Estimating burden of disease due to environmental factors with an emphasis on inadequate water, sanitation and hygiene

Jennyfer Wolf

A thesis submitted for the degree of
PhD by publication

University of East Anglia
School of Medicine
Norwich, England
September 2019

This copy of the thesis has been supplied on condition that anyone who consults it is understood to recognise that its copyright rests with the author and that use of any information derived therefrom must be in accordance with current UK Copyright Law. In addition, any quotation or extract must include full attribution.

Abstract

Environmental risks, including inadequate water, sanitation and hygiene (WASH), are major determinants of health and are responsible for much of the world's disease and deaths. Risk factor-attributable burden of disease assessments are important for prioritizing diseases and risk factors in policies and interventions. Risk factor exposure data and exposure-response information describing the association between the risk factor and the health outcome are used to calculate the population attributable fraction (PAF). The PAF signifies the proportion of ill health or deaths that could have potentially been prevented by removing the risk factor or by reducing it to an alternative level. It is used to calculate risk factor-attributable disease burden estimates.

The research presented and summarized here focuses on disease burden estimation attributable to environmental risk factors, especially to inadequate WASH. It includes research that improved availability of population-level data on relevant exposures, extended previous exposure classifications, generated and updated exposure-response relationships and estimated disease burden attributable to a range of environmental risk factors and for various adverse health outcomes. Research evaluating environmental health interventions as well as research examining factors associated with heterogeneous effectiveness of WASH interventions complements this work.

The presented work showed the great importance on health of environmental risk factors, provided important inputs for the monitoring of the Sustainable Development Goals (SDGs) and alternative methods and estimates to the Global Burden of Disease studies. It further highlighted the need for WASH interventions that lead to more radical WASH transitions, that target and reach whole communities and that consider response bias due to lack of blinding in subjectively assessed health outcomes. It further showed scarce evidence on the impacts on health of many environmental risk factors.

Table of contents

Acknowledgements

I am especially grateful to my supervisor at the World Health Organization (WHO) Dr Annette Prüss-Ustün who developed, organized and led most of the research presented here and who guided me throughout many years of my professional life. Additionally, thanks are due to the WHO water, sanitation and hygiene group, especially to Bruce Gordon and Dr Richard Johnston, for their technical expertise and continued support and to a large group of international experts that developed the framework for the water-, sanitation- and hygiene- (WASH-) related burden of disease assessments. I am grateful to have had the opportunity to contribute to WHO's research activities in the framework of quantifying health impacts from environmental risks to health.

I would also like to thank my supervisors from the Swiss Tropical and Public Health Institute Prof Daniel Mäusezahl and from the Universidad Peruana Cayetano Heredia Dr Stella Hartinger-Peña who enabled me to contribute to the design and set-up of an environmental health intervention and to conduct field work in Andean Peru. Great thanks are also due to the Peruvian research team, especially Dr Stella Hartinger-Peña, Angelika Fernandez and Hector Verastegui who led the field research in Peru, introduced me to the Peruvian culture and welcomed and hosted me so warmly.

I would like to express my special gratitude to my main thesis supervisor Prof Paul Hunter for giving me the opportunity to start and complete this PhD, for his guidance and continued support through each of the necessary stages and for many years of collaboration and scientific advice. Great thanks are also due to Dr Iain Lake and Dr Lee Hooper who provided valuable expertise and input on the PhD outline and to earlier versions of this work.

I am thanking my parents and my mother-in-law for their time and patience with our children that gave them the opportunity of having a great time with their grandparents while Eric and me were working and finalizing our theses.

I am greatly indebted to my husband, Eric, and our three sons, Jonathan, Leo and Jaron, who accompanied me during my time at the UEA and who enabled me to find the necessary time to work and complete this PhD during a period filled with changes and challenges. I am thanking my family for being my source of energy and happiness.

The publications on which this critical analysis is based and that are included at the end of this work were published open access and are permitted for unrestricted (non-commercial) re-use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abbreviations

CI	confidence interval
DALY	disability-adjusted life year
DHS	Demographic Health Survey
FAECI	Faecal Contamination Index
IHME	Institute of Health Metrics and Evaluation
JMP	WHO/UNICEF Joint Monitoring Programme for Water Supply, Sanitation and Hygiene
LPG	liquefied petroleum gas
MDG	Millennium Development Goal
MICS	Multiple Indicator Cluster Survey
PAF	population attributable fraction
RADWQ	Rapid Assessment of Drinking Water Quality
SBM	Swachh Bharat Mission
SDG	Sustainable Development Goal
WASH	water, sanitation and hygiene
WHO	World Health Organization
YLD	years lived with disease
YLL	years of life lost

1 Introduction

1.1 Background

Environmental risks such as polluted air, water or soil are important determinants of human health (1). About a quarter of global disease burden is estimated to be attributable[1] to environmental risk factors (3,4). Environmental pollution was estimated to be responsible for at least a three times higher disease burden than the burden resulting from the combined effect of AIDS, tuberculosis and malaria (5). The positive aspect about the high disease burden attributable to environmental risks is that most of these exposures could potentially be prevented with available methods, interventions and technologies (5).

Inadequate water, sanitation and hygiene (WASH) are important environmental health risks. In 2017, an estimated 785 million people lacked even a basic drinking water service, i.e., drinking water from an improved source, provided collection time is not more than 30 minutes for a roundtrip including queuing (6). More than 2 billion people were lacking a basic sanitation service, i.e., did not use an improved sanitation facility that is not shared with other households (6). Twenty-nine percent of the global population did not use safely managed drinking water, i.e., drinking-water from an improved water source which is located on premises, available when needed and free from faecal and priority chemical contamination (6). Fifty-five percent were not using safely managed sanitation, i.e., a sanitation facility which is not shared with other households and where excreta are safely disposed in situ or transported and treated off-site (6). The World Health Organization (WHO) recently estimated that inadequate WASH was responsible for nearly 2 million deaths in 2016, with the linkages between WASH and many diseases not yet quantified (7).

Disease burden estimation attributable to environmental exposures or risk factors raises awareness about the great importance of the environment for health. These

[1] Throughout this critical analysis, “attributable” disease burden refers to the proportion of disease that could have potentially been prevented through removal of the risk factor or reducing it to an alternative level. Attributable disease burden here does not include so-called “etiologic cases” (2) which are disease cases that occurred earlier in time due to exposure (see discussion for additional detail).

assessments include as essential components the quantification of the exposure to environmental risk factors and of the exposure-response relationships linking the risk factors and health outcomes. They extend beyond single epidemiological studies in individual populations and translate scientific results into health impacts of the exposed group or in the total population (8). Disease burden assessments thereby assist in setting priorities and choosing those interventions or guidelines with the largest expected public health impact. Furthermore, these assessments can determine health-related performance of governments or policies allowing comparisons across locations, identify high-risk populations, project exposures and associated disease burden into the future, provide the means to estimate the cost-effectiveness of interventions and guide the allocation of resources for health research (5,8).

1.2 Definition of environmental risk factors

In the presented work, environmental risk factors are defined, following previous work, as "all the physical, chemical and biological factors external to a person, and all related behaviours, but excluding those natural environments that cannot reasonably be modified" (3,9,10). This definition excludes alcohol and tobacco consumption, diet, unemployment, and environmental risk factors that usually cannot be modified such as pollen (3).

The focus of this work is on exposure to and health impacts from inadequate WASH. "Inadequate WASH" as used in this work spans a range of WASH services, behaviours and related health risks and includes especially drinking water and sanitation services and hygiene behaviours at household level (11,12). For specific health outcomes such as malaria, this definition includes water resources management (section 2.12 and (12)). Drinking water and sanitation service levels and presence of handwashing materials on premises are defined following the WHO/UNICEF Joint Monitoring Programme for Water Supply, Sanitation and Hygiene (JMP) (13–15) and are listed in Appendix 1 (A1.1).

1.3 Combining research on exposures and exposure-response relationships for risk factor-attributable disease burden estimation

The preferred method for calculating risk factor-attributable disease burden in this work follows a standardized approach, called comparative risk assessment (16,17). Comparative risk assessment uses common summary measures of population health such as deaths and disability-adjusted life years (DALYs) which can make results comparable between different populations or locations and open to scrutiny (8). Comparative risk assessments apply detailed exposure estimates and exposure-response relationships such as relative risks originating from systematic reviews of the available epidemiological evidence. These estimates are often disaggregated by location, sex and age group (18,19). Comparative risk assessments systematically evaluate changes in population health as a consequence of changing the exposure distribution of a risk factor (or group of risk factors) in the population (20). Where detailed exposure or exposure-response data were not available, disease burden estimates were calculated based on weaker exposure or exposure-response data, on knowledge of the disease transmission pathway or on expert opinion.

For the calculation of the burden of disease attributable to a risk factor using comparative risk assessment, the three following data inputs are needed (8):

1) the distribution of exposure to (different levels of) the risk factor of interest in the study population (Step A in Figure 1)
2) the exposure-response relationship between (different levels of) the risk factor and the health outcome(s) of interest (Step B in Figure 1)
3) overall disease statistics (e.g., deaths or DALYs in Figure 1) of the health outcome(s)

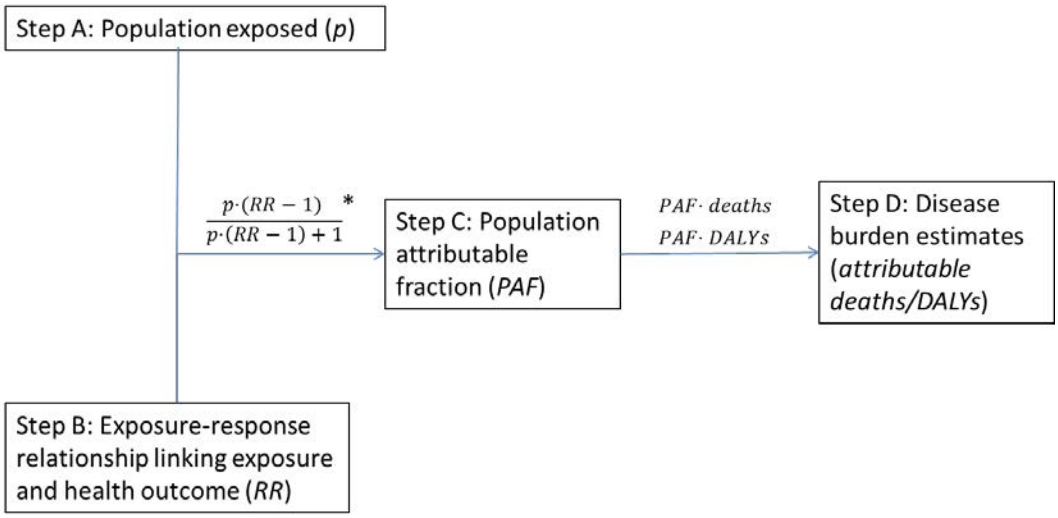


Figure 1: Simplified methodological approach and data requirements for disease burden estimation; p: population exposed, RR: relative risk, PAF: population attributable fraction, DALYs: disability-adjusted life years, * the PAF is usually calculated for population exposures and relative risks at different exposure levels (Equation 1), different PAF formulas are available, e.g., for the use of adjusted relative risks (Appendix 1 (A1.2))

The calculation of the risk factor-attributable disease burden requires the specification of a counterfactual minimum risk exposure level to which the current risk exposure and related disease burden are compared to. The counterfactual can be defined in various ways and includes the theoretical, the plausible, the feasible and the cost-effective minimum risk exposure levels (21). The theoretical minimum risk exposure level (or TMREL) presents the lowest population health risk which may not currently be attainable in practice and usually represents the preferred choice in burden of disease assessments. The plausible minimum risk exposure level represents what might be possible but not necessarily likely or feasible in the near future. The feasible minimum risk exposure level represents a level that has been observed in some population. Finally, the cost-effective minimum risk exposure distribution considers the costs of exposure reduction for guiding the choice of the alternative exposure scenario (21).

Figure 1 shows in a simplified and systematic manner, how the exposure distribution of the risk factor and the exposure-response relationship between the risk factor and the disease are used to calculate the population attributable fraction (PAF, step C in Figure 1). The PAF signifies the proportion the disease that could – under specific assumptions – have been prevented if exposure to the risk factor was removed or reduced to an alternative (counterfactual) level while other risk factors in the population remained unchanged (8,21). The assumptions that are made when estimating a PAF are that the risk factor and the outcome are causally related, the formerly exposed group immediately attains disease risk of the unexposed group after removal or reduction of the exposure and that the risk factor of interest is independent from other factors that influence disease risk (22). The PAF for burden of disease estimation is often calculated using the following formula:

$$\mathrm{PAF} = \frac{\sum_{j=1}^{n} p_j \cdot (RR_j - 1)}{\sum_{j=1}^{n} p_j \cdot (RR_j - 1) + 1} \quad (1)$$

where p_j is the proportion of the population exposed at exposure level j, RR_j is the relative risk at exposure level j and n is the total number of exposure levels. It should be noted that other PAF formulas are available especially for the use of adjusted relative risks (see Appendix 1 (A1.2) and related discussion).

WASH exposure levels and often also exposures to other environmental risks are related by similar mechanisms and policy interventions. The following formula has been proposed (18) and is used in this work for the estimation of the disease burden attributable to a cluster of risk factors (such as water, sanitation and hygiene together):

$$\mathrm{PAF} = 1 - \prod_{r=1}^{R} (1 - \mathrm{PAF}_r) \quad (2)$$

where r is the individual risk factor, and R the total number of risk factors accounted for in the cluster.

The PAF is then multiplied with the overall disease burden of the health outcome to derive the risk factor-attributable disease burden (Step D in Figure 1). Overall disease burden and attributable disease burden are often assessed as number of deaths (or injuries) or DALYs. DALYs are summary measures including both mortality and morbidity that assess the difference between the current situation and an ideal situation in which everyone lives perfectly healthy up to the standard life expectancy (8,23). More information on the calculation of DALYs is given in Appendix 1 (A1.3).

Limitations of risk factor-attributable disease burden assessments using comparative risk assessment methods include uncertainties in the different steps of the analysis process. These are uncertainties of assessing exposures, of estimating the exposure-response relationships and of disease burden calculation. Examples include the use of proxies in exposure assessment, inadequate capturing of non-linear relations, issues around the generalizability of relative risk estimates from a source to a target population and the appropriate application of different PAF formulas (23–25). Many of these limitations are detailed in the discussion.

1.4 Environmental risks and health – a history of global burden of disease assessments focusing on inadequate WASH

Note: Some of the global burden of disease assessments listed here are part of the main research presented in this critical analysis (sections 2.2-2.12). In this case, they are linked to the respective sections.

The first Global Burden of Disease study conducted for the year 1990 by the WHO in collaboration with the World Bank and the Harvard School of Public Health (26,27) examined the importance of ten risk factors. It provided the first global set of internally consistent disease burden estimates and introduced DALYs as a common health outcome metric (26,27). For estimating risk factor-attributable disease burden, epidemiological evidence and expert opinion were used (27). Poor water supply, sanitation and personal and domestic hygiene ranked second after malnutrition and was estimated to cause 7% of all DALYs in 1990 (26,27). In two subsequent analyses, environmental risks in general were estimated to be responsible for 23% (28) and 25-33% (10) of total DALYs in 1990. These two analyses differed regarding the number of disease categories addressed.

The 1990 Global Burden of Disease study was updated by the WHO for the years 2000, 2001, 2002 (29) and 2004 (30). These updates introduced major changes for risk factor-attributable disease burden assessments such as the comparison of current exposure distributions compared to counterfactual exposure distributions defined as the theoretical minimum risk (27). Of 26 risk factors examined, six were environmental. The disease burden attributed to inadequate WASH was calculated using a scenario approach (31) which combined different types of access to water and sanitation facilities or WASH-related behaviours such as water treatment or personal hygiene. Six typical exposure scenarios were defined for which corresponding exposure-response relationships could be identified. Three exposure scenarios extended beyond improved water and improved sanitation facilities and included improved water quality, continuous piped water or regulated water supply. The first exposure scenario or the counterfactual exposure level was defined as the theoretical minimum risk exposure level for which no diarrhoea transmission through inadequate WASH occurred. The assessment resulted in more than 2.2 million WASH-attributable deaths which represented 4% of all deaths in 1999 (31). However, none of the studies used for establishing the exposure-response relationships was blinded (27). Also, exposure-response relationships were based on different meta-analyses or even individual studies, thus constituting varying levels of quality of evidence (31). Exposure-response relationships might have therefore been influenced by bias and confounding at varying levels. The analysis was updated for the 2004 Global Burden of Disease study applying again the six exposure scenarios (32). It resulted in 1.9 million diarrhoeal deaths attributable to inadequate WASH representing 3.2% of global deaths in 2004 (32). Shortly after these assessments, the Environmental Burden of Disease Series was published by the WHO to provide practical guidance for conducting environmental burden of disease assessments at regional and national level (8).

Additionally, a comprehensive WHO environmental burden of disease assessment built on the comparative risk assessment performed for the year 2002 (4). It complemented the 2002 assessment by including more environmental risks, by systematically reviewing a broad range of diseases and injuries for environmental causes, by consulting experts to fill data gaps on the links between environmental risks and adverse health outcomes and by considering only the “reasonably modifiable environment” to increase policy relevance of disease burden estimates (33). This assessment estimated that 24% of the global disease burden and 36% of the disease burden in children under 15 years of age was attributable to environmental risks (4). A WHO companion publication summarized the WASH-attributable global disease burden as 9% of the overall disease burden (34). The comprehensive WHO environmental disease burden assessment was updated for the year 2012 (3,9) with an update of data tables again for 2016 (35). The 2012 assessment is part of the research presented in this critical analysis (section 2.6).

The 2010 Global Burden of Disease study was led by the Institute of Health Metrics and Evaluation (IHME) which was founded in 2007 (27). The comparative risk assessment for the 2010 Global Burden of Disease study analysed the disease burden of 67 risk factors and risk factor clusters (18). Inadequate water and sanitation (inadequate hygiene behaviours were not considered) fell significantly in ranking of relative importance of risk factors and was estimated to lead to only 337,000 deaths in 2010 and 0.9% of global DALYs (18). A major change of the comparative risk assessment of inadequate water and sanitation compared to previous global burden of disease assessments included that only two exposure scenarios for each the water and sanitation assessment were considered. These were improved water or sanitation facilities compared to unimproved water or sanitation facilities. This decision was based on a systematic review and meta-analysis (36) that did not find health impacts from improving water quality, based on the subgroup of water quality studies that were blinded (27). By using improved sanitation and water facilities as minimum risk exposures, the Global Burden of Disease study 2010 did not consider key exposures such as hygiene and did also not consider water quantity, quality, access, continuity and reliability (27). Starting with the comparative risk assessment for the Global Burden of Disease study 2010, the IHME published burden of disease estimates attributable to a range of environmental risk factors including inadequate WASH for the years 2013, 2015, 2016 and 2017 (24,37–39). After the 2010 assessment, the IHME revised and extended their WASH exposure scenarios and estimates are now updated annually.

The update for the year 2012 of the 2002 WHO burden of disease assessment from inadequate WASH (34) is included as main research in this critical analysis (section 2.5 (40)). This study differed from the previous WHO approach because of separate exposure scenarios for water, sanitation and hygiene. This was mainly due to the application of meta-regression techniques for deriving the exposure-response relationships (41). Compared to the Global Burden of Disease study 2010 by the IHME, exposure scenarios extended beyond improved water facilities and used safely stored drinking water that was filtered or boiled at household level as counterfactual exposure distribution (41). The latest WHO update for the WASH-attributable disease burden was conducted for the year 2016 and is also included in this critical analysis (section 2.12 (12)). Compared to the previous WHO assessment, it included additional exposure categories and a larger range of adverse health outcomes.

1.5 Aims and objectives

When I started to work on the research that is presented in this critical analysis, the main aim was to increase knowledge and awareness about the importance of environmental risks on human health. Accumulating evidence about the health impacts of environmental pollution and degradation such as climate change had highlighted the great importance of the subject and the need for additional evidence (e.g., (42–44)). When looking back on the whole body of research the main aim subsequently expands to increase the scope and to strengthen environmental burden of disease assessments with a focus on the burden of disease attributable to inadequate WASH.

This work has the following specific objectives:

i) To generate, improve and update data on various WASH exposure levels (Step A in Figure 1).

ii) To estimate exposure-response relationships between these exposure levels and selected health outcomes (Step B in Figure 1).

iii) To calculate and update the PAFs for environmental risk factors and the related attributable burden of disease (Steps C and D in Figure 1).

iv) To evaluate the effectiveness of environmental health interventions and to explore factors associated with their effectiveness.

2 List and summary of main research

2.1 Summary of included research

The eleven peer-reviewed scientific articles that are selected as main research for this critical analysis are grouped below as i) exposure assessment, ii) exposure-response relationship estimation, iii) disease burden calculation, and iv) effectiveness evaluation of environmental health interventions (two papers contributed to two of these groups). Subsequently in sections 2.2 to 2.12, the papers are listed in chronological order to better represent my own development in this area of research. The complete publications of the eleven peer-reviewed articles are included in Appendix 2 (A.2.1), followed by the confirmation of my contributions (A.2.2). The full list of my publications can be found in Appendix 1 (A1.4).

Exposure assessment

- **Wolf J**, Bonjour S, Prüss-Ustün A (2013) An exploration of multilevel modelling for estimating access to drinking-water and sanitation. J Water Health, doi: 10.2166/wh.2012.107
- Freeman MC, Stocks ME, Cumming O, Jeandron A, Higgins JP, **Wolf J**, Prüss-Ustün A, Bonjour S, Hunter PR, Fewtrell L, Curtis V. (2014) Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. Trop Med Int Health, doi: 10.1111/tmi.12339 [also included under "Exposure-response relationship estimation"]
- **Wolf J**, Johnston R, Freeman MC, Ram PK, Slaymaker T, Laurenz E, Prüss-Ustün A. (2018) Handwashing with soap after potential faecal contact: Global, regional and country estimates. Int J Epidemiol, doi: 10.1093/ije/dyy253
- **Wolf J**, Johnston R, Hunter PR, Gordon B, Medlicott K, Prüss-Ustün A. (2018) A Faecal Contamination Index for interpreting heterogeneous diarrhoea impacts of water, sanitation and hygiene interventions and overall, regional and country estimates of community sanitation coverage with a focus on low- and middle-income countries. Int J Hyg Environ Health, doi: 10.1016/j.ijheh.2018.11.005 [also included under "Effectiveness evaluation of environmental health interventions"]

Exposure-response relationship estimation

- **Wolf J**, Prüss-Ustün A, Cumming O, Bartram J, Bonjour S, Cairncross S, Clasen T, Colford JM Jr, Curtis V, De France J, Fewtrell L, Freeman MC, Gordon B, Hunter PR, Jeandron A, Johnston RB, Mäusezahl D, Mathers C, Neira M, Higgins JP. (2014) Assessing the impact of drinking water and sanitation on diarrhoeal disease in low- and middle-income settings: systematic review and meta-regression. Trop Med Int Health, doi: 10.1111/tmi.12331
- Freeman MC, Stocks ME, Cumming O, Jeandron A, Higgins JP, **Wolf J**, Prüss-Ustün A, Bonjour S, Hunter PR, Fewtrell L, Curtis V. (2014) Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. Trop Med Int Health, doi: 10.1111/tmi.12339 [also included under "Exposure assessment"]
- **Wolf J**, Hunter PR, Freeman MC, Cumming O, Clasen T, Bartram J, Higgins JPT, Johnston R, Medlicott K, Boisson S, Prüss-Ustün A. (2018) Impact of drinking water, sanitation and handwashing with soap on childhood diarrhoeal disease: updated meta-analysis and meta-regression. Trop Med Int Health, doi: 10.1111/tmi.13051

Disease burden calculation

- Prüss-Ustün A, Bartram J, Clasen T, Colford JM Jr, Cumming O, Curtis V, Bonjour S, Dangour AD, De France J, Fewtrell L, Freeman MC, Gordon B, Hunter PR, Johnston RB, Mathers C, Mäusezahl D, Medlicott K, Neira M, Stocks M, **Wolf J**, Cairncross S. (2014) Burden of disease from inadequate water, sanitation and hygiene in low- and middle-income settings: a retrospective analysis of data from 145 countries. Trop Med Int Health, doi: 10.1111/tmi.12329
- Prüss-Ustün A, **Wolf J**, Corvalán C, Neville T, Bos R, Neira M. (2016) Diseases due to unhealthy environments: an updated estimate of the global burden of disease attributable to environmental determinants of health. J Public Health, doi: 10.1093/pubmed/fdw085
- Prüss-Ustün A, **Wolf J**, Bartram J, Clasen T, Cumming O, Freeman MC, Gordon B, Hunter PR, Medlicott K, Johnston R (2019) Burden of disease from inadequate water, sanitation and hygiene for selected adverse health outcomes: an updated analysis with a focus on low- and middle-income countries. Int J Hyg Environ Health, doi: 10.1016/j.ijheh.2019.05.004

Effectiveness evaluation of environmental health interventions

- Hartinger SM, Lanata CF, Hattendorf J, Verastegui H, Gil AI, **Wolf J**, Mäusezahl D. (2016) Improving household air, drinking water and hygiene in rural Peru: a community-randomized–controlled trial of an integrated environmental home-based intervention package to improve child health. Int J Epidemiol, doi:10.1093/ije/dyw242
- **Wolf J**, Mäusezahl D, Verastegui H, Hartinger SM. (2017) Adoption of clean cookstoves after improved solid fuel stove programme exposure: a cross-sectional study in three Peruvian Andean regions. Int J Environ Res Public Health, doi: 10.3390/ijerph14070745
- **Wolf J**, Johnston R, Hunter PR, Gordon B, Medlicott K, Prüss-Ustün A. (2018) A Faecal Contamination Index for interpreting heterogeneous diarrhoea impacts of water, sanitation and hygiene interventions and overall, regional and country estimates of community sanitation coverage with a focus on low- and middle-income countries. Int J Hyg Environ Health. doi: 10.1016/j.ijheh.2018.11.005 [also included under "Exposure assessment"]

2.2 An exploration of multilevel modelling for estimating access to drinking-water and sanitation

Research in context

This research (45) developed a modelling approach for estimating access to improved drinking water and sanitation facilities by country and year. This model was the basis for subsequent modelling of various environmental and WASH exposures used for WASH-attributable burden of disease estimations (e.g., sections 2.4 (46), 2.5 (40), 2.10 (47), and 2.12 (12)).

I contributed to the development of the analytical framework and the analysis model. I was responsible for the data analysis and for preparing the draft publication.

Objectives

To develop estimates for access to improved water sources and sanitation facilities using multilevel modelling. To compare these estimates to current estimates of the JMP and to propose an alternative approach for monitoring and evaluating progress on the Millennium Development Goals (MDGs).

Main methods

Improved water sources included piped water on premises, public taps or standpipes, boreholes, tubewells, protected dug wells, protected springs, and rainwater collection (48). Improved sanitation facilities included non-shared flush/pour flush to piped sewer system, to septic tank or to pit latrine, ventilated improved pit latrines, composting toilets or pit latrines with slabs (48). Household-level data on access to improved water sources and improved sanitation facilities from the JMP database were used (11). A two-level linear model with a logit transformation of the dependent variable (proportion of population with access to improved water sources or improved sanitation by country and year), region as a fixed effect covariate and a random intercept and slope by county was applied. Subsequently, water quality data from nationally representative and comparable water quality tests (Rapid Assessment of Drinking Water Quality, RADWQ) conducted by the JMP between 2004 and 2007 in five countries (Ethiopia, Jordan, Nicaragua, Nigeria and Tajikistan) (49) complemented by two similar assessments performed in China and India were used to adjust estimates of access to improved water sources for water quality. Additionally, the proportion of the global population with access to improved, but shared sanitation was modelled using household survey data on access to shared sanitation from the JMP.

Main findings

It was estimated that the global proportion of the population without access to improved water sources declined from 23% in 1990 to 10% in 2015 while the absolute number of unserved people declined by only 40% globally. The global proportion of the population without access to improved sanitation declined from 50% to 34% while the number of unserved people declined by only a little more than 200 million people. Adjusting estimates for drinking water quality, the proportion of the world's population without access to microbiologically safe water in 2015 increased to 30%. If shared sanitation facilities of an otherwise improved technology (see above under "Main methods") were considered improved, only 23% of the world population would be classified as not having access to improved sanitation compared to 34% with the current classification.

Strengths and limitations

The strengths of multilevel modelling include a single model that produced continuous time series for all countries even in the presence of highly unbalanced data, e.g., countries with one or no data points. Limitations include the greater uncertainty of estimates when only limited country data were available (country estimates will be closer towards the model's mean or the fixed part of the model). Such estimates might be far from the actual country values if WASH service delivery in one country developed differently from other countries from which information was used (50). In addition, the model did not allow fixing the coverage estimate for drinking water or sanitation for 1990 at a certain value. This 1990 estimate was used as baseline to define global WASH targets such as the envisaged percentage point increase of global population coverage with improved water or sanitation. The addition of survey points might have therefore resulted in different baseline estimates and subsequently fluctuating global targets (51). Access to hygiene infrastructure or hygiene behaviours was not included and estimates did not extent beyond improved water and sanitation facilities. Modelling of disaggregated improved facilities (e.g., piped water vs. other improved) could have been realized using ordinal regression modelling. Additionally, results were not disaggregated beyond countries and therefore did not show differences and inequalities between areas and regions within individual countries. The adjustment of drinking water estimates for water quality were based on assessments on a limited number of countries and represented water quality measurements of different sources for one point in time.

Contributions of the research

The developed modelling approach contributed to the discussion of the JMP methodology for modelling facility access (51). It also formed the basis for subsequent exposure modelling for WHO risk factor-attributable burden of disease assessments and also for the monitoring of global targets and indicators. The analysis highlighted that, while meeting the MDG target for drinking water, global service provision was slower than population growth – leading to an increase of the unserved number of people in some world regions. The impact on MDG target achievement by taking drinking water quality and shared improved sanitation into account was shown. This highlighted the importance of further research and considerations of drinking water quality and shared sanitation.

2.3 Assessing the impact of drinking water and sanitation on diarrhoeal disease in low- and middle-income settings: systematic review and meta-regression

Research in context

This research (41) provided the exposure-response relationships (relative risks) between different levels of access to drinking water and sanitation or household water treatment and diarrhoeal disease. It thereby supplied an essential component for the WASH-attributable burden of disease assessment for the year 2012 (section 2.5 (40)). Section 0 (52) updates the systematic review for the burden of disease assessment for the year 2016 (section 2.12 (12)).

I contributed to the development of the analytical framework for the burden of disease assessment from inadequate WASH. I extracted the relevant data from intervention studies and led on the data analysis. I was responsible for preparing the draft publication.

Objectives

To assess the impacts on diarrhoeal disease of access to different levels of drinking water sources and sanitation facilities or use of household water treatment.

Main methods

A systematic literature review was conducted to identify studies that reported the effects on diarrhoeal disease of drinking water or sanitation interventions that could be grouped within the developed conceptual WASH models. Studies evaluating specific WASH interventions at the level of the household using randomised and non-randomised study designs were included as well as survey data analyses using certain matching methods to permit causal inference. Studies targeting non-representative parts of the population (such as people with HIV) or studies with a reported intervention implementation or compliance below 20% of targeted households were excluded. Random-effects meta-analysis and meta-regression were used to examine the effects of different levels of drinking water or sanitation access or household water treatment on diarrhoea morbidity. In an additional analysis, some results were adjusted for bias in non-blinded intervention studies based on empirical evidence (53).

Main findings

Sixty-one drinking water (75 total observations, six providing survey data) and eleven sanitation intervention (14 total observations, nine providing survey data) studies were included. The summary relative risks of diarrhoeal disease for the drinking water interventions were 0.66 (95% CI 0.60-0.71) and 0.72 (95% CI 0.56-0.88) for the sanitation interventions. Results from meta-regression suggested large diarrhoeal disease reductions for higher-quality piped water (relative risk 0.19 (95% CI 0.07-0.05)), filtered water that was safely stored in the household (relative risk 0.41 (95% CI 0.33-0.50), bias-adjusted relative risk 0.55 (95% CI 0.38-0.81)) and sewered sanitation (relative risk 0.31 (95% CI 0.27-0.36)) against the baseline of unimproved water or unimproved sanitation.

Strengths and limitations

The conceptual frameworks for the analysis of the different levels of drinking water and sanitation access and household water treatment were developed in collaboration with international WASH experts. Principles of network meta-analysis allowed the estimation of the relative risks for diarrhoea of transitions between exposure levels that had not been assessed in intervention studies. Some results were adjusted for likely bias due to non-blinding in interventions with subjective health outcomes (53,54). However, even though meta-regression is usually based on experimental studies, any identified associations are observational. As such meta-regression analyses do not have the weight of experimental studies (55). Results were from partly low quality intervention studies with imperfect compliance and implementation that differed considerably in terms of intervention implementation, and underlying pathogens, transmission pathways and populations. Results from household intervention studies might therefore underestimate the potential reduction of diarrhoeal disease burden that could be achieved through truly adequate WASH for all the population. Some pooled results were based on limited evidence and might therefore change with new evidence. Additionally, especially the sanitation observations included a large share of survey data analyses as data from intervention studies was scarce.

Contributions of the research

This analysis showed that the amount of diarrhoeal disease reduction was highly dependent on the respective level of WASH improvement. This finding supports considering health effects of improving WASH beyond improved facilities such as increased water quality and continuity of improved water sources and improved sanitation connected to a sewer system. Prior to this study, the 2010 Global Burden of Disease study had considerably downgraded the importance of adequate WASH by approximating safe drinking water and sanitation through improved water and sanitation facilities and by not considering health impacts from improving hygiene behaviours (18). This approach has subsequently been changed and the Global Burden of Disease studies now include higher levels of WASH service provision which increased WASH-attributable disease burden estimates (38). This systematic review and meta-analysis still provides the data basis for relative risk estimates of the most recent Global Burden of Disease study (56).

2.4 Hygiene and health: systematic review of handwashing practices worldwide and update of health effects

Research in context

This research (46) provided the exposure-response relationships (relative risks) for hygiene behaviours, such as handwashing with soap, and diarrhoeal disease. It additionally provided global, regional and country prevalence estimates for handwashing with soap after potential faecal contact. It thereby supplied crucial components (dose-response relationships and exposure information) for the burden of disease assessment of inadequate WASH for the year 2012 (section 2.5 (40)). Section 0 (52) updates the systematic review of hygiene interventions and its impact on diarrhoeal disease and section 2.10 (47) updates estimates for handwashing with soap prevalence.

I contributed to the development of the analytical framework for the burden of disease assessment from inadequate WASH. I led on the meta-analysis and meta-regression of hygiene promotion interventions. I contributed to the draft publication.

Objectives

To provide the first global, regional and country prevalence estimates for handwashing with soap after potential faecal contact. To update the exposure-response relationship between promotion of hygiene or handwashing with soap and diarrhoeal disease.

Main methods

Two systematic reviews were conducted to identify a) handwashing observation studies reporting the prevalence of observed handwashing with soap after using a toilet or after contact with excreta (including children's excreta) and b) hygiene promotion interventions reporting the effect on diarrhoeal disease. For the latter, studies evaluating hygiene interventions at individual, household, community or institutional level using randomised and non-randomised study designs were included as well as survey data analyses using certain matching methods to permit causal inference. Studies targeting non-representative parts of the population (such as people with HIV) were excluded. Multilevel modelling was used to estimate handwashing practise at country, regional and global levels. Evidence of diarrhoeal disease impacts from hygiene promotion interventions was pooled using random-effects meta-analysis and meta-regression. Results from non-blinded intervention studies were adjusted for likely bias.

Main findings

Based on 42 handwashing observation studies, it was estimated that 19% (95% CI 8%, 39%) of the world population wash hands with soap after potential faecal contact. Estimates ranged between 13% and 17% of the population in regions of low- and middle-income countries and 42% and 49% of the population in regions of high-income countries. Based on 26 hygiene promotion interventions (including one observation providing survey data), the pooled relative risk for diarrhoeal disease was 0.67 (95% CI 0.61, 0.74). In meta-regression, interventions focusing on the promotion of handwashing with soap yielded larger diarrhoea reductions (relative risk 0.60 (95% CI 0.53, 0.68)) which reduced to 0.77 (95% CI 0.32, 1.86) after adjustment for bias due to non-blinding.

Strengths and limitations

The systematic review on handwashing observation studies only included studies reporting observed handwashing. It excluded studies reporting self-reported hygiene behaviours which have been shown to considerably overestimate handwashing prevalence (57). Meta-regression allowed examining the effect on diarrhoea of different hygiene promotion strategies. However, even handwashing prevalence estimates from observed handwashing might be overestimated due to the presence of an observer (58). Limitations specific to the use of multi-level modelling and meta-regression analysis have already been discussed previously (sections 2.2 (45) and 2.3 (41)).

Contributions of the research

The systematic review and pooled analysis of observed handwashing prevalence was the first to provide country, regional and global estimates of observed handwashing with soap after potential faecal contact. It highlighted that handwashing with soap after potential faecal contact, an important and very cost-effective public health measure (59), was practised at low levels worldwide. The analysis of hygiene promotion interventions indicated that hygiene promotion focusing on handwashing with soap might have a larger effect on diarrhoeal disease than broader hygiene promotion.

Additionally, the analysis suggested that at least part of the observed health impact from hygiene promotion interventions might be due to reporting bias. Different to the Global Burden of Disease study which now uses presence of handwashing facilities as exposure (24), this research provided a closely matching exposure (prevalence of handwashing with soap) and exposure-response relationship (diarrhoea impacts from handwashing with soap promotion) for burden of disease estimation.

2.5 Burden of disease from inadequate water, sanitation and hygiene in low- and middle-income settings: a retrospective analysis of data from 145 countries

Research in context

This research (40) provided WASH-attributable diarrhoeal disease burden estimates for the year 2012. It used WASH exposure estimates and exposure-response relationships from research presented previously (sections 2.3 (41) and 2.4 (46)). This assessment is updated in section 2.12 (12) for the year 2016.

I contributed to the development of the analytical framework for the burden of disease assessment from inadequate WASH. I provided relevant data inputs for the analysis and reviewed the draft publication.

Objectives

To generate estimates of the diarrhoea burden attributable to inadequate WASH for the year 2012 with a focus on low- and middle-income settings.

Main methods

Comparative risk assessment methods combining exposure data and exposure response relationships with overall diarrhoeal disease burden figures were used to estimate the burden of disease attributable to inadequate WASH (17).

Main findings

Globally, 58% (95% CI 48%, 65%) of total diarrhoea deaths or 842,000 deaths were estimated to be attributable to inadequate WASH in 2012. Thirty-four percent (95% CI 16%, 45%) of total diarrhoea deaths were attributable to inadequate water and 19% (95% CI 7%, 29%) to inadequate sanitation in low- and middle-income settings. Twenty percent (95% CI 0%-60%) of total diarrhoeal deaths were attributable to inadequate hand hygiene. In children under five years of age, 361,000 WASH-attributable deaths were estimated, which represent 5.5% of all deaths in this age group in 2012.

Strengths and limitations

The comparative risk assessment took account of additional risk reduction when water quality and quantity were further improved over improved sources such as high-quality and continuously available household piped water. The analysis was limited due to scarce exposure data, e.g., considering water quality and handwashing prevalence, and scarce exposure-response data, e.g., for a functional and regulated piped water supply. Further limitations are discussed in the sections describing research that provided data inputs for this assessment (sections 2.2 (45), 2.3 (41) and 2.4 (46)). The minimum risk exposure level for the disease burden estimation, i.e., boiling or filtering water with subsequent safe storage, improved sanitation and handwashing with soap after potential faecal contact, likely did not reach a theoretical minimum risk exposure distribution which includes no disease risk from inadequate WASH (21). Further limitations include using a single disease outcome, i.e., diarrhoeal disease, though there was evidence for an impact of WASH on various other adverse health outcomes (60–62). Non-household settings such as health centres and schools were excluded.

Contributions of the research

This WHO WASH-attributable burden of disease assessment used different minimum risk exposure levels compared to the IHME Global Burden of Disease study 2010 (18). In contrast to the Global Burden of Disease study 2010, the counterfactual of the WHO disease burden analysis attributable to inadequate drinking water went beyond the provision of an improved drinking water source. The reason for this was that improved drinking water sources had been associated with considerable disease risk (63,64). Additionally and contrary to the Global Burden of Disease study 2010, this study included disease burden attributable to lack of handwashing with soap and results reflected adjustment for likely bias due to lack of blinding.

2.6 Diseases due to unhealthy environments: an updated estimate of the global burden of disease attributable to environmental determinants of health

Research in context

This research (9) assessed the disease burden attributable to a broad range of modifiable environmental risks for the year 2012. This assessment has also been published as a more detailed WHO report (3). It represented the update of the first comprehensive and systematic environmental burden of disease assessment for the year 2002 (4). These disease burden estimates have also been updated for the year 2016 (35).

I led on reviewing the scientific literature on the links between a broad range of environmental risks and adverse health outcomes. I was responsible for preparing the draft publication.

Objectives

To update burden of disease estimates attributable to the modifiable environment.

Main methods

Systematic literature reviews were conducted on the links between 133 diseases or injuries and environmental risks. PAFs were calculated using: i) comparative risk assessment, ii) more limited epidemiological calculation, iii) knowledge about the specific disease transmission pathway, and iv) expert surveys. The PAFs were multiplied with overall disease statistics (deaths and DALYs) to calculate disease burden figures attributable to the environment.

Main findings

Twenty-three percent (95% CI 13%-34%) of global deaths and 22% (95% CI 13%-32%) of global DALYs were attributable to environmental risks in 2012. Most of the environmental disease burden resulted from noncommunicable diseases. Cancers, ischaemic heart disease, stroke and chronic obstructive pulmonary disease (COPD) were the most important contributors to global deaths attributable to environmental risks. In addition to these diseases, conditions that majorly affect the young such as lower respiratory infections, diarrhoea, malaria, asthma, and neonatal conditions, as well as back and neck pain and accidents importantly contributed to global DALYs attributable to environmental risks. Young children and adults between 50 and 75 years of age were disproportionally affected.

Strengths and limitations

This burden of disease assessment reviewed the evidence of the links between 133 diseases or injuries and the environment. The majority of the estimates was based on comparative risk assessment methods and therefore represented high levels of evidence. However, many diseases and environmental risks were not included in the disease burden quantification because evidence was too limited. Additionally, environmental disease burdens occurring after a lag time from exposure were not adequately captured in this analysis. Environmental disease burden estimates were partly based on scarce evidence and assumptions. Also, a considerable part of the analysis was based on expert surveys which were however combined with methods of evidence synthesis.

Contributions of the research

Environmental burden of disease assessments seek to quantify and raise awareness about the importance of the environment on human health. These assessments can guide priority setting and decision making. This study presented the update of the first comprehensive environmental burden of disease assessment initially conducted for the year 2002 (4). It showed that there had been a major move from "traditional" and still important environmental risks such as inadequate WASH and household air pollution towards more "modern" risks such as ambient air pollution and exposure to chemicals and their large associated disease burden from noncommunicable diseases. Due to considering more risk factor-disease links, our estimates for the environmental disease burden were considerably higher than those of the corresponding Global Burden of Disease assessment for the year 2013 (38) (23% versus 16% of global deaths and 22% versus 12% of global DALYs). As this study focused on the modifiable environment, it highlighted the great potential of disease prevention from environmental protection.

2.7 Improving household air, drinking water and hygiene in rural Peru: a community-randomized-controlled trial of an integrated environmental home-based intervention package to improve child health.

Research in context

This work (65) is part of research in rural Peru (section 2.8 (66) and (67)) that was realized while I was working for the Swiss Tropical and Public Health Institute in collaboration with the Cayetano Heredia University in Lima, Peru. This work evaluated a randomized controlled trial that examined the effect of combined WASH and air pollution interventions on diarrhoea, respiratory infections and child growth. It contributed to evidence generation about environmental hazards. Results from such environmental health interventions are key inputs for exposure-response relationship assessment and risk factor-attributable disease burden estimation as presented in sections 2.3, 2.5, 2.9 and 2.12.

I was responsible for preparing the draft publication. Additionally, I contributed to the design and setup of a subsequent randomized controlled trial of a related environmental intervention package.

Objectives

To reduce respiratory infections and diarrhoea and to improve child growth through combining WASH and air pollution interventions.

Main methods

This community-randomized controlled field trial in rural Peru delivered an environmental intervention package consisting of in-kitchen water sinks with piped water connection, solar disinfection as point-of-use water treatment, hygiene promotion focusing on handwashing with soap and kitchen hygiene, and improved ventilated solid-fuel stoves. Young children were followed over 12 months to monitor diarrhoea and respiratory infections (weekly), anthropometrics (every two months) and to collect environmental microbiological samples (baseline, mid-term and endline). The control group received an attention control intervention to reduce likely bias through the non-blinded trial design.

Main findings

Children from 25 intervention communities experienced a mean of 1.8 diarrhoea episodes per child-year compared to 2.2 diarrhoea episodes in 26 control communities (relative risk 0.78, 95% CI 0.58-1.05, p=0.1). The relative risk for episodes of acute respiratory infections was 0.95 (95% CI 0.39, 1.65, p=0.5) and for acute lower respiratory infections 2.45 (95% CI 0.82, 7.39, p=0.1). No difference in height-for-age or weight-for-age was detected between intervention and control communities.

Strengths and limitations

This trial combined different environmental interventions for improving child health. Interventions acceptance was enhanced by designing the stoves and kitchen sinks in close collaboration with stakeholders and the communities and by placing emphasis on self-maintenance and repair (e.g., 85% of intervention households used the improved stoves two years after the study ended). An attention control intervention, i.e., an intervention implemented with the same intensity, such as same contact time, and with an anticipated outcome independent from the outcome of the main intervention (68,69), was implemented in the control group to prevent reporting bias from non-blinding and to reduce drop-out rates in the control group. Behaviour change, e.g., water treatment behaviour, was not assessed through self-report but through observation. However, observed compliance with the point-of-use solar water treatment was very low (10% of intervention households at end of follow-up). Water supply interruptions led to reduced compliance with the kitchen water sinks. Drinking water quality post-intervention was equivalently contaminated in intervention and control households. The improved stoves only modestly reduced air pollution and not to levels recommended by the WHO indoor air quality guidelines (70). Clean stoves such as liquefied petroleum gas (LPG) stoves were not implemented as gas was hardly available at the time in the study location. The attention control intervention might have itself reduced faecal environmental contamination and might have attenuated the intervention effect. Diarrhoea as well as incidence of lower respiratory infections was lower than anticipated and the study therefore lacked power to detect a significant effect on disease occurrence.

Contributions of the research

This trial was one of the first to combine potentially synergistic environmental interventions for reducing various household level risks to prevent several adverse health outcomes. The water intervention – piped water into the household that was additionally treated at point of use – aimed to achieve improvements in both water quantity and quality consistent with the concept of safely managed drinking water (11). It was shown that through extensive community engagement some environmental interventions were highly accepted and used.

2.8 Adoption of clean cookstoves after improved solid fuel stove programme exposure: a cross-sectional study in three Peruvian Andean regions

Research in context

This work (66) is another result from the research I conducted with the Swiss Tropical and Public Health Institute and the Cayetano Heredia University in rural Peru. It evaluated the effectiveness of various improved stove promotion programmes and explored factors associated with stove adoption. Such research can provide a better understanding of heterogeneous results of environmental health interventions. Through the research work in Peru, I gained experience in conducting fieldwork and data collection.

I contributed to the design and the development of the questionnaire and to checking questionnaire completion at the study site in Peru. I was responsible for the data analysis and for preparing the draft publication.

Objectives

To explore adoption and displacement of different stove types. To identify factors associated with stove adoption and displacement in rural Andean Peru.

Main methods

A questionnaire on cooking behaviours, types of cookstoves used, cleaning maintenance and repair of stoves, willingness to pay, demographic and socioeconomic variables of the household and fieldworker observations on the type and the condition of the stoves was developed and tested. Subsequently it was administered to 1,202 households in Cajamarca, Cuzco and La Libertad, three geographically and culturally diverse rural Andean regions. Eligibility criteria for households were previous participation in an improved stove promotion programme, use of biomass for cooking, Spanish as first language and a household head which was at least 18 years old. From all eligible households a convenience sample was drawn which was based on feasibility and balanced numbers between study sites (about 400 households per site were included). Multivariable logistic regression models were used to examine the associations between use and displacement of different stove types and a range of independent variables. The variables were chosen a-priori and were informed by a literature review on enablers and barriers of clean or improved stove uptake. Multiple imputation was used to complete missing information.

Main findings

Ninety-two percent of study households used a clean or improved stove as primary stove. However, stove stacking, i.e., the combination of different stove technologies such as the simultaneous use of clean, improved and unimproved stoves by one household, was frequent (69% of households). Thirty-five percent of households continued to use traditional stoves. Various household, socio-economic and stove variables could be identified that were associated with the uptake of improved or clean stoves or with the displacement of traditional stoves.

Strengths and limitations

This study included more than 1,200 households from three diverse and distant rural Andean regions. The questionnaire was developed based on prior literature, extensively field-tested and delivered by local study personnel. Due to the use of multiple imputation techniques data from all households could be used. However, cross-sectional studies are at risk of information and selection bias. Objective stove use monitors were not used; instead stove use was assessed through self-report which might have introduced bias. Additionally, recall bias might have been present as some stove promotion programmes dated back several years. Households willing to participate in our study and in stove promotion programmes might not be representative of the average rural Andean household. Also cross-sectional studies cannot establish the temporal sequence between exposure and outcome, e.g., knowing somebody able to build an improved stove can be an enabler for but also a consequence of using a particular stove.

Contributions of the research

This study indicated that nearly two thirds of households that participated in improved stove promotion programmes abandoned the use of traditional stoves. Most households relied on improved solid fuel stoves which can be regarded as interim technologies before clean stoves, such as LPG stoves, and required fuels become widely available (70). The identified enablers and barriers for improved or clean stove uptake and for the displacement of traditional stoves might inform future clean cookstove interventions.

2.9 Impact of drinking water, sanitation and handwashing with soap on childhood diarrhoeal disease: updated meta-analysis and meta-regression

Research in context

This work (52) presents the update of previously conducted research (sections 2.3 (41) and 2.4 (46)). It provided the updated exposure-response relationships (relative risks) between different WASH exposure categories and diarrhoeal disease. These were used for burden of disease calculations from inadequate WASH for the year 2016 presented in section 2.12 (12).

I contributed to the development of the updated analytical framework for WASH-attributable burden of disease assessments. I led on the systematic review, data extraction and data analysis. I was responsible for preparing the draft publication.

Objectives

To provide an updated assessment of the impacts of inadequate WASH on childhood diarrhoeal disease.

Main methods

The previous systematic reviews (41,46) were updated including literature published until early 2016 with the same inclusion and exclusion criteria as the previous reviews (sections 2.3 and 2.4). Meta-analysis and meta-regression were used to analyse the associations between different service levels of drinking water, sanitation or handwashing promotion with soap and diarrhoeal disease. Results from non-blinded studies of selected interventions were adjusted for reporting bias (41).

Main findings

This updated systematic review identified a total of 80 drinking water observations (eight observations providing survey data), 22 sanitation observations (eleven observations providing survey data) and 33 hygiene observations (one observation providing survey data). Random-effects meta-analysis yielded a pooled relative risk on diarrhoeal disease of 0.67 (95% CI 0.62, 0.73) for the water interventions, of 0.75 (95% CI 0.63, 0.88) for the sanitation interventions and of 0.70 (95% CI 0.64, 0.77) for the hygiene promotion studies. Evidence for greater disease reduction compared to other interventions was observed for point-of-use water filter interventions including safe storage (relative risk 0.39 (95% CI 0.32, 0.48)), higher-quality piped water to premises (relative risk 0.25 (95% CI 0.09, 0.67)), continuous piped water to premises (relative risk 0.64 (95% CI 0.42, 0.98)) and high community coverage with basic sanitation services (relative risk 0.55 (95% CI 0.34, 0.91)).

Strengths and limitations

Strengths and limitations of meta-regression that are described in section 2.3 about the initial systematic review and meta-analysis relate equally to this work. Compared to the 2014 meta-analysis (41), especially the exposure scenarios for drinking water and sanitation were extended to include higher levels and high coverage of services. Some of the effect estimates were based on scarce evidence such as the estimates for continuous piped water, higher-quality piped water and higher community sanitation coverage and might change when additional evidence emerges. Additionally, especially the sanitation observations included a large share of survey data analyses as data from intervention studies was scarce. WASH exposure classification in intervention studies was often poor, e.g., no disaggregation of unimproved sanitation was usually made. Additionally, use of or access to WASH services and a certain behaviour are only proxy indicators assumed to assess the amount of faecal contamination people are exposed to. There were substantial differences between the intervention studies relating to intervention type and uptake, study methods, settings, populations, pathogens present and transmission pathway dynamics.

Contributions of the research

The assessed WASH exposure levels included higher levels of service provision and were therefore in line with the Sustainable Development Goals (SDGs). This analysis highlighted that evidence on increased health effects from higher WASH service levels is accumulating but still limited. Results from this analysis might guide the choice of interventions according to their potential health impact and formed the basis for burden of disease assessments from inadequate WASH.

2.10 Handwashing with soap after potential faecal contact: Global, regional and country estimates

Research in context

This work (47) updated previous handwashing with soap prevalence estimates (section 2.4 (46)) using a revised methodology and thereby provided the necessary exposure data for the burden of disease estimates attributable to inadequate hygiene for the year 2016 (section 2.12 (12)).

I contributed to the development of the logical and analytical framework for this research. I extracted data on handwashing facility access and from handwashing observation studies identified from a systematic review. I was responsible for the data analysis and for preparing the draft publication.

Objectives

The principle aim was to quantify the current state of global handwashing practise. Specific study objectives were: 1) to quantify handwashing facility presence with soap and water on household premises, 2) to assess the association between handwashing facility presence and observed handwashing with soap, and 3) to derive country, regional and global estimates of handwashing with soap after potential faecal contact.

Main methods

Handwashing facility presence on household premises was estimated by country using multilevel modelling of country-level data on the proportion of the population with access to handwashing facilities (study objective 1). An updated (46) systematic literature review on household-level studies reporting observed handwashing with soap after potential faecal contact was conducted. Data was extracted from studies reporting both observed presence of a handwashing facility with soap and water and handwashing with soap at critical times. These data were analysed using a three-level Poisson model to estimate adjusted prevalences and prevalence ratios for handwashing with soap conditional on the presence of a handwashing facility (study objective 2). Handwashing with soap prevalence after potential faecal contact at country, regional and global levels was calculated by combining prevalence of a handwashing facility with soap and water on premises with the estimated prevalence of handwashing with soap conditional on handwashing facility presence (study objective 3).

Main findings

An estimated 73.5% (95% CI 63.2%, 81.8%) of the world population had access to a handwashing facility with soap and water on household premises in 2015. Handwashing with soap after potential faecal contact was about twice as likely (prevalence ratio 1.99, 95% CI 1.66, 2.39, $p<0.001$) where such a handwashing facility was present. An estimated 26.2% (95% CI 23.1%, 29.6%) of potential faecal contacts were followed by handwashing with soap in 2015.

Strengths and limitations

These updated handwashing with soap estimates represented a revised and improved modelling approach compared to the previous analysis of handwashing with soap prevalence (section 2.4 (46)). Also, substantially more countries were covered by their own national data in this assessment compared to the previous one (46). However, estimates of handwashing facility presence were still based on limited data. Also for many countries the mean for the respective region and income group needed to be extrapolated using multilevel modelling. The estimates for the association between the presence of a handwashing facility and observed handwashing with soap were based on only nine datasets from eight heterogeneous studies. These estimates were therefore only calculated for regional and not national levels.

Contributions of the research

This is the first study that used country-representative data on observed presence of a handwashing facility with soap and water on premises for deriving the prevalence of handwashing with soap at crucial times. Such data are now routinely collected in nationally-representative household surveys. Prior to this study only limited data on global handwashing with soap practice had been available and had been based on non-representative epidemiological studies (section 2.4 (46)). Disease burden estimates from inadequate hygiene of the Global Burden of Disease studies conducted by the IHME are based on just the presence of a handwashing facility as relevant exposure (without the translation to actual handwashing with soap)(24). Observed handwashing practice, likely the most reliable way to measure handwashing behaviours (71,72), is considered impractical to conduct routinely in national household surveys (58,73). The approach presented here may therefore be used to estimate handwashing behaviour at large scale which represents the matching exposure to the available exposure-response relationship for disease burden estimates from inadequate hygiene. This analysis showed that the prevalence of handwashing with soap remains at low levels even when necessary handwashing materials are present. Additionally, a considerable lack of hand hygiene data was observed.

2.11 A Faecal Contamination Index for interpreting heterogeneous diarrhoea impacts of water, sanitation and hygiene interventions and overall, regional and country estimates of community sanitation coverage with a focus on low- and middle-income countries

Research in context

First, this work (74) provided the first exposure estimates for high community sanitation coverage. The proportion of the global population living in communities with high coverage with basic sanitation forms the new sanitation minimum risk exposure level for the 2016 WHO disease burden estimation (section 2.12 (12)). High community sanitation coverage has increasingly been recognized as important for health (75–82). Second, this work followed a consensus meeting of WASH researchers (83) which had been conducted after the publication of several large WASH trials (84–86) that found limited health effects of improving WASH and especially sanitation. The work presented here contributed to explaining the observed heterogeneous effectiveness of WASH interventions.

I contributed to the development of the Faecal Contamination Index (FAECI). I conducted the literature search on relevant sanitation coverage levels. I was responsible for the data analysis of the association between the level of estimated faecal contamination and diarrhoea risk in WASH interventions as well as the analysis of cluster-level household survey data. I led on the preparation of the draft publication.

Objectives

First, to generate a simple, transparent and reasonable index of environmental faecal contamination that can be used to explain heterogeneous effectiveness on diarrhoeal disease of WASH interventions.

Second, to estimate the proportion of the population living in communities in which a specified percentage of the population has access to basic sanitation services by country, region and overall.

Main methods

First, the FAECI was developed using eight biologically plausible and frequently reported WASH indicators. Using this index, faecal contamination post-intervention was estimated in sanitation and WASH intervention studies. Subsequently the association between the estimated faecal contamination and the relative risk estimates for diarrhoeal disease from the individual WASH studies was analysed using meta-regression techniques.

Second, a literature search identified studies assessing health effects at various sanitation coverage levels. These studies were used to identify the health relevant thresholds for community sanitation coverage. Household survey microdata (at the level of the primary sampling unit) were analysed to calculate the proportion of the global population living in communities above a certain threshold of community sanitation coverage.

Main findings

First, the level of prevailing faecal contamination in the community post-intervention was strongly associated ($p<0.01$) with the relative risks for diarrhoeal disease. This suggested that continued faecal contamination might explain missing effectiveness of WASH interventions.

Second, forty-five percent (95% CI 35%, 56%) of the global population was estimated to live in communities in which more than 75% of the population was covered with basic sanitation services. Twenty-four percent (95% CI 15%, 35%) of the global population was estimated to live in communities in which more than 95% of the population was covered with basic sanitation services.

Strengths and limitations

First, the FAECI estimated faecal contamination easily and transparently and was able to explain heterogeneous effectiveness of WASH interventions. However, the FAECI used proxy indicators for faecal contamination which could have been chosen differently. More sophisticated approaches of modelling an unmeasured construct, here community faecal contamination, are available (e.g., (87)). Intervention studies with the lowest FAECI score were among the earlier conducted studies that reported on fewer of the chosen indicators. The score of these interventions was therefore assessed with greater uncertainty compared to the interventions that yielded a larger score. Safe management of sanitation and observed handwashing with soap – two indicators of the FAECI – needed to be inferred from other related information from the study reports. Missing values of other indicators were replaced with national mean values for the respective country, year and setting.

Second, the first estimates for high community sanitation coverage were developed. However, coverage was assessed for basic sanitation services and not for safely managed sanitation (6). Basic sanitation may not sufficiently lower faecal contamination in a community (88). Only 111 countries were covered with relevant household survey microdata for varying calendar years covering 78% of the world population and 92% of the population in low- and middle-income countries.

Contributions of the research

The score of the FAECI provided an explanation for the missing impact on diarrhoeal disease of recent large WASH trials (84–86). The publication of the results of these trials had resulted in widespread discussions about the health effectiveness of WASH interventions (83,89–92). The FAECI indicators may provide guidance on a minimum set of variables to be reported in any WASH intervention. This study further emphasized the need for more radical and transformative WASH interventions that successfully reduce faecal contamination in households and in the community. Additionally, this study provided the first estimates of high community sanitation coverage enabling a new counterfactual for the WHO burden of disease analysis attributable to inadequate WASH.

2.12 Burden of disease from inadequate water, sanitation and hygiene for selected adverse health outcomes: an updated analysis with a focus on low- and middle-income countries

Research in context

This paper (12) represented the update for the year 2016 of the previous WHO WASH-attributable burden of diarrhoeal disease assessment (section 2.5 (40)). It extended the scope of the previous analysis by including more health outcomes. The analysis presented here also used extended exposure information compared to other WASH-attributable burden of disease assessments. These included country-level estimates on the proportion of the population living in communities with a certain coverage with basic sanitation (section 2.11 (74)) and on the proportion of handwashing with soap after potential faecal contact (section 2.10 (47)). Furthermore, the present assessment applied updated exposure-response relationships for different WASH categories and exposure levels (section 2.9 (52)).

I contributed to the development of the analytical framework for the WASH-attributable burden of disease assessment and to calculating WASH-attributable disease burden estimates for various health outcomes. I delivered essential data input for the burden of disease assessment and was responsible for preparing the draft publication.

Objectives

To present WASH-attributable disease burden estimates for diarrhoea, respiratory infections, malnutrition, schistosomiasis, malaria, soil-transmitted helminth infections and trachoma for the year 2016.

Main methods

WASH-attributable disease burden was estimated preferably using comparative risk assessment methods, but also using more limited, in terms of available exposure or exposure-response data, epidemiological assessments. Modelled exposure data (11,45,47,74), based on household survey and census data, were combined with updated exposure-response relationships (52). Different counterfactuals were used for different diseases and included theoretical, plausible and feasible minimum risk exposure distributions (21). The resulting PAFs were multiplied with the total burden by disease.

Main findings

Sixty percent or 829,000 deaths of diarrhoeal disease, 13% of acute respiratory infections, 16% of malnutrition, 43% of schistosomiasis, 80% of malaria and 100% of both soil-transmitted helminths and trachoma were attributed to inadequate WASH. The overall WASH-attributable disease burden amounted to 1.6 million deaths (2.8% of deaths) and 104.6 million DALYs (3.9% of DALYs) in 2016.

Strengths and limitations

This assessment combined updated and revised exposure assessments with updated exposure-response relationships. It also included a broader range of health outcomes than previous assessments. Estimates for certain health outcomes and selected intervention types were adjusted for likely non-blinding bias. However, disease burden estimates for the different health outcomes represented different levels of evidence. WASH-attributable diarrhoea and respiratory infections were based on comparative risk assessments while the WASH-attributable burden of other health outcomes was based on more limited epidemiological assessments. Different counterfactuals for the different health outcomes were used such as the feasible, the plausible and the theoretical minimum risk exposure levels depending on the available evidence. For estimating the WASH-attributable burden of malaria, the counterfactual exposure distribution of all the population being exposed to safe water resource management was used. The exposure-response relationship linking water resource management and malaria is based on a systematic review conducted more than a decade ago and included only non-randomized intervention studies. The WASH-attributable malaria burden is therefore estimated with greater uncertainty. On the other hand, the total WASH-attributable burden of disease might still have been underestimated as many adverse health outcomes that are plausibly related to inadequate WASH have not been quantified. Future assessments should increasingly base their estimates on a theoretical minimum risk exposure level as the counterfactual. For most health outcomes this would likely include all the population using safely managed water and sanitation services and having access to essential hygiene conditions and performing essential hygiene practices, including handwashing, menstrual hygiene management and food hygiene (12,93). Additionally, estimates did not capture the burden from for example disease outbreaks, flooding and droughts or from certain populations such as refugees, internally displaced persons, and the homeless (12). Also certain exposure settings were not considered such as healthcare facilities, schools, workplaces and other public places (12).

Contributions of the research

These WASH-attributable disease burden estimates highlighted the importance on health of inadequate WASH. They provided an alternative to the disease burden estimates for the year 2016 from the IHME (37). Compared to the Global Burden of Disease study 2016, the assessment presented here adjusted estimates for likely non-blinding bias, used different counterfactuals and provided estimates for a larger range of disease outcomes. Additionally, handwashing with soap was used as the counterfactual exposure level while the IHME continues to use presence of a handwashing facility as exposure parameter which does not match the respective exposure-response relationship which relates to handwashing with soap promotion. These estimates provided the basis for reporting on SDG indicator 3.9.2 on WASH-attributable mortality (94).

3 Discussion

3.1 Main findings

The work summarized in this critical analysis generated, improved, and updated data on various WASH exposure levels (objective 1). It started off with developing a modelling approach for WASH exposure data over time able to incorporate unbalanced data, incomplete time series, non-linearity and missing data for whole countries (section 2.2 (45)). Initially used for access to improved drinking water and sanitation facilities (45), this approach was subsequently applied for modelling various WASH categories and exposure levels. A novel approach for estimating handwashing with soap prevalence was developed using nationally-representative household survey data on access to handwashing facilities. This analysis superseded the previous approach of modelling observed handwashing frequency from small-scale handwashing observation studies (sections 2.4 (46) and 2.10 (47)). It was highlighted that handwashing with soap after potential faecal contact was poorly practised throughout the world (46,47). Additionally, the handwashing prevalence estimates created the matching exposure for the generated exposure-response relationship linking handwashing with soap and health outcomes (sections 2.4 (46) and 2.9 (52)) for disease burden estimation from inadequate hygiene (sections 2.5 (40) and 2.12 (12)). The first global, regional and country-level exposure data for the proportion of the population living in communities above a certain level of sanitation coverage were generated by analysing cluster-level household survey data (section 2.11 (74)). This analysis highlighted that while 68% of the world population used at least basic sanitation, only 45% lived in communities in which at least 75% of households were covered with basic sanitation (74). These exposure estimates were used for a new sanitation counterfactual for the WHO WASH-attributable burden of disease assessment for the year 2016 (section 2.12 (12)).

The research presented here further estimated exposure-response relationships between WASH exposure levels and selected health outcomes (objective 2). The initial systematic review on WASH interventions was performed until 2013 (sections 2.3 (41) and 2.4 (46)), with subsequent update including literature published until early 2016 (section 2.9 (52)). Data were analysed using meta-analysis and meta-regression techniques to establish the exposure-response relationships between different levels of access to WASH and diarrhoea. Meta-regression in WASH research was first used by Hunter in 2009 to explain heterogeneous effectiveness of water treatment interventions (95). In the presented work, the application of meta-regression techniques was extended and included principles of network meta-analysis (sections 2.3 (41) and 2.9 (52)). These techniques could explain much of the observed heterogeneity of health impacts of WASH interventions. Additionally, they allowed the estimation of health impacts from transitions between exposure levels for which no direct evidence from intervention studies was available (41,52). These analyses highlighted the importance of higher level WASH services such as high-quality piped water, sewered sanitation and safe sanitation reaching high community coverage (41,52).

The generated exposures and exposure-response relationships were used to calculate and update the PAFs for specific risk factors and for estimating the WASH-attributable burden of disease (objective 3). The WASH-attributable burden of disease assessment for the year 2012 was conducted in collaboration between the WHO and WASH experts and attributed 842,000 diarrhoea deaths annually to inadequate WASH (section 2.5 (40)). A complementary assessment for the year 2012 estimated that 22% of the global disease burden was attributable to a large range of environmental risks (section 2.6 (3,9)). Updated WASH-attributable burden of disease figures were calculated for the year 2016 and resulted in 829,000 WASH-attributable diarrhoea deaths (section 2.12 (12)). This assessment included more health outcomes than previous assessments and estimated the WASH-attributable disease burden for diarrhoea, acute respiratory infections, schistosomiasis, protein-energy malnutrition, malaria, soil-transmitted helminth infections and trachoma (12).

Finally, the here presented work evaluated environmental health interventions and explored factors associated with their effectiveness (objective 4). A cluster randomized controlled trial assessed the health effects of a combined environmental health intervention package at household level (section 2.7 (65)). This trial combined different WASH interventions (point-of-use water treatment, piped water to households and hygiene and handwashing promotion) with the provision of improved cookstoves. However, it failed to demonstrate significantly improved health outcomes (65). A cross-sectional study evaluated improved or clean stove adoption and traditional stove displacement in more than 1,000 households from different Andean regions after various improved stove promotion programmes (section 2.8 (66)). This study also identified multiple factors associated with intervention uptake (66). Lastly, the development of a faecal contamination index enabled the explanation and interpretation of the observed heterogeneous effectiveness of sanitation and combined

WASH intervention studies using the estimated prevailing level of faecal contamination post-intervention in the community (section 2.11 (74)). This analysis indicated that current WASH interventions may not sufficiently lower exposure with faecal pathogens to achieve health outcomes (74).

The presented research is complemented by other related work that is presented in Appendix 1 (A1.4).

3.2 Strengths and limitations

The research presented in this critical analysis uniquely contributed to exposure assessment, exposure-response relationship generation and disease burden estimation attributable to environmental risks focusing on inadequate WASH. Parts of the research represented updates of previous work. One example was the disease burden assessment attributable to inadequate WASH for the year 2016 (section 2.12). These updates incorporated notable changes in methodology compared to the precursory work. Evaluations of environmental health interventions which contribute crucial inputs for risk factor-attributable disease burden assessments complement the presented work.

3.2.1 Exposure assessment

The WASH exposure assessments used proxy indicators such as access to WASH facilities intended to describe the level of faecal contamination or the amount of the specific pathogens people are exposed to through inadequate WASH. In the presented research, these proxies represented quite distal causes for the health outcome, such as the type of the drinking water facility (8). Water quality measurements, for example, would have constituted a more proximal cause (8). The use of more distal proxy indicators includes the greater risk of exposure misclassification and hence biased WASH-attributable disease burden estimates. It has for example been shown that water from improved sources was frequently faecally contaminated (63). The work presented in this critical analysis aimed to address the issue of proxy exposure indicators by extending exposure assessment beyond basic drinking water and sanitation services to higher levels of WASH services that are less likely to lead to exposure with faecal pathogens.

Multilevel modelling that was used for WASH exposure assessment has been criticized because of using information such as trends from other clusters, e.g., neighbouring countries, for a cluster with sparse or no data (50). However, the performance of the model was tested using cross-validation techniques (96) indicating that the model predicted reasonably well even for clusters without data (47). Other methods for modelling exposure to risk factors are available such as spatiotemporal Gaussian process regression used by the IHME (24,56). The performance of multilevel modelling and of Gaussian process regression for WASH exposure data has not been compared as different data sources were included in the IHME compared to the WHO assessments (56).

3.2.2 Exposure-response relationship estimation

For generating the exposure-response relationships, results from intervention studies with sometimes weak study designs, poor implementation and compliance that promoted very different technologies or behaviours were pooled. The evidence from intervention studies for certain WASH categories such as for sanitation was very scarce. Therefore also studies were included in the analyses that did not clearly specify an intervention but that analysed household survey data using matching methods to permit causal inference (97). Effect estimates from intervention studies generally relate to being invited to the intervention and are controlled for potential confounders (98). Effect estimates from observational studies on the other hand relate to actually participating in the “intervention” while potential confounders are not controlled for (98). The appropriateness of combining results from intervention and observational studies has therefore been questioned (98). Pooling results over many studies does not account for various other differences between studies such as the study setting and the quality of intervention implementation.

One frequent issue in WASH intervention studies is the lack of blinding participants to intervention status. Diarrhoea in WASH intervention studies is usually self-reported and it has been shown that subjectively assessed outcomes are prone to reporting bias (53,54). There are a couple of drinking-water intervention studies that aimed to blind their participants to intervention status (99–102). Different analyses conducted about a decade ago found that blinded water treatment interventions hardly reduced diarrhoea, suggesting that part of the health impact found in non-blinded water treatment interventions was in fact due to bias from lack of blinding (95,103). There were however multiple issues in the blinded water treatment interventions which might make them not suitable for determining the effect of non-blinding on intervention results. One issue was that these interventions applied point-of-use chlorine treatment as drinking-water intervention. There are certain diarrhoea pathogens, such as *Cryptosporidium* and *Guardia* that are resistant to chlorine treatment (104). *Cryptosporidium* is a particularly frequent pathogen in childhood diarrhoeal disease (105). Furthermore, truly blinding chlorine water treatment might be difficult: In one of the blinded studies (102), intervention households dropped out because they disliked the taste and smell of their water. Also in a recent double-blinded chlorine intervention study, many more intervention than control households complained about the taste and the smell of their drinking water (101). Additionally, 30% of drinking water samples had chlorine concentrations above the recommended thresholds for acceptable taste and odours and only a third of intervention households adhered to chlorine treatment throughout the intervention (101).

The WHO WASH-attributable disease burden research presented here is, to my knowledge, the first to have used a systematic and evidence-based approach developed by Welton et al. (106) to adjust risk estimates from intervention studies for non-blinding bias (41,52). The adjustment was based on a large meta-epidemiological study of more than 200 individual meta-analyses including nearly 2,000 trials from a range of different areas (53,106). Only results from point-of-use drinking water and hygiene promotion interventions were considered at increased risk of non-blinding bias and were therefore adjusted in contrast to water supply and sanitation interventions (103). Point-of-use drinking water and hygiene promotion interventions are household-level interventions which are usually more apparent to the recipients and have the clear and sole aim to improve health. Water-supply and sanitation interventions on the other hand are usually community-level interventions and do not solely concentrate on health outcomes but also on community and general development (41).

3.2.3 Disease burden calculation

Exposures to many environmental risks and risk factor-disease links have to date not been quantified (3). Examples include various adverse health effects that can plausibly be linked to inadequate WASH (12). Therefore, environmental burden of disease assessments are likely underestimating the true disease burden attributable to the environment. Burden of disease estimates attributable to various environmental risks or to inadequate WASH presented in this critical analysis are sometimes based on scarce evidence. Therefore, they are not always calculated using comparative risk assessments but using more limited exposure or exposure response information or even expert opinion (3).

Disease burden estimates are based on many assumptions that are made while assessing exposures and exposure-response relationships and calculating the PAF and are therefore quite uncertain. The assumptions that are made in exposure and exposure-response relationship assessment have been listed in previous sections. Another important source of uncertainty is the choice of the counterfactual exposure level, i.e., the level of exposure with the lowest assumed risk for health. The counterfactual importantly determines the size and the interpretation of the risk factor-attributable disease burden. Different counterfactual exposure distributions have been proposed including the theoretical, the plausible, the feasible and the cost-effective minimum risk (16). Usually, risk factor-attributable burden of disease assessments aim for a theoretical minimum risk exposure level to fully gauge the size of health impacts related to the risk factor (12,24). The theoretical minimum risk WASH exposure level may however be defined in different ways. There is evidence from studies that implementing Water Safety Plans on piped water in high-income countries resulted in reduced gastrointestinal disease (107,108). These findings indicate that even high levels of service provision, such as high-quality piped water, may exhibit residual WASH-attributable disease burden and thus do not constitute the "true" theoretical minimum risk. Often current WASH counterfactual exposure scenarios do not represent the theoretical minimum risk exposure level but more interim levels that likely pose considerable risks to health. One example would be basic WASH services (12). Additionally, counterfactual exposures and their related risk estimates are based on intervention studies with sometimes many limitations such as poor implementation and poor compliance. Often these interventions targeted individual households instead of whole communities. Such interventions are unlikely to reduce exposure with faecal or other pathogens to a large extent (74). Results from such interventions therefore likely underestimate the exposure-response relationships between WASH and health.

Due to the different sources of uncertainty when estimating risk factor-attributable disease burden, validation of estimates becomes very important. Validation of estimates seeks to determine how well the estimates correspond to the true exposure, the true exposure-response relationship or the true risk factor-attributable disease burden. Validation of exposure estimates is especially important when estimates are made for countries with no own source data and can be achieved with cross-validation techniques (96) as described in the research of section 2.10 (47). Unfortunately, validation of the exposure-response relationships and of the risk-factor attributable disease burden estimates is not possible at present as the true exposure-response relationship or the true risk factor-attributable disease burden in the target population is not known. This is an important limitation especially regarding the variability of disease burden estimates over time and between institutions.

The PAF is usually interpreted as the fraction of disease that would have been preventable through removal or reduction of the risk factor, however certain assumptions need to apply (22,109). There needs to be a causal relationship between exposure and disease. The relative risks describing the exposure-response relationship need to be free from confounding and bias. Truly effective interventions are required that are able to move everyone to the chosen counterfactual exposure distribution (110). Another assumption is that the formerly exposed group immediately attains disease risk of the unexposed group after removal or reduction of the exposure (22,109). Furthermore, a disease can usually be caused by more than one exposure. While the PAF for each risk factor is bounded by one (or 100%) the sum of the individual relevant exposures can (and usually does) exceed one (8,109). Whether the PAF of one exposure equals the preventable proportion of disease is therefore conditional on the assumption that all other relevant exposures are kept constant (109).

The PAF calculates the attributable disease burden or so-called “excess cases” of a disease or health outcome (2). Excess disease cases would not have occurred without exposure to the risk factor and are potentially preventable (2,23,111), They need to be differentiated from etiologic cases (2,23,104). Etiologic cases would have occurred without exposure (2,110,112,113) but are still caused by the risk factor (e.g., the risk factor led to an earlier disease onset). Often the number of excess cases is much smaller than the number of etiologic cases (2). Therefore, it can be argued that the PAF usually underestimates the health importance of a risk factor and that it indicates the lower bound of attributable burden (2,110). This is less important for infectious disease occurrence where probably all cases caused by the risk factor can be considered excess cases compared to mortality and chronic diseases.

Studies examining the linkages between environmental risks and disease are often of an observational design as it would be unethical to randomize a group of people to a (potential) hazardous exposure. Therefore, there is likely confounding in the risk factor-disease association and relative risks taken from the published literature are usually confounder-adjusted. Adjusted relative risks should however not be used in the presented PAF formula (Equation 1) but in alternative formulas (111). One formula requires the proportion of exposed disease cases (Equation A4, Appendix 1 (A1.2)). Another formula calculates stratum-specific (by confounder strata) attributable fractions which are subsequently weighted by the proportion of cases in each stratum and summed (Equation A5, Appendix 1 (A1.2))(25,111). Adjusted relative risks have often been used in Equation 1 which has been called the "partially adjusted" method (114). Using adjusted relative risks in Equation 1 was estimated to lead to a biased PAF of between 10% and 20% (25). The use of the alternative formulas that are appropriate for adjusted relative risks is often constrained by the additional data needs required for their computation (25). In current risk factor-attributable burden of disease analyses, usually stratum-specific PAFs for a range of potential confounders including age, sex and location are calculated (12,24). However and due to data availability, often the same exposure data and exposure-response relationships are applied across different confounder strata. There are various other factors acting as potential confounders, one notable example is socio-economic status. In WASH interventions in which a confounder such as socio-economic status will often positively confound the exposure-response relationship (i.e., crude relative risk > adjusted relative risk) the resulting PAF will be underestimated (25). This will usually be less important in randomized compared to non-randomized interventions as randomization aims for balanced covariate distributions between intervention and control groups. Relative risks from randomized studies are therefore usually less confounded than results from observational studies and are therefore more appropriately used in the presented PAF formula (Equation 1).

The exposure-response relationships used for calculating the PAFs were mostly derived from intervention studies. These studies had usually been conducted in population subgroups and not in the population for which the disease burden was subsequently calculated. To assure portability of an exposure-response relationship from a source to a target population, important assumptions are needed: Exposure is defined alike and the distribution of relevant confounders and effect-modifiers is the same in the source and the target population (23). It has been shown that small differences in relative risks and in the distribution of confounders and effect modifiers between the source and the target population resulted in considerable bias in the estimation of the PAF and the risk factor-attributable disease burden (114).

The PAFs from different exposures are often combined, for example to derive the overall environmental fraction of a disease (Equation 2). The application of this formula assumes independence between risk factors (e.g., being exposed to one factor does not increase the likelihood of being exposed to the other risk factor) and that the joint effects of the individual risk factors are multiplicative (23). The application of Equation 2 may have resulted in upward-biased estimates of the WASH-attributable disease burden as inadequate water, sanitation and hygiene are likely to be positively related to each other (115).

Priority setting for preventive action and choice of interventions should not be exclusively based on environmental burden of disease assessments. Social and ethical considerations need to be taken into account such as the priorities of a population and its risk perceptions as well as social consequences of the disease burden and related interventions (8). Another important issue is the availability and cost-effectiveness of interventions strategies (18). Also burden of disease assessments do usually not account for benefits other than health gains (8). A WASH intervention for example might not only improve health but also lead to increased security, empowerment of women and girls, dignity and time savings (116,117).

3.3 Impact on policy and practice of the presented research

PAFs and related risk factor-attributable burden of disease estimates quantify the importance of a risk factor on human health. They provide a bridge between the risk factor-disease association as usually derived in epidemiological studies and the prevalence of the risk factor in a given population (23). Even when relative risks are large the public health relevance of a risk factor might be small when only a small fraction of the population is exposed (23,111). The public health relevance might be large when there is substantial exposure with a risk factor with a small relative risk (23,111). The PAF can be interpreted as the proportion of disease cases or deaths that could have potentially been prevented given effective interventions to remove or reduce the risk factor were available. Results of burden of disease assessments are therefore relevant to policy-making, can guide the choice of the most urgent interventions and are easy to understand and to communicate (23,25,111).

Environmental disease burden estimates are important for raising awareness about the importance of environmental factors for health. Probably the most prominent example of the presented work is the comprehensive burden of disease assessment attributable to environmental risks (section 2.6 (3,9)). Results of this assessment were reported in over 170 newswires and newspapers in English, French and Spanish and in numerous other languages throughout the world (examples include (118–122)) and were also extensively communicated via social media (examples include (123,124)) and in a radio interview (125).

Following the publication of the WHO WASH-attributable burden of disease estimates for the year 2012 (section 2.5 (40)), the subsequent Global Burden of Disease study for the year 2013 changed its approach of estimating WASH-attributable disease burden (38). By using counterfactual exposure distributions that extended from improved drinking water and sanitation facilities to higher levels of WASH service provision including hygiene, estimated WASH-attributable disease burden increased by a factor of four between the Global Burden of Disease studies 2010 and 2013 (18,38). The IHME Global Burden of Disease study estimated 337,000 deaths from inadequate WASH in 2010 (18), which changed to 1,399,000 deaths in 2013 (38), 1,766,000 deaths in 2015 (39), 1,661,000 deaths in 2016 (37) and 1,610,000 in 2017 (24) (estimates for 2016 and 2017 include deaths from lower respiratory infections attributable to inadequate hygiene, Table 1). The Global Burden of Disease assessment for the year 2016 attributed 89% of global diarrhoea deaths to inadequate WASH (37) while the WHO assessment for the year 2016 attributed 60% of global diarrhoea deaths to inadequate WASH (section 2.12 (12)).

Table 1: WHO and GBD WASH-attributable disease burden estimates over time

Year of estimates	WASH-attributable diarrhoeal deaths (thousands)		Hygiene-attributable deaths from lower respiratory infections (thousands)	
	WHO	GBD (IHME)	WHO	GBD (IHME)
2010	-	337	-	-
2012	842	-	-	-
2013	-	1,399	-	-
2015	-	1,766*	-	-
2016	829	1,481	370	179
2017	-	1,422	-	188

* Includes diarrhoeal diseases, typhoid and paratyphoid fever; WASH: water, sanitation and hygiene, WHO: World Health Organization, GBD: Global Burden of Disease, IHME: Institute for Health Metrics and Evaluation

Reasons for the differences between the WHO estimates and those from the Global Burden of Disease study from the year 2013 onwards include different counterfactuals or minimum risk exposure levels and the adjustment for likely bias due to lack of blinding in the WHO assessments. In the Global Burden of Disease studies the minimum risk exposure levels were defined as high-quality drinking water that is filtered or boiled at point-of-use, sanitation connected to sewer or septic tank and access to handwashing stations with soap and water (24,37–39). In the WHO assessments, the minimum risk exposure level for drinking water was defined as water from any source that is filtered or boiled at household level (12,40). This choice was based on the scarcity of data for the exposure-response relationship between higher-quality piped water and disease (41,52). The current minimum risk exposure level for the WHO sanitation assessment is high, i.e., above 75% of the population, community coverage with basic sanitation facilities (12). For the hygiene assessment, the WHO uses the proportion of the population with access to handwashing facilities with soap and water but subsequently adjusts these estimates for actual handwashing with soap (47).

Transparency of methods and estimates seems especially important in light of such differing estimates. However, the earlier systematic review conducted by the IHME is only available as an abstract (36). The updated systematic review is only mentioned in the appendix of the comparative risk assessment for the Global Burden of Disease study 2017 and is described as an update of the here presented systematic review (section 2.3 (41))(56). In contrast, the search strategies, the included studies, the extracted variables, and the input as well as the results data at disaggregated level from the here presented systematic reviews, meta-analyses and WASH-attributable burden of disease assessments have been made available allowing re-calculation and data usage.

The WHO is reporting on several WASH-related SDG indicators, including the proportion of the population using safely managed sanitation services (Indicator 6.2.1), the proportion of wastewater safely treated (Indicator 6.3.1), and the mortality from unsafe water, sanitation and hygiene (Indicator 3.9.2) (94). The here presented WHO burden of disease estimates (sections 2.5 and 2.12) provided the data basis for the annual monitoring of the SDG target indicator 3.9.2 on WASH-attributable mortality (126).

The methods for risk factor-attributable burden of disease assessment that are described in this critical analysis have been used for an analysis of the potential impacts on health of the Indian Swachh Bharat Mission (SBM, Clean India Mission) which is a nation-wide campaign to end open defecation (127,128). Following the start of the SBM in 2014 and documented by household surveys, open defecation in rural India declined by about 12 percentage points per year between 2015 and 2019 compared to only 3 percentage points decline between 2000 and 2014 (6). The analysis which was conducted by the WHO with my contributions, estimated that the SBM could avert about 300,000 deaths from diarrhoea and protein-energy malnutrition provided the mission's goal of all the Indian population using safe sanitation by October 2019 was achieved (129). These results were quoted by the Indian Prime Minister in 2018 in his yearly speech on Independence Day and were also reported by the Indian media (130–132).

The knowledge and skills I acquired while conducting the research presented in this critical analysis enabled me to participate in discussions about environmental burden of disease assessments for example in Germany. Environmental health research is frequently subject to scientific misinformation that aims to influence public perceptions, reduce trust in research and impedes evidence-based policy making (133). Similarly, environmental disease burden assessments have been challenged regarding their validity and verity. One example is a recent debate in Germany about the disease burden attributable to NO_2 emissions (134,135). I contributed to frequently asked questions around environmental burden of disease assessments that were published on the WHO website and I am co-authoring a letter to the editor rebutting the criticism which was largely around calculating the PAF and the methods applied for calculating risk factor-attributable burden of disease estimates (136,137).

4 Concluding issues in WASH- and risk factor-attributable disease burden assessments and identified research needs

The research presented in this critical analysis demonstrated the importance of environmental risk factors on health including inadequate WASH. It also underlined the importance of selected issues in risk factor-attributable disease burden assessments, some of which are specific to inadequate WASH. Data gaps and needs for future research were identified.

For most environmental risks, data on exposures and exposure-response relationships are still scarce (5). To fill these data gaps, research on environmental risks encompassing all steps of risk-factor attributable disease burden assessment, including identification and mapping of exposures and quantification of exposure-response relationships, should be conducted (5).

Comparative risk assessment methods using theoretical minimum risk exposure distributions should ultimately replace alternative approaches for estimating risk factor-attributable disease burden that are based on lower quality data or more assumptions. More disaggregated exposure, exposure-response and disease data would allow WASH-attributable disease burden estimation for population subgroups of interest such as different socio-economic groups. Issues of comparative risk assessment methods include the appropriate use of adjusted relative risks for estimation of the PAF, the portability of the exposure-response relationship from various source populations to a target population with different underlying conditions and the choice of the most appropriate counterfactual.

Recently a few large, well-funded and well-conducted trials that yielded high implementation and compliance showed minimal health impacts from improving WASH (84–86). These trials provided or promoted basic WASH and only targeted households with pregnant women (84–86). Research has shown that much of the health impact from adequate WASH and especially from adequate sanitation is actually from community-level effects, i.e., whether a household is using safe sanitation impacts the health in neighbouring households (75,78–81). Even high coverage with basic sanitation services, as opposed to safely managed sanitation, might however not sufficiently reduce faecal contamination in a community (88). A consensus statement of researchers hypothesized that basic WASH services as implemented in these trials were unlikely to lead to health benefits and that higher level services covering the entire communities were needed (138). The research presented here contributed to this discussion by indicating that community faecal contamination needed to be reduced substantially before health impacts could be observed in intervention studies (section 2.11 (74)).

Risk factor-attributable, including WASH-attributable, burden of disease assessments usually rely on intervention studies whose results are pooled for establishing the exposure-response relationship. WASH interventions show great heterogeneity and apply different technologies and levels of services, provide infrastructure or promote certain behaviours. Accordingly, the presented research has shown that much of the observed difference in health impact is due to the type of intervention (sections 2.3 (41) and 2.9 (52)). Furthermore, health impact will likely depend on whether the intervention is tailored to the prevailing exposure routes of the local context (138).

A truly theoretical minimum risk exposure level in WASH-attributable disease burden assessments which might be approximated by all the population using safely managed WASH services would represent more comprehensively the amount of the disease burden that could be reduced through adequate WASH. Additionally, this would be in line with the targets of SDG 6 (94). For this, more radical or "transformative" (138) WASH interventions are needed that remove or substantially reduce faecal contamination in a community. Such interventions need to supply whole communities with water and sanitation network connections that provide continuous piped water free from contamination and safe sanitation and effective promotion of comprehensive hygiene behaviours. Such transitions from limited or basic WASH to safely managed WASH services have usually happened over decades in high-income countries and were accompanied with large though deferred population health improvements (138–141). As discussed above even safely managed WASH services might constitute risks to health which was shown through studies on Water Safety Plans (107,108). Depending on the local context, even more comprehensive WASH interventions might be needed, such as those also including reduced contact with animal faeces (142–144).

An additional limitation of relying on household interventions for WASH-attributable burden of disease assessments includes likely bias from lack of blinding in studies with self-reported health outcomes. The presented research adjusted for this bias based on prior evidence which resulted in non-significant health impact from certain point-of-use drinking water treatments and from hygiene promotion (sections 2.3 (41) and 2.9

(52)). This is in line with previous research (95,103). Alternative approaches are available that could be directly integrated in intervention design and implementation such as the use of negative control outcomes or attention control groups (145). Negative control outcomes are those outcomes that are not plausibly related to the intervention of interest, such as the prevalence of bruising or scrapes following a WASH intervention (146). In an attention control group an intervention that mimics the non-specific or theoretically inactive elements of the main intervention, such as intensity of contact, is implemented (68,69). The anticipated outcome of the attention control intervention needs to be independent from the outcome of the main intervention (68,69). An attention control group was used in the research presented here to reduce bias from lack of blinding and study drop-out (section 2.7 (65,67)). To further improve WASH interventions and their usability for disease burden analysis, research on intervention implementation, intervention quality, intermediate outcomes, determinants of intervention effectiveness and the relation between access and actual use of services would be useful (12).

Regarding the many limitations of intervention studies to derive the exposure-response relationships for disease burden estimation, the role of other study designs should be explored. One example are pre-existing, non-randomized interventions (147,148) which often happen in large and representative populations. Another example is the use of data from country-representative household surveys such as Multiple Indicator Cluster Surveys (MICS) and Demographic and Health Surveys (DHS) (149), potentially using matching methods for generating "intervention" and "control" groups (97). Using results of alternative study designs (27) might be an important step to increase data availability for example for the provision of higher level services and for settings such as high-income countries.

Future WASH-attributable burden of disease assessments might benefit from combined exposure scenarios of water, sanitation and hygiene because there are likely important linkages and interactions between the different WASH exposure categories. Such combined scenarios were already used in previous burden of disease assessments (31). This would also solve the discussed issue of using Equation 2 for combining different PAFs for a cluster of risk factors. Future assessments might also calculate the disease burden from several counterfactual scenarios, e.g. different definitions of the theoretical minimum risk but also plausible and feasible minimum risk exposure levels. This might also help explaining the varying size of WASH-attributable disease burden that has been observed over the last decade.

Major differences between estimates from recent WASH-attributable burden of disease assessments (12,18,24,27,37–40) highlight the need for developing harmonized approaches of assessing exposures, defining counterfactual distributions, and calculating exposure-response relationships and the associated disease burden. As burden of disease estimates have great policy relevance and often guide the choice of priorities and investments, environmental burden of disease assessments require clear communication of limitations and assumptions. Sensitivity analyses showing the impact of different assumptions on results should be conducted and presented.

References

1. Frumkin H, editor. Environmental Health: From Global to Local. 2. San Francisco, CA: Jossey-Bass; 2005.

2. Greenland S, Robins JM. Conceptual problems in the definition and interpretation of attributable fractions. Am J Epidemiol. 1988;128(6):1185–1197.

3. Prüss-Ustün A, Wolf J, Corvalán C, Bos R, Neira M. Preventing disease through healthy environments: A global assessment of the environmental burden of disease from environmental risks. Geneva, Switzerland: World Health Organization; 2016.

4. Prüss-Ustün A, Corvalán C. Preventing disease through healthy environments: Towards an estimate of the environmental burden of disease. Geneva, Switzerland: World Health Organization; 2006.

5. Landrigan PJ, Fuller R, Acosta NJ, Adeyi O, Arnold R, Baldé AB, et al. The Lancet Commission on pollution and health. Lancet. 2018;391(10119):462–512.

6. UNICEF, WHO. Progress on household drinking water, sanitation and hygiene 2000-2017. Special focus on inequalities. New York: United Nations Children's Fund and World Health Organization; 2019.

7. WHO. Safer Water, Better Health. Geneva, Switzerland: World Health Organization; 2019.

8. Prüss-Ustün A, Mathers C, Corvalán C, Woodward A. Introduction and methods: Assessing the environmental burden of disease at national and local levels. Geneva, Switzerland: World Health Organization; 2003. (Environmental burden of disease series). Report No.: 1.

9. Prüss-Ustün A, Wolf J, Corvalán C, Neville T, Bos R, Neira M. Diseases due to unhealthy environments: an updated estimate of the global burden of disease attributable to environmental determinants of health. J Public Health. 2016;39(3):464–475.

10. Smith KR, Corvalán CF, Kjellstrom T. How much global ill health is attributable to environmental factors? Epidemiology. 1999;10(5):573–584.

11. WHO, UNICEF. Home | JMP [Internet]. undated [cited 2019 Sep 9]. Available from: https://washdata.org/

12. Prüss-Ustün A, Wolf J, Bartram J, Clasen T, Cumming O, Freeman MC, et al. Burden of disease from inadequate water, sanitation and hygiene behaviours for selected adverse health outcomes: an updated analysis with a focus on low- and middle-income countries. Int J Hyg Environ Health. 2019;222(5):765–77.

13. WHO, UNICEF. Monitoring: Drinking water [Internet]. JMP. [cited 2019 Sep 9]. Available from: https://washdata.org/monitoring/drinking-water

14. WHO, UNICEF. Monitoring: Sanitation [Internet]. JMP. [cited 2019 Sep 9]. Available from: https://washdata.org/monitoring/sanitation

15. WHO, UNICEF. Monitoring: Hygiene [Internet]. JMP. [cited 2019 Sep 10]. Available from: https://washdata.org/monitoring/hygiene

16. Murray CJ, Lopez AD. On the comparable quantification of health risks: lessons from the Global Burden of Disease Study. Epidemiology. 1999;10(5):594–605.

17. Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJ, the Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. Lancet. 2002;360(9343):1347–60.

18. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2224–2260.

19. WHO. Comparative quantification of health risks. Geneva, Switzerland: World Health Organization; 2004.

20. Ezzati M. Annex 4.1: Comparative Risk Assessment in the Global Burden ofDisease Study and the Environmental Health Risks. In: Methodology for assessment of environmental burden of disease [Internet]. Geneva, Switzerland:

World Health Organization; 2000 [cited 2019 Sep 9]. p. 31–3. Available from: https://www.who.int/quantifying_ehimpacts/methods/en/wsh0007an4.pdf?ua=%201

21. Murray CJ, Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S. Comparative quantification of health risks: conceptual framework and methodological issues. Popul Health Metr. 2003;1(1):1.

22. Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions. Am J Public Health. 1998;88(1):15–19.

23. Steenland K, Armstrong B. An overview of methods for calculating the burden of disease due to specific risk factors. Epidemiology. 2006;512–519.

24. Stanaway JD, Afshin A, Gakidou E, Lim SS, Abate D, Abate KH, et al. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1923–1994.

25. Darrow LA, Steenland NK. Confounding and bias in the attributable fraction. Epidemiology. 2011;53–58.

26. Murray CJL, Lopez AD. The Global Burden of Disease. Geneva: World Health Organization, Harvard School of Public Health, World Bank; 1996.

27. Clasen T, Prüss-Ustün A, Mathers C, Cumming O, Cairncross S, Colford Jr JM. Estimating the impact of inadequate water, sanitation and hygiene on the global burden of disease: evolving and alternative methods. J Trop Med Int Health. 2014;19(8):884–93.

28. WHO. Health and Environment in Sustainable Development: Five Years after the Earth Summit. Geneva, Switzerland: World Health Organization; 1997.

29. WHO. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva, Switzerland: World Health Organization; 2002.

30. WHO. The Global Burden of Disease, 2004 update. Geneva, Switzerland: World Health Organization; 2008.

31. Prüss A, Kay D, Fewtrell L, Bartram J. Estimating the burden of disease from water, sanitation, and hygiene at a global level. Environ Health Perspect. 2002;110(5):537–542.

32. WHO. Global health risks, mortality and burden of disease attributable to selected major risks. Geneva, Switzerland; 2009.

33. Prüss-Üstün A, Corvalán C. How much disease burden can be prevented by environmental interventions? Epidemiology. 2007;18(1):167–178.

34. Prüss-Ustün A, Bos R, Gore F, Bartram J. Safer Water, Better Health. Geneva, Switzerland: World Health Organization; 2008.

35. WHO. Preventing disease through healthy environments: a global assessment of the burden of disease from environmental risks [Internet]. WHO. [cited 2020 Jan 12]. Available from: http://www.who.int/quantifying_ehimpacts/publications/preventing-disease/en/

36. Engell RE, Lim SS. Does clean water matter? An updated meta-analysis of water supply and sanitation interventions and diarrhoeal diseases. Lancet. 2013;381(Suppl 2):S44.

37. Gakidou E, Afshin A, Abajobir AA, Abate KH, Abbafati C, Abbas KM, et al. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1345–1422.

38. Forouzanfar MH, Alexander L, Anderson HR, Bachman VF, Biryukov S, Brauer M, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;386(10010):2287–323.

39. Forouzanfar MH, Afshin A, Alexander LT, Anderson HR, Bhutta ZA, Biryukov S, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–

2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388(10053):1659–1724.

40. Prüss-Ustün A, Bartram J, Clasen T, Colford JM Jr, Cumming O, Curtis V, et al. Burden of disease from inadequate water, sanitation and hygiene in low- and middle-income settings: a retrospective analysis of data from 145 countries. Trop Med Int Health. 2014;19(8):894–905.

41. Wolf J, Prüss-Ustün A, Cumming O, Bartram J, Bonjour S, Cairncross S, et al. Assessing the impact of drinking-water and sanitation on diarrhoeal disease in low-and middle-income settings: A systematic review and meta-regression. Trop Med Int Health. 2014;19(8):928–42.

42. Haines A. Climate Change and Health: Strengthening the Evidence Base for Policy. Am J Prev Med. 2008 Nov 1;35(5):411–3.

43. Frumkin H, Hess J, Luber G, Malilay J, McGeehin M. Climate Change: The Public Health Response. Am J Public Health. 2008 Mar 1;98(3):435–45.

44. Costello A, Abbas M, Allen A, Ball S, Bell S, Bellamy R, et al. Managing the health effects of climate change: Lancet and University College London Institute for Global Health Commission. Lancet. 2009 May 16;373(9676):1693–733.

45. Wolf J, Bonjour S, Prüss-Ustün A. An exploration of multilevel modeling for estimating access to drinking-water and sanitation. J Water Health. 2013;11(1):64–77.

46. Freeman MC, Stocks ME, Cumming O, Jeandron A, Higgins JPT, Wolf J, et al. Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. Trop Med Int Health. 2014;19(8):906–16.

47. Wolf J, Johnston R, Freeman MC, Ram PK, Slaymaker T, Laurenz E, et al. Handwashing with soap after potential faecal contact: Global, regional and country estimates for handwashing with soap after potential faecal contact. Int J Epidemiol. 2019;48(4):1204–18.

48. WHO, UNICEF. Progress on Sanitation and Drinking Water, 2010 update. Geneva, Switzerland: Unicef, World Health Organization; 2010.

49. JMP. Water quality monitoring [Internet]. [cited 2020 Jan 8]. Available from: https://washdata.org/monitoring/drinking-water/water-quality-monitoring

50. Fuller JA. Emerging Issues in Sanitation: Herd Protection, Sharing Between Households, and Joint Effects. [Michigan]: University of Michigan; 2015.

51. WHO, UNICEF. WHO/UNICEF JMP Task Force on Methods. 2014.

52. Wolf J, Hunter PR, Freeman MC, Cumming O, Clasen T, Bartram J, et al. Impact of drinking water, sanitation and hand washing with soap on childhood diarrhoeal disease: updated meta-analysis and meta-regression. Trop Med Int Health. 2018;23(5):508–25.

53. Savović J, Jones HE, Altman DG, Harris RJ, Jüni P, Pildal J, et al. Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. Ann Intern Med. 2012;157(6):429–438.

54. Wood L, Egger M, Gluud LL, Schulz KF, Jüni P, Altman DG, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. BMJ. 2008;336(7644):601.

55. Thompson SG, Higgins J. How should meta-regression analyses be undertaken and interpreted? Stat Med. 2002;21(11):1559–1573.

56. Stanaway JD, Afshin A, Gakidou E, Lim SS, Abate D, Abate KH, et al. Supplementary Appendix 1. In: Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017 [Internet]. Lancet; 2018 [cited 2019 Sep 9]. p. 60–3. Available from: https://ars.els-cdn.com/content/image/1-s2.0-S0140673618322256-mmc1.pdf

57. Biran A, Rabie T, Schmidt W, Juvekar S, Hirve S, Curtis V. Comparing the performance of indicators of hand-washing practices in rural Indian households. Trop Med Int Health. 2008;13(2):278–285.

58. Ram PK, Halder AK, Granger SP, Jones T, Hall P, Hitchcock D, et al. Is Structured Observation a Valid Technique to Measure Handwashing Behavior? Use of

Acceleration Sensors Embedded in Soap to Assess Reactivity to Structured Observation. Am J Trop Med Hyg. 2010 May 11;83(5):1070–6.

59. Townsend J, Greenland K, Curtis V. Costs of diarrhoea and acute respiratory infection attributable to not handwashing: the cases of India and China. Trop Med Int Health. 2016 Nov 1;22(1):74–81.

60. Ziegelbauer K, Speich B, Mäusezahl D, Bos R, Keiser J, Utzinger J. Effect of Sanitation on Soil-Transmitted Helminth Infection: Systematic Review and Meta-Analysis. PLoS Med. 2012 Jan 24;9(1):e1001162.

61. Emerson PM, Cairncross S, Bailey RL, Mabey DCW. Review of the evidence base for the 'F'and 'E'components of the SAFE strategy for trachoma control. Trop Med Int Health. 2000;5(8):515–527.

62. Humphrey JH. Child undernutrition, tropical enteropathy, toilets, and handwashing. Lancet Lond Engl. 2009;374(9694):1032–1035.

63. Bain R, Cronk R, Hossain R, Bonjour S, Onda K, Wright J, et al. Global assessment of exposure to faecal contamination through drinking water based on a systematic review. Trop Med Int Health. 2014 Aug 1;19(8):917–27.

64. Norman G, Pedley S, Takkouche B. Effects of sewerage on diarrhoea and enteric infections: a systematic review and meta-analysis. Lancet Infect Dis. 2010 Aug;10(8):536–44.

65. Hartinger SM, Lanata CF, Hattendorf J, Verastegui H, Gil AI, Wolf J, et al. Improving household air, drinking water and hygiene in rural Peru: a community-randomized–controlled trial of an integrated environmental home-based intervention package to improve child health. Int J Epidemiol. 2016;45(6):2089–2099.

66. Wolf J, Mäusezahl D, Verastegui H, Hartinger SM. Adoption of clean cookstoves after improved solid fuel stove programme exposure: a cross-sectional study in three Peruvian Andean regions. Int J Environ Res Public Health. 2017;14(7):745.

67. Hartinger SM, Lanata CF, Hattendorf J, Wolf J, Gil AI, Obando MO, et al. Impact of a child stimulation intervention on early child development in rural Peru: a cluster

randomised trial using a reciprocal control design. J Epidemiol Community Health. 2017;71(3):217–224.

68. Aycock DM, Hayat MJ, Helvig A, Dunbar SB, Clark PC. Essential considerations in developing attention control groups in behavioral research. Res Nurs Health. 2018;41(3):320–8.

69. Popp L, Schneider S. Attention placebo control in randomized controlled trials of psychosocial interventions: theory and practice. Trials. 2015 Apr 11;16(150).

70. WHO. WHO Guidelines for Indoor Air Quality: Household Fuel Combustion. Geneva, Switzerland: World Health Organization; 2014.

71. Ram PK. Practical Guidance for Measuring Handwashing Behavior: 2013 Update. New York, USA: Water and Sanitation Program; 2013.

72. Luby SP, Halder AK, Huda TM, Unicomb L, Johnston RB. Using child health outcomes to identify effective measures of handwashing. Am J Trop Med Hyg. 2011;85(5):882–892.

73. Loughnan LC, Ram PK, Luyendijk R. Measurement of handwashing behaviour in Multiple Indicator Cluster Surveys and Demographic and Health Surveys, 1985–2008. Waterlines. 2015;34(4):296–313.

74. Wolf J, Johnston R, Hunter PR, Gordon B, Medlicott KO, Prüss-Ustün A. A Faecal Contamination Index for interpreting heterogeneous diarrhoea impacts of water, sanitation and hygiene interventions and overall, regional and country estimates of community sanitation coverage with a focus on low- and middle-income countries. Int J Hyg Environ Health. 2019;222(2):270–82.

75. VanDerslice J, Briscoe J. Environmental interventions in developing countries: interactions and their implications. Am J Epidemiol. 1995;141(2):135–144.

76. Fuller JA, Villamor E, Cevallos W, Trostle J, Eisenberg JN. I get height with a little help from my friends: herd protection from sanitation on child growth in rural Ecuador. Int J Epidemiol. 2016 Jan 4;45(2):460–9.

77. Andres LA, Briceño B, Chase C, Echenique JA. Sanitation and Externalities: Evidence from Early Childhood Health in Rural India. The World Bank; 2014. (Policy Research Working Paper). Report No.: 6737.

78. Jung YT, Hum RJ, Lou W, Cheng Y-L. Effects of neighbourhood and household sanitation conditions on diarrhea morbidity: Systematic review and meta-analysis. PLoS One. 2017 Mar 15;12(3):e0173808.

79. Larsen DA, Grisham T, Slawsky E, Narine L. An individual-level meta-analysis assessing the impact of community-level sanitation access on child stunting, anemia, and diarrhea: Evidence from DHS and MICS surveys. PLoS Negl Trop Dis. 2017 Jun 8;11(6):e0005591.

80. Garn JV, Boisson S, Willis R, Bakhtiari A, al-Khatib T, Amer K, et al. Sanitation and water supply coverage thresholds associated with active trachoma: Modeling cross-sectional data from 13 countries. PLoS Negl Trop Dis. 2018;12(1):e0006110.

81. Fuller JA, Eisenberg JN. Herd protection from drinking water, sanitation, and hygiene interventions. Am J Trop Med Hyg. 2016;95(5):1201–1210.

82. Harris M, Alzua ML, Osbert N, Pickering A. Community-Level Sanitation Coverage More Strongly Associated with Child Growth and Household Drinking Water Quality than Access to a Private Toilet in Rural Mali. Environ Sci Technol. 2017 Jun 20;51(12):7219–27.

83. Rosenboom JW, Ban R. Seeking inputs for "consensus" meeting on sanitation interventions [Internet]. Sanitation Updates. 2018 [cited 2019 Sep 9]. Available from: https://sanitationupdates.wordpress.com/2018/04/23/seeking-inputs-for-consensus-meeting-on-sanitation-interventions/

84. Humphrey JH, Mbuya MN, Nitozini R, Moulton LH, Stoltzfus RJ, Tavengwa NV, et al. Independent and combined effects of improved water, sanitation, and hygiene, and improved complementary feeding, on child stunting and anaemia in rural Zimbabwe: a cluster-randomised trial. Lancet Glob Health. 2019;7:e132-47.

85. Luby SP, Rahman M, Arnold BF, Unicomb L, Ashraf S, Winch PJ, et al. Effects of water quality, sanitation, handwashing, and nutritional interventions on

diarrhoea and child growth in rural Bangladesh: a cluster randomised controlled trial. Lancet Glob Health. 2018 Mar 1;6(3):e302–15.

86. Null C, Stewart CP, Pickering AJ, Dentz HN, Arnold BF, Arnold CD, et al. Effects of water quality, sanitation, handwashing, and nutritional interventions on diarrhoea and child growth in rural Kenya: a cluster-randomised controlled trial. Lancet Glob Health. 2018;6(3):e316–e329.

87. Acock AC. Discovering structural equation modeling using Stata. Stata Press; 2013.

88. Huda TMN, Schmidt W-P, Pickering AJ, Unicomb L, Mahmud ZH, Luby SP, et al. Effect of Neighborhood Sanitation Coverage on Fecal Contamination of the Household Environment in Rural Bangladesh. Am J Trop Med Hyg. 2019 Mar 6;100(3):717–26.

89. Cumming O, Curtis V. Implications of WASH Benefits trials for water and sanitation. Lancet Glob Health. 2018 Jun 1;6(6):e613–4.

90. Coffey D, Spears D. Implications of WASH Benefits trials for water and sanitation. Lancet Glob Health. 2018 Jun 1;6(6):e615.

91. Arnold BF, Null C, Luby SP, Colford JM. Implications of WASH Benefits trials for water and sanitation – Authors' reply. Lancet Glob Health. 2018 Jun 1;6(6):e616–7.

92. Rosenboom JW, Ban R. Sanitation and health: what do we want to know? [Internet]. Sanitation Updates. 2018 [cited 2019 Sep 9]. Available from: https://sanitationupdates.wordpress.com/2018/08/02/sanitation-and-health-what-do-we-want-to-know/

93. WHO, UNICEF. Progress on drinking water, sanitation and hygiene: 2017 update and SDG baselines. Geneva, Switzerland: WHO, UNICEF; 2017.

94. United Nations. Sustainable Development Goals [Internet]. [cited 2019 Sep 8]. Available from: http://www.un.org/sustainabledevelopment/sustainable-development-goals/

95. Hunter PR. Household water treatment in developing countries: comparing different intervention types using meta-regression. Environ Sci Technol. 2009;43(23):8991–8997.

96. Arlot S, Celisse A. A survey of cross-validation procedures for model selection. Stat Surv. 2010;4(0):40–79.

97. Stuart EA. Matching methods for causal inference: A review and a look forward. Stat Sci. 2010;25(1):1–21.

98. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Chapter 40: When does it make sense to perform a meta-analysis? In: Introduction to meta-analysis. Wiley; 2009. p. 357–64.

99. Austin CJ. Investigation of in-house water chlorination and its effectiveness for rural areas of the Gambia. [New Orleans]: Tulane University School of Public Health and Tropical Medicine; 1993.

100. Jain S, Sahanoon OK, Blanton E, Schmitz A, Wannemuehler KA, Hoekstra RM, et al. Sodium Dichloroisocyanurate Tablets for Routine Treatment of Household Drinking Water in Periurban Ghana: A Randomized Controlled Trial. Am J Trop Med Hyg. 2010 Jan 1;82(1):16–22.

101. Boisson S, Stevenson M, Shapiro L, Kumar V, Singh LP, Ward D, et al. Effect of Household-Based Drinking Water Chlorination on Diarrhoea among Children under Five in Orissa, India: A Double-Blind Randomised Placebo-Controlled Trial. PLoS Med. 2013;10(8):e1001497.

102. Kirchhoff LV, McClelland KE, Pinho MDC, Araujo JG, De Sousa MA, Guerrant RL. Feasibility and efficacy of in-home water chlorination in rural North-eastern Brazil. J Hyg (Lond). 1985;94(02):173–180.

103. Cairncross S, Hunt C, Boisson S, Bostoen K, Curtis V, Fung IC, et al. Water, sanitation and hygiene for the prevention of diarrhoea. Int J Epidemiol. 2010;39(suppl 1):i193–i205.

104. Betancourt WQ, Rose JB. Drinking water treatment processes for removal of Cryptosporidium and Giardia. Vet Parasitol. 2004 Dec 9;126(1):219–34.

105. Kotloff KL, Nataro JP, Blackwelder WC, Nasrin D, Farag TH, Panchalingam S, et al. Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. Lancet. 2013;382(9888):209–22.

106. Welton NJ, Ades AE, Carlin JB, Altman DG, Sterne JAC. Models for potentially biased evidence in meta-analysis using empirically based priors. J R Stat Soc Ser A Stat Soc. 2009;172(1):119–136.

107. Gunnarsdottir MJ, Gardarsson SM, Elliott M, Sigmundsdottir G, Bartram J. Benefits of water safety plans: microbiology, compliance, and public health. Environ Sci Technol. 2012;46(14):7782–7789.

108. Setty KE, Kayser GL, Bowling M, Enault J, Loret J-F, Serra CP, et al. Water quality, compliance, and health outcomes among utilities implementing Water Safety Plans in France and Spain. Int J Hyg Environ Health. 2017 May 1;220(3):513–30.

109. Kowall B, Stang A. Stolpersteine bei der Interpretation des populationsattributablen Risikos. Gesundheitswesen. 2018;80(02):149–153.

110. Greenland S. Concepts and pitfalls in measuring and interpreting attributable fractions, prevented fractions, and causation probabilities. Ann Epidemiol. 2015;25(3):155–161.

111. Darrow LA. Commentary: errors in estimating adjusted attributable fractions. Epidemiology. 2014;25(6):917–918.

112. Robins JM, Greenland S. Estimability and estimation of excess and etiologic fractions. Stat Med. 1989;8(7):845–859.

113. Robins J, Greenland S. Estimability and estimation of expected years of life lost due to a hazardous exposure. Stat Med. 1991;10(1):79–93.

114. Flegal KM, Graubard BI, Williamson DF. Methods of calculating deaths attributable to obesity. Am J Epidemiol. 2004;160(4):331–338.

115. Ezzati M, Vander Hoorn S, Rodgers A, Lopez AD, Mathers CD, Murray CJ, et al. Estimates of global and regional potential health gains from reducing muliple major risk factors. Lancet. 2003;362(9380):271–280.

116. Bapat M, Agarwal I. Our Needs, Our Priorities; Women and Men from the Slums in Mumbai and Pune Talk About Their Needs for Water and Sanitation. Env Urban. 2003 Jan 10;15(2):71–86.

117. Bartram J, Cairncross S. Hygiene, Sanitation, and Water: Forgotten Foundations of Health. PLoS Med. 2010 Nov 9;7(11):e1000367.

118. Vidal J. Environmental risks killing 12.6 million people, WHO study says. The Guardian [Internet]. 2016 Mar 15 [cited 2020 Jan 7]; Available from: https://www.theguardian.com/environment/2016/mar/15/environmental-risks-killing-126-million-people-who-study-says

119. Tavernise S. Environmental Factors Like Pollution Cause a Quarter of Deaths, W.H.O. Says. The New York Times [Internet]. 2016 Mar 15 [cited 2020 Jan 7]; Available from: https://www.nytimes.com/2016/03/15/health/environmental-factors-like-pollution-cause-a-quarter-of-deaths-who-says.html

120. Deutsche Welle. WHO: Environment causes one in four deaths [Internet]. DW.COM. 2016 [cited 2020 Jan 7]. Available from: https://www.dw.com/en/who-environment-causes-one-in-four-deaths/a-19117118

121. Le Monde. Près d'un quart des morts dans le monde découlent d'une cause liée à l'environnement. Le Monde.fr [Internet]. 2016 Mar 15 [cited 2020 Jan 7]; Available from: https://www.lemonde.fr/pollution/article/2016/03/15/pres-d-un-quart-des-morts-dans-le-monde-decoulent-d-une-cause-liee-a-l-environnement_4882910_1652666.html

122. Planelles M. La mala calidad del medio ambiente causa 12,6 millones de muertes al año. El País [Internet]. 2016 Mar 15 [cited 2020 Jan 7]; Available from: https://elpais.com/internacional/2016/03/14/actualidad/1457959254_712347.html

123. World Health Organization (WHO) [Internet]. 2016 [cited 2020 Jan 7]. Available from: https://www.facebook.com/WHO/photos/a.167668209945237/1089308154447900/?type=3

124. World Health Organization (WHO). 12.6 million deaths per year are attributable to unhealthy environments http://goo.gl/lVEDpa #EnvironmentalHealthpic.twitter.com/IEkihfxZ65 [Internet]. @WHO. 2016 [cited 2020 Jan 7]. Available from: https://twitter.com/WHO/status/709664500333596672

125. BBC World Service - Health Check, The Crunch Effect: Why we Should Listen as we Eat [Internet]. BBC. 2016 [cited 2020 Jan 7]. Available from: https://www.bbc.co.uk/programmes/p03nqshj

126. GHO. SDG 3.9.2 WASH deaths (Public health and environment) [Internet]. WHO. 2016 [cited 2019 Aug 5]. Available from: https://apps.who.int/gho/data/node.imr.WSH_1?lang=en

127. Ministry of Drinking Water and Sanitation. Swachh Bharat Mission - Gramin [Internet]. [cited 2020 Jan 7]. Available from: http://swachhbharatmission.gov.in/sbmcms/index.htm

128. Ministry of Housing and Urban Affairs. Swachh Bharat Urban [Internet]. [cited 2020 Jan 7]. Available from: http://swachhbharaturban.gov.in/

129. WHO. World Health Organization, WHO lauds India's commitment to accelerated sanitation coverage [Internet]. SEARO. [cited 2020 Jan 3]. Available from: http://www.searo.who.int/mediacentre/features/2018/indias-commitment-accelerated-sanitation-coverage/en/

130. Modi's Swachh Bharat could save 3 lakh lives; WHO praises accelerated sanitation coverage in India [Internet]. The Financial Express. 2018 [cited 2020 Jan 3]. Available from: https://www.financialexpress.com/economy/modis-swachh-bharat-could-save-3-lakh-lives-who-praises-accelerated-sanitation-coverage/1268670/

131. Patel New. PM Modi misquotes WHO report on Swachh Bharat Mission saving 3 lakh lives [Internet]. India Today. 2018 [cited 2020 Jan 3]. Available from: https://www.indiatoday.in/india/story/pm-modi-misquotes-who-report-on-swachh-bharat-mission-saving-3-lakh-lives-1315124-2018-08-15

132. Three lakh lives saved: What WHO said about Swachh Bharat Mission impact [Internet]. The Indian Express. 2018 [cited 2020 Jan 3]. Available from: https://indianexpress.com/article/explained/fact-check-when-modi-got-swacch-bharat-mission-impact-a-bit-wrong-5307807/

133. Farrell J, McConnell K, Brulle R. Evidence-based strategies to combat scientific misinformation. Nat Clim Change. 2019;9:191–5.

134. Schneider A, Cyrys J, Breitner S, Kraus U, Peters A. Quantifizierung von umweltbedingten Krankheitslasten aufgrund der Stickstoffdioxid-Exposition in Deutschland. Helmholtz Zentrum München, im Auftrag des Umweltbundesamts; 2018.

135. Morfeld P, Erren TC. Warum ist die „Anzahl vorzeitiger Todesfälle durch Umweltexpositionen "nicht angemessen quantifizierbar? Gesundheitswesen. 2019;81(02):144–9.

136. Plaß D, Tobollik M, Devleesschauwer B, Grill E, Hoffmann B, Hurraß J, et al. Kritik an Population Attributable Fraction bei genauerem Hinsehen nicht gerechtfertigt. Gesundheitswesen. 2019;81(5):444–7.

137. WHO. Frequently asked questions on estimations of attributable burden of disease due to a risk factor [Internet]. WHO. 2019 [cited 2019 Sep 9]. Available from: http://www.who.int/quantifying_ehimpacts/faqs/en/

138. Cumming O, Arnold BF, Ban R, Clasen T, Esteves Mills J, Freeman MC, et al. The implications of three major new trials for the effect of water, sanitation and hygiene on childhood diarrhea and stunting: a consensus statement. BMC Med. 2019 Aug 28;17(173).

139. Alsan M, Goldin C. Watersheds in infant mortality: The role of effective water and sewerage infrastructure. 2018. (NBER Working Paper Series). Report No.: 21263.

140. Cutler D, Deaton A, Lleras-Muney A. The determinants of mortality. J Econ Perspect. 2006;20(3):97–120.

141. Bell F, Millward R. Public health expenditures and mortality in England and Wales, 1870–1914. Contin Change. 1998;13(2):221–249.

142. Ercumen A, Pickering AJ, Kwong LH, Arnold BF, Parvez SM, Alam M, et al. Animal Feces Contribute to Domestic Fecal Contamination: Evidence from E. coli Measured in Water, Hands, Food, Flies, and Soil in Bangladesh. Environ Sci Technol. 2017 Aug 1;51(15):8725–34.

143. Penakalapati G, Swarthout J, Delahoy MJ, McAliley L, Wodnik B, Levy K, et al. Exposure to animal feces and human health: A systematic review and proposed research priorities. Environ Sci Technol. 2017;51(20):11537–11552.

144. Zambrano LD, Levy K, Menezes NP, Freeman MC. Human diarrhea infections associated with domestic animal husbandry: a systematic review and meta-analysis. Trans R Soc Trop Med Hyg. 2014 Jun;108(6):313–25.

145. Lipsitch M, Tchetgen ET, Cohen T. Negative Controls: A Tool for Detecting Confounding and Bias in Observational Studies. Epidemiol Camb Mass. 2010 May;21(3):383–8.

146. Reese H, Routray P, Torondel B, Sinharoy SS, Mishra S, Freeman MC, et al. Assessing longer-term effectiveness of a combined household-level piped water and sanitation intervention on child diarrhoea, acute respiratory infection, soil-transmitted helminth infection and nutritional status: a matched cohort study in rural Odisha, India. Int J Epidemiol. 2019;

147. Arnold BF, Khush RS, Ramaswamy P, London AG, Rajkumar P, Ramaprabha P, et al. Causal inference methods to study nonrandomized, preexisting development interventions. Proc Natl Acad Sci. 2010;107(52):22605–22610.

148. Arnold B, Arana B, Mäusezahl D, Hubbard A, Colford JM. Evaluation of a pre-existing, 3-year household water treatment and handwashing intervention in rural Guatemala. Int J Epidemiol. 2009;38(6):1651–1661.

149. Geere J-A, Hunter P. The association of water carriage, water supply and sanitation usage with maternal and child health. A combined analysis of 49 Multiple Indicator Cluster Surveys from 41 countries. Int J Hyg Environ Health. 2019;in press.

150. Flegal KM. Bias in calculation of attributable fractions using relative risks from non-smokers only. Epidemiology. 2014;25(6):913.

151. Benichou J. A review of adjusted estimators of attributable risk. Stat Methods Med Res. 2001;10(3):195–216.

152. Salomon JA, Haagsma JA, Davis A, de Noordhout CM, Polinder S, Havelaar AH, et al. Disability weights for the Global Burden of Disease 2013 study. Lancet Glob Health. 2015;3(11):e712–e723.

Appendix 1

A1.1: The JMP service ladders for drinking water, sanitation and hygiene

Definitions are taken verbatim from the JMP website (11).

Drinking water

Safely managed drinking water: Drinking water from an improved water source which is located on premises, available when needed and free from faecal and priority chemical contamination.

Basic drinking water: Drinking water from an improved source, provided collection time is not more than 30 minutes for a roundtrip including queuing.

Limited drinking water*: Drinking water from an improved source for which collection time exceeds 30 minutes for a roundtrip including queuing.

Unimproved drinking water: Drinking water from an unprotected dug well or unprotected spring, surface drinking water which is water from a river, dam, lake, pond, stream, canal or irrigation canal.

Improved drinking water sources are those that have the potential to deliver safe water by nature of their design and construction, and include: piped water, boreholes or tubewells, protected dug wells, protected springs, rainwater, and packaged or delivered water. (13)

Sanitation

Safely managed sanitation: Use of improved facilities which are not shared with other households and where excreta are safely disposed in situ or transported and treated off-site.

Basic sanitation: Use of improved facilities which are not shared with other households.

Limited sanitation*: Use of improved facilities shared between two or more households.

Unimproved sanitation: Use of pit latrines without a slab or platform, hanging latrines or bucket latrines, and open defecation which is the disposal of human faeces in fields, forests, bushes, open bodies of water, beaches and other open spaces or with solid waste.

Improved sanitation facilities are those designed to hygienically separate excreta from human contact, and include: flush/pour flush to piped sewer system, septic tanks or pit latrines; ventilated improved pit latrines, composting toilets or pit latrines with slabs. (14)

Hygiene

Basic handwashing facility: Availability of a handwashing facility on premises with soap and water.

Limited handwashing facility: Availability of a handwashing facility on premises without soap and water.

No facility: No handwashing facility on premises.

Handwashing facilities may be fixed or mobile and include a sink with tap water, buckets with taps, tippy-taps, and jugs or basins designated for handwashing. Soap includes bar soap, liquid soap, powder detergent, and soapy water but does not include ash, soil, sand or other handwashing agents.

* In this work, limited drinking water and limited sanitation are usually grouped under unimproved drinking water and sanitation.

A1.2: Different PAF formulas

Different formulas with different properties are available for calculating the PAF (Table A1).

Table A1: PAF formulas and their properties

PAF formula	properties	
$\text{PAF} = \frac{(R_e - R_o)}{R_e}$	not valid when confounding is present	(A1)
$\text{PAF} = \frac{p_e \cdot (RR - 1)}{1 + p_e \cdot (RR - 1)}$	not valid when confounding is present	(A2)
$\text{PAF} = \frac{\sum_{j=1}^{n} p_j \cdot (RR_j - 1)}{\sum_{j=1}^{n} 1 + p_j \cdot (RR_j - 1)}$	same as Equation A2 but for various exposure levels	(A3)
$\text{PAF} = \frac{p_c \cdot (RR_{adj} - 1)}{RR_{adj}}$	valid when confounding is present	(A4)
$\text{PAF} = \sum_{i=1}^{z} W_i \frac{p_i \cdot (RR_i - 1)}{1 + p_i \cdot (RR_i - 1)}$	valid when confounding and effect modification are present	(A5)

where R_e is the risk of disease in the total population, R_o is the risk of disease in the unexposed population, p_e is the proportion of the population exposed, RR is the causal unadjusted relative risk associated with exposure, p_j is the proportion of the exposed population at exposure level j, RR_j is the unadjusted relative risk for exposure level j (relative to the baseline category), n is the number of exposure level, p_c is the proportion of cases exposed, RR_{adj} is the causal adjusted relative risk associated with exposure, p_i is the proportion of the population in stratum i who are exposed (adjustment factor form i joint strata), W_i is the proportion of cases among all cases in stratum i and z is the total number of strata.

Formulas A1, A2 and A5 are mathematically equivalent (25). Equation A3 is an extension of Equation A2 and includes more than two exposure levels. The first three formulas (Equations A1-A3) are not valid when there is confounding in the exposure-disease association and should only be used with unadjusted relative risks (22,111). The PAF calculated using Equation A4 is valid when relative risks needed adjustments for confounding factors and requires the proportion of cases exposed (111,150). Finally, PAFs calculated with Equation A5 remain valid when confounding and effect modification are present and is based on a weighted-sum of stratum-specific attributable fractions (111,151). Strata are defined by one or more adjustment factors and weighted by the proportion of cases in each stratum among all cases. This equation requires detailed information, namely exposure and disease prevalence and exposure-response relationships for each stratum. Further difficulties arise if adjustment factors are not categorical or if multiple adjustment factors lead to sparse data in the different strata (111). Note that this equation can also accommodate several exposure levels as in Equation A3.

A1.3: Definition and calculation of DALYs

DALYs are defined and calculated as:

$$\text{DALYs} = \text{YLL} + \text{YLD} \tag{A6}$$

where YLL are years of life lost due to premature mortality and YLD are years of life lived with disability due to disease incidence (8,23). YLL and YLD are calculated as follows:

$$\text{YLL} = \sum \text{N}_\text{i} \cdot \text{L}_\text{i} \tag{A7}$$

where N_i is the number of deaths from the specific cause in age group i and L_i is the standard remaining life expectancy at death from the cause of interest for age group i.

$$\text{YLD} = \text{I} \cdot \text{DW} \cdot \text{L} \tag{A8}$$

where I is the number of incident cases, DW is a disability weight and L is the mean duration of disease (8,23). Disability weights have values between 0 and 1 where 0 equals a state of full health and 1 equals death. They are supposed to indicate the amount of ill health associated with a single given health state (24). Disability weights are generated from surveys in different countries in which participants are presented two hypothetical individuals with different health states for judging which of the two persons they consider healthier (152).

A1.4: List of publications

Publications are ordered chronologically starting with the most recent. Those publications that are key papers for this PhD thesis are marked with an asterix (*). These publications are discussed in detail in sections 2.2 to 2.12 of the critical analysis. Note: In sections 2.2 to 2.12 publications are ordered differently and starting with the most dating-back publication to show the development of the presented research.

Journal articles

1. Cumming O, Arnold B, Ban R, Clasen T, Guiteras R, Gordon B, Howard G, Pickering A, Esteves Mills J, Hunter P, Johnston R, Prendergast A, Prüss-Ustün A, Rosenboom JW, Freeman M, Spears D, Sundberg S, **Wolf J**, Null C, Luby S, Humphrey J and Colford J (2019) The Implications of Three Major New Trials for the Effect of Water, Sanitation and Hygiene on Childhood Diarrhoea and Stunting - A Consensus Statement. BMC Med, doi: 10.1186/s12916-019-1410-x

2. * Prüss-Ustün A, **Wolf J**, Bartram J, Clasen T, Cumming O, Freeman MC, Gordon B, Hunter PR, Medlicott K, Johnston R (2019) Burden of disease from inadequate water, sanitation and hygiene for selected adverse health outcomes: an updated analysis with a focus on low- and middle-income countries, Int J Hyg Environ Health, doi: 10.1016/j.ijheh.2019.05.004

3. *** Wolf J**, Johnston R, Hunter PR, Gordon B, Medlicott K, Prüss-Ustün A (2018) A Faecal Contamination Index for interpreting heterogeneous diarrhoea impacts of water, sanitation and hygiene interventions and overall, regional and country estimates of community sanitation coverage with a focus on low- and middle-income countries. Int J Hyg Environ Health. doi: 10.1016/j.ijheh.2018.11.005.

4. *** Wolf J**, Johnston R, Freeman MC, Ram PK, Slaymaker T, Laurenz E, Prüss-Ustün A (2018) Handwashing with soap after potential faecal contact: Global, regional and country estimates. Int J Epidemiol, doi: 10.1093/ije/dyy253.

5. *** Wolf J**, Hunter PR, Freeman MC, Cumming O, Clasen T, Bartram J, Higgins JPT, Johnston R, Medlicott K, Boisson S, Prüss-Ustün A. (2018) Impact of

drinking water, sanitation and handwashing with soap on childhood diarrhoeal disease: updated meta-analysis and meta-regression. Trop Med Int Health, Volume 23, Issue 5, March 2018 doi: 10.1111/tmi.13051.

6. *** Wolf J**, Mäusezahl D, Verastegui H, Hartinger SM. (2017) Adoption of Clean Cookstoves after Improved Solid Fuel Stove Programme Exposure: A Cross-Sectional Study in Three Peruvian Andean Regions. Int J Environ Res Public Health. 2017 Jul 8;14(7). pii: E745. doi: 10.3390/ijerph14070745.

7. * Hartinger SM, Lanata CF, Hattendorf J, Verastegui H, Gil AI, **Wolf J**, Mäusezahl D. (2016) Improving household air, drinking water and hygiene in rural Peru: a community-randomized–controlled trial of an integrated environmental home-based intervention package to improve child health. Int J Epidemiol, doi:10.1093/ije/dyw242

8. * Prüss-Ustün A, **Wolf J**, Corvalán C, Neville T, Bos R, Neira M. (2016) Diseases due to unhealthy environments: an updated estimate of the global burden of disease attributable to environmental determinants of health. J Public Health, doi: 10.1093/pubmed/fdw085

9. Hartinger SM, Lanata CF, Hattendorf J, **Wolf J**, Gil AI, Ortiz Orbando M, Noblega M, Verastegui H, Mäusezahl D. (2016) Impact of a child stimulation intervention on early child development in rural Peru: A cluster randomised trial using a reciprocal control design. J Epidemiol Community Health, doi:10.1136/jech-2015-206536

10. *** Wolf J**, Prüss-Ustün A, Cumming O, Bartram J, Bonjour S, Cairncross S, Clasen T, Colford JM Jr, Curtis V, De France J, Fewtrell L, Freeman MC, Gordon B, Hunter PR, Jeandron A, Johnston RB, Mäusezahl D, Mathers C, Neira M, Higgins JP. (2014) Assessing the impact of drinking water and sanitation on diarrhoeal disease in low- and middle-income settings: systematic review and meta-regression. Trop Med Int Health, Volume 19, Issue 8, pages 928–942, August 2014 doi: 10.1111/tmi.12331

11. * Prüss-Ustün A, Bartram J, Clasen T, Colford JM Jr, Cumming O, Curtis V, Bonjour S, Dangour AD, De France J, Fewtrell L, Freeman MC, Gordon B, Hunter PR, Johnston RB, Mathers C, Mäusezahl D, Medlicott K, Neira M, Stocks M, **Wolf J**, Cairncross S. (2014) Burden of disease from inadequate

water, sanitation and hygiene in low- and middle-income settings: a retrospective analysis of data from 145 countries. Trop Med Int Health, Volume 19, Issue 8, pages 894–905, August 2014. doi: 10.1111/tmi.12329.

12. * Freeman MC, Stocks ME, Cumming O, Jeandron A, Higgins JP, **Wolf J**, Prüss-Ustün A, Bonjour S, Hunter PR, Fewtrell L, Curtis V. (2014) Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. Trop Med Int Health, Volume 19, Issue 8, pages 906–916, August 2014. doi: 10.1111/tmi.12339.

13. Prüss-Ustün A, **Wolf J**, Driscoll T, Degenhardt L, Neira M, Calleja JM. (2013) HIV Due to Female Sex Work: Regional and Global Estimates. PLoS ONE 23;8(5):e63476.

14. Bonjour S, Adair-Rohani H, **Wolf J**, Bruce NG, Mehta S, Prüss-Ustün A, Lahiff M, Rehfuess EA, Mishra V, Smith KR. (2013) Solid Fuel Use for Household Cooking: Country and Regional Estimates for 1980-2010. Environ Health Perspect. 2013 May 3.

15. * **Wolf J**, Bonjour S, Prüss-Ustün A (2013) An exploration of multilevel modelling for estimating access to drinking-water and sanitation. J Water Health. 2013 Mar;11(1):64-77.

16. **Wolf J**, Armstrong B (2012) The Association of Season and Temperature with Adverse Pregnancy Outcome in Two German States, a Time-Series Analysis. PLoS ONE 7(7): e40228. doi:10.1371/journal.pone.0040228

Reports and other grey literature

1. Plaß D, Tobollik M, Devleesschauwer B, Grill E, Hoffmann B, Hurraß J, Künzli N, Peters A, Rothenbacher D, Schneider A, Wichmann HE, Wintermeyer D, **Wolf J**, Zeeb H, Straff W. (2019) Kritik an Population Attributable Fraction bei genauerem Hinsehen nicht gerechtfertigt. Gesundheitswesen. 2019;81(5):444–7. doi: 10.1055/a-0915-1215

2. **Wolf J**, Prüss-Ustün A, Ivanov I, Mugdal S, Corvalán C, Bos R, Neira M. (2018) Preventing disease through a healthier and safer workplace. ISBN: 978-92-4-151377-7; World Health Organization, Geneva; Available from:

http://apps.who.int/iris/bitstream/handle/10665/272980/97892415137
77-eng.pdf?ua=1

3. World Health Organization (2017) Don't pollute my future! The impact of the environment on children's health. World Health Organization, Geneva. http://apps.who.int/iris/bitstream/10665/254678/1/WHO-FWC-IHE-17.01-eng.pdf, assessed 09.01.2018

4. International Programme on Chemical Safety (2016) The Public Health Impacts of Chemicals: Knowns and Unknowns. World Health Organization, Geneva.
apps.who.int/iris/bitstream/10665/206553/1/WHO_FWC_PHE_EPE_16.01_eng.pdf, assessed 08.07.2016

5. Prüss-Ustün A, **Wolf J**, Corvalán C, Bos R, Neira M. (2016) Preventing Disease through Healthy Environments: A global assessment of the burden of disease from environmental risks. ISBN 978 92 4 156519 6; World Health Organization, Geneva.

6. Wagner-Ahlfs C, **Wolf J** (2010): Miltefosin – Eine Fallstudie, wie öffentliche Erfindungen für arme Länder verfügbar gemacht werden können. Chemotherapie Journal 2010;19:63-9

7. Thaler J, Neugebauer J, **Wolf J**, Dakouré-Ouedraogo M, Köhler H, Wessel L, Zanré Y, Wacker J (2006): Auswirkungen einer prophylaktischen Gabe von Riboflavin an Schwangere auf die Häufigkeit der Malaria: Ergebnisse einer prospektiven randomisierten Studie. Geburtshilfe und Frauenheilkunde 2006;66:383-390

Appendix 2

A2.1: Publications included in this critical analysis

The following eleven peer-reviewed articles are included as main research in this critical analysis. They are included chronologically and in the same order as listed in sections 2.2-2.12.

© World Health Organization 2013
Journal of Water and Health | 11.1 | 2013

An exploration of multilevel modeling for estimating access to drinking-water and sanitation

Jennyfer Wolf, Sophie Bonjour and Annette Prüss-Ustün

ABSTRACT

Monitoring progress towards the targets for access to safe drinking-water and sanitation under the Millennium Development Goals (MDG) requires reliable estimates and indicators. We analyzed trends and reviewed current indicators used for those targets. We developed continuous time series for 1990 to 2015 for access to improved drinking-water sources and improved sanitation facilities by country using multilevel modeling (MLM). We show that MLM is a reliable and transparent tool with many advantages over alternative approaches to estimate access to facilities. Using current indicators, the MDG target for water would be met, but the target for sanitation missed considerably. The number of people without access to such services is still increasing in certain regions. Striking differences persist between urban and rural areas. Consideration of water quality and different classification of shared sanitation facilities would, however, alter estimates considerably. To achieve improved monitoring we propose: (1) considering the use of MLM as an alternative for estimating access to safe drinking-water and sanitation; (2) completing regular assessments of water quality and supporting the development of national regulatory frameworks as part of capacity development; (3) evaluating health impacts of shared sanitation; (4) using a more equitable presentation of countries' performances in providing improved services.

Key words | indicator, Millennium Development Goals, modeling, monitoring, sanitation, water

Jennyfer Wolf (corresponding author)
Sophie Bonjour
Annette Prüss-Ustün
Department for Public Health and Environment,
Evidence and Policy on Environmental Health,
World Health Organization,
20 Avenue Appia, CH-1211,
Geneva 27,
Switzerland
E-mail: *wolfj@who.int*

INTRODUCTION

Providing universal access to safe water and sanitation services could have prevented 1.9 million deaths and reduced global child mortality by 15% in 2004 (WHO 2009). Access to safe water and improved sanitation significantly reduces diarrheal diseases (Waddington *et al.* 2009; Cairncross *et al.* 2010) and other illnesses such as intestinal helminth infections, schistosomiasis and trachoma (Esrey *et al.* 1990; Ziegelbauer *et al.* 2012). One Millennium Development Goal (MDG) target is to halve, by 2015, the proportion of people without sustainable access to safe water and basic sanitation (United Nations 2012). However, in 2010 an estimated 2.5 billion people still lacked access to improved sanitation and 780 million to an improved water source (JMP 2012a). The term 'water' throughout this document refers to water for drinking, cooking and personal hygiene.

For future priority setting, we need reliable, reproducible, statistically sound estimates for country, regional and global access to safe water and sanitation. Since 1990, the World Health Organization (WHO)/United Nations Children's Fund (UNICEF) Joint Monitoring Programme (JMP) examines progress and trends in this connection (JMP 2010a). With the end of the MDG period approaching and the agenda for the post-MDG era under consideration, it is important to consider refinements of monitoring and evaluation. Current approaches are mostly limited to linear trends (JMP 2012a). Additionally, there has been debate whether estimates could be improved by considering water quality (Bain *et al.* 2012; JMP 2012a; Onda *et al.* 2012) and on the possible reclassification of certain sanitation services (JMP 2010a). Therefore we developed estimates for access to

doi: 10.2166/wh.2012.107

improved water sources and improved sanitation facilities using advanced modeling methods and reconsidered the definition of the access indicators depending on safety for health. The JMP task force on methods recommended that the JMP method be reviewed (JMP 2010b). The content of this paper may contribute to these discussions.

This article presents trends in access to safe water and sanitation over 25 years using available survey information and a sound modeling approach. Furthermore, we discuss the inclusion of water quality, different ways to consider shared sanitation and the potential impact such changes would have. Finally, we propose an alternative indicator to monitor the MDG targets which would more equitably represent the performance of countries.

METHODS

Data compilation and classification

We used the JMP database on access to improved water sources and improved sanitation facilities. It contains datasets collected through nationally representative household surveys and censuses (JMP 2010a). The data represent percentages of households using different improved sources/ facilities, disaggregated by urban and rural population. For the national level (urban and rural combined), nearly 1,100 data points for both water and sanitation were included. Detailed information about data sources and classification of a facility as improved or unimproved can be found in the JMP reports (JMP 2010a, 2012a). The survey estimates from the JMP datasets can be found on the JMP website (www.wssinfo.org/documents-links/documents/?tx_displaycontroller[type]=country_files). The number of surveys available ranged between zero and 30 with a mean of six per country. Out of 145 low and middle income countries (LMIC), 140 (for water) and 132 (for sanitation) are covered by at least one survey. A table with number of observations by time period and region is available in the Supplemental Material at www.who.int/quantifying_ehimpacts/en/index.html.

Prior to considering a dataset for estimation, the JMP examines every response category of the relevant questions of every survey to ensure they match those used for reporting purposes. In cases of discrepancies with national figures, usually attributable to the categories used, JMP engages with the national monitoring authorities to identify problems and seek solutions. To date, JMP have had such discussions in over 40 countries. Most of the discrepancies arise from differences in definitions of improved access, especially in the older datasets. One example consists in an 'uncovered' latrine type in China which was classified as 'unimproved', but which would fall under the 'improved' JMP classification – the seat was indeed uncovered, but the pit itself – which matters for the JMP definition – was actually covered. Recent discussions with Chinese survey authorities revealed the reasons for these differences. Adjustments not only changed Chinese sanitation coverage but had a significant impact on global figures.

In general, JMP harmonization exercises led to internationally adopted and harmonized core questions and response categories and hence to greater data comparability and accuracy of estimates. Additionally, recent surveys provide more disaggregation, and therefore less ambiguity. Several initiatives are contributing to the 'reconciliation' between past and recent datasets, such as the Accelerated Data Programme of the International Household Survey Network, which was established to improve the coordination and effectiveness of surveys (International Household Survey Network 2012). However, harmonization between historical and recent data remains a challenge and not always completely achievable.

Modeling approach

Criteria for model selection included: (a) closeness of modeled estimates to the survey points without following all within-country variability which might be partly due to systematic and non-systematic error; (b) transparency, simplicity and reproducibility of the model; and (c) ability to estimate for countries with little or no information. We therefore applied a linear two-level model with a logit-transformation of the dependent variable (access to improved water sources or improved sanitation), a cubic spline transformation of the main predictor (time), region (21-Global Burden of Disease (GBD)-Regions (Harvard University *et al.* 2009)) as a covariate and a random intercept and slope by country.

Multilevel modeling (MLM) creates continuous estimates over the specified time period. It considers the hierarchical structure of the whole dataset: survey points are correlated within countries which are assumed to be a random sample from a bigger population. Instead of calculating an intercept and regression slope separately for each country as is currently done in JMP, the multilevel model estimates an average intercept and an average slope with residual variances across countries. In practice, countries are assumed to follow the regional mean in case the trend information for the country is scarce or absent. When there is reliable information for a specific country (i.e. many data points and little within-country variability) the country curve will closely follow the country survey points, whereas for unreliable information (i.e. few country data points or high within-country variability) the estimates will still be close to the survey points but the trend will tend to follow the overall mean (Goldstein 2010; Hox 2010; Steele 2011).

We applied a two-level model allowing a random intercept and slope by country. The model was applied separately to the total, the rural and the urban population. Estimates were derived using maximum likelihood. The dependent variable was logit-transformed to restrict estimates and confidence intervals between zero and one (or 100%) and to use the specific shape of the logit curve with a slower increase when access approaches 100%. The logit transformation leads to increasingly asymmetric and narrow confidence intervals close to zero or 100% (De Onis *et al.* 2004). Likelihood ratio test and the Akaike Information Criterion (AIC) were used to decide the inclusion of random and fixed effects. We assumed unstructured covariance between the random intercept and random slope. Random effects and the dependent variable (after transformation) followed normal distributions (Quené & van den Bergh 2004). A cubic spline transformation of time (the main predictor) was chosen on inspection of the curves and to accommodate additional flexibility for future trends (see additional explanations in the Supplemental Material at www.who.int/quantifying_ehimpacts/en/index.html). Knots, which determine the flexibility of the curve, were set after 25, 50 and 75% of data points. Sensitivity analyses were performed with different transformations of the dependent and independent variable (different splines and random/fixed effects, non-logit transformation) and the choice of the final model was based on likelihood ratio tests, the AIC and inspection of the curves. For countries with no information, the regional mean trend was taken as the best estimate.

Confidence intervals on the national level were calculated as the square root of the combined fixed- and random-level variances, which were assumed to be independent. The regional estimates in Tables 1–3 were calculated as the population weighted average of the country estimates. The global estimate was calculated accordingly as the population weighted average of the regional estimates. Confidence intervals for regional and global estimates were calculated using regional and global standard errors derived as the square root of the weighted country variances. The country variances on the natural scale were estimated from the country logit variances using the delta method, which has been applied before and described in detail by De Onis *et al.* (2004). To calculate population numbers we used the population figures from the United Nations Population Division (2012).

We present estimates for WHO regions (Sub-Saharan Africa, the Americas, Eastern Mediterranean, Europe, South-East Asia, and Western Pacific – with high income countries (HIC) grouped separately (WHO 2012)) and, furthermore, disaggregated in urban and rural areas (Tables 1 and 2). For all analyses discussed in this paper, Equatorial Guinea was not considered a high income country but grouped with other Sub-Saharan African countries. All analyses were performed with Stata 12 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp. LP).

Water quality

Not all water sources that are classified as improved provide water with a quality that complies with WHO drinking water quality guidelines (WHO 2011) or are safe for health. Hence, the currently used MDG estimates should be corrected for access to safe water. Between 2004 and 2007, the JMP conducted nationally representative and comparable water quality tests in five pilot countries, the WHO/UNICEF Rapid Assessments of Drinking Water Quality (RADWQ) (JMP 2012b). These assessments covered Ethiopia, Jordan, Nicaragua, Nigeria, and Tajikistan, and tested water quality of different technologies for microbial and

Table 1 | Percentage of population without access to improved water sources, by region

		1990		2010		2015	
Region[a]		%	95% CI	%	95% CI	%	95% CI
Low and middle income countries							
Sub-Saharan Africa	Total	51.9	46.0, 57.8	35.9	29.7, 42.1	32.2	25.4, 39.0
	Urban	16.7		14.5		14.4	
	Rural	65.9		49.8		45.9	
Americas	Total	14.4	6.0, 22.8	5.8	2.8, 8.8	4.7	2.3, 7.1
	Urban	5.3		2.5		2.1	
	Rural	36.9		18.7		15.8	
Eastern Mediterranean	Total	21.5	14.7, 28.3	15.0	10.4, 19.6	13.7	9.0, 18.4
	Urban	7.4		6.2		6.3	
	Rural	31.4		22.1		20.1	
Europe	Total	10.5	6.2, 14.8	4.4	2.5, 6.3	3.6	1.9, 5.3
	Urban	2.9		1.1		0.9	
	Rural	22.5		9.9		8.4	
South-East Asia	Total	26.0	7.2, 44.8	11.9	2.2, 21.6	9.8	1.6, 18.0
	Urban	9.3		5.4		4.8	
	Rural	32.4		14.5		12.0	
Western Pacific	Total	32.7	0.1, 78.6	9.5	1.6, 40.9	6.8	1.1, 32.3
	Urban	4.1		1.7		1.4	
	Rural	44.4		16.8		12.9	
High income countries	Total	1.3	0.4, 4.1	0.5	0.2, 1.4	0.4	0.1, 1.2
	Urban	0.4		0.1		0.1	
	Rural	4.3		1.4		1.1	
World	Total	23.3	11.2, 35.4	11.8	7.2, 16.4	10.1	6.5, 13.7
	Urban	4.9		3.5		3.4	
	Rural	37.3		20.1		17.7	

[a]Grouped according to WHO regions and income category (WHO 2012).

chemical contamination for one point in time. Thermotolerant coliform bacteria were indicators for microbial contamination; fluoride, arsenic and nitrate were indicators for chemical contamination.

We also used similar assessments performed in China and India. In the Chinese assessment 1,604 and in the Indian 11,757 water sources were tested. Chinese RADWQ, however, covered one region only and tested total rather than thermotolerant coliforms. The Indian assessment was not conducted as an official RADWQ but followed the same methodology. It examined compliance to BIS 10500 (Bureau of Indian Standards 2005), which is based on WHO and national guidelines on drinking water quality. We only used the value for microbial water quality from the Indian RADWQ as chemical water quality testing was not done for arsenic. A systematic literature search in Medline and the internet did not yield any additional significant country representative data on water quality at point of use for low income countries. The total information on water quality, therefore, does not exceed one or two country representative surveys per large geographical region.

We compiled water quality estimates for piped to the household and non-piped improved sources from the above described assessments. We then extrapolated these water quality estimates from the respective countries to other countries in the same region (WHO region). We estimated piped water using MLM (see Supplemental material for details, available online at http://www.iwaponline.com/jwh/011/107.pdf) and non-piped improved sources as the difference between total improved and piped sources by country. We then multiplied the respective water quality proportions with those national estimates on piped and non-piped sources to estimate the population proportion without access to safe water in 2010. Water quality from unimproved

Table 2 | Percentage of population without access to improved sanitation, by region

		1990		2010		2015	
Region[a]		%	95% CI	%	95% CI	%	95% CI
Low and middle income countries							
Sub-Saharan Africa	Total	73.3	69.3, 77.3	66.1	61.6, 70.7	64.0	57.2, 70.8
	Urban	56.6		54.9		55.1	
	Rural	80.4		74.2		70.8	
Americas	Total	32.6	16.3, 48.9	21.1	8.9, 33.3	19.3	7.9, 30.7
	Urban	20.7		15.8		15.2	
	Rural	62.4		41.0		36.6	
Eastern Mediterranean	Total	51.3	42.0, 60.6	35.4	24.8, 46.0	32.9	22.0, 43.8
	Urban	23.1		18.1		18.0	
	Rural	70.3		49.6		44.7	
Europe	Total	19.5	10.8, 28.2	16.6	8.2, 25.0	16.4	7.4, 25.4
	Urban	13.5		13.0		13.1	
	Rural	31.0		22.4		21.1	
South-East Asia	Total	74.8	62.0, 87.6	56.2	35.7, 76.7	51.7	29.7, 73.7
	Urban	48.6		35.8		33.7	
	Rural	84.5		66.1		59.8	
Western Pacific	Total	67.4	28.9, 91.3	34.1	7.8, 76.0	27.1	5.6, 70.0
	Urban	45.2		24.6		20.7	
	Rural	76.9		41.8		33.3	
High income countries	Total	1.5	0.7, 3.0	0.6	0.3, 1.3	0.5	0.2, 1.2
	Urban	0.5		0.2		0.2	
	Rural	3.5		1.4		1.2	
World	Total	50.4	40.8, 60.0	36.5	25.6, 47.4	33.6	23.4, 43.8
	Urban	24.5		20.8		20.2	
	Rural	70.1		52.4		47.6	

[a]Grouped according to WHO regions and income category (WHO 2012).

sources was considered as 100% contaminated and water sources in HIC were assumed to be 100% safe.

Shared sanitation

Sanitation shared between households and public sanitation are on the increase in developing countries, but the boundaries between the two remain nebulous. Generally, shared facilities use improved technology. However, the JMP considers every shared sanitation technology as unimproved, given uncertainty about actual use, hygiene and safety for health.

The JMP adjusts for shared sanitation in its final estimates for access to improved sanitation by subtracting the mean over available survey estimates for shared sanitation use individually by country. However, this approach is currently not homogeneous, as for 34 LMIC no data on shared sanitation use are available, in which case no value will be subtracted. Therefore, JMP final estimates cannot be compared across countries, as the final value for access to improved sanitation sometimes includes and sometimes excludes shared sanitation facilities.

For our final estimates (as presented in Tables 1–3) we continued using the JMP classification and considered all shared sanitation as unimproved. We estimated shared sanitation use with a two level MLM for LMIC (see Supplemental material for additional information, available online at http://www.iwaponline.com/jwh/011/107.pdf).

Table 3 | Total population without access to improved water sources or improved sanitation, by region

Region[a]		1990 *n* (in million)	2010 *n* (in million)	2015 *n* (in million)
Low and middle income countries				
Sub-Saharan Africa	Water	263	300	304
	Sanitation	371	553	604
Americas	Water	63	34	29
	Sanitation	142	123	119
Eastern Mediterranean	Water	77	83	82
	Sanitation	183	194	198
Europe	Water	41	18	15
	Sanitation	77	67	67
South-East Asia	Water	343	215	187
	Sanitation	985	1,017	994
Western Pacific	Water	430	151	111
	Sanitation	886	540	442
High income countries	Water	13	5	4
	Sanitation	14	7	6
World	Water	1,229	806	733
	Sanitation	2,658	2,501	2,429

[a]Grouped according to WHO regions and income category (WHO 2012).

For shared sanitation use, only 192 country, 229 rural and 233 urban survey estimates were available. The regional mean was taken for LMIC with no information. For HIC, the proportion of shared sanitation use was assumed to be zero unless survey estimates were available for those countries, in which case their mean was extrapolated to the whole time period. Such estimated values for shared sanitation use were then deducted from the original survey points which indicate the use of improved shared and unshared facilities. The multilevel model was run on these estimates (survey points minus estimates for shared sanitation). For comparison, we subsequently recalculated global figures while considering shared sanitation of an improved technology as improved.

RESULTS

The complete time series (1990–2015) for each country is available at www.who.int/quantifying_ehimpacts/en/index.html. This site also contains additional information (number of surveys per time period and region, model equations, model evaluation, etc.) under 'Supplemental material'.

Country, regional and global trends

Complete data series between 1990 and 2015 for access to improved water sources and sanitation were generated for 193 WHO Member States. We estimate that, globally, the proportion of people without access to an improved water source will be reduced from 23% in 1990 to 10% in 2015. The number of unserved people, however, will be reduced by only 40%. Sub-Saharan Africa and the Eastern Mediterranean region will not halve their proportion of the unserved population. Furthermore, the number of people without access to an improved water source in these two regions is projected to increase by an additional 46 million people (Tables 1 and 3).

The global proportion of people without access to improved sanitation will be reduced from 50% in 1990 to 34% in 2015. The number of unserved people will decline only by little more than 200 million. If we were to apply the MDG target to regions, only Western Pacific would achieve the sanitation target by 2015 (Tables 2 and 3).

Figures 1 and 2 show the modeled global and regional trend in access to improved water sources and sanitation facilities between 1990 and 2015. The diamonds on the

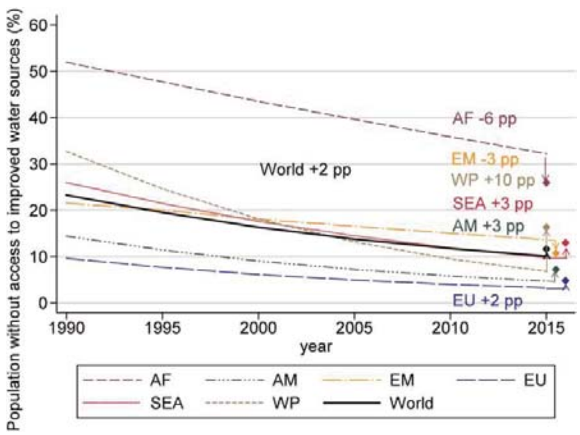


Figure 1 | Regional and global development towards the MDG water target. pp: percentage points, AF: Sub-Saharan Africa, AM: Americas, EM: Eastern Mediterranean, EU: Europe, SEA: South-East Asia, WP: Western Pacific, low and middle income countries only, world line includes high income countries. Diamond: MDG-target (if extrapolated to regions), numbers (pp): distance from MDG-target.

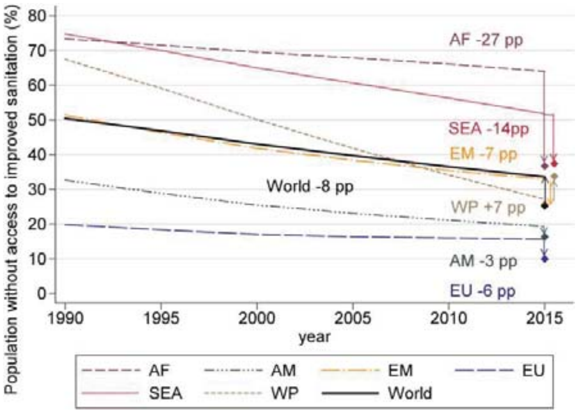


Figure 2 | Regional and global development towards the MDG sanitation target. pp: percentage points, AF: Sub-Saharan Africa, AM: Americas, EM: Eastern Mediterranean, EU: Europe, SEA: South-East Asia, WP: Western Pacific, low and middle income countries only, world line includes high income countries. Diamond: MDG-target (if extrapolated to regions), numbers (pp): distance from MDG-target.

Table 4 | Assumed regional microbial and overall compliance percentages (LMIC only)

Region[a]	Microbial compliance[b] Piped (%)	Microbial compliance[b] Other improved (%)	Overall compliance[c] Piped (%)	Overall compliance[c] Other improved (%)
Sub-Saharan Africa	83.1	67.2	78.9	63.2
Americas	89.9	34.0	89.0[d]	28.6[d]
Eastern Mediterranean	99.9	100[e]	97.8	100[e]
Europe	88.6	82.0	88.2	82.0
South-East Asia[f]	43.0	56.7	43.0[e]	56.7[e]
Western Pacific	99.0	53.7	98.0[d]	24.2[d]

[a]Grouped according to WHO regions (WHO 2012).
[b]Indicator: thermotolerant *Escherichia coli* (China: total coliforms).
[c]Indicators: thermotolerant *E. coli* (China: total coliforms), arsenic, nitrate, fluoride.
[d]Overall compliance not recorded, calculated assuming independence of individual estimates.
[e]Chemical compliance did not include arsenic and therefore overall compliance was not calculated.
[f]Compliance to BIS 10500 (Bureau of Indian Standards 2005).

right of the figure represent the MDG target globally and extrapolated to the region. The percentage points in the two figures indicate the difference between the MDG and the actual achievement; a minus indicates an estimated lagging behind the goal. Sub-Saharan Africa, for example, is estimated to miss the target of halving its population without access to improved water sources in 2015 by around six percentage points.

Access to services is consistently higher for urban compared to rural areas. However, the decrease in the proportion of the urban population without access to improved services between 1990 and 2015 was slower compared to the rural population (Tables 1 and 2). The total number of the urban population without access will rise globally between 1990 and 2015 from 109 to 130 million (access to an improved water source) and from 548 million to 765 million (access to improved sanitation).

Taking water quality into account

After adjusting our estimates with summary microbial and overall water quality (Table 4), calculated as described above, the proportion of the world's population without access to safe water in 2015 rose from 12 to 30% for microbiologically unsafe water and to 33% for overall unsafe water (Table 5).

Differing classifications of shared sanitation

Our final estimates on access to improved sanitation in Tables 2 and 3 and Figure 2 do not include shared facilities because we classified all shared sanitation as unimproved and deducted modeled estimates of shared sanitation use for each country from the original survey points. However, because of the ongoing controversy about the actual impact on health of shared facilities (see also Discussion section) we recalculated our estimates to show the approximate impact on results a different classification of shared sanitation might have. When all shared sanitation facilities of an improved technology were classified as 'improved', only 23% of the world population would be without access in 2015 compared to 34% with the current classification. Furthermore, the proportion of the population without access to improved sanitation would nearly halve between 1990 and 2015 (Table 6).

DISCUSSION

Results

The MDG drinking-water target has been met if access to improved water sources is equated with sustainable access

Table 5 | Estimates for not having access to safe water in 2010 adjusted for water quality

	Population unserved[b]	Population unserved adjusted microbial compliance[c]		Population unserved adjusted overall compliance[d]	
Region[a]	%	*N* in million	%	*N* in million	%
Low and middle income countries					
Sub-Saharan Africa	35.9	453	54.1	475	56.7
Americas	5.8	119	20.5	127	21.8[e]
Eastern Mediterranean	15.0	83	15.1[f]	90	16.3[f]
Europe	4.4	67	16.5	68	16.8
South-East Asia[g]	11.9	960	53.1	960[h]	53.1[h]
Western Pacific	9.5	374	23.6	520	32.8[e]
High income countries	0.5	5	0.5	5	0.5
World	11.8	2,062	30.1	2,244	32.7

[a]Grouped according to WHO regions and income category (WHO 2012).
[b]Without access to an improved water source.
[c]Adjusted for microbial quality.
[d]Adjusted for microbial and chemical quality.
[e]Overall compliance not recorded, calculated assuming independence of individual estimates.
[f]Only piped water was adjusted.
[g]Compliance to BIS 10500 (Bureau of Indian Standards 2005).
[h]Information available for microbial compliance only.

Table 6 | Global estimates when shared sanitation of an improved technology is classified as 'unimproved' versus 'improved'

	MLM[a] main estimates		MLM[a] estimate, recalculation	
	Shared sanitation as 'unimproved'		Shared sanitation as 'improved'	
Sanitation	*N* in million	(%)	*N* in million	(%)
Population not served 1990	2,658	(50.4)	2,402	(45.6)
Population not served 2010	2,501	(36.5)	1,821	(26.6)
Population not served 2015	2,429	(33.6)	1,656	(22.9)

[a]MLM: multilevel modeling.

to 'safe' water. We estimate that in 2015 only 10% of the world population will not have access to an improved water source. However, the sanitation target will be missed substantially if current trends continue. Alarmingly, the number of people without access to an improved water source or improved sanitation increased over time in some regions. This shows that the rates of improvement in access are generally not keeping up with population growth, especially in urban areas.

Generally, urban populations are considerably better served. Urbanization can facilitate the provision and lower the costs of facilities (Satterthwaite 2008). However, the comparatively small progress in those areas indicates that service provision is increasingly lagging behind population growth and rapid urbanization (JMP 2012a).

Modeling approach

We believe that MLM offers several advantages over traditional linear regression used by the JMP. Those include a single model for all countries, a flexible, still more stable curve, a continuous time series for all countries covering the whole MDG period, the additional information for countries with scarce data and the possibility to estimate for countries with no information. The JMP currently extrapolates the regression line over a limited number of years after the latest point and subsequently extends it horizontally (JMP 2012c). This leads to a sudden step in the estimates which is unlikely to happen in reality (Figures 3 and 4). Although global estimates of MLM differ only slightly from JMP estimates, they can differ substantially for individual countries, with up to 14 percentage points for access to an improved water source and 49 percentage points for access to improved sanitation. Furthermore, MLM proposes approximate estimates based on the regional mean for nine countries for water and 21 countries for

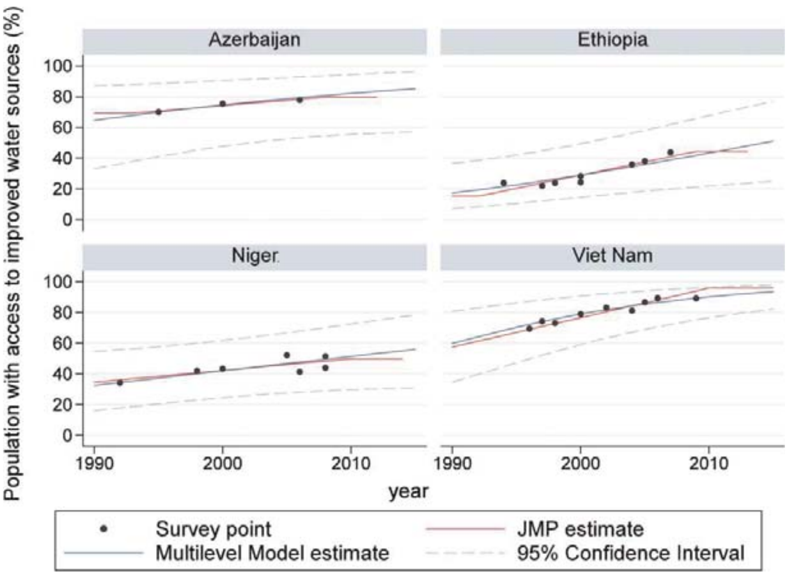


Figure 3 | Modeled access to an improved water source using multilevel modeling and JMP-methodology and survey data, country examples. JMP: Joint Monitoring Programme.

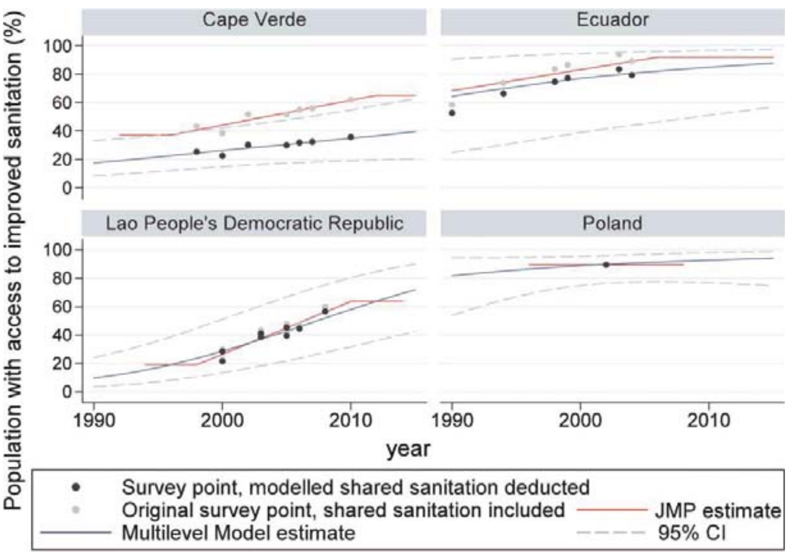


Figure 4 | Modeled access to improved sanitation using multilevel modeling and JMP-methodology, and survey data, country examples. JMP: Joint Monitoring Programme.

sanitation when no data are available. These estimates for countries without suitable survey data are indicative values only, to be used mainly for computing regional and global estimates, and are not meant to replace the more accurate measurements made by surveys or census. Current JMP method excludes countries without any survey point for computing regional or global estimates.

Some limitations should be noted. For countries with limited data, more information is used from other countries compared to countries with more information. We did not include further covariates into the model because they did not improve the model. In addition, forecasts to 2015 are based on current trends, meaning that policy or economic changes initiated after the last survey are not reflected. We also did not consider uncertainties associated with the survey estimates arising from sampling and non-sampling errors.

Consideration of water quality in monitoring the MDG targets

The MDG target addresses access to 'safe' water and 'basic' sanitation, whereas the indicators to monitor the targets are use of an 'improved' source or facility.

It was shown (JMP 2011; Bain *et al.* 2012) that considering representative data on water quality from the RADWQ considerably changes estimates for access to 'safe' water. To estimate access to actually 'safe' water on our estimates, we extrapolated national data on water quality of those assessments to countries in the same region and to the year 2010. Thereby, the number of people without access to safe water tripled and the unserved proportion increased by 21 percentage points in 2010. The currently used proxy indicator therefore might considerably overestimate the true access to safe water. However, data obtained by the RADWQ have to be interpreted with caution as they present a one-time measurement, do not consider seasonal fluctuations of water quality and use data collection methods that are not fully harmonized across countries (JMP 2010c). China, for example, reported total coliforms as indicator for microbial water quality whereas the other RADWQ measure thermotolerant *E. coli*. India did not test for contamination with arsenic and therefore overall compliance was not reported for South-East Asia. Our estimates are therefore not exact but highlight the difference between access to 'improved' services and actual safe access and the importance of collecting nationally representative water quality data by technology type.

If our estimates were adjusted for data on microbial compliance over the whole MDG period, they would show a shortfall towards the water target by around nine percentage points in 2015. This estimate, based on extrapolation of national data to the region, is remarkably close to a previous estimate based on modeling water quality using data from the five published RADWQ (Onda *et al.* 2012). In addition, our analysis includes field data for China and India, which together constitute about 37% of the world's population. This analysis therefore extends but also strengthens previous results. It should, however, be treated with caution because it is unlikely that compliance proportions remained constant over time and that country data can be extrapolated to other countries. More and better information on water quality would lead to more meaningful estimates.

Shared sanitation

'Shared sanitation' in the JMP dataset combines private sanitation shared between households, and public sanitation. Public sanitation was shown not to reduce morbidity in particular settings (Khan 1987). Additionally, it is often used by too many people, poorly maintained, far away, expensive and can pose a risk for interpersonal violence (Bapat & Agarwal 2003; World Bank 2006; Amnesty International 2010). This is likely to reduce its use and result in alternatives leading to contact with feces, like open defecation. Open defecation, even done by few people, has health impacts on the whole community by contaminating the environment and increasing the risk of infection (Saywell & Shaw 1999; Cairncross & Valdmanis 2006).

A bigger controversy exists around the health impacts of private facilities shared between households (Cairncross & Valdmanis 2006; Montgomery *et al.* 2010). Most of those facilities are used by few households and it was argued that a high proportion is probably safe for health (JMP 2010b). As limited resources and space, especially in densely populated urban areas, impedes the installation of one toilet per household (Saywell & Shaw 1999), this controversy deserves urgent clarification. We show in an exemplary calculation that classifying shared, otherwise improved sanitation as improved would have a huge impact on global figures. However, a different classification of (some) shared facilities as improved should be based on solid evidence. As this is currently not available, and furthermore data on shared sanitation use do not allow disaggregation into public or private sanitation, we classified all shared sanitation as unimproved, as done by JMP.

Additionally to the above, our model projects a constant increase of shared sanitation use between 1990 and 2015 worldwide (from 13% to 17%, or 511 million additional people).

Additional measure for progress

Halving a high proportion without access is much harder compared to halving a low one. This measure is, however, used to monitor the MDG target at global level (JMP 2012a). Halving a high proportion at country level means that a country supplied large parts of its population with services during the defined period. Poor countries are often in the difficult situation of both a high proportion without access and high population growth. They might have made remarkable progress in delivering services to many additional people, yet the percent reduction of the unserved proportion can be small. To acknowledge this, we show both the progress in reducing the proportion of the population without access ('MDG-type-progress', *x*-axis) and the progress in terms of the additional population served, meaning the total number of additional people served between 1990 and 2015 as a percentage of the 2015 population (*y*-axis) (Figures 5 and 6).

CONCLUSIONS

1. Multilevel modeling is transparent, flexible and easily reproducible, and offers several advantages over traditional linear regression. Those include continuous time series estimates for the whole MDG period for all countries even in the challenging but frequent situation of data scarcity.

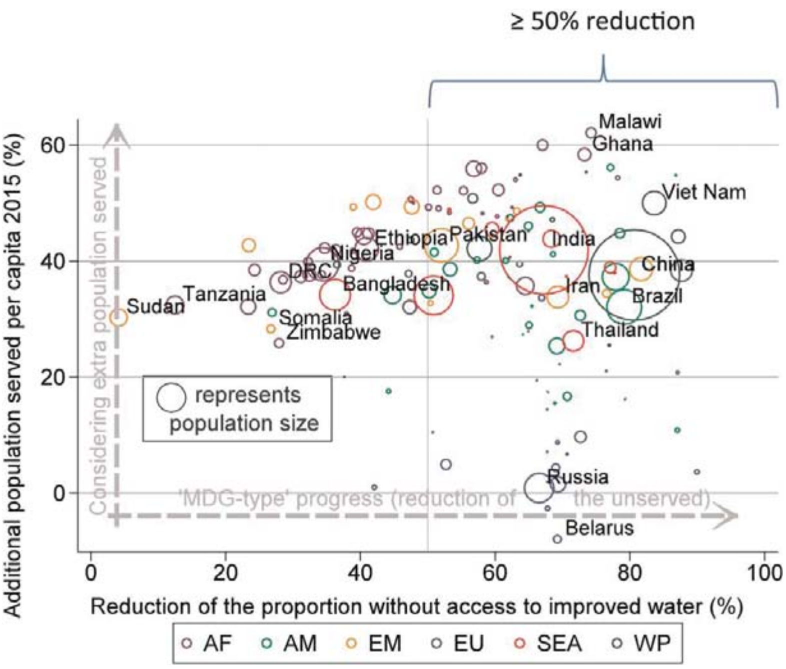


Figure 5 | Country progress on water: additional population served versus reduction of proportion of population unserved, between 1990 and 2015. AF: Sub-Saharan Africa, AM: Americas, EM: Eastern Mediterranean, EU: Europe, SEA: South-East Asia, WP: Western Pacific. Low and middle income countries only, scale does not cover all countries, ≥50% reduction would correspond to global MDG target.

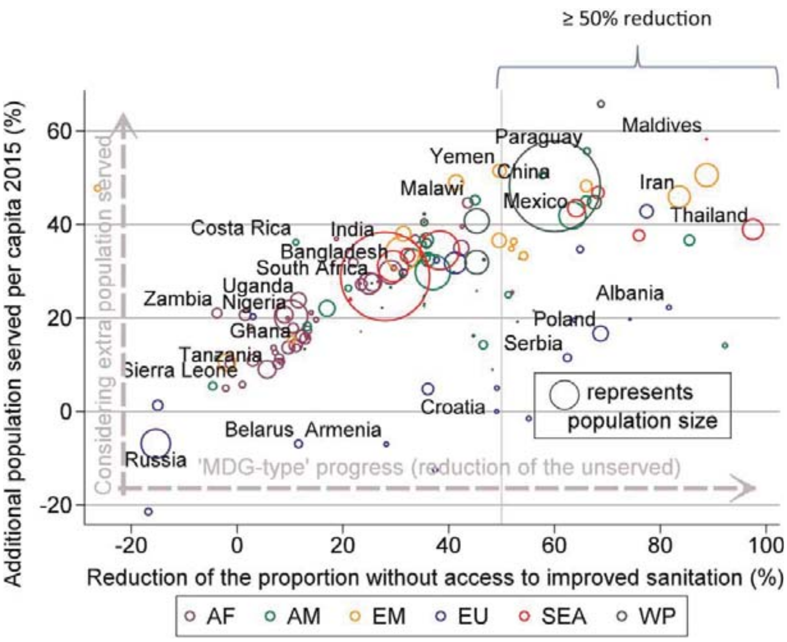


Figure 6 | Country progress on sanitation: additional population served versus reduction of proportion of population unserved, between 1990 and 2015. AF: Sub-Saharan Africa, AM: Americas, EM: Eastern Mediterranean, EU: Europe, SEA: South-East Asia, WP: Western Pacific. Low and middle income countries only, scale does not cover all countries, ≥50% reduction would correspond to global MDG target.

2. The MDG target for water, as measured by the indicator of access to improved drinking-water sources, will be achieved by 2015. The MDG target for sanitation is unlikely to be achieved. In some regions the number of people without access to services is rising, indicating that population growth and rapid urbanization have started to outpace new service provision.
3. Correction of the currently used MDG indicator for 'access to safe drinking-water' with information on water quality would provide a better account of the safety for health. Based on our approximation, it is unclear whether the MDG water target would actually be achieved by 2015, as representative data are currently available for only few developing countries and for one point in time. To regularly conduct national assessments of water quality is important and should be implemented after careful consideration of cost-effectiveness, sample location, timing and indicators.
4. At the moment the evidence is too scarce to clarify the ambiguity around the health impacts of shared sanitation. Changing the classification from shared facilities of an improved technology from unimproved to improved would have a huge impact not only on estimates but also on resource allocation and program planning, and should therefore be based only on solid evidence. We need more information on the proportion of shared sanitation, but also on the condition of those facilities and whether they are private or public. Furthermore, we do not have sufficient epidemiological evidence on the association between sharing sanitation facilities and morbidity.
5. Monitoring the reduction of the unserved proportion alone does not provide the full picture regarding progress made. Considering also the population that gained access during the relevant time period adds substantial information on actual efforts made by a country.

ACKNOWLEDGEMENT

We thank Abdou-Salam Savadogo for his valuable contribution to our work.

DISCLAIMER

The authors are staff members of the World Health Organization. The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions or policies of the World Health Organization.

REFERENCES

Amnesty International 2010 *Kenya: Insecurity and Indignity: Women's Experiences in the Slums of Nairobi, Kenya*. Amnesty International Publications, London, UK.

Bain, R., Gundry, S., Wright, J., Yang, H., Pedley, S. & Bartram, J. 2012 Accounting for water quality in monitoring access to safe drinking-water as part of the Millennium Development Goals: lessons from five countries. *Bull. World Health Org.* **90** (3), 228–235.

Bapat, M. & Agarwal, I. 2003 Our needs, our priorities; women and men from the slums in Mumbai and Pune talk about their needs for water and sanitation. *Environ. Urban.* **15** (2), 71–86.

Bureau of Indian Standards 2005 Indian Standard, Drinking Water Specification, Second Revision (No. 13.060.20). New Delhi.

Cairncross, S. & Valdmanis, V. 2006 Water supply, sanitation, and hygiene promotion. In: Jamison, D. T., Breman, J. G., Measham, A. R., Alleyne, G., Claeson, M., Evans, D. B., Jha, P., Mills, A. & Musgrove, P., editors. *Disease Control Priorities in Developing Countries*. Oxford University Press, Washington, pp. 771–792.

Cairncross, S., Hunt, C., Boisson, S., Bostoen, K., Curtis, V., Fung, I. C. H. & Schmidt, W. P. 2010 Water, sanitation and hygiene for the prevention of diarrhoea. *Int. J. Epidemiol.* **39** (suppl. 1), i193–i205.

De Onis, M., Blössner, M., Borghi, E., Morris, R. & Frongillo, E. A. 2004 Methodology for estimating regional and global trends of child malnutrition. *Int. J. Epidemiol.* **33** (6), 1260–1270.

Esrey, S. A., Potash, J. B., Roberts, L. & Shiff, C. 1990 Health Benefits from Improvements in Water Supply and Sanitation: Survey and Analysis of the Literature on Selected Diseases (WASH Technical Report No. 66). Environmental Health Project, USAID, Washington.

Goldstein, H. 2010 *Multilevel Statistical Models*, 4th edn. Wiley, UK.

Harvard University, Institute for Health Metrics and Evaluation, John Hopkins University, University of Queensland, World Health Organization 2009 Chapter 8: Analysis and Presentation of Regions. In: *GBD Study Operations Manual*, Final Draft.

Hox, J. 2010 *Multilevel Analysis, Techniques and Applications, 2nd edn. Quantitative Methodology Series*. Routledge, New York.

International Household Survey Network 2012 Accelerated Data Program. Available from: www.ihsn.org/adp/.

JMP 2010a *Progress on Sanitation and Drinking Water, 2010 Update*. UNICEF, World Health Organization, Geneva, Switzerland.

JMP 2010b JMP Sanitation and Method Task Force Meeting Report (Technical Task Force Meeting). New York.

JMP 2010c JMP Monitoring Drinking-water Quality Task Force Meeting Report (Technical Task Force Meeting). France.

JMP 2011 *Drinking Water: Equity, Safety and Sustainability, JMP Thematic Report in Drinking Water*. UNICEF, World Health Organization.

JMP 2012a *Progress on Drinking Water and Sanitation: 2012 Update*. UNICEF, World Health Organization.

JMP 2012b JMP > Welcome to the WHO & UNICEF Joint Monitoring Programme: documents. Available from: www.wssinfo.org/documents-links/documents/?tx_displaycontroller[type]=water_quality_reports.

JMP 2012c JMP > Welcome to the WHO & UNICEF Joint Monitoring Programme: method. Available from: www.wssinfo.org/definitions-methods/method/.

Khan, M. U. 1987 Limitation of communal latrines in changing the prevalence of parasites and diarrhoeal attack rate in Dhaka peri-urban slums. *Environ. Pollut.* **47** (3), 187–194.

Montgomery, M. A., Desai, M. M. & Elimelech, M. 2010 Comparing the effectiveness of shared versus private latrines in preventing trachoma in rural Tanzania. *Am. J. Trop. Med. Hyg.* **82** (4), 693–695.

Onda, K., LoBuglio, J. & Bartram, J. 2012 Global access to safe water: accounting for water quality and the resulting impact on MDG progress. *Int. J. Environ. Res. Public Health* **9** (3), 880–894.

Quené, H. & van den Bergh, H. 2004 On multi-level modeling of data from repeated measures designs: a tutorial. *Speech Commun.* **43** (1–2), 103–121.

Satterthwaite, D. 2008 Urbanization and sustainable development; Some notes for the presentation by David Satterthwaite for the UN Population Division.

Saywell, D. & Shaw, R. 1999 *On-plot Sanitation in Urban Areas (Technical Brief No. 61)*. WELL, London.

Steele, F. 2011 Module 5: Introduction to Multilevel Modelling Concepts. Available from: www.bristol.ac.uk/cmm/learning/course.html.

United Nations 2012 United Nations Millennium Development Goals. Available from: www.un.org/millenniumgoals/environ.shtml

United Nations Population Division 2012 United Nations Population Division Home Page. Available from: www.un.org/esa/population/.

Waddington, H., Snilstveit, B., White, H. & Fewtrell, L. 2009 *Water, Sanitation and Hygiene Interventions to Combat Childhood Diarrhoea in Developing Countries*.

International Initiative for Impact Evaluation, New Delhi, India.
WHO 2009 *Global Health Risks, Mortality and Burden of Disease Attributable to Selected Major Risks*. Geneva, Switzerland.
WHO 2011 *Guidelines for Drinking-water Quality*, 4th edn. Geneva, Switzerland.
WHO 2012 *World Health Statistics 2012*. Geneva, Switzerland.
World Bank 2006 *Kenya, Inside Informality: Poverty, Jobs, Housing and Services in Nairobi's Slums (No. 36347-KE)*. Water and Urban Unit 1, Africa Region, World Bank.
Ziegelbauer, K., Speich, B., Mäusezahl, D., Bos, R., Keiser, J. & Utzinger, J. 2012 Effect of sanitation on soil-transmitted helminth infection: systematic review and meta-analysis. *PLoS Med.* **9** (1), e1001162.

First received 15 June 2012; accepted in revised form 12 November 2012. Available online 17 December 2012

Tropical Medicine and International Health doi:10.1111/tmi.12331

VOLUME 19 NO 8 PP 928–942 AUGUST 2014

Systematic Review

Assessing the impact of drinking water and sanitation on diarrhoeal disease in low- and middle-income settings: systematic review and meta-regression

Jennyfer Wolf[1,2,3], Annette Prüss-Ustün[1], Oliver Cumming[4], Jamie Bartram[5], Sophie Bonjour[1], Sandy Cairncross[4], Thomas Clasen[6], John M. Colford Jr[7], Valerie Curtis[4], Jennifer De France[1], Lorna Fewtrell[8], Matthew C. Freeman[6], Bruce Gordon[1], Paul R. Hunter[9,10], Aurelie Jeandron[4], Richard B. Johnston[1,11], Daniel Mäusezahl[2,3], Colin Mathers[12], Maria Neira[1] and Julian P. T. Higgins[13,14]

1 *Department of Public Health and Environment, World Health Organization, Geneva, Switzerland*
2 *Swiss Tropical and Public Health Institute, Basel, Switzerland*
3 *University of Basel, Basel, Switzerland*
4 *London School of Hygiene and Tropical Medicine, London, UK*
5 *Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*
6 *Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA*
7 *School of Public Health, University of California, Berkeley, CA, USA*
8 *Centre for Research into Environment and Health, Aberystwyth University, Aberystwyth, UK*
9 *Norwich Medical School, University of East Anglia, Norwich, UK*
10 *Department of Environmental Health, Tshwane University of Technology, Pretoria, South Africa*
11 *EAWAG, Swiss Federal Institute of Aquatic Science and Technology, Dübendorf, Switzerland*
12 *Department of Health Statistics and Information Systems, World Health Organization, Geneva, Switzerland*
13 *School of Social and Community Medicine, University of Bristol, Bristol, UK*
14 *Centre for Reviews and Dissemination, University of York, York, UK*

Abstract

OBJECTIVE To assess the impact of inadequate water and sanitation on diarrhoeal disease in low- and middle-income settings.

METHODS The search strategy used Cochrane Library, MEDLINE & PubMed, Global Health, Embase and BIOSIS supplemented by screening of reference lists from previously published systematic reviews, to identify studies reporting on interventions examining the effect of drinking water and sanitation improvements in low- and middle-income settings published between 1970 and May 2013. Studies including randomised controlled trials, quasi-randomised trials with control group, observational studies using matching techniques and observational studies with a control group where the intervention was well defined were eligible. Risk of bias was assessed using a modified Ottawa–Newcastle scale. Study results were combined using meta-analysis and meta-regression to derive overall and intervention-specific risk estimates.

RESULTS Of 6819 records identified for drinking water, 61 studies met the inclusion criteria, and of 12 515 records identified for sanitation, 11 studies were included. Overall, improvements in drinking water and sanitation were associated with decreased risks of diarrhoea. Specific improvements, such as the use of water filters, provision of high-quality piped water and sewer connections, were associated with greater reductions in diarrhoea compared with other interventions.

CONCLUSIONS The results show that inadequate water and sanitation are associated with considerable risks of diarrhoeal disease and that there are notable differences in illness reduction according to the type of improved water and sanitation implemented.

keywords water, sanitation, diarrhoea, global burden of disease, risk estimates

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

Introduction

Diarrhoea is among the main contributors to global child mortality, causing one in ten child deaths (WHO 2009; Liu *et al.* 2012), and inadequate water and sanitation have long been associated with diarrhoea (Esrey & Habicht 1986; Esrey *et al.* 1991; Clasen *et al.* 2006, 2010; Waddington *et al.* 2009; Cairncross *et al.* 2010). In 2011, 11% of the world population reported using 'unimproved' drinking water supplies (defined as unprotected springs and dug wells, surface water and water stored in a tank) and 36% had 'unimproved' sanitation (defined as flush toilets not connected to a sewer or septic system, pit latrines without slab, bucket latrines or open defecation). 'Improved' and 'unimproved' drinking water and sanitation refer to specific sources and facilities as defined by the WHO/UNICEF Joint Monitoring Programme (JMP 2013) and are often taken as proxy indicators for appropriate and inappropriate water and sanitation. 'Inadequate' water and sanitation, as we define it for the purpose of this manuscript, means any drinking water or sanitation provision whose use poses a risk to health, which cannot be used safely, which is not available in sufficient quality or quantity or which is too distant for convenient access.

The 2010 Global Burden of Disease Study (GBD), by Lim *et al.* (2012), concluded that the impact of water and sanitation on diarrhoea was much smaller than previous GBD estimates (Prüss *et al.* 2002; Clasen *et al.* 2014). Their conclusion, based on a yet-to-be published systematic review, was that there was an increased risk of diarrhoea associated with unimproved water (RR 1.34, 95% CI 1.02–1.72) and unimproved sanitation (RR 1.33, 95% CI 1.02–1.74). They reported no additional benefit, however, from improved water quality or access over other improved water sources (such as public taps, protected springs or dug wells, boreholes and rainwater) after adjusting for potential bias due to lack of blinding (Lim *et al.* 2012; Engell & Lim 2013).

The 2010 GBD conclusions, with respect to the health impact associated with water and sanitation, represent a significant departure from previous estimates. This review was undertaken to update previous research and to explore the impact of other methods to adjust for non-blinding. Meta-regression was used to explore the impact of different types of improvement to drinking water or sanitation, as well as other study characteristics. The methods are described in line with the 'Preferred Reporting Items for Systematic Reviews and Meta-Analysis' (PRISMA) guideline (Moher *et al.* 2009) and include a PRISMA checklist (Online-only Appendix 1).

Methods

The objective of this study was to estimate the effect of different water and sanitation interventions on diarrhoeal disease morbidity, based on pooled estimates from existing studies. The protocol for this study was agreed, in advance, by an expert group convened by the World Health Organization (WHO) before the searches began.

Systematic literature review

Selection criteria and search strategy. Studies were sought that reported the effects on diarrhoea at the individual, household or community level of any drinking water or sanitation intervention providing they could be grouped within our conceptual models for drinking water and sanitation (Figures 1 and 2). Eligible study designs included:

- randomised (including cluster randomised) controlled trials;
- quasi-randomised and non-randomised controlled trials, when baseline data on the main outcome were available before the intervention was conducted (i.e. before and after studies with control group);
- case–control and cohort studies when they were related to an intervention;
- studies using time-series and interrupted time-series design; and
- observational studies using specific matching methods.

Studies were excluded if they mainly targeted institutions such as schools or the work place, or if they used non-representative population groups (e.g. people with HIV). We excluded studies in which the rate of implementation of the intervention was very low and studies that had very low compliance (<20%). A poor implementation rate might be reflected in similar rates of uptake in intervention and control groups: changes in morbidity cannot then confidently be attributed to the water or sanitation source or technology. As an example, Boisson *et al.* (2009) tested a novel portable water filter technology, but it was reportedly used by only 13% of the participants, and the authors themselves conclude that the health effect was likely not be due to the intervention and we excluded the study. Other studies in which interventions did not lead to differences in drinking water or sanitation access between intervention and control groups included Pradhan and Rawlings (2002) for household sanitation and Walker *et al.* (1999) for drinking water.

A wide range of single and combined water and sanitation interventions were eligible. Studies were included

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

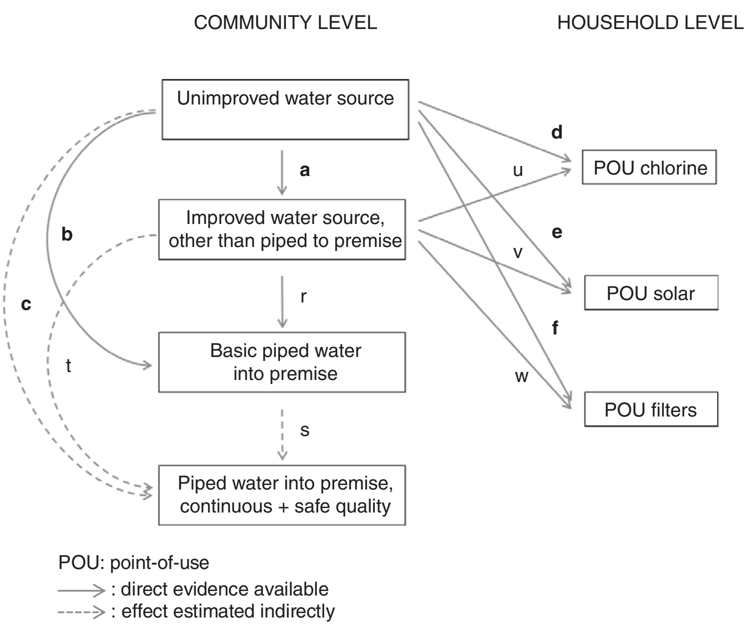


Figure 1 Conceptual framework for analysis of drinking water studies.

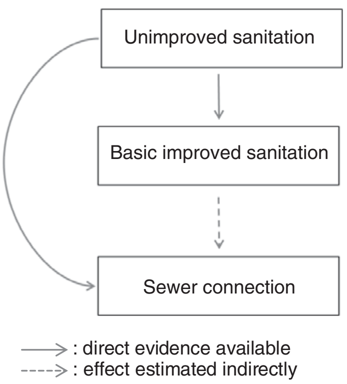


Figure 2 Conceptual framework for analysis of sanitation studies.

with participants of all ages from low- and middle-income settings. Due to the limited number of studies reporting mortality, studies had to report our primary outcome of diarrhoeal disease morbidity, regardless of aetiology and case confirmation. The main definition for diarrhoea was the WHO standard of at least three loose stools passed in the previous twenty-four hours (WHO 2005), but alternative case definitions were permitted providing that they could be assessed for validity. Studies were required to be published in a peer-reviewed journal or to have been assessed according to transparent criteria for methodological quality in a previously published systematic review.

Five databases were searched (Cochrane Library, MEDLINE & PubMed, Global Health, Embase and BIOSIS) in May 2013, using keyword and Medical Search Headings. The search terms and strategy are outlined in Online-only Appendix 2. In addition, reference lists of key articles (previously published systematic reviews and an unpublished literature review conducted by WHO) were examined, and subject experts and study authors were contacted to provide additional information and further relevant references where required. The search strategy was prepared and implemented in English, and only reports in English or French were considered. However, if a study published in a language other than English or French had been included in a previously published English or French language systematic review and the relevant data had been extracted and made available, this study was included in our analysis.

Data extraction and quality assessment. Titles and abstracts were screened by a single reviewer, and data extraction and quality assessment was carried out by two independent reviewers, using a structured and piloted form. Differences between reviewers over data extraction and quality assessment were reconciled with the intervention of a third abstractor, where required. The quality

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

assessment criteria were adapted from the Newcastle–Ottawa scale (Wells *et al.* undated) by Pope *et al.* (2010) for assessing the quality of studies for the health effects of interventions to reduce indoor air pollution. Specific quality criteria were adapted to each study type (intervention, cohort, case–control, cross-sectional) to assess the risk of sampling bias, bias in exposure and outcome measurements, bias in results analysis and reporting. The criteria are included in the data extraction form (Online-only Appendix 3).

The summary effect estimates were calculated as risk ratios (RR) with 95% confidence intervals (95% CI). For studies with multiple intervention arms (including factorial trials), we derived a single pair-wise comparison of the most comprehensive intervention compared with the least comprehensive intervention (or control) among the categories indicated in Figures 1 and 2, subject to availability of results. Where possible, we combined data across intervention arms falling within the same category (e.g. different methods for filtering at point of use). Whenever possible, effect estimates adjusted for clustering at household or community level were extracted.

Statistical analysis

General approach. Random-effects meta-analyses were conducted to examine, separately, the effect of improvements in drinking water or sanitation on diarrhoeal morbidity. Bayesian meta-regression was used to estimate the impact of different intervention types, baseline water and sanitation conditions and additional study characteristics (Thompson 1994). Other pre-specified covariates were retained in the model if the *P*-value was smaller than 0.2 or if they changed effect estimates of other variables by at least 15% (Kirkwood & Sterne 2003; McNamee 2003).

Systems for drinking water and sanitation provision lie on a continuum between poor and good supply/quality/facilities. Studies were grouped into categories according to the nature of the improvement, following conceptual models, as shown in Figures 1 and 2 and described in subsequent sections.

As a sensitivity analysis, 20% of studies with the lowest quality rating were excluded. For community- and household-level water interventions, separate sensitivity analyses were conducted as the studies tend to have different characteristics (with household-level interventions, for example, tending to be randomised controlled trials, while community-level interventions are often of a lower quality design – Clasen *et al.* 2006).

Potential for publication bias was examined with inspection of funnel plots and the use of Begg's and Egger's test. Analyses were performed with Stata 12 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp. LP). Bayesian meta-regression and bias adjustments were performed using WinBUGS (Lunn *et al.* 2000).

Analysis of drinking water interventions. The conceptual model used for the analysis of drinking water interventions is presented in Figure 1. Interventions were grouped as community-level (structural changes in supply) or household-level interventions (point-of-use treatment). Within point-of-use treatments, chlorine, solar disinfection and filter interventions were analysed separately. Within community-level interventions, studies were grouped according to whether the intervention led to an improved water source other than piped water (piped water means piped into premise throughout the article), a basic piped water source or a piped water source with a continuous supply and safe quality (referred to as higher-quality piped water).

We distinguish between 'basic piped water' and 'piped water, continuous and safe quality'. Practically, in all interventions providing piped water to households or premises, piped water was of non-optimal quality and/or supply was non-continuous requiring water storage in the households. The endpoint of these studies was therefore classified as 'basic piped water'. A 'piped water source, continuous and safe quality' is similar to the standard water supply in high-income countries. Studies of interventions that provide a continuous piped water supply of high water quality are currently not available for low- and middle-income settings besides one study (Hunter *et al.* 2010), which may come closest to the supplies typically encountered in high-income countries. We therefore approximated the transition from 'basic piped water' to 'piped water, continuous and safe quality' by the effect of safe water storage plus the effect of any quality improvements on a piped water system.

In Figure 1, the transitions a to f represent 'basic parameters' in the meta-regression model, each represented by a covariate. All other transitions are coded as combinations of these basic parameters: specifically, r = b – a, s = c – b, t = c – a, u = d – a, v = e – a and w = f – a. The model allows the indirect estimation of transitions that have not been directly observed (including those representing basic parameters), following ideas of network meta-analysis (Salanti *et al.* 2008).

Safe water storage in the household is an important component to prevent contamination and maintain adequate water quality (WHO 2013a). The effect of safe water storage was estimated by including a binary covariate to indicate either:

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

- when the intervention provided a safe storage container (i.e. a container with a narrow opening that prevents the introduction of objects) or
- when safe storage was an inherent part of the intervention (as with ceramic filters or solar disinfection of water in PET bottles).

The following further study characteristics were explored in meta-regression analyses:

- combined *vs.* single intervention, that is, plus additional hygiene education or sanitation provision;
- intention-to-treat *vs.* treatment-on-the-treated analysis;
- urban *vs.* rural settings;
- length of follow-up;
- sanitation provision at study baseline;
- provision of safe water storage;
- randomisation of study participants to the intervention;
- different interactions (see Online-only Appendix 4);
- type of household water treatment; and
- regional specificity (as dummy variable and according to WHO groupings – WHO 2013b).

Blinding study participants in household-level drinking water interventions. Studies where participants were blinded to point-of-use water quality interventions have consistently failed to show a statistically significant effect on diarrhoeal disease. As there are only three blinded household water interventions in low- and middle-income settings that meet the inclusion criteria (Kirchhoff *et al.* 1985; Jain *et al.* 2010; Boisson *et al.* 2013), it was felt that these were insufficient to define the potential bias associated with non-blinding. As diarrhoea in intervention studies is usually self-reported and non-blinding in subjectively assessed outcomes has been associated with bias (Wood *et al.* 2008; Savović *et al.* 2012), an additional analysis was performed, which incorporated bias adjustments based on empirical evidence (as described by Savović *et al.* (2012) and outlined below).

As community-level interventions are often less apparent to the recipient (study participant) than household-based interventions, it is likely that community-level interventions will be less prone to bias as a result of non-blinding. This idea is supported by the finding of similar results for community water or sanitation interventions when observational studies (examining survey data) and experimental studies were analysed separately. It is assumed that observational studies, using specific matching methods on survey data, are less prone to bias as a result of non-blinding because there is no single study hypothesis; the hypothesis regarding a potential impact of sanitation or water on diarrhoea would be just one of many possible hypotheses investigated in the survey. Such studies therefore offer an opportunity for limiting bias arising from non-blinding.

Meta-regression was repeated after making a bias adjustment in studies of household-level interventions. The result of each non-blinded study was separately adjusted by introducing bias through a prior distribution in a Bayesian framework (Welton *et al.* 2009). On the basis of the findings of Savović *et al.* (2012), who examined the distribution of bias due to lack of blinding in a large-scale meta-epidemiological study, three different prior distributions on size and direction of this bias were explored (Welton *et al.* 2009). These distributions incorporate variability in bias across studies and across meta-analyses. The prior which best represents the findings of the meta-epidemiological study (Savović *et al.* 2012) is based on the mean bias and the sum of all variance components. This is the preferred approach for the current analysis, as it will adjust the biased studies and should appropriately down-weight them. More information on bias adjustment for non-blinding and results with the other two prior distributions on size and direction of this bias are outlined in Online-only Appendix 4.

Analysis of sanitation interventions. Sanitation studies were grouped and analysed according to the conceptual model in Figure 2. We examined, in particular, the possibility of a differential effect of sewer connections over basic household improved sanitation (defined here as all other improved sanitation besides sewer connection). The following study characteristics were explored:

- combined *vs.* single intervention (i.e. plus additional hygiene education or water provision);
- urban *vs.* rural; and
- water provision at study baseline.

Results

Systematic search and quality grading

For water, of 6751 records identified through database searches and a further 68 identified through other sources, 3672 records were screened (after de-duplication) and 110 full-text articles were assessed for inclusion of which 61 were included for the meta-regression analysis.

For sanitation, of 12 502 records identified through database searches and a further 13 identified through other sources, 10 057 records were screened (after de-duplication) and 34 full-text articles were assessed for inclusion of which 11 were included for the meta-regression analysis. Figures 3 and 4 provide study flow

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

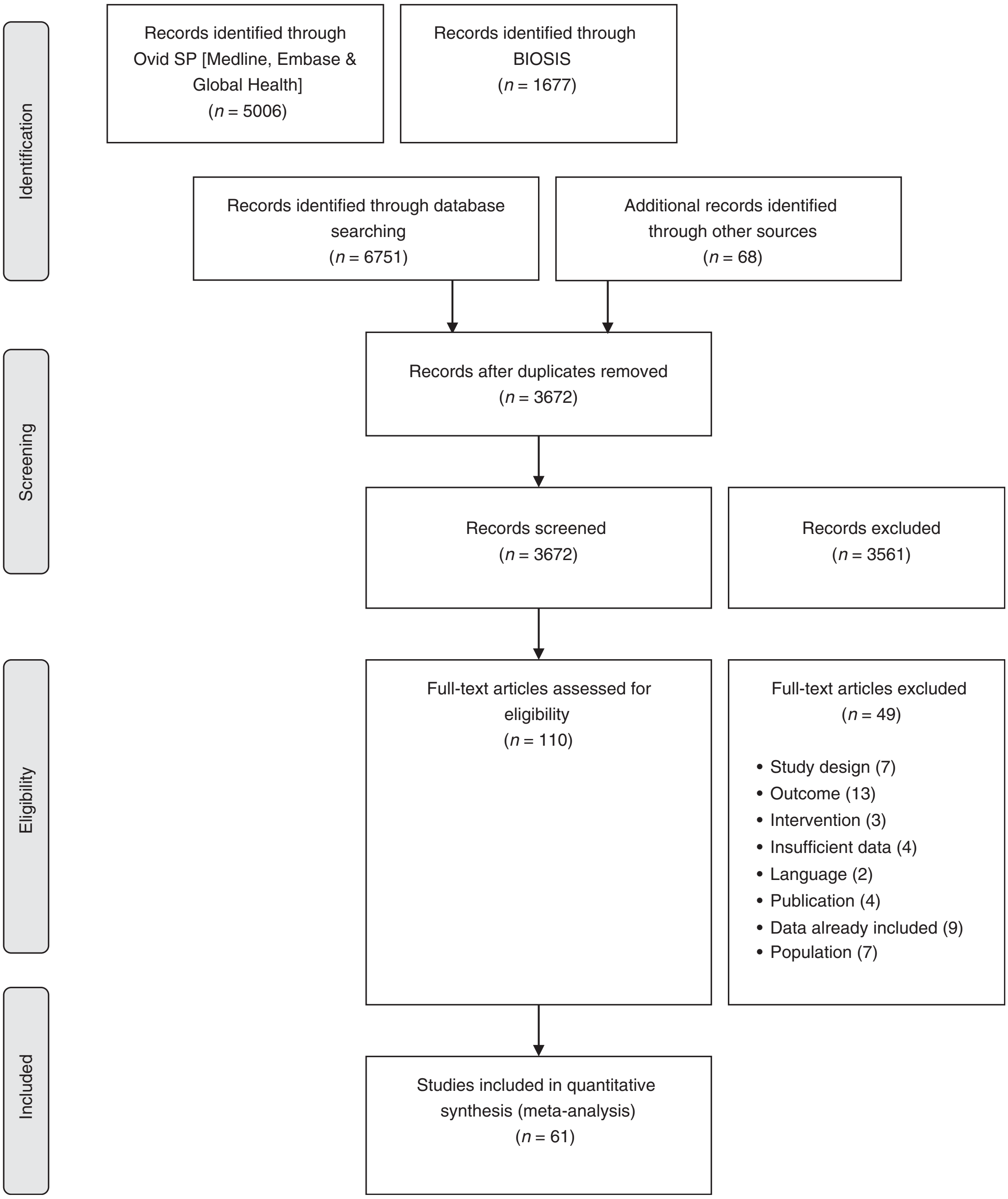


Figure 3 Flow chart of the selection process of drinking water studies.

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

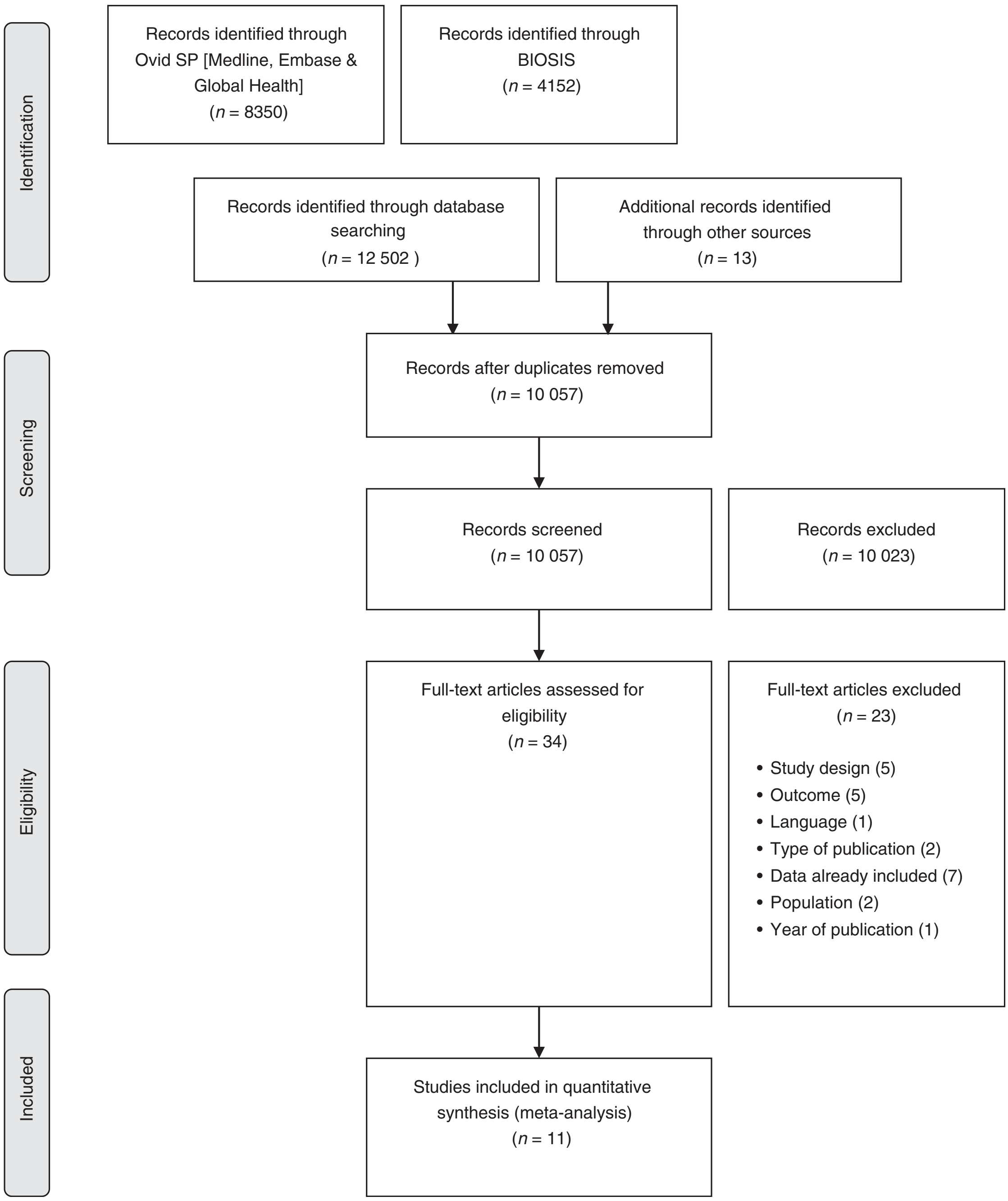


Figure 4 Flow chart of the selection process of sanitation studies.

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

Table 1 Included drinking water interventions according to study baseline and outcome

Baseline water	Outcome water	Comparisons	Transition (Figure 1)
Unimproved source	Improved community source	8	a
Unimproved source	Piped water	4	b
Improved community source	Piped water	7	r
Piped water	Higher-quality piped water	1	s
Unimproved source	POU chlorine treatment	16	d
Unimproved source	POU solar treatment	6	e
Unimproved source	POU filter treatment	14	f
Improved community source	POU chlorine treatment	4	u
Improved community source	POU solar treatment	5	v
Improved community source	POU filter treatment	3	w

POU = point-of-use, higher-quality piped water means quality improvements and safe storage of piped water.

diagrams of the number of studies screened and assessed for eligibility and included in the review. The Online-only Appendix 5 presents the citation, definitions and characteristics for all studies included in this analysis.

Analysis of water interventions

We included 68 comparisons of 61 individual studies from low- and middle-income settings. The number of observations describing each link between study baseline and outcome is listed in Table 1.

The summary risk ratio of all observations from the water interventions (all transitions), in a random-effects meta-analysis of the data, is 0.66 (0.60–0.71). Tables 2 and 3 show the results for individual transitions from the meta-regression analysis without and with bias adjustment for non-blinding.

The results from multivariable meta-regression before adjusting for non-blinding were nearly identical between Stata and WinBUGS. The results for chlorine and solar interventions were very similar and so, for convenience, they were combined in all analyses (in the context of Figure 1, this corresponds to setting d = e and hence u = v). Covariates retained in the model were provision of safe water storage and whether the intervention was a combined intervention.

Bias adjustment for non-blinding down weighs mainly estimates for point-of-use water treatment, higher-quality piped water and provision of safe water storage (Table 3).

The multivariable meta-regression model explained 53% of the between-study variance. Improved over unimproved sources are associated with only small reductions in diarrhoea, with a larger effect for piped water compared with other improved sources. The biggest protective effect on diarrhoeal disease was found for higher-quality (i.e. continuous and safe quality) piped water. Among household-level studies, filter interventions that also provided safe storage (for example, ceramic filters) were associated with a large reduction in diarrhoeal dis-

Table 2 Meta-regression results for water interventions, not adjusted for non-blinding

	Outcome water				
Baseline water	Improved community source	Basic piped water	Piped water, higher quality*	Chlorine/solar+*safe storage*	Filter+*safe storage*
Unimproved source	0.89 (0.78, 1.01)	0.77 (0.64, 0.92)	0.19 (0.07, 0.50)	0.82 (0.69, 0.96) *0.63 (0.55, 0.72)*	0.53 (0.41, 0.67) *0.41 (0.33, 0.50)*
Improved community source		0.86 (0.72, 1.03)	0.21 (0.08, 0.56)	0.92 (0.76, 1.10) *0.71 (0.61, 0.82)*	0.59 (0.45, 0.78) *0.46 (0.36, 0.58)*
Basic piped water			0.25 (0.09, 0.65)	1.07 (0.84, 1.34) *0.82 (0.67, 1.01)*	0.69 (0.51, 0.93) *0.53 (0.40, 0.69)*

*Continuous and safe water quality, based on limited evidence (Hunter *et al.* 2010) for quality improvements on basic piped water and should therefore be considered with caution.
Figures are relative risks (and 95% confidence intervals) and those in italics relate to additional safe storage.
Posterior estimates and credible interval limits were extracted as the median, 2.5% percentile and 97.5% percentile.
Results are adjusted for provision of safe water storage (RR 0.77 (0.64, 0.93)) and combined intervention (RR 0.84 (0.71, 0.99)).

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

Table 3 Meta-regression results for water interventions, adjusted for non-blinding

Baseline water	Outcome water				
	Improved community source	Basic piped water	Piped water, higher quality*	Chlorine/solar+*safe storage*	Filter+*safe storage*
Unimproved source	0.89 (0.78, 1.01)	0.77 (0.64, 0.92)	0.21 (0.08, 0.55)	0.99 (0.76, 1.27) *0.84 (0.61, 1.16)*	0.66 (0.47, 0.92) *0.55 (0.38, 0.81)*
Improved community source		0.86 (0.72, 1.03)	0.23 (0.09, 0.62)	1.11 (0.85, 1.44) *0.94 (0.68, 1.30)*	0.74 (0.52, 1.05) *0.62 (0.42, 0.93)*
Basic piped water			0.27 (0.10, 0.71)	1.29 (0.95, 1.74) *1.09 (0.76, 1.56)*	0.85 (0.58, 1.25) *0.72 (0.47, 1.11)*

*Continuous and safe water quality, based on limited evidence (Hunter *et al.* 2010) for quality improvements on basic piped water and should therefore be considered with caution.
Figures are relative risks (and 95% confidence intervals) and those in italics relate to additional safe storage.
Posterior estimates and credible interval limits were extracted as the median, 2.5% percentile and 97.5% percentile.
Results are adjusted for provision of safe water storage (RR 0.85 (0.69, 1.04)) and combined intervention (RR 0.83 (0.73, 1.01)).

ease. After taking account of safe water storage, the effects of ceramic and biosand filters were not significantly different from each other and so are grouped for further analysis. Chlorine and solar interventions did not appear to reduce diarrhoeal disease risk (applied to either unimproved or improved sources) after results were adjusted for non-blinding. There was some evidence of a greater diarrhoea risk reduction from improving household water storage and combining the water intervention with hygiene education and/or improved sanitation than through the water intervention alone (see footnotes of Table 2 and 3).

Analysis of sanitation interventions

We included 14 comparisons from low- and middle-income settings. Twelve observations compared improved sanitation facilities (other than sewer connections) with unimproved sanitation, and two observations had sewer connections as their outcome.

Table 4 Meta-regression results for sanitation interventions

Baseline sanitation	Outcome sanitation	
	Improved sanitation, no sewer	Sewer connection*
Unimproved sanitation	0.84 (0.77, 0.91)	0.31 (0.27, 0.36)
Improved sanitation, no sewer connection		0.37 (0.31, 0.44)

*Based on limited evidence (Pradhan & Rawlings 2002; Moraes *et al.* 2003) and should therefore be considered with caution.
Figures are relative risks (and 95% confidence intervals).
Results are adjusted for combined intervention (RR 0.88 (0.77, 1.01)).

The final model explained 97% of the between-study variance. The overall relative risk for improved over unimproved sanitation on diarrhoea, based on meta-analysis, was 0.72 (0.59, 0.88). The results of multivariable meta-regression are shown in Table 4. A larger association between sewer interventions and reduction in diarrhoea was observed compared with other improved sanitation.

Excluding 20% of studies with the lowest quality rating did not significantly change estimates, either for the water or the sanitation analysis. Funnel plot asymmetry was observed among the studies of household-level water quality interventions, which may be due to publication bias. There was no evidence of funnel plot asymmetry in studies of community-level water or sanitation improvements with or without sewer interventions. Funnel plots and results of statistical tests examining evidence for publication bias are shown in the Online-only Appendix 4.

Water and sanitation intervention studies typically report diarrhoeal levels in children up to 5 years of age, with impacts in other age groups less frequently reported. Data on other age groups were extracted wherever possible, and the results for all ages compared with children under five. The effect estimates were found to be very similar and mostly within the confidence interval of the under-five age group. It has therefore been assumed that the estimates derived here can be used for all ages.

Discussion

Results

The results show that there are large potential reductions in diarrhoeal disease risk through improvements to both water and sanitation in low- and middle-income settings.

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

For water, the most effective household-level intervention was found to be a point-of-use filter in combination with safe water storage. At the community level, introduction of high-quality piped water (i.e. water supplied continuously to the household of good microbial water quality) was found to be most effective. There were also differences in the impact of sanitation interventions, and there is evidence that sewer interventions are associated with a greater reduction in diarrhoea than basic household sanitation. These results are largely consistent with previously published reviews, where provision of improved community water supply was associated with a limited reduction in diarrhoeal illness (Waddington *et al.* 2009), and some water quality interventions (especially water filters) had a significant impact on reducing illness (Clasen *et al.* 2006; Hunter 2009; Waddington *et al.* 2009; Cairncross *et al.* 2010). This is also true for sanitation, as sanitation interventions in previous analyses have been shown to reduce diarrhoea by 30–40% (Waddington *et al.* 2009; Cairncross *et al.* 2010), with a larger effect observed for sewer connection (Norman *et al.* 2010).

The effect estimates for higher-quality piped drinking water and sewer connection should, however, be treated with caution. We approximated the transition from 'basic piped water' to 'piped water, continuous and safe quality' by the effect of safe water storage plus the effect of any quality improvements on a piped water system. We acknowledge that this is likely an underestimate as it accounts for the quality aspect but not any benefits derived through greater water access and its impact on, for example, personal hygiene. Source water quality improvement on piped water was estimated from one single study (Hunter *et al.* 2010), although the results are consistent with evidence from high-income countries (Payment *et al.* 1991; Colford *et al.* 2009). The effect of a sewered system was derived from two observations (Pradhan & Rawlings 2002; Moraes *et al.* 2003). Given the small number of observations used to derive these results, generalisation should be made only with caution. For example, in the intervention study that provided source water quality improvements on a piped water supply (Hunter *et al.* 2010), it is possible that the baseline piped water may have been of poorer quality than 'typical' piped water in low- and middle-income settings. However, reclassifying the baseline water in this study as unimproved in the analysis barely changed the diarrhoeal effect estimates. Given the limited evidence base, it is likely that these estimates may change considerably as additional evidence becomes available. They do, however, indicate the large potential benefits of improving water and sanitation and call for a disaggregation of the 'improved' levels defined by JMP (JMP 2013).

The finding of potentially important disease reduction beyond improved non-piped and also basic piped water sources is eminently plausible. Water from those improved sources is frequently contaminated during collection, transport and household storage (Wright *et al.* 2004; Rufener *et al.* 2010). Household piped water in low- and middle-income settings is frequently non-continuous (e.g. Brown *et al.* 2013) which presents two microbial risks, namely infiltration into non-pressurised distribution systems and recontamination or growth during household storage. In addition, community and non-continuous household water supply may reduce the amount of water available for hygiene purposes. Water availability and distance to the water source are both associated with risk of diarrhoea (Wang & Hunter 2010; RSS 2011; Pickering & Davis 2012). Reliable at-home water supplies were shown to increase water availability and key hygiene practices (Evans *et al.* 2013). The current analysis further suggests that improved water storage is associated with decreased risk of diarrhoea; a finding which has been previously described (Roberts *et al.* 2001; Günther & Schipper 2013). The beneficial effect of filters over both unimproved and improved sources remained significant and substantial after bias adjustment for non-blinding. This may reflect the fact that even water from improved sources is frequently of poor quality (Bain *et al.* 2012, 2014; Wolf *et al.* 2013). The smaller effect seen from chlorine and solar treatments could be explained if a significant proportion of diarrhoea episodes was caused by agents that are less susceptible to those treatments, non-exclusive use (Mäusezahl *et al.* 2009), and/or there is low uptake (compliance) of the intervention (as the need for adequate compliance has been shown in previous epidemiological modelling – Hunter *et al.* 2009; Brown & Clasen 2012; Enger *et al.* 2013).

Household members with improved sanitation may still be exposed to high levels of pathogens from faecal material if their neighbours have no improved sanitation (Root 2011; Baker & Ensink 2012), or when on-site sanitation is not managed hygienically. In urban areas, especially, latrines have been observed to fill and overflow, which can lead to major contamination of the surrounding area (Carter 2013). Introduction of sewered sanitation at large scale in urban areas in low- and middle-income settings would be expected to have a positive impact on health, although care must be taken that sewage is appropriately treated to avoid the diarrhoeal disease burden being shifted 'downstream' to the receiving communities (Baum *et al.* 2013). As such, it is acknowledged that sewered systems with appropriate sewage treatment are costly, and in some settings, decentralised systems for managing on-site sanitation

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

may be more cost-effective and appropriate (Norman *et al.* 2010).

Limitations

Effect estimates are from heterogeneous interventions and therefore only approximate the impact of improving water and sanitation on diarrhoea. Study quality is generally low which confirm previous analyses (Waddington *et al.* 2009; Cairncross *et al.* 2010; Clasen *et al.* 2010). Blinding and randomisation of study participants in water and sanitation interventions is often not possible and sometimes may not be desirable as blinding could negatively influence compliance and community dynamics which are important components for the adoption of interventions (Hartinger *et al.* 2011). Sanitation studies especially are often quasi-randomised (Capuno *et al.* 2011; Kumar & Vollmer 2013) which can introduce bias. Additionally, some point-of-use interventions have been shown to have low acceptability to the population (Boisson *et al.* 2009; Luoto *et al.* 2012) leading to poor adoption, and even an effective point-of-use treatment will have little impact on health if it is not consistently applied (Enger *et al.* 2013). In addition, few point-of-use interventions are effective against all typical classes of pathogens, and post-treatment contamination is frequent (Wright *et al.* 2004; Stauber *et al.* 2012). Even piped water interventions frequently provide low-quality non-continuous water which therefore requires storage, point-of-use treatment or the use of alternative water sources (Wang *et al.* 1989; Brown *et al.* 2013). Better quality water and sanitation interventions showed greater effectiveness in reducing diarrhoeal disease (Clasen *et al.* 2006). An attempt was made to account for some of these limitations by exploring health impacts beyond basic improved water and sanitation, by the use of specific bias adjustments and different sensitivity analyses.

We applied a bias adjustment to account for non-blinding, based on the findings of Savović *et al.* (2012). These, however, are based on clinical interventions, and there is little evidence that the pooled estimated bias is representative for the type of interventions covered in this article. The estimate is, however, specific to subjectively assessed outcomes (such as self-reported diarrhoea), and we believe that it represents the best currently available evidence on the effect of bias due to non-blinding.

Currently, only the impact of water and sanitation on diarrhoeal morbidity has been considered. Many other health effects (such as intestinal parasite infections, impaired nutritional status and possibly environmental enteropathy) have been associated with inadequate water and sanitation (Korpe & Petri 2012; Ziegelbauer *et al.* 2012; Dangour *et al.* 2013; Lin *et al.* 2013). Furthermore, inadequate water and sanitation have been associated with reduced school attendance (Freeman *et al.* 2012) and personal security issues, especially for women (Bapat & Agarwal 2003; Talaat *et al.* 2011). Unfortunately, quantitative evidence on these effects is currently very limited.

Meta-regression yields observational associations between variables, and is therefore prone to bias (Thompson & Higgins 2002). Use of water sources and sanitation facilities was defined at study level, although it may vary within the community. This can underestimate the true baseline or outcome effect. To include access as a continuous variable is currently not possible as many studies omit this information.

General discussion

The choice of what level of water and sanitation to consider as representing the highest attainable degree of safety (i.e. the counterfactual) has major implications in terms of the burden of disease that is attributable to inadequate water and sanitation. The analysis demonstrates health benefits beyond those achievable with basic improved water and sanitation, and it seems that health gains can be maximised when high-quality drinking water is available in sufficient quantities in the home and the sanitation system effectively prevents exposure to faecal material (through isolation and/or appropriate treatment). Thus, the results suggest that use of facilities defined as 'improved', as used in the 2010 GBD study (Lim *et al.* 2012), should not be construed as use of fully safe and adequate water and sanitation, devoid of an associated disease burden.

Service levels are frequently lower in low- and middle-income countries than those in high-income countries, but it is suggested that high-level services could represent a reference against which the risk for lower levels of water and sanitation could be estimated. Even defining high-level water services (i.e. high-quality water piped continuously to the home) as the counterfactual may lead to underestimates of the burden of disease. In Iceland, for example, the introduction of water safety plans was associated with a significant reduction of diarrhoea in the population (Gunnarsdottir *et al.* 2012). Also, tap water in California, USA, meeting all the required quality standards, was still associated with gastrointestinal illness (Colford *et al.* 2009). However, at present, data limitations preclude the setting of even higher counterfactuals for water and sanitation.

The systematic literature reviews and analyses reported in this paper have led to the identification of areas where evidence is missing on the linkages between water, sanitation and health. It is believed that effect estimates from

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

meta-analyses would greatly benefit from more well-conducted and reported water and sanitation intervention studies complying to, for example, the CONSORT Statement for randomised controlled trials (Schulz *et al.* 2010) or the STROBE Statement for observational studies (Von Elm *et al.* 2007). Studies applying a factorial design might be a promising approach to assess different interventions simultaneously and, given a sufficiently large sample size, interactions between different WASH interventions (Montgomery *et al.* 2003). Studies reporting consistently not only on health outcome but also on implementation and compliance would enable inclusion of this information in future analyses. Additionally, research on underlying factors that strengthen intervention implementation and increase people's acceptance, adoption and sustained use is still rare. Improved methods for using natural experiments or pre-existing development interventions, in which exposure is not artificially manipulated, also seem to be a promising way forward (Arnold *et al.* 2009; Craig *et al.* 2012). Furthermore, impacts resulting from inadequate water and sanitation other than diarrhoea morbidity are currently under-researched. More evidence on these topics would enable more meaningful estimates of the potential health benefits of improving water and sanitation to be made.

Conclusions

Inadequate drinking water and sanitation are associated with considerable risks for diarrhoeal disease. The choice of a suitable approach that can differentiate health effects between different improvements in water and sanitation relative to the baseline is crucial for meaningful estimates. However, evidence from well-conducted intervention studies assessing exclusive use of adequate access and supply of safe water or universal use of effective sanitation is still very limited.

Acknowledgements and disclaimer

The study was partially funded by the United Kingdom Department for International Development (DFID). The funder had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript. Thomas Clasen has participated in research and consulting services supported by Unilever and Vestergaard-Frandsen, which manufacture and sell household or other point of use water filtration devices. We would like to thank Wolf-Peter Schmidt and Sophie Boisson from the London School of Hygiene and Tropical Medicine for their advice and inputs into the review component. Some authors are staff members of the World Health Organization (WHO) or other institutions. The authors alone are responsible for the views expressed in this publication, which do not necessarily represent the views, decisions or policies of the WHO, DFID or other institutions. This article should not be reproduced for use in association with the promotion of commercial products, services or any legal entity. The WHO does not endorse any specific organisation or products. Any reproduction of this article cannot include the use of the WHO logo.

References

Arnold B, Arana B, Mäusezahl D, Hubbard A & Colford JM Jr (2009) Evaluation of a pre-existing, 3-year household water treatment and handwashing intervention in rural Guatemala. *International Journal of Epidemiology* **38**, 1651–1661.

Bain R, Gundry S, Wright J, Yang H, Pedley S & Bartram J (2012) Accounting for water quality in monitoring access to safe drinking-water as part of the Millennium Development Goals: lessons from five countries. *Bulletin of the World Health Organization* **90**, 228–235.

Bain R, Cronk R, Hossain R *et al.* (2014) Assessment of the level of exposure to fecally contaminated drinking water in developing countries. *Tropical Medicine and International Health* **19** [Epub ahead of print]

Baker SM & Ensink J (2012) Helminth transmission in simple pit latrines. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **106**, 709–710.

Bapat M & Agarwal I (2003) Our needs, our priorities; women and men from the slums in Mumbai and Pune talk about their needs for water and sanitation. *Environment & Urbanization* **15**, 71–86.

Baum R, Luh J & Bartram J (2013) Sanitation: a global estimate of sewerage connections without treatment and the resulting impact on MDG progress. *Environmental Science & Technology* **47**, 1994–2000.

Boisson S, Schmidt W-P, Berhanu T, Gezahegn H & Clasen T (2009) Randomized controlled trial in rural Ethiopia to assess a portable water treatment device. *Environmental Science & Technology* **43**, 5934–5939.

Boisson S, Stevenson M, Shapiro L *et al.* (2013) Effect of household-based drinking water chlorination on diarrhoea among children under five in Orissa, India: a double-blind randomised placebo-controlled trial. *PLoS Medicine* **10**, e1001497.

Brown J & Clasen T (2012) High adherence is necessary to realize health gains from water quality interventions. *PLoS One* **7**, e36735.

Brown J, Hien VH, McMahan L *et al.* (2013) Relative benefits of on-plot water supply over other "improved"sources in rural Vietnam. *Tropical Medicine & International Health* **18**, 65–74.

Cairncross S, Hunt C, Boisson S *et al.* (2010) Water, sanitation and hygiene for the prevention of diarrhoea. *International Journal of Epidemiology* **39**(suppl 1), i193–i205.

Capuno J, Tan CAR & Fabella VM (2011) Do piped water and flush toilets prevent child diarrhea in rural Philippines?

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

Asia-Pacific Journal of Public Health. Retrieved. September 18, 2013. from http://aph.sagepub.com/content/early/2011/12/08/1010539511430996.abstract.

Carter RC (2013) Editorial: What happens when the pit latrine is full? *Waterlines* **32**, 185–186.

Clasen T, Schmidt WP, Rabie T, Roberts I & Cairncross S (2006) Interventions to improve water quality for preventing diarrhoea (Review). *Cochrane Database of Systematic Reviews* **3**, 1–52.

Clasen TF, Bostoen K, Schmidt WP *et al.* (2010) Interventions to improve disposal of human excreta for preventing diarrhoea. *Cochrane Database of Systematic Reviews* **6**, 1–30.

Clasen T, Pruss-Ustun A, Mathers C, Cumming O, Cairncross S & Colford JM Jr. (2014) Estimating the impact of inadequate water, sanitation and hygiene on the global burden of disease: evolving and alternative methods. *Tropical Medicine and International Health* **19** [Epub ahead of print]

Colford JM Jr, Hilton JF, Wright CC *et al.* (2009) The Sonoma water evaluation trial: a randomized drinking water intervention trial to reduce gastrointestinal illness in older adults. *American Journal of Public Health* **99**, 1988–1995.

Craig P, Cooper C, Gunnell D *et al.* (2012) Using natural experiments to evaluate population health interventions: new Medical Research Council guidance. *Journal of Epidemiology and Community Health* **66**, 1182–1186.

Dangour AD, Watson L, Cumming O *et al.* (2013) Interventions to improve water quality and supply, sanitation and hygiene practices, and their effects on the nutritional status of children. *Cochrane Database of Systematic Reviews* **8** CD009382

Engell RE & Lim SS (2013) Does clean water matter? An updated meta-analysis of water supply and sanitation interventions and diarrhoeal diseases. *Lancet* **381**, S44.

Enger KS, Nelson KL, Rose JB & Eisenberg JNS (2013) The joint effects of efficacy and compliance: a study of household water treatment effectiveness against childhood diarrhea. *Water Research* **47**, 1181–1190.

Esrey SA & Habicht J-P (1986) Epidemiologic evidence for health benefits from improved water and sanitation in developing countries. *Epidemiologic Reviews* **8**, 117–128.

Esrey SA, Potash JB, Roberts L & Shiff C (1991) Effects of improved water supply and sanitation on ascariasis, diarrhoea, dracunculiasis, hookworm infection, schistosomiasis, and trachoma. *Bulletin of the World Health Organization* **69**, 609.

Evans B, Bartram J, Hunter P *et al.* (2013) *Public Health and Social Benefits of at-House Water Supplies*. University of Leeds, UK.

Freeman MC, Greene LE, Dreibelbis R *et al.* (2012) Assessing the impact of a school-based water treatment, hygiene and sanitation programme on pupil absence in Nyanza Province, Kenya: a cluster-randomized trial. *Tropical Medicine & International Health* **17**, 380–391.

Gunnarsdottir MJ, Gardarsson SM, Elliott M, Sigmundsdottir G & Bartram J (2012) Benefits of water safety plans: microbiology, compliance, and public health. *Environmental Science & Technology* **46**, 7782–7789.

Günther I & Schipper Y (2013) Pumps, germs and storage: The impact of improved water containers on water quality and health. *Health Economics* **22**, 757–774.

Hartinger SM, Lanata CF, Hattendorf J *et al.* (2011) A community randomised controlled trial evaluating a home-based environmental intervention package of improved stoves, solar water disinfection and kitchen sinks in rural Peru: Rationale, trial design and baseline findings. *Contemporary Clinical Trials* **32**, 864–873.

Hunter PR (2009) Household water treatment in developing countries: comparing different intervention types using meta-regression. *Environmental Science & Technology* **43**, 8991–8997.

Hunter PR, Zmirou-Navier D & Hartemann P (2009) Estimating the impact on health of poor reliability of drinking water interventions in developing countries. *Science of The Total Environment* **407**, 2621–2624.

Hunter PR, Ramírez Toro GI & Minnigh HA (2010) Impact on diarrhoeal illness of a community educational intervention to improve drinking water quality in rural communities in Puerto Rico. *BMC Public Health* **10**, 219.

Jain S, Sahanoon OK, Blanton E *et al.* (2010) Sodium dichloroisocyanurate tablets for routine treatment of household drinking water in periurban Ghana: a randomized controlled trial. *American Journal of Tropical Medicine and Hygiene* **82**, 16–22.

JMP (2013) *Progress on Sanitation and Drinking-Water. 2013 Update*. World Health Organization, UNICEF, Geneva, Switzerland.

Kirchhoff LV, McClelland KE, Pinho MDC, Araujo JG, De Sousa MA & Guerrant RL (1985) Feasibility and efficacy of in-home water chlorination in rural North-eastern Brazil. *Journal of Hygiene* **94**, 173–180.

Kirkwood B & Sterne JAC (2003) Chapter 29: Regression modelling. In: *Essential Medical Statistics*, 2nd edn Blackwell Science, Oxford, UK, pp. 315–342.

Korpe PS & Petri WA Jr (2012) Environmental enteropathy: critical implications of a poorly understood condition. *Trends in Molecular Medicine* **18**, 328–336.

Kumar S & Vollmer S (2013) Does access to improved sanitation reduce childhood diarrhea in rural India? *Health Economics* **22**, 410–427.

Lim SS, Vos T, Flaxman AD *et al.* (2012) A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* **380**, 2224–2260.

Lin A, Arnold BF, Afreen S *et al.* (2013) Household environmental conditions are associated with enteropathy and impaired growth in rural Bangladesh. *American Journal of Tropical Medicine and Hygiene* **89**, 130–137.

Liu L, Johnson HL, Cousens S *et al.* (2012) Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet* **379**, 2151–2161.

Lunn DJ, Thomas A, Best N & Spiegelhalter D (2000) WinBUGS: a Bayesian modelling framework: concepts, structure, and extensibility. *Statistics and Computing* **10**, 325–337.

Luoto J, Mahmud M, Albert J *et al.* (2012) Learning to dislike safe water products: results from a randomized controlled trial

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

of the effects of direct and peer experience on willingness to pay. *Environmental Science & Technology* **46**, 6244–6251.

Mäusezahl D, Christen A, Pacheco GD *et al.* (2009) Solar drinking water disinfection (SODIS) to reduce childhood diarrhoea in rural Bolivia: a cluster-randomized, controlled trial. *PLoS Medicine* **6**, e1000125.

McNamee R (2003) Confounding and confounders. *Occupational and Environmental Medicine* **60**, 227–234.

Moher D, Liberati A, Tetzlaff J & Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of Internal Medicine* **151**, 264–269.

Montgomery AA, Peters TJ & Little P (2003) Design, analysis and presentation of factorial randomised controlled trials. *BMC Medical Research Methodology* **3**, 26. doi:10.1186/1471-2288-3-26.

Moraes LRS, Azevedo Cancio J, Cairncross S & Huttly S (2003) Impact of drainage and sewerage on diarrhoea in poor urban areas in Salvador, Brazil. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **97**, 153–158.

Norman G, Pedley S & Takkouche B (2010) Effects of sewerage on diarrhoea and enteric infections: a systematic review and meta-analysis. *Lancet Infectious Diseases* **10**, 536–544.

Payment P, Richardson L, Siemiatycki J, Dewar R, Edwardes M & Franco E (1991) A randomized trial to evaluate the risk of gastrointestinal disease due to consumption of drinking water meeting current microbiological standards. *American Journal of Public Health* **81**, 703–708.

Pickering AJ & Davis J (2012) Freshwater availability and water fetching distance affect child health in sub-Saharan Africa. *Environmental Science & Technology* **46**, 2391–2397.

Pope DP, Mishra V, Thompson L *et al.* (2010) Risk of low birth weight and stillbirth associated with indoor air pollution from solid fuel use in developing countries. *Epidemiologic Reviews* **32**, 70–81.

Pradhan M & Rawlings LB (2002) The impact and targeting of social infrastructure investments: lessons from the Nicaraguan Social Fund. *World Bank Economic Review* **16**, 275–295. World Bank

Prüss A, Kay D, Fewtrell L & Bartram J (2002) Estimating the burden of disease from water, sanitation, and hygiene at a global level. *Environmental Health Perspectives* **110**, 537–542.

Roberts L, Chartier Y, Chartier O, Malenga G, Toole M & Rodka H (2001) Keeping clean water clean in a Malawi refugee camp: a randomized intervention trial. *Bulletin of the World Health Organization* **79**, 280–287.

Root GPM (2011) Sanitation, community environments, and childhood diarrhoea in rural Zimbabwe. *Journal of Health, Population and Nutrition* **19**, 73–82.

RSS (2011) Review evidence on minimum household water security requirements for health protection. Research Division, Royal Scientific Society Amman-Jordon. http://www.mdgfund.org/sites/default/files/ENV_STUDY_Jordan_Minimum%20hosehole%20water%20security.pdf

Rufener S, Mäusezahl D, Mosler H-J & Weingartner R (2010) Quality of drinking-water at source and point-of-consumption—drinking cup as a high potential recontamination risk: A field study in Bolivia. *Journal of Health & Population Nutrition* **28**, 34–41.

Salanti G, Higgins JPT, Ades AE & Ioannidis JPA (2008) Evaluation of networks of randomized trials. *Statistical Methods in Medical Research* **17**, 279–301.

Savović J, Jones HE, Altman DG *et al.* (2012) Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. *Annals of Internal Medicine* **157**, 429–438.

Schulz KF, Altman DG & Moher D & For the CONSORT Group (2010) CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMJ* **340**: c332–c332.

Stauber CE, Kominek B, Liang KR, Osman MK & Sobsey MD (2012) Evaluation of the impact of the plastic BioSand filter on health and drinking water quality in rural Tamale, Ghana. *International Journal of Environmental Research and Public Health* **9**, 3806–3823.

Talaat M, Afifi S, Dueger E *et al.* (2011) Effects of hand hygiene campaigns on incidence of laboratory-confirmed influenza and absenteeism in schoolchildren, Cairo. *Egypt. Emerging Infectious Diseases* **17**, 619–625.

Thompson SG (1994) Systematic review: why sources of heterogeneity in meta-analysis should be investigated. *British Medical Journal* **309**, 1351–1355.

Thompson SG & Higgins J (2002) How should meta-regression analyses be undertaken and interpreted? *Statistics in Medicine* **21**, 1559–1573.

Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC & Vandenbroucke JP (2007) The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Preventive Medicine* **45**, 247–251.

Waddington H, Snilstveit B, White H & Fewtrell L (2009). *Water, Sanitation and Hygiene Interventions to Combat Childhood Diarrhoea in Developing Countries*. International Initiative for Impact Evaluation, New Delhi, India.

Walker I, del Cid R, Ordoñez F & Rodríguez F (1999). *Ex-Post Evaluation of the Honduran Social Investment Fund (FHIS 2)*. World Bank, Washington, DC. http://www.esa.hn/pub/FHIS%20Expost%20Evaluation.pdf.

Wang X & Hunter PR (2010) A systematic review and meta-analysis of the association between self-reported diarrheal disease and distance from home to water source. *American Journal of Tropical Medicine and Hygiene* **83**, 582–584.

Wang ZS, Shepard DS, Zhu YC *et al.* (1989) Reduction of enteric infectious disease in rural China by providing deep-well tap water. *Bulletin of the World Health Organization* **67**, 171.

Wells GA, Shea B, O'Connell D *et al.* (undated) *The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-analyses*. Ottawa Hospital. Research Institute. Retrieved. from http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

Welton NJ, Ades AE, Carlin JB, Altman DG & Sterne JAC (2009) Models for potentially biased evidence in meta-analysis

© 2014 John Wiley & Sons Ltd
The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

using empirically based priors. *Journal of the Royal Statistical Society: Series A (Statistics in Society)* **172**, 119–136.

WHO (2005). *The treatment of Diarrhoea. A Manual for Physicians and Other Senior Health Workers*, 4th edn. WHO, Geneva, Switzerland.

WHO (2009) *Global health risks, Mortality and Burden of Disease Attributable to Selected Major Risks*. WHO, Geneva, Switzerland. Retrieved. April 30, 2012. from http://www.who.int/healthinfo/global_burden_disease/global_health_risks/en/index.html.

WHO (2013a) *Safe Household Water Storage*. WHO. Retrieved. December 5, 2013. from http://www.who.int/household_water/research/safe_storage/en/.

WHO (2013b) *World Health Statistics 2013*. World Health Organization, Geneva, Switzerland

Wolf J, Bonjour S & Prüss-Ustün A (2013) An exploration of multilevel modeling for estimating access to drinking-water and sanitation. *Journal of Water and Health* **11**, 64–77.

Wood L, Egger M, Gluud LL *et al.* (2008) Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *British Medical Journal* **336**, 601.

Wright J, Gundry S & Conroy R (2004) Household drinking water in developing countries: a systematic review of microbiological contamination between source and point-of-use. *Tropical Medicine & International Health* **9**, 106–117.

Ziegelbauer K, Speich B, Mäusezahl D, Bos R, Keiser J & Utzinger J (2012) Effect of sanitation on soil-transmitted helminth infection: systematic review and meta-analysis. *PLoS Medicine* **9**, e1001162.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. PRISMA checklist.
Appendix S2. Literature search strategy.
Appendix S3. Data extraction form.
Appendix S4. General extra information.
Appendix S5. List of included intervention studies.

Corresponding Author Jennyfer Wolf, Swiss Tropical and Public Health Institute, Basel, Switzerland. Tel.: +41 61 284 87 44; Fax: +41 61 284 81 05; E-mail: jennyfer.wolf@unibas.ch

© 2014 John Wiley & Sons Ltd

The World Health Organization retains copyright and all other rights in the manuscript of this article as submitted for publication.

VOLUME 19 NO 8 PP 906–916 AUGUST 2014

Systematic Review

Hygiene and health: systematic review of handwashing practices worldwide and update of health effects

Matthew C. Freeman[1], Meredith E. Stocks[1], Oliver Cumming[2], Aurelie Jeandron[2], Julian P. T. Higgins[3,4], Jennyfer Wolf[5,6,7], Annette Prüss-Ustün[5], Sophie Bonjour[5], Paul R. Hunter[8,9], Lorna Fewtrell[10] and Valerie Curtis[2]

1 *Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA*
2 *London School of Hygiene and Tropical Medicine, London, UK*
3 *School of Social and Community Medicine, University of Bristol, Bristol, UK*
4 *Centre for Reviews and Dissemination, University of York, York, UK*
5 *Department of Public Health and Environment, World Health Organization, Geneva, Switzerland*
6 *Swiss Tropical and Public Health Institute, Basel, Switzerland*
7 *University of Basel, Basel, Switzerland*
8 *Norwich Medical School, University of East Anglia, Norwich, UK*
9 *Department of Environmental Health, Tshwane University of Technology, Pretoria, South Africa*
10 *Centre for Research into Environment and Health, Aberystwyth University, Aberystwyth, UK*

Abstract

OBJECTIVE To estimate the global prevalence of handwashing with soap and derive a pooled estimate of the effect of hygiene on diarrhoeal diseases, based on a systematic search of the literature.
METHODS Studies with data on observed rates of handwashing with soap published between 1990 and August 2013 were identified from a systematic search of PubMed, Embase and ISI Web of Knowledge. A separate search was conducted for studies on the effect of hygiene on diarrhoeal disease that included randomised controlled trials, quasi-randomised trials with control group, observational studies using matching techniques and observational studies with a control group where the intervention was well defined. The search used Cochrane Library, Global Health, BIOSIS, PubMed, and Embase databases supplemented with reference lists from previously published systematic reviews to identify studies published between 1970 and August 2013. Results were combined using multilevel modelling for handwashing prevalence and meta-regression for risk estimates.
RESULTS From the 42 studies reporting handwashing prevalence we estimate that approximately 19% of the world population washes hands with soap after contact with excreta (i.e. use of a sanitation facility or contact with children's excreta). Meta-regression of risk estimates suggests that handwashing reduces the risk of diarrhoeal disease by 40% (risk ratio 0.60, 95% CI 0.53–0.68); however, when we included an adjustment for unblinded studies, the effect estimate was reduced to 23% (risk ratio 0.77, 95% CI 0.32–1.86).
CONCLUSIONS Our results show that handwashing after contact with excreta is poorly practiced globally, despite the likely positive health benefits.

keywords hygiene, diarrhoea, handwashing, risk estimates, meta-analysis

Introduction

Handwashing with soap at key times has been shown to reduce diarrhoeal disease and acute respiratory infection (Curtis & Cairncross 2003; Rabie & Curtis 2006; Aiello *et al.* 2008). Alongside adequate sanitation, handwashing with soap after stool contact is an important barrier to the faecal–oral spread of diarrhoea because it prevents pathogens from reaching the domestic environment and hence their subsequent ingestion. Handwashing with soap before contact with food and water also reduces the secondary transmission of pathogens from the environment

 © 2014 John Wiley & Sons Ltd

to a new host (Curtis *et al.* 2000). Beyond diarrhoeal disease, handwashing is also thought to play a role in reducing the transmission of infections such as pneumonia, influenza, helminths, trachomae, neonatal infections, HIV-associated infections and environmental enteropathies (Aiello *et al.* 2008; Blencowe *et al.* 2011; Curtis *et al.* 2011; Ejere *et al.* 2012; Ejemot *et al.* 2012; ; Filteau 2009; ; Freeman *et al.* 2013; Greenland *et al.* 2013; Isaac *et al.* 2008; WHO 2009). Further, hand hygiene is essential for disease control in commercial and domestic food preparation as well as in health care, day care, educational and occupational settings (Roberts *et al.* 2000; Bowen *et al.* 2007; Ejemot *et al.* 2012). Previous studies have suggested that promoting hand hygiene may be one of the most cost-effective means of reducing the global burden of disease (Cairncross & Valdmanis 2006).

The purpose of this article was to obtain key inputs for the development of the first regional and global estimates of handwashing with soap following faecal exposure, in view of updating the estimates of the burden of disease for the impact of this behaviour on diarrhoeal disease. We systematically reviewed the prevalence of the relevant hand hygiene practices worldwide and updated the evidence linking hand hygiene practices to the prevention of diarrhoea. In both cases, we present adjusted estimates due to known biases. The methods are described in line with the 'Preferred Reporting Items for Systematic Reviews and Meta-Analysis' (PRISMA) guideline (Moher *et al.* 2009) and include a PRISMA checklist (Appendix S1). The results provide a basis for estimating the global burden of disease from inadequate hand hygiene practices (Prüss-Ustün *et al.* 2014).

Methods

We systematically reviewed the literature for observed handwashing prevalence and applied multilevel modelling to estimate handwashing practices worldwide, by region and by country. To estimate the effect of different hygiene interventions on diarrhoeal disease morbidity, we reviewed the literature and used meta-regression techniques. The protocol for this study was reviewed and agreed upon by an expert group convened by the World Health Organization (WHO) the searches began.

Exposure prevalence: selection criteria, search strategy and data extraction

Because self-report is known to dramatically overestimate rates of handwashing with soap (Biran *et al.* 2008), studies were sought that reported the observed prevalence of handwashing with soap after using a toilet or after contact with excreta (including children's excreta). We included contact with children's excreta both because evidence for the impact of the specific times for handwashing is limited (see Luby *et al.* 2011 for the only available study), and because handwashing after handling child faeces is a plausible proxy for handwashing in general. Similarly, though in most observational studies, it is not known whether the subject uses the latrine for defecation, handwashing after toilet use is a relevant proxy for handwashing after contact with excreta. Hospital- and school-based handwashing studies were excluded, as they are not representative of the general population.

A systematic search was conducted for studies published between 1990 and August 2013 using PubMed, Embase and ISI Web of Knowledge. No restrictions were placed on language or study type. The database search was supplemented with data identified in a previous review (Curtis *et al.* 2009) and with additional Google Scholar searches of author names identified during the systematic database search. In addition, experts were contacted for unpublished handwashing observations.

Studies were selected for inclusion using a two-step review process. Titles and abstracts of all studies identified in the search were screened for relevance. The full text of each of the relevant articles was then reviewed and studies were excluded if they did not provide data on the prevalence of observed handwashing with soap. Data were extracted from each study using a standard protocol. Data extracted included information on study setting (country), observation location (home or public setting), timeframe of survey, population subgroup, sample size, a description of how handwashing prevalence was measured and specific prevalence estimates for any of the handwashing occasions, such as after toilet use or after cleaning up after a child (Appendix S5).

Impact estimates: selection criteria, search strategy and data extraction

Studies were eligible for inclusion if they were published between 1970 and August 2013 and reported on the impact of a hygiene promotion program on diarrhoea. Eligible study designs included randomised controlled trials, quasi-randomised controlled trials, observational studies using matching techniques and observational studies with a control group, where the intervention was well defined. In addition to studies concerning individual, household and community hygiene interventions, institutional interventions (e.g. in day-care centres and schools) were also included on the assumption that associated behaviours may plausibly affect household protection (unlike the water and sanitation meta-regression by Wolf *et al.* 2014). Studies assessing the impact of handwashing with soap were excluded if they were on non-representative population groups (e.g. HIV-positive children) or if there was no control group. The primary outcome was diarrhoeal disease morbidity regardless of aetiology and case confirmation. The main definition for diarrhoea was the WHO standard of at least three loose stools passed in the previous 24 h (WHO 2005), but alternative case definitions were permitted.

Five databases were searched (Cochrane Library, PubMed, Global Health, Embase and BIOSIS) – using keyword and medical search headings. Reference lists of key articles (previously published systematic reviews and an unpublished literature review conducted by the WHO) were examined and subject experts and study authors were contacted to provide additional information where required. The search strategy was prepared in English, and only studies available in English or French were considered unless the relevant data had been extracted and made available in a previously published English or French language systematic review.

Titles and abstracts were screened by a single reviewer, and data extraction and quality assessment was carried out by two independent reviewers, using a structured and piloted form. Differences between reviewers over data extraction and quality assessment were reconciled with the intervention of a third abstractor, where required. The quality assessment criteria were adapted from the Newcastle-Ottawa scale (Wells *et al.* undated) for assessing the quality of studies for the health effects of interventions to reduce indoor air pollution (Pope *et al.* 2010). Specific quality criteria were adapted to study design (intervention, cohort, case–control, cross-sectional), to assess the risk of bias in sampling, exposure and outcome measurement, results, analysis and reporting.

Exposure prevalence: statistical analysis

We estimated the proportion of country populations washing hands with soap using data from the prevalence surveys. Multilevel modelling was used to obtain the proportion of the population washing hands with soap for the year 2012. A linear two-level model, with WHO regions (WHO 2013) as covariates and a random intercept by country, provided an estimate for countries using a methodology similar to (Wolf *et al.* 2013). Country means were estimated without weighting by sample size as surveys were not designed to be country-representative, and their variability was likely to be due to different settings (e.g. public restroom in motorway or university, or home) or population groups. For countries with only one survey, the survey value was used for country reporting but not for estimation of the regional mean. Regional estimates were calculated as the mean of prevalence from countries with surveys, without weighting by country population (this choice was made because country population is not likely to drive handwashing prevalence). The means for the two regions without surveys (Eastern Mediterranean low- and middle-income and Eastern Mediterranean high-income regions) were obtained from the mean of prevalence of low- and middle-income and high-income countries, respectively. The global mean was obtained by a regional population-weighted mean of regional prevalence. Uncertainty intervals were estimated by bootstrap sampling from the survey points.

Impact estimates: Statistical analysis

The summary effect estimates were calculated as risk ratios (RR) with 95% confidence intervals (CI). Studies with multiple intervention arms could provide more than one effect estimate, providing each arm had a separate control. Whenever possible we extracted effect estimates that were adjusted for clustering at household or community level.

Random-effects meta-analyses were conducted to examine the effect of hygiene promotion interventions on diarrhoeal morbidity. Meta-regression was used to assess the impact of different intervention types and further study characteristics that could potentially influence results (Thompson 1994). Additional pre-specified covariates were retained in the model if the *P*-value was smaller than 0.2 or if they changed effect estimates of other variables by at least 15% (Kirkwood & Sterne 2003; McNamee 2003).

We explored the following further study characteristics in meta-regression analysis:

- interventions focused on handwashing only *vs*. those covering a broad range of hygiene promotion messages;
- handwashing interventions with and without the provision of soap;
- high-income *vs*. low- and middle-income countries;
- improved water and/or improved sanitation at baseline;
- urban *vs*. rural area;
- length of follow-up (as continuous variable, or more or less than 12 months); and
- randomised *vs*. non-randomised.

As a sensitivity analysis, we excluded the studies with the lowest quality rating (12% of all hygiene studies). Additionally, we checked whether excluding the only

 © 2014 John Wiley & Sons Ltd

study that used survey data changed the results (Fan & Mahal 2011).

Relating to the reasoning in Wolf *et al.* (2014) for non-blinding bias adjustment in household-level interventions with subjective assessed outcomes, we believe such an approach is also appropriate for hygiene intervention studies. It is not possible to blind educational interventions. Therefore, meta-regression was repeated with the result of each study separately adjusted by introducing bias through a prior distribution in a Bayesian framework (Welton *et al.* 2009). On the basis of the findings of Savović *et al.* (2012), who examined the distribution of bias due to lack of blinding in a large-scale meta-epidemiological study, different prior distributions on size and direction of this bias were explored (Welton *et al.* 2009). These distributions incorporate variability in bias across studies and across meta-analyses. The prior which best represents the findings of the meta-epidemiological study (Savović *et al.* 2012) is based on the mean bias and the sum of all variance components. This is the preferred approach for the current analysis, as it will adjust the biased studies and should appropriately down-weight them. More information on bias adjustment for non-blinding is provided in Supporting Information (Appendix S6).

The potential for an association between study size and effect size, which may be due to publication bias, was examined using funnel plots and statistical tests (Begg's and Egger's test). Analyses were performed with Stata 12 (Stata Statistical Software Release 12; StataCorp., College Station, TX, USA). Bayesian meta-regression and bias adjustments were performed using WinBUGS (Lunn *et al.* 2000).

Results

Prevalence of handwashing with soap

The initial search for handwashing with soap prevalence identified 2881 unique publications. Only 24 of these studies were found to provide prevalence data for handwashing with soap for at least one of the specified times of interest. Fifteen additional data sets were identified from the previous review conducted by Curtis *et al.* 2009 and two additional data sets were provided by contacted authors. Figure 1 provides the search flow diagram of the number of studies screened for eligibility and included in the calculations of pooled handwashing prevalence estimates for countries and regions. Study details for the 42 identified studies are presented in Appendix S2.

We estimate that 19% of people worldwide wash their hands with soap after contact with excreta. The regional mean prevalence of handwashing with soap ranges between 13% and 17% in low- and middle-income regions, and between 42% and 49% in high-income regions (Table 1). Country-level prevalence estimates can be found in Table 2. Country means in low- and middle-income regions vary between 5% and 25% of handwashing after contact with excreta, and between 48% and 72% in high-income countries. Israel and the Republic of Korea have lower handwashing prevalence than other high-income countries. They also are at the lower band of income within the high-income category (at time of surveys) and are geographically located outside the larger high-income regions. Given the availability of studies, we were not able to measure the changes in handwashing with soap prevalence over time.

Impact of handwashing promotion on diarrhoea

Figure 2 provides a flow diagram for the systematic search of publications linking handwashing with soap to diarrhoea outcomes. We identified 920 unique publications, of which 26 were retained for quantitative meta-analysis. Appendix S4 presents the citation, definitions and characteristics for each of the 26 studies included in the meta-analysis.

Of the 26 included studies, 14 employed interventions focused on handwashing messages while 12 delivered general hygiene education, which includes programs where handwashing with soap was only one component of a larger set of messages. Among the 14 handwashing-focused studies, 11 specifically mentioned and provided soap, but did not generally provide information on the actual use of soap. The summary effect size of all hygiene promotion interventions in a random-effects meta-analysis of all 26 observations was a 33% reduction in the risk of diarrhoea [risk ratio (RR) 0.67, 95% confidence interval (CI) 0.61–0.74]. We found a 40% reduction in the risk of diarrhoea from the promotion of handwashing with soap (RR 0.60, 95% CI 0.53–0.68) and a 24% reduction in the risk of diarrhoea for general hygiene education alone (RR 0.76, 95% CI 0.67–0.86). Promotion of handwashing (with provision of soap or where soap was used) was thus associated with greater reduction of diarrhoea than broader hygiene education ($P = 0.01$) (Table 3).

When testing for length of follow-up, there was weak evidence ($P = 0.17$) that the impact of the intervention on diarrhoea declined with time after initial implementation, with an approximately 10% increase in diarrhoea risk after one year, compared to the initial reported levels. This association was, however, strongly driven by a single study (Wilson *et al.* 1991), which showed a partic-

© 2014 John Wiley & Sons Ltd

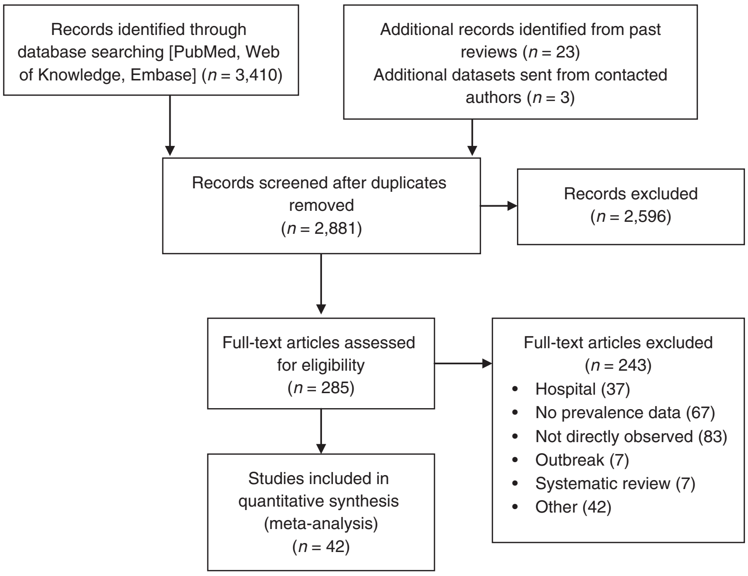


Figure 1 Flowchart describing study selection in handwashing prevalence.

Table 1 Mean prevalence of handwashing with soap by region

Region	Number of studies	Prevalence of handwashing with soap, (%) (95% CI)
Africa	13	14 (11, 18)
Americas HI	7	49 (33, 65)
Americas LMI	2	16 (7, 33)
Eastern Mediterranean HI*	–	44 (34, 57)
Eastern Mediterranean LMI*	–	15 (9, 24)
Europe HI	5	44 (29, 56)
Europe LMI	1	15 (6, 30)
South-East Asia	11	17 (7, 36)
Western Pacific HI	2	43 (25, 57)
Western Pacific LMI	2	13 (6, 25)
World	43	19 (8, 39)

LMI, low- and middle-income; HI, high-income; –, not available.
*No data available for Eastern Mediterranean (Emr); the mean for LMI countries was used for EmrLMI, and mean for HI countries for EmrHI, respectively.

ularly strong effect immediately post-intervention. Study duration was, therefore, not retained as covariate in the final analysis. No association was found between diarrhoea risk and the other tested covariates. The included covariates explained 32% of the between-study variance.

Omitting the studies with the poorest quality ratings, or the single study with a particularly high effect size immediately post-intervention, did not change the results of the model. A funnel plot of the hygiene promotion studies is shown in Appendix S3. Statistical tests for asymmetry were not statistically significant, although the plot does not exhibit the expected funnel shape, which is probably due to the variety of different study designs.

Interventions reporting the impact of handwashing with soap on diarrhoea mostly provide results for the association between maternal caregiver handwashing and diarrhoea among children under 5 years, with impacts on other age groups less frequently reported. Data on other age groups were extracted wherever possible and the results for all ages compared with children under five. No difference by age group was detected and so it has been assumed that the estimates derived here can be used for all ages.

© 2014 John Wiley & Sons Ltd

Table 2 Mean prevalence of handwashing with soap by country

Region	Country	No. of Studies	Prevalence estimate, (%) (95% CI) without sample weighting
Afr	Burkina Faso	1	8 (4, 14)
	Ethiopia	1	22 (13, 34)
	Ghana	3	13 (6, 22)
	Kenya	5	15 (7, 29)
	Senegal	1	19 (12, 30)
	Uganda	1	15 (9, 24)
	Tanzania	1	5 (3, 10)
AmrHI	USA	7	49 (32, 65)
AmrLMI	Peru	2	16 (7, 32)
EurHI	Israel	1	12 (5, 26)
	Netherlands	1	50 (34, 66)
	United Kingdom	3	52 (34, 70)
EurLMI	Kyrgyzstan	1	16 (7, 32)
Sear	Bangladesh	7	18 (10, 27)
	India	3	15 (3, 27)
	Thailand	1	25 (15, 38)
WprHI	New Zealand	1	72 (44, 89)
	Republic of Korea	1	17 (9, 33)
WprLMI	China	2	13 (6, 24)

Afr, Africa; Amr, Americas; Emr, Eastern Mediterranean; Eur, Europe; Sear, Southeast Asia; Wpr, Western Pacific; LMI, low- and middle-income; HI, high-income.

Studies of hygiene cannot be blinded and generally rely on self-reported diarrhoea. We therefore introduced bias adjustments based on empirical evidence for all studies (Savović *et al.* 2012), in the same way as in the meta-regression on drinking water and sanitation (Wolf *et al.* 2014), with the results shown in Table 3. After adjusting for bias, while handwashing with soap leads to a marked reduction in the risk of diarrhoea, the result is no longer statistically significant.

Discussion

A systematic review of global handwashing showed that handwashing after possible contact with excreta is still far from universally practiced. The global mean prevalence of handwashing was estimated at 19%. Although this result is based on only 43 studies from 19 countries, the studies show remarkably little variability within regions of the same income level. The high-income countries with data on handwashing frequency show rates varying between 48% and 72%, and low-income countries show lower rates varying between 5% and 25%.

To our knowledge, this is the first systematic review of observed handwashing prevalence. We used data from studies that employed direct observation of handwashing behaviour rather than self-reported behaviour, as self reporting is known to overestimate real handwashing rates greatly (Biran *et al.* 2008). However, the presence of an observer has consistently been shown to lead to biased results due to increased handwashing behaviour (Ram *et al.* 2010; Pedersen *et al.*, 1986; Munger & Harris 1989). We would expect such bias to inflate our estimate, meaning that 19% is likely an overestimate of the global prevalence of handwashing. For this reason, it is even more pressing to determine handwashing promotional strategies that are effective and engender long-lasting behaviour change.

The risk ratio for the reduction in diarrhoeal disease risk from handwashing with soap (RR 0.60), before adjusting for potential bias due to lack of blinding, is largely consistent with previous estimates. It is found across types of study design and is robust to changes in inclusion criteria. Courtesy bias – the tendency of participants (who know they are in the intervention group, i.e. they are non-blinded) to provide answers to please the investigator – is a concern, as it may lead to over-reporting of handwashing behaviours and under-reporting of diarrhoea, thus an overestimation of the effect of the intervention. This effect has been discussed in the context of point-of-use water-treatment studies (Schmidt & Cairncross 2009) and may also apply to hygiene interventions (Luby *et al.* 2006). An additional challenge is that observations may lead to a Hawthorne effect (the effect,

© 2014 John Wiley & Sons Ltd

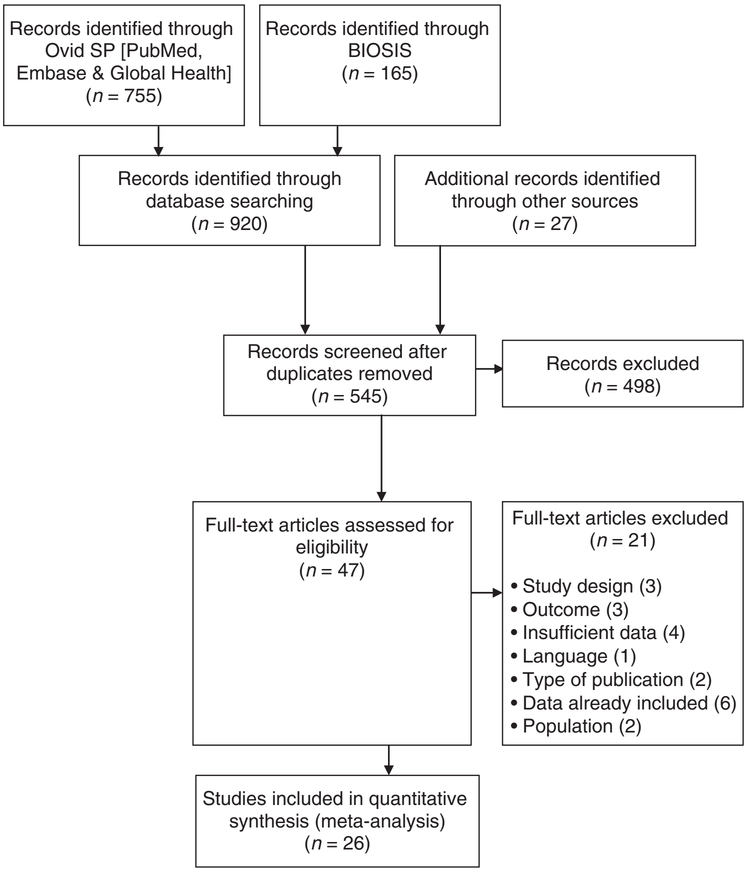


Figure 2 Flowchart describing the selection of studies on the effect of handwashing on diarrhoea.

Table 3 Meta-regression results for hygiene interventions, without and with bias adjusted for non-blinding

Bias adjustment for non-blinding	All hygiene education studies (*n* = 26)	Handwashing with soap only (*n* = 14)	General hygiene education only (*n* = 12)
No adjustment	0.67 (0.61, 0.74)	0.60 (0.53, 0.68)	0.76 (0.67, 0.86)
Adjustment	0.86 (0.36, 2.09)	0.77 (0.32, 1.86)	0.97 (0.40, 2.36)

usually positive, of being under investigation generally) which can result either in an overstatement or understatement of the effectiveness of the hygiene interventions (Ram *et al.* 2010).

In the absence of evidence as to the existence and magnitude of bias due to non-blinding, we chose to make a correction to our effect estimates based on the distribution of bias in a large-scale meta-epidemiological study of medical and pharmacological interventions (Savović *et al.* 2012). This is our best estimate of likely bias in the absence of further evidence (Wolf *et al.* 2014). The adjustment reduces the estimate of the effect of handwashing with soap on diarrhoea from an RR of 40% to an RR of 23%, an estimate that is not significant at the 5% level.

One short-term intervention study that reported observations of the amount of soap use, and employed an objective measure of illness (rectal swabs), showed strong

© 2014 John Wiley & Sons Ltd

reductions in the transmission of shigellosis following handwashing compared to a non-handwashing control group (Khan 1982). This comparatively high-quality study (in terms of both exposure and outcome assessment) does provide convincing evidence that hand hygiene has the potential to reduce risk of diarrhoea when there is sufficient motivation for people to comply. To improve our estimates of the health impact of handwashing with soap, future research should:

- employ objective outcome measures
- measure compliance with the intervention and
- explore the impact of courtesy bias, including how much it can be minimised by reducing perceived links between an intervention and the measurement of impact.

We used direct observation in this study because no gold standard measures of handwashing exist, and it is considered a more accurate measure than self-report. While additional studies that rely on observation may not be advisable given the known bias and cost, the need for more precise measures of handwashing behaviour remain. Newly emerging sensor technologies are likely to provide more accurate measures (Fleischman *et al.* 2011; Ford *et al.* 2014). While still costly and only realistic in high-income settings, data from studies in low-income setting may not be far off. Objective measures of illness are also improving that rely on immune response or provide pathogen specific phylogenics (Wu *et al.* 2010; Lammie *et al.* 2012), and do not rely on self-reported diarrhoea.

Even when we reduce the effect estimate for suspected courtesy bias, a concurrent publication suggests that handwashing with soap could reduce the burden of disease by some 296 872 (95% CI 0–882 159) lives a year based on 2012 data (Prüss-Ustün *et al.* 2014). As argued by Curtis and Cairncross in their review (2003), it is reasonable to assume that reductions of diarrhoeal morbidity would result in great reductions in mortality. This is a large number that does not take into account other possible health effects of handwashing. Two recent meta-analyses, for example, have investigated the link between hygiene and respiratory infections. A systematic review by Rabie and Curtis (2006) found a mean reduction in acute respiratory infections of 16% (95% CI 6–40%) from eight studies in community and institutional settings in high-income countries. In a review of 16 studies of various hand hygiene interventions (soap, sanitiser, education) from low-, middle- and high-income countries in both community and institutional settings, Aiello *et al.* (2008) found mean reduction in respiratory illness of 21% (95% CI 5–34%). In addition, as part of an observational study, handwashing has been reported to reduce neonatal mortality (Rhee *et al.* 2008). In a study that included, but was not limited to, handwashing promotion found reductions in worm infection in China (Bieri *et al.* 2013). Personal hygiene reduces the risk of severe trachoma infection (Emerson *et al.* 2000), mitigates the effects of Severe Acute Respiratory Syndrome (Fung & Cairncross 2006) and is recommended to address the risk of influenza pandemics (Cowling *et al.* 2009). However, the evidence on hand hygiene and diseases other than diarrhoeal infections in developing countries is too limited and the evidence from developed countries too heterogeneous to currently draw quantitative conclusions in view of population health impacts.

Further questions remain for research in handwashing. It is not yet clear which handwashing occasions are the most important. Although handwashing with soap after contact with faecal material (e.g. after defecation) provides an important barrier to faecal–oral transmission, it does not prevent secondary transmission (e.g. before preparing food and feeding children – Nizame *et al.* 2013). It is not clear how often hands should be washed, given the tendency for hands to become rapidly recontaminated in normal daily activity (Devamani 2001; Ram *et al.* 2011). It is currently not clear what are the optimal, and practical, hand-cleansing rates to prevent the transmission of respiratory and other pathogens. In addition, it is still not clear as to which hands matter most – is it the mother's, the child's, or those of people outside the family potentially vectoring novel pathogens?

With an overall average of 19% of the world population washing their hands with soap after using the toilet, much promotional work is still needed to increase the frequency of this practice, especially in the poorest countries with the highest disease burdens. The success of recent efforts to promote hand hygiene (Biran *et al.* 2014) is encouraging (Curtis *et al.* 2009), though it is clear that scaled approaches to improve handwashing with soap are needed.

Acknowledgements

The study was partially funded by the United Kingdom Department for International Development (DFID). The funder had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript. Some authors are staff members of the World Health Organization (WHO) or other institutions. The authors alone are responsible for the views expressed in this publication, which do not necessarily represent the

© 2014 John Wiley & Sons Ltd

views, decisions, or policies of the WHO, the UK DFID or other institutions. This article should not be reproduced for use in association with the promotion of commercial products, services or any legal entity. WHO does not endorse any specific organisation or products. Any reproduction of this article cannot include the use of the WHO logo.

References

Aiello AE, Coulborn RM, Perez V & Larson EL (2008) Effect of hand hygiene on infectious disease risk in the community setting: a meta-analysis. *American Journal of Public Health* **98**, 1372–1381.

Bieri FA, Gray DJ, Williams GM *et al.* (2013) Health-education package to prevent worm infections in Chinese schoolchildren. *The New England Journal of Medicine* **368**, 1603–1612.

Biran A, Rabie T, Schmidt W, Juvekar S, Hirve S & Curtis V (2008) Comparing the performance of indicators of handwashing practices in rural Indian households. *Tropical Medicine & International Health* **13**, 278–285.

Biran A, Schmidt W-P, Varadharajan KS *et al.* (2014) Effect of a behaviour-change intervention on handwashing with soap in india (superamma): a cluster-randomised trial. *The Lancet Global Health* **2**, e145–e154.

Blencowe H, Cousens S, Mullany LC *et al.* (2011) Clean birth and postnatal care practices to reduce neonatal deaths from sepsis and tetanus: a systematic review and Delphi estimation of mortality effect. *BMC Public Health* **11** (Suppl. 3), S11.

Bowen A, Ma H, Jianming O *et al.* (2007) A cluster-randomized controlled trial evaluating the effect of a handwashing-promotion program in Chinese primary schools. *American Journal of Tropical Medicine and Hygiene* **76**, 1166–1173.

Cairncross S & Valdmanis V (2006) Water supply, sanitation, and hygiene promotion. In: *Disease Control Priorities in Developing Countries*, 2nd edn (eds DT Jamison, JG Breman, AR Measham, G Alleyne, M Claeson, DB Evans, P Jha, A Mills & P Musgrove) World Bank, Washington, DC, Available at: http://www.ncbi.nlm.nih.gov/books/NBK11755/ (Accessed 13 December 2013).

Clasen T, Bartram J, Colford J, Luby S, Quick R & Sobsey M (2009) Comment on 'Household water treatment in poor populations: is there enough evidence for scaling up now?'. *Environmental Science & Technology* **43**, 5542–5544.

Cowling BJ, Chan K-H, Fang VJ *et al.* (2009) Facemasks and hand hygiene to prevent influenza transmission in households: a cluster randomized trial. *Annals of Internal Medicine* **151**, 437–446.

Curtis V & Cairncross S (2003) Effect of washing hands with soap on diarrhoea risk in the community: a systematic review. *The Lancet Infectious Diseases* **3**, 275–281.

Curtis V, Cairncross S & Yonli R (2000) Domestic hygiene and diarrhoea – pinpointing the problem. *Tropical Medicine & International Health* **5**, 22–32.

Curtis VA, Danquah LO & Aunger RV (2009) Planned, motivated and habitual hygiene behaviour: an eleven country review. *Health Education Research* **24**, 655–673.

Curtis V, Schmidt W, Luby S, Florez R, Touré O & Biran A (2011) Hygiene: new hopes, new horizons. *The Lancet Infectious Diseases* **11**, 312–321.

Devamani C (2001) Bacterial recontamination of hands following handwashing and associated risk factors in rural Andhra Pradesh, India. Infectious and Tropical Diseases. MSc. London School of Hygiene and Tropical Medicine.

Ejemot RI, Ehiri JE, Meremikwu MM & Critchley JA (2012) Hand washing for preventing diarrhoea. *Cochrane Database Systematic Review* CD004265.

Ejere HOD, Alhassan MB & Rabiu M (2012) Face washing promotion for preventing active trachoma. *Cochrane Database Systematic Review* CD003659.

Emerson PM, Cairncross S, Bailey RL & Mabey DC (2000) Review of the evidence base for the 'F' and 'E' components of the SAFE strategy for trachoma control. *Tropical Medicine & International Health* **5**, 515–527.

Fan VY-M & Mahal A (2011) What prevents child diarrhoea? The impacts of water supply, toilets, and hand-washing in rural India. *Journal of Development Effectiveness* **3**, 340–370.

Filteau S (2009) The HIV-exposed, uninfected African child. *Tropical Medicine & International Health* **14**, 276–287.

Fleischman DS, Webster GD, Judah G, de Barra M, Aunger R & Curtis VA (2011) Sensor recorded changes in rates of hand washing with soap in response to the media reports of the H1N1 pandemic in Britain. *BMJ Open* **1**, e000127.

Ford EW, Boyer BT, Menachemi N & Huerta TR (2014) Increasing hand washing compliance with a simple visual cue. *American Journal of Public Health*, e1–e6.

Freeman MC, Clasen T, Brooker SJ, Akoko DO & Rheingans R (2013) The impact of a school-based hygiene, water quality and sanitation intervention on soil-transmitted helminth reinfection: a cluster-randomized trial. *The American Journal of Tropical Medicine and Hygiene* **89**, 875–883.

Fung IC-H & Cairncross S (2006) Effectiveness of handwashing in preventing SARS: a review. *Tropical Medicine & International Health* **11**, 1749–1758.

Greenland K, Cairncross S, Cumming O & Curtis V (2013) Can we afford to overlook hand hygiene again? *Tropical Medicine & International Health* **18**, 246–249.

Isaac R, Alex RG & Knox TA (2008) Malabsorption in wasting HIV disease: diagnostic and management issues in resource-poor settings. *Tropical Doctor* **38**, 133–134.

Khan MU (1982) Interruption of shigellosis by hand washing. *Transactions of the Royal Society of Tropical Medicine & Hygiene* **76**, 164–168.

Kirkwood BR & Sterne JAC (2003) Chapter 29: Regression modelling. In: *Essential Medical Statistics*, 2nd edn (eds Kirkwood BR & Sterne JAC). Blackwell Science, Hoboken, NJ, pp. 315–342.

 © 2014 John Wiley & Sons Ltd

Lammie PJ, Moss DM, Brook Goodhew E *et al.* (2012) Development of a new platform for neglected tropical disease surveillance. *International Journal for Parasitology* **42**, 797–800.

Luby SP, Agboatwalla M, Painter J *et al.* (2006) Combining drinking water treatment and hand washing for diarrhoea prevention, a cluster randomised controlled trial. *Tropical Medicine & International Health* **11**, 479–489.

Luby SP, Halder AK, Huda T, Unicomb L, Johnson RB. (2011) The effect of handwashing at recommended times with water alone and with soap on child diarrhea in rural Bangladesh: an observational study. *PLoS Medicine* **8**, e1001052.

Lunn DJ, Thomas A, Best N & Spiegelhalter D (2000) WinBUGS: a Bayesian modelling framework: concepts, structure, and extensibility. *Statistics and Computing* **10**, 325–337.

McNamee R (2003) Confounding and confounders. *Occupational and Environmental Medicine* **60**, 227–234.

Moher D, Liberati A, Tetzlaff J & Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of Internal Medicine* **151**, 264–269.

Munger K & Harris SJ (1989) Effects of an observer on hand washing in a public restroom. *Perceptual and Motor Skills* **69**, 733–734.

Nizame FA, Unicomb L, Sanghvi T *et al.* (2013) Handwashing before food preparation and child feeding: a missed opportunity for hygiene promotion. *The American Journal of Tropical Medicine and Hygiene* **89**, 1179–1185.

Pedersen DM, Keithly S & Brady K (1986) Effects of an observer on conformity to handwashing norm. *Perceptual and Motor Skills* **62**, 169–170.

Pope DP, Mishra V, Thompson L *et al.* (2010) Risk of low birth weight and stillbirth associated with indoor air pollution from solid fuel use in developing countries. *Epidemiologic Reviews* **32**, 70–81.

Prüss-Ustün A, Bartram J, Clasen T *et al.* (2014) Burden of diarrhoeal disease from inadequate water, sanitation and hygiene in low- and middle-income settings: a retrospective analysis of data from 147 countries. *Tropical Medicine & International Health*. doi: 10.1111/tmi.12329.

Rabie T & Curtis V (2006) Handwashing and risk of respiratory infections: a quantitative systematic review. *Tropical Medicine & International Health* **11**, 258–267.

Ram PK, Halder AK, Granger SP *et al.* (2010) Is structured observation a valid technique to measure handwashing behavior? Use of acceleration sensors embedded in soap to assess reactivity to structured observation *The American Journal of Tropical Medicine and Hygiene* **83**, 1070–1076.

Ram PK, Jahid I, Halder AK *et al.* (2011) Variability in hand contamination based on serial measurements: implications for assessment of hand-cleansing behavior and disease risk. *The American Journal of Tropical Medicine and Hygiene* **84**, 510–516.

Rhee V, Mullany LC, Khatry SK *et al.* (2008) Maternal and birth attendant hand washing and neonatal mortality in southern Nepal. *Archives of Pediatrics & Adolescent Medicine* **162**, 603–608.

Roberts L, Jorm L, Patel M, Smith W, Douglas RM & McGilchrist C (2000) Effect of infection control measures on the frequency of diarrheal episodes in child care: a randomized, controlled trial. *Pediatrics*, **105** (pt 1), 743–746.

Savović J, Jones HE, Altman DG *et al.* (2012) Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. *Annals of Internal Medicine* **157**, 429–438.

Schmidt W-P & Cairncross S (2009) Household water treatment in poor populations: is there enough evidence for scaling up now? *Environmental Science & Technology* **43**, 986–992.

Thompson SG (1994) Systematic review: why sources of heterogeneity in meta-analysis should be investigated. *British Medical Journal* **309**, 1351–1355.

Wells GA, Shea B, O'Connell D *et al.* (undated) The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa Hospital. Research Institute. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

Welton N, Ades A, Carlin J, Altman D & Sterne J (2009) Models for potentially biased evidence in meta-analysis using empirically based priors. *Journal of the Royal Statistical Society: Series A (Statistics in Society)* **172**, 119–136.

WHO (2005) *The Treatment of Diarrhoea. A Manual for Physicians and Other Senior Health Workers*, 4th edn. WHO, Geneva, Switzerland.

WHO (2013) *World Health Statistics 2013*. World Health Organization, Geneva.

Wilson JM, Chandler GN, Muslihatun & Jamiluddin (1991) Hand-washing reduces diarrhoea episodes: a study in Lombok, Indonesia. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **85**, 819–821.

Wolf J, Bonjour S & Prüss-Ustün A (2013) An exploration of multilevel modeling for estimating access to drinking-water and sanitation. *Journal of Water and Health* **11**, 64–77.

Wolf J, Prüss-Ustün A, Cumming O *et al.* (2014) Assessing the impact of drinking-water and sanitation on diarrhoeal disease in low- and middle-income settings: a systematic review and meta-regression. *Tropical Medicine and International Health*. doi: 10.1111/tmi.12331.

World Health Organisation (2009) WHO Guidelines on Hand Hygiene in Health Care: a Summary. First Global Patient Safety Challenge. Clean Care is Safer Care. http://www.chp.gov.hk/files/pdf/who_ier_psp_200907_eng.pdf (Accessed December 2013).

Wu GD, Lewis JD, Hoffmann C *et al.* (2010) Sampling and pyrosequencing methods for characterizing bacterial communities in the human gut using 16s sequence tags. *BMC Microbiology* **10**, 206.

© 2014 John Wiley & Sons Ltd

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. PRISMA guidelines checklist.

Appendix S2. Details of studies on hygiene and diarrhoea.

Appendix S3. Publication bias.

Appendix S4. Details of studies on hygiene and diarrhoea.

Appendix S5. Sample data extraction sheet.

Appendix S6. Blinding study participants in hygiene promotion interventions.

Corresponding Author Matthew C. Freeman, Department of Environmental Health, Rollins School of Public Health, Emory University, 1518 Clifton Road NE, CNR 2027, Atlanta, GA, USA. E-mail: mcfreem@emory.edu

© 2014 John Wiley & Sons Ltd

VOLUME 19 NO 8 PP 894–905 AUGUST 2014

Burden of disease from inadequate water, sanitation and hygiene in low- and middle-income settings: a retrospective analysis of data from 145 countries

Annette Prüss-Ustün[1], Jamie Bartram[2], Thomas Clasen[3], John M. Colford Jr[4], Oliver Cumming[5], Valerie Curtis[5], Sophie Bonjour[1], Alan D. Dangour[5], Jennifer De France[1], Lorna Fewtrell[6], Matthew C. Freeman[3], Bruce Gordon[1], Paul R. Hunter[7,8], Richard B. Johnston[1,9], Colin Mathers[10], Daniel Mäusezahl[11,12], Kate Medlicott[1], Maria Neira[1], Meredith Stocks[3], Jennyfer Wolf[1,11,12] and Sandy Cairncross[5]

1 *Department of Public Health and Environment, World Health Organization, Geneva, Switzerland*
2 *Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*
3 *Rollins School of Public Health, Emory University, Atlanta, GA, USA*
4 *School of Public Health, University of California, Berkeley, Berkeley, CA, USA*
5 *London School of Hygiene and Tropical Medicine, London, UK*
6 *Centre for Research into Environment and Health, Aberystwyth University, Aberystwyth, UK*
7 *Norwich Medical School, University of East Anglia, Norwich, UK*
8 *Department of Environmental Health, Tshware University of Technology, Pretoria, South Africa*
9 *EAWAG, Swiss Federal Institute of Aquatic Science and Technology, Dübendorf, Switzerland*
10 *Department of Health Statistics and Information Systems, World Health Organization, Geneva, Switzerland*
11 *Swiss Tropical and Public Health Institute, Basel, Switzerland*
12 *University of Basel, Basel, Switzerland*

Abstract

OBJECTIVE To estimate the burden of diarrhoeal diseases from exposure to inadequate water, sanitation and hand hygiene in low- and middle-income settings and provide an overview of the impact on other diseases.

METHODS For estimating the impact of water, sanitation and hygiene on diarrhoea, we selected exposure levels with both sufficient global exposure data and a matching exposure-risk relationship. Global exposure data were estimated for the year 2012, and risk estimates were taken from the most recent systematic analyses. We estimated attributable deaths and disability-adjusted life years (DALYs) by country, age and sex for inadequate water, sanitation and hand hygiene separately, and as a cluster of risk factors. Uncertainty estimates were computed on the basis of uncertainty surrounding exposure estimates and relative risks.

RESULTS In 2012, 502 000 diarrhoea deaths were estimated to be caused by inadequate drinking water and 280 000 deaths by inadequate sanitation. The most likely estimate of disease burden from inadequate hand hygiene amounts to 297 000 deaths. In total, 842 000 diarrhoea deaths are estimated to be caused by this cluster of risk factors, which amounts to 1.5% of the total disease burden and 58% of diarrhoeal diseases. In children under 5 years old, 361 000 deaths could be prevented, representing 5.5% of deaths in that age group.

CONCLUSIONS This estimate confirms the importance of improving water and sanitation in low- and middle-income settings for the prevention of diarrhoeal disease burden. It also underscores the need for better data on exposure and risk reductions that can be achieved with provision of reliable piped water, community sewage with treatment and hand hygiene.

keywords burden of disease, diarrhoea, water, sanitation, hygiene

Introduction

Information on the burden of disease, its causes and prevention is fundamental to health policy. Among other things, an improved understanding of the disease burden and the relative contribution of key risks points towards opportunities for preventive action in a context of increasing healthcare costs (OECD 2013).

In recognition of the value of this information, several comprehensive disease burden studies, focusing mainly on

© 2014 The Authors. Tropical Medicine and International Health published by John Wiley & Sons Ltd.
This is an open access article under the terms of the Creative Commons Attribution License,
which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

diarrhoeal diseases, have been undertaken in recent decades (Murray & Lopez 1996; WHO 2002, 2004, 2009; Prüss-Ustün *et al.* 2008; Lim *et al.* 2012). These report important changes in the roles of various risk factors (Clasen *et al.* 2014).

Inadequate drinking water, sanitation and hygiene (WASH) are important risk factors, particularly in low-income settings. In 2011, an estimated 768 million people relied on 'unimproved' water supplies (as defined by the WHO/UNICEF Joint Monitoring Program for Water and Sanitation – JMP), which are thought to have high levels of pathogen contamination (WHO & UNICEF 2013a). Many more use sources that are classified as 'improved' but are still unsafe for consumption (Bain *et al.* 2014). More than 2.5 billion people lack access to an improved sanitation facility (WHO & UNICEF 2013a). Inadequate hand hygiene practices have been estimated to affect 80% of the population globally (Freeman *et al.* 2014b).

The health risks from inadequate WASH have been documented previously (Esrey *et al.* 1991; Fewtrell *et al.* 2005; Waddington *et al.* 2009). However, the unpublished review on which the 2010 Global Burden of Disease (GBD) study is based (Lim *et al.* 2012) departed from earlier reviews by finding no additional benefit from further improvements such as higher water quality or continuous piped supply over the exposure defined as using 'other improved water supplies' (Engell & Lim 2013). A more recent systematic review, however, is largely consistent with previous evidence (Wolf *et al.* 2014).

Estimating the impact of WASH on diarrhoeal diseases has commonly been assessed with comparative risk assessment methods (Ezzati *et al.* 2002; WHO 2004; Lim *et al.* 2012), although other methods such as population intervention models could also be considered (Clasen *et al.* 2014). Other diseases cannot currently be estimated with such methods due to insufficient evidence and require alternative approaches. As these would require considerable additional assessments and analyses, they are not analysed in detail in this article.

Accrual of substantive recent evidence, as well as trends in the total diarrhoea burden, justifies the revision of methods and estimates of the burden of diarrhoeal disease associated with inadequate WASH. While the estimate presented focuses mainly on low- and middle-income settings, the approach used can accommodate a wider range of settings. An overview of previous findings on the impacts of WASH on other diseases than diarrhoea is also provided.

Methods

Framework for estimation

For the purpose of this assessment, we defined WASH to include the following transmission pathways: (i) ingestion of water – for example diarrhoea, arsenicosis, fluorosis; (ii) lack of water linked to inadequate personal hygiene – for example diarrhoea, trachoma, scabies; (iii) poor personal, domestic or agricultural hygiene – for example diarrhoea, Japanese encephalitis; (iv) contact with water – for example schistosomiasis; (v) vectors proliferating in water – for example malaria; and (vi) contaminated water systems – for example legionellosis (Prüss *et al.* 2002). The impact of WASH on most diseases cannot be precisely estimated, because of insufficient information on global exposures of concern or lack of widely applicable risk estimates matching the exposures. Table 1 provides

Table 1 Diseases related to water, sanitation and hygiene

Disease outcomes and range of the fraction of disease globally attributable to WASH*			
Contribution of WASH not quantified at global level	0–33%	33–66%	66–100%
Hepatitis A, E, F	Onchocerciasis	Lymphatic filariasis	Ascariasis
Legionellosis		Malaria	Hookworm
Scabies		Undernutrition and its consequences	Trichuriasis
Arsenicosis		Drowning	Dengue
Fluorosis			Schistosomiasis
Methaemoglobinaemia			Japanese encephalitis
			Trachoma

WASH, water, sanitation and hygiene.
Includes diseases other than diarrhoea.
Adapted from: Prüss-Ustün and Corvalán (2007), Prüss-Ustün *et al.* (2008).
*Estimates based on previous assessments combining systematic literature reviews with expert opinion.

© 2014 The Authors. Tropical Medicine and International Health published by John Wiley & Sons Ltd.

an overview of main diseases related to WASH and previously estimated attributable fractions by disease. An overview of previous results is provided in the Discussion section.

The burden of diarrhoea associated with inadequate WASH can, however, be estimated using comparative risk assessment methods (Ezzati *et al.* 2002; WHO 2004; Lim *et al.* 2012) and is addressed in detail in this article. This approach estimates the proportional reduction in disease or death that would occur if exposures were reduced to an alternative baseline level bearing a minimum risk (also referred to as theoretical minimum risk), while other conditions remain unchanged. It is derived from the proportion of people exposed to the conditions of interest and the relative risk of disease related to the exposure.

Proportion of the population exposed and relative risk values were specified by level of exposure, age group and sex. Estimates were calculated for the 145 low- and middle-income countries (WHO Member States with income levels defined by the World Bank for 2012), which were then grouped into the six WHO Regions (WHO 2013b, Supporting Information). The estimation was performed for the year 2012 (WHO 2013a).

Selection of exposure-risk pairs for diarrhoeal disease

Water. Exposure levels were selected according to the availability of exposure data and corresponding exposure-risk information (Wolf *et al.* 2013, 2014) and included the following: (i) using an unimproved water source; (ii) using an improved water source other than piped to premises; (iii) using basic piped water on premises (improved source); and (iv) using a water filter or boiling water in the household (on water from an unimproved or improved source).

As piped water on premises is often intermittent and of suboptimal quality, the risks associated with having access to a 'basic' piped water supply in most settings of low- and middle-income countries are not equal to zero. A single study (meeting the criteria for the systematic review – Wolf *et al.* 2014) was identified which could inform this estimate of risk (i.e. by demonstrating the effect of improving water quality through the better operation of an existing piped water system in a context relevant to a low- or middle-income country). This study (Hunter *et al.* 2010) showed a significant and large reduction in diarrhoea and had an effect size of 0.32 (95% CI: 0.14–0.74). This evidence is also supported by information from disease outbreaks resulting from contaminated piped water (Mermin *et al.* 1999) and by interventions to further improve water supply systems in developed countries (Gunnarsdottir *et al.* 2012).

However, given that only one study is currently available on the improvement beyond piped water to premises, a conservative approach was taken and the next best exposure level was used as the counterfactual (i.e. baseline) exposure (which consists of using a filter to treat water at household level – Wolf *et al.* 2014). Household water filtering is therefore used as a proxy for further improvement beyond currently available improved water sources.

It has been documented that lower water use (Cairncross & Feachem 1993; Royal Scientific Society 2013) and increasing distance to a water source (Tonglet *et al.* 1992; Galiani *et al.* 2007; Pickering & Davis 2012; Evans *et al.* 2013) have been associated with an increased risk of diarrhoea. The number of studies identified, however, was not sufficient to derive a pooled estimate. To account for this, in the current analysis, people living at distances greater than a 30-min round trip from their water source were assumed to have unimproved water.

Among assessed household water treatment methods, after adjusting for bias introduced through non-blinding of study participants, only use of a filter showed significant reductions in diarrhoeal disease morbidity; the effect of other methods, such as solar disinfection and chlorination, became non-significant after adjusting for bias (Wolf *et al.* 2014). Boiling of drinking water is a widespread practice in certain areas (Rosa & Clasen 2010), and while boiling may be an effective water treatment, recontamination has been reported (Clasen *et al.* 2008; Rosa *et al.* 2010). Only one study, however, has reported on the health effect of this practice (Iijima *et al.* 2001) and, for the purposes of this analysis, people who boil their drinking water have been classified with those who filter their water. Safe storage was assumed for all households filtering or boiling their water as information on recontamination was not available. Households filtering or boiling their water, with subsequent safe storage, represent the minimum risk group in this analysis.

The exposure levels for inadequate drinking water, used in this analysis, along with additional levels of exposure to water with improved quality or quantity that are not currently supported by sufficient epidemiological evidence, are shown in Figure 1. This approach can accommodate further exposure levels when supported by sufficient evidence. The exposure–risk relationships (taken from Wolf *et al.* 2014) are summarised in Table 2.

Sanitation. The only exposure levels for inadequate sanitation with both globally representative exposure data and sufficient evidence for its effect on diarrhoea were the use of an improved or unimproved sanitation facility (as defined by JMP – WHO & UNICEF 2013b). Evidence based on two studies suggests that further reduction in

 © 2014 The Authors. Tropical Medicine and International Health published by John Wiley & Sons Ltd.

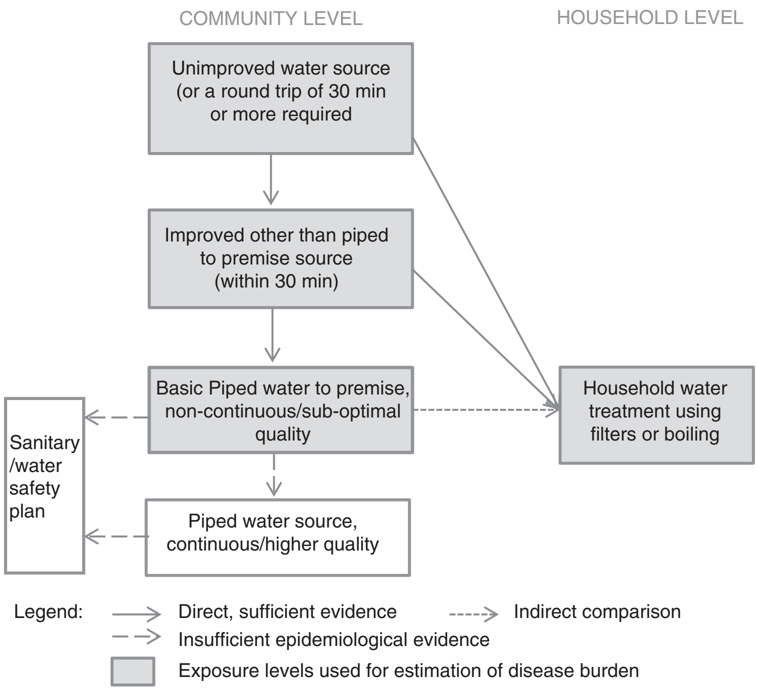


Figure 1 Exposure levels and associated risks for drinking water-related burden of disease estimates.

Table 2 Effect sizes used for estimating diarrhoeal disease burden estimates from inadequate drinking water

	Outcome water		
Baseline water	Improved source other than piped to premise	Basic piped water to premise‡	Filter and safe storage in the household*
Unimproved source	0.89 (0.78–1.01)	0.77 (0.64–0.92)	0.55 (0.38–0.81)
Improved source other than piped to premise		0.86 (0.72–1.03)	0.62 (0.42–0.93)
Basic piped water to premise‡			0.72 (0.47–1.11)†

Not all steps of this body of evidence may be significant; however, risk estimates of the overall chain of improvements in water and sanitation are significant.
Adapted from: Wolf *et al.* (2014); Figures constitute relative risks (and 95% confidence intervals).
*Estimate for filtering water in the household also used for boiling water.
†Obtained through indirect comparison with improved non-piped or community water source in the meta-regression.
‡possibly non-continuous, and/or of sub-optimal quality.

diarrhoea morbidity can be achieved with sewer connections in urban settings (although it should be noted that potential adverse impacts of untreated sewage on receiving communities have not been well studied). As the evidence for sewer connection was limited, it was not retained for the current diarrhoeal disease burden estimates. The overall effect for access to an improved sanitation facility on reduction in diarrhoea morbidity used was 28% (RR 0.72, 95% CI 0.59–0.88) from Wolf *et al.* (2014).

Hygiene. An updated review of the evidence linking interventions of the promotion of hand hygiene with soap and diarrhoea morbidity (Freeman *et al.* 2014b) showed a 40% reduction in diarrhoea (RR 0.60, 95% CI 0.53–0.68). When correcting for bias due to non-blinding in studies using subjective health outcomes (Savović *et al.* 2012), this estimate changes to 0.77 (95% CI 0.32–1.86) and becomes non-significant. It should be noted, however, that this bias correction is based on a wide array of medical

© 2014 The Authors. Tropical Medicine and International Health published by John Wiley & Sons Ltd.

interventions, which may be of limited applicability to this type of intervention. A 23% reduction in diarrhoeal disease risk remains the best estimate of the effect of handwashing promotion.

Estimation of the proportion of people exposed

We drew on the definitions of the use of improved water sources, piped water to premises and improved sanitation of the JMP (WHO & UNICEF 2013b). Exposure by country was estimated by multilevel modelling as previously described (Wolf *et al.* 2013) based on over 1400 data points from national and international household surveys and censuses reported by JMP (WHO & UNICEF 2013b). Households with a travel time to the water source >30 min were deducted from improved sources at community level. We applied a linear two-level model with a logit transformation of the dependant variable (use of improved water source, improved sanitation or piped water to premises) to obtain estimates for the year 2012 (Wolf *et al.* 2013). The model also used a cubic spline transformation of the main predictor (time) and WHO region (WHO 2013b) as covariates, as well as a random intercept and slope by country.

Travel time of >30 min was reported by 178 household surveys [Demographic Health Surveys (USAID 2014), Multiple Indicator Cluster Surveys (UNICEF 2014), World Health Surveys (WHO 2014)] from 79 countries and was estimated for the year 2012 using a similar but simplified approach with a linear two-level model, with time and region as covariates and a random intercept and slope by country.

The proportion of country populations practising water treatment in the household was estimated using data from 78 household surveys [Demographic Health Surveys (USAID 2014), Multiple Indicator Cluster Surveys (UNICEF 2014), World Health Surveys (WHO 2014)] from 68 countries containing information on reported household water treatment (including chlorination, boiling, filtering, solar disinfection and others). A similar modelling approach as for travel time >30 min was used to obtain the proportion of households boiling or filtering their drinking water for the year 2012, with the difference that it did not use a random slope at country level. For countries with no information, the regional mean trend was taken as the best estimate.

Based on a review of water quality (Bain *et al.* 2014), no significant proportion of households in low- and middle-income settings are currently assumed to benefit from regulated and fully functional piped water supply systems.

The hand-washing prevalence, based on 75 observations, was taken from the systematic review reported by Freeman *et al.* (2014b).

Population-attributable fractions of diarrhoeal disease for individual risk factor and for the cluster

For each risk factor, the population-attributable fraction (PAF) was estimated by comparing current exposure distributions to a counterfactual distribution, for each exposure level, sex and age group, and by country:

$$\mathrm{PAF} = \frac{\sum_{i=1}^{n} p_i(\mathrm{RR}_i - 1)}{\sum_{i=1}^{n} p_i(\mathrm{RR}_i - 1) + 1} \quad (1)$$

where p_i and RR_i are the proportion of the exposed population and the relative risk at exposure level i, respectively, and n is the total number of exposure levels.

Exposure to inadequate WASH is related by similar mechanisms and policy interventions. The following formula has been proposed for the estimation of burden attributable to a cluster of risk factors (Lim *et al.* 2012):

$$\mathrm{PAF} = 1 - \prod_{r=1}^{R}(1 - \mathrm{PAF}_r) \quad (2)$$

where r is the individual risk factor and R the total number of risk factors accounted for in the cluster. This formula assumes that risk factors are independent. This assumption is likely to be an oversimplification for WASH as, for instance, handwashing promotion is unlikely to be effective if water quantity is limited. However, this approach has been applied in the assessment for ease of interpretation of the results, and in the absence of a more suitable approach.

Estimation of burden of diarrhoeal disease

The burden of disease attributable to each risk factor (AB), or to the cluster of risk factors, in deaths or disability-adjusted life years (DALYs), was obtained by multiplying the PAFs by the total burden of disease of diarrhoea (B):

$$\mathrm{AB} = \mathrm{PAF} \times \mathrm{B} \quad (3)$$

The PAFs were applied equally to burden of disease in deaths and DALYs, and we assumed that the case fatality related to WASH was the same as the mean case fatality of diarrhoeal diseases.

 © 2014 The Authors. Tropical Medicine and International Health published by John Wiley & Sons Ltd.

Uncertainty estimates

To estimate uncertainty intervals, we developed a Monte Carlo simulation of the results with 5000 draws of the exposure distribution, and of the relative risks. As lower and upper uncertainty estimates, we used the 2.5 and 97.5 percentiles of the attributable fractions, attributable deaths and DALYs resulting from the Monte Carlo analysis (Palisade 2013).

Results

The worldwide distribution of exposure and the resulting attributable deaths and DALYs from diarrhoeal disease associated with inadequate WASH practices were estimated for the year 2012.

Exposure estimates

In low- and middle-income countries, it was found that in 31% of households people report boiling or filtering their water; 31% of households use piped water to premises; 27% use a non-piped or community water source; 12% use only an unimproved water source and do not filter or boil their water; and on the sanitation side, 58% of households were estimated to use an improved sanitation facility, respectively.

Handwashing after using a sanitation facility or contact with faecal material is practised by 19% of people worldwide (based on observation data), with a mean of 14% in low- and middle-income countries, and 43% in high-income countries (Freeman *et al.* 2014b). The estimated regional distribution of exposure is presented in Table 3 (drinking water) and Table 4 (sanitation and hygiene); more detail by country is provided in the Supporting Information.

Estimates of the burden of diarrhoeal disease

The resulting burden of diarrhoea, in low- and middle-income countries, linked to these exposures amounts to 502 000 deaths associated with inadequate water and 280 000 deaths due to inadequate sanitation from a total of 1.50 million diarrhoeal deaths in the year 2012.

In addition, it was estimated that 297 000 deaths could be prevented by the promotion of hand hygiene, although this estimate is based on an effect size which is not statistically significant. The estimate without adjusting for non-blinding would be 539 000 deaths.

Together (using Equation 2), the deaths attributable to inadequate water and sanitation amount to 685 000. Adding (bias-adjusted) inadequate hand hygiene increases this estimate to 842 000 deaths, which represents 1.5%

Table 3 Distribution of the population to exposure levels of drinking water, by region, for 2012

Region	Use of piped water on premises		Use of non-piped or community sources		Use of unimproved water sources		
	Proportion of total population by region						
Filtering/boiling in the household	Without	With	Without	With	Without	With	Total*
Sub-Saharan Africa	0.16	0.03	0.36	0.04	0.38	0.04	1.00
America, LMI	0.58	0.30	0.05	0.01	0.05	0.01	1.00
Eastern Mediterranean, LMI	0.54	0.04	0.25	0.01	0.15	0.01	1.00
Europe, LMI	0.54	0.27	0.10	0.05	0.03	0.02	1.00
South-East Asia	0.16	0.09	0.48	0.14	0.09	0.04	1.00
Western Pacific, LMI	0.31	0.35	0.13	0.14	0.04	0.04	1.00
Total LMI	0.31	0.18	0.27	0.09	0.12	0.03	1.00

LMI, low and middle income.
*The total may not equal the sum of numbers displayed in the rows due to rounding error.

© 2014 The Authors. Tropical Medicine and International Health published by John Wiley & Sons Ltd.

of the global disease burden in 2012. A regional summary of attributable deaths and DALYs for each of the risk factors is provided in Tables 5–7, and the cluster data are shown in Table 8. Detail by country can be found in the Supporting Information.

Among children under 5 years, 361 000 deaths could have been prevented through reduction of these risks in low- and middle-income settings, representing 5.5% of the total burden of disease in this age group.

Table 4 Distribution of the population to exposure levels of sanitation and hygiene, by region, for 2012

Region	Access to improved sanitation facility	Prevalence of handwashing after contact with excreta
	Proportion of total population	
Sub-Saharan Africa	0.35	0.14
America, HI	–	0.49
America, LMI	0.83	0.16
Eastern Mediterranean, HI	–	0.44
Eastern Mediterranean, LMI	0.68	0.14
Europe, HI	–	0.44
Europe, LMI	0.87	0.15
South-East Asia	0.47	0.17
Western Pacific, HI	–	0.43
Western Pacific, LMI	0.64	0.13
Total	–	0.19
Total HI	–	0.43
Total LMI	0.58	0.14

LMI, low and middle income; HI, high income; –, not estimated.

Discussion

These estimates of the burden of diarrhoea attributable to inadequate WASH are lower than previous estimates coordinated by WHO (WHO 2009) and higher than the recent estimate of the 2010 GBD study (Lim *et al.* 2012). There is strong evidence that the number of deaths due to diarrhoeal disease has dropped considerably since 2004 (WHO 2009; Liu *et al.* 2012; Lozano *et al.* 2012) due to a combination of improved management of diarrhoeal disease (especially the use of oral rehydration therapy) and better access to water and sanitation. This is in line with the lower burden of diarrhoeal disease estimates in both the 2010 GBD study and the current work. The larger burden of diarrhoeal disease found in this study, compared with the 2010 GBD study, can be explained by the different counterfactuals used, the consideration in this study of disease burden due to poor hand hygiene and to the adjustments made to account for bias resulting from the lack of blinding

Table 5 Diarrhoea burden attributable to inadequate water by region, 2012

Region	PAF (95% CI)	Deaths (95% CI)	DALYs (in 1000s) (95% CI)
Sub-Saharan Africa	0.38 (0.19–0.50)	229 316 (106 664–300 790)	17 587 (8152–23 065)
America, LMI	0.26 (0.14–0.33)	6441 (624–9748)	522 (39–801)
Eastern Mediterranean, LMI	0.36 (0.19–0.46)	50 409 (22 498–66 604)	4046 (1784–5351)
Europe, LMI	0.16 (0.10–0.26)	1676 (196–2606)	174 (19–271)
South-East Asia	0.32 (0.11–0.44)	207 773 (59 708–293 068)	10 748 (3097–15 160)
Western Pacific, LMI	0.20 (0.09–0.27)	6448 (2005–9469)	716 (198–1081)
Total LMI	0.34 (0.16–0.45)	502 061 (217 119–671 945)	33 793 (14 930–44 871)

DALYs, disability-adjusted life years; PAF, population-attributable fraction; LMI, low and middle income.

Table 6 Diarrhoea burden attributable to inadequate sanitation by region, 2012

Region	PAF (95% CI)	Deaths (95% CI)	DALYs (in 1000s) (95% CI)
Sub-Saharan Africa	0.21 (0.07–0.31)	126 294 (42 881–186 850)	9694 (3291–14 333)
America, LMI	0.09 (0.03–0.15)	2370 (774–3724)	188 (61–295)
Eastern Mediterranean, LMI	0.17 (0.06–0.26)	24 441 (8339–36 809)	1914 (651–2887)
Europe, LMI	0.03 (0.01–0.06)	352 (107–597)	36 (11–61)
South-East Asia	0.19 (0.06–0.28)	123 279 (42 116–185 426)	6376 (2177–9595)
Western Pacific, LMI	0.11 (0.04–0.17)	3709 (1171–5954)	444 (136–737)
Total LMI	0.19 (0.07–0.29)	280 443 (95 699–417 482)	18 650 (6380–27 769)

DALYs, disability-adjusted life years; PAF, population-attributable fraction; LMI, low and middle income.

© 2014 The Authors. Tropical Medicine and International Health published by John Wiley & Sons Ltd.

Table 7 Diarrhoea burden attributable to inadequate hand hygiene by region, 2012

Region	PAF (95% CI)	Deaths (95% CI)	DALYs (in 1000s) (95% CI)
Sub-Saharan Africa	0.20 (0–0.61)	122 955 (0–365 911)	9411 (0–28 006)
America, HI	0.13 (0–0.45)	–	–
America, LMI	0.20 (0–0.60)	5026 (0–15 013)	416 (0–1243)
Eastern Mediterranean, HI	0.14 (0–0.48)	–	–
Eastern Mediterranean, LMI	0.21 (0–0.61)	28 699 (0–85 369)	2314 (0–6884)
Europe, HI	0.14 (0–0.48)	–	–
Europe, LMI	0.19 (0–0.59)	1972 (0–5975)	202 (0–611)
South-East Asia	0.20 (0–0.60)	131 519 (0–392 018)	6857 (0–20 444)
Western Pacific, HI	0.16 (0–0.50)	–	–
Western Pacific, LMI	0.21 (0–0.61)	6690 (0–19 891)	758 (0–2253)
Total	0.20 (0–0.60)	–	–
Total HI	0.14 (0–0.47)	–	–
Total LMI	0.20 (0–0.60)	296 860 (0–885 355)	19 958 (0–59 491)

DALYs, disability-adjusted life years; PAF, population-attributable fraction; LMI, low and middle income; HI, high income; –, not estimated.

Table 8 Diarrhoea deaths attributable to the cluster of inadequate water, and inadequate sanitation and hand hygiene

	Inadequate water, sanitation and hand hygiene		Inadequate water and sanitation	
Region	PAF (95% CI)	Deaths (95% CI)	PAF (95% CI)	Deaths (95% CI)
Sub-Saharan Africa	0.61 (0.55–0.66)	367 605 (326 795–402 438)	0.51 (0.47–0.55)	307 493 (276 989–335 899)
America, LMI	0.46 (0.36–0.50)	11 519 (9310–13 616)	0.32 (0.28–0.34)	8125 (7101–9158)
Eastern Mediterranean, LMI	0.58 (0.47–0.66)	81 064 (65 359–94 707)	0.47 (0.40–0.53)	65 700 (55 266–75 876)
Europe, LMI	0.35 (0.28–0.46)	3564 (2462–4678)	0.19 (0.19–0.27)	1970 (1654–2280)
South-East Asia	0.56 (0.36–0.70)	363 904 (225 359–477 720)	0.45 (0.31–0.57)	291 763 (193 198–383 423)
Western Pacific, LMI	0.44 (0.31–0.54)	14 160 (10 035–18 009)	0.29 (0.23–0.33)	9429 (7519–11 242)
Total LMI	0.58 (0.48–0.65)	841 818 (699 059–963 626)	0.47 (0.40–0.53)	684 479 (580 456–780 463)

PAF, population-attributable fraction; LMI, low and middle income.

in studies on different household water treatment interventions.

The estimate of diarrhoeal disease burden attributable to inadequate WASH practices is limited by the underlying evidence, which remains scarce for the transition between an improved water source and a functional and regulated water supply system. The evidence is also limited on sanitation; in particular, there is a dearth of information on wastewater and excreta management from improved facilities and the impact this has on downstream communities when it is disposed of, untreated, to the environment. In addition, a conservative effect size was chosen for the impact of hand hygiene on diarrhoea, based on figures adjusted for possible bias (Freeman *et al.* 2014b). This approach is, thus, more conservative than previous estimates (Curtis & Cairncross 2003).

Exposure data are limited in terms of representative measures of water quality. Handwashing prevalence has not yet been widely assessed, although studies have shown surprisingly little variation across countries and population groups within income groups (Freeman *et al.* 2014b). Surveys reporting the use of household water treatment options have shown some over-reporting. This would, however, have led to an underestimation of diarrhoeal disease burden in this analysis as households reported as filtering or boiling their water were assigned as having no risk related to inadequate WASH.

Certain potentially relevant exposure/exposure-risk pairs cannot yet be considered. These include, for example, incomplete community sanitation (i.e. incomplete community coverage) meaning that contact with excreta may persist within the community. Another example consists in improved sanitation facilities without treatment, which are likely to result in exposure of receiving communities to untreated sewage and could affect 22% of the global population (Baum *et al.* 2013). Also, this assessment is limited to non-outbreak situations.

The global assessment of exposure to faecal contamination through drinking water (Bain *et al.* 2014) has highlighted that piped water supplies in the American,

© 2014 The Authors. Tropical Medicine and International Health published by John Wiley & Sons Ltd.

European and Western Pacific low- and middle-income regions show particularly low contamination in urban areas, with <10% of investigated samples faecally contaminated. The relative risks from the meta-regression (Wolf *et al.* 2014) may overrate the risks of water sources with such low proportions of contamination, as they have been relatively poorly investigated in the underlying epidemiological literature. If assuming that urban piped supplies in those regions carry no increased risk for diarrhoea, the total diarrhoea burden from inadequate water sources would have decreased from 502 000 to 497 000 deaths in 2012, with 2800 fewer deaths in the American region, 700 fewer deaths in the European region and 1500 fewer deaths in the Western Pacific region, respectively. The contamination of piped water in those regions may, however, have been underestimated because (i) studies tend to take place in formal urban areas and especially in capital cities, (ii) the assessment reported the per cent of samples containing contamination rather than compliance with WHO guidelines, and (iii) the focus was on water quality at the source and not stored at home or sampled just before consumption (Bain *et al.* 2014).

The current estimation has focused on diarrhoeal diseases and has not re-analysed the impact on other diseases, which have been linked to inadequate WASH, including soil-transmitted helminth infections (Ziegelbauer *et al.* 2012), vector-borne diseases (Emerson *et al.* 2000), environmental enteropathy (Humphrey 2009). Furthermore, improved WASH has been shown to significantly reduce undernutrition (Dangour *et al.* 2013), a major cause of mortality in children under 5 years of age (Black *et al.* 2013). Previous estimates, based on literature reviews combined with expert opinion, have, however, attempted to provide quantitative estimates of other diseases than diarrhoea, with the following results: In 2004, 881 000 deaths were attributed to water supply, sanitation and hygiene, mainly through the effect on undernutrition and its consequences, but also from schistosomiasis and lymphatic filariasis. The impacts of water resource management, mainly on malaria but also dengue and Japanese encephalitis, were estimated to amount to 557 000 deaths in the same year. Finally, safer water environments could have prevented 244 000 deaths from drowning, globally (Prüss-Ustün & Corvalán 2007; Prüss-Ustün *et al.* 2008). Although these figures would require an update, they indicate that the impacts of WASH on other diseases combined are likely to be even higher than those on diarrhoea.

The estimation of diarrhoeal disease burden relies on proxies such as access to water and sanitation facilities rather than water quality, water quantity or behaviours associated with these facilities (such as consistent or exclusive use by individuals) which are also a determining factor in characterising actual exposure. They were selected because of the available exposure information and their best match in the latest findings on risk estimates from the epidemiological literature. Greater precision of estimates is expected with better assessment of these more proximal risks and their population exposures. In addition, in common with a number of other disease burden estimates (Lim *et al.* 2012), the estimate is based on risk estimates for morbidity rather than mortality.

Due to these limitations, it is unlikely that this estimate accounts for the full health benefits in diarrhoea reduction that could be achieved by improvements in WASH. By relying on evidence of interventions that have often only achieved limited or partial compliance, this disease burden reflects reduction in diarrhoea that can be achieved with currently documented interventions in low- and middle-income countries. It is unlikely that the estimate accounts for the full reduction in burden that could be achieved by well-functioning water supply or sewage systems. For example, this estimate does not reflect health benefits that may be achieved through improvements following the implementation of management systems such as water safety plans (Gunnarsdottir *et al.* 2012), a proactive, comprehensive approach to managing risks throughout the water supply system. In addition, the estimates do not account for the potential impact of improvements to institutional settings, such as health centres and schools, and where studies have shown impact on other age groups (Dreibelbis *et al.* 2014; Freeman *et al.* 2014a).

Through the reassessment of the evidence linking drinking water to diarrhoea using a more scaled approach (Wolf *et al.* 2014), it has been possible to develop an estimate that takes account of the reduction in risks when further improving water quality or quantity over what is currently defined as an ‘improved source’, which was not carried out in more basic assessments (Lim *et al.* 2012). Indeed, improved water sources have been shown to carry important contamination and risks to a significant share of the population (Bain *et al.* 2014).

The separate assessment of the risks of WASH is not ideal, as those risk factors are likely to have linkages in terms of both exposure and effects on diarrhoeal risk. This choice was made, however, to facilitate policy interpretation, and because of the availability of factor-specific data sets. Nevertheless, the validity of some of these aspects, such as joint interventions, has been assessed in

 © 2014 The Authors. Tropical Medicine and International Health published by John Wiley & Sons Ltd.

the meta-regression (Wolf *et al.* 2014) by testing the significance of covariates.

It is acknowledged that this assessment does not account for a number of relevant exposures including access to a continuous supply of safe piped water, community sewerage which prevents exposure to untreated wastewater or excreta (rather than focusing on household exposure alone) – evidence in this area is still limited. The counterfactual for the current assessment corresponds to currently achievable options that have been documented in developing countries and does not yet take into account the improvements that could be made beyond such a status. Although this assessment is limited to low- and middle-income settings, it is acknowledged that health risks exist even in apparently well-managed drinking water systems in developed countries (Zmirou *et al.* 1995; Naumova *et al.* 2005; Lake *et al.* 2007; Tinker *et al.* 2009), and further improvements have been shown to reduce health risks (Gunnarsdottir *et al.* 2012). This assessment does, however, act as a step towards a more comprehensive future estimate.

Conclusion

This updated estimate of the diarrhoeal disease burden due to inadequate WASH has made use of a meta-regression approach to the evidence, based on specific information of baseline and outcome situation for each relevant study. This approach has resulted in a more refined estimate of disease burden according to exposure specificities. It can accommodate further consolidation as evidence accrues. It confirms the important role of the provision of safe water, adequate sanitation and hygiene promotion to protect health. Previous finding indicating an important impact of WASH on other diseases than diarrhoea further strengthens these findings.

Acknowledgements and disclaimer

The study was partially funded by the United Kingdom Department for International Development (DFID). The funder had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript. Some authors are staff members of the World Health Organization (WHO) or other institutions. The authors alone are responsible for the views expressed in this publication, which do not necessarily represent the views, decisions or policies of the WHO, the UK DFID or other institutions. This article should not be reproduced for use in association with the promotion of commercial products, services or any legal entity. The WHO does not endorse any specific organisation or products. Any reproduction of this article cannot include the use of the WHO logo.

Conflict of interest

Thomas Clasen has participated in research and consulting services supported by Unilever and Vestergaard-Frandsen, which manufacture and sell household or other point of use water filtration devices.

References

Bain R, Cronk R, Bonjour S *et al.* (2014) Assessment of the level of exposure to fecally contaminated drinking water in developing countries. *Tropical Medicine and International Health* (this issue).

Baum R, Luh J & Bartram J (2013) Sanitation: a global estimate of sewerage connections without treatment and the resulting impact on MDG progress. *Environmental Science & Technology* **47**, 1994–2000.

Black RE, Victora CG, Walker SP *et al.* (2013) Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet* **382**, 427–477.

Cairncross S & Feachem R (1993). *Environmental Health Engineering in the Tropics. An Introductory Text.* John Wiley & Sons, Chichester.

Clasen T, Mclaughlin C, Nayaar N *et al.* (2008) Microbiological effectiveness and cost of disinfecting water by boiling in semi-urban India. *American Journal of Tropical Medicine & Hygiene* **79**, 407–413.

Clasen T, Prüss-Ustün A, Mathers C, Cumming O, Cairncross S & Colford JM Jr (2014) Estimating the impact of unsafe water, sanitation and hygiene on the global burden of disease: evolving and alternative methods. *Tropical Medicine & International Health* (this issue).

Curtis V & Cairncross S (2003) Effect of washing hands with soap on diarrhoea risk in the community: a systematic review. *The Lancet Infectious Diseases* **3**, 275–281.

Dangour AD, Watson L, Cumming O *et al.* (2013) Interventions to improve water quality and supply, sanitation and hygiene practices, and their effects on the nutritional status of children. *The Cochrane Database of Systematic Reviews* **8**, CD009382.

Dreibelbis R, Freeman MC, Greene LE, Saboori S & Rheingans R (2014) The impact of school water, sanitation, and hygiene interventions on the health of younger siblings of pupils: a cluster-randomized trial in Kenya. *American Journal of Public Health* **104**, e91–e97.

Emerson PM, Cairncross S, Bailey RL & Mabey DC (2000) Review of the evidence base for the 'F' and 'E' components of the SAFE strategy for trachoma control. *Tropical Medicine & International Health* **5**, 515–527.

Engell RE & Lim S (2013) Does clean water matter? An updated meta-analysis of water supply and sanitation interventions and diarrhoeal diseases. *The Lancet* **381**, S44.

Esrey SA, Potash JB, Roberts L & Shiff C (1991) Effects of improved water supply and sanitation on ascariasis, diarrhoea,

© 2014 The Authors. Tropical Medicine and International Health published by John Wiley & Sons Ltd.

dracunculiasis, hookworm infection, schistosomiasis, and trachoma. *Bulletin of the World Health Organization* **69**, 609–621.

Evans B, Bartram J, Hunter P *et al.* (2013) *Public Health and Social Benefits of At-House Water Supplies*. University of Leeds, Leeds, UK.

Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S & Murray CJL (2002) Selected major risk factors and global and regional burden of disease. *Lancet* **360**, 1347–1360.

Fewtrell L, Kaufmann RB, Kay D, Enanoria W, Haller L & Colford JM (2005) Water, sanitation, and hygiene interventions to reduce diarrhoea in less developed countries: a systematic review and meta-analysis. *The Lancet Infectious Diseases* **5**, 42–52.

Freeman MC, Clasen T, Dreibelbis R *et al.* (2014a) The impact of a school-based water supply and treatment, hygiene, and sanitation programme on pupil diarrhoea: a cluster-randomized trial. *Epidemiology & Infection* **142**, 340–351.

Freeman M, Stocks M, Cumming O *et al.* (2014b) Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. *Tropical Medicine and International Health* (this issue).

Galiani S, Gonzalez-Rozada M & Schargrodsky E (2007) *Water Expansions in Shantytowns: Health and Savings*. Inter-American Development Bank, Washington, DC.

Gunnarsdottir MJ, Gardarsson SM, Elliott M, Sigmundsdottir G & Bartram J (2012) Benefits of water safety plans: microbiology, compliance, and public health. *Environmental Science & Technology* **46**, 7782–7789.

Humphrey JH (2009) Child undernutrition, tropical enteropathy, toilets, and handwashing. *Lancet* **374**, 1032–1035.

Hunter PR, Ramírez Toro GI & Minnigh HA (2010) Impact on diarrhoeal illness of a community educational intervention to improve drinking water quality in rural communities in Puerto Rico. *BMC Public Health* **10**, 219.

Iijima Y, Karama M, Oundo JO & Honda T (2001) Prevention of bacterial diarrhea by pasteurization of drinking water in Kenya. *Microbiology & Immunology* **45**, 413–416.

Lake IR, Harrison FC, Chalmers RM *et al.* (2007) Case-control study of environmental and social factors influencing cryptosporidiosis. *European Journal of Epidemiology* **22**, 805–811.

Lim SS, Vos T, Flaxman AD *et al.* (2012) A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet* **380**, 2224–2260.

Liu L, Johnson HL, Cousens S *et al.* (2012) Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. *Lancet* **379**, 2151–2161.

Lozano R, Naghavi M, Foreman K *et al.* (2012) Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* **380**, 2095–2128.

Mermin JH, Villar R, Carpenter J *et al.* (1999) A massive epidemic of multidrug-resistant typhoid fever in Tajikistan associated with consumption of municipal water. *The Journal of Infectious Diseases* **179**, 1416–1422.

Murray C & Lopez AD (1996) *The Global Burden of Disease*. World Health Organization, Harvard School of Public Health, World Bank, Geneva.

Naumova EN, Christodouleas J, Hunter PR & Syed Q (2005) Effect of precipitation on seasonal variability in cryptosporidiosis recorded by the North West England surveillance system in 1990–1999. *Journal of Water and Health* **3**, 185–196.

OECD (2013) *Public Spending on Health and Long-Term Care: A New Set of Projections*. Organization for Economic Cooperation and Development, Paris.

Palisade (2013) @Risk 6. http://www.palisade.com/risk

Pickering AJ & Davis J (2012) Freshwater availability and water fetching distance affect child health in sub-Saharan Africa. *Environmental Science & Technology* **46**, 2391–2397.

Prüss A, Kay D, Fewtrell L & Bartram J (2002) Estimating the burden of disease from water, sanitation, and hygiene at a global level. *Environmental health perspectives* **110**, 537–542.

Prüss-Ustün A & Corvalán C (2007) How much disease burden can be prevented by environmental interventions? *Epidemiology* **18**, 167–178.

Prüss-Ustün A, Bos R, Gore F & Bartram J (2008) *Safer Water, Better Health*. World Health Organization, Geneva, Switzerland.

Rosa G & Clasen T (2010) Estimating the scope of household water treatment in low- and medium-income countries. *The American Journal of Tropical Medicine and Hygiene* **82**, 289–300.

Rosa G, Miller L & Clasen T (2010) Microbiological effectiveness of disinfecting water by boiling in rural Guatemala. *American Journal of Tropical Medicine & Hygiene* **82**, 473–477.

Royal Scientific Society (2013) *To Identify Minimum Household Water Security Requirements for Health Protection*. Royal Scientific Society, Amman, Jordan.

Savović J, Jones HE, Altman DG *et al.* (2012) Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. *Annals of Internal Medicine* **157**, 429–438.

Tinker SC, Moe CL, Klein M *et al.* (2009) Drinking water residence time in distribution networks and emergency department visits for gastrointestinal illness in Metro Atlanta, Georgia. *Journal of Water and Health* **7**, 332–343.

Tonglet R, Isu K, Mpese M, Dramaix M & Hennart P (1992) Can improvements in water supply reduce childhood diarrhoea? *Health Policy and Planning* **7**, 260–268.

UNICEF (2014) *Multiple Indicator Cluster Survey (MICS)*. United Nations Children's Fund, New York. http://www.unicef.org/statistics/index_24302.html.

USAID (2014) *DHS Program*. US Agency for International Development. http://dhsprogram.com/.

 © 2014 The Authors. Tropical Medicine and International Health published by John Wiley & Sons Ltd.

Waddington H, Snilstveit B, White H & Fewtrell L (2009) *Water, Sanitation and Hygiene Interventions to Combat Childhood Diarrhoea in Developing Countries*. The International Initiative for Impact Evaluation (3ie), New Delhi, India.

WHO (2002) *The World Health Report 2002 – Reducing Risks, Promoting Healthy Life*. World Health Organization, Geneva, Switzerland.

WHO (2004) *Comparative Quantification of Health Risks*. World Health Organization, Geneva.

WHO (2009) *The Global Burden of Disease: 2004 Update*. World Health Organization, Geneva.

WHO (2013a) Global health observatory – data repository [Online]. http://apps.who.int/ghodata/files/84/ghodata.html.

WHO (2013b) *WHO Regional Offices* [Online]. World Health Organization, Geneva. http://www.who.int/about/regions/en/

WHO (2014) *World Health Survey (WHS)* [Online]. Geneva. http://www.who.int/healthinfo/survey/en/

WHO & UNICEF (2013a) *Progress on Sanitation and Drinking-Water. 2013 Update*. World Health Organization, Geneva.

WHO & UNICEF (2013b) WHO/UNICEF Joint Monitoring Programme (JMP) for water supply and sanitation [Online]. http://www.wssinfo.org/data-estimates/introduction/.

Wolf J, Bonjour S & Prüss-Ustün A (2013) An exploration of multilevel modeling for estimating access to drinking-water and sanitation. *Journal of Water and Health* **11**, 64–77.

Wolf J, Prüss-Ustün A, Cumming O *et al.* (2014) Review of the evidence relating drinking-water and sanitation to diarrhoea: a meta-regression. *Tropical Medicine and International Health* (this issue).

World Bank (2012) *Country and Lending Groups, July 2012*. World Bank, Washington, DC.

Ziegelbauer K, Speich B, Mäusezahl D, Bos R, Keiser J & Utzinger J (2012) Effect of sanitation on soil-transmitted helminth infection: systematic review and meta-analysis. *PLoS Medicine* **9**, e1001162.

Zmirou D, Rey S & Courtois X (1995) Residual microbiological risk after simple chlorine treatment of drinking ground water in small community systems. *European Journal of Public Health* **5**, 75–81.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Deaths attributable to inadequate water, sanitation, and hygiene by low- and middle-income countriesa for the year 2012.

Table S2. Deaths attributable to the combined inadequate water and sanitation, and to the combined inadequate water, sanitation and hygiene by low- and middle-income countrya, for the year 2012.

Corresponding Author Annette Prüss-Ustün, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland. E-mail: pruessa@who.int

© 2014 The Authors. Tropical Medicine and International Health published by John Wiley & Sons Ltd.

Journal of Public Health | Vol. 39, No. 3, pp. 464–475 | doi:10.1093/pubmed/fdw085 | Advance Access Publication September 12, 2016

Diseases due to unhealthy environments: an updated estimate of the global burden of disease attributable to environmental determinants of health

A. Prüss-Ustün[1], J. Wolf[2,3,5], C. Corvalán[4], T. Neville[1], R. Bos[1], M. Neira[1]

[1]Department of Public Health, Environmental and Social Determinants of Health, World Health Organization, 1211 Geneva, Switzerland
[2]Department of Epidemiology and Public Health, Swiss Tropical and Public Health Institute, 4051 Basel, Switzerland
[3]University of Basel, 4003 Basel, Switzerland
[4]Faculty of Health, University of Canberra, ACT 2617, Australia
[5]Present address: World Health Organization, Geneva, Switzerland
Address correspondence to A. Prüss-Ustün, E-mail: pruessa@who.int

ABSTRACT

Background The update of the global burden of disease attributable to the environment is presented. The study focuses on modifiable risks to show the potential health impact from environmental interventions.

Methods Systematic literature reviews on 133 diseases and injuries were performed. Comparative risk assessments were complemented by more limited epidemiological estimates, expert opinion and information on disease transmission pathways. Population attributable fractions were used to calculate global deaths and global disease burden from environmental risks.

Results Twenty-three percent (95% CI: 13–34%) of global deaths and 22% (95% CI: 13–32%) of global disability adjusted life years (DALYs) were attributable to environmental risks in 2012. Sixty-eight percent of deaths and 56% of DALYs could be estimated with comparative risk assessment methods. The global disease burden attributable to the environment is now dominated by noncommunicable diseases. Susceptible ages are children under five and adults between 50 and 75 years. Country level data are presented.

Conclusions Nearly a quarter of global disease burden could be prevented by reducing environmental risks. This analysis confirms that eliminating hazards and reducing environmental risks will greatly benefit our health, will contribute to attaining the recently agreed Sustainable Development Goals and will systematically require intersectoral collaboration to be successful.

Keywords environment, morbidity and mortality, public health

Introduction

Attribution of the burden of disease to environmental risks highlights the importance of environmental protection for people's health and can inform priority setting for targeted management of environmental determinants. Ten years ago the global burden of disease attributable to the environment was estimated for the first time in a comprehensive, systematic and transparent way.[1] The study concluded that as much as 24% of disability adjusted life years (DALYs) and 23% of deaths were due to modifiable environmental risks.[1]

The health impacts of specific risk factors have traditionally been assessed separately.[2,3] A comprehensive account of the consequences of unhealthy environments that are modifiable outlines the full potential of disease prevention that can be achieved by reconsidering the way we shape our environment. Since the last assessment 10 years ago,[1] considerable more evidence has become available which justifies an updated assessment. We present here the methods and results of a new study which updates the previous analysis, by compiling the most recent synthesized and other key

A. Prüss-Ustün, senior scientist
J. Wolf, consultant to the World Health Organization
C. Corvalán, Adjunct professor
T. Neville, consultant to the World Health Organization
R. Bos, independent consultant
M. Neira, Director

© The World Health Organization [2016]. Published by Oxford University Press on behalf of The Faculty of Public Health.
This is an Open Access article distributed under the terms of the Creative Commons Attribution 3.0 IGO License (https://creativecommons.org/licenses/by/3.0/igo/), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.

evidence on each disease and injury and their links to the environment.[4] We present environmental burden of disease both in terms of environment-attributable mortality and DALYs, a weighted measure of death and disability.

The aim of the study is to quantify the links between disease or injury and environmental risks using CRAs and alternative methods and to derive an estimate of the environmental disease burden, overall, by region and country. For policy relevance, we deliberately focus on those risks which could be prevented or reduced by feasible interventions which modify the environment. The assessment was completed by a review of effective interventions for each of the investigated diseases.

Methods

Defining the environment in the context of public health

Environmental health has been defined as that part of public health that addresses all the physical, chemical and biological determinants of health external to a person, and all the related factors impacting behaviours.[5] Included under environment for the purpose of this study are exposure to pollution and chemicals (e.g. air, water, soil, products), physical exposures (e.g. noise, radiation), the built environment (e.g. housing, land-use, infrastructure), other anthropogenic changes (e.g. climate change, vector breeding places), related behaviours and the work environment. Excluded are life style factors and behaviours which have no or only minor relations with the physical environment such as diet, tobacco or alcohol consumption, environments which cannot reasonably be modified (e.g. wetlands, pollen), or social conditions and unemployment. These risks are further detailed in Supplementary File (A1). The focus is placed on disease which can be prevented, either with almost immediate effect, or with longer term transformations.

Systematic literature review

For each of the 133 disease and injury groups,[2] we searched the literature systematically using Pubmed and Google Scholar for population health impacts from environmental risks and effects of interventions addressing those risks. The search strategy included a range of different MeSH (Medical Subject Headings) terms and keywords on each of the diseases or injuries, combined with terms for 'environment', 'occupation', relevant environmental risks and any of the occupational groups at risk, starting from the year 2004 until 2014. Older literature was taken from the earlier study[1] and major projects of risk assessments were reviewed. Furthermore, the literature and data repositories were screened for documented and publicly available data and information on population health impacts, effects of interventions, exposure-response relationships, transmission pathways and causality. Global estimates of population impacts from environmental risks were completed with national or regional estimates, results of systematic reviews and meta-analyses on disease reduction from interventions or on environmental determinants; and finally by individual studies on interventions and environmental determinants. The focus on evidence of interventions underlines risk reductions that are already feasible, whereas other risk reductions may not yet be feasible or performed at large scale. Only risk factors with an established link of causality to health were further considered.

Estimation of the population attributable fraction

The population attributable fraction (PAF) of a risk factor is the proportional reduction in population death or disease that would occur if exposure to this factor was removed or reduced to an achievable, alternative (or counterfactual) exposure distribution.[6] To calculate the PAF of a risk factor to a disease, the following information is needed: (i) the exposure distribution to the risk factor within the population of interest, (ii) the relative risk (RR) linking each level of exposure to the specific disease or injury, and (iii) an alternative (counterfactual) exposure distribution to which environmental risks could be reduced. The counterfactual exposure distributions were based either on evidence from interventions, removal of pathways which have been eliminated elsewhere, or exposures achieved in some populations or areas.

According to the results of the systematic literature review (see above), four different approaches were used to estimate the fraction of diseases attributable to environmental risks in the following order of priority: (i) CRAs, which generally provide estimates based on the highest levels of evidence and most comprehensive data,[7–10] (ii) estimates based on more limited exposure information and/or exposure-risk relationships, (iii) diseases with a transmission pathway dependent on specific modifiable environmental conditions were fully attributed to the environment (such as intestinal nematode infections which require contamination of the environment by human excreta), and (iv) expert surveys.

Estimation of burden of disease attributable to the environment

In priority, we used systematic global estimates of population impacts from environmental risks (CRA type of assessments).[2,11–13] These assessments are systematic evaluations of changes in population health resulting from modifying the population distribution of exposure from the current situation as compared to an alternative exposure, in combination with corresponding exposure-risk relationships. In these assessments, exposure is assessed for country populations as much as possible, the extrapolability of exposure-response relationship screened. CRA type of assessments are the method of choice and represent the highest level of evidence for environmental health conditions with a clear, established link between exposure and health outcome, such as exposure to air pollution or inadequate water and sanitation, chemicals or radiation. However, often available data is too limited to perform CRA type of assessments such as for insect vectors of diseases or rodent reservoirs of zoonoses which are more difficult to measure or which show a level of variation that is hard to translate in a disease burden, and alternative methods as specified below needed to be used.

Information on estimating disease burden from a combination of different risks is given in Supplementary File (A2).

When sufficient exposure distributions, or exposure-risk estimates or other important information was missing to perform CRA type of assessments, estimates based on more limited epidemiological data were performed, such as for HIV/AIDS, Hepatitis B, other sexually transmitted diseases, suicide and underweight.

Additional information can be found in the full WHO report on this work.[4] For several diseases, approximate epidemiological estimations were also used to support expert opinion (e.g. unintentional injuries from fires).

Certain infectious diseases are solely transmitted through pathways which depend on specific modifiable environmental conditions, such as intestinal nematode infections which require contamination of the environment by human excreta. These diseases were fully attributed to the environment on the basis of their transmission pathway.

When estimates of population impacts from environmental risks were not available or could not be developed in the framework of this study, experts were asked to provide a best estimate of the fraction of the specific disease of the global population attributable to the reasonably modifiable environment, as well as the 95% confidence interval (CI). Experts were selected on the basis of their publications in the area of the disease or the relevant environmental risk factor. They were provided with abstracts of search results of the systematic reviews described earlier, as well as an initial estimate that was based on pooled estimates from the literature. Three or more experts were chosen for each disease or injury. More information on generating PAFs and confidence intervals from the experts' replies is given in Supplementary File (A3).

Where the body of evidence resulting from the updated literature review did not substantially differ or was unlikely to justify a change in experts' estimation of PAF, the results of the expert survey of the previous study[1] were taken.

To calculate the fraction of disease attributable to a risk factor for any defined population, compiled or estimated PAFs were multiplied by the corresponding WHO disease statistics,[2] by disease or injury, country, sex and age group, and for deaths and DALYs. Equations are listed in Supplementary File (A4).

Compilation of main intervention areas

The evidence on effectiveness of interventions was further compiled by disease in order to summarize the main intervention areas.

Results

Results of environment-attributable deaths and disease burden, the attributable fractions, as well as the respective estimation method are listed in Table 1. The environmental fractions of the burden of selected diseases are shown in Fig. 1. Out of the 133 diseases or injuries, 101 had significant links with the environment, and 92 of them have been at least partially quantified. These 92 were grouped in 66 main disease and injury groups. Of these, global CRAs were available for 20 groups, of which 12 could be exclusively used for those diseases and eight needed to be completed by expert opinion. Eight diseases could be assessed (Table 1) on the basis of more limited epidemiological data, and four further disease PAFs were based on their transmission pathways. The PAFs of the remaining 31 diseases were fully estimated through expert surveys. More than 100 experts provided more than 250 quantitative replies. In terms of estimated environmental disease burden (in DALYs), as much as 56% could be estimated with CRA-type methods (of which 36% with a combination of risk factors), 40% were based on expert surveys (of which 8% in the 2015 round), 3% on estimations using more limited data, and 1% based on transmission pathways (Table 1).

A description of the underlying evidence and region-specific results for each disease or injury are detailed in the report along with compiled effectiveness of environmental interventions. Based on a summary of the literature review on interventions, we report a mapping of diseases to main strategies for disease reduction through environmental improvements in Table 2, which are further detailed in the full report.[1]

Environmental risks contributed 23% (95% CI = 13–34%) of the global burden measured in deaths, corresponding

Table 1 Global deaths, disease burden (in DALYs) and fractions attributable to the environment for 2012, and methods used

Disease	*Deaths (in 2012)*	*DALYs (in 2012)*	*Attributable fraction (in DALYs) (95% CI)*	*Estimation method used*
Total	12 624 495	596 412 171	22 (13–32)	
Infectious and parasitic diseases				
Respiratory infections				
Lower respiratory infections	566 361	51 752 605	35 (27–41)	a[e]
Upper respiratory infections and otitis	1190	989 751	14 (5–22)	d_{2005}
Diarrhoeal diseases	845 810	56 606 914	57 (34–72)	a[f]
Intestinal nematode infections				
Ascariasis	3297	1 353 195	100	c
Trichuriasis	0	664 771	100	c
Hookworm disease	<10	3 211 578	100	c
Parasitic and vector diseases				
Malaria	258 702	23 074 449	42 (28–55)	d_{2005}
Trachoma	0	298 711	100	c
Schistosomiasis	17 871	3 301 300	82 (71–92)	d_{2015}
Chagas disease	4371	295 450	56 (28–80)	d_{2005}
Lymphatic filariasis	<10	1 893 574	67 (39–89)	d_{2005}
Onchocerciasis	0	59 827	10 (7–13)	d_{2005}
Leishmaniasis	12 952	903 053	27 (9–40)	d_{2005}
Dengue	27 249	1 369 867	95 (89–100)	d_{2005}
HIV/AIDS[#]	137 985	7 780 321	10 (8–13)	b
Sexually transmitted diseases excluding HIV/AIDS[#]			8 (4–17)	
Syphilis	286	17 567	6 (3–14)	b
Chlamydia	108	115 567	8 (3–16)	b
Gonorrhoea	105	63 588	12 (7–25)	b
Trichomoniasis	0	6599	4 (2–6)	b
Hepatitis B	2828	111 446	2 (1–4)	b
Tuberculosis	166 687	7 688 971	18 (5–40)	(b), d_{2005}
Other infectious diseases	160 418	11 463 450	27 (17–37)	d_{2005}
Neonatal and nutritional conditions				
Neonatal conditions	270 087	25 819 566	11 (2–27)	d_{2005}
Childhood underweight	27 291	2 834 186	15 (10–19)	b
Noncommunicable diseases				
Lung cancer	568 632	13 902 105	36 (17–52)	a[e]
Other cancers	1 097 144	31 047 781	16 (7–41)	(a), d_{2005}
Mental, behavioural and neurological disorders				
Unipolar depressive disorders	536	8 473 707	12 (5–35)	d_{2015}
Bipolar disorder	30	528 985	4 (0–9)	d_{2015}
Schizophrenia	839	561 463	4 (1–9)	d_{2015}
Alcohol use disorders	17 104	5 121 132	16 (6–38)	d_{2015}
Drug use disorders	10 213	1 663 568	11 (2–36)	d_{2015}
Anxiety disorders	13	5 479 365	20 (5–42)	d_{2015}
Eating disorders	636	158 276	7 (0–20)	d_{2015}
Pervasive developmental disorders	–	546 443	7 (0–26)	d_{2015}
Childhood behavioural disorders	–	742 156	12 (3–36)	d_{2015}
Idiopathic intellectual disability	106	193 742	6 (1–25)	d_{2015}
Alzheimer's disease and other dementias	41 936	1 088 036	6 (1–13)	d_{2015}

Continued

Table 1 Continued

Disease	*Deaths (in 2012)*	*DALYs (in 2012)*	*Attributable fraction (in DALYs) (95% CI)*	*Estimation method used*
Parkinson's disease	8293	171 015	7 (2–14)	d_{2015}
Epilepsy	30 031	3 023 792	15 (2–30)	d_{2015}
Multiple sclerosis	1141	69 729	6 (1–22)	d_{2015}
Migraine	<10	2 585 608	14 (2–36)	d_{2015}
Non-migraine headache	–	310 613	17 (2–46)	d_{2015}
Other mental, behavioural and neurological conditions	43 297	1 985 121	11 (2–24)	d_{2015}
Sense organ diseases				
Cataracts	–	1 669 157	24 (14–33)	a^f
Deafness	–	4 787 242	22 (19–25)	a^g
Cardiovascular diseases				
Rheumatoid arthritis	10 928	934 393	17 (6–30)	a^g
Hypertensive heart disease	93 652	2 146 830	9 (5–15)	a^g
Ischaemic heart disease	2 273 811	58 561 915	35 (26–46)	a^e
Stroke	2 476 553	58 985 984	42 (24–53)	a^e
Other circulatory diseases	49 291	1 355 822	3 (1–5)	a^g
Respiratory diseases				
Chronic obstructive pulmonary disease	1 193 589	32 280 160	35 (20–48)	a^e
Asthma	169 449	11 055 150	44 (26–53)	(a), d_{2005}
Chronic kidney diseases	27 143	759 826	3 (1–5)	a^g
Musculoskeletal diseases				
Rheumatoid arthritis	6934	217–314	2 (1–4)	d_{2005}
Osteoarthritis	829	3 606 529	20 (11–29)	d_{2005}
Back and neck pain	158	14 627 733	27 (17–41)	a^g, d_{2015}
Other musculoskeletal diseases	20 666	4 961 741	15 (6–24)	d_{2005}
Congenital anomalies	27 770	2 621 857	5 (1–10)	d_{2005}
Unintentional injuries				
Road traffic accidents	497 079	31 000 887	39 (23–64)	(a), d_{2005}
Unintentional Poisonings	137 339	7 824 627	73 (53–90)	(a), d_{2005}
Falls	208 469	12 671 696	30 (15–58)	(a), d_{2005}
Fires	199 776	13 665 389	76 (58–91)	(a), (b), d_{2015}
Drownings	268 166	16 948 334	73 (43–94)	(a), d_{2005}
Other unintentional injuries	393 136	23 133 586	43 (20–74)	(a), d_{2005}
Intentional injuries				
Suicide	164 394	8 119 700	21 (13–30)	b
Interpersonal violence	81 730	5 101 921	16 (3–28)	d_{2005}

HIV/AIDS = human immunodeficiency virus/acquired immunodeficiency syndrome; a: comparative risk assessment type, b: calculation based on limited epidemiological data, c: disease transmission pathway, d_{2015}: expert survey 2015, d_{2005}: expert survey 2005; ( ) Estimates available, but completion by expert survey as main risk-factor disease pair not assessed. [e] Source: Combination of various risk factors developed for this analysis, WHO, based on references.[9,11–13] [f] Source: WHO.[10,11] [g] Source:[13]; see disease-specific sections and Technical Annex of full report for further information.

to 12.6 million deaths in 2012, and 22% (95% CI = 13–32%) in DALYs. In children under 5 years, as much as 26% of deaths and 25% of DALYs are attributable to the environment.

Global deaths attributable to the environment are dominated by 8.2 million deaths from noncommunicable diseases, followed by 2.5 million deaths related to infectious, parasitic, neonatal and nutritional diseases, and 2.0 million deaths from injuries. The difference is much less important in terms of disease burden, with 276, 202 and 118 million DALYs attributable to the environment in noncommunicable diseases; infectious, parasitic, neonatal and nutritional diseases; and injuries, respectively. Whereas there are significantly more deaths from noncommunicable diseases,

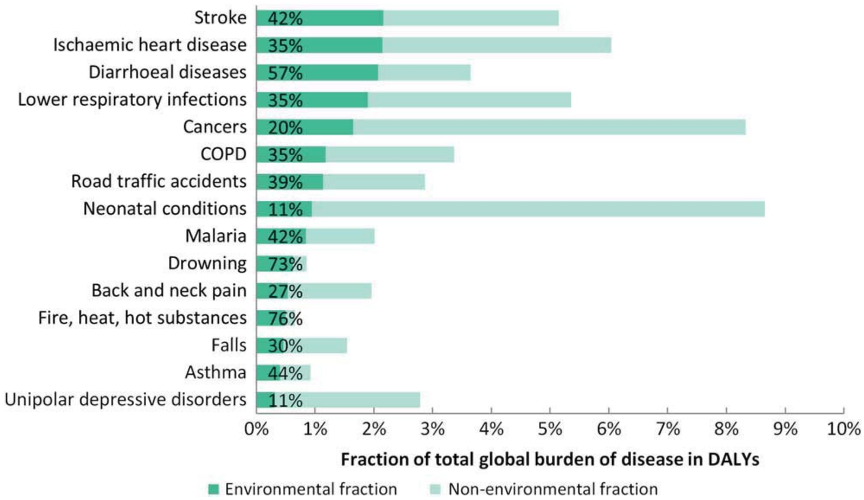


Fig.1 Environmental fraction of burden of selected diseases (percentages relate to the environmental share of the respective disease).

infectious, parasitic, neonatal and nutritional diseases and injuries affect the young to a greater extent and therefore lead to relatively higher losses of DALYs relative to noncommunicable diseases (Fig. 2).

Figure 2 shows that overall disease burden attributable to the environment (thick grey line) peaks for the very young and for adults aged 50–75 years. These two age groups show important susceptibilities to environmental conditions. Children are mainly affected by communicable diseases. For the age group between 50 and 75 years the contributions of infectious diseases and injuries are still significant, while noncommunicable diseases, in particular cardiovascular diseases due to ambient and household air pollution, become very important. Box 1 highlights the shift from environmental disease burden from communicable to noncommunicable diseases between 2002 and 2012.

Age-standardized deaths and DALYs by country are provided in Tables A1 and A2 of the Supplementary File. While the highest burden of environment-attributable disease is still in Sub-Saharan Africa and dominated by infectious, parasitic, neonatal and nutritional disease burden, the per capita deaths from noncommunicable diseases are now higher in most other regions of the world. Figure 3 shows environmentally related deaths per 100 000 population by gross national income (GNI). The size of the bubbles is proportional to country population. There is a reduction of deaths with increasing income up to a GNI of around 25 000. At larger incomes there is no difference in death rates, with most countries having around 50 deaths per 100 000.

Discussion

What is already known on the topic and what this study adds

Compared to our estimates for 2002, we see a major shift in the importance of environmental factors in noncommunicable disease aetiology. This is due to (i) the composition of the global disease burden which is now dominated by noncommunicable diseases,[14] (ii) increased evidence on environmental determinants of noncommunicable diseases, and (iii) growing importance of environmental factors that contribute to noncommunicable diseases such as air pollution. As the world population continues to age rapidly, the trend of environmental risks predominantly affecting noncommunicable diseases is expected to become more pronounced.

One hundred and one out of 133 diseases and injuries were at least partially attributable to manageable environmental factors, as compared to 85 out of 102 in the previous study. In addition, the share of estimates based on the highest evidence level, i.e. using CRA type of approaches, has considerably increased and now reaches 56% (for DALYs), as compared to less than 10% in the previous study. In these high-evidence assessments, exposures are being assessed at country level or higher resolution, such as by age and gender to the extent possible and where appropriate, and the transferability of exposure-risk relationships to other population groups than where assessed are being verified or adjusted. This adds to the comprehensiveness and strength of evidence of the previous report.

Nevertheless, our numbers show that environmental factors continue to contribute to a large disease burden from

Table 2 Main areas of strategies for disease reduction through environmental improvements

Disease or Injury[a]	*Main areas*
Infectious and parasitic diseases	
Respiratory infections	Household fuel use for cooking, heating and lighting, ambient air pollution, second-hand smoke, housing improvements (to prevent chilling, crowding).
Diarrhoeal diseases	Drinking water quality, improved sanitation facilities, recreational water quality, personal and community hygiene, animal excreta management, agricultural practices, climate change.
Intestinal nematode infections	Sanitation facilities and hygiene to prevent contamination of the environment with excreta, safe management of wastewater for irrigation.
Malaria	Environmental modification, including drainage, land levelling, filling depressions, pools and ponds, mosquito proof drinking water storage; environmental manipulation, including aquatic vegetation management, safe storage of domestic water, managing peri-domestic waste; reduced contact between humans and disease vectors screening of houses; livestock distribution.
Trachoma	Access to improved sanitation facilities; effective management of human waste; domestic water supplies, fly control, personal hygiene.
Schistosomiasis	Management of human waste, safe drinking water supply, improved irrigation infrastructure and safe irrigation and other agricultural practices; workers' protection to avoid contact with contaminated water (such as wearing rubber boots).
Chagas disease	Management of peri-domestic areas (such as filling cracks in house walls, clearing areas around houses of wood stacks, maintaining goat corrals and chicken dens clean of organic debris).
Lymphatic filariasis	Modification of drainage and wastewater ponds, freshwater collection and irrigation schemes; impact depends on locally relevant disease vectors.
Onchocerciasis	Improved design and operation of water resources development projects (particularly dams).
Leishmaniasis	Housing improvements, such as eliminating soil and wall cracks, removal of organic material in the peri-domestic environment, workers' personal protection.
Dengue	Management of water bodies around the house such as removing standing water from open water containers, urban infrastructure improvements, and solid waste management.
Japanese encephalitis	Irrigation management in rice-growing areas and distribution of farm animals (mainly pigs), personal protection methods.
HIV/AIDS and sexually transmitted diseases	Programmes to reduce occupational transmission among sex workers and migrant workers such as construction workers, seasonal agricultural labourers, truck drivers and sailors.
Hepatitis B and C	Occupational transmission among sex workers and migrant workers for hepatitis B;accidental needle-stick injuries in healthcare workers.
Tuberculosis	Exposure of miners and other occupational groups to airborne particles such as silica or coal dust, possibly exposure to household fuel combustion smoke and second-hand smoke. Managing setting-specific conditions, such as in prisons, hospitals and refugee camps.
Neonatal and nutritional conditions	
Neonatal conditions	Household air pollution from fuel combustion, mothers' exposure to environmental tobacco smoke, poor water and sanitation in birth settings.
Childhood underweight	Provision of adequate water, sanitation and hygiene, adaptive management addressing climate change acting on food insecurity.
Cancers	Household air pollution from fuel combustion, ambient air pollution, second-hand smoke, ionizing radiation, ultraviolet radiation, exposure to chemicals, exposures at work and in other settings.
Noncommunicable diseases	
Neuropsychiatric disorders	Occupational stress has been linked to depression and anxiety; posttraumatic stress disorders to disasters such as floods, earthquakes, and fires, which could in part be prevented by environmental measures (e.g., floods by hydraulic infrastructure or land use patterns, or their mitigation of climate change, the impact of earthquakes and fires through more adequate buildings); forced resettlements in the context of development projects; drug use and alcohol disorder to the occupational environment such as working in the entertainment industry; epilepsy to occupational head trauma; Parkinson's disease to exposure to chemicals such as pesticides; intellectual disability to childhood exposure to lead and methylmercury; insomnia to noise and occupational stress; migraine to bright lights, poor air quality and odours. Exercise and physical activity fostered by supportive environments can reduce depression and anxiety.

Continued

Table 2 Continued

Disease or Injury[a]	*Main areas*
Cataracts	Protection from ultraviolet radiation, reduction of household air pollution from combustion smoke.
Hearing loss	Managing occupational exposure to high noise levels.
Cardiovascular diseases	Reducing or eliminating indoor and outdoor air pollution, second-hand smoke, exposure to lead, stressful working conditions, shift work.
Chronic obstructive pulmonary disease	Reducing or eliminating household air pollution from combustion smoke, ambient air pollution, exposure to dusts in the workplace.
Asthma	Reducing or eliminating air pollution, second-hand smoke, exposure to indoor mould and dampness, occupational exposure to allergens.
Musculoskeletal diseases	Managing occupational stressors, such as heavy lifting, vibrations, prolonged sitting and poor work postures; need to carry large quantities of water over significant distances for domestic use.
Congenital anomalies	Mothers' exposure to second-hand smoke, chemicals.
Unintentional injuries	
Road traffic accidents	Design of the roadways (e.g. sidewalks, bicycle lanes, restricted traffic, traffic-calming measures), land-use planning; traffic intensification in development areas with big infrastructure projects.
Unintentional poisonings	Safe handling and storage of chemicals, adequate product information, adequate choice of chemicals, workers' protection (e.g. protective clothing).
Falls	Safety of housing and working environment.
Fires, heat and hot substances	Safety of cooking, lighting and heating equipment, in particular open fires, unsafe stoves or the use of candles or kerosene lamps, building fire codes, use of flammable materials in the home, safety of occupational environments and practices, climate change.
Drownings	Safety of water environments (community infrastructure, physical barriers, prevention and rescue services), public awareness, regulations (e.g. on transportation on waterways), workers' safety measures, climate change-induced flood risks.
Other unintentional injuries	Protection from animal bites and contact with venomous plants, safety of mechanical equipment (including sports equipment, agricultural and industrial machinery), safety of off-road transportation, protection from exposure to ionizing radiation or electric currents.
Intentional injuries	
Self-harm	Access to toxic chemicals such as pesticides, access to firearms.
Interpersonal violence	Access to firearms, urban design (e.g. mobility, visibility), workers' protection.
Related risk factors	
Physical inactivity	Workplace activity, prolonged sitting at the workplace, travel modes, transport infrastructure and land use patterns (walkability, urban density, land use diversity), availability of suitable parks and open spaces.
Obesity	Factors favouring physical activity.

[a] Disease groups have been aggregated as compared to Table 1, as several disease subgroups have similar reduction strategies.

communicable diseases in many low and middle income countries. In these countries, environmental risks leading to infectious diseases especially in children, such as household air pollution, unsafe drinking-water and poor sanitation and personal hygiene are still highly prevalent.[11,15] Furthermore the burden from respiratory and intestinal infections in these countries remains high.[14] At the same time they experience the double burden of communicable and noncommunicable diseases.

Our results differ from the Global Burden of Disease Study 2013 (GBD 2013)[8] which attributed 12% of global DALYs and 16% of global mortality to environmental risks, mainly because we used a broader scope of the definition of environment and complementary methods of assessment. Those risks comprise unsafe water, sanitation and hygiene; air pollution (ambient particulate matter, ozone and household air pollution); second-hand smoke; lead and residential radon exposure; and occupational risks[8] (NB: here we do not count burden attributable to physical inactivity/low physical activity as also for our analysis we did not quantify the environmental part of the burden from this risk factor). Our analysis covers a broader range of environmental risks adding noise (only included as occupational noise in GBD 2013); various chemicals; risks associated with poor housing, the recreational environment, water resource management, land use and the built environment; other community risks;

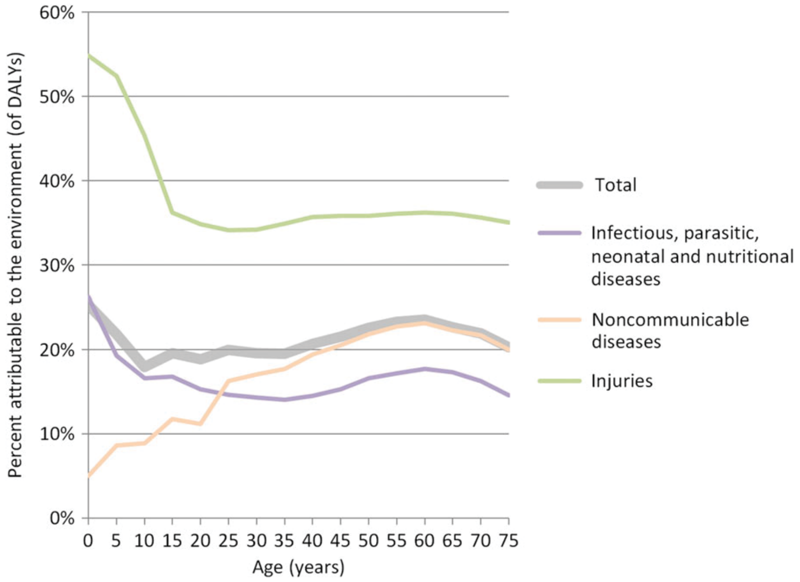


Fig. 2 Environmental disease burden of overall; infectious, parasitic, neonatal and nutritional nutritional; noncommunicable diseases and injuries by age.

Box 1: Trends of the environmental share of burden of disease by disease group.

- Infectious, parasitic, neonatal and nutritional: PAF from 31% in 2002 to 20% in 2012
- Noncommunicable diseases: PAF from 17% in 2002 to 22% in 2012
- Injuries: PAF from 37% in 2002 to 38% in 2012
- Overall: PAF from 23.3% in 2002 to 22.7% in 2012

radiation and climate change. Additionally, we consider more risk-factor disease links. Furthermore, GBD 2013 rated high blood pressure as most important risk factor, causing alone as much as 19% of global deaths and 8% of all DALYs.[8] Some of this burden can however be attributed to environmental factors such as air pollution,[16,17] arsenic[18] and lead exposure,[19] occupational risks[20] and environmental noise.[21]

Limitations of this study

A large part of this analysis is based on surveys of expert opinion and the uncertainties of such estimates are relatively large. However, experts were provided with the body of evidence that was identified during the systematic searches on the particular disease and its links to the respective environmental risks. We only updated this process when justified by a significant change in evidence. Further uncertainties relate to data limitations and assumptions made in e.g. CRA type of analyses.[8,11–13] Also key exposures at younger ages, which may result in noncommunicable diseases at older ages could not be adequately captured in this study.

Certain diseases or environmental risk factors were not included in our analysis, either because there was insufficient evidence and therefore health effects were not quantifiable (e.g. changed, damaged or depleted ecosystems and exposure to endocrine disrupting substances), or because the risk factor(s) caused a relatively small disease burden, or is/are of regional significance but do not feature at a global scale. Environmental risks not readily modifiable, e.g. pollen, were not considered.

Additional conservative approaches have been chosen for this analysis as compared to the previous one in order to increase methodological rigour. For example, (a) only the main environmental risks were quantified where CRA estimates were available, and (b) the exposures of similar risks were combined before the estimation of health impacts. The environmental disease burden measured in DALYs between 2002 and 2012 is not directly comparable as some of the basic parameters as discounting and age-weighting for DALY estimation changed during this period.[22] Using the same methods, the change would have been greater, as more deaths are now due to noncommunicable diseases, which tend to occur at older ages, and induce fewer years of life lost (and fewer DALYs).

We have not considered health impacts of social determinants.[23] There is, however, a strong link between the

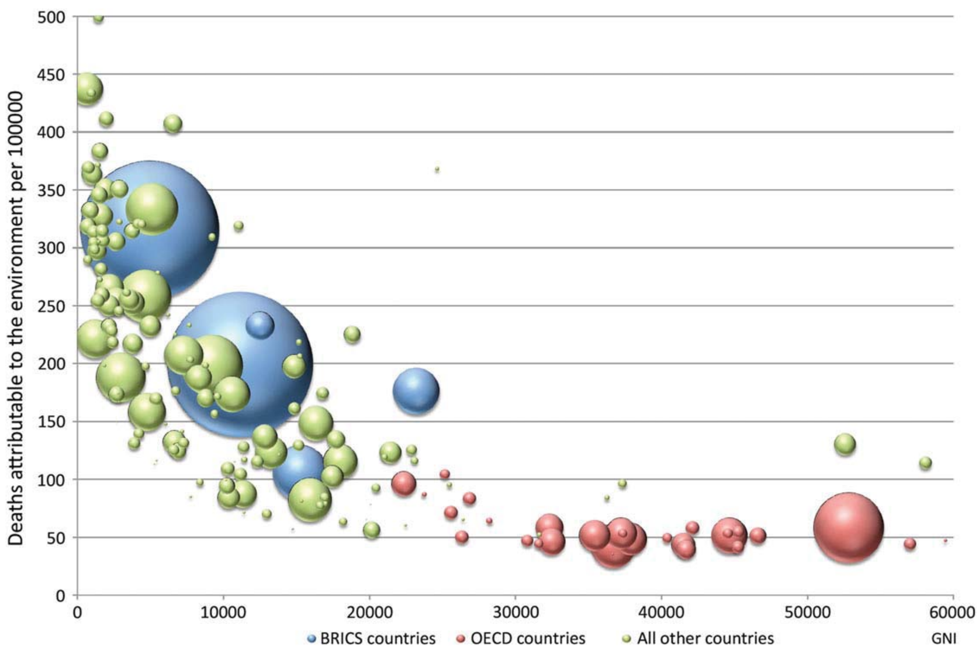


Fig. 3 Environmental burden of disease (deaths per 100 000 population, *y*-axis) by gross national income per capita (*x*-axis); each bubble represents a country, bubble size represents population size; BRICS: Brazil, Russia, India, China, South Africa; OECD: Organisation for Economic Co-operation and Development.

conditions of people's daily lives and environmental risks to health. The lower people's socioeconomic status the more likely they are to be exposed to environmental risks, such as chemicals, air pollution and poor housing, water, sanitation and hygiene. Poor people and communities are therefore likely to benefit most from environmental interventions as they are disproportionally affected by adverse environments.[24]

Policy implications

In principle, and given the methods and definitions chosen, the attributable burden here equates what can be prevented if the risks were removed. While we currently have solutions for reducing many of the prevailing risks, interventions that are affordable and that could completely eliminate certain risks such as ambient air pollution at a larger scale may require further development. Others, such as use of solid fuels, could be removed with almost immediate effect if the necessary means were made available. Yet for exposures which seem unavoidable in the short term, approaches are being considered which would require certain transformations in the way we currently produce and consume.

Important calls for action are coming from two main global platforms. One of them was created by the adoption of the SDGs in September 2015.[25] It was significant that the Heads of State gathered at a Special Session of the UN General Assembly did not agree on another agenda or declaration, but made a pledge to 'the transformation of our earth'. Full adherence to the obligations created by this pledge, even if only moral could result in important improvements on the reduction of environmental risks. The Supplementary File (A5, Table A3) gives further information on SDGs and their links with a healthy environment. The other is climate change. International efforts to reduce our carbon footprint (one such example is the recent Paris Agreement, the first global agreement to reduce climate change[26]) would lead to innovative interventions with positive ramifications to several key environmental factors, including to air pollution, water, chemicals, among others.

Conclusions

This analysis, which confirms that reducing environmental exposures can greatly improve our health and is critical for attaining the SDGs, has been generated considering a large list of environmental risk factors and risk factor-disease links. For half of those links, CRA types of assessment were available basing the results on solid evidence.

In conclusion, our results convey good news as we included only those environmental exposures that are amenable to change, meaning that interventions exist for removing a large part of global disease burden. A prerequisite would be a stronger focus on primary prevention placing a healthy environment at the centre of such an effort. This is not a task for ministries of health alone. Tackling environmental risks requires intersectoral collaboration. After nearly 50 years of actively promoting this concept, whether referred to as intersectoral action, breaking down silos or the nexus approach, it remains elusive as ever. The statement 'intersectoral collaboration: loved by all, funded by no-one' points to obstacles, mainly vested interests, that have burdened this approach ever since it was included as part of the WHO/UNICEF Alma Ata Declaration on Primary Health Care in 1978. Environmental health, quintessentially intersectoral, has suffered most from this lack of progress. There remain a number of health sector-specific functions (monitoring, surveillance), but for the actual interventions the health sector will have to create the enabling environment for intersectoral action. Investing in environmental interventions pays off for governments; it reduces the transfer of hidden costs from other sectors to the health sector. This new report provides the evidence base for intersectoral action providing the evidence to systematically consider the integration of measures into all policy areas.

Supplementary data

Supplementary data are available at the *Journal of Public Health* online

Acknowledgements

We are extremely grateful to the more than 100 experts from around the world and the colleagues from many WHO Departments who provided advice and input and assisted in the evaluation of impacts of the environment on disease (for a complete list of persons see report (2)).

Funding

This work was supported by the Centers for Disease Control and Prevention's National Institute for Occupational Safety and Health, USA, under Cooperative Agreement 5E11OH010676-02.

References

1 Prüss-Üstün A, Corvalán C. Preventing disease through healthy environments [Internet]. World Health Organization Geneva; 2006. Available from: http://cdrwww.who.int/entity/quantifying_ehimpacts/publications/preventingdiseasebegin.pdf (20 December 2015, date last accessed).

2 World Health Organization. Global Health Observatory (GHO) data [Internet]. WHO. undated. Available from: http://www.who.int/gho/en/ (16 July 2015, date last accessed).

3 IHME. GBD 2013, GBD Compare [Internet]. Available from: http://vizhub.healthdata.org/gbd-compare/ (13 January 2016, date last accessed).

4 Prüss-Ustün A, Wolf J, Corvalán C *et al.* Preventing disease through healthy environments: A global assessment of the environmental burden of disease from environmental risks [Internet]. World Health Organization; 2016. Available from: http://www.who.int/quantifying_ehimpacts/publications/preventing-disease/en/ (18 March 2016, date last accessed).

5 World Health Organization. Environmental health [Internet]. undated. Available from: http://www.who.int/topics/environmental_health/en/ (16 July 2015, date last accessed).

6 World Health Organization. Metrics: Population Attributable Fraction (PAF) [Internet]. undated. Available from: http://www.who.int/healthinfo/global_burden_disease/metrics_paf/en/index.html (15 Novenber 2015, date last accessed).

7 World Health Organization. Global health risks: Mortality and burden of disease attributable to selected major risks. 2009.

8 Forouzanfar MH, Alexander L, Anderson HR *et al.* Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;**386**(**10010**):2287–323.

9 Ezzati M, Lopez AD, Rodgers A *et al.* Selected major risk factors and global and regional burden of disease. *Lancet* 2002;**360**(**9343**):1347–60.

10 Prüss-Ustün A, Mathers C. *Introduction and Methods. Assessing the Environmental Burden of Disease at National and Local Levels.* Geneva, Switzerland: World Health Organization, 2003.

11 Prüss-Ustün A, Bartram J, Clasen T *et al.* Burden of disease from inadequate water, sanitation and hygiene in low- and middle-income settings: a retrospective analysis of data from 145 countries. *Trop Med Int Health* 2014;**19**(**8**):894–905.

12 World Health Organization. *Burden of Disease from Household Air Pollution for 2012.* Geneva, Switzerland: World Health Organization, 2014.

13 World Health Organization. *Burden of Disease from Ambient Air Pollution for 2012.* Geneva, Switzerland: World Health Organization, 2014.

14 Naghavi M, Wang H, Lozano R *et al.* Global, regional, and national age–sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;**385**(**9963**):117–71.

15 Bonjour S, Adair-Rohani H, Wolf J *et al.* Solid fuel use for household cooking: country and regional estimates for 1980–2010. *Environ Health Perspect* 2013;**121**(**7**):784–90.

16 Baumgartner J, Schauer JJ, Ezzati M *et al.* Indoor air pollution and blood pressure in adult women living in rural China. *Environ Health Perspect* 2011;**119**(**10**):1390–5.

17 Fuks KB, Weinmayr G, Foraster M *et al.* Arterial blood pressure and long-term exposure to traffic-related air pollution: an analysis in the European Study of Cohorts for Air Pollution Effects (ESCAPE). *Environ Health Perspect* 2014;**122**(**9**):896–905.

18 Abhyankar LN, Jones MR, Guallar E *et al.* Arsenic exposure and hypertension: a systematic review. *Environ Health Perspect* 2012;**120** (**4**):494–500.

19 Navas-Acien A, Schwartz BS, Rothenberg SJ *et al.* Bone lead levels and blood pressure endpoints: a meta-analysis. *Epidemiology* 2008;**19** (**3**):496–504.

20 Babu GR, Jotheeswaran AT, Mahapatra T *et al.* Is hypertension associated with job strain? A meta-analysis of observational studies. *Occup Env Med* 2014:220–7.

21 van Kempen E, Babisch W. The quantitative relationship between road traffic noise and hypertension: a meta-analysis. *J Hypertens* 2012;**30**(**6**):1075–86.

22 Murray CJL, Vos T, Lozano R *et al.* Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**(**9859**):2197–223.

23 World Health Organization. Social determinants of health [Internet]. Available from: http://www.who.int/social_determinants/en/ (21 July 2015, date last accessed).

24 Marmot M, Allen J, Bell R *et al.* WHO European review of social determinants of health and the health divide. *Lancet* 2012;**380**(**9846**):1011–29.

25 United Nations. Sustainable Development Goals [Internet]. undated [cited 2015 Dec 14]. Available from: http://www.un.org/sustainabledevelopment/development-agenda/

26 2015 United Nations Climate Change Conference. In: Wikipedia, the free encyclopedia [Internet]. 2015. Available from: https://en.wikipedia.org/w/index.php?title=2015_United_Nations_Climate_Change_Conference&oldid=695179642 (14 December 2015, date last accessed).

International Journal of Epidemiology, 2016, 2089–2099
doi: 10.1093/ije/dyw242
Advance Access Publication Date: 6 November 2016
Original article

Interventions

Improving household air, drinking water and hygiene in rural Peru: a community-randomized–controlled trial of an integrated environmental home-based intervention package to improve child health

SM Hartinger[1,2], CF Lanata[2], J Hattendorf[1,3], H Verastegui[2], AI Gil[2], J Wolf[1,3] and D Mäusezahl[1,3,*]

[1]Swiss Tropical and Public Health Institute, Basel, Switzerland, [2]Instituto de Investigación Nutricional, Lima, Peru, [3]University of Basel, Basel, Switzerland and

*Corresponding author. Department of Public Health and Epidemiology, Swiss Tropical and Public Health Institute, PO Box, CH-4002 Basel, Switzerland. E-mail: Daniel.Maeusezahl@unibas.ch

Accepted 3 August 2016

Abstract

Background: Diarrhoea and acute lower respiratory infections are leading causes of childhood morbidity and mortality, which can be prevented by simple low-cost interventions. Integrated strategies can provide additional benefits by addressing multiple health burdens simultaneously.
Methods: We conducted a community-randomized–controlled trial in 51 rural communities in Peru to evaluate whether an environmental home-based intervention package, consisting of improved solid-fuel stoves, kitchen sinks, solar disinfection of drinking water and hygiene promotion, reduces lower respiratory infections, diarrhoeal disease and improves growth in children younger than 36 months. The attention control group received an early child stimulation programme.
Results: We recorded 24 647 child-days of observation from 250 households in the intervention and 253 in the attention control group during 12-month follow-up. Mean diarrhoea incidence was 2.8 episodes per child-year in the intervention compared with 3.1 episodes in the control arm. This corresponds to a relative rate of 0.78 [95% confidence interval (CI): 0.58–1.05] for diarrhoea incidence and an odds ratio of 0.71 (95% CI: 0.47–1.06) for diarrhoea prevalence. No effects on acute lower respiratory infections or children's growth rates were observed.
Conclusions: Combined home-based environmental interventions slightly reduced childhood diarrhoea, but the confidence interval included unity. Effects on growth and respiratory outcomes were not observed, despite high user compliance of the interventions. The absent effect on respiratory health might be due to insufficient household air

© The Author 2016. Published by Oxford University Press on behalf of the International Epidemiological Association

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

quality improvements of the improved stoves and additional time needed to achieve attitudinal and behaviour change when providing composite interventions.

Key words: Community-randomised trial, integrated interventions, household air pollution, household water treatment, improved cook stove, kitchen hygiene, hand-washing

Key Messages

- Combined kitchen–environmental interventions, including an improved solid-fuel stove, a kitchen sink, solar treatment of drinking water and hygiene promotion, are successfully implemented at the household level. Convenience gains from improved cooking stoves and kitchen sinks are highly valued by the beneficiaries.
- Integrated home-based interventions might have reduced childhood diarrhoea, but failed to impact respiratory infections and child growth.
- Reasons for the lack of an effect on respiratory health might be due to insufficient reduction of household air pollution of the improved stoves and duration of follow-up.

Introduction

Diarrhoea and acute lower respiratory infections (ALRI) remain leading causes of childhood morbidity and mortality.[1] Unsafe drinking water, poor sanitation, lack of personal hygiene and poor household air quality are considered amongst the most important risk factors for those diseases.[2,3]

Interventions to improve drinking water, sanitation and hygiene have been shown consistently to reduce diarrhoeal disease.[4–7] Similarly, the odds for acute respiratory infections (ARI) were 3.5 times and for pneumonia 78% higher in children exposed to biomass fuels compared with non-exposed children.[8,9] A randomized–controlled trial providing improved solid-fuel stoves to rural households in Guatemala found a rate ratio of 0.84 [95% confidence interval (CI): 0.63, 1.13] for physician-diagnosed childhood pneumonia comparing households in the intervention to those in the control group which reduced to 0.67 (95% CI: 0.45, 0.98) after multiple imputation and limited to severe pneumonia.[10]

Combining potentially synergistic interventions has been advocated before in the drinking-water and sanitation sector.[11,12] In the presented trial, we combine interventions to tackle various household-related risks simultaneously. The interventions for this study were developed using a participatory approach during a six-month pilot phase.[13,14] We identified and convened main stakeholders and beneficiaries to develop an intervention package that generates healthy household environments, addresses local beliefs and cultural views, and has potentially synergistic effects on household health and livelihoods. Additionally, the attention control group received an early child stimulation intervention to reduce bias from the open, i.e. non-blinded, trial design, which was judged to be especially important in home-based interventions.[4,15]

The main objective was to reduce respiratory infections and diarrhoea and to improve child growth in children less than 36 months, through an integrated environmental home-based intervention package (IHIP), comprising improved solid-fuel stoves, kitchen sinks, solar disinfection of drinking water and hygiene promotion.

Methods

Ethics

The study was approved by the ethical review board of the Nutritional Research Institute (Instituto de Investigación Nutricional, IIN), the cantonal ethical review board of Basel, Switzerland, Switzerland (Ethikkommission beider Basel, EKBB), the Cajamarca Regional Health Authority and the Peruvian National Institute of Health (Instituto Nacional de Salud, INS: 2-05-70-08-012). It was registered at a national (INS) and an international trial registry (ISRCTN: 'ISRCTN28191222'). Community leaders and local authorities signed an agreement with the IIN and Swiss Tropical and Public Health Institute (Swiss TPH) after screening for eligibility and before randomization. The principal caregiver of each study child gave written informed consent before study implementation. Sick study children were evaluated by the study physician or referred for treatment.

Site and population

The study was conducted from September 2008 to January 2010 in the San Marcos province, located 60 kilometres south-east of Cajamarca city, in northern Peru. We chose this area because of its well-separated and accessible communities and because, to our knowledge, no major health promotion programmes were currently implemented. The province is located between 2200 and 3900 metres above sea level. Most of the population are small-scale farmers. At the time of the study, most people were using an unventilated traditional stove or open fire for cooking and heating within their homes. About 80% of the population had a piped-water system with a faucet available in the household's yard.

Study design

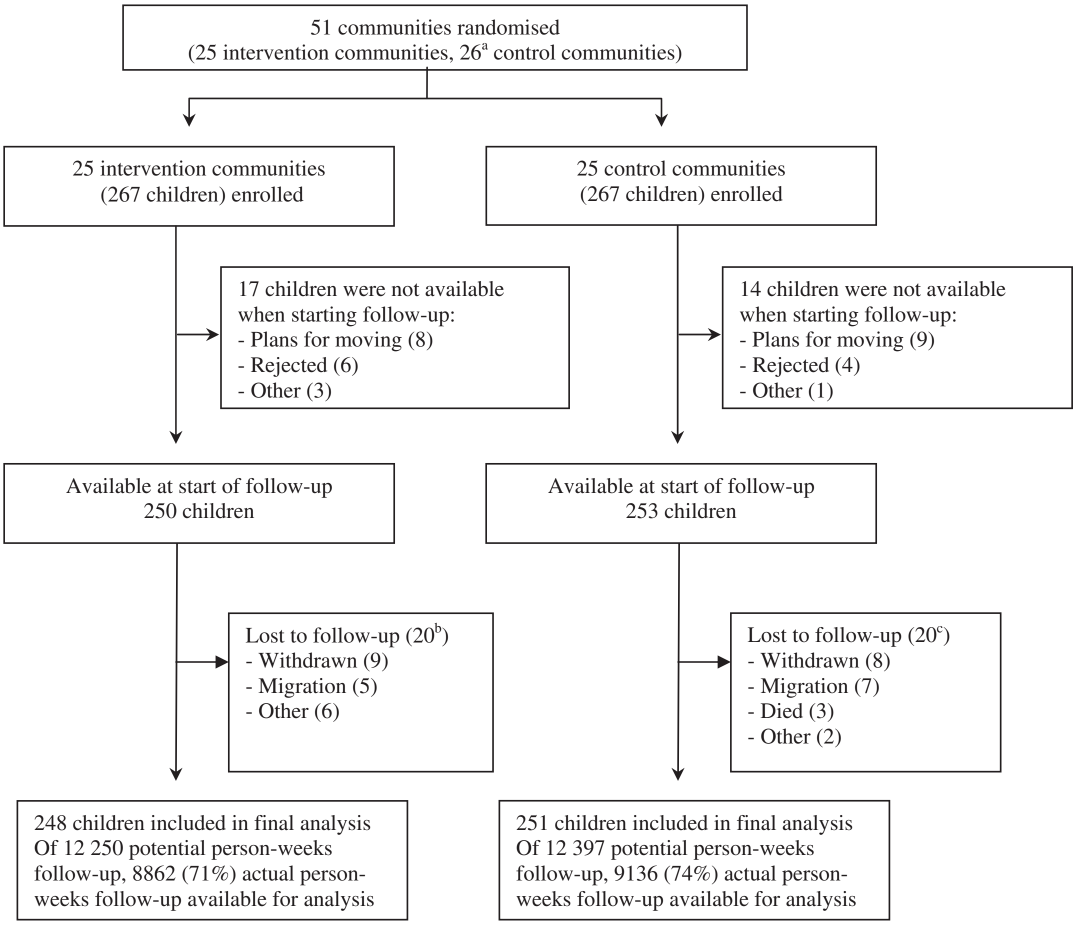
We implemented a community-randomized–controlled field trial to evaluate the IHIP interventions on reducing acute diarrhoeal illness and ARI, and improving child growth over a 12-month surveillance period. Our primary sampling units were the communities. Sample size was calculated for cluster-randomized trials using the approach of Hayes and Bennett.[14] The trial was powered to detect an incidence rate (IR) reduction of 22% with 80% power at a 5% level of significance, assuming five episodes of ARI and five episodes of diarrhoea per child-year of observation and a coefficient of variation of $k = 0.2$. Fifty-six communities were identified by a house-to-house screening. We included only 51 communities, as five communities were very small, with fewer than four children. Three of the five communities were joined to adjacent communities and the other two were excluded because of remoteness. Within the included communities, one child aged 6–35 months was randomly selected from each eligible household willing to participate. Eligibility criteria included use of solid fuels, no public sewage connection and no intention to move during the study period. Randomization was performed at the village level. The 51 communities were randomized using covariate-based constrained randomization—a procedure that can balance individual- and group-level covariates in the experimental units, here the communities, in a group-randomized study.[14,15] Randomization, enrolment and baseline data collection took place between September 2008 and January 2009 (Figure 1). Blinding of the interventions was not possible. To counteract potential unbalance of dropouts between study arms and non-blinding bias, an early child stimulation intervention, which seemed unlikely to have an impact on child diarrhoea and respiratory infections, was implemented as attention control. More details on study design can be found elsewhere.[16]

Development of interventions

The components of the IHIP interventions were developed with a participatory approach during a six-month pilot phase in neighbouring communities not enrolled in the trial.[15,16] We identified and convened main stakeholders and beneficiaries to develop an intervention package that generates healthy household environments, addresses local beliefs and cultural views, and has potentially synergistic effects on household health and livelihoods. We investigated efficacy and acceptability of the interventions, i.e. providing the stoves, kitchen sinks and plastic bottles for solar water treatment, and hygiene education. With the community members' involvement, an improved solid-fuel stove called the 'OPTIMA-improved stove' and a kitchen sink providing piped water within the household's kitchen were developed.[17] The stoves were built with local materials to enable self-maintenance and repair. Nine months after installation, all stoves were revisited and repaired as needed by the original stove builders. Mothers/caretakers were also trained in solar drinking-water disinfection (SODIS) according to standard procedures.[18] Mothers were instructed to wash their own and children's hands with soap or detergent after defecation, after changing diapers, before food preparation and before eating. Additionally, mothers were instructed to separate animals and their excreta from the kitchen environment. The IHIP highlights include:

- components: an improved ventilated solid-fuel stove, a kitchen sink with in-kitchen water connection, a point-of-use water-quality intervention applying solar disinfection to drinking water and a hygiene intervention focusing on hand-washing with soap and kitchen hygiene;
- aims: to reduce childhood respiratory infections and diarrhoea via reduced household air pollution, increased quality and quantity of drinking water and water used for hygiene purposes, and improved personal and kitchen hygiene;
- development: community engagement in the design and development of the interventions (namely involvement of local and regional stakeholders to assure development-, health- and education-sector engagement in the design and post-intervention scale-up phases).

More information on stove performance, the microbiological efficacy of SODIS and the qualitative assessment of perceptions are described elsewhere.[16,17,19,20] The intervention in the control communities was based on the National WawaWasi early child development (ECD)



[a] One community (12 children) declined to participate during enrolment
[b] Two children without any follow-up data excluded from final analysis
[c] Two children without any follow-up data excluded from final analysis

Figure 1. Flow of participants.

programme, which provided psychomotor and cognitive stimulation in children under four years of age at day-care centres.[21] Together with WawaWasi experts, we adapted the intervention to be applied at the household level and trained field staff. Mothers were trained in the use of the ECD toys and materials and instructed to play with their children for at least 30 minutes every day.

Training of field staff

Four teams, which received extensive specific training, were responsible for data collection. The field research team collected morbidity data and was trained in interviewing techniques, data recording, identification of signs and symptoms of child diarrhoea, and ALRI severity symptoms, as well as measuring respiratory rates. Additionally, the team collected spot-check observations using a checklist on household hygiene and environmental health conditions (e.g. presence of SODIS bottles on the roof or kitchen). The health promoters locally hired elementary school teachers, implemented and promoted the interventions and collected monthly compliance data. The anthropometric team was trained in measuring child weight and height in a standardized way. The environmental team collected environmental samples to test for faecal contamination of mothers' hands, drinking water and kitchen cloths.

Implementation

The IHIP interventions (improved solid-fuel stoves and kitchen sinks) were installed between October 2008 and January 2009. Households without connection to piped water were connected during sink installation. SODIS and personal, child and kitchen hygiene were reinforced monthly during 12-month follow-up. Each child in the control group received six sets of toys approximately every two months, depending on the child's progress and age.[16,17] The promotion of the interventions was done with the same intensity in both groups.

Data collection

Follow-up took place from February 2009 to January 2010. Field workers visited each household weekly and collected morbidity data from the mother/caretaker on daily signs and symptoms of child diarrhoea and respiratory illness. If diarrhoea was observed, additional information on severity was collected (sunken eyes, dry mouth, tongue and mucous membranes and thirstiness). If a child had cough or fever on the day of the household visit or the previous day, we looked for danger signs[22] to assess the severity of the respiratory illness by recording noisy and/or fast breathing, rhonchus/wheezing, lower chest in-draw, malaise and lack of appetite. If any of the severity signs were present, the child was examined and treated by our study physician on the same day or referred to local healthcare services. Specific questions determined the child's health at the moment of the weekly home visit, including seeking outpatient care, hospitalization and type of medical treatment.

Height and weight were collected every two months. In deviation to the original protocol, height and weight measurements were done only once per visit instead of repeating the measurements three times. Environmental samples from the mother's hands, kitchen cloths and drinking water were collected at baseline, mid-term and end of the surveillance period.[23] However, we did not collect data on breastfeeding or child-feeding practices as potential confounders of diarrhoea and anthropometric outcomes.

Outcome measurements

Diarrhoea was defined as three or more liquid or semiliquid stools in a 24-hour period or one stool with blood and/or mucus.[24] An episode was defined to begin on the first day of diarrhoea and ended the last day of diarrhoea, followed with at least two consecutive non-diarrhoeal days.

ARI was defined as a child presenting cough and/or difficulty breathing. ALRI was defined as a child presenting cough or difficulty breathing, with a raised respiratory rate (>50 per min in children aged 6–11 months and >40 per min in children aged $\geq$12 months) on two consecutive measurements.[22,25] An episode was defined to begin on the first day of cough or difficulty breathing and ended with the last day of the same combination, followed by at least seven days without those symptoms.[25]

Stunting, wasting and underweight as defined by the World Health Organization (WHO) were used to evaluate child nutritional status.[26]

Statistical analysis

We applied an intention-to-treat analysis comparing incidence rate of diarrhoea and respiratory infection per child-year in intervention vs control communities. Longitudinal prevalence (LP) was calculated as the number of illness days per days under observation. All children with at least one day of follow-up were included in the analysis. Generalized estimating equation (GEE) models were fitted to adjust for correlation within villages.[27] The unadjusted model included only the design factors and the intervention effect. Further models adjusted for child's age and sex. No imputation of missing data has been performed.

The statistical models included the log link function for negative binomial (relative rate RR) and logit for binomial distributed data (odds ratio OR). The logarithm of days under observation was included as offset variable in the count models. The statistical analyses were performed using SAS software v9.3 (PROC GENMOD, SAS Institute Inc.). Data management, cleaning and descriptive analysis were done using R V3.0.0 (R development core team). The coefficient of variation (k) and the 95% credible interval were estimated via Bayesian generalized random effects models using WinBUGS 1.4.

Results

Of the 51 communities, 25 communities (267 households) were randomized to the intervention and 26 (267 households) to the control arm (Figure 1). One community in the control group declined to participate. Further details on participant flow before start of follow-up are described elsewhere.[16] The final analysis included 248 children from intervention and 251 children from control communities. Information on morbidity was collected for about 18 000 person-weeks, representing 71% and 74% of the total possible observation time in intervention and control arms.

Baseline characteristics were balanced between study arms with the exception of access to piped water (Table 1). Both study groups were 'poor' according to national standards (Table 1).[28] Despite the high coverage of piped-water supply (80%), about 65% of drinking-water samples were contaminated with *Escherichia coli* and 10% of these were faecally contaminated with diarrhoeagenic *E. coli*.[23]

Table 1. Demographics and socio-economic characteristics of 503 households in rural Peru

Characteristics	Intervention arm		Control arm	
	Number	Mean (SD) or %	Number	Mean (SD) or %
Demography				
Number of household members	226	5.0 (1.6)	234	4.6 (1.5)
Age in years of enrolled children	250	2.1 (0.7)	253	2.1 (0.7)
Female children	250	50%	253	50%
National poverty indicators[a]				
1 unsatisfied basic need	224	17%	231	23%
2 unsatisfied basic need	224	25%	231	28%
3 unsatisfied basic need	224	40%	231	35%
4 unsatisfied basic need	224	14%	231	10%
Household characteristics				
Household with latrines	245	80%	239	84%
Piped-water supply	245	74%	239	82%
Microbiological indicators[b]				
Drinking water	88	68%	94	64%
Kitchen wipes	56	34%	35	25%
Mother's hands	95	27%	109	22%
Anthropometrics				
Height-for-age Z-scores [median (IQR)]	196	−2.2 (−2.7, −1.4)	194	−2.0 (−2.5, −1.4)
Weight-for-age Z-scores [median (IQR)]	201	−0.8 (−1.2, −0.2)	202	−0.7 (−1.2, −0.1)

[a]The National Poverty Indicators comprise five basic parameters: (i) inappropriate infrastructure; (ii) crowding; (iii) lack of access to basic sanitation; (iv) having at least one child of school age not attending school; and (v) family head with at least three dependents with incomplete primary-level education. A household is considered 'poor' if they have one unsatisfied basic need.[27]

[b]*E. coli*-positive samples.

Further socio-demographic, household and environmental baseline context is also described elsewhere.[16]

Diarrhoea morbidity

Children in the intervention arm reported a total of 301 diarrhoea episodes, which corresponds to a mean of 1.8 episodes per child-year. In the control arm, 375 episodes and a mean of 2.2 episodes per child-year occurred. The mean episode length of 2.8 days was shorter in the intervention arm compared with 3.1 days in the control arm (Table 2). The statistical analysis estimated that children in the intervention communities had 22% fewer diarrhoea episodes per year compared with children in control communities [RR: 0.78, 95% CI: 0.58–1.05, $p = 0.10$]. A similar result was found for the LP of diarrhoea, with an OR of 0.71 (95% CI: 0.47–1.06, $p = 0.09$) (Table 3). The clustering coefficient k was 0.39 (95% confidence interval: 0.25–0.57). The prevalence of child diarrhoea indicated no evident temporal effect throughout the follow-up period (Figure 2). To confirm that findings were not sensitive to the choice of covariates, we reanalysed including piped water and/or latrine ownership in the model. None of the models yielded major changes in the point estimates or confidence intervals.

Respiratory infections

The total number of ARI episodes was 831 in the intervention group and 877 in the control group (Table 2). Out of these, we achieved 68% and 63% of respiratory rate measurements in the intervention and control groups, respectively, corresponding to 554 and 563 ARI episodes with respiratory rate assessment. In about 50% of ARI episodes, the child had already received medical treatment before respiratory rate assessment. The total numbers of ALRI episodes were 25 in the intervention and 10 in the control group (Table 2). The RR for ARI episodes was 0.95 (0.39, 1.65; *p*-value 0.53) and 2.45 (95% CI: 0.82 to 7.39; *p*-value 0.11) for ALRI. The ORs associated with cough or difficulty breathing prevalence, and cough or difficulty breathing and fever prevalence were close to 1 (Table 3). Prevalences over time are illustrated in Figure 3.

Anthropometric measurements

At baseline, children of both study arms had similar frequencies of stunting (median of −2.2 and −2.0 *z*-scores below average WHO growth standards in intervention and control arm) and underweight (median −0.8 and −0.7). At the end of follow-up, no difference was observed between intervention and control children for height-for-age (−2.1 and −1.9 *z*-score, respectively) or weight-for-age (−0.6 and −0.7, respectively).

Table 2. Descriptive statistics of main diarrhoeal and respiratory health outcomes and anthropometric measurements

Health conditions	Class or parameter	Intervention ($N = 248$)	Control ($N = 251$)
Days under observation	Median (IQR)	265 (225–293)	276 (235–297)
Days under observation	Total	62 031	63 952
Diarrhoeal illness			
Number of episodes	Median (IQR)	1 (0–2)	1 (0–2)
Days with diarrhoea	Median (IQR)	2 (0–4)	2 (0–6)
Total number of days with diarrhoea	Total	827	1125
Total number of episodes	Total	301	375
Total number of persistent episodes (>14 days' duration)	Total	0	4
Mean length of episode (days)		2.8	3.1
Diarrhoea incidence (number of episodes/child-year)	Mean	1.8	2.2
Diarrhoea prevalence (number of diarrhoeal days/child-year)	Mean	4.9	6.6
Number of diarrhoeal episodes with blood	Total	17	24
Number of diarrhoeal episodes with vomiting	Total	51	54
Respiratory infections			
Days with cough or difficulties breathing	Median (IQR)	17 (8–25)	14 (8–26)
Total number of days with cough or difficulties breathing	Total	4534	4635
Total number of days with cough or difficulties breathing and fever	Total	951	1034
Total number of ARI episodes	Total	831	877
Percentage of ARI episodes seen with respiratory rate measurements	%	68% (554)	63% (563)
Total number of ALRI episodes	Total	25/554[a]	10/563[b]
Number of children with at least one ALRI episode	Total	17	10
Anthropometrics			
Height-for-age Z-scores [median (IQR)]	Median (IQR)	–2.1 (–2.7/–1.3)	–1.9 (–2.5/–1.4)
Weight-for-age Z-scores [median (IQR)]	Median (IQR)	–0.6 (–1.1/–0.2)	–0.7 (–1.2/–0.2)

ARI, acute respiratory infections; ALRI, acute lower respiratory infections.

[a]In 255/554 episodes, the mother started medical treatment before the field worker assessed the respiratory rate.

[b]In 218/563 episodes, the mother started medical treatment before the field worker assessed the respiratory rate.

Table 3. Effect of the intervention on diarrhoea and acute respiratory infections

Outcome	Crude model[a]			Age sex model[b]		
($n = 499$)	RR/OR	95% CI	*p*-value	RR/OR	95% CI	*p*-value
Number of diarrhoea episodes[c] (RR)	0.78	0.58, 1.05	0.10	0.79	0.60, 1.03	0.09
Diarrhoea prevalence (OR)	0.71	0.47, 1.06	0.09	0.72	0.49, 1.05	0.09
Episodes with blood (OR)	0.80	0.39, 1.65	0.55	0.80	0.39, 1.65	0.54
Number of ARI episodes (RR)	0.95	0.82, 1.10	0.53	0.95	0.82, 1.10	0.51
Number of ALRI episodes (RR)	2.45	0.82, 7.39	0.11	2.47	0.84, 7.29	0.10
Cough or difficulty breathing prevalence (OR)	0.97	0.79, 1.19	0.80	0.97	0.79, 1.19	0.79
Cough or difficulty breathing and fever prevalence (OR)	0.89	0.71, 1.12	0.33	0.89	0.71, 1.12	0.33

Number of episodes: number of episodes per child-year; prevalence: number of days ill per days under observation; ARI, acute respiratory infections; ALRI, acute lower respiratory infections.

[a]Adjusted for design factor (intra-village correlation).

[b]Adjusted for child's age and sex and design factor (intra-village correlation).

[c]Clustering coefficient $k = 0.39$.

Microbiological samples

A total of 1994 samples of drinking water, kitchen cloths and mothers' hands were collected throughout the study. We observed an *E. coli* geometric mean of CFU/100 ml of 9 (CI 95% 3.6–22.4) for drinking-water samples at baseline, 6.1 (CI 95% 0.7–48.2) at mid-study and 2.9 (CI 95% 1.9–4.5) at end-of-study evaluations in the intervention households. A similar decline in the *E. coli* geometric mean was observed for control households.

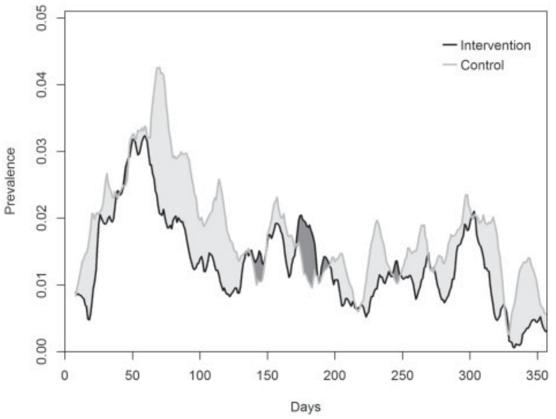


Figure 2. Diarrhoea prevalence over time. Presented are unweighted moving averages using a bandwidth of two weeks.

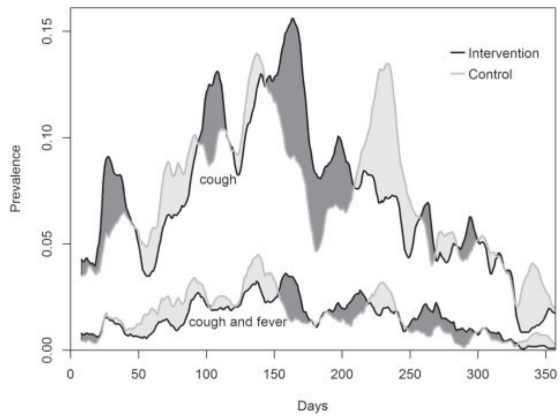


Figure 3. Cough or difficulty breathing prevalence and cough or difficulty breathing and fever prevalence over time. Presented are unweighted moving averages using a bandwidth of two weeks.

Compliance

Indicators and methods of measuring compliance in this trial are detailed in the Supplementary data, available at *IJE* online. Field workers that carried out weekly spot-check observations of compliance observed an initial prevalence of SODIS use of 60% with a steady decline throughout follow-up. At study end, SODIS was only practised by 10% of the IHIP intervention group. Self-reported use by mothers was around 90%, with a slight decrease at study end. Compliance of the improved-stove and kitchen-sink use is based on monthly maternal reporting. Ninety per cent of all mothers reported using the improved stove daily and two-thirds reported using the kitchen sink for washing utensils and children's hands daily. Lack of continuous water flow (based on seasonal water availability) and interrupted water supply were two limitations for use.

Discussion

Our community-randomized–controlled trial in 51 rural Peruvian communities consisting of improved solid-fuel stoves, kitchen sinks, hygiene promotion and SODIS treatment might have reduced child diarrhoea episodes by 22% (RR 0.78, 95% CI: 0.49–1.05) and diarrhoea prevalence by 29% (OR 0.71, 95%, CI: 0.47, 1.06). Although the confidence intervals included unity, the observed effect is consistent with lower numbers of persistent diarrhoea, bloody stool episodes, shorter duration of illness (Table 2) and episodes requiring treatment in the intervention arm (data not shown). Objective environmental indicators such as faecal contamination of drinking water also corroborate the observed diarrhoea reduction. No effects on children's ARI, ALRI and growth were found.

We combined different interventions that individually impact childhood diarrhoea: piped water delivered to the household's kitchen, household drinking-water treatment and hygiene education. A recent systematic review of drinking-water and sanitation improvements found diarrhoea risk reductions when basic piped water to the household or premise was introduced on a formerly improved community water source.[4] Supplying reliable drinking water directly to the household's kitchen increases water availability and is thereby a prerequisite for hygienic practices.[29] Water availability and distance to the water source were shown to be associated with reduced diarrhoea risk.[30–32]

The mentioned review found additional diarrhoea reductions for SODIS treatment on top of piped water to the household but there was no effect of this intervention on any baseline water source when results were adjusted for non-blinding.[4] Different blinded household-level drinking-water quality studies showed no effect on diarrhoeal disease reduction.[33–35]

Also, the effect of hygiene promotion was thought to be susceptible to bias from unblinded designs.[5] Non-blinding in intervention studies with subjective outcomes, like caregiver's report of diarrhoea, was associated with significant overestimation of the intervention effect.[35,36] To counteract this bias, we implemented a different intervention in the control group. The baseline water source might further explain the different findings of previously published SODIS intervention studies that showed larger impacts of SODIS on diarrhoeal disease—they were all conducted on unimproved or improved community water sources[37–44] whereas, in our intervention, 80% of study participants already received piped water within their premises or yards. Additionally, at the end of follow-up, only 10% of study households were using SODIS. Low compliance in SODIS interventions has been described before despite extensive promotion campaigns.[45] Our interventions did not lead to the provision of high-quality drinking water that has been associated with larger diarrhoea reductions.[4] Additionally, having focused even more on babies, hand-washing at key times and the creation of clean playing and feeding environments could have led to increased diarrhoea reduction.[46] Furthermore, the ECD intervention that we implemented in the attention control group is likely to have positively influenced playing and feeding environments and might therefore have attenuated the intervention effect. We nevertheless judged a control intervention to be highly important to prevent increased drop-out in the control group and reporting bias from the non-blinded design. Additionally, the area had received hand-washing promotion through local health centres before; therefore, there was a general understanding of appropriate hand-washing practices in both the intervention and the control groups. Finally, our study was sufficiently powered to detect a 22% reduction in diarrhoea episodes assuming five episodes per person-year of observation. However, we observed a mean of two diarrhoea episodes.

We did not observe a reduction in ARI and ALRI episodes. Potential reasons are: (i) insufficient power to detect reduction in ARI and especially ALRI, of which only a few cases were observed; (ii) the improved stove substantially lowered air pollution,[18,19,47] but not to levels recommended by the WHO (indoor air quality guidelines were not available at the time of the study)[48]; (c) limitations of timely respiratory rate assessment, as we examined children only once per week; and (d) limitations to clinically diagnose ALRI.

The RESPIRE study, the first randomized–controlled trial on improved solid-fuel stoves, suggested a mean CO exposure reduction of 50% to achieve impact on physician-diagnosed pneumonia.[10] In our study, we found only small reductions of CO and $PM_{2.5}$ pollutants that were more pronounced in better-maintained stoves. We measured exposure data only once and seven months after stove implementation.[18,19,47] The best-functioning stoves achieved a 45% and 27% mean reduction of $PM_{2.5}$ and CO, respectively, in mothers' personal exposure.[19] It is possible that, after the introduction of the stoves, study participants spent more time in the then less-smoky kitchens, which led to increased total exposure to air pollutants. Project-initiated repairs were carried out nine months after the stoves had been installed. At this point, 35% of our stoves needed minor repairs, e.g. re-plastering, and 1% needed major repairs, e.g. a broken chimney valve. Two years after the end of the study, an evaluation showed that around 85% of the Optima-improved cooking stoves were still in use (defined as at least five times a week, twice a day).

A further limitation was the monitoring frequency for ARI and ALRI. Respiratory rate measurements were only available for about two-thirds of all reported ARI episodes. In addition, in 40% of the remaining ARI episodes, the child had already attended a health centre and/or received treatment at the time of the household visit. Therefore, the true ALRI incidence is likely higher, but this should be balanced between intervention and control communities. Hence, the observed 25 and 10 ALRI episodes in the intervention and control arm should be interpreted with caution considering also that, of the 25 observed episodes in the intervention arm, almost one-third were recorded in a single very sick child. Additionally, a more objective way of defining ALRI, e.g. through chest x-rays, could have produced more correct estimates[24] but would have added substantially to costs and training requirements, which was not feasible for this study.

We could not blind the application of our interventions. Open trial designs can, however, benefit from and harness the community dynamics generating interest and motivation for a demand-driven replication. Furthermore, we believe that the selection of a highly valued intervention in the control arm (early child stimulation) reduced non-blinding/reporting bias and drop-out rates. Additionally, we used standardized data-collection tools and independent morbidity data-collection teams to minimize social desirability bias.

In conclusion, our intervention is one of the first studies to focus on addressing several household burdens simultaneously. Improved drinking-water quality and quantity, personal and kitchen hygiene and indoor air quality provide a healthy household environment that can translate into many aspects of life, including better health and poverty reduction. Even though we found no strong evidence for health impacts, the IHIP could be successfully delivered and was highly accepted.

Funding

This work was supported by the UBS Optimus Foundation, Freiwillige Akademische Gesellschaft, Basel, Stiftung Emilia-Guggenheim-Schnurr, Basel. The funders of the study had no involvement in study design, data collection, analysis or interpretation of the data, nor were they involved in the writing of this paper or in the decision to submit the paper for publication.

Acknowledgements

The authors wish to express their appreciation and thank the study families for their kind participation and local authorities for their continuous support throughout the study. We would also like to express our gratitude to the field teams, especially to Mrs Selene

Flores, who was instrumental in logistic support provided for the study. Author contributions—the principal investigators: Mäusezahl, Lanata; study concept and design: Mäusezahl, Lanata; obtained funding: Mäusezahl, Lanata; acquisition of data: Hartinger, Lanata, Gil; data entry: Hartinger, Gil, analysis and interpretation of data: Hattendorf, Hartinger, Mäusezahl, Lanata; drafting of the manuscript: Hartinger, Hattendorf, Mäusezahl, Wolf; statistical analysis: Hattendorf, Hartinger; critical revision of the manuscript: Hattendorf, Lanata, Gil, Mäusezahl, Wolf. Trial registry: http://www.controlled-trials.com/ISRCTN28191222.

Conflict of interest: The authors have no conflicts of interest to declare.

References

1. Walker CLF, Rudan I and Liu L *et al*. Global burden of childhood pneumonia and diarrhoea. *Lancet* 2013;**381**:1405–16.
2. Prüss-Ustün A, Bartram J and Clasen T *et al*. Burden of disease from inadequate water, sanitation and hygiene in low- and middle-income settings: a retrospective analysis of data from 145 countries. *Trop Med Int Health* 2014;**19**:894–905.
3. IHME. GBD 2013, *GBD Compare*. http://vizhub.healthdata.org/gbd-compare/ (13 January 2016, date last accessed).
4. Wolf J, Prüss-Ustün A and Cumming O *et al*. Assessing the impact of drinking-water and sanitation on diarrhoeal disease in low-and middle-income settings: a systematic review and meta-regression. *Trop Med Int Health* 2014;**19**:928–42.
5. Freeman MC, Stocks ME and Cumming O *et al*. Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. *Trop Med Int Health* 2014;**19**:906–16.
6. Clasen TF, Bostoen K and Schmidt WP *et al*. Interventions to improve disposal of human excreta for preventing diarrhoea. *Cochrane Database Syst Rev*. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007180.pub2/pdf/standard (30 January 2013, date last accessed).
7. Cairncross S, Hunt C and Boisson S *et al*. Water, sanitation and hygiene for the prevention of diarrhoea. *Int J Epidemiol* 2010;**39(Suppl 1)**:i193–205.
8. Dherani M, Pope D and Mascarenhas M *et al*. Indoor air pollution from unprocessed solid fuel use and pneumonia risk in children aged under five years: a systematic review and meta-analysis. *Bull World Health Organ* 2008;**86**:390–8C.
9. Po JY, FitzGerald JM and Carlsten C. Respiratory disease associated with solid biomass fuel exposure in rural women and children: systematic review and meta-analysis. *Thorax* 2011;**66**:232–9.
10. Smith KR, McCracken JP and Weber MW *et al*. Effect of reduction in household air pollution on childhood pneumonia in Guatemala (RESPIRE): a randomised controlled trial. *Lancet* 2011;**378**:1717–26.
11. Eisenberg JNS, Scott JC and Porco T. Integrating disease control strategies: balancing water sanitation and hygiene interventions to reduce diarrheal disease burden. *Am J Public Health* 2007;**97**:846.
12. VanDerslice J and Briscoe J. Environmental interventions in developing countries: interactions and their implications. *Am J Epidemiol* 1995;**141**:135–44.
13. Hayes RJ and Bennett S. Simple sample size calculation for cluster-randomized trials. *Int J Epidemiol* 1999;**28**:319–26.
14. Moulton LH. Covariate-based constrained randomization of group-randomized trials. *Clin Trials* 2004;**1**:297–305.
15. Hartinger SM, Lanata CF and Hattendorf J *et al*. A community randomised controlled trial evaluating a home-based environmental intervention package of improved stoves, solar water disinfection and kitchen sinks in rural Peru: rationale, trial design and baseline findings. *Contemp Clin Trials* 2011;**32**:864–73.
16. Hartinger SM, Lanata CF and Gil AI *et al*. Combining interventions: improved chimney stoves, kitchen sinks and solar disinfection of drinking water and kitchen clothes to improve home hygiene in rural Peru. *Field Actions Science Reports: The Journal of Field Actions, Special Issue 6*. http://factsreports.revues.org/1627 (3 May 2013, date last accessed).
17. SODIS: *Willkommen bei SODIS*. http://www.sodis.ch/index (1 April 2015, date last accessed).
18. Commodore AA, Hartinger SM and Lanata CF *et al*. Carbon monoxide exposures and kitchen concentrations from cookstove-related woodsmoke in San Marcos, Peru. *Int J Occup Environ Health* 2013;**19**:43–54.
19. Hartinger SM, Commodore AA and Hattendorf J *et al*. Chimney stoves modestly improved Indoor Air Quality measurements compared with traditional open fire stoves: results from a small-scale intervention study in rural Peru. *Indoor Air* 2013;**23**:342–52.
20. Cueto S, Guerrero G and Leon J *et al*. *Promoting early childhood development through a public programme: Wawa Wasi in Peru*. Report No. 51, University of Oxford, Department of International Development, Young Lives, 2009. http://www.grade.org.pe/en/publicaciones/859-promoting-early-childhood-development-through-a-public-programme-wawa-wasi-in-peru/ (9 September 2016, date last accessed).
21. World Health Organization. *Integrated Management of Childhood Illness, Chart Booklet*. March 2014. http://whqlibdoc.who.int/publications/2008/9789241597289_eng.pdf (9 September 2016, date last accessed).
22. Gil AI, Lanata CF and Hartinger SM *et al*. Fecal contamination of food, water, hands, and kitchen utensils at the household level in rural areas of Peru. *J Environ Health* 2014;**76**:102–8.
23. World Health Organization. *The Treatment of Diarrhoea: A Manual for Physicians and Other Senior Health Workers*, 4th edn. WHO, 2005. http://www.who.int/maternal_child_adolescent/documents/9241593180/en/ (9 September 2016, date last accessed).
24. Lanata CF, Rudan I and Boschi-Pinto C *et al*. Methodological and quality issues in epidemiological studies of acute lower respiratory infections in children in developing countries. *Int J Epidemiol* 2004;**33**:1362–72.
25. World Health Organization. *The WHO Child Growth Standards*. http://www.who.int/childgrowth/en/ (1 April 2015, date last accessed).
26. Durán Pacheco G, Hattendorf J and Colford JM *et al*. Performance of analytical methods for overdispersed counts in cluster randomized trials: sample size, degree of clustering and imbalance. *Stat Med* 2009;**28**:2989–3011.
27. Instituto Nacional de Estadística e Informática (INEI) 2007. https://www.inei.gob.pe/ (19 January 2016, date last accessed).

28. Evans BE, Bartram J and Hunter P *et al*. *Public Health and Social Benefits of At-House Water Supplies*. University of Leeds, 2013. http://r4d.dfid.gov.uk/pdf/outputs/water/61005-DFID_HH_water_supplies_final_report.pdf (1 April 2014, date last accessed).
29. Wang X and Hunter PR. A systematic review and meta-analysis of the association between self-reported diarrheal disease and distance from home to water source. *Am J Trop Med Hyg* 2010;**83**:582–4.
30. Pickering AJ and Davis J. Freshwater availability and water fetching distance affect child health in sub-Saharan Africa. *Environ Sci Technol* 2012;**46**:2391–7.
31. Royal Scientific Society Amman-Jordan (RSS). *Review Evidence on Minimum Household Water Security Requirements for Health Protection*. Research Division, Royal Scientific Society Amman-Jordon, 2011. http://www.mdgfund.org/sites/default/files/ENV_STUDY_Jordan_Minimum%20hosehole%20water%20security.pdf (9 September 2016, date last accessed).
32. Boisson S, Stevenson M and Shapiro L *et al*. Effect of household-based drinking water chlorination on diarrhoea among children under five in Orissa, India: a double-blind randomised placebo-controlled trial. *PLoS Med* 2013;**10**:e1001497.
33. Kirchhoff LV, McClelland KE and Pinho MDC *et al*. Feasibility and efficacy of in-home water chlorination in rural North-eastern Brazil. *Journal of Hygiene* 1985;**94**:173–80.
34. Jain S, Sahanoon OK, Blanton E and Schmitz A *et al*. Sodium dichloroisocyanurate tablets for routine treatment of household drinking water in Periurban Ghana: a randomized controlled trial. *Am J Trop Med Hyg* 2010;**82**:16–22.
35. Savović J, Jones HE and Altman DG *et al*. Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. *Ann Intern Med* 2012;**157**:429–38.
36. Wood L, Egger M and Gluud LL *et al*. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ* 2008;**336**:601.
37. Conroy RM, Elmore-Meegan M and Joyce T *et al*. Solar disinfection of drinking water and diarrhoea in Maasai children: a controlled field trial. *Lancet* 1996;**348**:1695–7.
38. Conroy RM, Meegan ME and Joyce T *et al*. Solar disinfection of water reduces diarrhoeal disease: an update. *Arch Dis Child* 1999;**81**:337–8.
39. Conroy RM, Meegan ME and Joyce T *et al*. Solar disinfection of drinking water protects against cholera in children under 6 years of age. *Arch Dis Child* 2001;**85**:293–5.
40. du Preez M, Conroy RM and Ligondo S *et al*. Randomized intervention study of solar disinfection of drinking water in the prevention of dysentery in Kenyan children aged under 5 years. *Environ Sci Technol* 2011;**45**:9315–23.
41. McGuigan KG, Samaiyar P and du Preez M *et al*. High compliance randomized controlled field trial of solar disinfection of drinking water and its impact on childhood diarrhea in rural Cambodia. *Environ Sci Technol* 2011;**45**:7862–7.
42. Rai BB, Pal R and Kar S *et al*. Solar disinfection improves drinking water quality to prevent diarrhea in under-five children in Sikkim, India. *J Glob Infect Dis* 2010;**2**:221.
43. Rose A, Roy S and Abraham V *et al*. Solar disinfection of water for diarrhoeal prevention in southern India. *Arch Dis Child* 2006;**91**:139–41.
44. Graf J, Togouet SZ and Kemka N *et al*. Health gains from solar water disinfection (SODIS): evaluation of a water quality intervention in Yaounde, Cameroon. *J Water Health* 2010;**8**:779–96.
45. Mäusezahl D, Christen A and Pacheco GD *et al*. Solar drinking water disinfection (SODIS) to reduce childhood diarrhoea in rural Bolivia: a cluster-randomized, controlled trial. *PLoS Med* 2009;**6**:e1000125.
46. Ngure FM, Reid BM and Humphrey JH *et al*. Water, sanitation, and hygiene (WASH), environmental enteropathy, nutrition, and early child development: making the links. *Ann NY Acad Sci* 2014;**1308**:118–28.
47. Commodore AA, Zhang JJ and Chang Y *et al*. Concentrations of urinary 8-hydroxy-2′-deoxyguanosine and 8-isoprostane in women exposed to woodsmoke in a cookstove intervention study in San Marcos, Peru. *Environ Int* 2013;**60**:112–22.
48. World Health Organization. *Indoor Air Quality Guidelines: Household Fuel Combustion*. World Health Organization, 2014. http://www.who.int/indoorair/publications/household-fuel-combustion/en/ (30 November 2015, date last accessed).

International Journal of
Environmental Research and Public Health

MDPI

Article

Adoption of Clean Cookstoves after Improved Solid Fuel Stove Programme Exposure: A Cross-Sectional Study in Three Peruvian Andean Regions

Jennyfer Wolf [1,2], Daniel Mäusezahl [1,2,*], Hector Verastegui [3] and Stella M. Hartinger [1,2,3]

1 Swiss Tropical and Public Health Institute, 4051 Basel, Switzerland; jennyfer.wolf@unibas.ch (J.W.); stella.hartinger.p@upch.pe (S.M.H.)
2 Centre for African Studies, University of Basel, Petersplatz 1, 4001 Basel, Switzerland
3 Universidad Peruana Cayetano Heredia, Av. Honorio Delgado 430, Urb. Ingeniería, S.M.P., 31 Lima, Peru; hector.verastegui.h@upch.pe
* Correspondence: daniel.maeusezahl@unibas.ch; Tel.: +41-(0)-61-284-81-78

Academic Editor: Ling Tim Wong
Received: 8 May 2017; Accepted: 3 July 2017; Published: 8 July 2017

Abstract: This study examined measures of clean cookstove adoption after improved solid fuel stove programmes in three geographically and culturally diverse rural Andean settings and explored factors associated with these measures. A questionnaire was administered to 1200 households on stove use and cooking behaviours including previously defined factors associated with clean cookstove adoption. Logistic multivariable regressions with 16 pre-specified explanatory variables were performed for three outcomes; (1) daily improved solid fuel stove use, (2) use of liquefied petroleum gas stove and (3) traditional stove displacement. Eighty-seven percent of households reported daily improved solid fuel stove use, 51% liquefied petroleum gas stove use and 66% no longer used the traditional cookstove. Variables associated with one or more of the three outcomes are: education, age and civil status of the reporting female, household wealth and size, region, encounters of problems with the improved solid fuel stove, knowledge of somebody able to build an improved solid fuel stove, whether stove parts are obtainable in the community, and subsidy schemes. We conclude that to be successful, improved solid fuel stove programmes need to consider (1) existing household characteristics, (2) the household's need for ready access to maintenance and repair, and (3) improved knowledge at the community level.

Keywords: clean cookstoves; adoption; stove stacking; Peru; household air pollution; improved solid fuel stove; liquefied petroleum gas

1. Introduction

Nearly three billion people continue to use solid fuels for cooking, heating and lighting [1]. Exposure to solid fuel smoke often through the use of traditional cookstoves ("traditional cookstove" includes open indoor fire in this article) is associated with adverse health impacts like respiratory infections [2,3], ischemic heart disease [4], stroke [5], lung cancer [6], and cataract formation [5,7]. Household air pollution was ranked the eighth leading health risk factor and was associated with nearly three million deaths in 2015 [8]. The use of traditional cookstoves has furthermore been shown to lead to negative social and environmental impacts through excess time and money spent [9], contribution to outdoor air pollution [10,11], deforestation and climate change [12].

To mitigate the negative impacts of burning solid fuels for cooking, efforts to promote the adoption of clean cookstoves are undertaken. The Global Alliance for Clean Cookstoves was created to foster household adoption of clean cookstoves and fuels [13]. Additionally, one of the Sustainable

Development Goals calls for access to affordable, reliable, sustainable and modern energy for all [14]. However, programmes promoting clean cookstoves frequently experienced problems; households did not sufficiently or sustainably use the new stove, nor did maintain or repair it when broken [15,16]. Near-exclusive use of clean cookstoves is essential to sufficiently reduce air pollution levels to achieve positive health impacts [17,18]. Often, however, clean cookstoves are just added to the traditional stoves leading to a parallel use of cooking devices ("stove stacking") [19].

Research on clean cookstove adoption has discovered enablers and barriers for clean cookstove adoption. Puzzolo et al. [20] identified factors related to the cooking technology, the household, community, programme and societal level. A Chinese literature review identified stove design, knowledge and awareness, household characteristics, market development, financial support and favourable policies as important enablers for clean cookstove and fuel adoption [21]. Household wealth and education, demographics, stove programme characteristics, and costs were described as important factors across settings [22–26].

Evaluation of promotion programmes needs to assess whether households use and value the new stove. An additional important measure is the displacement of traditional stoves when clean cookstoves are introduced [17]. Knowledge of enabling and hindering factors is essential for programme monitoring and future efforts. Here we present results from 1200 questionnaires administered to rural Andean households that had previously taken part in an improved solid fuel stove (IS) promotion programme. The objectives of this study were to explore adoption and displacement of different stove types as well as associated factors in diverse rural Andean regions where the use of solid fuels is widespread.

2. Materials and Methods

2.1. Study Settings

The study was conducted between February and November 2014 in three rural Andean Peruvian regions: Cajamarca, Cuzco and La Libertad. In rural Peru, wood is the most important cooking fuel and is exclusively used by over 40% of households. Many more use wood in combination with other solid or with clean fuels such as liquefied petroleum gas (LPG). LPG is used exclusively by only 5% of the rural population [27]. The study sites were selected purposively because of (i) large IS promotion programmes which had been conducted within the last 15 years, (ii) geographical and cultural differences between the regions, (iii) knowledge of the study sites and availability of data on e.g., the number of households exposed to IS promotion programmes, and (iv) a sufficiently high number of households in the communities. More information on the study sites can be found in the Supplementary Material (Text S1).

2.2. Sampling, Inclusion Criteria and Selection of Households

For the study site selection we identified the number of IS promotion programmes in the province, districts and communities of the area from local non-governmental organisations (NGOs), municipal and community authorities. We then sampled households from available census lists from all communities in the study sites. A household was considered eligible for the study (i) if it had previously taken part in an IS promotion programme of a governmental, non-governmental or research institution, (ii) if it used biomass (wood, carbon, dung, etc.) for cooking (alone or in combination), (iii) if it spoke Spanish as first language, and (iv) if its household head was at least 18 years old. From all eligible households, a convenience sample was drawn; households in a distance perimeter of a one hour car's drive from the community centre and accessible within a maximum of 20 min walk from a main road were visited. Only households willing to participate were interviewed. Data collection on stove use and potentially explanatory variables was performed as described in the section below.

2.3. Study Design and Data Collection

The questionnaire for this cross-sectional study was informed by recent literature on indices of clean cookstove adoption [28] and their enablers and barriers [20–26]. The questionnaire was pre-tested by our field staff before the start of the study. Where there were doubts about the comprehensibility of questions or related answers, changes were applied immediately and re-checked. After having completed pre-testing, we piloted the questionnaire in 20 households in San Marcos, Cajamarca. Additional modifications were made as needed. The final questionnaire took approximately two hours to complete. It included both open and closed questions and was written in Spanish. The main topics included clean cookstove adoption, i.e., questions on cooking behaviours, types of cookstoves present in the household, patterns of cookstove use, cleaning, maintenance and repair, willingness to pay for an IS or its parts and fieldworker observations and demographic, socio-economic and livelihood variables. All interviewers received at least three days of specific training on the questionnaire and performed practice interviews before commencing the study. A questionnaire-based interview was conducted with the female household head and field supervisors reviewed each questionnaire after completion for errors or missing values. More information on the questionnaire can be obtained from the corresponding author.

We also conducted a total of 25 focus group discussions (FGDs) in the three regions to explore, for example, general perceptions of the different stoves and barriers and enablers for their adoption. Results of FGDs will be presented elsewhere.

2.4. Data Analysis

We used multivariable logistic regression models to examine three outcomes of interest: (a) reported daily IS use, (b) reported LPG stove use, and (c) reported displacement of the traditional stove (i.e., the traditional cookstove was no longer used). Sixteen independent variables were chosen a priori to be included in the regression models. These variables were chosen based on a review of the literature and included (i) demographics and household variables (region, age, education and civil status of reporting female, household size, household wealth index, land ownership (where the house is built)), (ii) knowledge and awareness variables (education and internet use), (iii) price and costing variables (household wealth index, firewood needs to be bought, stove programme, taking part in national gas programme), (iv) stove design variables (stove programme, problems with IS), variables describing the supply chain, the clean cookstove market and an enabling environment (knowledge of somebody who can build an IS, IS parts can be obtained in the community, local authorities/leaders support IS use, taking part in the national gas programme). Variables, their categorisation and missing values are listed in Table S1. Education was categorised as zero years, one to six years—which corresponds to primary school—and above six years of schooling. All 16 explanatory variables were included in all three regression models independent of their p-value or the effect on the estimate of one of the other variables. Effect estimates presented in this paper are therefore adjusted for all other variables in the model.

Complete information was available for 87% of all participating households, i.e., for 13% of households there was at least one of the independent variables for logistic regression analyses missing (Table S1). Multiple imputation using chained equations was performed to impute missing data. More details can be found in the Supplementary Material (Text S2 and Tables S2–S5). Results of the logistic regression models presented in this article are based on the imputed dataset.

Analyses were performed using Stata/IC 14 (StataCorp, 2015, Stata Statistical Software, College Station, TX, USA).

2.5. Ethics

The study was approved by the ethical review boards of the Universidad Peruana Cayetano Heredia in Lima, Peru, and the University of Basel, Switzerland (through the ethics commission 'Ethikkommission Nordwest- und Zentralschweiz' (EKNZ)). All household heads signed written informed consent prior to participation.

3. Results

In the three regions, Cajamarca, Cuzco and La Libertad, stove use data and data on potentially explanatory variables were collected from 48, 12 and 23 communities, respectively. In total, 1202 households participated and 400 questionnaires were administered in Cajamarca, 400 in Cuzco and 402 in La Libertad. We excluded 169 households or 14% of all data from the analysis. Of those, 99 households were excluded because they had not taken part in a stove programme, but had adopted their own IS following experiences with cooking on their neighbour's or friend's IS. The remainder were excluded because of implausible values in the stove use variables. Demographics and further information on the 1033 remaining households are given in Table 1.

Table 1. Background and stove adoption information for 1033 households in three regions of Peru.

Demographics and Further Explanatory Variables	n (%)
Region	
Cajamarca	344 (33.3)
Cuzco	331 (32.0)
La Libertad	358 (34.7)
Age of reporting female	
<35	245 (23.7)
35–<45	289 (28.0)
45–<55	249 (24.1)
≥55	230 (22.3)
Education of reporting female (years of schooling)	
0	133 (12.9)
1–6	701 (67.9)
≥7	177 (17.1)
Civil status of reporting female (married/civil partnership vs. single/separated/divorced/widowed)	876 (84.8)
Household size, ≥5 persons	473 (45.8)
Wealth index [a]	
1. Quintile (lowest)	207 (20.0)
2. Quintile	212 (20.5)
3. Quintile	215 (20.8)
4. Quintile	197 (19.1)
5. Quintile (highest)	202 (19.6)
Land ownership (where house is built)	915 (88.6)
Internet use	341 (33.0)
Firewood is bought	362 (35.0)
Stove programme	
IIN	147 (14.2)
Sembrando	191 (18.5)
Juntos	183 (17.7)
Municipalidad	118 (11.4)
NINA	237 (22.9)
others (various, programmes with <5% coverage)	157 (15.2)
Participation in national gas programme	189 (18.3)
Year of stove programme participation	
≤2008	197 (19.1)
2009	161 (15.6)
2010	193 (18.7)
2011	209 (20.2)
2012	105 (10.2)
2013	50 (4.8)

Table 1. *Cont.*

Demographics and Further Explanatory Variables	*n* (%)
Problems with IS	338 (32.7)
Knowledge of somebody who can build an IS	332 (32.1)
IS parts can be obtained in the community	174 (16.8)
Local authorities/leaders support IS use	435 (42.1)
Stove use and adoption	
Primary cookstove	
IS	902 (87.3)
LPG stove	43 (4.2)
Traditional cookstove [b]	86 (8.3)
Secondary cookstove	
IS	80 (7.7)
LPG stove	469 (45.4)
Traditional cookstove	167 (16.2)
None	317 (30.7)
Daily IS use	900 (87.1)
LPG stove use	529 (51.2)
Traditional stove displacement	677 (65.5)

[a] The index is constructed from: (i) number of people per room; (ii) presence of consumer durables; (iii) presence of housing characteristics; (iv) flooring material; (v) drinking-water source; (vi) toilet facility. The original index includes presence of LPG/electricity stove and type of cooking fuel, two variables that we have excluded for the wealth index used in this analysis [29]. [b] Includes tulpia (open fire) and traditional cookstove with or without chimney. Acronyms: IIN: Instituto de Investigación Nutricional; IS: improved solid fuel stove; LPG: liquefied petroleum gas.

3.1. Stove Use and Adoption

Numbers and percentages of households using clean and traditional stoves as the primary or secondary cookstove, using the IS daily, using the LPG stove and having displaced the traditional stove are shown in Table 1. Some 87% of women stated that they used the IS daily, 51% that they used the LPG stove (in general) and 66% that they did not use traditional cookstoves. Ninety-two percent of households stated that they used clean cookstoves as the primary cooking technology, with the IS being the most important reported primary cookstove. In case a secondary cookstove was mentioned, this was mostly an LPG stove. Fieldworker observations on households reporting the IS as the primary or secondary stove revealed a missing or broken chimney in 3.5% and 6.1% and no closed combustion chamber in 13% of all observations. Eighteen percent of all households stated that they participated in the national gas programme “Fondo de Inclusión Social Energético” (FISE) [30], 69% practised stove stacking (i.e., mentioned using a secondary stove) and 54% and 79% were willing to pay (any amount of money) for a new IS or replacement parts in case the current stove would break.

3.2. Multivariable Analysis of Factors Associated with Clean Cookstove Adoption

Results of the multivariable logistic regression models examining daily IS use, use of the LPG stove and traditional stove displacement are presented in Table 2. Taking part in the national gas programme FISE [30] was an almost perfect predictor of being a gas user. This variable was therefore not included in the regression model but analysis of gas use was performed including only those households that had not taken part in the national FISE programme (n = 844). In the following paragraphs, we list the explanatory variables that are associated with one of the three outcomes which we define as a p-value of ≤ 0.05. If a variable consists of several categories, such as education, we refer to the overall p-value as given in Table 2.

Table 2. Results of multivariable logistic regression analysis of daily IS use, LPG stove use and traditional stove displacement, Peru 2014.

	Daily IS Use (*n* = 1033)		LPG Stove Use (*n* = 844)		Traditional Stove Displacement (*n* = 1033)	
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Region		0.3		0.3		<0.0001
Cajamarca	1		1		1	
La Libertad	1.27 (0.44, 3.68)		1.19 (0.48, 2.94)		2.42 (1.19, 4.93)	
Cuzco	2.46 (0.83, 7.29)		1.71 (0.87, 3.36)		4.48 (2.28, 8.79)	
Age of reporting female		0.4		1		0.002
<35	1		1		1	
35–<45	0.75 (0.44, 1.28)		0.89 (0.56, 1.42)		0.59 (0.39, 0.89)	
45–<55	1.26 (0.68, 2.32)		0.94 (0.57, 1.54)		0.43 (0.28, 0.67)	
≥55	0.96 (0.49, 1.87)		0.93 (0.53, 1.63)		0.49 (0.3, 0.81)	
Education of reporting female (years of schooling)		0.02		0.02		0.2
0	1		1		1	
1–6	0.90 (0.46, 1.76)		2.09 (1.22, 3.6)		1.39 (0.89, 2.17)	
≥7	0.44 (0.20, 0.99)		2.47 (1.26, 4.87)		1.03 (0.57, 1.84)	
Civil status of reporting female, married/civil partnership vs. single/separated/divorced/widowed	1.75 (1.06, 2.88)	0.03	0.97 (0.62, 1.54)	0.9	0.98 (0.65, 1.47)	0.9
Household size, ≥5 persons	1.25 (0.82, 1.91)	0.3	0.80 (0.56, 1.13)	0.2	0.64 (0.47, 0.88)	0.005
Wealth index		0.9		<0.0001		0.001
1. Quintile (lowest)	1		1		1	
2. Quintile	1.05 (0.57, 1.93)		2.41 (1.4, 4.15)		1.40 (0.92, 2.14)	
3. Quintile	0.77 (0.43, 1.4)		2.03 (1.17, 3.51)		1.81 (1.17, 2.8)	
4. Quintile	0.93 (0.48, 1.78)		5.05 (2.92, 8.74)		1.27 (0.81, 1.99)	
5. Quintile (highest)	0.91 (0.46, 1.79)		10.17 (5.67, 18.22)		2.74 (1.65, 4.54)	
Land ownership	1.06 (0.58, 1.93)	0.9	0.97 (0.57, 1.65)	0.9	0.77 (0.47, 1.26)	0.3
Internet use	1.36 (0.85, 2.18)	0.2	1.28 (0.89, 1.83)	0.2	1.07 (0.76, 1.5)	0.7
Firewood is bought	0.80 (0.52, 1.23)	0.3	1.09 (0.76, 1.55)	0.6	1.28 (0.92, 1.77)	0.1
Stove programme		0.2		0.07		0.1
IIN	1		1		1	
Sembrando	2.32 (0.74, 7.25)		1.04 (0.44, 2.47)		1.48 (0.73, 2.98)	
Juntos	2.37 (0.68, 8.27)		2.61 (0.99, 6.9)		0.80 (0.36, 1.78)	
Municipalidad	3.21 (0.75, 13.76)		1.13 (0.4, 3.21)		0.66 (0.27, 1.64)	
NINA	1.42 (0.28, 7.32)		1.43 (0.47, 4.34)		0.51 (0.19, 1.39)	
others (various, <5%)	3.91 (1.11, 13.78)		1.39 (0.57, 3.43)		0.93 (0.45, 1.93)	
Year of stove programme participation		0.2		0.1		0.2
≤2008	1		1		1	
2009	0.48 (0.13, 1.86)		0.54 (0.2, 1.46)		0.96 (0.43, 2.14)	
2010	0.33 (0.09, 1.24)		0.90 (0.36, 2.26)		1.00 (0.46, 2.17)	
2011	0.41 (0.11, 1.61)		0.87 (0.34, 2.25)		1.24 (0.53, 2.91)	
2012	0.77 (0.19, 3.22)		1.61 (0.62, 4.16)		1.42 (0.62, 3.25)	
2013	0.31 (0.07, 1.38)		0.98 (0.33, 2.88)		3.23 (1.18, 8.84)	
Problems with IS	0.62 (0.41, 0.93)	0.02	1.13 (0.8, 1.6)	0.5	0.65 (0.48, 0.88)	0.005
Knowledge of somebody who can build IS	2.01 (1.24, 3.27)	0.01	0.68 (0.47, 0.98)	0.04	1.02 (0.74, 1.41)	0.9
IS parts can be obtained in community	0.84 (0.51, 1.39)	0.5	1.23 (0.81, 1.87)	0.3	1.48 (1, 2.2)	0.05
Local authorities/leaders support IS use	0.94 (0.58, 1.52)	0.8	0.85 (0.57, 1.26)	0.4	0.99 (0.7, 1.39)	0.9

3.2.1. Daily IS Use

Variables associated with daily IS use in the multivariable logistic regression analysis were years of schooling and civil status of the reporting female (odds ratios, ORs,) and *p*-values of all variables are given in Table 2, second column). Encountering problems with the IS was negatively associated (OR 0.62 (0.41, 0.93)) and knowledge of somebody able to build or repair an IS was positively associated with daily IS use (OR 2.01 (1.24, 3.27)).

3.2.2. LPG Stove Use

Variables associated with LPG stove use in the multivariable logistic regression analysis were years of schooling (e.g., OR 2.47 (1.26, 4.87) for ≥7 years compared to no schooling) and wealth index (e.g., OR 10.17 (5.67, 18.22) for the fifth quintile compared to the first quintile). Knowledge of somebody able to build an IS was negatively associated with LPG stove use (OR 0.68 (0.47, 0.98)) (Table 2, third column for all ORs and *p*-values).

3.2.3. Traditional Stove Displacement

Variables associated with the displacement of the traditional stove in the multivariable logistic regression analysis were region, age of the reporting female, household size and wealth index. Encountering problems with the IS was negatively associated (OR 0.65 (0.48, 0.88)) and the possibility to obtain IS parts in the community was positively associated with traditional stove displacement (OR 1.48 (1, 2.2)) (Table 2, fourth column for all ORs and *p*-values).

Tables comparing results from analysis of imputed data and complete cases are shown in Tables S3–S5.

4. Discussion

In this study, more than 1000 households had participated in various IS promotion programmes in geographically and culturally diverse rural Andean regions. We show that a large proportion of households report daily clean cookstove use as their main or even as their exclusively used technology, i.e., no concurrent use of traditional cookstoves. Various characteristics are associated with daily IS use, LPG stove use and displacement of the traditional cookstove.

4.1. Stove Use and Adoption

Households in our study reported that the IS is their primary stove, however, LPG stoves play an increasing role in household cooking. In a similar setting in Mexico, 50–70% of households continued to use the IS ten months after intervention implementation and only 10% did not adopt it [31]. Usage of the IS was shown to decline during the first months after implementation and then to stabilise [16,31]. In our study in which most households participated in a stove programme several years ago (Table 1), we believe that this stable phase of IS use had been reached. The parallel use of multiple cookstoves (or stove stacking) is common (69% of households). Eighty-five percent of those households combine the IS as the primary stove with either the LPG (63%) or the traditional stove (22%). These numbers vary by region: in Cuzco 76% of all households practicing stove stacking use the IS as the primary plus the LPG stove as the secondary stove, whereas in Cajamarca this number is only 50% and more households (33% of all households practicing stove stacking) combine the IS with a traditional stove. Exclusive IS use is a rare phenomenon, as clean cookstoves seldom meet all household needs [19,32]. However, 66% of households reported not using the traditional cookstove, but using either the IS exclusively or in combination with the LPG stove. During our previous research activity in Cajamarca in 2009 [33,34], household use of LPG was still uncommon. However, having accepted the IS as new cooking technology might have increased households' acceptance of other clean stoves, a phenomenon also described in Mexico [31]. From focus group discussions that we conducted within the framework of this study, we discovered that households were highly enthusiastic about LPG stoves. However, these stoves were not considered as true replacements for solid fuel stoves and mostly used for minor cooking activities of short duration (such as breakfast preparation and heating dinner). Reasons given in focus groups were the high price of LPG and alteration in the taste of traditional meals.

All three measures of stove use, i.e., daily IS use, LPG stove use and traditional stove displacement, are important to achieve health effects and to describe different phases after clean cookstove promotion. A household might, for example, use the IS but might not yet have switched to LPG or discontinued using the traditional stove. Indeed, use of the IS or the LPG stove might be a prerequisite for traditional stove displacement. In this sense, traditional stove displacement might reflect sustained changes after clean cookstove promotion. In our study, 70% of households that reported daily IS use, also reported traditional stove displacement, as compared to only 35% in households with no daily IS use. Similarly, 73% of households using the LPG stove reported traditional stove displacement compared to 57% of households not using the LPG stove.

4.2. Factors Associated with Cookstove Adoption and Displacement

In-depth understanding of local enablers and barriers has been postulated to be key for successful clean cookstove interventions [35,36]. We selected our list of potential important factors based on prior evidence and explored them in a specific local context. Similar to what has been described before, some of our enabling and hindering factors are relevant for more than one outcome. Variables associated with clean cookstove adoption (i.e., with one of our three outcomes) can be grouped in demographics (education, age, civil status and region), household (household size, household wealth index), community (knowledge of somebody able to build or repair an IS and whether IS parts are obtainable in the community), stove (encounters of problems with the IS) and policy characteristics (subsidy schemes such as the national gas programme FISE). Women with higher education had higher odds of adopting the LPG stove, but lower odds of using the IS daily. Higher education was consistently associated with increased uptake of clean cookstoves in previous research [20,21,23,24]. In the present settings where the IS has become a standard cooking technology (reflected by high usage), LPG stoves might be perceived as new and modern and as a stove that more educated and wealthy households can access initially. Related to that, women in the lowest age group had higher odds of displacing the traditional stove and higher household wealth was associated with both traditional stove displacement and LPG stove use. Higher wealth might be especially important in rural areas where LPG is usually more expensive [20]. Women living with a partner had higher odds of using the IS daily than single, separated, divorced or widowed women which might be due to the fact that these women cook more often and for more people. Similarly, a bigger household size was associated with a decreased chance of traditional stove displacement, which is consistent with previous research showing LPG stove uptake being larger in smaller households [20]. Experiencing problems with the IS decreased the chance that the household was using the IS daily and also that it had displaced the traditional stove. Fieldworker observations reporting no or a broken chimney of the IS were associated with less daily IS use, less use of the LPG stove and less traditional stove displacement (data not shown). Negative experiences with IS durability are likely to reduce motivation for its use and confidence to abolish traditional stoves. Indeed, stove stacking with traditional cookstoves has been described as a strategy to cope with uncertainties regarding income, fuel prices and access to fuels [19]. Problems with the programme stove were also found to be much lower in communities were new stoves were rapidly taken up compared to communities where uptake took longer [31]. Two more factors, knowledge of somebody with the ability to build or repair an IS (positively associated with daily IS use and negatively associated with LPG use) and whether IS parts are obtainable in the community (positively associated with traditional stove displacement), underline the importance of stove functioning and possibilities for repair and maintenance through a functioning supply chain for clean cookstove adoption. Region was also associated with traditional stove displacement with households in La Libertad and in Cuzco, having higher odds of not using traditional stoves which might be related to policy and programme characteristics. Variables associated with the use of the LPG stove were only examined in the group of households not taking part in the national gas programme [30]. All except one of the 189 households that participated in this programme stated that they used the LPG stove, making the FISE a very strong predictor for LPG uptake. The Peruvian government in 2012 initiated the programme FISE to promote household LPG use for example via subsidies. It has been shown before that initial costs of LPG stoves and cylinders and the high price of LPG in general are among the most important barriers for uptake [20,22] with subsidies being an important measure to raise adoption rates [21]. More information on the different stove programmes is provided Texts S3 and S4, Tables S6 and S7.

4.3. Limitations

In cross-sectional study designs, there are a number of different biases that might occur such as selection and information bias. In this study, households were selected from areas in which IS promotion programmes had been conducted. From these areas we included all households having participated in a programme (overall less than 5% of households declined). First, households willing to participate in our study might not be representative of all rural Peruvian households who have taken part in a stove programme. They might have been more or less satisfied with the programme or their respective stove and felt the need to express this. Second, households willing to participate in a stove programme might differ from the average rural Andean household. We nevertheless believe that our results are largely generalisable to the rural Peruvian Andean context as we included a large number of households from geographically and culturally diverse regions.

Furthermore, cross-sectional studies cannot establish temporal sequence between exposure and outcome. Knowledge of somebody able to build an IS was associated with daily IS use, but it is possible that because household members used an IS they knew somebody who could build or repair it. Furthermore, our outcomes and exposures are self-reported which might overestimate actual clean cookstove use. A recent study in Rwanda showed differences between observed and reported IS use [37] (54% observed, 78% reported). A similar observation was made in a humanitarian crisis setting in Darfur, Sudan [38]. Another study found similar results in relation to whether stove use was reported or measured [39]. A study in rural Mexico introducing IS reported similar displacement of the open fire (57% compared to 66% displacement of traditional stoves in this study) [19]. Nevertheless, objective assessment of stove use, for example, with stove use monitors might have led to more accurate outcome assessments [38,39], which was, however, not possible for this study. We believe that in this setting the risk of reporting bias might be smaller as questions on cookstove use were less related to the respective IS promotion programme as there were a considerable number of different programmes which were mostly conducted several years ago. This might, on the other hand, have led to recall bias especially on information on the respective stove promotion programmes. The questionnaire had been designed to evaluate IS use and adoption. Therefore, fieldworker observations relate only to the IS. Observations listing for example all present stoves in the home would have been useful to validate reported IS and LPG stove use and displacement of the traditional stove. We could not examine all potential enablers and barriers described previously and also not all variables that had been included in the questionnaire for this purpose. For example, questions around perceptions of time and money savings, benefits for health and safety and cleanliness of the kitchen were answered very uniformly across households. It was described before that households stated high satisfaction with the programme stove which was not necessarily related to real satisfaction [39]. Finally, we did not assess use of a specific cookstove for cooking the main meal or for other household tasks such as heating water or the home.

5. Conclusions

In the Peruvian Andes the transition to clean cookstoves appears to be in process after many years of IS and more recent LPG stove promotion. Only one third of all households report traditional cookstove use and only 8% as the primary stove. These households should be considered in future programmes to achieve desired health impacts. Due to household preferences and related monetary costs, LPG stoves are currently unlikely to completely replace solid fuel stoves. However, LPG stoves offer advantages which might make them very suitable secondary stoves, potentially able to further reduce the role of traditional cookstoves if household economic constraints are carefully considered beyond current subsidy schemes. Factors influencing stove adoption are related to stove maintenance and repair at community-level and a functioning supply chain. Preferences for a certain cookstove seem further influenced by just a few demographic, household, community, stove and public policy characteristics that can be considered for programme planning. The results of our study on more than 1000 households from three geographically and culturally diverse rural Andean settings provide an important evaluation of IS promotion programmes and add to the growing evidence on factors promoting or hindering clean cookstove adoption. The study findings assist in designing successful clean cookstove interventions for the future.

Supplementary Materials: The following are available online at http://www.mdpi.com/1660-4601/14/7/745/s1, Text S1: Background information titled: The three study regions, Table S1: Independent variables for logistic regression analysis; lists and describes all 16 independent variables and the amount of missing data, Text S2: Methods section titled: Multiple imputations using chained equations; a detailed description about assumptions and methods underlying multiple imputation of missing independent variables, Table S2: Comparison between observations with missing variables and observations that are fully observed; compares observations that have no missing values in any of the variables with observations that have missing observations in one or more of variables, Table S3: Results of multivariable logistic regression analysis of daily IS use, analysis of complete cases and imputed data; comparison of the respective regression model when complete cases versus imputed data is used, Table S4: Results of multivariable logistic regression analysis of LPG stove use, analysis of complete cases and imputed data; comparison of the respective regression model when complete cases versus imputed data is used, Table S5: Results of multivariable logistic regression analysis of traditional cookstove displacement, analysis of complete cases and imputed data; comparison of the respective regression model when complete cases versus imputed data is used, Text S3: Background information titled: Information on institutions/programmes promoting improved stoves in Peru, Table S6: Number of improved solid fuel stoves by region, Table S7: Description of institutions and programmes promoting improved solid fuel stoves; gives detailed information on the institution/stove programme, the stove model, technical specifications, type of fuel and stove certification, Text S4: Background information titled: The national gas programme FISE.

Acknowledgments: The study was funded by the Global Alliance for Clean Cookstoves. We are very grateful to the participating households in Cajamarca, La Libertad and Cuzco, our field teams and field supervisors. Additionally, we thank Valerie Paz-Soldan and Valerie Baquerizo for general supervision of data collection and helpful comments on the questionnaire. Furthermore, we thank Veronika Jäger for valuable inputs and critical review of the manuscript.

Author Contributions: Daniel Mäusezahl and Stella M. Hartinger conceived and designed the study; Stella M. Hartinger and Hector Verastegui conducted the fieldwork; Jennyfer Wolf analyzed the data; Jennyfer Wolf wrote the paper.

Conflicts of Interest: The authors declare no conflict of interest. The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results.

References

1. Bonjour, S.; Adair-Rohani, H.; Wolf, J.; Bruce, N.G.; Mehta, S.; Prüss-Ustün, A.; Lahiff, M.; Rehfuess, E.A.; Mishra, V.; Smith, K.R. Solid Fuel Use for Household Cooking: Country and Regional Estimates for 1980–2010. *Environ. Health Perspect.* **2013**, *121*, 784–790. [CrossRef] [PubMed]
2. Kurmi, O.P.; Semple, S.; Simkhada, P.; Smith, W.C.S.; Ayres, J.G. COPD and chronic bronchitis risk of indoor air pollution from solid fuel: A systematic review and meta-analysis. *Thorax* **2010**, *65*, 221–228. [CrossRef] [PubMed]
3. Dherani, M.; Pope, D.; Mascarenhas, M.; Smith, K.R.; Weber, M.; Bruce, N. Indoor air pollution from unprocessed solid fuel use and pneumonia risk in children aged under five years: A systematic review and meta-analysis. *Bull. World Health Organ.* **2008**, *86*, C390–C398.
4. Uzoigwe, J.C.; Prum, T.; Bresnahan, E.; Garelnabi, M. The Emerging Role of Outdoor and Indoor Air Pollution in Cardiovascular Disease. *N. Am. J. Med. Sci.* **2013**, *5*, 445–453. [CrossRef] [PubMed]
5. World Health Organization. World Health Organization. Global Health Observatory (GHO) Data. In *Global Health Observatory (GHO) Data*; WHO: Geneva, Switzerland. Available online: http://www.who.int/gho/en/ (accessed on 14 June 2016).
6. Bruce, N.; Dherani, M.; Liu, R.; Hosgood, H.D., III; Sapkota, A.; Smith, K.R.; Straif, K.; Lan, Q.; Pope, D. Does household use of biomass fuel cause lung cancer? A systematic review and evaluation of the evidence for the GBD 2010 study. *Thorax* **2015**, *70*, 433–441. [CrossRef] [PubMed]
7. Smith, K.R.; Bruce, N.; Balakrishnan, K.; Adair-Rohani, H.; Balmes, J.; Chafe, Z.; Dherani, M.; Hosgood, H.D.; Mehta, S.; Pope, D.; et al. Millions dead: How do we know and what does it mean? Methods used in the comparative risk assessment of household air pollution. *Annu. Rev. Public Health* **2014**, *35*, 185–206. [CrossRef] [PubMed]

8. Forouzanfar, M.H.; Afshin, A.; Alexander, L.T.; Anderson, H.R.; Bhutta, Z.A.; Biryukov, S.; Brauer, M.; Burnett, R.; Cercy, K.; Charlson, F.J.; et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: A systematic analysis for the Global Burden of Disease Study 2015. *Lancet* **2016**, *388*, 1659–1724. [CrossRef]
9. Ruiz-Mercado, I.; Masera, O.; Zamora, H.; Smith, K.R. Adoption and sustained use of improved cookstoves. *Energy Policy* **2011**, *39*, 7557–7566. [CrossRef]
10. Künzli, N. Commentary: Abating climate change and lung cancer! *Int. J. Epidemiol.* **2011**, *40*, 729–730. [CrossRef] [PubMed]
11. Chafe, Z.A.; Brauer, M.; Klimont, Z.; Van Dingenen, R.; Mehta, S.; Rao, S.; Riahi, K.; Dentener, F.; Smith, K.R. Household Cooking with Solid Fuels Contributes to Ambient $PM_{2.5}$ Air Pollution and the Burden of Disease. *Environ. Health Perspect.* **2014**, *122*, 1314–1320. [CrossRef] [PubMed]
12. World Bank. *Household Cookstoves, Environment, Health, and Climate Change: A New Look at an Old Problem*; The World Bank: Washington, DC, USA, 2011.
13. Global Alliance for Clean Cookstoves. Our Mission. Available online: http://cleancookstoves.org/about/our-mission/ (accessed on 8 March 2016).
14. United Nations. *The Sustainable Development Goals Agenda*; UN: New York, NY, USA; Available online: http://www.un.org/sustainabledevelopment/development-agenda/ (accessed on 14 December 2015).
15. Hanna, R.; Duflo, E.; Greenstone, M. *Up in Smoke: The Influence of Household Behavior on the Long-Run Impact of Improved Cooking Stoves*; National Bureau of Economic Research: Cambridge, MA, USA, 2012.
16. Pillarisetti, A.; Vaswani, M.; Jack, D.; Balakrishnan, K.; Bates, M.N.; Arora, N.K.; Smith, K.R. Patterns of stove usage after introduction of an advanced cookstove: The long-term application of household sensors. *Environ. Sci. Technol.* **2014**, *48*, 14525–14533. [CrossRef] [PubMed]
17. Johnson, M.A.; Chiang, R.A. Quantitative guidance for stove usage and performance to achieve health and environmental targets. *Environ. Health Perspect.* **2015**, *123*, 820–826. [CrossRef] [PubMed]
18. World Health Organization. *Indoor Air Quality Guidelines: Household Fuel Combustion*; WHO: Geneva, Switzerland, 2014.
19. Ruiz-Mercado, I.; Masera, O. Patterns of Stove Use in the Context of Fuel–Device Stacking: Rationale and Implications. *EcoHealth* **2015**, *12*, 42–56. [CrossRef] [PubMed]
20. Puzzolo, E.; Stanistreet, D.; Pope, D.; Bruce, N.; Rehfuess, E. *Factors Influencing the Largescale Uptake by Households of Cleaner and More Efficient Household Energy Technologies*; EPPI-Centre: London, UK, 2013.
21. Shen, G.; Lin, W.; Chen, Y.; Yue, D.; Liu, Z.; Yang, C. Factors influencing the adoption and sustainable use of clean fuels and cookstoves in China—A Chinese literature review. *Renew. Sustain. Energy Rev.* **2015**, *51*, 741–750. [CrossRef]
22. Global Alliance for Clean Cookstoves. *Igniting Change: A Strategy for Universal Adoption of Clean Cookstoves and Fuels*; GACC: Washington, DC, USA, 2011.
23. Lewis, J.J.; Pattanayak, S.K. Who adopts improved fuels and cookstoves? A systematic review. *Environ. Health Perspect.* **2012**, *120*, 637–645. [CrossRef] [PubMed]
24. Beyene, A.D.; Koch, S.F. Clean fuel-saving technology adoption in urban Ethiopia. *Energy Econ.* **2013**, *36*, 605–613. [CrossRef]
25. Thurber, M.C.; Warner, C.; Platt, L.; Slaski, A.; Gupta, R.; Miller, G. To promote adoption of household health technologies, think beyond health. *Am. J. Public Health* **2013**, *103*, 1736–1740. [CrossRef] [PubMed]
26. Shankar, A.; Johnson, M.; Kay, E.; Pannu, R.; Beltramo, T.; Derby, E.; Harrell, S.; Davis, C.; Petach, H. Maximizing the benefits of improved cookstoves: Moving from acquisition to correct and consistent use. *Glob. Health Sci. Pract.* **2014**, *2*, 268–274. [CrossRef] [PubMed]
27. Instituto Nacional de Estadística e Informática. INEI Estadisticas: Población y Vivienda. Available online: http://www.inei.gob.pe/estadisticas/indice-tematico/poblacion-y-vivienda/ (accessed on 5 November 2015).
28. Troncoso, K. *A Recipe for Developing Adoption & Impact Indices*; Global Alliance for Clean Cookstoves: Washington, DC, USA, 2014.
29. Rheingans, R.; Anderson, J.D.; Luyendijk, R.; Cumming, O. Measuring disparities in sanitation access: Does the measure matter? *Trop. Med. Int. Health* **2014**, *19*, 2–13. [CrossRef] [PubMed]
30. FISE. Fondo de Inclusión Social Energético. Available online: http://www.fise.gob.pe/index.html (accessed on 15 January 2016).

31. Pine, K.; Edwards, R.; Masera, O.; Schilmann, A.; Marrón-Mares, A.; Riojas-Rodríguez, H. Adoption and use of improved biomass stoves in Rural Mexico. *Energy Sustain. Dev.* **2011**, *15*, 176–183. [CrossRef]
32. Rehfuess, E.A.; Puzzolo, E.; Stanistreet, D.; Pope, D.; Bruce, N. Enablers and barriers to large-scale uptake of improved solid fuel stoves: A systematic review. *Environ. Health Perspect.* **2014**, *122*. [CrossRef] [PubMed]
33. Hartinger, S.M.; Lanata, C.F.; Hattendorf, J.; Gil, A.I.; Verastegui, H.; Ochoa, T.; Mäusezahl, D. A community randomised controlled trial evaluating a home-based environmental intervention package of improved stoves, solar water disinfection and kitchen sinks in rural Peru: Rationale, trial design and baseline findings. *Contemp. Clin. Trials* **2011**, *32*, 864–873. [CrossRef] [PubMed]
34. Hartinger, S.M.; Lanata, C.F.; Gil, A.I.; Hattendorf, J.; Verastegui, H.; Mäusezahl, D. Combining interventions: Improved chimney stoves, kitchen sinks and solar disinfection of drinking water and kitchen clothes to improve home hygiene in rural Peru. *Field Actions Sci. Rep.* **2012**, *6*, 1–10.
35. Thomas, E.; Wickramasinghe, K.; Mendis, S.; Roberts, N.; Foster, C. Improved stove interventions to reduce household air pollution in low and middle income countries: A descriptive systematic review. *BMC Public Health* **2015**, *15*. [CrossRef] [PubMed]
36. Alam, A.; Tawale, N.; Patel, A.; Dibley, M.J.; Jadhao, S.; Raynes-Greenow, G. Household Air Pollution Intervention Implications: Findings from Qualitative Studies and a Field Trial of Clean Cookstoves in Two Rural Villages in India. *Int. J. Environ. Res. Public Health* **2016**, *13*. [CrossRef] [PubMed]
37. Rosa, G.; Majorin, F.; Boisson, S.; Barstow, C.; Johnson, M.; Kirby, M.; Ngabo, F.; Thomas, E.; Clasen, T. Assessing the Impact of Water Filters and Improved Cook Stoves on Drinking Water Quality and Household Air Pollution: A Randomised Controlled Trial in Rwanda. *PLoS ONE* **2014**, *9*. [CrossRef] [PubMed]
38. Wilson, D.L.; Coyle, J.; Kirk, A.; Rosa, J.; Abbas, O.; Adam, M.I.; Gadgil, A.J. Measuring and Increasing Adoption Rates of Cookstoves in a Humanitarian Crisis. *Environ. Sci. Technol.* **2016**, *50*, 8393–8399. [CrossRef] [PubMed]
39. Ruiz-Mercado, I.; Canuz, E.; Walker, J.L.; Smith, K.R. Quantitative metrics of stove adoption using Stove Use Monitors (SUMs). *Biomass Bioenergy* **2013**, *57*, 136–148. [CrossRef] [PubMed]

© 2017 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).

Check for updates

VOLUME 23 NO 5 PP 508–525 MAY 2018

Systematic Review

Impact of drinking water, sanitation and handwashing with soap on childhood diarrhoeal disease: updated meta-analysis and meta-regression

Jennyfer Wolf[1], Paul R. Hunter[2,3], Matthew C. Freeman[4], Oliver Cumming[5], Thomas Clasen[4], Jamie Bartram[6], Julian P. T. Higgins[7], Richard Johnston[1], Kate Medlicott[1], Sophie Boisson[1] and Annette Prüss-Ustün[1]

1 *Department of Public Health, Environment and Social Determinants of Health, WHO, Geneva, Switzerland*
2 *The Norwich School of Medicine, University of East Anglia, Norwich, UK*
3 *Department of Environmental Health, Tshwane University of Technology, Pretoria, South Africa*
4 *Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA*
5 *Department of Disease Control, London School of Hygiene and Tropical Medicine, London, UK*
6 *Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*
7 *School of Social and Community Medicine, University of Bristol, Bristol, UK*

Abstract

OBJECTIVES Safe drinking water, sanitation and hygiene are protective against diarrhoeal disease; a leading cause of child mortality. The main objective was an updated assessment of the impact of unsafe water, sanitation and hygiene (WaSH) on childhood diarrhoeal disease.
METHODS We undertook a systematic review of articles published between 1970 and February 2016. Study results were combined and analysed using meta-analysis and meta-regression.
RESULTS A total of 135 studies met the inclusion criteria. Several water, sanitation and hygiene interventions were associated with lower risk of diarrhoeal morbidity. Point-of-use filter interventions with safe storage reduced diarrhoea risk by 61% (RR = 0.39; 95% CI: 0.32, 0.48); piped water to premises of higher quality and continuous availability by 75% and 36% (RR = 0.25 (0.09, 0.67) and 0.64 (0.42, 0.98)), respectively compared to a baseline of unimproved drinking water; sanitation interventions by 25% (RR = 0.75 (0.63, 0.88)) with evidence for greater reductions when high sanitation coverage is reached; and interventions promoting handwashing with soap by 30% (RR = 0.70 (0.64, 0.77)) *vs.* no intervention. Results of the analysis of sanitation and hygiene interventions are sensitive to certain differences in study methods and conditions. Correcting for non-blinding would reduce the associations with diarrhoea to some extent.
CONCLUSIONS Although evidence is limited, results suggest that household connections of water supply and higher levels of community coverage for sanitation appear particularly impactful which is in line with targets of the Sustainable Development Goals.

keywords diarrhoea, hygiene, meta-analysis, sanitation, review, water

Introduction

The Sustainable Development Goals (SDGs) adopted by 193 Member States at the UN General Assembly in 2015 aim to substantially improve water and sanitation globally and include two specific targets within Goal 6 for drinking water, sanitation and hygiene (WaSH) [1]:

- 6.1 By 2030, achieve universal and equitable access to safe and affordable drinking water for all.
- 6.2 By 2030, achieve access to adequate and equitable sanitation and hygiene for all and end open defecation, paying special attention to the needs of women and girls and those in vulnerable situations.

Progress towards the Millennium Development Goals (MDGs) which preceded the SDGs was monitored globally based on the use of improved drinking water supplies and sanitation facilities. The SDGs aim at higher water and sanitation service provision and are being monitored

This article is the updated review of doi: 10.1111/tmi.12331.

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.
This is an open access article distributed under the terms of the Creative Commons Attribution IGO License, which permits unrestricted use, distribution and reproduction in any medium, provided that the original work is properly cited. In any reproduction of this article there should not be any suggestion that WHO or the article endorse any specific organization or products. The use of the WHO logo is not permitted. This notice should be preserved along with the article's URL.

Table 1 Global indicators for drinking water, sanitation and hygiene in the MDG and SDG periods

	MDG Indicator	SDG Indicators and further details
Drinking water	Proportion of population using an improved drinking water source*	Proportion of population using safely managed drinking water services† Safely managed drinking water services: Use of an improved drinking water source, which is located on premises, available when needed, and compliant with faecal and priority chemical standards‡ Basic drinking water services: use of an improved drinking water source provided collection time is not more than 30 min for a roundtrip including queuing‡ Limited drinking water services: use of an improved drinking water source where collection time exceeds 30 min for a roundtrip to collect water including queuing‡
Sanitation	Proportion of population using an improved sanitation facility which is not shared with other households*	Proportion of population using safely managed sanitation services, including a handwashing facility with soap and water† Safely managed sanitation services: Use of an improved sanitation facility which is not shared with other households, and where excreta are safely disposed *in situ* or transported and treated offsite‡ Basic sanitation services: Use of an improved sanitation facility which is not shared with other households‡ Limited sanitation services: Use of an improved sanitation facility which is shared between two or more households‡
Hygiene	None	Proportion of population using safely managed sanitation services, including a handwashing facility with soap and water†

MDG, Millennium Development Goal; SDG, Sustainable Development Goal.
*Official list of MDG indicators (United Nations Statistics Division 2008).
†Official list of SDG Indicators (Division 2016).
‡For a listing of improved drinking water sources and sanitation facilities, see https://washdata.org/.

using indicators which include elements of service quality that were not captured by the MDG indicators (Table 1) [2]. Moreover, while the MDGs did not include a hygiene target, SDG 6 specifically includes a place for handwashing with water and soap in the household.

Achieving the SDG WaSH targets will be challenging. In 2015, only 68% of the world population used improved sanitation, meaning that 2.4 billion people still lacked even simple sanitation facilities like pit latrines and septic tanks. Although 91% of the world population used improved drinking water sources in 2015, 663 million people still used unimproved sources such as unprotected springs, wells and surface water [3]. Furthermore, it has been estimated that 10% of improved drinking water sources are heavily contaminated with faecal material, that is, contain at least 100 *Escherichia coli* or thermotolerant coliform bacteria per 100 ml [4], underlining that improved water sources do not guarantee water that is safe for drinking. Estimates suggest that only 19% of the world population washes hands with soap after contact with excreta [5]. Those that lack access are typically the poorest and most marginalised, which adds importantly to the costs and the efforts of reaching universal coverage [3].

Inadequate WaSH is considered as an important risk for diarrhoea [6–8] and has been linked to many other adverse health- and non-health consequences, such as other infectious diseases, poor nutritional status, reduced security and spare time [9–13]. Diarrhoea remains among the most important causes for global child mortality and is estimated to account for approximately 600 000 deaths in children under 5 years annually [14].

This updated systematic review and meta-analysis provide new estimates for the impact of WaSH interventions on childhood diarrhoea. New WaSH studies have been published including studies on continuous water supply and rigorous studies of improved sanitation which permit adaptation and extension of the exposure scenarios previously presented and which better align with the SDG6 targets for water, sanitation and hygiene improvements. Our updated analysis of the latest evidence on water, sanitation and hygiene and diarrhoea is key for guiding the choice of interventions according to their potentially highest health benefits and provides a basis for estimating the global burden of disease from WaSH.

Methods

The protocol for this study was agreed, in advance, by an expert group convened by WHO in 2013. Participating experts who took part in this initial meeting are listed in Appendix S4. The update of this systematic review is registered within PROSPERO [15] under the registration number CRD42016043164. Appendix S1 shows the

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

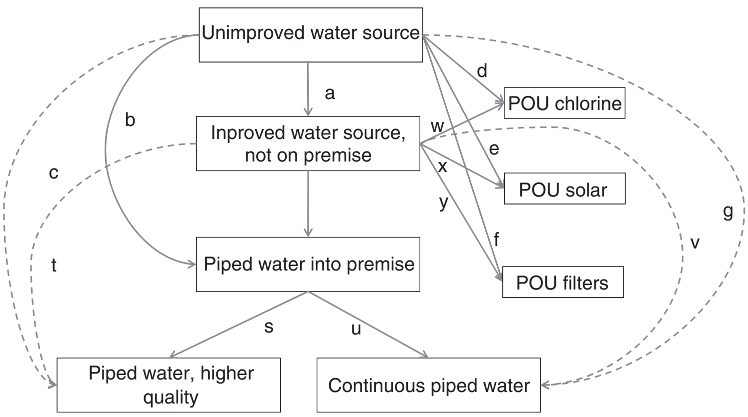


Figure 1 Conceptual framework for the analysis of drinking water studies. POU: point-of-use; ⟶ direct evidence available, - -> effect estimated indirectly, 'improved water source' according to the WHO/UNICEF Joint Monitoring Programme (JMP) not including piped water into premises, POU chlorine includes chlorination and flocculation; additional covariates are examined in meta-regression.

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist.

Systematic literature review

Selection criteria and search strategy. We included any study reporting the effect on diarrhoea morbidity in children less than 5 years of age of any WaSH intervention providing they reported sufficient data to allow for characterisation in accordance with the conceptual models for WaSH that were generated by mapping the available evidence (Figures 1 and 2) [16]. More information on the conceptual framework is given in the paper on the initial systematic review [16]. If data on children under five were not available, we included estimates for all ages or older children. Only studies with a clearly specified intervention matching our pre-defined exposure scenarios (Figures 1 and 2) that provided improved household or community water supply or sanitation facilities or promoted handwashing with soap were included in this review. Interventions needed to be tested against a control group that did not receive the respective intervention (s) or that received a control or placebo intervention. Eligible study designs included

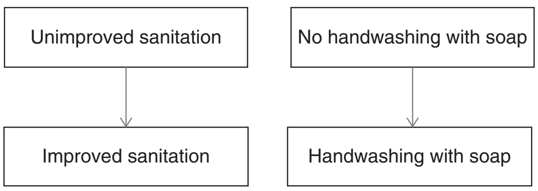


Figure 2 Conceptual frameworks for the analysis of sanitation and hygiene studies. Additional covariates are examined in meta-regression.

- randomised (including individual and cluster randomised) controlled trials;
- quasi-randomised and non-randomised controlled trials, the latter when baseline data on the main outcome were available before the intervention was conducted (i.e. before and after studies with a concurrent control group);
- case–control and cohort studies when they were related to a clearly specified intervention;
- studies using time-series and interrupted time-series design; and
- studies without a clearly specified intervention analysing cross-sectional household survey data but with appropriate matching methods to permit causal inference [17].

For the purpose of this analysis, we will refer to studies listed under 1. to 4. as 'studies evaluating specific interventions' and studies listed under 5. 'survey data analyses'.

We included single and combined water and sanitation interventions that reported relative risk estimates or the relevant data for their calculations. For water and sanitation, we restricted study location to households in low- and middle-income settings, that is low- and middle-income countries according to the World Bank classification [18] and interventions in low-income settings in high-income countries, whereas for hygiene, we also included studies performed in institutions such as day-care centres/homes and primary schools from high-income settings because we assume these settings represent the high potential for faecal pathogen transmission. We only included hygiene interventions that included a handwashing component and excluded interventions concerning hand sanitisers such as alcohol-based handrubs in Correa *et al.* [19]. For the water and sanitation analysis,

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

we excluded studies that mainly targeted institutions like schools or the work place and, in general, we excluded studies where the study population was considered to be non-representative with regard to the exposure–outcome relationship of interest (e.g. interventions targeting HIV+ population). Included effect estimates were usually based on intention-to-treat analyses rather than estimates in those who actually adopted the intervention, despite often low compliance levels.

Interventions including both a drinking water and a sanitation component were included in both water and sanitation analysis. As hygiene interventions are often added as an additional component to water and sanitation interventions, studies included in the hygiene analysis needed to report effect estimates separately for the hygiene component, needed to be exclusive hygiene interventions or to clearly have the hygiene intervention as the main component.

Studies were included in the review only if they were published in a peer-reviewed scientific journal in English or French or to have been assessed according to transparent criteria for methodological quality in a previously conducted systematic review. Studies published in languages other than English or French were included provided the relevant data were available in a previous systematic review published in English or French.

Non-randomised studies with baseline differences in diarrhoea occurrence that were not accounted for in the analysis were not included in the analyses as the effect estimate related to the intervention could not reasonably be estimated.

We systematically searched Pubmed, Embase, Scopus and Cochrane Library using both keywords and MeSH terms to identify WASH studies and their impact on diarrhoeal disease. The update covered the search between 1 January 2012 and early 2016 (February for the search on water and sanitation interventions and May for hygiene). As such the systematic review now covers studies published from 1970 until early 2016 [16]. The search strategy and search terms for the four databases are detailed in Appendix S2. The reference sections of systematic reviews on WaSH were also searched. References were also provided from subject-matter experts, including co-authors of this study and those included in the acknowledgements section.

Data extraction and quality assessment. Study title and abstract screening, data extraction and quality assessment were primarily performed by a single reviewer. A second reviewer subsequently checked inclusion of studies and data extraction. Data extraction was carried out using a structured and piloted form [16]. Differences between reviewers over data extraction were reconciled with a third reviewer, where required. Authors were contacted for additional details when required for extraction or calculation of effect estimates or classification of the studies.

Study quality was assessed using a revised and previously published version [20] of the Newcastle-Ottawa scale [21] that we used in our previous reviews for WaSH interventions [5, 16]. Quality criteria were adapted for studies evaluating specific interventions and survey data analyses (Appendix S5). Study quality scores were used to identify and exclude the lowest-rated studies for sensitivity analyses.

Where possible we extracted the adjusted relative risk from the paper in the following order of preference:

1. longitudinal prevalence ratio, that is the proportion of time ill,
2. prevalence ratio/risk ratio,
3. rate ratio,
4. odds ratio.

When these values were not given in the paper, we calculated relative risks and confidence intervals from data presented in the paper. Where confidence intervals could not be calculated, the study was excluded from meta-analysis. Standard errors of the log relative risk were calculated using standard formulae [22]. Odds ratios can overstate the estimated intervention effect especially when the respective disease is frequent and effect estimates are large (further away from 1) [23]. Therefore, odds ratios were converted to risk ratios using the control group risk as given in the respective paper [22, 24]. Risk ratios, prevalence ratios, rate ratios and means ratios were combined without any conversion.

For one study presenting adjusted odds ratios [25], the control group risk was not given. Effect estimates of this study were included as odds ratio. We, however, performed a sensitivity analysis converting the odds ratios of this study to risk ratios with a – conservatively high – assumed control group diarrhoea prevalence of 30% over the preceding week.

Where possible, we combined effect estimates across intervention arms falling within the same category (e.g. different methods for filtering drinking water at point of use). When multiple relevant effect estimates were given within a study, we included independent subgroups (separate intervention and separate control group in different settings) from a single study separately. In the case of multiple comparisons within a study (e.g. effect estimates for different POU water interventions) but with the same control group or different effect sizes across relevant age groups or for the same individuals over time, effect estimates were combined using methods described in

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

Borenstein *et al.* [26]. In brief, effect estimates from different participants, for example from different relevant age groups, were combined as independent subgroups, whereas different effect estimates on the same participants, for example collected at different time points, were combined taking into account the correlation between the effect estimates. In the case of water interventions, multiple comparisons were often not combined if the groups were not sufficiently similar (e.g. water intervention separately and water intervention plus hygiene education). In these cases, including factorial designs, we derived a single pairwise comparison of the most comprehensive intervention compared with the least comprehensive intervention (or control; comprehensive according to Figure 1 with, e.g. a piped water intervention being more comprehensive than an improved, not on premises water source). We, however, chose preferably intervention arms that did not combine different components of WaSH (e.g. water interventions without an additional hygiene or sanitation component).

Statistical analysis

General approach. Random effects meta-analysis was conducted separately by WaSH component to examine the association with diarrhoeal morbidity. Random effects meta-regression was used to examine drinking water interventions according to our conceptual framework (Figure 1) and to examine further pre-specified covariates as indicated below. Bayesian meta-regression was used to adjust study results of point-of-use drinking water treatment and hygiene interventions for non-blinding bias (described in more detail below). Following our previous approach [16], we adjusted only point-of-use and hygiene interventions for non-blinding bias as these interventions usually aim exclusively to improve health which is apparent to the recipient, whereas water and sanitation interventions that improve supply are often less apparent to the recipient and have aims beyond health such as community development, environmental hygiene benefits and time savings of water collection.

Possible publication bias was examined with inspection of funnel plots and the use of Egger's test. Analyses were performed with Stata 14 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). Bayesian meta-regression and bias adjustments were performed using WinBUGS version 1.4 [27].

Analysis of drinking water interventions. The conceptual model for the analysis of drinking water interventions is shown in Figure 1. Interventions were grouped as structural changes in supply, for example, from unimproved over improved towards different levels of piped water to premises, and point-of-use treatment in the household, for example, chlorine, solar and filter treatment. As more studies have been published, our conceptual framework for the drinking water analysis has been adjusted to include two additional categories of piped water to premises services (Figure 1): treatment of piped water to improve its quality and a continuous supply of piped water (vs. an intermittent supply).

In Figure 1, transitions a to g present basic parameters in the meta-regression model, each represented by a covariate. All other transitions are coded as combinations of these parameters, specifically: $r = b - a$, $s = c - b$, $t = c - a$, $u = g - b$, $v = g - a$, $w = d - a$, $x = e - a$, $y = f - a$. The model allows the indirect estimation of transitions that have not been directly observed (including those representing basic parameters), following ideas of network meta-analysis [28]. The adapted exposure scenario aligns more closely with the SDGs which aim at higher water service provision than just improved water supply.

The *a priori* model for the meta-regression of drinking water interventions included seven binary variables presenting the basic parameters outlined in Figure 1 plus two additional variables, that is, whether safe water storage was provided and whether the intervention included also hygiene education and/or a sanitation intervention (from now called 'combined intervention'). The association of safe water storage and diarrhoea was estimated by including a binary covariate that was coded one for interventions providing a safe storage container (i.e. a container with a narrow opening that prevents the introduction of objects either separately or inherently in ceramic filter interventions). Additional assessed covariates included access to improved or unimproved sanitation in the study population, interventions in rural compared to urban or mixed areas, survey data analysis *vs.* studies evaluating specific interventions and time of follow-up in studies evaluating specific interventions. The covariates were examined as indicator variables and time of follow-up as indicator and as continuous variable. As sensitivity analyses, we excluded cross-sectional, non-intervention studies, non-randomised studies, the quintile of studies evaluating specific interventions with the lowest quality rating, studies that did not report on diarrhoea in children <5 years and studies published before 2012.

Blinding study participants in point-of-use drinking water interventions. Most WaSH interventions are unblinded and diarrhoea is self-reported in most intervention evaluation studies which may lead to biased reports of diarrhoea [29, 30]. We performed an additional analysis that

 © 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

incorporates bias adjustments for the POU water quality interventions based on empirical evidence [29]. This Bayesian meta-regression analysis was performed by subtracting a bias factor from the log risk ratio from each non-blinded study. This bias factor is based on 234 meta-analyses including a total of 1970 trials across a broad range of clinical areas, settings and types of experimental interventions including curative and preventive interventions [29]. The bias factor was given a prior distribution in the shape of a normal distribution with mean 0.25 and variance 0.2, reflecting findings from the BRANDO meta-epidemiological study [29]. Further descriptions of this approach can be found in Appendix S4.

Analysis of sanitation interventions. We examined the overall association between sanitation interventions and diarrhoea morbidity with random effects meta-analysis. We also examined the association of sewer connections and diarrhoea as compared to improved sanitation at the household-level alone using meta-regression with two binary variables to describe the transitions from unimproved to improved sanitation other than sewer and to sewer connections plus a binary variable indicating a combined intervention. We also examined a disaggregation of unimproved sanitation into open defecation and use of unimproved sanitation facilities in studies that disaggregated accordingly.

Other examined covariates were access to improved or unimproved drinking water in the study population at baseline, the level of community sanitation coverage reached after the intervention, whether the sanitation intervention provided sanitation promotion only as compared to interventions that provided also sanitation hardware (e.g. latrine construction or material), survey data analyses *vs.* studies evaluating specific interventions, time of follow-up in studies evaluating specific interventions and whether the intervention was a combined intervention, that is, aiming also at water or hygiene improvements. Community coverage was examined as indicator variable with two categories ≤75% and >75% sanitation coverage after the intervention and as a continuous variable (percentage with access to sanitation in the intervention group after the intervention). The choice of the categories was informed by a recent study that found changes in the relationship between sanitation and diarrhoea prevalence at about 75% [31]. Other covariates were examined as indicator variables and time of follow-up as indicator and as continuous variable. Time of follow-up as indicator variable in the analysis of sanitation studies was examined with a cut-off of 24 months as compared to the analysis of water and hygiene studies with a cut-off of 12 months to reflect the generally longer duration of sanitation studies (median duration of sanitation, water and hygiene interventions was 24, 8 and 8 months, respectively).

As sensitivity analyses, we excluded survey data analyses, non-randomised studies, the quintile of studies evaluating specific interventions with the lowest quality rating, studies that did not report on diarrhoea in children <5 years and studies published before 2012.

Analysis of hygiene interventions. The overall association between hygiene interventions and diarrhoea morbidity was examined using random effects meta-analysis, as were the following covariates using meta-regression: exclusive promotion of handwashing with soap *vs.* broader hygiene education, provision of soap, high-income *vs.* low- and middle-income countries, community *vs.* institutional (e.g. day-care, schools) interventions and time of follow-up in studies evaluating specific interventions. These were examined as indicator variables and time of follow-up as indicator and as continuous variable.

As sensitivity analyses, survey data analyses, non-randomised studies, the quintile of studies evaluating specific interventions with the lowest quality rating, studies that did not report on diarrhoea in children <5 years, studies published before 2012, studies in institutional settings, studies in household setting and studies from high-income countries were excluded.

An additional analysis was performed to adjust effect estimates of unblinded studies for the assumed effect of non-blinding bias as described before.

Results

Systematic literature search

Studies on water and sanitation were searched simultaneously, hygiene studies in a separate literature search. The electronic searches of four databases yielded 11 723 water and sanitation studies, along with a further 120 identified through scanning the reference sections of previous systematic reviews or provided from subject-matter experts, which was then reduced to 8700 after de-duplication. Separate electronic searches of the same four databases yielded 363 hygiene studies, along with a further nine identified through scanning the reference sections of previous systematic reviews, which was then reduced to 308 after de-duplication. Hence, 8779 and 308 titles and abstracts were screened respectively for water and sanitation, and hygiene, from which 80 full water and sanitation texts and 11 full hygiene texts were assessed for inclusion. Finally, 14 new water studies, eight new sanitation studies (Figure 3) and eight new hygiene studies (Figure 4) were included for quantitative meta-analysis alongside those studies identified in our previous water and sanitation [16] and hygiene [5] reviews. The complete databases therefore comprise 73 studies providing 80 observations for drinking water, 19 studies providing 22 observations for sanitation and 33 studies providing 33 observations for hygiene. Appendix S3 presents citations and characteristics for all WASH studies included in the analysis.

Analysis of drinking water interventions

We included 80 observations from 73 individual studies, with 14 additional observations from 14 studies not included in our previous review [16]. The number of observations describing each link between study baseline and outcome is listed in Table 2. Effect estimates of individual observations are listed in Appendix S3. Forest plots separated by type of drinking water intervention are shown in Appendix S4.

Random effects meta-analysis of all 80 observations yielded a pooled effect estimate of 0.67 (0.62, 0.73) with an I^2 of 92% indicating considerable heterogeneity of effect estimates between studies. Results of random effects meta-regression according to Figure 1 (without bias adjustment for non-blinding) are presented in Table 3a with the effect estimates of provision of safe water storage and combined interventions in the table footnote. The meta-regression model explained 39% of the between-study variance. Further covariates, examined in the full meta-regression model, included access to improved *vs.* unimproved sanitation (RR 0.98 (0.80, 1.21)), interventions in rural *vs.* urban or mixed areas (RR 1.00 (0.87, 1.17)), survey data analyses *vs.* studies evaluating specific interventions (RR 1.00 (0.74, 1.34)) and time of follow-up in studies evaluating specific interventions as continuous (in months: RR 1.00 (0.99, 1.00) and as indicator variable ≥12 months *vs.* <12 months: RR 1.02 (0.86, 1.21)) showed no association with diarrhoea and did not considerably change effect estimates of the other variables in the model (i.e. no confounding, all effect estimates changed less than 5%). There were no missing values for any of these covariates. Results of the analysis adjusting for bias due to lack of blinding are presented in Table 3b. After adjusting for bias, there was no evidence that POU chlorine treatment or POU solar treatment was beneficial (confidence intervals widely cross

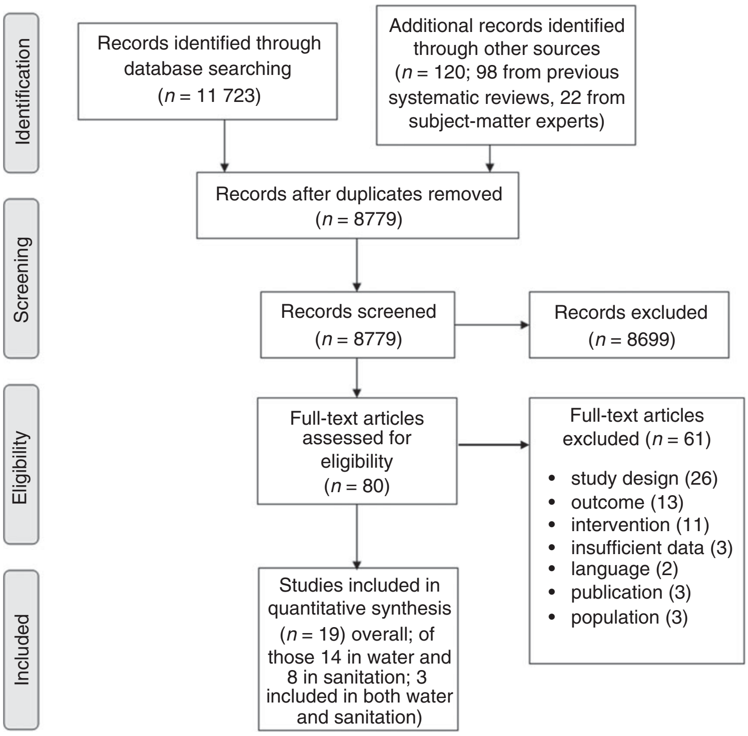


Figure 3 PRISMA Flow chart [75] of the selection process of drinking water and sanitation studies (update only).

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

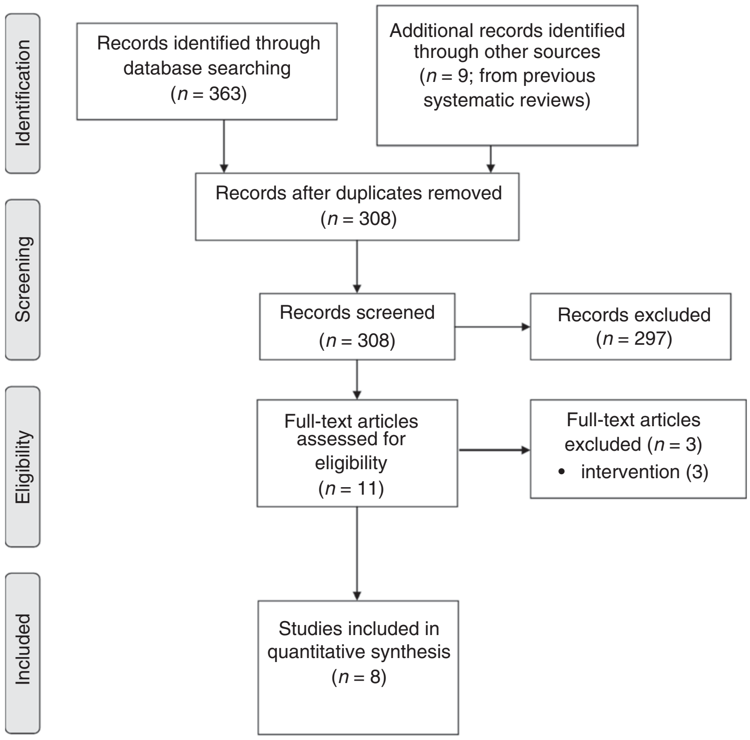


Figure 4 PRISMA Flow chart [75] of the selection process of hygiene studies (update only).

Table 2 Included drinking water interventions according to study baseline and outcome

Baseline water	Outcome water	Comparisons	Transition (Figure 1)
Unimproved source	Improved source, not on premises	11	a
Unimproved source	Piped water	6	b
Improved source, not on premises	Piped water	7	r
Piped water	Piped water, higher quality	1	s
Piped water	Continuous piped water	2	u
Unimproved source	POU chlorine treatment	18	d
Unimproved source	POU solar treatment	5	e
Unimproved source	POU filter treatment	15	f
Improved source, not on premises	POU chlorine treatment	5	w
Improved source, not on premises	POU solar treatment	6	x
Improved source, not on premises	POU filter treatment	3	y
Total		79*	

POU, point-of-use; 'piped water' means piped to premises.
*Comparisons add up to 79 observations (as compared to 80 included observations) as one study provided improved water storage only [74].

one, columns 6 and 7 of Table 3b) whereas filtering of unimproved and improved sources, excluding piped water to premises, remains significantly beneficial (column 8 of Table 3b).

Sensitivity analyses. Excluding survey data analyses (eight observations from five individual studies) yielded a pooled estimate of 0.65 (0.60, 0.71), I^2: 92% in meta-analysis. Effect estimates for individual transitions

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

Table 3 (a) Risk ratios for drinking water interventions, not adjusted for non-blinding. (b) Risk ratios for drinking water interventions, adjusted for non-blinding in point-of-use water interventions

	Outcome water						
Baseline water	Improved source, not on premises	Piped water	Piped water, higher quality*	Continuous piped water*	POU chlorine treatment	POU solar treatment	POU filter treatment filter + *safe storage*†
(a)							
Unimproved source	0.89 (0.77, 1.02)	0.77 (0.64, 0.93)	0.25 (0.09, 0.67)	0.64 (0.42, 0.98)	0.76 (0.64, 0.91)	0.67 (0.54, 0.84)	0.49 (0.38, 0.64) *0.39 (0.32, 0.48)*
Improved source, not on premises		0.87 (0.72, 1.04)	0.28 (0.10, 0.76)	0.73 (0.48, 1.10)	0.86 (0.71, 1.04)	0.76 (0.62, 0.92)	0.55 (0.41, 0.74) *0.44 (0.34, 0.56)*
Piped water			0.32 (0.12, 0.86)	0.84 (0.57, 1.22)	0.99 (0.78, 1.26)	0.87 (0.67, 1.13)	0.64 (0.46, 0.88) *0.50 (0.38, 0.66)*
(b)							
Unimproved source	0.89 (0.77, 1.02)	0.77 (0.64, 0.92)	0.25 (0.09, 0.66)	0.64 (0.42, 0.97)	0.91 (0.70, 1.18)	0.88 (0.60, 1.27)	0.60 (0.42, 0.84) *0.52 (0.35, 0.77)*
Improved source, not on premises		0.87 (0.72, 1.04)	0.28 (0.10, 0.75)	0.72 (0.47, 1.10)	1.02 (0.78, 1.35)	0.99 (0.68, 1.42)	0.67 (0.46, 0.97) *0.59 (0.39, 0.88)*
Piped water			0.32 (0.12, 0.84)	0.83 (0.57, 1.21)	1.18 (0.86, 1.60)	1.14 (0.76, 1.70)	0.77 (0.53, 1.14) *0.68 (0.44, 1.04)*

(a) Results are adjusted for provision of safe water storage (0.79 (0.64, 0.98)) and combined intervention (0.84 (0.70, 1.00)).
(b) Results are adjusted for provision of safe water storage (0.87 (0.69, 1.11)) and combined intervention (0.85 (0.72, 1.01)).
*Based on limited evidence, one observation with 'piped water, higher quality' as outcome [34] and two observations with 'continuous piped water' as outcome [32, 33].
†Some point-of-use filter treatments include safe drinking water storage as an integrated component, such as ceramic filter interventions that filter the water in a closed water container with a tap.

 © 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

between exposure scenarios did not change besides the transition to continuous piped water (one of two studies describing this transition analysed survey data, e.g. from unimproved to continuous piped: 0.71 (0.39, 1.27) instead of 0.65 (0.42, 0.98), from improved community source to continuous piped: 0.81 (0.45, 1.46) instead of 0.73 (0.48, 1.10) and from piped to continuous piped: 0.93 (0.55, 1.58) instead of 0.84 (0.57, 1.22)).

Excluding the eleven studies evaluating specific interventions with the lowest quality rating yielded a pooled effect estimate of 0.67 (0.62, 0.73), excluding non-randomised studies a pooled effect estimate of 0.62 (0.56, 0.68), excluding studies that did not report diarrhoea in children <5 years a pooled effect estimate of 0.69 (0.65, 0.75) and excluding studies published before 2012 a pooled effect estimate of 0.69 (0.59, 0.81) in meta-analysis as compared to the pooled estimate of the whole dataset of 0.67 (0.62, 0.73).

Converting the odds ratios of Clasen *et al.* [25] to risk ratios with the assumed control group risk of 30% only slightly reduced the estimates for filter interventions (e.g. from unimproved source to filter: 0.51 (0.39, 0.66) instead of 0.49 (0.38, 0.64) and from improved community source to filter: 0.57 (0.42, 0.76) instead of 0.55 (0.41, 0.74)).

Analysis of sanitation interventions

We included 22 observations from 19 individual studies, eight additional observations from eight studies compared to the previous review. Random effects meta-analysis of all 22 observations yielded an effect estimate of 0.75 (0.63, 0.88), I^2: 95% (Figure 5). Effect estimates of individual observations are listed in Appendix S3.

Eighteen observations reported the association between improved household sanitation facilities and diarrhoea compared to unimproved sanitation and two observations respectively of sewer connection compared to unimproved and improved sanitation facilities. From 12 of the 13 intervention studies, a measure of sanitation coverage after the intervention could be extracted (Appendix S3).

Examining improved household sanitation and sewer connection separately in meta-regression resulted in an effect estimate of 0.84 (0.73, 0.98) for improved household sanitation and 0.60 (0.39, 0.92) for sewer connection compared to a baseline of unimproved sanitation and 0.71 (0.47, 1.07) of sewer connection compared to a baseline of improved household sanitation (adjusted for combined interventions: RR 0.65 (0.48, 0.89)). This model explained 59% of the between-study variance. When disaggregating unimproved sanitation into open defecation and unimproved sanitation facilities (16 of the 22 observations allowed this disaggregation), there was no difference in diarrhoea risk between open defecation and unimproved sanitation facilities (RR 1.00 (0.71, 1.42)) and hence no difference in effect estimates for improved household sanitation and sewer connection *vs.* a baseline of either open defecation or unimproved sanitation facilities.

Meta-regression results of the further examined covariates were 1.19 (0.79, 1.79) for baseline access to an improved *vs.* unimproved water source, 0.96 (0.64, 1.44) for latrine promotion only *vs.* also provision of latrine hardware, 1.26 (0.90, 1.78) for survey data analyses *vs.* studies evaluating specific interventions, 1.32 (0.72, 2.43) for studies evaluating specific interventions with a follow-up time of more than 24 months *vs.* those up to 24 months and 1.01 (0.99, 1.04) for each one month increase in follow-up time, and 0.59 (0.43, 0.81) for combined *vs.* single interventions. Studies evaluating specific interventions that led to a sanitation coverage up to 75% reduced diarrhoea on average by 24% (RR 0.76 (0.51, 1.13)) in the intervention compared to the control group, and those with sanitation coverage above 75% after the intervention by 45% (RR 0.55 (0.34, 0.91) in the intervention compared to the control group. There were no missing values for any of these covariates besides one missing observation for community coverage in one intervention study. Here, we used listwise deletion, that is the record was excluded from the respective analysis.

Sensitivity analyses. Excluding survey data analyses yielded a pooled effect estimate of 0.68 (0.50, 0.91), excluding the study with the lowest quality rating a pooled effect estimate of 0.75 (0.63, 0.89), excluding non-randomised studies a pooled effect estimate of 0.96 (0.87, 1.06), excluding studies that did not report diarrhoea in children <5 years a pooled effect estimate of 0.76 (0.64, 0.91) and excluding studies published before 2012 a pooled effect estimate of 0.88 (0.81, 0.94) in meta-analysis as compared to the pooled estimate of the whole dataset of 0.75 (0.63, 0.88). Forest plots by intervention type (improved household sanitation and sewer), community coverage (up to and above 75%) and for randomised studies are shown in Appendix S4.

Analysis of hygiene interventions

We included 33 observations from 33 individual studies, eight additional observations compared to the previous review. Random effects meta-analysis of all 33 observations yielded an effect estimate of 0.70 (0.64, 0.77), I^2: 89% (Figure 6). A Bayesian bias-adjusted analysis to account for lack of blinding in all of the studies changed

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

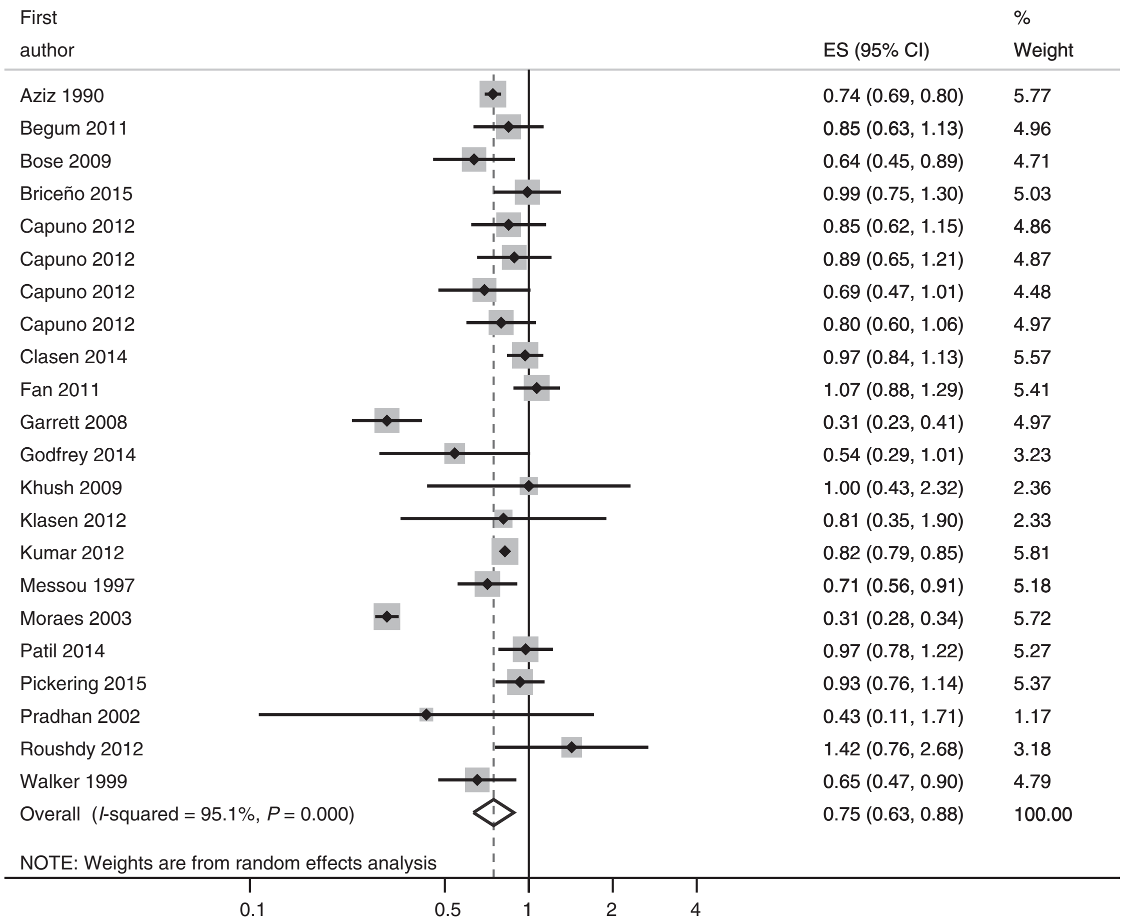


Figure 5 Forest plot of included sanitation interventions.

the effect estimate to 0.90 and introduced considerable uncertainty (95% confidence interval from 0.37 to 2.17) (Table 3). Effect estimates of individual observations are listed in Appendix S3.

In meta-regression, there was no evidence for an association of exclusive promotion of handwashing *vs.* broader hygiene education (RR 0.91 (0.76, 1.09)), the provision of soap (RR 0.88 (0.73, 1.05)), high-income *vs.* low- and middle-income countries (RR 1.01 (0.82, 1.24)), community *vs.* institutional interventions (RR 1.02 (0.83, 1.24)) and time of follow-up in studies evaluating specific interventions as continuous (in months: RR 1.01 (1.00, 1.02) and as indicator variable ≥12 months *vs.* <12 months: RR 1.12 (0.93, 1.36) and diarrhoea. There were no missing values for any of these covariates.

Sensitivity analyses. Excluding one survey data analysis yielded a pooled effect estimate of 0.71 (0.64, 0.78), excluding the five studies evaluating specific interventions with the lowest quality rating yielded a pooled effect estimate of 0.68 (0.62, 0.74), excluding non-randomised studies a pooled effect estimate of 0.74 (0.65, 0.83), excluding studies that did not report diarrhoea in children <5 years a pooled effect estimate of 0.70 (0.64, 0.78), excluding studies published before 2012 a pooled effect estimate of 0.92 (0.84, 1.02), excluding institutional-level studies a pooled effect estimate of 0.70 (0.62, 0.79), excluding household-level studies a pooled effect estimate of 0.69 (0.59, 0.81) and excluding studies conducted in high-income countries a pooled effect estimate of 0.70 (0.62, 0.78) in meta-analysis as compared to the pooled estimate of the whole dataset of 0.70 (0.64, 0.77).

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

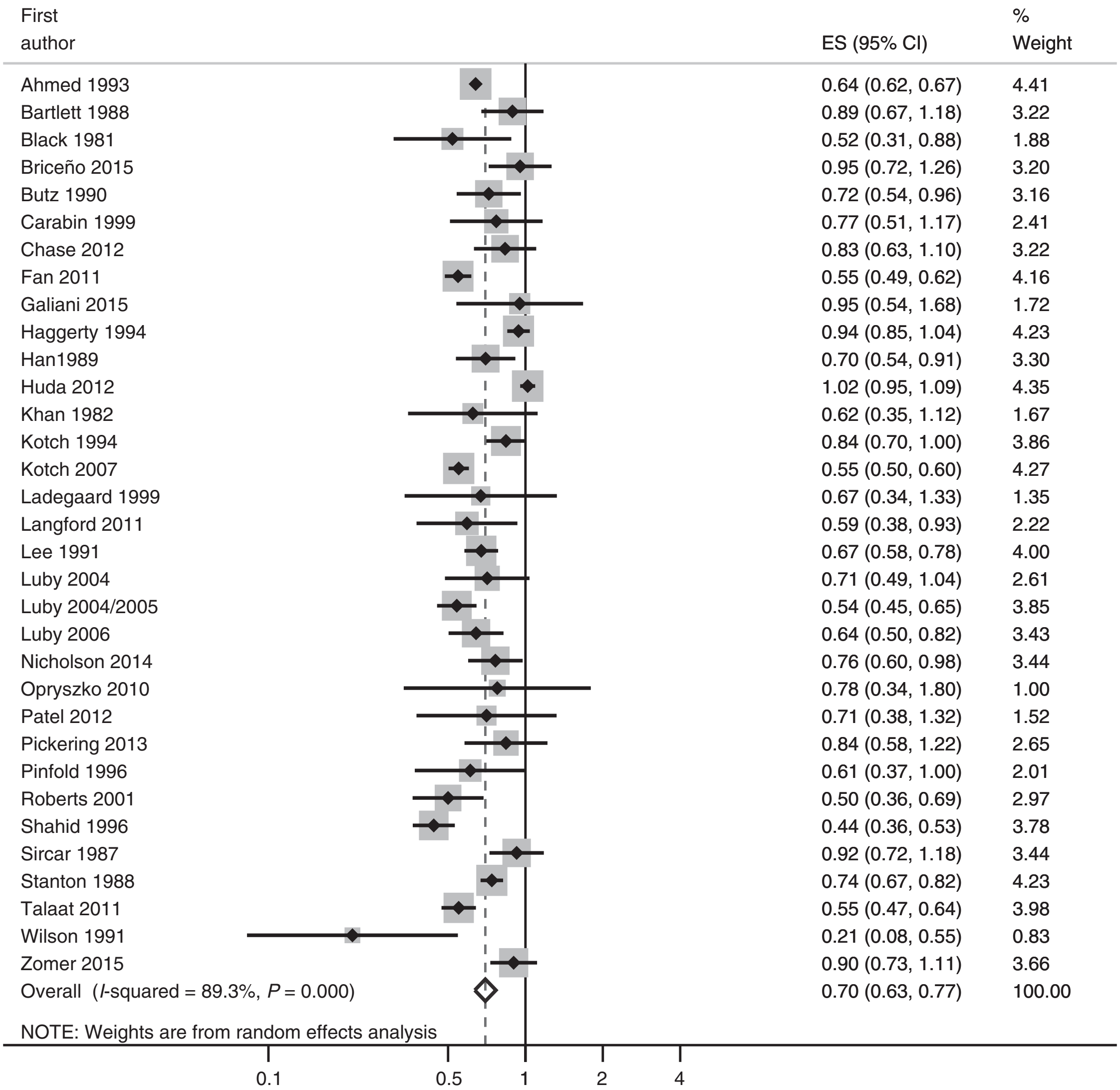


Figure 6 Forest plot of included hygiene interventions.

There was no evidence of funnel-plot asymmetry and small study effects in any of the WaSH meta-analyses (Appendix S4).

Discussion

Main findings

Our results show large potential reductions in the risk of diarrhoeal disease through the delivery of interventions aiming at improvements in drinking water, sanitation and hygiene. For water, the greatest reductions are for a piped water to premises supply that has been treated to improve its quality (75% based on limited evidence) and for POU-filtered water that is safely stored in the household (61% or 48% reduction before and after adjustment for non-blinding) compared to a baseline of unimproved drinking water.

For sanitation, our overall estimates show a 25% mean diarrhoea risk reduction compared to no intervention.

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

Interventions reaching high sanitation coverage, that is above 75%, in the community were associated with a diarrhoea risk reduction of 45%. Also, sewer connections were associated with larger diarrhoea risk reduction than improved household sanitation (40% *vs.* 16%). In both water and sanitation analyses, diarrhoea morbidity is reduced further when the intervention is combined with other components of WaSH.

Hygiene interventions reduce diarrhoea compared to no intervention (30% reduction before adjustment for non-blinding), but the 10% reduction found after adjustment for non-blinding is not statistically significant.

Limitations

Study limitations. We conducted systematic searches across multiple databases for published literature but relevant grey literature was only identified from the review of historic systematic reviews or when supplied by subject-matter experts. There is a risk therefore that relevant studies may have been missed although comparison with previous systematic reviews suggests that our searches were comprehensive.

Some of the meta-regression effect estimates – indicated above (Table 3a and b) – are based on a small number of studies and should be interpreted with caution. Effect estimates for the transition from piped water to a continuous piped supply are based on only two studies which evaluated this change [32, 33] and the transition from piped water to treated piped water is based on only one study [34]. Of the two studies comparing continuous piped to intermittent piped water, one is a cross-sectional, non-intervention study [33]. We excluded this study in a sensitivity analysis which led to a considerable change in the effect estimate for this transition. Also, the results of the sanitation and hygiene meta-analysis were sensitive to excluding studies published before 2012 (hygiene and sanitation) and excluding non-randomised studies (sanitation). Sanitation coverage of 75% was reached in only five studies [35–39]. These five studies are heterogeneous and include one combined water and sanitation intervention and three sewered sanitation interventions. Larger effect estimates might therefore also be due to study characteristics other than community coverage. As the evidence is scarce, the analysis of sanitation coverage also does not take into account baseline sanitation coverage or coverage in the control group – factors that could substantially impact intervention effects. Effect estimates for these transitions are likely to change as new evidence emerges.

Usually, WaSH interventions are unblinded and often rely on self-reported diarrhoea, which is likely to present a high risk of biased reports of diarrhoea that can lead to over-estimation of effect estimates [29, 30]. We attempt to adjust for this limitation by adjusting point-of-use drinking water and hygiene interventions for the assumed effect of non-blinding bias. WaSH exposure classification is often poor. We could not, for example, always differentiate between several types of unimproved sanitation such as shared sanitation (of an otherwise acceptable type), unimproved facilities and open defecation [3] as this information is not clearly reported in many sanitation studies and, indeed, comparison groups may be using a broad range of facilities within a single study. It is possible that these different unimproved sanitation categories exhibit different impacts on health [40–43]. Some studies reported open defecation separately from other unimproved facilities and our analysis found no differential impact on diarrhoea morbidity. This one-time binary measure of mainly practising open defecation or mainly using unimproved sanitation facilities is a simplification and might therefore be subject to fluctuation and measurement error. A community might have high access to unimproved household sanitation but still many community members might practise open defecation [44]. Similarly, unsafe containment, emptying, transport and treatment of faecal waste from improved facilities may discharge excreta back into the environment.

Effectiveness trials of WaSH interventions have typically not achieved high coverage or high compliance [45]. This is particularly the case for recent studies of rural onsite sanitation interventions: in Tanzania, latrine construction rates increased only from 39% to 51% [46]; in India, only around 40% of intervention households had a functional or improved toilet post-intervention and use of these facilities remained limited [47, 48]; and in Mali, latrine coverage was 65% in the intervention arm *vs.* 35% in control households while open defecation remained common [44]. None of the included studies analyses a fully safely managed chain of excreta management. Our effect estimates therefore remain a conservative estimate of the potential impact on diarrhoea through interventions reaching high coverage and compliance.

Limitations of the analysis. Results from meta-regression are observational associations between variables and are therefore prone to bias [49]. WaSH at baseline and outcome was defined at study level, although may vary within the community. This can underestimate the true baseline or outcome effect.

The I^2 statistic, a measure of inconsistency across study findings, was high in the water, sanitation and hygiene analysis [50]. This is consistent with the substantial

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

differences among the studies in terms of intervention type and uptake, study methods, settings, populations, pathogens present and transmission pathways dynamics. We applied meta-regression techniques to explore the reasons for this variance. Results suggest that only part of the variance can be explained and that effect estimates might vary substantially depending on study, intervention and implementation characteristics.

Effect estimates included in this review are usually based on intention-to-treat analysis which might again underestimate the true health impact of WaSH interventions which usually achieve low coverage and lower compliance [45, 51]. Exposure reductions are influenced by many factors such as baseline WaSH and changes in supply, use and maintenance. We tried to account for some of these by examining baseline WaSH, time of follow-up and further covariates. We did not, however, adjust effect estimates for compliance which is crucially important for any health impact. A modelling study on household water treatment concluded that diarrhoea risk decreased proportionally with pathogen removal only when compliance was almost 100% [52, 53]. Assuming a compliance of 80–90%, which is seldom reached in WaSH interventions, diarrhoeal disease was much less reduced [52, 53]. However, compliance is often poorly measured or not measured at all in WaSH intervention evaluations [4] and can be assessed by self-report, observations or measurements (e.g. chlorine in drinking water). Results will differ according to which method is chosen and whether compliance is assessed at a single time point or continuously over time. Self-reported household water treatment users in Zambia reported inconsistently on compliance to household water treatment at two different time points [54].

Our exposure scenarios for drinking water do not include bottled or packaged water. Bottled water consumption is estimated to have increased to 391 billion litres in 2017 compared to 212 billion litres in 2007 [55]. Bottled water can show very small levels of faecal contamination [3, 56–59] and was associated with decreased risk for diarrhoea compared to piped water [60]. Research also showed that different kinds of bottled water can exhibit very different diarrhoea disease risks [61]. We did not include bottled water into our exposure scenarios as there is little evidence from interventions of its effect on diarrhoeal disease. The issue should, however, be given further attention and taken into account in future estimates if evidence permits.

Our assessment is limited to diarrhoeal disease, although systematic reviews have assessed the impact of inadequate WaSH on many other health outcomes such as soil-transmitted helminth infections [13], trachoma [12] and schistosomiasis [62]. Additional benefits, such as livelihood impacts, impacts on well-being and environmental consequences, are likely [2]. Furthermore, our water and sanitation and, partially, hygiene analysis are limited to household access and does not include health impact from access to WaSH in institutions such as schools and healthcare facilities.

We limited our search to studies on diarrhoea morbidity rather than diarrhoea mortality as outcome in our search strategy even though mortality studies can be considered a higher level of evidence, one reason being the greater robustness of the outcome. However, the current evidence base from mortality studies is weak, with very scarce studies of generally limited quality. We are only aware of three WaSH studies which report mortality from diarrhoeal disease ([63, 64] and one unpublished study described in Wagner and Lanoix [65]). None of these studies would have met our inclusion criteria: two studies were observational (one case–control study without relation to a clearly specified intervention [63] and one analysing cross-sectional data [64]) and for the unpublished study not enough data were available to judge eligibility.

General interpretation

Our results are broadly consistent with previous evidence. A Cochrane review on interventions to improve water quality for preventing diarrhoea found insufficient evidence for improved community water sources and included no evidence of reliable piped water to households [7]. The same review found that POU water quality interventions reduced diarrhoea by an average of 23% for chlorination, 31% for flocculation and disinfection, 38% for solar water treatment, 53% for biosand filters and 61% for ceramic filters, all prior to adjustment for non-blinding. Previous reviews on sanitation and diarrhoea estimated somewhat larger associations between interventions aiming at improvements in sanitation and diarrhoea [6, 8]. This might be partially due to a number of recent effectiveness trials that did not significantly reduce diarrhoea [44, 46–48]. Our hygiene effect estimate (not adjusted for non-blinding bias) is consistent with unadjusted pooled estimates from a recent update of a Cochrane review on hygiene interventions [66]. An analysis of Demographic and Health Survey (DHS) data found similar results of increased diarrhoea reduction of combined WaSH interventions [67]. These estimates, consistent with protective effects, are comparable to other published estimates but are drawn from unblinded studies relying on subjective outcomes and may therefore be exaggerated due to biased reports of diarrhoea. We add

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

to the available evidence as we present effect estimates conditional on baseline access and adjusted for further covariates and have moreover adjusted selected effect estimates for potential bias arising from non-blinding.

We find evidence for larger diarrhoea reduction for interventions reaching high sanitation coverage in the community compared to those reaching low coverage. In previous research [31, 68, 69], full community coverage was associated consistently with large diarrhoea reductions: a simulation study estimated nearly 60% diarrhoea reduction for a village with full sanitation coverage compared to a village where everybody practices open defecation [68]. Similarly, an analysis of Indian national data concluded a 47% diarrhoea reduction could be expected in children living in a village with complete sanitation coverage compared to children in villages without sanitation [31]. In both studies, 75% of the diarrhoea reduction was attributed to the indirect or community effect that adequate sanitation has on members of other households in the community. An analysis of 29 Demographic and Health Surveys across sub-Saharan Africa and South Asia found that below 60% coverage, improved sanitation was associated with 18% and at 100% coverage with 56% of diarrhoea reduction [69]. Sanitation coverage was also associated with improvements in children's anthropometric status [70, 71] and reduced child mortality [72]. Introducing sewered sanitation in low- and middle-income settings would be expected to have positive health impacts, although care must be taken that sewage is appropriately treated to avoid the diarrhoeal disease burden being shifted 'downstream' to the receiving communities [73].

We identified important evidence gaps while working on this review and analysis. Impact evaluations should report both diarrhoea mortality and morbidity and the exact WaSH exposure both at baseline and follow-up in terms of access and behaviour (e.g. access to facilities and use). Sanitation interventions should aim to yield high community coverage which is crucial for maximum health gains and is important for adding evidence on the direct and indirect health effects of sanitation. Studies providing microbiologically high-quality piped drinking water continuously to households are needed to estimate which effect of safe drinking water on diarrhoea could be maximally achievable. Studies achieving high compliance and considering non-household exposures would be very important to truly disentangle the effect of WaSH interventions on diarrhoea morbidity.

Acknowledgement and disclaimer

We thank Meredith Stocks for her valuable contributions to the systematic review on hygiene interventions. We thank the following researchers for the provision of additional information on their work: Lindsey Novak, Luis Andres, Claire Chase, Minal Patel, Isabel Günther and Samuel Godfrey. We thank the authors of two reviews, the first one conducted by the World Bank and specifically Luis Andres, Christian Borja-Vega and Ronald Gomez-Suarez (World Bank 2016b) and the second one conducted by Thomas Clasen for the WHO sanitation guidelines, for the provision of their search results.

The study was partially funded by the United Kingdom Department for International Development (DFID). The funder had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Thomas Clasen has participated in research and consulting services supported by Unilever and Vestergaard, which manufacture and sell household or other point of use water filtration devices. Jamie Bartram currently conducts research on drinking water supply and household water treatment which is funded by Suez Environnement and Medentech. Some authors are staff members of WHO or other institutions. The authors alone are responsible for the views expressed in this publication, which do not necessarily represent the views, decisions or policies of the institutions with which they are affiliated. This article should not be reproduced for use in association with the promotion of commercial products, services or any legal entity. WHO does not endorse any specific organisation or products.

References

1. UN General Assembly Resolution A/RES/70/1. Transforming our world: the 2030 Agenda for Sustainable Development [Internet]; 2015. (Available from: http://www.un.org/en/ga/search/view_doc.asp?symbol=A/RES/70/1) [7 Dec 2016]
2. Hutton G, Chase C. The knowledge base for achieving the sustainable development goal targets on water supply, sanitation and hygiene. *Int J Environ Res Public Health* 2016: **13**: 536.
3. UNICEF, WHO. 25 Years Progress on Sanitation and Drinking Water, 2015 Update and MDG Assessment [Internet]. UNICEF and World Health Organization: Geneva, Switzerland; 2015. (Available from: http://files.unicef.org/publications/files/Progress_on_Sanitation_and_Drinking_Water_2015_Update_pdf) [19 Feb 2018]
4. Bain R, Cronk R, Hossain R *et al.* Global assessment of exposure to faecal contamination through drinking water based on a systematic review. *Trop Med Int Health* 2014: **19**: 917–927.
5. Freeman MC, Stocks ME, Cumming O *et al.* Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. *Trop Med Int Health* 2014: **19**: 906–916.

 © 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

6. Cairncross S, Hunt C, Boisson S *et al.* Water, sanitation and hygiene for the prevention of diarrhoea. *Int J Epidemiol* 2010: **39**(suppl 1): i193–i205.
7. Clasen TF, Alexander KT, Sinclair D *et al.* Interventions to improve water quality for preventing diarrhoea. *Cochrane Database Syst Rev*. 2015: **10**: CD004794.
8. Waddington H, Snilstveit B, White H, Fewtrell L. Water, sanitation and hygiene interventions to combat childhood diarrhoea in developing countries [Internet]. International Initiative for Impact Evaluation New Delhi; 2009. (Available from: http://zunia.org/uploads/media/knowledge/3ie%20SR0011249554991.pdf) [31 Jan 2013]
9. Bapat M, Agarwal I. Our needs, our priorities; women and men from the slums in Mumbai and Pune talk about their needs for water and sanitation. *Env Urban* 2003: **15**: 71–86.
10. Benova L, Cumming O, Campbell OM. Systematic review and meta-analysis: association between water and sanitation environment and maternal mortality. *Trop Med Int Health* 2014: **19**: 368–387.
11. Dangour AD, Watson L, Cumming O *et al.* Interventions to improve water quality and supply, sanitation and hygiene practices, and their effects on the nutritional status of children. *Cochrane Database Syst Rev* 2013: **8**.
12. Stocks ME, Ogden S, Haddad D, Addiss DG, McGuire C, Freeman MC. Effect of water, sanitation, and hygiene on the prevention of trachoma: a systematic review and meta-analysis. *PLoS Med* 2014: **11**: e1001605.
13. Strunz EC, Addiss DG, Stocks ME, Ogden S, Utzinger J, Freeman MC. Water, sanitation, hygiene, and soil-transmitted Helminth infection: a systematic review and meta-analysis. *PLoS Med* 2014: **11**: e1001620.
14. WHO. Global Health Observatory (GHO) data [Internet]. WHO; 2016. (Available from: http://www.who.int/gho/en/) [24 Jun 2016]
15. Centre for Reviews and Dissemination, University of York. PROSPERO: International prospective register of systematic reviews [Internet]. (Available from: http://www.crd.york.ac.uk/PROSPERO/) [21 Jul 2016].
16. Wolf J, Prüss-Ustün A, Cumming O *et al.* Assessing the impact of drinking-water and sanitation on diarrhoeal disease in low-and middle-income settings: a systematic review and meta-regression. *Trop Med Int Health* 2014: **19**: 928–942.
17. Stuart EA. Matching methods for causal inference: a review and a look forward. *Stat Sci* 2010: **25**: 1–21.
18. World Bank. World Bank Country and Lending Groups – World Bank Data Help Desk [Internet]; 2016. Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups [19 Oct 2016]
19. Correa JC, Pinto D, Salas LA, Camacho JC, Rondón M, Quintero J. A cluster-randomized controlled trial of handrubs for prevention of infectious diseases among children in Colombia. *Rev Panam Salud Pública* 2012: **31**: 476–484.
20. Pope DP, Mishra V, Thompson L *et al.* Risk of low birth weight and stillbirth associated with indoor air pollution from solid fuel use in developing countries. *Epidemiol Rev* 2010: **32**: 70–81.
21. Wells G, Shea B, O'Connell D *et al.* The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses [Internet]. Ottawa Hospital. Research Institute. (Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp)
22. Higgins J, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions [Internet]*. Version 5.1.0. The Cochrane Collaboration; 2011. (Available from: www.cochrane-handbook.org) [updated Mar 2011]
23. Davies HTO, Crombie IK, Tavakoli M. When can odds ratios mislead? *BMJ* 1998: **316**: 989–991.
24. Zhang J, Kai FY. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *JAMA* 1998: **280**: 1690–1691.
25. Clasen T, Parra GG, Boisson S, Collin S. Household-based ceramic water filters for the prevention of diarrhea: a randomized, controlled trial of a pilot program in Colombia. *Am J Trop Med Hyg* 2005: **73**: 790–795.
26. Borenstein M, Hedges L, Higgins JP, Rothstein HR. Part 5: complex data structures. *Introduction to Meta-Analysis*, 1st ed. Chichester, UK: John Wiley & Sons, Ltd; 2009. pp. 213–245.
27. Lunn DJ, Thomas A, Best N, Spiegelhalter D. WinBUGS-a Bayesian modelling framework: concepts, structure, and extensibility. *Stat Comput* 2000: **10**: 325–337.
28. Salanti G, Higgins JP, Ades AE, Ioannidis JP. Evaluation of networks of randomized trials. *Stat Methods Med Res* 2008: **17**: 279–301.
29. Savović J, Jones HE, Altman DG *et al.* Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. *Ann Intern Med* 2012: **157**: 429–438.
30. Wood L, Egger M, Gluud LL *et al.* Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ* 2008: **336**: 601.
31. Andres LA, Briceño B, Chase C, Echenique JA. Sanitation and Externalities: Evidence from Early Childhood Health in Rural India. The World Bank; 2014. (Policy Research Working Paper). Report No.: 6737.
32. Ercumen A, Arnold BF, Kumpel E *et al.* Upgrading a piped water supply from intermittent to continuous delivery and association with waterborne illness: a matched cohort study in Urban India. *PLoS Med* 2015: **12**: e1001892.
33. Roushdy R, Sieverding M, Radwan H. The impact of water supply and sanitation on child health: Evidence from Egypt. New York, NY, USA: Population Council; 2012. (Poverty, Gender, and Youth Working Paper). Report No.: 24.
34. Hunter PR, Toro GIR, Minnigh HA. Impact on diarrhoeal illness of a community educational intervention to improve drinking water quality in rural communities in Puerto Rico. *BMC Public Health* 2010: **10**: 219.
35. Aziz KMA, Hoque BA, Hasan KZ *et al.* Reduction in diarrhoeal diseases in children in rural Bangladesh by

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

environmental and behavioural modifications. *Trans R Soc Trop Med Hyg* 1990: **84**: 433–438.
36. Klasen S, Lechtenfeld T, Meier K, Rieckmann J. Benefits trickling away: The health impact of extending access to piped water and sanitation in urban Yemen. Göttingen: Georg-August-Universität; 2012. pp. 1–35. Report No.: 110.
37. Moraes LRS, Cancio JA, Cairncross S, Huttly S. Impact of drainage and sewerage on diarrhoea in poor urban areas in Salvador, Brazil. *Trans R Soc Trop Med Hyg* 2003: **97**: 153–158.
38. Pradhan M, Rawlings LB. The impact and targeting of social infrastructure investments: Lessons from the Nicaraguan Social Fund [Internet]; 2002. pp. 275–295. (Available from: http://wber.oxfordjournals.org/content/16/2/275.short) [12 Feb 2013]
39. Walker I, Del Cid R, Ordoñez F, Rodríguez F. Ex-post evaluation of the Honduran Social Investment Fund (FHIS 2). World Bank Wash DC [Internet]; 1999. (Available from: http://www.esa.hn/pub/FHIS%20Expost%20Evaluation.pdf) [10 Mar 2014]
40. Fuller JA, Clasen T, Heijnen M, Eisenberg JNS. Shared sanitation and the prevalence of diarrhea in young children: evidence from 51 countries, 2001–2011. *Am J Trop Med Hyg* 2014: **91**: 173–180.
41. Günther I, Niwagaba CB, Lüthi C *et al.* When is shared sanitation improved sanitation?-The correlation between number of users and toilet hygiene [Internet]. University Library of Munich, Germany; 2012. (Available from: https://ideas.repec.org/p/pra/mprapa/45830.html) [14 Apr 2016]
42. Heijnen M, Cumming O, Peletz R *et al.* Shared sanitation versus individual household latrines: a systematic review of health outcomes. *PLoS ONE* 2014: **9**: e93300.
43. Spears D, Ghosh A, Cumming O. Open defecation and childhood stunting in India: an ecological analysis of new data from 112 districts. *PLoS ONE* 2013: **8**: e73784.
44. Pickering AJ, Djebbari H, Lopez C, Coulibaly M, Alzua ML. Effect of a community-led sanitation intervention on child diarrhoea and child growth in rural Mali: a cluster-randomised controlled trial. *Lancet Glob Health* 2015: **3**: e701–e711.
45. Garn JV, Sclar GD, Freeman MC *et al.* The impact of sanitation interventions on latrine coverage and latrine use: a systematic review and meta-analysis. *Int J Hyg Environ Health* 2017; **220**(2, part B): 329–340.
46. Briceño B, Coville A, Martinez S. Promoting Handwashing and Sanitation: Evidence from a Large-Scale Randomized Trial in Rural Tanzania. The World Bank; 2015. (Policy Research Working Paper). Report No.: 7164.
47. Clasen T, Boisson S, Routray P *et al.* Effectiveness of a rural sanitation programme on diarrhoea, soil-transmitted helminth infection, and child malnutrition in Odisha, India: a cluster-randomised trial. *Lancet Glob Health* 2014: **2**: e645–e653.
48. Patil SR, Arnold BF, Salvatore AL *et al.* The effect of India's total sanitation campaign on defecation behaviors and child health in rural Madhya Pradesh: a cluster randomized controlled trial. *PLoS Med* 2014: **11**: e1001709.
49. Thompson SG, Higgins J. How should meta-regression analyses be undertaken and interpreted? *Stat Med* 2002: **21**: 1559–1573.
50. Borenstein M, Hedges L, Higgins JP, Rothstein HR. Chapter 16: identifying and quantifying heterogeneity. *Introduction to Meta-Analysis*. Chichester, UK: Wiley; 2009. p. 357–364.
51. Kolb deWilde C, Milman A, Flores Y, Salmerón J, Ray I. An integrated method for evaluating community-based safe water programmes and an application in rural Mexico. *Health Policy Plan*. 2008: 23: 452–464.
52. Brown J, Clasen T. High adherence is necessary to realize health gains from water quality interventions. *PLoS ONE* 2012: **7**: e36735.
53. Enger KS, Nelson KL, Rose JB, Eisenberg JNS. The joint effects of efficacy and compliance: a study of household water treatment effectiveness against childhood diarrhea. *Water Res* 2013: **47**: 1181–1190.
54. Rosa G, Kelly P, Clasen T. Consistency of use and effectiveness of household water treatment practices among urban and rural populations claiming to treat their drinking water at home: a case study in Zambia. *Am J Trop Med Hyg* 2016: **94**: 445–455.
55. statista. Bottled water consumption worldwide from 2007 to 2017 (in billion liters) [Internet]. Statista; 2016. (Available from: http://www.statista.com/statistics/387255/global-bottled-water-consumption/) [28 Jul 2016].
56. Bain R, Cronk R, Wright J, Yang H, Slaymaker T, Bartram J. Fecal contamination of drinking-water in low- and middle-income countries: a systematic review and meta-analysis. *PLoS Med* 2014: **11**: e1001644.
57. Williams AR, Bain RES, Fisher MB, Cronk R, Kelly ER, Bartram J. A systematic review and meta-analysis of fecal contamination and inadequate treatment of packaged water. *PLoS ONE* 2015: **10**: e0140899.
58. Wright J, Dzodzomenyo M, Wardrop NA *et al.* Effects of sachet water consumption on exposure to microbe-contaminated drinking water: household survey evidence from Ghana. *Int J Environ Res Public Health* 2016: **13**: 303.
59. Fisher MB, Williams AR, Jalloh MF, Saquee G, Bain RE, Bartram JK. Microbiological and chemical quality of packaged sachet water and household stored drinking water in Freetown, Sierra Leone. *PLoS ONE* 2015: **10**: e0131772.
60. Sima LC, Desai MM, McCarty KM, Elimelech M. Relationship between use of water from community-scale water treatment refill kiosks and childhood diarrhea in Jakarta. *Am J Trop Med Hyg* 2012: **87**: 979–984.
61. Hunter PR, Risebro H, Yen M *et al.* Water source and diarrhoeal disease risk in children under 5 years old in Cambodia: a prospective diary based study. *BMC Public Health* 2013: **13**: 1.
62. Grimes JE, Croll D, Harrison WE, Utzinger J, Freeman MC, Templeton MR. The relationship between water, sanitation and schistosomiasis: a systematic review and meta-analysis. *PLoS Negl Trop Dis* 2014: **8**: e3296.

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

63. Victora CG, Smith PG, Vaughan JP *et al*. Water supply, sanitation and housing in relation to the risk of infant mortality from diarrhoea. *Int J Epidemiol* 1988: **17**: 651–654.
64. Bhalotra S., Diaz-Cayeros A, Miller G, Miranda A, Venkataramani A. Urban water disinfection and mortality decline in developing countries [Internet]. Cambridge, UK: National Bureau of Economic Research; 2017. (NBER Working Paper Series). Report No.: 23239. (Available from: http://www.nber.org/papers/w23239) [20 Feb 2018]
65. Wagner EG, Lanoix JN. Water supply for rural areas and small communities [Internet]. World Health Organization; 1959. (Monograph Series). Report No.: 42. (Available from: http://www.who.int/water_sanitation_health/dwq/monograph42.pdf) [27 Feb 2018]
66. Ejemot-Nwadiaro RI, Ehiri JE, Arikpo D, Meremikwu MM, Critchley JA. Hand washing promotion for preventing diarrhoea. *Cochrane Database Syst Rev* 2015::CD004265.
67. Fuller JA, Westphal JA, Kenney B, Eisenberg JNS. The joint effects of water and sanitation on diarrhoeal disease: a multicountry analysis of the Demographic and Health Surveys. *Trop Med Int Health* 2015: **20**: 284–292.
68. Fuller JA. Emerging Issues in Sanitation: Herd Protection, Sharing Between Households, and Joint Effects. University of Michigan; 2015.
69. Jung YT, Lou W, Cheng Y-L. Exposure-response relationship of neighbourhood sanitation and children's diarrhea. *Trop Med Int Health* 2017: **22**: 857–865.
70. Fuller JA, Villamor E, Cevallos W, Trostle J, Eisenberg JN. I get height with a little help from my friends: herd protection from sanitation on child growth in rural Ecuador. *Int J Epidemiol* 2016: **45**: 460–469.
71. Hammer J, Spears D. Village Sanitation and Children's Human Capital: Evidence from a Randomized Experiment by the Maharashtra Government. The World Bank; 2013. (Policy Research Working Paper). Report No.: 6580.
72. Geruso M, Spears D. Neighborhood sanitation and infant mortality [Internet]. Cambridge, UK: National Bureau of Economic Research; 2015. (NBER Working Paper Series). Report No.: 21184. (Available from: http://www.nber.org/papers/w21184) [20 Feb 2018]
73. Baum R, Luh J, Bartram J. Sanitation: a global estimate of sewerage connections without treatment and the resulting impact on MDG progress. *Environ Sci Technol* 2013: **47**: 1994–2000.
74. Günther I, Schipper Y. Pumps, germs and storage: the impact of improved water containers on water quality and health. *Health Econ* 2013: **22**: 757–774.
75. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009: **151**: 264–269.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1 PRISMA checklist
Appendix S2 Search Strategy
Appendix S3 Included WaSH studies
Appendix S4 General further information
Appendix S5 Quality ratings

Corresponding Author Annette Prüss-Ustün, Department of Public Health, Environment and Social Determinants of Health, World Health Organization, 20 Avenue Appia, Geneva, Switzerland. Tel.: +41 22 791 35 84; E-mail: pruessa@who.int

© 2018 World Health Organization; licensed by WHO Published by John Wiley & Sons Ltd.

International Journal of Epidemiology, 2019, 1204–1218
doi: 10.1093/ije/dyy253
Advance Access Publication Date: 10 December 2018
Original article

Infectious Disease

Handwashing with soap after potential faecal contact: global, regional and country estimates

Jennyfer Wolf,[1]* Richard Johnston,[1] Matthew C Freeman,[2] Pavani K Ram,[3] Tom Slaymaker,[4] Eric Laurenz[5] and Annette Prüss-Ustün[1]

[1]Department of Public Health, Environmental and Social Determinants of Health, World Health Organization, Geneva, Switzerland, [2]Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA, [3]School of Public Health and Health Professions, University of Buffalo, Buffalo, NY, USA, [4]Division of Data, Research and Policy, UNICEF, New York City, NY, USA and [5]Fraunhofer ISE, Fraunhofer Institute for Solar Energy Systems, Freiburg, Germany

*Corresponding author. Department of Public Health, Environmental and Social Determinants of Health, World Health Organization, 1211 Geneva, Switzerland. E-mail: jennyfer.wolf@gmail.com

Editorial decision 11 October 2018; Accepted 9 November 2018

Abstract

Background: Limited data have been available on the global practice of handwashing with soap (HWWS). To better appreciate global HWWS frequency, which plays a role in disease transmission, our objectives were to: (i) quantify the presence of designated handwashing facilities; (ii) assess the association between handwashing facility presence and observed HWWS; and (iii) derive country, regional and global HWWS estimates after potential faecal contact.

Methods: First, using data from national surveys, we applied multilevel linear modelling to estimate national handwashing facility presence. Second, using multilevel Poisson modelling on datasets including both handwashing facility presence and observed HWWS after potential faecal contact, we estimated HWWS prevalence conditional on handwashing facility presence by region. For high-income countries, we used meta-analysis to pool handwashing prevalence of studies identified through a systematic review. Third, from the modelled handwashing facility presence and estimated HWWS prevalence conditional on the presence of a handwashing facility, we estimated handwashing practice at country, regional and global levels.

Results: First, approximately one in four persons did not have a designated handwashing facility in 2015, based on 115 data points for 77 countries. Second the prevalence ratio between HWWS when a designated facility was present compared with when it was absent was 1.99 (1.66, 2.39) $P<0.001$ for low- and middle-income countries, based on nine datasets. Third, we estimate that in 2015, 26.2% (23.1%, 29.6%) of potential faecal contacts were followed by HWWS.

Conclusions: Many people lack a designated handwashing facility, but even among those with access, HWWS is poorly practised. People with access to designated

© World Health Organization, 2018. All rights reserved. The World Health Organization has granted the Publisher permission for the reproduction of this article.
This is an Open Access article distributed under the terms of the Creative Commons Attribution 3.0 IGO License (https://creativecommons.org/licenses/by/3.0/igo/), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.

handwashing facilities are about twice as likely to wash their hands with soap after potential faecal contact as people who lack a facility. Estimates are based on limited data.

Key words: Diarrhoea, hygiene, hand disinfection, handwashing facility, global estimates

Key Messages

- One in four persons worldwide did not have access to a handwashing facility with soap and water on premises in 2015.
- In 2015, handwashing with soap occurred in about 26% after events of potential faecal contact, globally. In regions with high access to handwashing facilities, handwashing with soap was performed by about 51%, and in regions with more limited access, by about 22% after events of potential faecal contact.
- Though additional data and analyses are needed, quantifying the presence of handwashing facilities with soap and water on premises may be used to estimate actual handwashing behaviour.
- Important gaps exist for country-representative data on presence of designated handwashing facilities and on handwashing behaviour at household level, for all regions of the world and particularly for high-income countries.

Introduction

Handwashing with soap (HWWS) is an important public health behaviour as it reduces exposure to faecal pathogens and other infectious agents, thereby reducing gastrointestinal[1,2] and respiratory infections.[3] Interventions that successfully promote HWWS are considered very cost-effective.[4] However, HWWS was estimated to be practised in only 19% of cases after potential faecal contact, globally.[1]

The proportion of people using a handwashing facility with soap and water on premises is a global indicator of the Sustainable Development Goals (SDG indicator 6.2.1b).[5] Country-representative data on this indicator are collected in household surveys such as demographic and health surveys (DHS) and multiple indicator cluster surveys (MICS) and assessed through observation by enumerators.[6,7] The presence of handwashing materials at household level was associated with observed HWWS, hand cleanliness and child health.[8–10] However, recent randomized controlled trials of interventions which provided handwashing materials and promoted handwashing with soap, combined with improvements in drinking water and sanitation, resulted in ambiguous health impacts.[11–13] The absence of a handwashing facility with soap and water on premises does not preclude that hands are washed, but in situations where the handwashing facility is located off-site or water and soap need to be fetched, routine handwashing after potential faecal contact, or other key times such as before preparing food or eating, is less likely to occur.[8]

Handwashing practice recorded during structured observations is considered the most reliable way to measure actual handwashing behaviours,[14,15] though some limitations exist with regard to bias.[16] Structured observations are considered impractical to conduct routinely in national household surveys, given cost and logistical constraints.[7,16] This study quantifies the link between observed HWWS and the presence of a designated handwashing facility, defined as a specific place within the premises of a household which has both soap and water. Previous estimates of HWWS practice were based on research studies reporting observed handwashing prevalence after potential faecal contact.[1] These studies were usually not nationally representative, were conducted in various settings and were therefore not comparable between countries. The updatepresented here is based on nationally representative household survey data that are harmonized across countries and that cover an increasingly large number of countries around the world.

The purpose of this analysis was to quantify the current state of global handwashing practice. To that end, we had the following three objectives: (i) to quantify presence of designated handwashing facilities at national, regional and global levels; (ii) to assess the association between presence of a designated handwashing facility and observed HWWS at crucial time points; and (iii) to derive country, regional and global estimates of HWWS practice after potential faecal contact.

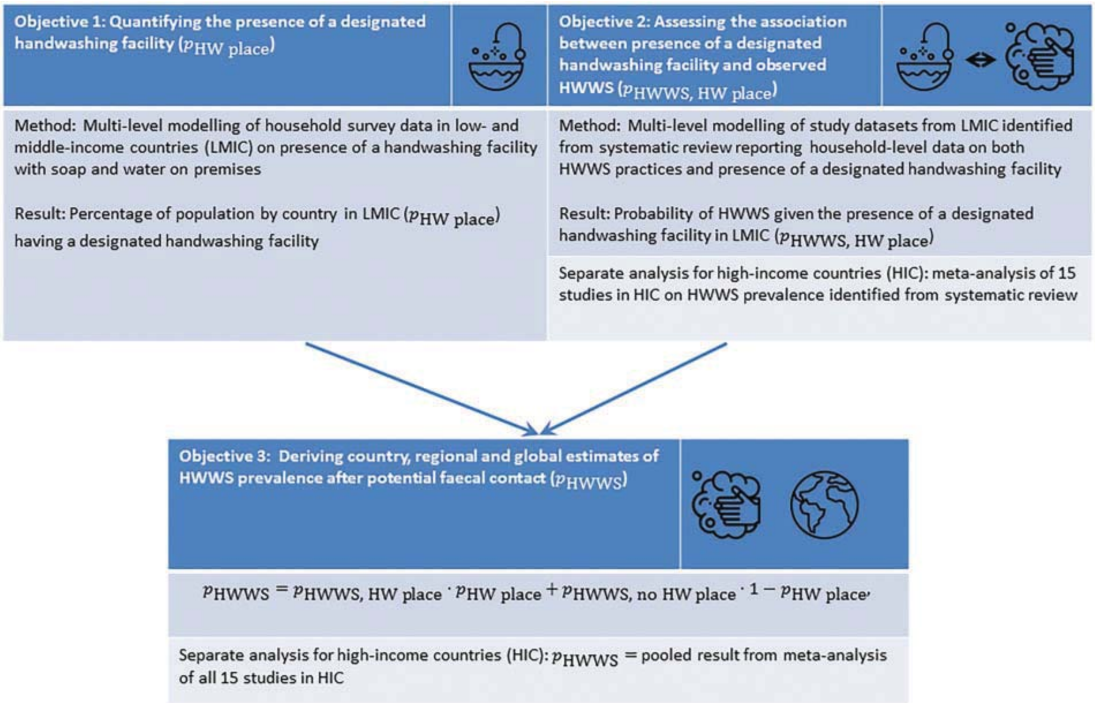


Figure 1. Overview of objectives, methods and results; HIC: high-income countrie; LMIC: low- and middle-income countries. Icons made by pongsakornred, Freepik, and turkkub from www.flaticon.com.

Methods

We have summarized the key methodological approaches below; but as this work uses various methods and analysis steps, we have included a figure explaining the relationship between the three objectives (Figure 1). An additional table listing the methods used for each objective in detail is provided in the Supplementary Appendix A.0.1 (available as Supplementary data at *IJE* online). We are following guidelines for accurate and transparent health estimates reporting (GATHER)[17,18] and have included a GATHER checklist in Supplementary Appendix A.0.2. Data analysis code can be obtained from the corresponding author.

Objective 1: quantifying the presence of a designated handwashing facility

We extracted country data on household presence of a designated handwashing facility from the WHO/UNICEF Joint Monitoring Programme for Water Supply, Sanitation and Hygiene (JMP) global database. This compiles data collected through nationally representative household surveys and censuses, and represents proportions of households that have a handwashing facility with soap and water available on premises, i.e. within the dwelling, yard or plot (defined above as and named within this manuscript as a 'designated handwashing facility').[19]

We modelled a continuous time series of estimates for 194 countries using a two-level (data points clustered within countries) linear multilevel model (MLM) with a random intercept by country. This approach allowed us to estimate values for countries with and without data points. The dependent variable (survey estimate of presence of a designated handwashing facility) was logit-transformed to restrict estimates between 0 and 1 (or between 0 and 100%). Covariates (fixed effects) included in the model were a continuous time variable (year, centred by its median), a factor variable indicating regional grouping (the six WHO regions: AFR, AMR, EMR, EUR, SEAR and WPR[20]) and a factor variable indicating the country's income level. Countries' income levels were grouped as low-, lower-middle-, upper-middle- and high-income economies for the year 2015,[21] as the main outcome of the analysis was modelled country estimates for 2015. Urban and rural areas were modelled separately. Estimates for countries with no data point ($n = 118$, Table 1) were extrapolated from the mean urban and rural values for the respective year, region and income level (i.e. the model prediction for the fixed part). Further model details are included in Supplementary Appendix A.1.2 (available as

Supplementary data at *IJE* online). Supplementary Appendix A.3.4 (available as Supplementary data at *IJE* online) lists in column H whether the modelled estimate is based on own country values or whether it was extrapolated from the mean value.

Confidence intervals (CIs) of the presence of a designated handwashing facility by urban and rural areas and for countries with data points were derived using the Monte Carlo method with random draws ($n = 10\ 000$) of the fixed and random effects coefficient sets and the 2.5 and 97.5 percentiles of the hereby created model predictions. For countries without data points (thus without random effect coefficients to be varied), confidence intervals were approximated as 95% prediction intervals of a standard fixed effects linear model for the respective region. The prediction interval PI was applied to the model output (main estimate y) of the MLM to yield approximate lower and upper confidence limits CL ($= y \pm PI/2$). The MLM was implemented in Stata 14.[22] Confidence intervals for urban and rural areas at country level were derived in R[23] using the 'arm'-package.[24]

Country estimates and their 95% CIs were derived using country population figures for urban and rural areas from the United Nations Population Division (2017 revision).[25] Country estimates were calculated as population-weighted means of the urban and rural modelled values; 95% CIs were derived with standard formulae. The standard error (SE) at country level was estimated with an approach using the delta method which is described in detail here[26] for a similar context and in the Supplementary Appendix (Equation A3), available as Supplementary data at *IJE* online. The same approach was used to calculate regional and global estimates and their 95% CIs.

As a sensitivity analysis, we modelled presence of a designated handwashing facility using only the more recent survey data since 2009, as before 2009 handwashing measurements in DHS and MICS had not yet been harmonized across countries.[7]

The predictive performance of the model was assessed using cross-validation.[27] As modelled results are presented for the year 2015, and as it was necessary to extrapolate to many countries with no survey point at all, leave-one-out cross validation was used for the number n of countries with a survey point for the year 2015 ($country_1, \ldots, country_n$). The model was fitted n times, each time setting all survey points for $country_i$ as missing ($country_i$ formed the 'test set' in round n). Subsequently, $country_i$ model prediction was compared with $country_i$ actual survey value for the year 2015 and the root mean squared error across n rounds was calculated.

Table 1. Number of survey data points available by country on proportions of households with an observed designated handwashing facility

Number of countries	Number of data points[a]
117	0
48	1
23	2
4	3
1	4
1	5
Total = 194	Total = 115

[a]A data point comprises one estimate for urban and rural areas separately.

Objective 2: assessing the association between presence of a designated handwashing facility and observed HWWS

Systematic review of observed HWWS prevalence after potential faecal contact

We updated the results of our previous systematic review[1] to identify any study that reported proportion of observed HWWS after potential faecal contact, published from August 2013 to February 2016, using PubMed, Embase and ISI Web of Knowledge. No restrictions were placed on language or study type. The search strategy was identical to that in the previous review and used the following keywords: [observ*] AND [hand wash*], [handwash*], [soap]. The database search was supplemented with data identified in a previous review[28] and with additional Google Scholar searches of author names identified during the systematic database search. In addition, subject matter experts were contacted for unpublished handwashing observations.

We included any study that reported HWWS practice assessed with structured observations in adults and children. Though direct observation has shown to change participant behaviours,[16] this bias is lower than what has been found with self-report.[29] Therefore, studies were sought that reported the observed prevalence of HWWS after using a toilet or after potential contact with human excreta (including children's excreta). There are several key events for HWWS, including food preparation, eating or feeding a child, but we focused on HWWS after potential contact with faecal pathogens such as after defecation, after using the toilet and after potential contact with child faeces. Contrary to our previous systematic review, we excluded handwashing observation studies in day care centres and schools (pre-, primary, middle and high school) and refugee camps, as such settings might not be representative for handwashing at household level.

Studies were selected for inclusion using a two-step review process. Titles and abstracts of all studies identified in the search were screened for relevance. The full text of each of the relevant articles was then reviewed, and studies were excluded if they did not provide observational data on the prevalence of observed HWWS. Data were extracted from each study using a standard protocol and included information on study setting (country), observation location (home or public setting), time frame of survey, population subgroup, sample size, a description of how handwashing prevalence was measured and specific prevalence estimates for any of the handwashing occasions, such as after toilet use or after cleaning up after a child. Characteristic of included studies and their references are listed in Supplementary Appendix A.2.1 (available as Supplementary data at *IJE* online).

Multilevel analysis of the association between presence of a designated handwashing facility and observed HWWS

Inclusion criteria and study selection. For analysing the association between presence of a designated handwashing facility and HWWS, studies were assembled from the systematic review that reported both observed presence of a designated place for handwashing and HWWS at critical times (i.e. after faecal exposure and before food contact), assessed through structured observations. Additional study datasets were provided from subject matter experts. Studies needed to fulfil the following further criteria to be included in the analysis: (i) the study needed to be conducted at household-level; (ii) in case of post-intervention data, the control group needed to be identifiable; and (iii) the study needed to have been conducted within the past 20 years (1998–2017).

In case of intervention data, we included data from both intervention and control groups at study baseline if available (e.g. Nepal, Zimbabwe[30,31]). However, in most studies data on the observed designated handwashing facility and structured observations of HWWS were available post-intervention only. From these studies, we used post-intervention data and we used data from control households only. For the Zimbabwe study,[31] data on observed designated handwashing facilities and HWWS were available at study baseline and post-intervention. Here we added post-intervention data from the control group in case these households had not been included at baseline.

Exposure definition. The exposure of interest was defined as an observed designated handwashing facility (defined above as a designated place within the premises of a household which has both soap and water) that could include a specific handwashing hardware, such as a tippy tap or washbasin, or be any set place that householders consider their designated handwashing place. Soap in this context includes any kind of soap or detergent but excludes mud, sand or ash. In most studies, householders were asked to show the place where household members usually washed hands and the presence of soap and water was observed. In two datasets, information on the designated handwashing facility was given for the primary and secondary (or tertiary) handwashing facility (Nepal, Tanzania). In these datasets, the main exposure was present (coded 1) when soap and water were present at any of the observed handwashing facilities.

Outcome definition. The primary outcome was observed HWWS after potential faecal contact. Both hands needed to be washed with soap. Potential faecal contact in this analysis includes visiting the toilet, defaecation and cleaning a child's bottom or changing its nappies, but does not include potential contact with animal faeces. Any handwashing occasion by any household member reported in the primary studies and related to the respective exposure was included in the analysis. Though the literature search had focused on observed HWWS after potential faecal contact, we also analysed the available data to investigate the association between presence of a designated handwashing facility and observed HWWS before food contact. Food contact in this analysis includes preparing, cooking or serving food, eating, and feeding or breastfeeding a child. We excluded handwashing observations when either the designated handwashing facility or HWWS could not be observed.

Statistical analysis. To estimate adjusted prevalences and prevalence ratios from binary outcome data, we used Poisson regression with robust standard errors.[32,33] We used a three-level model (handwashing observations clustered within households, households clustered within countries (or studies) to estimate HWWS prevalence after potential faecal contact, and to account for the clustering of observations within households and countries (or studies). HWWS was included as a binary variable and coded '1' if HWWS occurred after potential faecal contact and coded '0' if the respective contact occurred but hands were not washed or not washed with soap or only one hand was washed with soap. Presence or absence of a designated handwashing facility was included as a binary variable. Absence includes presence of a handwashing facility on premises that are not equipped with soap and water, as well as no place for handwashing on premises. As further fixed effect covariates, we included binary variables for the respective WHO region[20] (Supplementary Appendix 1.1, available as Supplementary data at *IJE* online). As determinants for washing own hands might be different from washing children's hands, we analysed data restricted to handwashing occasions among adults. More details on the model are included in Supplementary Appendix A.2.3 (available as Supplementary data at *IJE* online).

We used the 'margins' command in Stata[34] to predict adjusted HWWS prevalence after potential faecal contact at regional level for households with and without a designated handwashing facility, for each region represented by included studies (AFR, AMR, SEAR, and WPR).[34] We predicted the average adjusted HWWS prevalence after potential faecal contact for households having or not having a designated handwashing facility for the remaining regions (low- and middle-income countries only) not represented by included studies (EMR and EUR).[34] To account for the uncertainty of estimates for the latter, 95% prediction intervals were approximated based on the standard deviation of the available country-level adjusted prevalences. Analyses were performed in Stata 14.[22]

High-income countries: meta-analysis of observed HWWS prevalence after potential faecal contact

As the selected studies for the analysis of the association between presence of a designated handwashing facility and observed HWWS were conducted exclusively in low- and middle-income countries, we conducted random effects meta-analysis on observed HWWS prevalence after potential faecal contact in high-income country studies identified in the systematic review, to approximate the proportion of HWWS after potential faecal contact in those countries.

Objective 3: deriving country, regional and global estimates of HWWS prevalence after potential faecal contact

To estimate HWWS prevalence p_{HWWS} after potential faecal contact at country level for low- and middle-income countries in 2015, we applied the following formula:

$$p_{\text{HWWS}} = p_{\text{HWWS, HW place}} \cdot p_{\text{HW place}} + p_{\text{HWWS, no HW place}} \cdot 1 - p_{\text{HW place}}, \quad (1)$$

where $p_{\text{HWWS, HW place}}$ is the estimated HWWS prevalence after potential faecal contact in the presence of an observed designated handwashing facility (estimated at regional level, Table 4), the proportion $p_{\text{HW place}}$ is the modelled estimate of presence of a designated handwashing facility at country level and $p_{\text{HWWS, no HW place}}$ is the estimated HWWS prevalence after potential faecal contact without having a designated handwashing facility (Tables 2 and 4). The estimates for $p_{\text{HWWS, HW place}}$ and $p_{\text{HWWS, no HW place}}$ at country level are extrapolated from modelled results at regional level (see objective 2). This projection from regional to country level results in an increase of the confidence intervals, just as the inverse operation—the aggregation from country to regional level—would lead to a decrease, as the uncertainties at country level would partially offset each other (Supplementary Appendix Equations A3 and A.3.1, available as Supplementary data at *IJE* online). For estimating HWWS prevalence after potential faecal contact for high-income countries, the pooled HWWS prevalence from the meta-analysis (objective 2) was taken. To estimate the proportion of potential faecal events that were followed by HWWS at regional and global level for low-, middle- and high-income countries, we calculated population-weighted means of the country estimates. As we do not know the total number of potential faecal contacts by country and region, we assume an equal average number of faecal contacts by person across countries and regions, and use total population by country and region to calculate the regional and global estimates. The calculation of the 95% confidence intervals for these estimates at country, regional and global levels is described in Supplementary Appendix A.3.2, A.3.3 (available as Supplementary data at *IJE* online).

As a sensitivity analysis, we re-calculated regional and global handwashing prevalence, applying the approach for low- and middle-income countries to high-income countries. We did so by using formula 1 for high-income countries, where $p_{\text{HW place}}$ is the modelled estimate of presence of a designated handwashing facility for high-income countries, $p_{\text{HWWS, HW place}}$ is the pooled estimate of handwashing prevalence from meta-analysis from all handwashing observation studies in high-income countries and $p_{\text{HWWS, no HW place}}$ was approximated with the mean handwashing prevalence without a designated handwashing facility from the analysis of the nine low- and middle-income country datasets (Table 4).

Results

Objective 1: quantifying the presence of a designated handwashing facility

Data availability

The dataset consisted of 115 data points for urban and rural areas each, over the time period 2000 to 2016. A total of 77 countries had at least one data point available, including 76 low- and middle-income countries [of those, 38 countries in the WHO African Region (AFR), 14 countries in the WHO Region of the Americas (AMR), eight in the WHO Eastern Mediterranean Region (EMR), eight in the WHO European Region (EUR), five in the WHO South-East Asia Region (SEAR) and three in the WHO Western Pacific Region (WPR)] and one high-income

Table 2. Percentage of population having access to a designated handwashing facility in 2015, by area

Area	Percentage of population (95% CI) with access to a designated handwashing facility in 2015
AFR LMI	17.7 (14.8, 21.0)
AMR LMI	83.3 (72.2, 90.5)
EMR LMI	68.3 (59.2, 76.1)
EUR LMI	95.7 (91.8, 97.8)
SEAR LMI	69.4 (39.5, 88.7)
WPR LMI	89.6 (67.7, 97.3)
Urban	84.1 (75.6, 90.1)
Rural	61.2 (40.7, 78.3)
Low- and middle-income countries	69.5 (56.8, 79.8)
High-income countries	95.0 (89.8, 97.7)
World	73.5 (63.2, 81.8)

AFR, WHO African Region; AMR, WHO Region of the Americas; EMR, WHO Eastern Mediterranean Region; EUR, WHO European Region; SEAR, WHO South-East Asia Region; WPR, WHO Western Pacific Region; LMI, low- and middle-income.

country (Barbados).[20] More information on the regional grouping is listed in Supplementary Appendix A.1.1, available as Supplementary data at *IJE* online). Only 29 countries had more than one data point available, making it difficult to determine trends (Table 1).

Modelled results of handwashing facility presence

Table 2 lists percentage of population having access to a designated handwashing facility by area. We estimate that in 2015, 73.5% of the world population had access to a designated handwashing facility. In high-income countries, 95% of the population have access to a designated handwashing facility compared with 69.5% in low- and middle-income countries. A similar difference is estimated between urban and rural areas, with 84.1% in urban compared with 61.2% in rural areas.

The root mean squared error (RMSE) from cross-validation was 11.1% for urban and 7.3% for rural areas, indicating that on average the model estimate for the year 2015 for a country without any survey point is respectively 11.1 and 7.3 percentage points away from the 'true' value (which is approximated here with the survey point for 2015 for the respective country).

When modelling the presence of a designated handwashing facility based on uniformly collected data in MICS/ DHS from 2009 onwards (removing 13 data points for both urban and rural areas which originated from before 2009), the estimated percentage of population with access to a designated handwashing facility changed only slightly (AFR LMI: 17.1; AMR LMI: 83.0; EMR LMI: 66.4; EUR LMI: 95.9; SEAR LMI: 68.3; WPR LMI: 89.8; urban: 84.1; rural: 60.1; low- and middle-income countries: 68.9; high-income countries: 94.9; world: 73.0).

Objective 2: assessing the association between presence of a designated handwashing facility and observed HWWS

Data availability

The systematic review identified a total of 42 studies of which 15 were conducted in high-income countries (Figure 2). Nine datasets (five studies were identified through the systematic database search and three that had not been published at the time of the analysis were provided from subject matter experts) from eight low- and middle-income countries, in four out of six WHO regions, reported both presence of a designated handwashing facility and structured observations of handwashing after potential faecal contact, and thus were included in the analysis of objective 2.

Multilevel analysis of the association between presence of a designated handwashing facility and observed HWWS

The eight studies (providing nine datasets), reporting both presence of a designated handwashing facility and structured observations of handwashing after potential faecal contact, were combined to estimate the association between presence of a designated handwashing facility and HWWS after potential faecal contact. Data from Zimbabwe urban and rural sites were different parts of one study from the same research group. Table 3 lists characteristics of included studies. Further suitable studies that were identified from the systematic search but not included in the analysis are listed, with reasons for exclusion, in Supplementary Appendix A.2.4 (available as Supplementary data at *IJE* online).

The pooled dataset includes 3953 observed potential handwashing occasions after potential faecal contact. Of those, hands were washed with soap in 18.6% of potential handwashing occasions. In the presence of a designated handwashing facility, hands were washed with soap in 25% of potential handwashing occasions compared with 12% in the absence of a designated facility. The 28 observations with missing values in the variable indicating the presence of a handwashing place with soap and water (0.7% of all observations) were excluded from the analysis (i.e. listwise deletion).

From the three-level Poisson model there was very strong evidence ($P<0.001$) for an association between presence of a designated handwashing facility and observed HWWS after potential faecal contact in structured observations. After taking account of the clustering of

Table 3. Characteristics of included datasets for estimating the association between presence of a designated handwashing facility and observed HWWS

Country (WHO region)	Year	Setting	Interventions	Baseline/endline	Household member role (for SO)	Sample size	HWWS after faecal contact	References
Ethiopia (AFR)	2012/ 2013	Rural	Four hygiene arms against control	HW place endline only (self-reported in baseline), so base- & endline	Mixed	59 households, 78 faecal contacts(controls)	7.7%	36
Senegal (AFR)	2011	Urban/rural	Hygiene arm against control	SO endline only, HW place base- & endline	Mixed (primary caregiver, other adults, children)	88 households, 231 faecal contacts (controls)	14.3%	37
Tanzania (AFR)	2012	Rural	Three intervention arms (hygiene, sanitation & hygiene + sanitation) against control	Only endline data	Mixed	185 households, 239 faecal contacts (controls)	12.1%	38
Zimbabwe (AFR), two datasets included	urban: 2014 (baseline)/2015 (endline); rural: 2016 (baseline)/2017 (endline)	Urban & rural dataset	Hygiene arm against control (SO) (with pre-intervention data) (intervention and control group included)	SO and HW place base- & endline	Mixed (primary caregiver, other adults, children)	211 rural + 388 urban households, 322 rural + 432 urban faecal contacts(all groups at baseline, controls at endline)	4.6% total (5.3% rural, 4.2% urban)	31
Peru (AMR)	2011	Rural	Two intervention arms against control	SO endline only, HW place base- & endline	Mixed (primary caregiver, other adults, children)	282 households, 421 faecal contacts	33.3%	39
Bangladesh (SEAR)	2013	Urban	Two intervention arms (vaccination & vaccination + hygiene) against control	SO endline only, HW base- & endline	Primary caregiver	112 households, 39 faecal contacts	18%	40
Nepal (SEAR)	2012	Rural	Baseline data (intervention and control group included)	Only baseline data	Mixed (primary caregiver, other adults, children)	1008 households, 1690 faecal contacts	23.7%	30
Viet Nam (WPR)	2010/ 2011	Rural	Two hygiene arms against control	SO endline only, HW place base- & endline	Primary caregiver and children up to 5 years	200 households, 501 faecal contacts (controls)	16.8%	41

AFR, WHO African Region; AMR, WHO Region of the Americas; EMR, WHO Eastern Mediterranean Region; EUR, WHO European Region; SEAR, WHO South-East Asia Region; WPR, WHO Western Pacific Region; HW, handwashing; SO, structured observations; HWWS, handwashing with soap.

observations in households and countries (or studies), and after adjusting for study region, the prevalence of HWWS where a designated handwashing facility was present was 1.99 (95% CI 1.66, 2.39) times higher than in the absence of a designated facility, Note that in the absence of a designated handwashing facility, householders could still fetch water and soap to wash their hands, use the neighbour's facility etc..

There was also very strong evidence ($P < 0.001$) for an association between having a designated handwashing facility and observed HWWS before food contact (there were a total of 12 052 potential handwashing occasions before food contact, of which hands were washed in 5%). After taking account of the clustering of observations in households and countries (or studies) and after adjusting for study region, the prevalence of HWWS in presence of a designated handwashing facility was present was 2.57 (95% CI 2.26, 2.92) times higher than in the absence of a designated facility.

After restricting to adult handwashing, there remained 2578 observed potential handwashing occasions after potential faecal contact and 7554 potential handwashing occasions before food contact. Of those, hands were washed with soap in 19.1% of potential handwashing occasions after potential faecal contact and in 4% of potential handwashing occasions before food contact. The association between presence of a designated handwashing facility and adult HWWS after potential faecal or before food contact remained very strong ($P < 0.001$) and of similar size compared with the analysis including data on children's handwashing (prevalence ratios for HWWS after potential faecal contact 2.02 (95% CI 1.77, 2.32) and before food contact 2.42 (1.96, 3.00)).

High-income countries: meta-analysis of HWWS prevalence after potential faecal contact

Supplementary Appendix A.2.1 (available as Supplementary data at *IJE* online) includes citations, number of observed HWWS events after potential faecal exposure, number of observed faecal contact events and characteristics for all 15 studies in high-income countries included in random effect meta-analysis. The pooled HWWS proportion after potential faecal contact was 51% (95% CI: 43%, 59%) (independent of presence of a designated handwashing facility, Figure 3). The I^2 of 99.5% indicates high heterogeneity of HWWS between studies.[42] Subgroup meta-analysis by study region did not lead to a relevant reduction of I^2 (>95% within subgroups), which resulted in the choice of the pooled estimate over all 15 studies. We additionally examined the 15 studies for potential outliers.[43] Jeong 2007[44] was identified as outlier, and the removal of this study changed the pooled estimate from 51% to 53%. A forest plot of the meta-analysis of all studies identified in the systematic review, separately by high- versus low- and middle-income countries, is placed in Supplementary Appendix A.2.2 (available as Supplementary data at *IJE* online).

HWWS prevalence results by presence of a handwashing facility and by region

Adjusted HWWS prevalences after potential faecal contact by presence of a designated handwashing facility and by region are given in Table 4. Predicted HWWS prevalences by presence/absence of a designated handwashing facility for low- and middle-income regions are derived from the analysis described in objective 2. Proportions of HWWS after potential faecal contact for high-income regions are taken from the meta-analysis of all identified studies in high-income countries described in the same objective. Supplementary Appendix A.3.4 (available as Supplementary data at *IJE* online) lists under column I how HWWS estimates were generated by country.

Objective 3: deriving country, regional and global estimates of HWWS prevalence after potential faecal contact

HWWS prevalences after potential faecal contact, by country for low- and middle-income countries, are computed on the basis of the estimates of presence of a designated handwashing facility at country- evel (objective 1) and the adjusted regional predictions of HWWS after potential faecal contact by presence/absence of a designated facility (objective 2, Table 4) using formula 1. For high-income countries, handwashing prevalence was estimated using the result from meta-analysis (objective 2, Figure 2).

Using this approach, we estimate that, worldwide, 26.2% of potential faecal contacts were followed by HWWS in 2015 (Table 5). Country estimates for HWWS after potential faecal contact are provided in Supplementary Appendix A.3.4 (available as Supplementary data at *IJE* online).

When calculating the regional (high-income countries) and global proportions of faecal contacts followed by HWWS using formula 1 as described above (sensitivity analysis described in Methods) also for high-income countries, estimates changed only slightly (48.7% instead of 50.6% for high-income countries and 25.9% instead of 26.2% for the world).

Discussion

This analysis shows that 27% of the world population—nearly two billion people—lack a designated handwashing facility (objective 1). People who have access to a designated

Table 4. Predicted HWWS prevalence by presence of a designated handwashing facility and by region

Area	Predicted HWWS (95% CI) after potential faecal contact (proportion)	
	In households without designated handwashing facility	In households with designated handwashing facility
AFR, LMI	0.071 (0.033, 0.110)	0.142 (0.056, 0.227)
AMR, LMI	0.198 (0.165, 0.231)	0.394 (0.362, 0.426)
EMR, LMI	0.128 (0.040, 0.337)	0.254 (0.078, 0.578)
EUR, LMI	0.128 (0.040, 0.337)	0.254 (0.078, 0.578)
SEAR, LMI	0.163 (0.144, 0.182)	0.325 (0.277, 0.373)
WPR, LMI	0.090 (0.074, 0.107)	0.180 (0.167, 0.193)
High-income countries	0.506 (0.426, 0.585)[a]	

Values for LMI regions are predicted adjusted prevalences at representative (regional) values (AFR, SEAR and WPR) and average (pooled across regions) adjusted prevalence (AMR, EMR and EUR) calculated from the multilevel logistic model.

HWWS, handwashing with soap; AFR, WHO African Region; AMR, WHO Region of the Americas; EMR, WHO Eastern Mediterranean Region; EUR, WHO European Region; SEAR, WHO South-East Asia Region; WPR, WHO Western Pacific Region; LMI, low- and middle-income.

[a]Value taken from meta-analysis on studies in high-income countries (objective 2, Figure 2).

handwashing facility, defined here as a specific place within the premises of a household which has both soap and water, are about twice as likely to wash hands with soap after potential faecal contact and 2.6 times as likely to wash hands with soap before food contact, compared with people without a designated facility (objective 2). Only 26% of potential faecal contacts (i.e. after visiting the toilet, after defaecation, after cleaning a child's bottom or changing its nappies) were followed by HWWS (objective 3).

We provide country, regional and global HWWS estimates after potential faecal contact. These estimates are based on modelled estimates of survey data on the presence of designated handwashing facilities. The modelled estimates were converted to estimated HWWS practice using predicted handwashing prevalence in the presence or absence of a designated handwashing facility.

Compared with our previous estimate of 19% HWWS after potential faecal contact,[1] the estimates from the current analysis presented here are slightly higher. Whereas it is possible that a real global trend exists due to efforts of improving HWWS after potential faecal contact globally,[45] it is more likely that this new estimate represents our revised and improved modelling approach. We use a revised and extended methodology compared with our assessment in 2012 which had relied solely on a systematic review of observed HWWS. We now use country-representative data on presence of essential handwashing materials at a designated handwashing facility, converting them into handwashing practice based on an analysis of the association between presence of a designated handwashing facility and handwashing behaviour. Many more countries are now covered by national data compared with the previous approach (76 versus 28 low- and middle-income countries).

Strengths and limitations

Objective 1

The estimates for presence of a designated handwashing facility are based on 115 data points. For 118 of 194 countries there was no data point, and for 48 countries there was only one data point. Trends over time were estimated based on the overall trend from available data points. For countries with no data, the mean for the respective region and income group was used. As such, the reliability of estimates for different regions and countries varies. Results from cross-validation showed, however, that the model predicted was sufficiently close to the actual survey data point even for countries with no data point. Our modelling approach offers several advantages, including a single model for all countries, a continuous time series and the use of information from other country data for countries with few data or no data.

Objective 2

Estimates for the association between presence of a designated handwashing facility and observed HWWS are derived by regions and are based on nine datasets from eight heterogeneous studies in low- and middle-income countries, covering various subgroups of populations in four out of six regions. For EMR and EUR regions, HWWS practice was assumed as the average adjusted predicted prevalence based on all included studies. As such, estimates of the association between presence of a designated handwashing facility and observed HWWS are based on limited evidence. However, the proportion of observed HWWS is consistently low across the nine datasets (Table 3). The African region is covered by four datapoints which are all lower than any other datapoint for any different region.

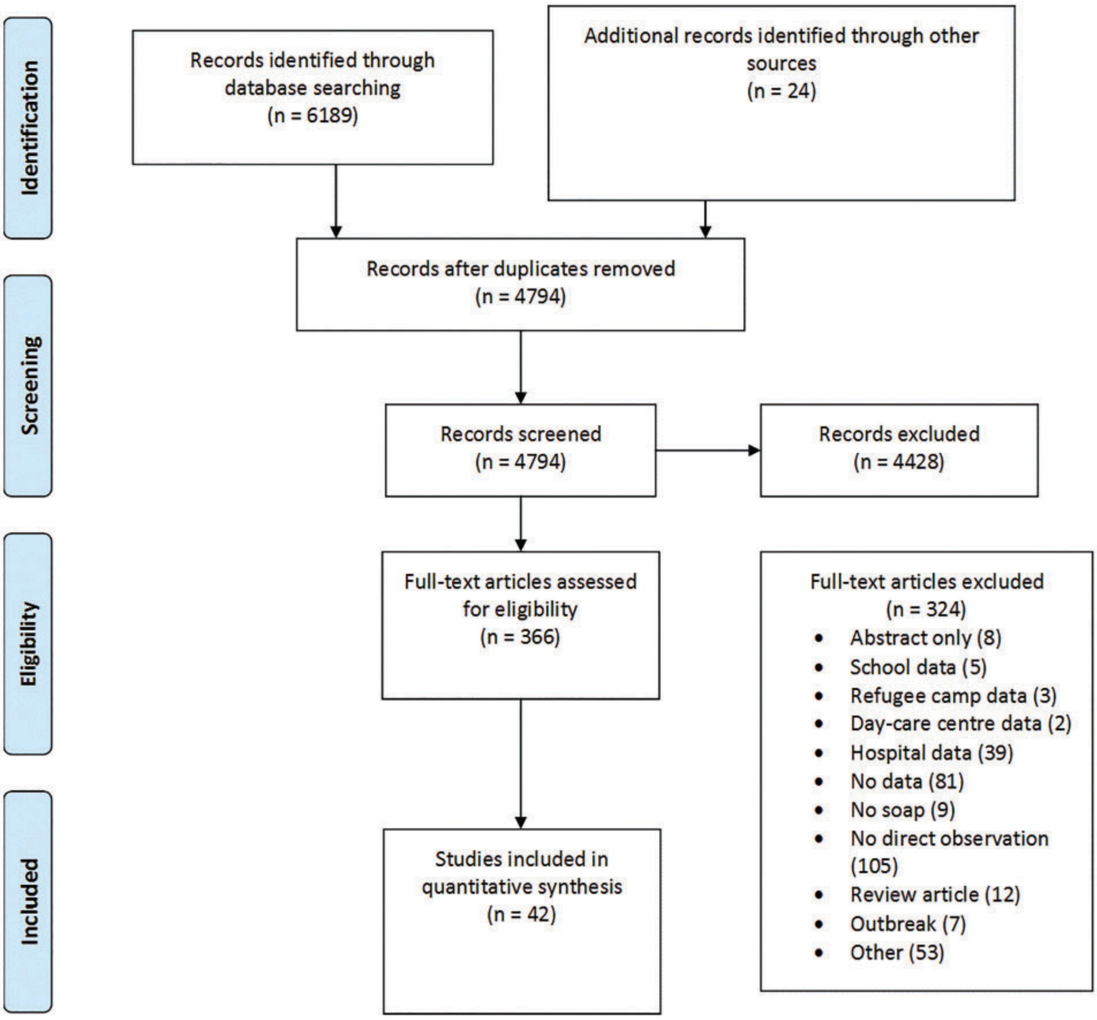


Figure 2. PRISMA flow chart[35] of selection process of handwashing observation studies.

Removing one of the datasets at a time changed the predicted mean HWWS after potential faecal contact only to a minor extent [from 0.25 predicted HWWS in households with a basic handwashing facility, including all studies to a minimum of 0.2 (excluding Nepal), and to a maximum of 0.27 (excluding Viet Nam)]. Furthermore, overall handwashing prevalence after potential faecal contact—irrespective of handwashing facility presence—across the nine datasets, taking account of clustering within studies, is 14%, which is close to the pooled estimate of 17% from all 27 observations from low- and middle-income countries. This indicates that HWWS rates across these settings are consistently low (forest plot in Supplementary Appendix A.2.2, available as Supplementary data at *IJE* online).

Of the 15 studies conducted in high-income countries, there was only one[46] that was conducted at household level; the rest were conducted in public settings, which may limit their generalizability to the household setting. In the one household-level study, hands were washed with soap in about 80% after visiting the toilet but only in 42% after changing a dirty nappy.[46] Studies conducted in public settings will mostly include potential handwashing occasions after visiting the toilet, whereas household-level studies will also include occasions after cleaning a child's bottom or changing its nappies. In the household-level study, 57% of potential faecal contacts were followed by HWWS, which is however close to the pooled estimate of 51% for all high-income countries, and close to the handwashing prevalence found for a study conducted in the same

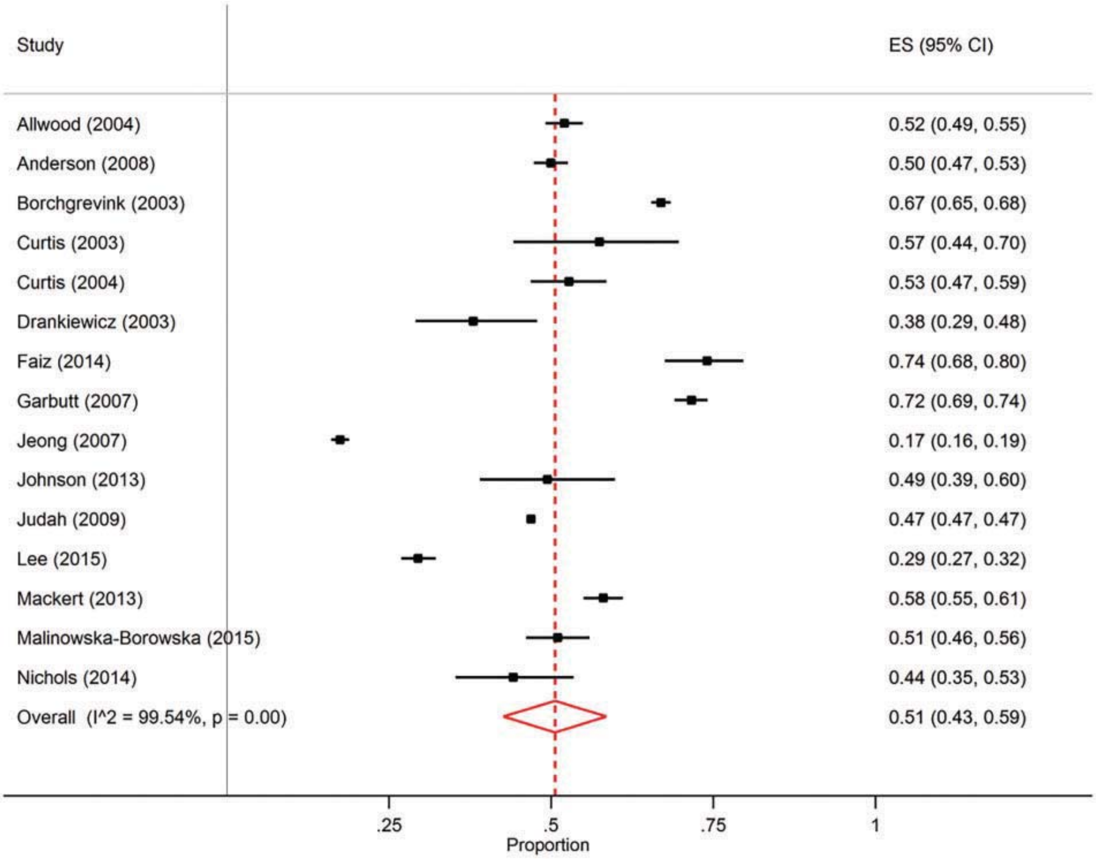


Figure 3. Forest plot of handwashing observation studies in high-income countries.

country but in a public setting.[47] The I^2 statistic, a measure of inconsistency across study findings,[42] was very high, which indicates that results for individual high-income countries might vary to a larger extent from the pooled estimate, and likely reflects substantial differences among the studies in terms of study design and methods, settings and populations.

Objective 3

This study provides important input to the SDG indicator 3.9.2 (Mortality from water, sanitation and hygiene),[5] estimating population exposures to inadequate handwashing practices. HWWS estimates are based on a novel approach using country-representative data on presence of a designated handwashing facility, converting them into actual handwashing practice. We assumed that the average number of potential faecal contacts per person was the same across regions but might not be correct for different reasons, e.g. different number of children per caregiver. Due to data scarcity for high-income countries, the estimate of HWWS for high-income countries is not based on modelled estimates from national household surveys (as are the estimates for low- and middle-income countries), but only on smaller observational studies reporting handwashing behaviour. The sensitivity analysis using modelled estimates for high-income countries yielded, however, very similar estimates for HWWS practice.

Further discussion

This analysis proposes an approach for estimating HWWS practice after potential faecal contact, including after toilet use, which is based on adjusted nationally representative household survey data and the probability of HWWS by presence/absence of a designated handwashing facility.

We quantify the presence and importance of designated handwashing places as a crucial first step for achieving the desired handwashing behaviour. This analysis suggests that data on the presence of designated handwashing facilities at household level could be used to assess actual

Table 5. Percentage of faecal contacts that are followed by HWWS (in 2015), by area

Area	Percentage (95% CI) of faecal contacts followed by HWWS
AFR, LMI	8.4 (5.0, 13.6)
AMR, LMI	36.1 (33.0, 39.4)
EMR, LMI	21.4 (8.2, 45.2)
EUR, LMI	24.9 (7.8, 56.3)
SEAR, LMI	27.6 (22.5, 33.3)
WPR, LMI	17.1 (15.5, 18.7)
Low- and middle-income countries	21.7 (18.7, 25.1)
High-income countries	50.6 (42.6, 58.5)
World	26.2 (23.1, 29.6)

The estimate for low- and middle-income countries is the combined estimate from the six regions above.

HWWS, handwashing with soap; AFR, WHO African Region; AMR, WHO Region of the Americas; EMR, WHO Eastern Mediterranean Region; EUR, WHO European Region; SEAR, WHO South-East Asia Region; WPR, WHO Western Pacific Region; LMI, low- and middle-income.

handwashing behaviour when handwashing facility presence is adjusted by the association with actual observed handwashing. This could be highly valuable for aggregated HWWS estimates (i.e. at country level) because data on handwashing facility presence are reliable and efficient and—whereas structured observations can estimate handwashing behaviour directly—structured observations are also too time consuming to be integrated in national data collection.[6,14] This analysis also suggests that using handwashing facility presence for estimating handwashing behaviour, without further adjustment, would grossly overestimate actual handwashing prevalence, as we show that in low- and middle-income countries only 25% of potential faecal contacts in households with access to a designated handwashing facility are followed by HWWS. We show that HWWS practice after potential faecal contact is low, in particular in low- and middle-income-countries but also in high-income countries. There are further substantial differences between HWWS in sub-Saharan Africa (WHO AFR region) and low- and middle-income countries from other regions. In sub-Saharan Africa, access to designated handwashing facilities is much lower than in other world regions (Table 2). Even in the presence of a designated handwashing facility, HWWS was lower in sub-Saharan Africa compared with other low- and middle-income regions (12% versus 29% of all potential faecal contacts). Given that HWWS is associated with the risk of diarrhoea and acute respiratory infections,[48,49] it is important to take action at national and international levels to reduce this important global public health risk.

Conclusions

HWWS is practised in around 26% of cases after potential faecal contact. To effectively promote HWWS, there is a need to increase handwashing facilities equipped with soap and water in or around the home. As HWWS remains limited even in the presence of a designated handwashing facility, efforts to promote handwashing behaviour need to be conducted simultaneously. This analysis uses nationally representative survey data and derived HWWS estimates, and is in line with individual HWWS observation studies. It suggests that the presence of a designated handwashing facility could be used to estimate actual handwashing behaviour. However, our estimates are based on limited data, i.e. 115 survey data points covering 77 countries for access to designated handwashing facilities and nine datasets from eight low- and middle-income countries, to analyse the association between presence of a designated handwashing facility and observed handwashing behaviour. There is a need for greater data availability on hand hygiene, in particular for: (i) data at household level reporting observed handwashing behaviour, including reporting of the presence of handwashing facilities for low-, middle- and especially high-income countries; and (ii) nationally representative data on presence of handwashing facilities for high-income countries and those low- and middle-income countries not yet covered by such data.

Supplementary Data

Supplementary data are available at *IJE* online.

Funding

This work was supported by the United Kingdom Department for International Development (DFID) [204700–101]. Those acknowledged have confirmed their agreement.

Acknowledgements

We thank Ben Arnold for reviewing the paper and for repeated advice on data analysis. We are grateful to Meredith Stocks and Heather Amato (Emory University) for their valuable contribution to the systematic review. We thank Adam Biran (LSHTM), Hans-Joachim Mosler (Eawag), Nadja Contzen (Eawag), Jonathan Lilje (Eawag), Max Friedrich (Eawag), Claire Chase (World Bank) and Wit Wichaidit (University at Buffalo) for their great efforts in providing the raw data of their studies and advice on any upcoming data queries.

Conflict of interest: None declared.

References

1. Freeman MC, Stocks ME, Cumming O *et al*. Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. *Trop Med Int Health* 2014;**19**:906–16.

2. Ejemot-Nwadiaro RI, Ehiri JE, Arikpo D, Meremikwu MM, Critchley JA. Hand washing promotion for preventing diarrhoea. *Cochrane Database Syst Rev* 2015;**9**:CD004265.
3. Rabie T, Curtis V. Handwashing and risk of respiratory infections: a quantitative systematic review. *Trop Med Int Health* 2006;**11**:258–67.
4. Townsend J, Greenland K, Curtis V. Costs of diarrhoea and acute respiratory infection attributable to not handwashing: the cases of India and China. *Trop Med Int Health* 2017;**22**:74–81.
5. United Nations. Sustainable Development Goals. 2015. http://www.un.org/sustainabledevelopment/sustainable-development-goals/ (18 October 2016, date last accessed).
6. Kumar S, Loughnan L, Luyendijk R *et al*. Handwashing in 51 countries: analysis of proxy measures of handwashing behavior in multiple indicator cluster surveys and demographic and health surveys, 2010–13. *Am J Trop Med Hyg* 2017;**97**:447–59.
7. Loughnan LC, Ram PK, Luyendijk R. Measurement of handwashing behaviour in multiple indicator cluster surveys and demographic and health surveys, 1985–2008. *Waterlines* 2015;**34**: 296–13.
8. Ram PK, Sahli M, Arnold B *et al*. *Global Scaling up Handwashing: Validity of Rapid Measures of Handwashing Behavior: An Analysis of Data From Multiple Impact Evaluations in the Global Scaling up Handwashing Project*. Washington, DC: Water and Sanitation Program, World Bank Group, 2014.
9. Halder AK, Tronchet C, Akhter S, Bhuiya A, Johnston R, Luby SP. Observed hand cleanliness and other measures of handwashing behavior in rural Bangladesh. *BMC Public Health* 2010;**10**: 1.
10. Luby SP, Halder AK. Associations among handwashing indicators, wealth, and symptoms of childhood respiratory illness in urban Bangladesh. *Trop Med Int Health* 2008;**13**:835–44.
11. Null C, Stewart CP, Pickering AJ *et al*. Effects of water quality, sanitation, handwashing, and nutritional interventions on diarrhoea and child growth in rural Kenya: a cluster-randomised controlled trial. *Lancet Glob Health* 2018;**6**:e316–29.
12. Stewart CP, Kariger P, Fernald L *et al*. Effects of water quality, sanitation, handwashing, and nutritional interventions on child development in rural Kenya (WASH Benefits Kenya): a cluster-randomised controlled trial. *Lancet Child Adolesc Health* 2018; **2**:269–80.
13. Luby SP, Rahman M, Arnold BF *et al*. Effects of water quality, sanitation, handwashing, and nutritional interventions on diarrhoea and child growth in rural Bangladesh: a cluster randomised controlled trial. *Lancet Glob Health* 2018;**6**:e302–15.
14. Ram PK. *Practical Guidance for Measuring Handwashing Behavior: 2013 Update. Water and Sanitation Program*, 2013. https://www.wsp.org/sites/wsp.org/files/publications/WSP-Practical-Guidance-Measuring-Handwashing-Behavior-2013-Update.pdf (19 November 2018, date last accessed).
15. Luby SP, Halder AK, Huda TM, Unicomb L, Johnston RB. Using child health outcomes to identify effective measures of handwashing. *Am J Trop Med Hyg* 2011;**85**:882–92.
16. Ram PK, Halder AK, Granger SP *et al*. Is structured observation a valid technique to measure handwashing behavior? Use of acceleration sensors embedded in soap to assess reactivity to structured observation. *Am J Trop Med Hyg* 2010;**83**:1070–76.
17. Stevens GA, Alkema L, Black RE *et al*. Guidelines for accurate and transparent health estimates reporting: the GATHER statement. *PLoS Med* 2016;**13**:e1002056.
18. GATHER. Guidelines for Accurate and Transparent Health Estimates Reporting]. Gather Statement. http://gather-statement.org/ (16 April 2018, date last accessed).
19. WHO, UNICEF. *Hygiene*. https://washdata.org/monitoring/hygiene (19 October 2017, date last accessed).
20. WHO. *WHO Regional Groupings. World Health Stat 2017 Monit Health SDGs Sustain Dev Goals*. 2017 http://apps.who.int/iris/bitstream/10665/255336/1/9789241565486-eng.pdf.
21. World Bank. *World Bank Country and Lending Groups – World Bank Data Help Desk*. 2016. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups (19 October 2016, date last accessed).
22. StataCorp. *Stata Statistical Software: Release 14*. College Station, TX: Statacorp, 2015.
23. R Core Team. *R: A Language and Environment for Statistical Computing*. Vienna: R Foundation for Statistical Computing, 2015.
24. Gelman A, Su Y-S. *arm: Data Analysis Using Regression and Multilevel/Hierarchical Models. R Package Version 1.9-3*. 2016. https://CRAN.R-project.org/package=arm (19 November 2018, date last accessed).
25. United Nations Population Division. *World Population Prospects 2017*. 2017.. https://esa.un.org/unpd/wpp/ (19 October 2017, date last accessed).
26. De Onis M, Blössner M, Borghi E, Morris R, Frongillo EA. Methodology for estimating regional and global trends of child malnutrition. *Int J Epidemiol* 2004;**33**:1260–70.
27. Arlot S, Celisse A. A survey of cross-validation procedures for model selection. *Stat Surv* 2010;**4**:40–79.
28. Curtis VA, Danquah LO, Aunger RV. Planned, motivated and habitual hygiene behaviour: an eleven country review. *Health Educ Res* 2009;**24**:655–73.
29. Biran A, Rabie T, Schmidt W, Juvekar S, Hirve S, Curtis V. Comparing the performance of indicators of hand-washing practices in rural Indian households. *Trop Med Int Health* 2008;**13**: 278–85.
30. Vujcic J, Ram PK. *PPPHW Program Baseline Data Analysis: Report; Version 4*. Buffalo, NY: University at Buffalo, 2013.
31. EAWAG. *Handwashing Campaigns in Rural and Urban Zimbabwe*. 2017. https://www.ranasmosler.com/single-post/2017/07/06/Evaluation-report (6 October 2017, date last accessed).
32. Barros AJ, Hirakata VN. Alternatives for logistic regression in cross-sectional studies: an empirical comparison of models that directly estimate the prevalence ratio. *BMC Med Res Methodol* 2003;**3**:21.
33. Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol* 2004;**159**: 702–06.
34. Williams R. *Using Stata's Margins Command to Estimate and Interpret Adjusted Predictions and Marginal Effects*. University of Notre Dame, 2017.. https://www3.nd.edu/∼rwilliam/stats/Margins01.pdf (12 October 2017, date last accessed).
35. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009;**151**:264–69.

36. Contzen N, Meili IH, Mosler H-J. Changing handwashing behaviour in southern Ethiopia: a longitudinal study on infrastructural and commitment interventions. *Soc Sci Med* 2015;**124**:103–14.
37. Borja-Vega C, Briceño B, Garcia V. *Senegal - WSP Global Scaling up Handwashing Behavior Impact Evaluation 2009-2011, Baseline and Endline Surveys*. World Bank, 2016. http://microdata.worldbank.org/index.php/catalog/2557 (19 November 2018, date last accessed).
38. Briceño B, Coville A, Martinez S. *Promoting Handwashing and Sanitation: Evidence From a Large-scale Randomized Trial in Rural Tanzania*. Washington, DC: World Bank, 2015.
39. Galiani S, Gertler P, Ajzenman N, Orsola-Vidal A. Promoting handwashing behavior: the effects of large-scale community and school-level interventions. *Health Econ* 2016;**25**:1545–59.
40. Qadri F, Ali M, Chowdhury F *et al*. Feasibility and effectiveness of oral cholera vaccine in an urban endemic setting in Bangladesh: a cluster randomised open-label trial. *Lancet* 2015; **386**:1362–71.
41. Chase C, Do Q-T. *Handwashing Behavior Change at Scale: Evidence From a Randomized Evaluation in Vietnam*. Washington, DC: World Bank, 2012.
42. Higgins J, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**:557–60.
43. Viechtbauer W, Cheung MW-L. Outlier and influence diagnostics for meta-analysis. *Res Synth Methods* 2010;**1**:112–25.
44. Jeong J, Choi J, Jeong I, Paek K, In H, Park K. [A nationwide survey on the hand washing behavior and awareness]. *J Prev Med Public Health* 2007;**40**:197–204.
45. WHO, UNICEF. *Progress on Drinking Water, Sanitation and Hygiene: 2017 Update and SDG Baselines*. Geneva: WHO, UNICEF, 2017.
46. Curtis V, Biran A, Deverell K, Hughes C, Bellamy K, Drasar B. Hygiene in the home: relating bugs and behaviour. *Soc Sci Med* 2003;**57**:657–72.
47. Curtis V. *Hand Washing at LSHTM—The Shocking Truth*. Seattle, WA: Institute for Health Metrics and Evaluation, 2004.
48. Wolf J, Hunter PR, Freeman MC *et al*. Impact of drinking water, sanitation and hand washing with soap on childhood diarrhoeal disease: updated meta-analysis and –regression. *Trop Med Int Health*. 2018. https://onlinelibrary.wiley.com/doi/abs/10.1111/tmi.13051 (18 March 2018, date last accessed).
49. Aiello AE, Coulborn RM, Perez V, Larson EL. Effect of hand hygiene on infectious disease risk in the community setting: a meta-analysis. *Am J Public Health* 2008;**98**: 1372–81.

International Journal of Hygiene and Environmental Health 222 (2019) 270–282

Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.com/locate/ijheh

A Faecal Contamination Index for interpreting heterogeneous diarrhoea impacts of water, sanitation and hygiene interventions and overall, regional and country estimates of community sanitation coverage with a focus on low- and middle-income countries

Jennyfer Wolf[a,*], Richard Johnston[a], Paul R. Hunter[b,c], Bruce Gordon[a], Kate Medlicott[a], Annette Prüss-Ustün[a]

[a] Department of Public Health, Environment and Social Determinants of Health, World Health Organization, 20 Avenue Appia, Geneva, Switzerland
[b] The Norwich School of Medicine, University of East Anglia, Norwich, UK
[c] Department of Environmental Health, Tshwane University of Technology, Pretoria, South Africa

ARTICLE INFO

Keywords:
Sanitation
Diarrhea
Estimates
Fecal contamination
Sanitation coverage
Community

ABSTRACT

Objectives: The impact on diarrhoea of sanitation interventions has been heterogeneous. We hypothesize that this is due to the level of prevailing faecal environmental contamination and propose a Faecal Contamination Index (FAECI) of selected WASH indicators (*objective 1*). Additionally, we provide estimates of the proportion of the population living in communities above certain sanitation coverage levels (*objective 2*).
Methods: Objective 1: Faecal contamination post-intervention was estimated from WASH intervention reports. WASH indicators composing the FAECI included eight water, sanitation and hygiene practice indicators, which were selected for their relevance for health and data availability at study- and country-level. The association between the estimated level of faecal environmental contamination and diarrhoea was examined using meta-regression. *Objective 2*: A literature search was conducted to identify health-relevant community sanitation coverage thresholds. To estimate total community coverage with basic sanitation in low- and middle-income countries, at relevant thresholds, household surveys with data available at primary sampling unit (PSU)-level were analysed according to the identified thresholds, at country-, regional- and overall level.
Results: Objective 1: We found a non-linear association between estimated environmental faecal contamination and sanitation interventions' impact on diarrhoeal disease. Diarrhoea reductions were highest at lower faecal contamination levels, and no diarrhoea reduction was found when contamination increased above a certain level. *Objective 2*: Around 45% of the population lives in communities with more than 75% of coverage with basic sanitation and 24% of the population lives in communities above 95% coverage, respectively.
Conclusions: High prevailing faecal contamination might explain interventions' poor effectiveness in reducing diarrhoea. The here proposed Faecal Contamination Index is a first attempt to estimate the level of faecal contamination in communities. Much of the world's population currently lives in faecally contaminated environments as indicated by low community sanitation coverage.

1. Introduction

Drinking water, sanitation and hygiene (WASH) interventions may amongst others provide community water access or household water connections, source or point-of-use water quality improvements, on-site sanitation or sewer connections, handwashing promotion or general hygiene education (Fewtrell et al., 2005). These interventions have been shown to improve health (Freeman et al., 2017; Prüss-Ustün et al., 2008; Wolf et al., 2018a) and to have many non-health benefits such as improvements in equity, dignity, safety, time savings and cognitive

Abbreviations: WASH, water sanitation and hygiene; FAECI, Faecal Contamination Index; PSU, primary sampling unit; SDG, Sustainable Development Goal; JMP, WHO/UNICEF Joint Monitoring Programme for Water Supply Sanitation and Hygiene; DHS, Demographic and Health Survey; MICS, Multiple Indicator Cluster Survey

* Corresponding author.
E-mail addresses: jennyfer.wolf@gmail.com, wolfj@who.int (J. Wolf), johnstonr@who.int (R. Johnston), paul.hunter@uea.ac.uk (P.R. Hunter), gordonb@who.int (B. Gordon), medlicottk@who.int (K. Medlicott), pruessa@who.int (A. Prüss-Ustün).

https://doi.org/10.1016/j.ijheh.2018.11.005
Received 23 August 2018; Received in revised form 26 October 2018; Accepted 19 November 2018
1438-4639/ © 2018 World Health Organization. Published by Elsevier Gmbh. This is an open access article under the CC BY 3.0 license (http://creativecommons.org/licenses/BY 3.0/IGO/).

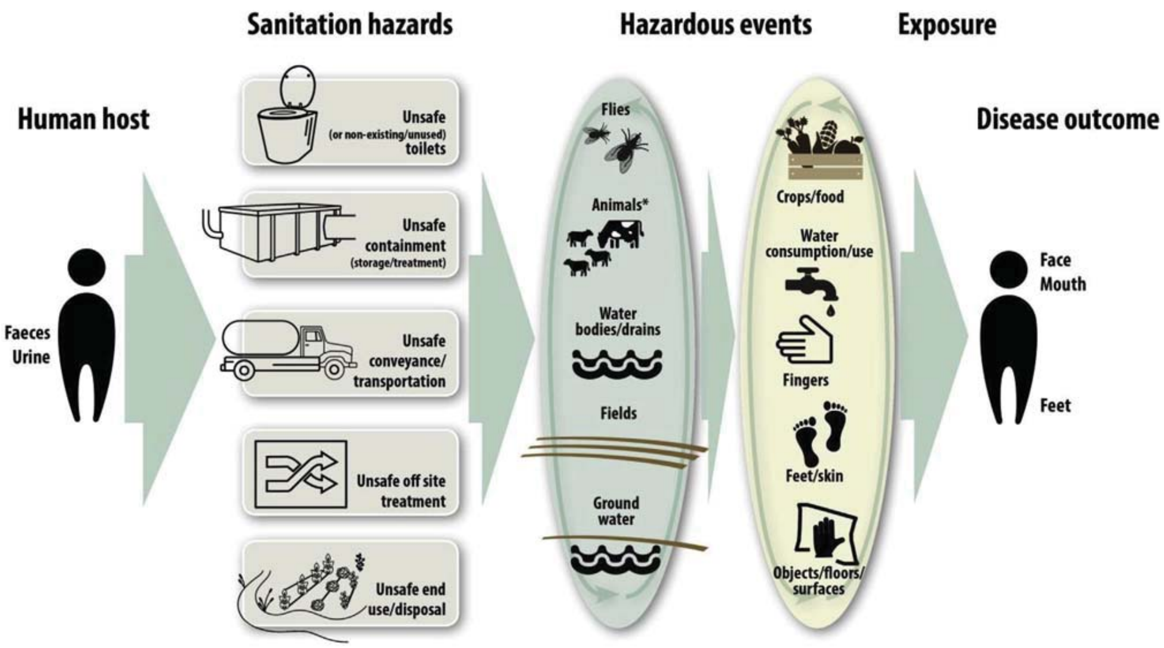


Fig. 1. The health impacts from unsafe sanitation through various transmission pathways (Figure taken from (WHO, 2018a)), * Refers to animals as mechanical vectors. Transmission of animal excreta-related pathogens to human hosts is not represented in this diagram.

development, educational attainment and national economic and overall development (Bapat and Agarwal, 2003; Bartram and Cairncross, 2010; Sclar et al., 2017). Access to safely managed sanitation services, i.e. toilets from which excreta are treated and disposed of safely, is therefore part of Sustainable Development Goal (SDG) 6 (United Nations, 2018).

Recent large, well-designed and well-conducted WASH trials and intervention studies, which included sanitation improvements with high intervention fidelity, did however not yield expected effects on diarrhoeal and nutritional outcomes (Humphrey, 2018; Luby et al., 2018; Null et al., 2018; Reese et al., 2018), which motivated ongoing discussions among researchers, practitioners and funders (Arnold et al., 2018; Coffey and Spears, 2018; Cumming and Curtis, 2018; Rosenboom and Ban, 2018a, 2018b).

It has long been argued that the - measurable - impact of WASH interventions on diarrhoea depends on the number and type of faecal pathogens that people are exposed to through a variety of transmission pathways in their homes and communities (Briscoe, 1984; VanDerslice and Briscoe, 1995) (Fig. 1). In communities with very high levels of faecal contamination, an intervention that successfully reduces faecal exposure through one exposure pathway might still translate in no or only slight diarrhoea reduction, in particular if other important pathways remain (VanDerslice and Briscoe, 1995). The SaniPath study, for example, has provided insights into pathways of exposure to faecal contamination, has revealed high levels of faecal environmental contamination in low-income settings and identified the consumption of contaminated food as the main fecal exposure pathway for children (Robb et al., 2017). Another example is faecally contaminated drinking water, which can result from inadequate sanitation and hygiene and which has been shown to be a frequent problem even in so-called "improved" drinking water sources (Bain et al., 2014). Public and occupational settings might offer important additional exposure routes through for example contaminated soil and open drains (Antwi-Agyei et al., 2016; Berendes et al., 2018).

There is consistent and considerable evidence that entire communities benefit from sanitation improvements in individual households, e.g., (Andres et al., 2014; Fuller et al., 2016; Garn et al., 2018; Jung et al., 2017a; Larsen et al., 2017; VanDerslice and Briscoe, 1995). The health impacts from sanitation might even primarily result from protective effects on the community rather than from direct benefits to individual households (Andres et al., 2014; Fuller and Eisenberg, 2016; Harris et al., 2017). High community coverage of sanitation might be especially important for densely-populated areas with frequent person-to-person contact and little free space (Berendes et al., 2017).

This paper is motivated by two main objectives: The first is to estimate faecal environmental contamination post-intervention from sanitation intervention reports and to use these estimates to explain heterogeneous impacts on diarrhoeal disease. For this purpose we propose for the first time a Faecal Contamination Index (FAECI) of selected WASH indicators. The second objective is to provide country, regional and overall estimates of the proportion of the population living in communities above a certain level of coverage with basic sanitation services with a focus on low- and middle-income countries to complete data on faecal environmental contamination in general and on WASH indicators used for the FAECI.

2. Methods

2.1. Estimation of faecal environmental contamination using a composite index and assessing the association between faecal contamination and the impact of sanitation interventions on diarrhoeal disease

2.1.1. Construction of the Faecal Contamination Index (FAECI)

A set of WASH indicators was selected to develop a Faecal Contamination Index (FAECI), on the basis of biological plausibility, demonstrated association with diarrhoeal disease (Ram et al., 2014; Wolf et al., 2018a), data availability at country-level and frequent reporting in research trials. Since poor sanitation is a primary cause of faecal environmental contamination, half of the eight indicators relate to sanitation practices. Two indicators were selected for drinking water and two for hand hygiene. Seven of the indicators refer to the proportion of the population (at the scale of the intervention) that:

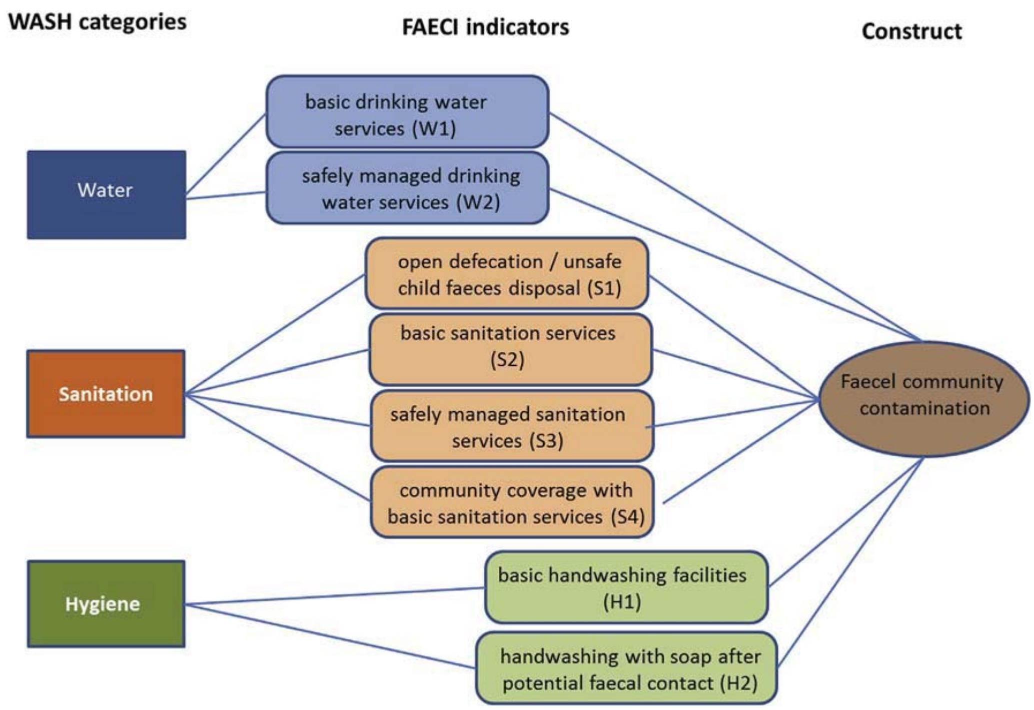


Fig. 2. WASH indicators for assessing faecal environmental contamination.

1. practice open defecation or unsafe disposal of child faeces (S1),
2. use or have access to basic sanitation services, i.e., improved sanitation facilities that are not shared between two or more households (S2),
3. use or have access to safely managed sanitation services, i.e., basic sanitation services that ensure safe disposal or safe transport and treatment of excreta (S3),
4. use or have access to basic drinking water services, i.e., water from improved sources that require no more than 30 min to collect water from (W1),
5. use or have access to safely managed water services, i.e., improved sources accessible on premises, which provide water free from contamination and available when needed (W2),
6. have access to basic handwashing facilities, i.e., handwashing facilities with soap and water on premises (H1),
7. wash hands with soap after potential faecal contact (H2).

An eighth indicator (S4) refers to community sanitation coverage, i.e. the proportion of the population within a community that uses or has access to basic sanitation services. The eight indicators are shown in Fig. 2.

Indicators S2, S3, S4, W1 and W2 refer to either use of or access to services dependent on the information available from the study report. S1 and H2 are indicators of behaviours whereas H1 assesses access to services. More information on the indicators and scoring of interventions is provided in Table 1. We subjectively chose 75% and 50% as the cut-off values for most indicators as a simplified approach and in order to get a good distribution of scores. S1 (open defection/unsafe child faeces disposal), S3 (safely managed sanitation services) and W1 (basic drinking water services) received more stringent cut-off values because we assumed high potential faecal contamination of the environment from open defecation and unsafely managed sanitation services (WHO, 2018a). Most of the world's population is now covered with improved drinking water sources (WHO and UNICEF, 2017), which are however often faecally contaminated (Bain et al., 2014). A rather high cut-off value for W1 ensured a better distribution of scores. Improved drinking-water and sanitation facilities are defined following the JMP (WHO and UNICEF, 2017).

The first six indicators are assessed regularly (S1: only open defecation) through nationally-representative household surveys and are compiled and reported globally by the JMP every two years (WHO and UNICEF, undated). Child faeces are considered safely disposed of if the child him/herself uses a toilet or latrine, or if another person puts or rinses the child's faeces into a toilet or latrine (Water and Sanitation Program, 2015). The proportion of the population using safely managed drinking water services, safely managed sanitation services and a handwashing facility with soap and water are global indicators of the Sustainable Development Goals (SDG indicator 6.1.1 and 6.2.1) (United Nations, n.d.). The population using basic drinking water and sanitation services, and with access to handwashing facilities also contribute to monitoring of SDG targets on poverty (indicator 1.4.1). Structured observation of handwashing with soap after potential faecal contact is considered the most reliable way to measure actual hand hygiene behaviour (Luby et al., 2011; Ram, 2013) and has been estimated by country for the year 2015 based on the JMP global database and nationally-representative household surveys (Wolf et al., 2018b) (H2). The proportion of community sanitation coverage (S4) has recently been examined as an important determinant for reducing diseases and other health conditions related to basic sanitation services (Jung et al., 2017a; Larsen et al., 2017; Wolf et al., 2018a). Community sanitation coverage represents a distinct pathway for faecal contamination from household-level sanitation (S2). Estimates of community sanitation coverage are now being presented in this work at national, regional and overall level for low- and middle-income countries (Objective 2).

2.1.2. Estimating faecal environmental contamination in published sanitation intervention studies using the FAECI

The potential level of faecal environmental contamination using the FAECI was estimated in sanitation interventions identified in a recent systematic review (Wolf et al., 2018a). This review included sanitation

Table 1
Indicators for assessing faecal environmental contamination: scoring and further information.

WASH category	Scoring [number of points][a]	Notes
Sanitation	(percentages usually relate to percentage of population)	
S1. Open defecation (OD)/unsafe child faeces disposal	[0] < 5% OD, unsafe child faeces disposal [1] 5%–10% [2] > 10% OD	If open defecation was not directly reported in the study, we used information on sanitation coverage and reported use of toilets. If child faeces disposal was not reported in the study we assumed that there was no unsafe child faeces disposal.
S2. Basic sanitation services	[0] ≥75% use or access to basic sanitation services [1] ≥50%- < 75% [2] < 50%	This indicator usually measures the proportion of the study population that has been provided with or that uses the intervention facilities. It also reflects functionality of services if such information is available.
S3. Safely managed sanitation services	[0] < 5% use or access to unsafely managed sanitation (such as open drains/flush on street) [1] 5%–10% [2] > 10%	Due to data constraints, this indicator assesses evidence against safe management of sanitation facilities (such as open drains, overflowing toilets, unimproved facilities). Sanitation facilities were assumed to be safely managed when the three following conditions were met: there was no indication of unsafe management, intervention facilities were basic sanitation services and the majority of the study group was covered with these facilities. The same cut-offs for scoring as for OD/unsafe child faeces disposal are applied as we assumed high potential faecel contamination from facilities with evidence against safe management.
S4. Community coverage with basic sanitation services	[0] ≥75% community coverage with basic sanitation services [1] ≥60%- < 75% [2] < 60%	This indicator assesses coverage with the intervention facilities of the whole community. It is referring to use of sanitation if such information is available.
Drinking water		
W1. Basic drinking water services	[0] ≥ 90% use or access to a basic drinking water service [1] ≥75%- < 90%, or ≥ 90% but evidence for household water storage [2] < 75%	Basic drinking water services are defined as improved drinking water sources from which water is available in < 30min round-trip (WHO and UNICEF, 2017). As the time to collect water is often not reported in intervention studies, we use here the proportion of improved drinking water sources without the information on distance. If information on this indicator was not available from the study, it was replaced with country-representative data for the respective country, setting and year (WHO and UNICEF, undated).
W2. Safely managed drinking water services	[0] ≥75% use or access to safely managed drinking water services [1] ≥50%- < 75% [2] < 50%	Safely managed drinking water services include water that is accessible on premises, available when needed and free from contamination. As the continuity of supply is often not reported in sanitation interventions studies, safely managed drinking water services are operationalized as the proportion of improved drinking water supplies on premises that is free from contamination. If information on this indicator is not available from the respective study, it has been replaced with country-representative data for the respective country, setting and year (WHO and UNICEF, undated).
Hygiene		
H1. Basic handwashing facilities	[0] ≥ 75% access to basic handwashing facilities [1] ≥50% - < 75% [2] < 50%	This indicator measures access to a handwashing facility on premises that is equipped with water and soap. If presence of basic handwashing facility was not given, the value was replaced with country representative JMP data for the respective country, setting and year (WHO and UNICEF, undated) or from an analysis modelling the presence of basic handwashing facilities at country level (Wolf et al., 2018b).
H2. Handwashing with soap after potential faecal contact	[0] ≥75% wash hands with soap after potential faecal contact [1] ≥50% - < 75% [2] < 50%	This indicator reflects observed handwashing with soap (HWWS) after potential faecal contact. If observed HWWS is not reported, the indicator was approximated by reported HWWS or by the proportion of basic handwashing facilities (Wolf et al., 2018b)

[a] A high score represents high estimated faecal contamination.

Table 2
Search terms for literature search.

	Search terms
Construct 1	(prevalence[tw] OR incidence[tw] OR risk[tw] OR exposure[tw] OR exposed[tw] OR outcome[tw] OR epidemiology[tw] OR epidemiological[tw] OR impact[tw] OR effect[tw] OR evaluation[tw] OR odds[tw])
Boolean operator	AND
Construct 2	(neighbourhood[tiab] OR neighbourhoods[tiab] OR neighborhood[tiab] OR neighborhoods[tiab] OR village[tiab] OR villages[tiab] OR community[tiab] OR communities[tiab] OR "herd protection"[tiab] OR "herd protective"[tiab] OR coverage[tiab])
Boolean operator	AND
Construct 3	(toilet*[tiab] OR latrine*[tiab] OR pit[tiab] OR pits[tiab] OR sanita*[tiab] OR feces[tiab] OR faeces[tiab] OR fecal[tiab] OR faecal[tiab] OR excre*[tiab] OR sewage[tiab] OR sewer*[tiab] OR sewerage[tiab] OR open defecation"[tiab] OR Toilet Facilities"[MeSH] OR Toilet Training"[MeSH] OR Sanitation[MeSH] OR Feces[MeSH] OR Sewage[MeSH])

interventions that reported the effect on diarrhoea morbidity of any improvements in sanitation access or use conducted at the level of the household or community. Interventions in non-household settings such as schools, healthcare facilities, or workplaces were not included. Interventions needed to be tested against a control group that did not receive the respective intervention(s) or that received a control or placebo intervention. Eligible study designs included randomized controlled trials, quasi-randomized and non-randomized controlled trials when baseline data on the main outcome were available, case–control and cohort studies when they were related to a clearly specified

Table 3
Included sanitation and combined WASH interventions.

reference	country	setting	intervention type	improvement of access versus sanitation promotion*	RR (lcl, ucl), p-value#	FAECI post-intervention (intervention group)‡
Aziz et al. (1990)	Bangladesh	rural	improved household sanitation plus hygiene education and improved water supply	sanitation access	**0.74 (0.69, 0.80), p < 0.01**	9
Briceño et al. (2015)	Tanzania	rural	improved household sanitation	sanitation promotion	0.99 (0.75, 1.30)	15
Clasen et al. (2014)	India	rural	improved household sanitation	sanitation access	0.97 (0.83, 1.12)	13
Garrett et al. (2008)	Kenya	rural	improved household sanitation plus hygiene education and improved water supply	sanitation promotion	**0.31 (0.23, 0.41)**	16
Godfrey et al. (2014)	Mozambique	rural	improved household sanitation	sanitation promotion	0.54 (0.29, 1.01)	15
Humphrey (2018)	Zimbabwe	rural	improved household sanitation plus hygiene education and improved water supply	sanitation access	1.18 (0.87, 1.61), p = 0.3	10
Khush and London (2009)	India	rural	improved household sanitation plus hygiene education and improved water supply	sanitation promotion	1.00 (0.43, 2.32)	12
Klasen et al. (2012)	Yemen	urban	sewer intervention	sanitation access	0.81 (0.35, 1.90)	7
Luby et al. (2018)	Bangladesh	rural	improved household sanitation	sanitation access	**0.61 (0.46, 0.81)**	11
Messou et al. (1997)	Ivory Coast	rural	improved household sanitation plus hygiene education and improved water supply	sanitation access	**0.71 (0.56, 0.91)**	9
Moraes et al. (2003)	Brazil	urban	sewer intervention	sanitation access	**0.31 (0.28, 0.34), p < 0.0001**	3
Null et al. (2018)	Kenya	rural	improved household sanitation	sanitation access	0.99 (0.88, 1.1)	11
Patil et al. (2014)	India	rural	improved household sanitation	sanitation promotion	0.97 (0.78, 1.22)	15
Pickering et al. (2015)	Mali	rural	improved household sanitation	sanitation promotion	0.93 (0.76, 1.14), p = 0.5	15
Pradhan and Rawlings (2002)	Nicaragua	urban	sewer intervention	sanitation access	0.43 (0.11, 1.71)	3
Reese et al. (2018)	India	rural	improved household sanitation plus hygiene education and improved water supply	sanitation access	0.98 (0.78, 1.23), p = 0.9	9
Walker et al. (1999)	Honduras	rural	improved household sanitation	sanitation access	**0.65 (0.47, 0.90)**	6

RR: relative risk, lcl: lower 95% confidence limit, ucl: upper 95% confidence limit, improved household sanitation include any improvements to sanitation facilities at household level, sewer interventions provide households with connections to the public sewer system, relative risks in bold indicate results significant at $p < 0.05$ (confidence limits do not include 1), * "sanitation access" means that the intervention provided (most of) the intervention hardware, it does not exclude sanitation promotion, "sanitation promotion" means that the intervention or project promoted the building of sanitation facilities but did not build or provide them to households, # p-value only added when it could be extracted alongside the relative risk from the publication of the respective intervention study, ‡ the FAECI score can reach a maximum of 16, a high FAECI represents high estimated faecal environmental contamination.

intervention and studies using time-series designs (Wolf et al., 2018a). Additionally to the interventions identified from the systematic review (Wolf et al., 2018a), more recently conducted sanitation and WASH trials and intervention studies based on the same inclusion criteria were included (Table 3). When a study made sanitation interventions in both a combined WASH and an exclusive sanitation intervention arm, we selected the exclusive sanitation arm. Each study was evaluated on each of the eight WASH indicators both in the intervention (after the intervention) and the control group. Each indicator was given a score depending on the level of (assumed) faecal contamination for the respective indicator, between zero and two points. Missing information on hygiene or drinking water was extrapolated for the respective country, year and region (urban or rural) from national mean values (WHO and UNICEF, undated; Wolf et al., 2018b). Two raters (AP and JW) independently assessed each study. Discrepancies were discussed and – in case no agreement could be reached – a third person consulted (RJ). The scores of all indicators were added up giving equal weight to each indicator. A large FAECI score represents high estimated faecal contamination in the community or the environment.

2.1.3. Analysis of the association between estimated faecal contamination (using the FAECI) and the effectiveness of sanitation interventions on diarrhoeal disease

Relative risk estimates for diarrhoeal disease prevalence or incidence were extracted from a recent systematic review (Wolf et al., 2018a) or directly from the sanitation interventions if not included in the review. As odds ratios can overstate the estimated intervention effect (Davies et al., 1998), these were converted to risk ratios using the control group risk as given in the respective paper (Higgins and Green, 2011; Zhang and Kai, 1998). Meta-regression analysis was used to assess the association between the relative risk estimates as outcome and the FAECI as continuous explanatory variable. To assess a hypothesized non-linear relationship between the relative risk estimates and the FAECI, a squared term of the FAECI was introduced in the meta-regression model. Because of the limited number of studies ($n = 17$) we decided a-priori that no further polynomials would be tested. We however examined the effect of urban versus rural setting (binary variable), combined WASH versus exclusive sanitation interventions (binary variable) and the size of the difference between the FAECI scores in intervention and control group ("delta FAECI", continuous variable). We also examined the association between the relative risk estimates and the delta FAECI, i.e., the difference between the FAECI score in the intervention and the control group, as single predictive variable – in the meta-regression model. Data analysis was performed using Stata 14 (StataCorp, 2015). Studentized deleted residuals were examined for each study visually departing from the overall trend to examine potential outliers, which can distort results and conclusions from any meta-analytic model (Viechtbauer and Cheung, 2010).

2.2. Estimation of country, regional and total proportions of the population from low- and middle-income countries living in communities in which basic sanitation coverage exceeds a defined threshold

2.2.1. Literature search to establish health-relevant community sanitation coverage thresholds

We searched PubMed (in January 2018) combining both MeSH terms and keywords in order to identify studies assessing health effects from improving sanitation services at various community coverage levels (Table 2). We restricted the search to the last 10 years and excluded animal studies (used the humans filter in PubMed).

Sanitation coverage in a community is defined here as the proportion of people in a community that use basic sanitation services. A community has been defined as a "group of people with diverse characteristics who are linked by social ties, share common perspectives, and engage in joint action in geographical locations or settings" (MacQueen et al., 2001). Communities in the current analysis are represented by the survey clusters, or primary sampling units (PSUs), which usually consist of geographic areas that group together approximately 100 households (ICF International, 2012).

2.2.2. Data extraction from national household surveys

We searched the JMP household survey data repository in July 2017 for relevant microdata at PSU-level from Demographic Health Surveys (DHS) (The DHS Program, undated) or Multiple Indicator Cluster Surveys (MICS) (UNICEF, undated), for 195 countries and territories collected since 1998 and containing information on household sanitation access and on data sampling (i.e. specifying the PSU and household weights). When several household surveys with relevant microdata at PSU-level were available we only extracted data from the most recent survey. Extracted data was substituted, if available, by harmonized files prepared by the JMP after specific country consultations. For five countries (Nicaragua, Ecuador, Brazil, China, and Sri Lanka) non-DHS/non-MICS survey data were used as they contained the relevant data and DHS or MICS survey data were not available or had been collected a longer time ago (Nicaragua: ENDESA (Encuesta Nicaragüense de Demografía y Salud) 2011 (UNFPA Nicaragua, 2016); Ecuador: ENEMDU (Encuesta Nacional de Empleo, Desempleo y Subempleo) 2016 (Instituto Nacional de Estadística y censos, 2016); Brazil: PNAD (Pesquisa Nacional por Amostra de Domicílios) 2015 (Instituto Brasileiro de Geografia e Estatística, undated); China: SAGE (WHO Study on global AGEing and adult health) 2008 (WHO, n.d.); Sri Lanka: WHS (World Health Survey) 2003 (World Bank, 2013). A pooled dataset was created combining all countries for which microdata at PSU-level were available. Variables indicating proportion of households using improved sanitation facilities and basic sanitation services were calculated following the JMP definitions (WHO and UNICEF, 2017). Population weights were used in the analysis to estimate the proportion of people living in communities with defined sanitation coverage and to account for the fact that not all households were selected with equal probability into the survey sample. Population weights were calculated by multiplying the household weight as given in the surveys with the number of de jure household members (usual household members, i.e. not only those present at the time of the survey).

2.2.3. Analysis of the population living in communities above a defined threshold of sanitation coverage

Data were analysed taking account of cluster sampling in survey data collection (using the svy-command in Stata). To calculate the percentage of the population living in communities above a defined threshold of coverage with basic sanitation services by country, two analysis steps were performed: first, the proportion of the population within the PSU using basic sanitation services was calculated. Second, the mean proportion of the national population living in clusters having at least a certain basic sanitation coverage level was calculated weighted by the mean of population weights by PSU.

Confidence intervals at country-level were generated using the standard error of the mean at country-level (Statalist - archive, 2009). Regional and global estimates and their 95% confidence intervals were derived using country population figures from the United Nations Population Division for the year 2016 (2017 revision) (United Nations Population Division, undated). Standard errors at regional and global levels were estimated with an approach using the delta method ((De Onis et al., 2004), formula in Appendix A – Main (A.1)). Data analysis was performed in Stata 14 (StataCorp, 2015).

We are following guidelines for accurate and transparent health estimates reporting ("GATHER: Guidelines for Accurate and Transparent Health Estimates Reporting," n.d.; Stevens et al., 2016) and have included a GATHER-checklist as an Appendix (Appendix B – Gather Checklist). Data analysis code can be obtained from the corresponding author upon request. Ethical clearance was not needed for this work as this study did not involve any human or animal participation or personal data. All data was anonymised and informed consent of the

WASH intervention studies was obtained at the time of original data collection.

3. Results

3.1. Estimation of faecal environmental contamination using a composite index and assessing the association between faecal contamination and the impact of sanitation interventions on diarrhoeal disease

3.1.1. Estimating faecal environmental contamination in published sanitation intervention studies using the FAECI

A total of 17 intervention studies were included (Table 3). Of those, six were combined WASH interventions including a sanitation component, and 11 were exclusive sanitation interventions. Fourteen interventions improved household sanitation and three interventions provided sewer connections. Table 3 shows the FAECI scores post-intervention in the intervention group. The scores for all eight indicators for all 17 studies both in the intervention and control groups are included in Appendix C - Faecal contamination score of sanitation interventions.

The frequency of reporting of the eight WASH indicators post-intervention in the intervention group in the 17 sanitation studies is shown in Fig. 3. While the four sanitation indicators could always be extracted from the study reports, the two hygiene indicators but also drinking water quality were more rarely reported.

3.1.2. Analysis of the association between estimated faecal contamination and the effectiveness of sanitation interventions on diarrhoeal disease

Using meta-regression analysis, estimated faecal environmental contamination as represented by the score of the FAECI and the squared FAECI score were strongly associated with the relative risks of diarrhoea of intervention studies ($p = 0.006$). The model including all studies explained 53% of the between-study variance. Additional binary indicators of urban versus rural setting and sanitation versus combined WASH interventions, and a continuous indicator for the difference of the FAECI between intervention and control group (the "delta FAECI") were not significantly associated with diarrhoea risk and did not change

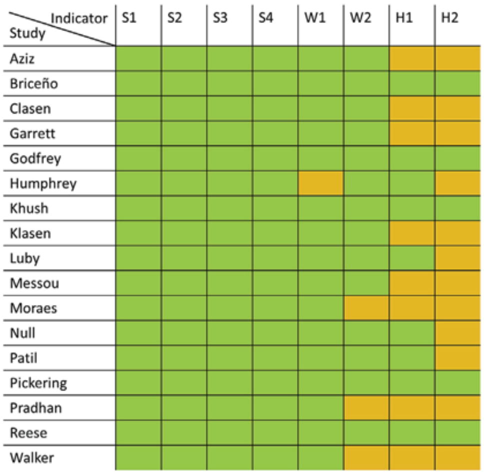


Fig. 3. Reporting of the eight WASH indicators in the intervention group post-intervention by sanitation study; green: indicator reported, orange: indicator not reported, S1: open defecation/unsafe child faeces disposal, S2: basic sanitation services, S3: safely managed sanitation services, S4: community coverage with basic sanitation services, W1: basic drinking water services, W2: safely managed drinking water services, H1: basic handwashing facilities, H2: handwashing with soap after potential faecal contact. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

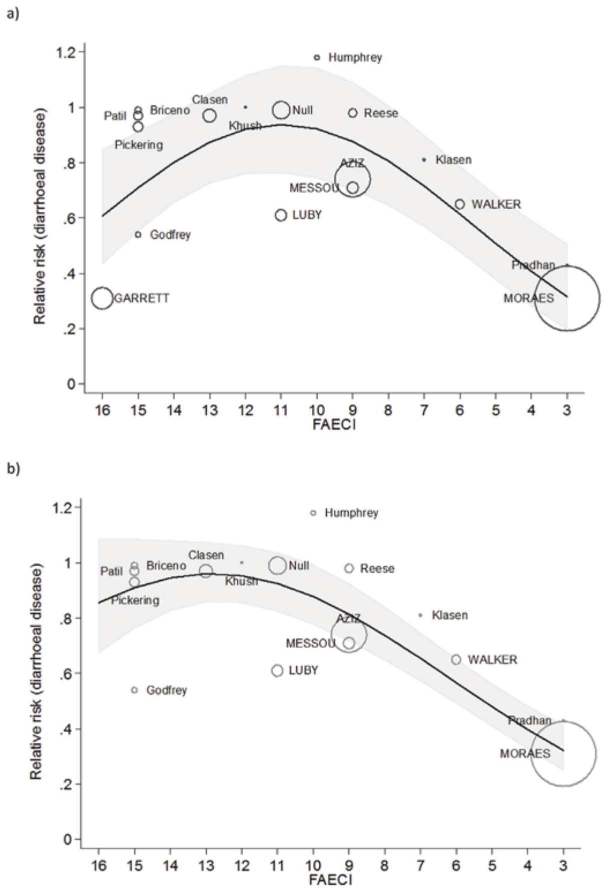


Fig. 4. Relative risks of diarrhoeal disease as a function of the FAECI a) including all studies, b) excluding one study identified as a potential outlier; black line: predicted mean relative risks, shaded area: 95% confidence interval, circles represent relative risk estimates of individual studies, circle sizes are drawn proportional to the inverse of the relative risk's variance to emphasize differences in the precision of the estimates, first author name written in uppercase means significant relative risk estimates at $p < 0.05$, FAECI: Faecal Contamination Index.

the association of the other variables in the model.

Predicted relative risks from the meta-regression model ranged from a minimum of 0.32 (0.20, 0.51) at a FAECI of three (low estimated faecal contamination, note: as none of the included sanitation interventions yielded a FAECI score below 3, we did not predict relative risks for scores below three) to 0.94 (0.77, 1.15) at a FAECI of 11 (high estimated faecal contamination). The majority of interventions with a FAECI score between 8 and 13 did not show a significant effect of diarrhoea and hence also the predicted relative risks from the model were equivalent to no effect (i.e., confidence intervals include 1, $p > 0.05$). At a FAECI of 14–16 predicted relative risks declined again due to two studies that show low relative risks at a high FAECI (Fig. 4, a).

Using studentized deleted residuals, one study (Garrett et al., 2008) was identified as an outlier (Viechtbauer and Cheung, 2010). Running the meta-regression model excluding this study showed very strong associations ($p < 0.0001$) between the FAECI score, its squared term and the relative risk estimates of the interventions (Fig. 4, b). This model explained 88% of the between-study variance and also did not show the decline of predicted mean relative risk estimates at a large FAECI.

Table 4
Studies investigating the existence of community sanitation coverage thresholds for diarrhoea impacts.

citation	location	level of sanitation service provision	community coverage threshold	impact	study design
Andres et al. (2014)	India, rural	basic sanitation services	two thresholds: ~30% (before 30% basically no change on diarrhoea) and ~75% (around 50% of diarrhoea reduction after 75%)	47% diarrhoea reduction in children communities in a village with 100% sanitation coverage compared to children in communities with 0% coverage	cross-sectional
Harris et al. (2017)	Mali, rural	sanitation facilities (including basic, shared and unimproved)	no threshold (tested for 20%, 40% and 60% sanitation coverage), no association between increased sanitation coverage and diarrhoea	–	cross-sectional
Jung et al. (2017b)	various low-income	basic sanitation services	threshold at 60%	56% diarrhoea reduction at 100% community coverage with basic sanitation (OR 0.44 (0.29, 0.67)), 18% diarrhoea reduction < 60% coverage (OR 0.82 (0.77, 0.87))	cross-sectional (DHS surveys)
Larsen et al. (2017)	various	sanitation facilities (including improved and unimproved private facilities)	threshold between 30% and 100%	6% diarrhoea reduction (AOR 0.94 (0.91–0.97)) for children with household-level sanitation access in communities with 100% vs. 1–30% coverage	meta-analysis of survey data
Wolf et al. (2018a)	various	mainly basic sanitation services, depending on study	threshold at ≥75%	45% diarrhoea reduction in high coverage studies versus 24% in low coverage studies (five studies with ≥85% community coverage (RR 0.55 (0.34, 0.91)) versus 16 studies ≤65% coverage (RR 0.76 (0.51, 1.13)))	systematic review and meta-analysis of intervention studies

OR: odds ratio, AOR: adjusted odds ratio, RR: relative risk; basic sanitation includes improved sanitation facilities that are not shared between two or more households (WHO and UNICEF, 2017).

The delta FAECI, included separately and in combination with its squared term, was not significantly associated with the effect sizes of the interventions.

3.2. Estimation of country, regional and total proportions of the population from low- and middle-income countries living in communities in which basic sanitation coverage exceeds a defined threshold

3.2.1. Literature search to establish health-relevant community sanitation coverage thresholds

From an initial list of 3800 citations, we selected 145 studies for abstract review and subsequently 49 studies for full text review. Of those, five studies reported the association between community coverage thresholds and diarrhoeal disease impacts (Table 4). Based on the recent systematic review and meta-analysis of intervention studies (Wolf et al., 2018a), and support from three of the other four studies (Andres et al., 2014; Jung et al., 2017b; Larsen et al., 2017), we chose 75% as a threshold for reporting as this threshold was the most frequently reported one, and 95% as a threshold indicating near complete coverage.

Furthermore, there was evidence for an association between community coverage with basic sanitation and malnutrition (Alderman et al., 2003; Cameron et al., 2017; Fuller et al., 2016; Gertler et al., 2015; Harris et al., 2017; Larsen et al., 2017; Vyas et al., 2016), infectious diseases (Fuller and Eisenberg, 2016), anaemia (Larsen et al., 2017), trachoma (Garn et al., 2018), cognitive development (Cameron et al., 2017) and child mortality (Geruso and Spears, 2015). For soil-transmitted helminths, one study found an association with community sanitation (Forrer et al., 2016), and one did not (Oswald et al., 2017).

3.2.2. Data extraction from national household surveys

From the JMP data repository we identified a total of 111 countries for which survey microdata on use of basic sanitation services at PSU-level were available. The countries and territories included cover 29 out of 31 low-income, 47 out of 52 lower middle-income, 33 out of 57 upper middle-income and 2 (Trinidad and Tobago and Uruguay) out of 55 high-income countries and territories (Table 5).

Surveys had been conducted between the years 1998 and 2017 (mean and median at 2012). 78% (87/111) of surveys were collected after 2010. The included countries cover 78% of the world population and 92% of the population in low- and middle-income countries. A complete list of countries included in the analysis, the survey type, year, region and income status are provided in Appendix D - Country estimates. About four hundred (401) observations (each observation represents a household) were deleted because of duplicates of households in the same PSU and country. In total, over 2 million (2,034,497) observations in a total of 93,269 PSUs were included. The mean and median number of PSUs per survey was 840 and 448 respectively and ranged from a minimum of 100 PSUs (Saint Lucia) to a maximum of 28,524 PSUs (India). The mean and median number of households surveyed per cluster was 22 and 21 respectively and ranged from a minimum of 1 household to a maximum of 764 households.

3.2.3. Analysis of the population living in communities above a defined threshold of sanitation coverage

The percentage of the population living in communities in which more than 75% and 95% of the population are covered with basic sanitation services by country is given in Appendix D - Country estimates and is shown in Fig. 5. Regional and total aggregates are given in Table 6.

Table 5
Number of countries and territories with available data at community-level (PSU-level) on use of basic sanitation services by region.

Region	Number of countries with community-level data on basic sanitation services	Total number of low- and middle-income countries by region	Total number of countries by region
African Region	42	46	47
Region of the Americas[a]	22	26	35
Eastern Mediterranean Region	14	15	22
European Region	16	20	53
South-East Asia Region	10	11	11
Western Pacific Region	7	20	27
Total	111	138	195

[a] Includes Uruguay and Trinidad and Tobago as high-income countries; basic sanitation includes improved sanitation facilities that are not shared between two or more households (WHO and UNICEF, 2017).

4. Discussion

4.1. Main results

4.1.1. Faecal environmental contamination in sanitation intervention studies and its association with the effectiveness of sanitation interventions on diarrhoeal disease

The analysis shows a non-linear association between the estimated level of faecal contamination in the community, as assessed by the FAECI, and impacts of sanitation interventions on diarrhoeal disease. It suggests that sanitation interventions are more effective at reducing diarrhoea at lower levels of faecal contamination, and that interventions are less likely to show diarrhoea reductions if faecal contamination in the community remains above a certain level.

4.1.2. Estimates of the population living in communities above a defined threshold of sanitation coverage

The percentage of the population from low- and middle-income countries living in communities with more than 75% and 95% coverage with basic sanitation services is estimated at 45% and 24% respectively. Large regional discrepancies exist, with less than a third of the African and South-East Asian population living in communities covered with > 75% basic sanitation services.

Table 6
Regional and total estimates of the percentage of the population from low- and middle-income countries living in communities with high sanitation coverage.

	population (percentage (95% CI)) living in communities with the given level of basic sanitation coverage	
Region	**> 75%**	**> 95%**
African Region	13.3% (11.1%, 16.0%)	6.2% (4.4%, 8.8%)
Region of the Americas	75.8% (73.7%, 77.7%)	46.1% (43.9%, 48.2%)
Eastern Mediterranean Region	54.8% (51.9%, 57.6%)	35.7% (32.1%, 39.6%)
European Region	93.3% (91.3%, 94.9%)	79.6% (77.4%, 81.6%)
South-East Asia Region	31.9% (30.9%, 32.9%)	12.7% (9.3%, 17.1%)
Western Pacific Region	63.2% (26.3%, 89.2%)	30.6% (5.8%, 75.8%)
Total	45.3% (34.7%, 56.4%)	23.7% (14.9%, 35.4%)

CI: confidence interval, results apply to low- and middle income countries, regions according to WHO regional groupings (WHO, 2018b), basic sanitation includes improved sanitation facilities that are not shared between two or more households (WHO and UNICEF, 2017).

4.2. General discussion

Faecal environmental contamination was assessed combining a set of WASH indicators that cover many household- and community-level transmission pathways for diarrhoeal disease (compare to Fig. 1). Our

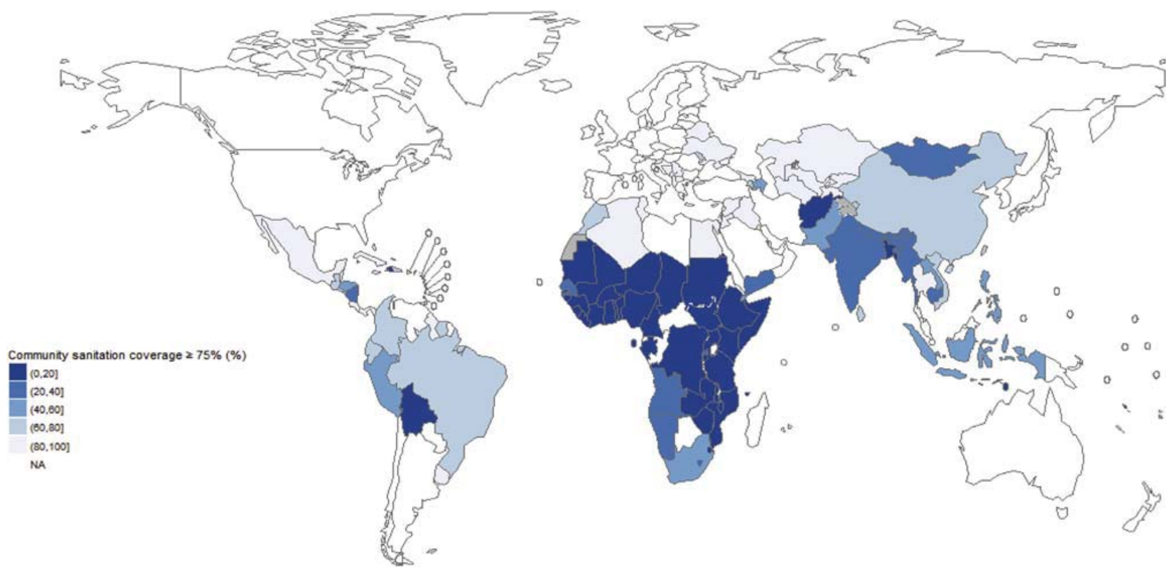


Fig. 5. Community sanitation coverage ≥75% by country;"Community sanitation coverage" means the percentage of the population living in communities in which access with basic sanitation services ≥75%, basic sanitation includes improved sanitation facilities that are not shared between two or more households (WHO and UNICEF, 2017).

results show that estimated faecal contamination is an important determinant of a sanitation intervention's potential to reduce diarrhoeal disease. The level of faecal environmental contamination therefore assists in interpreting differing results from WASH interventions for diarrhoeal disease reduction. The different WASH indicators on which information is collected can provide guidance on a minimum set of indicators for monitoring and reporting in all WASH research studies in order to semi-quantitatively assess the likelihood of faecal contamination after the intervention.

Some of the WASH indicators measure behaviours (S1 and H2) while another access to or presence of specific infrastructure (H1) or both depending on the study's reporting (S2, S3, S4, W1, W2). Improving use of or access to services requires different intervention strategies. Examples include health risk communication and education for improving use (Anthonj et al., 2018) and subsidy and hardware provision interventions for improving access (Garn et al., 2017). Improved data on use of services or facilities could probably improve estimates of faecal contamination.

The analysis suggests that settings with low faecal contamination post-intervention are more likely to show impacts on diarrhoeal disease than settings with high prevailing faecal contamination. In poor settings, which often carry the burden of considerable faecal contamination of the environment, sanitation and WASH interventions are crucially important, and should be considered as a necessary but possibly insufficient step for achieving disease reduction (Clasen et al., 2014). In the spirit to “leave no one behind” and get communities to a sufficiently reduced level of faecal environmental contamination, WASH interventions should continue to be made in these highly contaminated settings, to progressively reduce faecal contamination among these most vulnerable populations. The lack of impacts on diarrhoea after a WASH intervention cannot necessarily be interpreted as an intervention's ineffectiveness, a point that has already been made more than 20 years ago (VanDerslice and Briscoe, 1995). The outcome of any single intervention depends not only on whether that intervention is used sustainably but also on what other transmission pathways are important in the context of the study communities (Robb et al., 2017). Even in settings with high faecal contamination before the intervention, disease reduction may be achieved if the level of faecal contamination is reduced below a certain level. This underlines the importance of interventions that reach entire communities ensuring that everyone uses a toilet that safely contains excreta (WHO, 2018a) and that progressively reduces faecal contamination of the environment– which many interventions of the past failed to achieve (Sclar et al., 2016). WASH interventions need plans for operation and maintenance, oversight and regulation, monitoring and an accompanying enabling environment to ensure sustainability and prevent back slippage. Sanitation Safety Planning (SSP) is a local level risk assessment and management tool that can be used to identify priority risks along the sanitation chain and make improvements to technology, behaviours and management to reduce exposure. SSP also helps coordinate improvements and monitoring by multiple actors along the sanitation chain (WHO, 2015). Deleting one study (Garrett et al., 2008) identified as an outlier increased the strength of association between the FAECI and the relative risk estimates of the interventions. The excluded study might indeed be different from the other sanitation studies as it was conducted in a very sparsely populated area, where contact with community faecal contamination may have been reduced..

We had initially planned to validate the FAECI on another WASH category and attempted to extract data on the FAECI indicators from 14 drinking water filtration interventions. However, none of the filtration intervention studies reported whether sanitation facilities were safely managed, the presence of a handwashing facility with soap and water or observed handwashing with soap. While most filtration studies reported the presence of latrines or toilets it was often not clear whether these facilities were of an improved or unimproved technology. This underlines the importance of a minimum set of WASH indicators that should be reported in all WASH intervention studies independent of the WASH category addressed.

The FAECI should be regarded as a first attempt to simply, transparently and reasonably estimate the level of faecal contamination in a community environment in a way that is comparable across various intervention locations. We believe that even with slightly different indicators or different scoring, the general results and broad conclusions would be similar. We had – for example - constructed a different version of the index that included a combined measure of unsafe disposal or presence of child and animal faeces, which was however not pursued due to data scarcity on animal faeces or animal presence. Analysis of the estimated faecal contamination assessed with this modified index led to basically the same results as the here proposed one (results in Appendix A – Main, A.2). The index is semi-quantitative and does not intend to present an exact measure of faecal contamination. We caution against interpreting the size of the score too precisely and using the score of the FAECI for influencing targeting of resources. Future developments could include harmonized definitions for the proposed indicators, examine non-household settings such as schools, healthcare facilities and workplaces and explore more sophisticated approaches to estimating faecal contamination such as a latent variable approaches that treats faecal environmental contamination as an unobserved variable that can be modelled from a set of observed variables (Cai, 2012).

The FAECI includes community sanitation coverage as one indicator, which has recently been shown to have various health benefits independent from household-scale sanitation coverage (e.g., studies listed in Table 4 and (Fuller and Eisenberg, 2016; Garn et al., 2018; Jung et al., 2017a)). This paper provides the first country, regional and total estimates of the population from low- and middle-income countries living in communities with defined coverage levels of basic sanitation services that are based on nationally-representative and standardized data. It thereby completes harmonized and country-level data availability on the proposed minimum set of WASH indicators.

4.3. Limitations

4.3.1. Faecal environmental contamination in sanitation intervention studies using the FAECI and its association with the effectiveness of sanitation interventions on diarrhoeal disease

For the proposed FAECI score, the different WASH indicators receive equal weighting though the strength of their associations with health may differ and there are likely important interactions (Kolsky and Blumenthal, 1995). Poor sanitation services will generally have a higher impact on the overall FAECI compared to poor drinking water supply or hand hygiene as four indicators relate to sanitation. This is justified as open defecation and poor sanitation can be considered the fundamental drivers of faecal contamination in a community (Daniels et al., 2016). In addition, although ingestion of unsafe water potentially increases faecal exposure, increased water availability in general protects against faecal exposure and disease (Pickering and Davis, 2012; Wang and Hunter, 2010). Some indicators are related to each other. If, for example, sanitation facilities remain mainly of an unimproved technology post-intervention, both S2 and S3 and usually also S4 will receive a high score. However, these indicators allow a differentiation between different levels of access to basic sanitation. We did not assess the applicability of the FAECI on other health outcomes (e.g. stunting), which may show different thresholds of estimated faecal contamination.

Not all indicators were reported in all included studies. Studies with the lowest estimated faecal contamination reported less information relevant for the FAECI indicators compared to the rest of the studies, which might have influenced the size of the FAECI (Fig. 3) (Moraes et al., 2003; Pradhan and Rawlings, 2002; Walker et al., 1999). None of the sanitation studies reported safe management of sanitation facilities or water sources as defined by the JMP (WHO and UNICEF, 2017), which required an adaptation of the definitions for this study (details in

Table 1). No study reported observed handwashing with soap after potential faecal contact (H2). For the five studies for which information on this indicator could be extracted, we inferred low actual handwashing with soap from low self-reported handwashing or high contamination of hands. Study data on some of the indicators are likely to be subject to information bias. People under observation might wash their hands more frequently than they usually do (Hawthorne effect) and self-reported behaviour, such as on open defecation, might lead to under-reported open-defecation (McCambridge et al., 2014; Savović et al., 2012).

The FAECI does not include an exhaustive list of potential pathways for transmission of faecal pathogens (Fig. 1). Indicators are only proxy-measures, i.e., they do not provide an exact measure of faecal contamination. Due to data limitations, the indicator on handwashing with soap (H2) includes only handwashing after potential faecal contact and omits food-related handwashing occasions. Again mainly due to data limitations, food and soil contamination or contamination via flies (Bauza et al., 2018; Chavasse et al., 1999; Gautam, 2015; Morita et al., 2017) is not included. These pathways are partly dependent on the indicator (S1), which assesses presence of human faeces in the environment. Alternative ways for introducing faeces in the environment, such as wastewater irrigation (Qadir et al., 2010), are however not covered. The index also lacks information on the presence of animal faeces, which can represent an important pathway for diarrhoeal disease transmission (Ercumen et al., 2017; Penakalapati et al., 2017; Zambrano et al., 2014). The presence of animal faeces post intervention was reported by only one (Pickering et al., 2015) of the included studies. Though currently not included in the index, the presence of animal faeces should be reported in any WASH intervention study with diarrhoea or other health outcomes.

4.3.2. Analysis of the association between estimated faecal contamination and the effectiveness of sanitation interventions on diarrhoeal disease

Results from meta-regression, as used in this analysis, are observational and do not establish causation between the predictor and the outcome (Thompson and Higgins, 2002). As the sample size – the number of sanitation interventions – is limited, the assessment of the association between covariates and the outcome is limited. The I^2 statistic, a measure of inconsistency across study findings (Borenstein et al., 2009, p. 16), was high (92%), which is consistent with our hypothesis of substantial differences in background characteristics such as different levels of faecal environmental contamination but might also reflect differences in terms of intervention type and uptake, study methods, settings, and populations. Results from meta-regression suggest that estimated faecal environmental contamination can explain an important part of the variance.

4.3.3. Estimates of the population living in communities above a defined threshold of sanitation coverage

The estimates are based on a limited number (n = 111) of mostly low- and middle-income countries. Furthermore, even though most surveys were conducted recently, 16 surveys data back to before 2010 (Appendix D - Country estimates). Especially for these countries it is likely that community coverage with basic sanitation services has increased by a certain extent. Use of sanitation facilities in DHS or MICS is self-reported and may therefore be biased; selection bias, e.g., from non-response, might be an additional source of bias in cross-sectional survey data (Levin, 2006).

Due to data constraints at cluster-level of national household surveys, estimates of community sanitation coverage are estimates of coverage with basic sanitation services and not necessarily safely managed services. In 2015, the JMP estimated that 68% of the world population used basic sanitation services of which only 39% were estimated to be safely managed (WHO and UNICEF, 2017). Community coverage estimates with safely managed sanitation services would therefore likely to be considerably lower than estimates for community coverage with basic sanitation services.

Not all previous evidence showed that greater community sanitation coverage leads to positive health outcomes (Harris et al., 2017; Oswald et al., 2017). One of those studies reported continuing high levels of open defecation and coverage included any sanitation facility (Harris et al., 2017). In the other study, community coverage levels with any kind of latrine as well as access to an improved drinking water source remained under 60% even in the high sanitation coverage group (Oswald et al., 2017). Higher sanitation coverage might have no impact on faecal contamination or health if facilities are not safe (Berendes et al., 2017; Daniels et al., 2016), if community coverage remains low (Odagiri et al., 2016), or if alternative pathways for transmission of faecel material exist (Yajima et al., 2009).

5. Conclusions

A large proportion of the world's population lives in communities that are vulnerable to significant faecal contamination from poor management of excreta. We propose a first attempt to estimate the level of faecel contamination in an intervention setting. Results of the analysis suggest that WASH interventions are more likely to lead to reductions of diarrhoeal disease when faecal contamination of the living environment has been reduced below some threshold level. This underlines the importance of interventions that reach whole communities assuring that everybody uses a safe toilet and sanitation system that separates excreta from human contact along the whole sanitation chain. WASH interventions may show no impact on diarrhoea because of persisting faecal contamination due to for example incomplete community coverage or use of sanitation facilities that do not safely contain faecal material or treat it to a level suited to the end use or disposal type. Such interventions might nevertheless be necessary interim steps to reduce faecal environmental contamination for achieving disease reduction in the future. The assessment of a minimum set of WASH indicators is useful for the evaluation of the prevailing major pathways of faecal transmission and of the intervention's effectiveness.

Conflicts of interest

None.

Acknowledgement and disclaimer

The study was partially funded by the United Kingdom Department for International Development. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.Some authors are staff members of the World Health Organization or other institutions. The authors alone are responsible for the views expressed in this publication, which do not necessarily represent the views, decisions or policies of the institutions with which they are affiliated. This article should not be reproduced for use in association with the promotion of commercial products, services or any legal entity. The WHO does not endorse any specific organization or products.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijheh.2018.11.005.

References

Alderman, H., Hentschel, J., Sabates, R., 2003. With the help of one's neighbors: externalities in the production of nutrition in Peru. Soc. Sci. Med. 56, 2019–2031. https://doi.org/10.1016/S0277-9536(02)00183-1.

Andres, L.A., Briceño, B., Chase, C., Echenique, J.A., 2014. Sanitation and Externalities: Evidence from Early Childhood Health in Rural India (No. 6737), Policy Research Working Paper. The World Bank.

Anthonj, C., Fleming, L., Godfrey, S., Ambelu, A., Bevan, J., Cronk, R., Bartram, J., 2018. Health risk perceptions are associated with domestic use of basic water and sanitation services-evidence from rural Ethiopia. Int. J. Environ. Res. Publ. Health 15. https://doi.org/10.3390/ijerph15102112.
Antwi-Agyei, P., Biran, A., Peasey, A., Bruce, J., Ensink, J., 2016. A faecal exposure assessment of farm workers in Accra, Ghana: a cross sectional study. BMC Publ. Health 16. https://doi.org/10.1186/s12889-016-3266-8.
Arnold, B.F., Null, C., Luby, S.P., Colford, J.M., 2018. Implications of WASH Benefits trials for water and sanitation – authors' reply. Lancet Glob. Health 6, e616–e617. https://doi.org/10.1016/S2214-109X(18)30229-8.
Aziz, K.M.A., Hoque, B.A., Hasan, K.Z., Patwary, M.Y., Huttly, S.R., Rahaman, M.M., Feachem, R.G., 1990. Reduction in diarrhoeal diseases in children in rural Bangladesh by environmental and behavioural modifications. Trans. R. Soc. Trop. Med. Hyg. 84, 433–438.
Bain, R., Cronk, R., Wright, J., Yang, H., Slaymaker, T., Bartram, J., 2014. Fecal contamination of drinking-water in low- and middle-income countries: a systematic review and meta-analysis. PLoS Med. 11 e1001644. https://doi.org/10.1371/journal.pmed.1001644.
Bapat, M., Agarwal, I., 2003. Our needs, our priorities; women and men from the slums in Mumbai and pune talk about their needs for water and sanitation. Environ. Urbanization 15, 71–86. https://doi.org/10.1177/095624780301500221.
Bartram, J., Cairncross, S., 2010. Hygiene, sanitation, and water: forgotten foundations of health. PLoS Med. 7 e1000367. https://doi.org/10.1371/journal.pmed.1000367.
Bauza, V., Byrne, D.M., Trimmer, J.T., Lardizabal, A., Atiim, P., Asigbee, M.A.K., Guest, J.S., 2018. Child soil ingestion in rural Ghana – frequency, caregiver perceptions, relationship with household floor material and associations with child diarrhoea. Trop. Med. Int. Health 23, 558–569. https://doi.org/10.1111/tmi.13050.
Berendes, D., Kirby, A., Clennon, J.A., Raj, S., Yakubu, H., Leon, J., Robb, K., Kartikeyan, A., Hemavathy, P., Gunasekaran, A., Ghale, B., Kumar, J.S., Mohan, V.R., Kang, G., Moe, C., 2017. The influence of household- and community-level sanitation and fecal sludge management on urban fecal contamination in households and drains and enteric infection in children. Am. J. Trop. Med. Hyg. 96, 1404–1414. https://doi.org/10.4269/ajtmh.16-0170.
Berendes, D.M., Kirby, A.E., Clennon, J.A., Agbemabiese, C., Ampofo, J.A., Armah, G.E., Baker, K.K., Liu, P., Reese, H.E., Robb, K.A., Wellington, N., Yakubu, H., Moe, C.L., 2018. Urban sanitation coverage and environmental fecal contamination: links between the household and public environments of Accra, Ghana. PLoS One 13 e0199304. https://doi.org/10.1371/journal.pone.0199304.
Borenstein, M., Hedges, L., Higgins, J.P., Rothstein, H.R., 2009. Chapter 16: identifying and quantifying heterogeneity. Introduction to Meta-analysis. Wiley, pp. 357–364.
Briceño, B., Coville, A., Martinez, S., 2015. Promoting Handwashing and Sanitation: Evidence from a Large-Scale Randomized Trial in Rural Tanzania (No. 7164). Policy Research Working Paper. The World Bank.
Briscoe, J., 1984. Intervention studies and the definition of dominant transmission routes. Am. J. Epidemiol. 120, 449–456.
Cai, L., 2012. Latent variable modeling. Shanghai Arch. Psychiatr. 24, 118–120. https://doi.org/10.3969/j.issn.1002-0829.2012.02.010.
Cameron, L., Chase, C., Joseph, G., Pinto, R., 2017. Child Stunting and Cognitive Impacts of Water, Sanitation and Hygiene in Indonesia (Draft Report).
Chavasse, D., Shier, R., Murphy, O., Huttly, S., Cousens, S., Akhtar, T., 1999. Impact of fly control on childhood diarrhoea in Pakistan: community-randomised trial. Lancet 353, 22–25. https://doi.org/10.1016/S0140-6736(98)03366-2.
Clasen, T., Prüss-Ustün, A., Mathers, C., Cumming, O., Cairncross, S., Colford Jr., J.M., 2014. Estimating the impact of inadequate water, sanitation and hygiene on the global burden of disease: evolving and alternative methods. J. Trop. Med. Int. Health.
Coffey, D., Spears, D., 2018. Implications of WASH Benefits trials for water and sanitation. Lancet Glob. Health 6, e615. https://doi.org/10.1016/S2214-109X(18)30225-0.
Cumming, O., Curtis, V., 2018. Implications of WASH Benefits trials for water and sanitation. Lancet Glob. Health 6, e613–e614. https://doi.org/10.1016/S2214-109X(18)30192-X.
Daniels, M.E., Smith, W.A., Schmidt, W.-P., Clasen, T., Jenkins, M.W., 2016. Modeling Cryptosporidium and giardia in ground and surface water sources in rural India: associations with latrines, livestock, damaged wells, and rainfall patterns. Environ. Sci. Technol. 50, 7498–7507.
Davies, H.T.O., Crombie, I.K., Tavakoli, M., 1998. When can odds ratios mislead? BMJ 316, 989–991.
De Onis, M., Blössner, M., Borghi, E., Morris, R., Frongillo, E.A., 2004. Methodology for estimating regional and global trends of child malnutrition. Int. J. Epidemiol. 33, 1260–1270. https://doi.org/10.1093/ije/dyh202.
Ercumen, A., Pickering, A.J., Kwong, L.H., Arnold, B.F., Parvez, S.M., Alam, M., Sen, D., Islam, S., Kullmann, C., Chase, C., Ahmed, R., Unicomb, L., Luby, S.P., Colford, J.M., 2017. Animal feces contribute to domestic fecal contamination: evidence from E. coli measured in water, hands, food, flies, and soil in Bangladesh. Environ. Sci. Technol. 51, 8725–8734. https://doi.org/10.1021/acs.est.7b01710.
Fewtrell, L., Kaufmann, R.B., Kay, D., Enanoria, W., Haller, L., Colford, J.M., 2005. Water, sanitation, and hygiene interventions to reduce diarrhoea in less developed countries: a systematic review and meta-analysis. Lancet Infect. Dis. 5, 42–52.
Forrer, A., Khieu, V., Schindler, C., Schär, F., Marti, H., Char, M.C., Muth, S., Odermatt, P., 2016. Ivermectin treatment and sanitation effectively reduce strongyloides stercoralis infection risk in rural communities in Cambodia. PLoS Neglected Trop. Dis. 10 e0004909. https://doi.org/10.1371/journal.pntd.0004909.
Freeman, M.C., Garn, J.V., Sclar, G.D., Boisson, S., Medlicott, K., Alexander, K.T., Penakalapati, G., Anderson, D., Mahtani, A.G., Grimes, J.E., 2017. The impact of sanitation on infectious disease and nutritional status: a systematic review and meta-analysis. Int. J. Hyg Environ. Health 220, 928–949.
Fuller, J.A., Eisenberg, J.N., 2016. Herd protection from drinking water, sanitation, and hygiene interventions. Am. J. Trop. Med. Hyg. 95, 1201–1210.
Fuller, J.A., Villamor, E., Cevallos, W., Trostle, J., Eisenberg, J.N., 2016. I get height with a little help from my friends: herd protection from sanitation on child growth in rural Ecuador. Int. J. Epidemiol. 45, 460–469. https://doi.org/10.1093/ije/dyv368.
Garn, J.V., Boisson, S., Willis, R., Bakhtiari, A., al-Khatib, T., Amer, K., Batcho, W., Courtright, P., Dejene, M., Goepogui, A., 2018. Sanitation and water supply coverage thresholds associated with active trachoma: modeling cross-sectional data from 13 countries. PLoS Neglected Trop. Dis. 12 e0006110.
Garn, J.V., Sclar, G.D., Freeman, M.C., Penakalapati, G., Alexander, K.T., Brooks, P., Rehfuess, E.A., Boisson, S., Medlicott, K.O., Clasen, T.F., 2017. The impact of sanitation interventions on latrine coverage and latrine use: a systematic review and meta-analysis. Int. J. Hyg Environ. Health 220, 329–340. https://doi.org/10.1016/j.ijheh.2016.10.001.
Garrett, V., Ogutu, P., Mabonga, P., Ombeki, S., Mwaki, A., Aluoch, G., Phelan, M., Quick, R.E., 2008. Diarrhoea prevention in a high-risk rural Kenyan population through point-of-use chlorination, safe water storage, sanitation, and rainwater harvesting. Epidemiol. Infect. 136, 1463–1471.
GATHER: Guidelines for Accurate and Transparent Health Estimates Reporting [WWW Document], n.d. . Gather Statement. URL http://gather-statement.org/(accessed 4. 16.18).
Gautam, O., 2015. Food Hygiene Intervention to Improve Food Hygiene Behaviours, and Reduce Food Contamination in Nepal: an Exploratory Trial (PhD Thesis). London School of Hygiene & Tropical Medicine.
Gertler, P., Shah, M., Alzua, M., Cameron, L., Martinez, S., Patil, S., 2015. How Does Health Promotion Work? Evidence from the Dirty Business of Eliminating Open Defecation (No. 20997), NBER Working Paper Series. National Bureau of Economic Research.
Geruso, M., Spears, D., 2015. Neighborhood Sanitation and Infant Mortality (No. 21184), NBER Working Paper Series. National Bureau of Economic Research, Cambridge, UK.
Godfrey, S., Van Der Velden, M., Muianga, A., Vigh, M., Gunning, J.W., Elbers, C., 2014. Impact study of the One Million Initiative rural water and sanitation programme in Mozambique. Waterlines 33, 35–44.
Harris, M., Alzua, M.L., Osbert, N., Pickering, A., 2017. Community-level sanitation coverage more strongly associated with child growth and household drinking water quality than access to a private toilet in rural Mali. Environ. Sci. Technol. 51, 7219–7227. https://doi.org/10.1021/acs.est.7b00178.
Higgins, J., Green, S. (Eds.), 2011. Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Collaboration [updated March 2011] Version 5.1.0.
Humphrey, J.H., 2018. Sanitation Hygiene Infant Nutrition Efficacy (SHINE) Trial in Zimbabwe: Rationale, Design, Methods, Intervention Uptake.
ICF International (Ed.), 2012. Demographic and Health Survey Sampling and Household Listing Manual, Measure DHS. ICF International, Calverton, Maryland, U.S.A.
Instituto Brasileiro de Geografia e Estatística, undated. National Household Sample Survey [WWW Document]. URL https://ww2.ibge.gov.br/english/estatistica/populacao/trabalhoerendimento/pnad2013/default.shtm (accessed 6.18.18).
Instituto Nacional de Estadística y censos, 2016. ENEMDU – 2016. In: Inst. Nac. Estad. Censos, . http://www.ecuadorencifras.gob.ec/enemdu-2016/ accessed 6.18.18.
Jung, Y.T., Hum, R.J., Lou, W., Cheng, Y.-L., 2017a. Effects of neighbourhood and household sanitation conditions on diarrhea morbidity: systematic review and meta-analysis. PLoS One 12 e0173808. https://doi.org/10.1371/journal.pone.0173808.
Jung, Y.T., Lou, W., Cheng, Y.-L., 2017b. Exposure-response relationship of neighbourhood sanitation and children's diarrhea. Trop. Med. Int. Health 22, 857–865.
Khush, R., London, A., 2009. Evaluating the Sustainability and Impacts of Water, Sanitation & Hygiene Interventions. Aquaya Institute.
Klasen, S., Lechtenfeld, T., Meier, K., Rieckmann, J., 2012. Benefits Trickling Away: The Health Impact of Extending Access to Piped Water and Sanitation in Urban Yemen (Discussion Papers No. 110). Georg-August-Universität, Göttingen.
Kolsky, P.J., Blumenthal, U.J., 1995. Environmental health indicators and sanitation-related disease in developing countries: limitations to the use of routine data sources. World Health Stat. Q. Rapp. Trimest. Stat. Sanit. Mond. 48, 132–139.
Larsen, D.A., Grisham, T., Slawsky, E., Narine, L., 2017. An individual-level meta-analysis assessing the impact of community-level sanitation access on child stunting, anemia, and diarrhea: evidence from DHS and MICS surveys. PLoS Neglected Trop. Dis. 11 e0005591. https://doi.org/10.1371/journal.pntd.0005591.
Levin, K.A., 2006. Study design III: cross-sectional studies. Evid. Base Dent. 7, 24–25. https://doi.org/10.1038/sj.ebd.6400375.
Luby, S.P., Halder, A.K., Huda, T.M., Unicomb, L., Johnston, R.B., 2011. Using child health outcomes to identify effective measures of handwashing. Am. J. Trop. Med. Hyg. 85, 882–892.
Luby, S.P., Rahman, M., Arnold, B.F., Unicomb, L., Ashraf, S., Winch, P.J., Stewart, C.P., Begum, F., Hussain, F., Benjamin-Chung, J., Leontsini, E., Naser, A.M., Parvez, S.M., Hubbard, A.E., Lin, A., Nizame, F.A., Jannat, K., Ercumen, A., Ram, P.K., Das, K.K., Abedin, J., Clasen, T.F., Dewey, K.G., Fernald, L.C., Null, C., Ahmed, T., Colford, J.M., 2018. Effects of water quality, sanitation, handwashing, and nutritional interventions on diarrhoea and child growth in rural Bangladesh: a cluster randomised controlled trial. Lancet Glob. Health 6, e302–e315. https://doi.org/10.1016/S2214-109X(17)30490-4.
MacQueen, K.M., McLellan, E., Metzger, D.S., Kegeles, S., Strauss, R.P., Scotti, R., Blanchard, L., Trotter, R.T., 2001. What is community? An evidence-based definition for participatory public health. Am. J. Public Health 91, 1929–1938.
McCambridge, J., Witton, J., Elbourne, D.R., 2014. Systematic review of the Hawthorne effect: new concepts are needed to study research participation effects. J. Clin. Epidemiol. 67, 267–277.
Messou, E., Sangaré, S.V., Josseran, R., Le, C.C., Guélain, J., 1997. Effect of hygiene measures, water sanitation and oral rehydration therapy on diarrhea in children less than five years old in the south of Ivory Coast. Bull. Soc. Pathol. Exot. 1990 (90),

44–47.
Moraes, L.R.S., Cancio, J.A., Cairncross, S., Huttly, S., 2003. Impact of drainage and sewerage on diarrhoea in poor urban areas in Salvador, Brazil. Trans. R. Soc. Trop. Med. Hyg. 97, 153–158.
Morita, T., Perin, J., Oldja, L., Biswas, S., Sack, R.B., Ahmed, S., Haque, R., Bhuiyan, N.A., Parvin, T., Bhuyian, S.I., Akter, M., Talukder, K.A., Shahnaij, M., Faruque, A.G., George, C.M., 2017. Mouthing of soil contaminated objects is associated with environmental enteropathy in young children. Trop. Med. Int. Health 22, 670–678. https://doi.org/10.1111/tmi.12869.
Null, C., Stewart, C.P., Pickering, A.J., Dentz, H.N., Arnold, B.F., Arnold, C.D., Benjamin-Chung, J., Clasen, T., Dewey, K.G., Fernald, L.C., 2018. Effects of water quality, sanitation, handwashing, and nutritional interventions on diarrhoea and child growth in rural Kenya: a cluster-randomised controlled trial. Lancet Glob. Health 6, e316–e329.
Odagiri, M., Schriewer, A., Daniels, M.E., Wuertz, S., Smith, W.A., Clasen, T., Schmidt, W.-P., Jin, Y., Torondel, B., Misra, P.R., 2016. Human fecal and pathogen exposure pathways in rural Indian villages and the effect of increased latrine coverage. Water Res. 100, 232–244.
Oswald, W.E., Stewart, A.E.P., Kramer, M.R., Endeshaw, T., Zerihun, M., Melak, B., Sata, E., Gessese, D., Teferi, T., Tadesse, Z., Guadie, B., King, J.D., Emerson, P.M., Callahan, E.K., Freeman, M.C., Flanders, W.D., Clasen, T.F., Moe, C.L., 2017. Association of community sanitation usage with soil-transmitted helminth infections among school-aged children in Amhara Region, Ethiopia. Parasites Vectors 10, 91. https://doi.org/10.1186/s13071-017-2020-0.
Patil, S.R., Arnold, B.F., Salvatore, A.L., Briceño, B., Ganguly, S., Colford, J.M., Gertler, P.J., 2014. The effect of India's total sanitation campaign on defecation behaviors and child health in rural Madhya Pradesh: a cluster randomized controlled trial. PLoS Med. 11, e1001709. https://doi.org/10.1371/journal.pmed.1001709.
Penakalapati, G., Swarthout, J., Delahoy, M.J., McAliley, L., Wodnik, B., Levy, K., Freeman, M.C., 2017. Exposure to animal feces and human health: a systematic review and proposed research priorities. Environ. Sci. Technol. 51, 11537–11552.
Pickering, A.J., Davis, J., 2012. Freshwater availability and water fetching distance affect child health in sub-Saharan Africa. Environ. Sci. Technol. 46, 2391–2397. https://doi.org/10.1021/es203177v.
Pickering, A.J., Djebbari, H., Lopez, C., Coulibaly, M., Alzua, M.L., 2015. Effect of a community-led sanitation intervention on child diarrhoea and child growth in rural Mali: a cluster-randomised controlled trial. Lancet Glob. Health 3, e701–711. https://doi.org/10.1016/S2214-109X(15)00144-8.
Pradhan, M., Rawlings, L.B., 2002. The Impact and Targeting of Social Infrastructure Investments: Lessons from the Nicaraguan Social Fund.
Prüss-Ustün, A., Bos, R., Gore, F., Bartram, J., 2008. Safer Water, Better Health. World Health Organization, Geneva.
Qadir, M., Wichelns, D., Raschid-Sally, L., McCornick, P.G., Drechsel, P., Bahri, A., Minhas, P.S., 2010. The challenges of wastewater irrigation in developing countries. Agric. Water Manag., Compr. Assess. Water Manag. Agric. 97, 561–568. https://doi.org/10.1016/j.agwat.2008.11.004.
Ram, P.K., 2013. Practical Guidance for Measuring Handwashing Behavior: 2013 Update. Water and Sanitation Program.
Ram, P.K., Sahli, M., Arnold, B., Colford, J.M., Chase, C., Briceño, B., Orsola-Vidal, A., Gertler, P., 2014. Global Scaling up Handwashing: Validity of Rapid Measures of Handwashing Behavior: an Analysis of Data from Multiple Impact Evaluations in the Global Scaling up Handwashing Project. Water and Sanitation Program. World Bank Group, Washington.
Reese, H., Routray, P., Torondel, B., Sclar, G.D., Delea, M., Sinharoy, S., Zambrano, L., Caruso, B., Suar, M., Clasen, T., 2018. Effect of a Combined Household-level Piped Water and Sanitation Intervention in Rural Odisha, India on Diarrheal Diseases, Respiratory Infection, Soil-transmitted Helminth Infection, and Undernutrition.
Robb, K., Null, C., Teunis, P., Yakubu, H., Armah, G., Moe, C.L., 2017. Assessment of fecal exposure pathways in low-income urban neighborhoods in Accra, Ghana: rationale, design, methods, and key findings of the SaniPath study. Am. J. Trop. Med. Hyg. 97, 1020–1032.
Rosenboom, J., Ban, R., 2018a. Seeking inputs for "consensus" meeting on sanitation interventions. Sanit. Updat.
Rosenboom, J., Ban, R., 2018b. Sanitation and health: what do we want to know? Sanit. Updat.
Savović, J., Jones, H.E., Altman, D.G., Harris, R.J., Jüni, P., Pildal, J., Als-Nielsen, B., Balk, E.M., Gluud, C., Gluud, L.L., 2012. Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. Ann. Intern. Med. 157, 429–438.
Sclar, G.D., Garn, J.V., Penakalapati, G., Alexander, K.T., Krauss, J., Freeman, M.C., Boisson, S., Medlicott, K.O., Clasen, T., 2017. Effects of sanitation on cognitive development and school absence: a systematic review. Int. J. Hyg Environ. Health 220, 917–927.
Sclar, G.D., Penakalapati, G., Amato, H.K., Garn, J.V., Alexander, K., Freeman, M.C., Boisson, S., Medlicott, K.O., Clasen, T., 2016. Assessing the impact of sanitation on indicators of fecal exposure along principal transmission pathways: a systematic review. Int. J. Hyg Environ. Health 219, 709–723.
StataCorp, 2015. Stata Statistical Software: Release, vol 14.
Statalist - archive, 2009. RE: st: saving svy mean estimates? https://www.stata.com/statalist/archive/2009-04/msg00240.html accessed 6.18.18.
Stevens, G.A., Alkema, L., Black, R.E., Boerma, J.T., Collins, G.S., Ezzati, M., Grove, J.T., Hogan, D.R., Hogan, M.C., Horton, R., 2016. Guidelines for accurate and transparent health estimates reporting: the GATHER statement. PLoS Med. 13 e1002056.
The DHS Program Demographic and health surveys. undated. https://dhsprogram.com/ accessed 6.18.18.
Thompson, S.G., Higgins, J., 2002. How should meta-regression analyses be undertaken and interpreted? Stat. Med. 21, 1559–1573.
UNFPA Nicaragua, 2016. Encuesta Nicaragüense de Demografía y Salud ENDESA 2011 – 2012. Informe final [WWW Document]. http://nicaragua.unfpa.org/es/publicaciones/encuesta-nicarag%C3%BCense-de-demograf%C3%ADa-y-salud-endesa-2011-%E2%80%93-2012-informe-final accessed 6.18.18.
UNICEF, undated. MICS [WWW Document]. URL http://mics.unicef.org/(accessed 6.18.2018).
United Nations, 2018. Goal 6: Ensure Availability and Sustainable Management of Water and Sanitation for All — SDG Indicators. https://unstats.un.org/sdgs/report/2017/Goal-06/, Accessed date: 29 May 2018.
United Nations, n.d. Sustainable Development Goals [WWW Document]. URL http://www.un.org/sustainabledevelopment/sustainable-development-goals/(accessed 10.18.2016).
United Nations Population Division, undated. World Population Prospects 2017 [WWW Document]. URL https://esa.un.org/unpd/wpp/(accessed 10.19.17).
VanDerslice, J., Briscoe, J., 1995. Environmental interventions in developing countries: interactions and their implications. Am. J. Epidemiol. 141, 135–144.
Viechtbauer, W., Cheung, M.W.-L., 2010. Outlier and influence diagnostics for meta-analysis. Res. Synth. Methods 1, 112–125.
Vyas, S., Kov, P., Smets, S., Spears, D., 2016. Disease externalities and net nutrition: evidence from changes in sanitation and child height in Cambodia, 2005–2010. Econ. Hum. Biol. 23, 235–245. https://doi.org/10.1016/j.ehb.2016.10.002.
Walker, I., del Cid, R., Ordoñez, F., Rodríguez, F., 1999. Ex-post Evaluation of the Honduran Social Investment Fund (FHIS 2). World Bank Wash, DC.
Wang, X., Hunter, P.R., 2010. A systematic review and meta-analysis of the association between self-reported diarrheal disease and distance from home to water source. Am. J. Trop. Med. Hyg. 83, 582–584. https://doi.org/10.4269/ajtmh.2010.10-0215.
Water and Sanitation Program, 2015. Scaling up Rural Sanitation and Hygiene. Management of Child Feces: Current Disposal Practices, Research Brief. World Bank Group.
WHO, 2018a. Guidelines on Sanitation and Health. [WWW Document]. WHO. http://www.who.int/water_sanitation_health/sanitation-waste/sanitation/sanitation-guidelines/en/, Accessed date: 23 July 2018.
WHO, 2018b. Annex C: WHO regional groupings. In: World Health Statistics 2018: Monitoring Health for the SDGs. Geneva, pp. 86.
WHO, 2015. Sanitation Safety Planning. Manual for Safe Use and Disposal of Wastewater, Greywater and Excreta. World Health Organization, Geneva.
WHO, n.d. WHO Study on global AGEing and adult health (SAGE) [WWW Document]. URL http://www.who.int/healthinfo/sage/en/(accessed 8.6.18).
WHO, UNICEF, 2017. Progress on Drinking Water, Sanitation and Hygiene: 2017 Update and SDG Baselines. WHO, UNICEF, Geneva.
WHO, UNICEF, undated. Home | JMP [WWW Document]. URL https://washdata.org/(accessed 6.3.18).
Wolf, J., Hunter, P.R., Freeman, M.C., Cumming, O., Clasen, T., Bartram, J., Higgins, J.P.T., Johnston, R., Medlicott, K., Boisson, S., Prüss-Ustün, A., 2018a. Impact of drinking water, sanitation and hand washing with soap on childhood diarrhoeal disease: updated meta-analysis and –regression. Trop. Med. Int. Health 23. https://doi.org/10.1111/tmi.13051.
Wolf, J., Johnston, R., Freeman, M., Ram, P.K., Slaymaker, T., Laurenz, E., Prüss-Ustün, A., 2018b. Handwashing with soap after potential faecal contact: global, regional and country estimates. Int. J. Epidemiol accepted for publication.
World Bank, 2013. Sri Lanka - World Health Survey 2003. WHS 2003) | Data Catalog. https://datacatalog.worldbank.org/dataset/sri-lanka-world-health-survey-2003 accessed 6.18.18.
Yajima, A., Jouquet, P., Do, T.D., Dang, T.C.T., Tran, C.D., Orange, D., Montresor, A., 2009. High latrine coverage is not reducing the prevalence of soil-transmitted helminthiasis in Hoa Binh province, Vietnam. Trans. R. Soc. Trop. Med. Hyg. 103, 237–241. https://doi.org/10.1016/j.trstmh.2008.08.012.
Zambrano, L.D., Levy, K., Menezes, N.P., Freeman, M.C., 2014. Human diarrhea infections associated with domestic animal husbandry: a systematic review and meta-analysis. Trans. R. Soc. Trop. Med. Hyg. 108, 313–325. https://doi.org/10.1093/trstmh/tru056.
Zhang, J., Kai, F.Y., 1998. What's the relative risk?: a method of correcting the odds ratio in cohort studies of common outcomes. Jama 280, 1690–1691.

International Journal of Hygiene and Environmental Health 222 (2019) 765–777

Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.com/locate/ijheh

Burden of disease from inadequate water, sanitation and hygiene for selected adverse health outcomes: An updated analysis with a focus on low- and middle-income countries

Annette Prüss-Ustün[a,*], Jennyfer Wolf[a], Jamie Bartram[b], Thomas Clasen[c], Oliver Cumming[d], Matthew C. Freeman[c], Bruce Gordon[a], Paul R. Hunter[e,f], Kate Medlicott[a], Richard Johnston[a]

[a] Department of Public Health, Environment and Social Determinants of Health, World Health Organization, Geneva, Switzerland
[b] Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
[c] Department of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA
[d] Department of Disease Control, London School of Hygiene and Tropical Medicine, London, UK
[e] The Norwich School of Medicine, University of East Anglia, Norwich, UK
[f] Department of Environmental Health, Tshwane University of Technology, Pretoria, South Africa

ARTICLE INFO

Keywords:
Burden of disease
Comparative risk assessment
Drinking water
Water
Sanitation
Hygiene
Diarrhoea
Hand washing

ABSTRACT

Background: To develop updated estimates in response to new exposure and exposure-response data of the burden of diarrhoea, respiratory infections, malnutrition, schistosomiasis, malaria, soil-transmitted helminth infections and trachoma from exposure to inadequate drinking-water, sanitation and hygiene behaviours (WASH) with a focus on low- and middle-income countries.

Methods: For each of the analysed diseases, exposure levels with both sufficient global exposure data for 2016 and a matching exposure-response relationship were combined into population-attributable fractions. Attributable deaths and disability-adjusted life years (DALYs) were estimated for each disease and, for most of the diseases, by country, age and sex group separately for inadequate water, sanitation and hygiene behaviours and for the cluster of risk factors. Uncertainty estimates were computed on the basis of uncertainty surrounding exposure estimates and relative risks.

Findings: An estimated 829,000 WASH-attributable deaths and 49.8 million DALYs occurred from diarrhoeal diseases in 2016, equivalent to 60% of all diarrhoeal deaths. In children under 5 years, 297,000 WASH-attributable diarrhoea deaths occurred, representing 5.3% of all deaths in this age group. If the global disease burden from different diseases and several counterfactual exposure distributions was combined it would amount to 1.6 million deaths, representing 2.8% of all deaths, and 104.6 million DALYs in 2016.

Conclusions: Despite recent declines in attributable mortality, inadequate WASH remains an important determinant of global disease burden, especially among young children. These estimates contribute to global monitoring such as for the Sustainable Development Goal indicator on mortality from inadequate WASH.

1. Introduction

Global burden of disease assessments are important to identify priorities for improving population health and tracking changes in the relative importance of different diseases, injuries and risk factors (Murray and Lopez, 2013). The burden of disease from inadequate drinking water, sanitation and hygiene behaviours (WASH) has been estimated at various times in previous decades (Forouzanfar et al., 2016, 2015; Gakidou et al., 2017; Lim et al., 2012; Murray and Lopez, 1996; Prüss-Ustün et al., 2014, 2008; Stanaway et al., 2018; WHO, 2004, 2002); inadequate drinking water as used in this work includes unsafe water and water with insufficient access. While some of these

Abbreviations: CRA, comparative risk assessment; DALYs, disability-adjusted life years; HICs, high-income countries; JMP, WHO/UNICEF Joint Monitoring Programme for Water Supply, Sanitation and Hygiene; LMICs, low- and middle-income countries; WASH, water, sanitation and hygiene behaviours

* Corresponding author. Department of Public Health, Environment and Social Determinants of Health, World Health Organization, 20 Avenue Appia, Geneva, Switzerland.

E-mail addresses: pruessa@who.int (A. Prüss-Ustün), jennyfer.wolf@gmail.com, wolfj@who.int (J. Wolf), jbartram@email.unc.edu (J. Bartram), thomas.f.clasen@emory.edu (T. Clasen), Oliver.Cumming@lshtm.ac.uk (O. Cumming), matthew.freeman@emory.edu (M.C. Freeman), gordonb@who.int (B. Gordon), paul.hunter@uea.ac.uk (P.R. Hunter), medlicottk@who.int (K. Medlicott), johnstonr@who.int (R. Johnston).

https://doi.org/10.1016/j.ijheh.2019.05.004
Received 21 December 2018; Received in revised form 3 May 2019; Accepted 3 May 2019
1438-4639/ © 2019 World Health Organization; licensee Elsevier. This is an open access article under the CC BY 3.0 license (http://creativecommons.org/licenses/BY 3.0/IGO/).

Table 1
Adverse health outcomes that are at least partly attributable to inadequate water, sanitation and hygiene behaviours.

Global WASH-attributable disease burden not quantified	Global WASH-attributable disease burden estimates available	
Health outcomes	Health outcomes	Main WASH exposure
Arsenicosis	**Ascariasis**	sanitation
Cyanobacterial toxins	Cancer (bladder)	drinking water
Fluorosis	Dengue	water resource management/water bodies
Hepatitis A, E	**Diarrhoeal diseases**	drinking water, sanitation, hygiene behaviours*
Lead poisonings	Drowning[d]	recreational water/water bodies
Legionellosis	**Hookworm disease**[a]	Sanitation
Leptospirosis	Japanese Encephalitis	water resource management/agricultural practices
Methaemoglobinaemia	Lymphatic filariasis	water resource management/water bodies
Neonatal conditions and maternal outcomes	**Malaria**[d]	water resource management/water bodies
Poliomyelitis	Musculoskeletal diseases	drinking water
Scabies	Onchocerciasis	water resource management
Spinal injury	**Protein-energy malnutrition**[a,b,c]	drinking water, sanitation, hygiene behaviours*
	Respiratory infections[c]	hygiene behaviours*
	Schistosomiasis[a,b,c,d]	drinking water, sanitation, hygiene behaviours*, water resource management/ agricultural practices/recreational water
	Trachoma[a,c]	sanitation, hygiene behaviours*
	Trichuriasis[a]	Sanitation

The listed diseases are based on prior work (Prüss-Ustün et al., 2016, 2008). Health outcomes quantified in this article are written in bold. *hygiene behaviours include hand hygiene(diarrhoeal diseases, protein-energy malnutrition, trachoma), face hygiene (trachoma), food hygiene (hookworm) and bathing (schistosomiasis).

assessments focused on diarrhoeal disease (Forouzanfar et al., 2015; Lim et al., 2012; Murray and Lopez, 1996; Prüss-Ustün et al., 2014; WHO, 2002) others also assessed the WASH-attributable disease burden of other health outcomes such as soil-transmitted helminth infections, malaria, trachoma, schistosomiasis, lymphatic filariasis, lower respiratory infections, and protein energy malnutrition (Forouzanfar et al., 2016; Gakidou et al., 2017; Prüss-Ustün et al., 2008; Stanaway et al., 2018; WHO, 2004). These assessments present very different burden of disease estimates because of differences in methods used, scope of the estimates, and ongoing improvements in WASH in many regions (Clasen et al., 2014).

Despite improvements, inadequate WASH remains a major global risk factor: In 2015, 844 million people lacked a basic drinking water service, i.e., a drinking water source protected from recontamination within 30 min' round-trip to collect water, and nearly 30% of the global population did not use a safely managed drinking water service—a drinking water source located on premises, available when needed and free from contamination (WHO and UNICEF, 2017). In terms of access to sanitation, 2.3 billion people were lacking a basic sanitation service—an improved sanitation facility that is not shared with other households—and more than 60% were not using a safely managed sanitation service—a sanitation facility that safely disposes excreta in-situ or that ensures that excreta are safely treated off-site (WHO and UNICEF, 2017). Estimates suggest that one in four persons worldwide does not have access to a handwashing facility with soap and water on premises and that only 26% of potential faecal contacts are followed by handwashing with soap (Wolf et al., 2018b). Furthermore, only 45% of the population live in communities in which coverage with basic sanitation services is above 75% (Wolf et al., 2018c).

The objective of this paper is to present updated WASH-attributable burden of diarrhoeal disease estimates for the year 2016 and to add the WASH-attributable burden of further selected adverse health outcomes including respiratory infections, malnutrition, schistosomiasis, malaria, soil-transmitted helminth infections and trachoma. It needs to be acknowledged that – depending on the available evidence - not all estimates are based on the same level of evidence, use different counterfactual exposure distributions and apply different assumptions. To reduce this disease burden from a broad range of diseases, very different intervention strategies would be required which are further outlined below. This paper provides the basis for reporting on Sustainable Development Goal indicator (3.9.2) on WASH-attributable mortality (United Nations, 2018).

2. Methods

2.1. Framework for estimation

"Inadequate WASH" as used in this article spans a range of WASH services, behaviours and related risks for specific health outcomes, including, amongst others, drinking water, sanitation and hygiene (e.g., diarrhoea, protein-energy malnutrition), and water resources management (e.g., malaria). Sanitation and drinking water services, and presence of a handwashing facility with soap and water on premises are defined following the WHO/UNICEF Joint Monitoring Programme for Water Supply, Sanitation and Hygiene (JMP)(WHO and UNICEF, undated). Table 1 presents a list of adverse health outcomes that can at least partly be attributed to inadequate WASH and whether this relation has previously been quantified. Some of the outcomes from Table 1 for which global WASH-attributable disease burden estimates are available (right column) are not included in this analysis as high quality evidence on the exposure-response relationship is lacking.

This disease burden assessment for the year 2016 preferably includes adverse health outcomes for which the WASH-attributable fraction of disease burden can be estimated using comparative risk assessment (CRA, respective diseases are diarrhoea, ARI and schistosomiasis). CRAs are based on detailed, i.e., by level of exposure, age group and sex, exposure and exposure-response information (Ezzati et al., 2002; WHO, 2004). In addition, we present WASH-attributable disease burden estimates from other health outcomes for which sufficient exposure and exposure-response data was available but which are based on weaker evidence, more assumptions and different counterfactual exposure distributions (malnutrition, malaria, soil-transmitted helminth infections and trachoma). WASH-attributable burden of disease estimates were calculated for 132 low- and middle-income countries as the available epidemiological evidence originates mainly from these settings. For diarrhoea (only for hygiene as risk factor) and acute respiratory infections, estimates were calculated for 183 low-, middle- and high-income countries. Countries are WHO Member States with income levels defined by the World Bank for 2016 (World Bank, 2016) which were grouped into the six WHO Regions (Sub-Saharan Africa, America, Eastern Mediterranean, Europe, South-East Asia, and Western Pacific (WHO, 2017a)). Data on total deaths and disability-adjusted life years (DALYs) by disease or condition were taken from the WHO Global Health Observatory for the year 2016 (WHO, 2018a). These data are publicly available and can be assessed from the following website (WHO, 2018b).

2.2. Population attributable fractions of disease for individual risk factors and for the cluster of risks

Disease burden attributable to a risk factor is estimated using the population attributable fraction (PAF) which is the proportion of disease or death that could be prevented if exposures were reduced to an alternative or counterfactual scenario, while other conditions remain unchanged (Ezzati et al., 2002; WHO, 2004). The calculation of the PAF requires the proportion of the population exposed to the different levels of the risk factor and the corresponding exposure-response relationship (Vander Hoorn et al., 2004):

$$PAF = \frac{\sum_{j=1}^{n} p_j\,(RR_j - 1)}{\sum_{j=1}^{n} p_j(RR_j - 1) + 1} \quad (1)$$

where p_j is the proportion of the population exposed at exposure level j, RR_j is the relative risk at exposure level j and n is the total number of exposure levels.

Exposure levels of drinking water, sanitation and hygiene are related by similar mechanisms and policy interventions. The following formula has been proposed for the estimation of burden attributable to a interlinked cluster of risk factors (Lim et al., 2012) (relevant for the diarrhoea and schistosomiasis burden):

$$PAF = 1 - \prod_{r=1}^{R} (1 - PAF_r) \quad (2)$$

where r is the individual risk factor, and R the total number of risk factors accounted for in the cluster.

2.3. Choice of counterfactual exposure levels for WASH-attributable disease burden estimation

The counterfactual exposure distribution can be defined in various ways including the theoretical, the plausible, the feasible and the cost-effective minimum risk exposure distributions (Murray et al., 2003). The theoretical minimum risk exposure distribution refers to the exposure level with the lowest population health risk, irrespective of whether this level is currently attainable in practice. The plausible minimum risk exposure distribution refers to a level which is imaginable without necessarily being likely or feasible in the near future. The feasible minimum risk exposure distribution is a level that has been observed in some population and the cost-effective minimum risk exposure distribution considers the costs of exposure reduction for choosing the alternative exposure scenario (Murray et al., 2003).

Depending on the type and quality of the available evidence, we chose different definitions of the counterfactual exposure distribution for the various adverse health outcomes included in this analysis (Table 2). For WASH-attributable diarrhoeal disease burden estimation, we applied the plausible minimum risk exposure distribution which includes that all the population boils and filters their drinking water and prevents recontamination, lives in a community in which coverage with basic sanitation services exceeds 75% and practices handwashing with soap after potential faecal contact. The WASH-attributable burden of malnutrition estimates are based on the diarrhoea estimates using a pooled analysis of the fraction of stunting attributable to repeated diarrhoea episodes (Checkley et al., 2008). We also used the plausible minimum risk exposure distribution for the hygiene-attributable disease burden of acute respiratory infections. For trachoma and soil-transmitted helminth infections, we used the theoretical minimum risk exposure distribution and assume that the burden of these diseases could be completely prevented through adequate WASH, based on current knowledge on disease transmission which basically occurs through inadequate sanitation and hygiene. The theoretical minimum risk

Table 2
Information on counterfactual, outcome association and potential for bias by health outcome.

health outcome	WASH counterfactual exposure definition	prevalence of WASH counterfactual exposure in 2016	RR for/association between WASH counterfactual exposure and outcome# (against lowest level of exposure, e.g., unimproved WASH)	counterfactual definition used	potential for bias
diarrhoea	water: household water treatment using filtering or boiling	33.1% (WHO and UNICEF, undated)	RR 0.52 (0.35, 0.77)* (Wolf et al., 2018a)	plausible minimum risk	predominately non-blinded intervention studies but bias-adjustment performed
	sanitation: basic sanitation in a community > 75% sanitation coverage	45.3% (Wolf et al., 2018c)	RR 0.55 (0.34, 0.91) (Wolf et al., 2018a)		
	hygiene: handwashing with soap after potential faecal contact	26.2% (Wolf et al., 2018b)	RR 0.86 (0.35, 2.07)* (Wolf et al., 2018a)		
acute respiratory infections	hygiene: handwashing with soap after potential faecal contact	26.2% (Wolf et al., 2018b)	RR 0.84 (0.79, 0.89) (Rabie and Curtis, 2006)	plausible minimum risk	predominantly non-blinded intervention studies
protein-energy malnutrition	*same as for diarrhoea*	*same as for diarrhoea*	combining the PAF for stunting attributable to diarrhoea (25% (8%, 38%)) (Checkley et al., 2008) with the PAF of WASH-attributable diarrhoeal disease (60% (54%, 65%))	*same as for diarrhoea*	includes only WASH-attributable burden via diarrhoea, only stunting is considered as indicator for malnutrition
schistosomiasis	basic drinking water and basic sanitation services	basic drinking water: 87.2%; basic sanitation: 62.0% (WHO and UNICEF, undated)	basic drinking water: RR 0.53 (0.47, 0.61) (Grimes et al., 2014); basic sanitation: RR 0.65 (0.54, 0.78) (Freeman et al., 2017)	feasible minimum risk	RR estimates from observational studies only
malaria	safe water resource management	0% (Keiser et al., 2005)	RR 0.21 (0.13–0.33) (Keiser et al., 2005)	theoretical minimum risk	disease burden estimates based on stronger assumptions
soil-transmitted helminth infections	safely managed water and safely managed sanitation services, essential hygiene conditions and essential hygiene practices	NA	RR 0	theoretical minimum risk	disease burden estimates based on stronger assumptions
trachoma	safely managed water and safely managed sanitation services, essential hygiene conditions and essential hygiene practices	NA	RR 0	theoretical minimum risk	disease burden estimates based on stronger assumptions

RR: relative risk, NA: not applicable, # separate RR for water, sanitation and hygiene are combined using equation (2), * adjusted for potential non-blinding bias.

exposure distribution is approximated here as all the population using safely managed drinking water, i.e., a basic drinking water service accessible on premises, available when needed and free from contamination, safely managed sanitation, i.e., a basic sanitation service that safely disposes excreta in-situ or that ensures that excreta are safely treated off-site, and all the population having access to essential hygiene conditions and performing essential hygiene practices that help maintain health and prevent the spread of disease, including hand- and facewashing, menstrual hygiene management and food hygiene (WHO and UNICEF, undated). Also for the WASH-attributable malaria burden estimates, we used the theoretical minimum risk exposure distribution of all the population being exposed to safe water resource management for which a corresponding exposure-response relationship from meta-analysis is available (Keiser et al., 2005). For the WASH-attributable schistosomiasis disease burden estimation, the applied counterfactual is equivalent to a feasible minimum risk exposure distribution which is access to basic drinking water and sanitation services. This is again due to the available matching exposure-response relationships for these exposures (Freeman et al., 2017; Grimes et al., 2014).

2.4. Estimation of burden of disease attributable to inadequate WASH

The burden of disease attributable to each risk factor (AB), or to the cluster of risk factors, in deaths or DALYs, was obtained by multiplying the PAF by the total burden of each respective disease (B):

$$AB = PAF \text{ x } B \quad (3)$$

The PAFs were applied equally to burden of disease in deaths and DALYs and we assumed that the WASH-attributable case fatality was the same as the mean case fatality of the respective diseases.

2.5. Uncertainty estimates

To estimate uncertainty intervals, we developed a Monte Carlo simulation of the results with 5000 draws of the exposure distribution, and of the relative risks. As lower and upper uncertainty estimates we used the 2.5 and 97.5 percentiles of the PAFs, attributable deaths and DALYs resulting from the Monte Carlo analysis. Uncertainty estimates were calculated using @RISK-software, version 6 (@RISK, n.d.).

We are following guidelines for accurate and transparent health estimates reporting (GATHER)("GATHER: Guidelines for Accurate and Transparent Health Estimates Reporting," n.d.; Stevens et al., 2016) and have included a GATHER-checklist as a Supplementary File (S3).

2.6. The WASH-attributable burden of diarrhoeal disease

2.6.1. Adjustment for non-blinding bias of interventions for exposure-response estimation

Open trials – that is where participants are not blinded to their allocation – which use subjective outcome measures, such as self-reported diarrhoea, are at high risk of bias (Savović et al., 2012; Wood et al., 2008). Exposure-response relationships linking point-of-use drinking water or hygiene interventions and diarrhoea were therefore bias-adjusted based on empirical evidence (Savović et al., 2012)(Tables S1 and S2 in the Supplementary File 1) using a previously published method (Wolf et al., 2018a, 2014). These two types of WASH interventions were chosen for bias adjustment as these interventions usually aim exclusively to improve health which is apparent to the recipient. A detailed description of this approach can also be found in the Supplementary File S1. We present WASH-attributable diarrhoeal disease burden as bias-adjusted estimates in the main text and additionally as non-adjusted estimates in the Supplementary File S1, Tables S3–S5, to show the magnitude of this adjustment and for comparability with other burden of disease assessments.

Drinking water

Fig. 1 shows drinking water exposure levels and Tables 2 and S1 (Supplementary File 1) show matching exposure-response relationships used for WASH-attributable burden of diarrhoeal disease estimation.

Exposure estimates: Data on the relevant exposure levels was available through country-representative household surveys and censuses reported by the JMP (WHO and UNICEF, undated). Estimates for the year 2016 were derived using multilevel modeling (Wolf et al., 2013) of about 1400 data points for each of the different categories of drinking water supply and about 130 data points for each of the different categories of household water treatment. Exposure estimates for the different levels of drinking water relevant for burden of disease calculation are available by country as a Supplementary File (S2).

Exposure-response relationship: As the evidence on additional improvements – such as improvements in water quality and availability - on piped water to premises remains limited, we chose household water filtering or boiling with prevention of recontamination as the counterfactual exposure level. Corresponding exposure-response relationships were taken from the most recent meta-analysis (Wolf et al., 2018a). (Tables 2 and S1 in the Supplementary File 1)

Sanitation

Fig. 2 shows sanitation exposure levels. Tables 2 and S2 (Supplementary File 1) shows the matching exposure-response relationship used for WASH-attributable burden of diarrhoeal disease estimation.

Exposure estimates: Sanitation exposure data was available from the JMP (WHO and UNICEF, undated). Exposure estimates of access to basic sanitation services in a community with greater than 75% coverage with basic sanitation services is based on an analysis of survey data at cluster-level (Wolf et al., 2018c). Exposure estimates for the different levels of sanitation relevant for burden of disease calculation are available by country as a Supplementary File (S2).

Exposure-response relationship: New evidence has recently emerged on additional benefits on diarrhoeal disease from safe sanitation when people live in communities with high sanitation coverage (e.g., (Fuller and Eisenberg, 2016; Jung et al., 2017b, 2017a)). This has led to using basic sanitation services in a community in which more than 75% of people are covered with basic sanitation services as the counterfactual exposure scenario. The choice of the cut-off at 75% sanitation coverage is based on prior sanitation intervention studies which found increased diarrhoea reductions after that point (Wolf et al., 2018c, 2018a).

As a sensitivity analysis, we included the recently published results of four WASH intervention studies (Humphrey et al., 2019; Luby et al., 2018; Null et al., 2018; Reese et al., 2018) in the calculation of the exposure-response relationship between inadequate sanitation and diarrhoeal disease. Results of these studies had not been published at the time of the systematic review and meta-analysis that provided the exposure-response relationships for this burden of disease assessment (Wolf et al., 2018a).

Hygiene

Fig. 2 shows hygiene exposure levels and Tables 2 and S2 (Supplementary File 1) show matching exposure-response relationships used for burden of disease estimation.

Exposure estimates: Exposure estimates are based on "having a handwashing facility with soap and water on premises", i.e., a basic handwashing facility (WHO and UNICEF, 2018a), and are available through country-representative household surveys such as Demographic Health Surveys and Multiple Indicator Cluster Surveys through the JMP (WHO and UNICEF, undated). Because access to a basic handwashing facility would overestimate actual handwashing practices, this proxy indicator has been converted to actual handwashing with soap prevalence based on an analysis of the association between presence of a basic handwashing facility and observed handwashing with soap (Wolf et al., 2018b). Exposure estimates for handwashing with soap after potential faecal contact are available by country as a Supplementary File (S2).

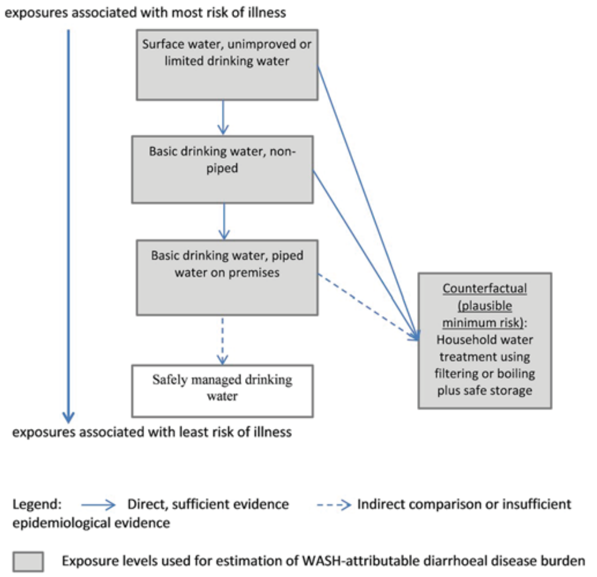


Fig. 1. Exposure levels for drinking water-related burden of diarrhoeal disease estimates.
Note: these exposure levels are used for the WASH-attributable burden of diarrhoeal disease assessment, exposure levels used for the assessment of other diseases vary. "limited", "unimproved" and "basic" facilities and services follow definitions of the WHO/UNICEF Joint Monitoring Programme for Water Supply, Sanitation and Hygiene (JMP) (WHO and UNICEF, undated). "Counterfactual" signifies the counterfactual exposure distribution used for the diarrhoeal disease assessment and presents the plausible minimum exposure distribution. The theoretical minimum risk exposure distribution (which is not used for this analysis) would be "safely managed drinking water". The length of the different arrows in not intended to quantify differences in disease risk.

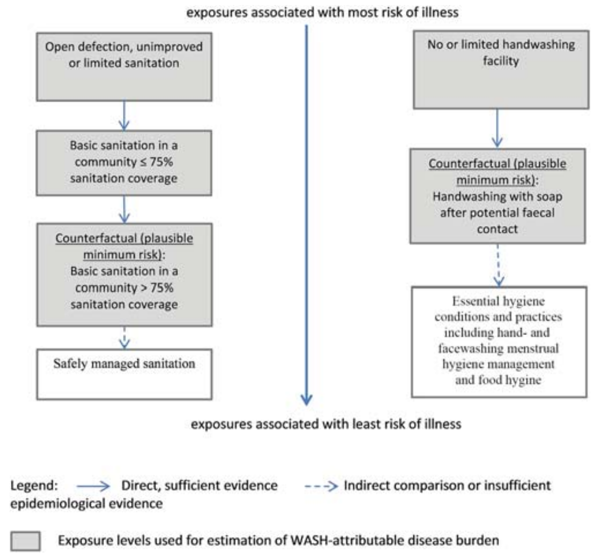


Fig. 2. Exposure levels for sanitation-related (left) and hygiene-related (right) burden of disease estimates.
Note: these exposure levels are used for the WASH-attributable burden of diarrhoeal disease and – for hygiene - acute respiratory infections assessment, exposure levels used for burden of disease estimation of other diseases vary. "limited", "unimproved" and "basic" facilities and services follow definitions of the WHO/UNICEF Joint Monitoring Programme for Water Supply, Sanitation and Hygiene (JMP) (WHO and UNICEF, undated). "Counterfactual" signifies the counterfactual exposure distribution used for the diarrhoeal disease and respiratory infections assessment and presents the plausible minimum exposure distribution. The theoretical minimum risk exposure distribution (which is not used for the diarrhoea and respiratory infections analysis) would be "Safely managed sanitation" and "Essential hygiene conditions and practices including hand- and facewashing, menstrual hygiene management and food hygiene". The length of the different arrows in not intended to quantify differences in disease risk.

Exposure-response relationship: The relative risk from a recent systematic review and meta-analysis of WASH intervention studies and diarrhoeal disease (Wolf et al., 2018a) associated with the sub-group of studies focusing on "handwashing promotion" matched best the exposure and was therefore taken for burden of disease calculation.

2.7. The WASH-attributable burden of further selected health outcomes

2.7.1. Acute respiratory infections

Hands act frequently as carriers for respiratory pathogens which can enter the body via hand-to-face contact (Warren-Gash et al., 2013). In addition, some forms of respiratory viral disease are transmitted via the faecal-oral route (Rabie and Curtis, 2006).

Exposure estimates: Only inappropriate hygiene is considered as risk factor for acute respiratory infections. The same hygiene exposure data as for the analysis of the WASH-attributable diarrhoeal disease burden were taken (handwashing with soap after potential faecal contact derived from access to a handwashing facility with soap and water (Wolf et al., 2018b)).

Exposure-response relationship: The relative risk of 0.84 for washing hands with soap and respiratory infections is based on a meta-analysis of seven intervention studies in high-income countries (HICs) (Rabie and Curtis, 2006) which is similar to a more recent pooled estimate from low- and middle-income countries (LMICs) based on only three studies (Mbakaya et al., 2017). Only one of the seven hand-hygiene intervention studies was blinded and used a placebo hand-sanitizer in the control group (White et al., 2001).

2.7.2. Protein-energy malnutrition

Inadequate WASH can be linked to nutritional status via diarrhoea, environmental enteropathy, (subclinical) enteropathogen infections and soil-transmitted helminth infections (Dangour et al., 2013; MAL-ED Network Investigators, 2017; Schnee et al., 2018).

Exposure estimates: As the WASH-attributable malnutrition estimates are based on the WASH-attributable diarrhoea estimates, the same exposure levels are used as for the WASH-attributable diarrhoeal disease burden estimation.

Exposure-response relationship: A pooled analysis of nine prospective datasets from five countries estimated that 25% of stunting could be attributed to repeated diarrhoea episodes in children (Checkley et al., 2008). This estimate is combined with the fraction of WASH-attributable diarrhoeal disease burden in children under five to estimate the fraction of the WASH-attributable malnutrition burden.

As a sensitivity analysis, disease burden of protein-energy malnutrition was calculated using diarrhoea estimates that were not adjusted for non-blinding bias.

2.7.3. Schistosomiasis

Schistosomiasis can occur when people contact water containing certain aquatic snails that have been infested with parasitic worms; these worms have a human life cycle and are discharged through human excreta (WHO, 2018c).

Exposure estimates: The relevant exposure levels for the analysis of the WASH-attributable schistosomiasis burden were use of basic drinking water and sanitation services and surface, unimproved or limited drinking water and open defecation, unimproved or limited sanitation. Data on these exposures were available through the JMP

(WHO and UNICEF, undated) with estimates derived for 2016 as described for diarrhoea (Wolf et al., 2013)(Supplementary File S2).

Exposure-response relationship: The pooled relative risk from meta-analysis of 0.53 (0.47, 0.61) links access to basic drinking water services versus surface, unimproved or limited drinking water (Grimes et al., 2014). The pooled relative risk of 0.65 (0.54, 0.78) for sanitation links basic sanitation services and open defecation, unimproved or limited sanitation and is the mean relative risk combining the association between sanitation and *Schistosoma mansoni* and *S. haematobium* weighted by the precision of the estimates (Freeman et al., 2017). These relative risks include data from observational studies only (cross-sectional and case-control design).

As a sensitivity analysis we calculated the WASH-attributable schistosomiasis burden using a population attributable fraction (PAF) of 82% as previously estimated through an expert survey (Prüss-Ustün et al., 2016). This 82% relates to the fraction of schistosomiasis that was assumed to be preventable through adequate WASH while it was acknowledged that probably 100% of schistosomiasis burden could be attributed to environmental risks (Prüss-Ustün et al., 2016).

2.7.4. Malaria

Environmental management in malaria prevention often includes water resource management - for example, the installation, cleaning and maintenance of drains, the systematic elimination of standing water pools, the siting of settlements away from vector breeding sites (dry-belting) - but also measures applied to the human habitat such as mosquito-proofing of houses (Keiser et al., 2005).

Exposure estimates: Globally, very limited water resource management have been undertaken and environmental management interventions almost disappeared when dichlorodiethyltrichloroethane (DDT) appeared (Keiser et al., 2005). Therefore the relevant exposure levels are universally implemented safe water resource management as theoretical minimum risk exposure distribution versus no safe water resource management.

Exposure-response relationship: The exposure-response relationship is taken from a meta-analysis of the relation between environmental management and malaria occurrence (Keiser et al., 2005). We chose the more conservative – in terms of the size of the relative risk estimate - approach which was based on stronger evidence, and selected an exposure-response relationship (risk ratio) of 0.21 (0.13–0.33) for modification of human habitation – as compared to 0.12 (0.08, 0.18) for environmental modification.

As a sensitivity analysis we calculated the WASH-attributable malaria burden using previously estimated regional PAFs that were based on expert opinion (Prüss-Ustün et al., 2016).

2.7.5. Soil-transmitted helminth infections

This assessment includes the most predominant soil-transmitted helminths – *Ascaris lumbricoides*, *Trichuris trichiura* and the hookworms. Transmission occurs uniquely through the release of nematode eggs in human excreta from infected individuals into the environment. After the release from the human body, the eggs need to mature for about three weeks to become infective. Susceptible individuals are infected via ingestion of these eggs or penetration of their skin by, or direct ingestion of, the larvae. Also re-infection only occurs due to contact with infective stages in the environment (WHO, 2018d). It is therefore assumed that infections with soil-transmitted helminths would completely cease in case the theoretical minimum exposure level – universal use of safely managed water and safely managed sanitation services, universal access to essential hygiene conditions and universal practice of essential hygiene - would be achieved. The total disease burden from infections with soil-transmitted helminths was therefore entirely attributed to inadequate WASH (Prüss-Ustün et al., 2016).

2.7.6. Trachoma

Trachoma is transmitted via personal contact (e.g., via hands and clothes) and by flies that have been in contact with the discharge of the eyes or the nose of an infected person (WHO, 2018e). It is assumed that through safe disposal of faeces and especially hygiene (face- and handwashing and cleaning of clothes) transmission of trachoma would cease which is also supported through historical evidence (Hu et al., 2010; Mohammadpour et al., 2016). The overall disease burden from trachoma was therefore assumed to be fully attributable to inadequate WASH (Prüss-Ustün et al., 2016). For trachoma, we used the same theoretical minimum exposure level as for soil-transmitted helminths of universal safely managed drinking water, safely managed sanitation, essential hygiene conditions and hygiene practices.

3. Results

3.1. Exposure estimates

The relevant exposures for WASH-attributable disease burden estimation include access to services and WASH-related behaviours. Water resource management is the relevant exposure for WASH-attributable burden of malaria estimation. In LMICs, 58% of the population used piped water on premises; 30% used a non-piped basic water service; and 13% used surface, unimproved or limited drinking water in 2016 (Table 3). 33% of the population reported boiling or filtering their water. In LMICs, 62% used basic sanitation services and 45% of the population lived in communities with basic sanitation coverage above 75% (Table 4). Worldwide, 74% of the population had access to a basic handwashing facility, 70% in LMICs and 95% in HICs. This resulted in 26% of the global population, 22% in LMICs and 51% in HICs, washing hands with soap after potential faecal contact (Table 5).

3.2. Estimates of the WASH-attributable burden of diarrhoeal disease

The total number of diarrhoeal deaths in 2016 was 1.4 million (WHO, 2018f). Of those, 485,000 deaths were attributable to inadequate water, 432,000 to inadequate sanitation and 165,000 to inadequate hygiene behaviours after adjusting for the likely effect of non-blinding bias (Tables 6–9). Inadequate WASH together caused 829,000 diarrhoeal deaths which correspond to about 60% of total diarrhoeal deaths in 2016 that would have been preventable through improving drinking water and sanitation services and handwashing with soap.

In children under five years of age, 477,000 diarrhoeal deaths occurred in 2016. Of those 297,000 or 62.2% (adjusted for non-blinding bias) were attributable to inadequate WASH.

Not adjusting the disease burden estimates for non-blinding bias resulted in a total of 1,025,000 deaths which correspond to 74% of total diarrhoeal deaths and 1.8% of all deaths being attributable to inadequate WASH in 2016 (Supplementary File S1, Tables S3–S5).

Inclusion of the results of four additional WASH interventions (Humphrey et al., 2019; Luby et al., 2018; Null et al., 2018; Reese et al., 2018) published after we conducted the systematic review and meta-analysis on WASH interventions and diarrhoeal disease (Wolf et al., 2018a), changed the exposure-response relationship for basic sanitation in low-coverage communities to 0.82 (0.63, 1.06) and in high coverage communities to 0.58 (0.40, 0.84) as compared to 0.76 (0.51, 1.13) and 0.55 (0.34, 0.91) for low- and high-coverage communities respectively without these four studies (Tables 2 and S2 in the Supplementary File 1). This resulted in a reduction of diarrhoeal deaths attributable to inadequate sanitation from 432,000 to 396,000.

3.3. Estimates of the WASH-attributable burden of other adverse health outcomes

3.3.1. Acute respiratory infections

Thirteen percent of the overall disease burden of acute respiratory infections was attributable to inadequate handwashing with soap which amounted to 370,000 deaths in 2016 (Table 10). WASH-attributable disease burden from acute respiratory infections by region is given in Table S6 in the Supplementary File 1.

3.3.2. Protein-energy malnutrition

Combining the fraction of diarrhoeal disease burden attributed to inadequate WASH in children below five years of age (adjusted estimate) with the estimate of 25% of stunting attributable to repeated diarrhoea episodes by country (Checkley et al., 2008) resulted in the attribution of 16% of malnutrition to inadequate water, sanitation and hygiene for 2016 (Table 10). These estimates do not include the consequences of protein-energy malnutrition on other diseases and associated mortality. WASH-attributable disease burden from protein-energy malnutrition by region is given in Table S7 in the Supplementary File 1.

Using non-adjusted diarrhoea estimates to calculate the WASH-attributable protein-energy malnutrition burden resulted in the attribution of 20% of malnutrition to inadequate WASH and in 34,000 WASH-attributable deaths in children below five years of age (Supplementary File S1, Table S8).

3.3.3. Schistosomiasis

Using the available exposure and exposure-response information, it is estimated that 43% or 10,400 deaths could have been prevented by improving drinking water and sanitation services in 2016 (Table 10). Inadequate drinking water is responsible for 5700 deaths and inadequate sanitation for 6300 deaths. WASH-attributable disease burden from schistosomiasis by region is given in Table S9 in the Supplementary File 1.

The sensitivity analysis using the previously estimated PAF of 82% based on expert survey (Prüss-Ustün et al., 2016) would result in about 20,000 WASH-attributable Schistosomiasis deaths.

3.3.4. Malaria

It is estimated that 80% of malaria was attributable to non-existent water resource management which resulted in 355,000 WASH-attributable malaria deaths in 2016 (Table 10).

A sensitivity analysis using previously estimated regional PAFs for malaria that were based on expert survey (Prüss-Ustün et al., 2016) resulted in 187,000 WASH-attributable malaria deaths in 2016.

3.3.5. Soil-transmitted helminth infections and trachoma

Assuming 100% of soil-transmitted helminth infections and trachoma cases are attributable to inadequate WASH, over 6000 deaths could have been prevented in 2016 through safely managed water and sanitation, access to essential hygiene conditions and practice of essential hygiene behaviours (Table 10).

WASH-attributable disease burden estimates (in deaths and DALYs) by country and health outcome is detailed in Supplementary Files S4 (deaths) and S5 (DALYs).

Table 4
Distribution of the population to exposure levels of sanitation, by region, for 2016.

Region	Percentage of population	
	using basic sanitation services	living in communities with > 75% basic sanitation coverage
Sub-Saharan Africa, LMICs	30.8	13.3
America, LMICs	85.1	75.8
Eastern Mediterranean, LMICs	69.1	54.8
Europe, LMICs	92.5	93.3
South-East Asia, LMICs	50.9	31.9
Western Pacific, LMICs	75.1	63.2
Total LMICs	62.0	45.3

LMICs: low and middle income countries.

Table 5
Distribution of the population to exposure levels of hygiene, by region, for 2016.

Region	Percentage of population washing hands with soap after potential faecal contact
Sub-Saharan Africa, all	8.4
America, LMICs	36.2
Eastern Mediterranean, LMIC	21.6
Europe, LMICs	24.9
South-East Asia, all	27.8
Western Pacific, LMICs	17.1
Total	26.3
Total HICs	50.6
Total LMICs	21.8

LMICs: low and middle income countries, HICs: high income countries.

4. Discussion

It is estimated that 1.6 million deaths and 105 million DALYs are attributable to inadequate WASH, including only diseases which could be quantified, representing 2.8% of total deaths and 3.9% of total DALYs in 2016. Of those, 829,000 deaths are due to diarrhoeal disease. Sixty per cent of the overall diarrhoea burden, 13% of the burden from acute respiratory infections, 16% of the burden of protein-energy malnutrition, 43% of the schistosomiasis burden, 80% of the malaria burden and 100% of both the burden from soil-transmitted helminth infections and trachoma burden are attributed to inadequate WASH.

4.1. Discussion of results

Compared to our previous burden of diarrhoeal disease assessment

Table 3
Distribution of the population to exposure levels of drinking water, by region, for 2016.

Region	Percentage of population using						Total
	piped water on premises		basic drinking water, not piped on premises		surface, unimproved or limited water		
	not filtered or boiled[a]	filtered or boiled	not filtered or boiled	filtered or boiled	not filtered or boiled	filtered or boiled	
Sub-Saharan Africa, LMICs	25.5	3.1	29.6	2.0	35.8	4.0	100
America, LMICs	58.3	32.3	4.6	1.1	2.9	0.8	100
Eastern Mediterranean, LMICs	53.8	4.8	26.0	0.7	13.7	0.9	100
Europe, LMICs	55.6	29.3	6.9	4.1	2.5	1.7	100
South-East Asia, LMICs	24.9	12.7	38.6	13.0	7.2	3.5	100
Western Pacific, LMICs	28.5	50.7	8.8	8.3	1.6	2.1	100
Total LMICs	34.1	23.5	22.6	7.0	10.2	2.6	100

[a] Filtering or boiling means point-of-use water treatment at household-level. The total may not equal the sum of numbers displayed in the rows due to rounding.
LMICs: low- and middle-income countries.

Table 6
Diarrhoea burden attributable to inadequate water by region, 2016

Region	PAF	(95% CI)	Deaths	(95% CI)	DALYs (in 1 000s)	(95% CI)
Sub-Saharan Africa, LMICs	0.40	(0.22–0.51)	259,073	(140,144–330,643)	16,837	(9120–21,472)
America, LMICs	0.27	(0.02–0.42)	6246	(480–9469)	506	(22–776)
Eastern Mediterranean, LMICs	0.39	(0.19–0.50)	48,947	(24,067–63,413)	3675	(1778–4764)
Europe, LMICs	0.20	(0.02–0.31)	959	(86–1500)	137	(2–215)
South-East Asia, LMICs	0.31	(0.12–0.43)	163,760	(64,307–225,941)	7798	(3067–10,750)
Western Pacific, LMICs	0.21	(0.08–0.30)	5756	(2069–8320)	493	(160–725)
Total LMICs	0.36	(0.19–0.47)	484,741	(231,153–639,285)	29,446	(14,149–38,702)

DALYs: disability-adjusted life years, PAF: population-attributable fraction; LMICs: low- and middle-income countries; for the analysis of burden of diarrhoeal disease attributed to inadequate water the counterfactual exposure distribution (plausible minimum risk) of filtering/boiling of water from any water source with subsequent safe storage was compared to the actual exposure distribution for 2016.

for the year 2012 (Prüss-Ustün et al., 2014), we now attribute about 17,000 less deaths to inadequate water (2012: 502,000 deaths, 2016: 485,000 deaths), 152,000 additional deaths to inadequate sanitation (2012: 280,000 deaths, 2016: 432,000 deaths) and 132,000 less deaths to inadequate hygiene behaviours (2012: 297,000 deaths, 2016: 165,000 deaths). Especially the methods for exposure assessment of both inadequate sanitation and inadequate hygiene behaviours have been revised using updated evidence. The consideration of health impacts from poor sanitation coverage in the community led to a significant increase of disease burden from inadequate sanitation. Furthermore, we are no longer relying on observations of handwashing frequency which are usually not nationally representative. Diarrhoea deaths attributable to inadequate WASH also changed due to reductions in overall diarrhoeal mortality (WHO, 2018a) and updated exposure-response relationships (Wolf et al., 2018a).

For comparison with similar estimates, the comparative risk assessment for the year 2016 for the Global Burden of Disease Study conducted by the Institute for Health Metrics and Evaluation attributed 89% of diarrhoea deaths and 8% of deaths from acute respiratory infections to inadequate WASH (Gakidou et al., 2017) – compared to 60% and 13% in this assessment. Differences compared to our estimates are mainly due to our approach of adjusting some WASH interventions for non-blinding bias (only diarrhoeal disease burden estimates, see discussion below), different approaches of exposure assessment and different minimum risk exposure (counterfactual) levels. The Institute for Health Metrics and Evaluation considers sewered sanitation as the sanitation counterfactual, which is however not necessarily supported by recent evidence nor for rural areas (Baum et al., 2013; WHO and UNICEF, 2017). Community sanitation coverage is not taken into account and availability of basic handwashing facilities is used as exposure parameter which does not match the parameter of the exposure-response relationship which is handwashing with soap at times of potential pathogen exposure.

Recent WASH disease burden estimates have varied considerably: in 2010 the Global Burden of Disease Study estimated 337,000 deaths from inadequate WASH (Lim et al., 2012) while subsequently reporting 1,399,000 deaths in 2013 (Forouzanfar et al., 2015), 1,766,000 deaths in 2015 (Forouzanfar et al., 2016), 1,661,000 deaths in 2016 (Gakidou et al., 2017) and 1,610,000 in 2017 (Stanaway et al., 2018). The initial increase was mainly due to the fact that the first counterfactuals for estimating WASH-attributable burden of disease were improved drinking water sources and improved sanitation facilities as defined by the JMP (WHO and UNICEF, undated). Improved drinking water sources are often unreliable and of poor water quality while improved sanitation is often not safely managed and does not protect the community (Bain et al., 2014; Clasen et al., 2014; WHO and UNICEF, 2017). More recent WASH-attributable global burden of disease assessments recognize health impacts from improvements in drinking water and sanitation beyond improved water sources and sanitation facilities, i.e., piped water sources, household water treatment and sewered sanitation, and from considering personal hygiene as separate risk factor. Since the 2015 assessment, more diseases have been added in the Global Burden of Disease assessments such as typhoid and paratyphoid fever in 2015 (Forouzanfar et al., 2016) and acute respiratory infections in 2016 and 2017 (Gakidou et al., 2017; Stanaway et al., 2018).

The positive side of a high WASH-attributable disease burden is the great potential for disease burden reduction. In theory, the entire estimated disease burden could have been prevented through interventions. These interventions vary depending on the health outcome and the chosen counterfactual exposure distribution. Diarrhoea, acute respiratory infections, malnutrition and schistosomiasis will require improvements of drinking water and sanitation services and increased handwashing with soap. The same is true for soil-transmitted helminth infections and trachoma, however to completely prevent these infections more radical and comprehensive WASH interventions are required (safely managed drinking water and sanitation services, access to essential hygiene conditions and practice of essential hygiene behaviours). Additionally, the prevention of soil-transmitted helminth infections might require the proper treatment of human waste and adequate food hygiene to prevent infections that occur through the use of human faeces as fertilizer (Anuar et al., 2014; Strunz et al., 2014). Trachoma prevention might include the need for a stronger emphasis on comprehensive hygiene practices including facewashing (Stocks et al., 2014). Finally to reduce the WASH-attributable malaria disease

Table 7
Diarrhoea burden attributable to inadequate sanitation by region, 2016

Region	PAF	(95% CI)	Deaths	(95% CI)	DALYs (in 1 000s)	(95% CI)
Sub-Saharan Africa, LMICs	0.37	(0.36–0.38)	236,134	(229,625–241,875)	15,303	(14,866–15,684)
America, LMICs	0.14	(0.13–0.16)	3261	(2949–3529)	257	(229–280)
Eastern Mediterranean, LMICs	0.27	(0.24–0.30)	34,425	(30,473–37,781)	2538	(2260–2775)
Europe, LMICs	0.03	(0.02–0.03)	134	(91–161)	20	(14–24)
South-East Asia, LMICs	0.29	(0.25–0.33)	152,986	(129,778–173,011)	7245	(6131–8208)
Western Pacific, LMICs	0.17	(0.15–0.20)	4780	(4041–5413)	403	(332–464)
Total LMICs	0.32	(0.30–0.34)	431,720	(407,090–452,623)	25,765	(24,519–26,825)

DALYs: disability-adjusted life years, PAF: population-attributable fraction; LMICs: low- and middle-income countries; for the analysis of burden of diarrhoeal disease attributed to inadequate sanitation the counterfactual exposure distribution (plausible minimum risk) of having access to basic sanitation in a community with > 75% coverage with basic sanitation facilities was compared to the actual exposure distribution for 2016.

Table 8
Diarrhoea burden attributable to inadequate hygiene behaviours by region, 2016

Region	PAF	(95% CI)	Deaths	(95% CI)	DALYs (in 1 000s)	(95% CI)
Sub-Saharan Africa, all	0.13	(0–0.61)	85,166	(0–394,782)	5516	(0–25,622)
America, LMICs	0.10	(0–0.47)	2227	(0–10,741)	183	(0–886)
America, HICs	0.08	(0–0.41)	930	(0–4967)	25	(0–131)
Eastern Mediterranean, LMICs	0.12	(0–0.57)	15,013	(0–72,270)	1130	(0–5440)
Eastern Mediterranean, HICs	0.08	(0–0.41)	34	(0–186)	5	(0–27)
Europe, LMICs	0.11	(0–0.54)	537	(0–2605)	72	(0–352)
Europe, HICs	0.08	(0–0.40)	1216	(0–6371)	29	(0–151)
South-East Asia, all	0.11	(0–0.50)	56,419	(0–264,975)	2656	(0–12,477)
Western Pacific, LMICs	0.12	(0–0.55)	3347	(0–15,182)	298	(0–1350)
Western Pacific, HICs	0.08	(0–0.40)	310	(0–1645)	6	(0–31)
Total	0.12	(0–0.56)	165,200	(0–780,443)	9919	(0–46,598)

DALYs: disability-adjusted life years, PAF: population-attributable fraction; LMICs: low- and middle-income countries, HICs: high-income countries; for the analysis of burden of diarrhoeal disease attributed to inadequate hygiene behaviours the counterfactual exposure distribution (plausible minimum risk) of handwashing with soap after potential faecal contact was compared to the actual exposure distribution for 2016.

burden, interventions will be required that lead to environmental modification and manipulation, including water resource management as main component, and changes of the human habitat, including siting of settlements away from breeding sites (Keiser et al., 2005).

4.2. Limitations

This WASH-attributable burden of disease assessment is limited to some selected diseases and adverse health outcomes and does not take into account a large amount of other adverse health outcomes (examples are given in Table 1) that are at least partly WASH-attributable and that could be prevented through improved WASH management. Additionally, the here presented estimates do not capture disease burden from, for example, water-borne disease outbreaks, flooding and droughts or disease burden in certain populations such as refugees, internally displaced persons, and the homeless or certain exposure settings such as healthcare facilities, schools, workplaces and other public places. Additionally, adequate WASH and treatment of wastewater (from households, intensive livestock raising and industry) can reduce environmental drivers of antimicrobial resistance (Bürgmann et al., 2018; O'Neill, 2016; WHO, 2014), an increasingly serious threat to global public health (WHO, 2018g). WASH-attributable disease burden estimates refer predominantly to LMICs as most of the epidemiological evidence originates from these countries.

This analysis considers WASH-attributable deaths and DALYs from a range of diseases and conditions including diarrhoea, acute respiratory infections, protein-energy malnutrition, schistosomiasis, malaria, soil-transmitted helminth infections and trachoma. Some WASH-attributable disease burden estimates, i.e., for diarrhoea and respiratory infections, are based on CRA and the exposure-response relationship on meta-analysis of intervention studies. The remaining diseases have been estimated using more limited exposure or exposure-response information which required more assumptions. WASH-attributable disease burden estimates for the latter diseases include therefore greater uncertainties. The WASH-attributable estimates of the burden of respiratory infections are calculated using a dose-response relationship from intervention studies not adjusted for likely bias due to non-blinding. The malnutrition estimates are based on the diarrhoea estimates and therefore omit other pathways through which WASH can have an impact on malnutrition such as subclinical enteric infections and environmental enteropathy (Rogawski and Guerrant, 2017). In addition, these estimates include only stunting and omit other forms of malnutrition such as underweight and wasting. Stunting, compared to wasting and underweight, is the more severe form of malnutrition, is associated with chronic and recurrent undernutrition, e.g., from frequent infectious disease, and prevents children from reaching their physical and cognitive potential (WHO, 2018h). There is usually considerable overlap between stunting, wasting and underweight (Myatt et al., 2018). The estimate of the fraction of WASH-attributable stunting is based on the fraction of stunting attributable to repeated diarrhoea episodes (Checkley et al., 2008) which is combined with the fraction of WASH-attributable diarrhoea. In young children from low-income countries (where the bulk of the global burden of diarrhoea occurs) repeated diarrhoea episodes are the norm: e.g., children under three years old experience on average three episodes of diarrhoea every year (WHO, 2017b). Recent findings from the GEMS study suggested that children with both moderate/severe and less-severe diarrhoea had a significantly increased risk for stunting (Kotloff et al., 2019). Global health estimates for diarrhoeal disease burden which are used for WASH-attributable disease burden estimation can be subject to considerable under-reporting, especially for countries without well-functioning death registration systems for which estimates rely heavily on surveys and censuses (WHO, 2018i).Our estimate of 16% of malnutrition is broadly consistent with a Cochrane review that concluded that

Table 9
Diarrhoea burden attributable to the cluster of inadequate water, sanitation and hygiene behaviours by region, 2016

Region	PAF	(95% CI)	Deaths	(95% CI)	DALYs (in 1 000s)	(95% CI)
Sub-Saharan Africa, all	0.67	(0.62–0.72)	431,700	(398,398–462,156)	27,997	(25,822–29,968)
America, LMICs	0.43	(0.35–0.51)	9861	(8050–11,623)	799	(639–952)
America, HICs	0.08	(0.00–0.25)	930	(0–4967)	25	(0–131)
Eastern Mediterranean, LMICs	0.60	(0.50–0.70)	76,387	(62,928–87,982)	5718	(4787–6531)
Eastern Mediterranean, HICs	0.08	(0.00–0.25)	34	(0–186)	5	(0–27)
Europe, LMICs	0.31	(0.22–0.39)	1481	(1053–1899)	207	(148–265)
Europe, HICs	0.08	(0.00–0.17)	1216	(0–6371)	29	(0–151)
South-East Asia, all	0.56	(0.43–0.68)	295,070	(225,467–356,569)	13,981	(10,634–16,948)
Western Pacific, LMICs	0.43	(0.32–0.53)	11,661	(8651–14,501)	1008	(715–1282)
Western Pacific, HICs	0.08	(0.00–0.23)	310	(0–1645)	6	(0–31)
Total	0.60	(0.54–0.65)	828,651	(753,021–901,072)	49,774	(45,835–53,596)

DALYs: disability-adjusted life years, PAF: population-attributable fraction; LMICs: low- and middle-income countries, HICs: high-income countries.

Table 10
Summary of WASH-attributable disease burden, 2016

disease	PAF	95% CI	method for PAF estimation	counterfactual exposure level	deaths	DALYs
Schistosomiasis	0.43	0.40–0.46	CRA	feasible minimum risk (universal access to/use of basic water and sanitation services)	10,405	1,095,658
total WASH-attributable disease burden using a feasible minimum risk					**10,405**	**1,095,658**
Diarrhoea	0.60*	0.54–0.65	CRA	plausible minimum risk (universal filtering/boiling of water + safe storage. access to/use of basic sanitation in communities > 75% basic sanitation coverage, HWWS after potential faecal contact)	828,651*	49,773,959*
Acute respiratory infections	0.13	0.08–0.16	CRA	plausible minimum risk (universal HWWS after potential faecal contact)	370,370	17,308,136
Protein-energy malnutrition	0.16*	0.15–0.17	based on diarrhoeal estimates	plausible minimum risk (see diarrhoea)	28,194*	2,995,329*
total WASH-attributable disease burden using a plausible minimum risk					**1,227,215**	**70,077,424**
Malaria	0.80	0.67–0.87	comparing universal safe water resource management (WRM) against no WRM	theoretical minimum risk (universal safe WRM)	354,924	29,707,805
Soil-transmitted helminth infections	1	1–1	burden completely WASH-attributed	theoretical minimum risk (universal safely managed water and sanitation, access to essential hygiene conditions and practice of essential hygiene behaviours)	6248	3,430,614
Trachoma	1	1–1	burden completely WASH-attributed	theoretical minimum risk (universal safely managed water and sanitation, access to essential hygiene conditions and practice of essential hygiene behaviours)	< 10	244,471
total WASH-attributable disease burden using a theoretical risk					**361,175**	**33,382,890**

PAF: population attributable fraction, CI: confidence interval, DALYs: disability-adjusted life years, CRA: comparative risk assessment, HWWS: handwashing with soap, theoretical minimum risk: use of safely managed water and sanitation services, access to essential hygiene conditions and practice of essential hygiene behaviour, plausible minimum risk: boiling/filtering of drinking water with subsequent safe storage, access to/use of basic sanitation in a community with > 75% basic sanitation coverage, handwashing with soap after potential faecal contact, feasible minimum risk: access to/use of basic drinking water and basic sanitation services, disease burden estimates are for low- and middle-income countries, diarrhoea and acute respiratory infections include disease burden in high-income countries from inadequate hygiene.

WASH interventions might have a small benefit on length growth (Dangour et al., 2013). The schistosomiasis exposure-response function is based on observational studies only (Freeman et al., 2017; Grimes et al., 2014) and the counterfactual exposure distribution is use of basic water and sanitation services which represents a feasible minimum risk exposure distribution only. The counterfactual exposure distribution for malaria – universal exposure to safe water resource management (Keiser et al., 2005) – differs from the exposure distributions of the other diseases which are related to the use of certain WASH services. From the above it can be concluded that our disease burden estimates are likely underestimating the true disease burden of inadequate WASH.

While some have argued that the counterfactual exposure distribution used for risk factor-attributable disease burden estimation should represent what can be achieved through interventions (Greenland, 2002; Steenland and Armstrong, 2006), others advocate the use of multiple exposure distributions including those which might not be achievable by currently available interventions to appreciate the size of the problem (Murray et al., 2003). Based on the available evidence – especially regarding the exposure-response relationship – our WASH-attributable disease burden estimates are based on different – including feasible, plausible and theoretical minimum risk – counterfactual definitions. Especially the feasible (only used for schistosomiasis) but also the plausible minimum risk exposure levels represent interim levels on which further improvements are possible and necessary. These interim exposure levels should be replaced with the theoretical minimum risk exposure distribution of safely managed water and sanitation, access to essential hygiene conditions and practice of essential hygiene behaviours when the available evidence allows this. The JMP currently provides country-level data for access to safely managed drinking water and sanitation services only for a limited number of countries (WHO and UNICEF, 2018b). In addition, there is to date no matching exposure-response relationship from meta-analysis between safely managed drinking water or sanitation and disease outcome. Even the theoretical minimum risk exposure distribution might underestimate the true WASH-attributable disease burden which is supported by evidence of residual WASH-attributable diarrhoea burden in high-income countries (Gunnarsdottir et al., 2012; Setty et al., 2017). Evidence on health impacts of Water Safety Plans which are implemented increasingly throughout the world (WHO and IWA, 2017) could potentially strengthen the theoretical minimum risk exposure distribution for burden of disease assessment and add estimates for high-income countries in the future (Gunnarsdottir et al., 2012; Setty et al., 2017). Exposure levels do also not include bottled or packaged water which is used increasingly in many countries (statista, 2016). Bottled water was frequently shown to be of high microbial quality (Bain et al., 2014; Fisher et al., 2015; UNICEF and WHO, 2015; Williams et al., 2015; Wright et al., 2016) and was associated with a decreased risk for diarrhoea compared to piped water (Sima et al., 2012). Both country-level exposure data and the matching exposure-response relationship between bottled water use and health outcome are currently lacking. Changing from a feasible or plausible minimum risk exposure level to a theoretical minimum risk exposure level as the counterfactual for WASH-attributable disease burden estimation (relevant for diarrhoea, acute respiratory infections, malnutrition, and schistosomiasis) might considerably increase WASH-attributable disease burden estimates. This is supported by historical evidence of large reductions of child and overall mortality following improvements towards safely managed water and sanitation infrastructure in high-income countries (Alsan and Goldin, 2018; Bell and Millward, 1998; Cutler et al., 2006).

The WASH-attributable burden of disease assessment from most included diseases is based on WASH interventions, many of which were poorly implemented, had low compliance and promoted or installed technologies with disputable effectiveness. Therefore, the estimated WASH-attributable disease fractions can be interpreted as estimates of the fractions of disease preventable through implementing these interventions. We do adjust the diarrhoeal disease burden estimates for the likely overestimation of health impacts due to non-blinding by adjusting the results of each non-blinded point-of-use drinking water and hygiene intervention (Wolf et al., 2018a, 2014). This approach down-weights biased studies and – in our case – results in reduced estimated health impacts. The above cited issues on poor WASH interventions are however likely to underestimate the disease burden attributable to inadequate WASH. This is one more reason why our assessment assures conservative estimates which are at the lower end of the assumed truth. The WASH-attributable disease burden estimates from diarrhoea, soil-transmitted helminth infections and protein-energy malnutrition have undergone country consultations which ensure the use of all available and eligible exposure and disease data and compatible data categories.

The formula combining disease burden estimates from water, sanitation and hygiene (eq. (2)) assumes that risk factors are independent (Steenland and Armstrong, 2006). This assumption is likely to be an oversimplification for WASH as, for instance, handwashing promotion is unlikely to be effective if water quantity is limited. However, this approach has been applied in the assessment for ease of interpretation of the results, and in the absence of a more suitable approach.

WASH-attributable morbidity for some diseases in our analysis (diarrhoea, schistosomiasis) is estimated separately for the different components of WASH (water, sanitation and hygiene are analysed in three separate models). This approach ignores that the different WASH components affect disease in conjunction. The meta-regression model (Wolf et al., 2018a) that was used to generate the exposure-response relationships between WASH and diarrhoea, however adjusted for baseline WASH of the other categories and included further covariates. A multi-risk model might nevertheless be the preferred approach for WASH-attributable disease burden assessment in the future. Including all three WASH components in one model would also take account of the fact that the three risk factors (inadequate water, inadequate sanitation and inadequate hygiene) are often likely to vary simultaneously, e.g. improving access to or use of water facilities might improve hygiene behaviours and sanitation at the same time.

The here presented WASH-attributable burden of disease estimates required different assumptions. We show through different sensitivity analyses that disease burden estimates can change by as much as a factor of two depending on assumptions, applied exposure-response relationships and counterfactual definitions. Especially the WASH-attributable schistosomiasis disease burden estimates, generated using the feasible minimum risk exposure distribution, are likely to be underestimated. Accordingly, estimates based on expert survey were considerably higher. Care should be taken to consider the approximate nature of the estimates which are however suitable to gauge the size of the problem, to compare the relative importance of diseases and risk factors and to monitor changes over time.

The attributable burden signifies the reduction in current or future disease burden if past exposure to a risk factor had been equal to the counterfactual exposure distribution (Murray et al., 2003). An assumption that is made when stating the PAF is that the formerly exposed group immediately attains disease risk of the unexposed group after removal or reduction of the exposure (Kowall and Stang, 2018; Rockhill et al., 1998). This is often not the case and additionally differs between different health outcomes. For example, diarrhoea disease reduction is likely to happen more immediate than changes in nutritional status, universal water resource management may take a considerable time to implement but once it is established disruption of mosquito habitats will probably follow quite quickly. These different time lags that are not apparent from the PAF need to be considered and are important for interpreting results, prevention efforts, research and policy.

5. Conclusions

An important fraction of overall deaths and DALYs in low- and middle-income countries is attributable to inadequate WASH. Burden of disease estimates have an approximate nature as they do not capture the complete list of WASH-attributable adverse health outcomes, exposed settings and populations and are dependent on assumptions, exposure-response functions and chosen counterfactual definitions that are often still based on imperfect WASH interventions.

To improve estimates of health benefits from WASH there is a need for well-designed trials that evaluate the effectiveness of safely managed water and sanitation services, access to essential hygiene conditions and practice of essential hygiene behaviours that reach high coverage and use in the communities. To improve health outcomes there is a strong need for research on implementation systems, intervention quality and intermediate outcomes such as exposure to faecal pathogens in the community. Additionally, data from high-income countries on WASH exposure distributions and exposure-response relationships might strengthen future definitions of the theoretical minimum exposure distribution and might enable more comprehensive WASH disease burden assessments.

Acknowledgments and disclaimer

The study was partially funded by the United Kingdom Department for International Development (DFID). The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. Some authors are staff members of the World Health Organization or other institutions. The authors alone are responsible for the views expressed in this publication, which do not necessarily represent the views, decisions or policies of the institutions with which they are affiliated. This article should not be reproduced for use in association with the promotion of commercial products, services or any legal entity. The WHO does not endorse any specific organization or products.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijheh.2019.05.004.

References

Alsan, M., Goldin, C., 2018. Watersheds in Infant Mortality: the Role of Effective Water and Sewerage Infrastructure (No. 21263). NBER Working Paper Series.
Anuar, T.S., Salleh, F.M., Moktar, N., 2014. Soil-transmitted helminth infections and associated risk factors in three orang asli tribes in peninsular Malaysia. Sci. Rep. 4, 4101. https://doi.org/10.1038/srep04101.
Bain, R., Cronk, R., Wright, J., Yang, H., Slaymaker, T., Bartram, J., 2014. Fecal contamination of drinking-water in low- and middle-income countries: a systematic review and meta-analysis. PLoS Med. 11, e1001644. https://doi.org/10.1371/journal.pmed.1001644.
Baum, R., Luh, J., Bartram, J., 2013. Sanitation: a global estimate of sewerage connections without treatment and the resulting impact on MDG progress. Environ. Sci. Technol. 47, 1994–2000.
Bell, F., Millward, R., 1998. Public health expenditures and mortality in England and Wales, 1870–1914. Continuity Change 13, 221–249.
Bürgmann, H., Frigon, D., H Gaze, W., M Manaia, C., Pruden, A., Singer, A.C., F Smets, B., Zhang, T., 2018. Water and sanitation: an essential battlefront in the war on antimicrobial resistance. FEMS Microbiol. Ecol. 94. https://doi.org/10.1093/femsec/fiy101.
Checkley, W., Buckley, G., Gilman, R.H., Assis, A.M., Guerrant, R.L., Morris, S.S., Mølbak, K., Valentiner-Branth, P., Lanata, C.F., Black, R.E., 2008. Multi-country analysis of the effects of diarrhoea on childhood stunting. Int. J. Epidemiol. 37, 816–830. https://doi.org/10.1093/ije/dyn099.
Clasen, T., Prüss-Ustün, A., Mathers, C., Cumming, O., Cairncross, S., Colford Jr., J.M., 2014. Estimating the impact of inadequate water, sanitation and hygiene on the global burden of disease: evolving and alternative methods. J. Trop. Med. Int. Health.
Cutler, D., Deaton, A., Lleras-Muney, A., 2006. The determinants of mortality. J. Econ. Perspect. 20, 97–120.
Dangour, A.D., Watson, L., Cumming, O., Boisson, S., Che, Y., Velleman, Y., Cavill, S., Allen, E., Uauy, R., 2013. Interventions to improve water quality and supply,

sanitation and hygiene practices, and their effects on the nutritional status of children. Cochrane Database Syst. Rev. 8.
Ezzati, M., Lopez, A.D., Rodgers, A., Vander Hoorn, S., Murray, C.J., the Comparative Risk Assessment Collaborating Group, 2002. Selected major risk factors and global and regional burden of disease. Lancet 360, 1347–1360.
Fisher, M.B., Williams, A.R., Jalloh, M.F., Saquee, G., Bain, R.E., Bartram, J.K., 2015. Microbiological and chemical quality of packaged sachet water and household stored drinking water in Freetown, Sierra Leone. PLoS One 10, e0131772.
Forouzanfar, M.H., Alexander, L., Anderson, H.R., Bachman, V.F., Biryukov, S., Brauer, M., Burnett, R., Casey, D., Coates, M.M., Cohen, A., others, 2015. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 386, 2287–2323.
Forouzanfar, M.H., Afshin, A., Alexander, L.T., Anderson, H.R., Bhutta, Z.A., Biryukov, S., Brauer, M., Burnett, R., Cercy, K., Charlson, F.J., others, 2016. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 388, 1659–1724.
Freeman, M.C., Garn, J.V., Sclar, G.D., Boisson, S., Medlicott, K., Alexander, K.T., Penakalapati, G., Anderson, D., Mahtani, A.G., Grimes, J.E., 2017. The impact of sanitation on infectious disease and nutritional status: a systematic review and meta-analysis. Int. J. Hyg Environ. Health 220, 928–949.
Fuller, J.A., Eisenberg, J.N., 2016. Herd protection from drinking water, sanitation, and hygiene interventions. Am. J. Trop. Med. Hyg. 95, 1201–1210.
Gakidou, E., Afshin, A., Abajobir, A.A., Abate, K.H., Abbafati, C., Abbas, K.M., Abd-Allah, F., Abdulle, A.M., Abera, S.F., Aboyans, V., 2017. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 390, 1345–1422.
GATHER Guidelines for Accurate and Transparent Health Estimates Reporting. [WWW Document], n.d. . Gather Statement. http://gather-statement.org/ accessed 4.16.18.
Greenland, S., 2002. Causality theory for policy uses of epidemiological measures. In: Summary Measures of Population Health: Concepts, Ethics, Measurement, and Application. World Health Organization, Geneva.
Grimes, J.E., Croll, D., Harrison, W.E., Utzinger, J., Freeman, M.C., Templeton, M.R., 2014. The relationship between water, sanitation and schistosomiasis: a systematic review and meta-analysis. PLoS Neglected Trop. Dis. 8, e3296.
Gunnarsdottir, M.J., Gardarsson, S.M., Elliott, M., Sigmundsdottir, G., Bartram, J., 2012. Benefits of water safety plans: microbiology, compliance, and public health. Environ. Sci. Technol. 46, 7782–7789.
Hu, V.H., Harding-Esch, E.M., Burton, M.J., Bailey, R.L., Kadimpeul, J., Mabey, D.C.W., 2010. Epidemiology and control of trachoma: systematic review. Trop. Med. Int. Health 15, 673–691. https://doi.org/10.1111/j.1365-3156.2010.02521.x.
Humphrey, J.H., Mbuya, M.N., Nitozini, R., Moulton, L.H., Stoltzfus, R.J., Tavengwa, N.V., Mutasa, K., Majo, F., Mutasa, B., Mangwadu, G., Chasokela, C.M., Chigumira, A., Chasekwa, B., Smith, L.E., Tielsch, J.M., Jones, A.D., Manges, A., Maluccio, J.A., Prendergast, A., 2019. Independent and combined effects of improved water, sanitation, and hygiene, and improved complementary feeding, on child stunting and anaemia in rural Zimbabwe: a cluster-randomised trial. Lancet Glob. Health 7, e132–e147.
Jung, Y.T., Hum, R.J., Lou, W., Cheng, Y.-L., 2017a. Effects of neighbourhood and household sanitation conditions on diarrhea morbidity: systematic review and meta-analysis. PLoS One 12, e0173808. https://doi.org/10.1371/journal.pone.0173808.
Jung, Y.T., Lou, W., Cheng, Y.-L., 2017b. Exposure-response relationship of neighbourhood sanitation and children's diarrhea. Trop. Med. Int. Health 22, 857–865.
Keiser, J., Singer, B.H., Utzinger, J., 2005. Reducing the burden of malaria in different eco-epidemiological settings with environmental management: a systematic review. Lancet Infect. Dis. 5, 695–708. https://doi.org/10.1016/S1473-3099(05)70268-1.
Kotloff, K.L., Nasrin, D., Blackwelder, W.C., Wu, Y., Farag, T., Panchalingham, S., Sow, S.O., Sur, D., Zaidi, A.K.M., Faruque, A.S.G., Saha, D., Alonso, P.L., Tamboura, B., Sanogo, D., Onwuchekwa, U., Manna, B., Ramamurthy, T., Kanungo, S., Ahmed, S., Qureshi, S., Quadri, F., Hossain, A., Das, S.K., Antonio, M., Hossain, M.J., Mandomando, I., Acácio, S., Biswas, K., Tennant, S.M., Verweij, J.J., Sommerfelt, H., Nataro, J.P., Robins-Browne, R.M., Levine, M.M., 2019. The incidence, aetiology, and adverse clinical consequences of less severe diarrhoeal episodes among infants and children residing in low-income and middle-income countries: a 12-month case-control study as a follow-on to the Global Enteric Multicenter Study (GEMS). Lancet Glob. Health 7, e568–e584. https://doi.org/10.1016/S2214-109X(19)30076-2.
Kowall, B., Stang, A., 2018. Stolpersteine bei der Interpretation des populationsattributablen Risikos. Gesundheitswesen 80, 149–153.
Lim, S.S., Vos, T., Flaxman, A.D., Danaei, G., Shibuya, K., Adair-Rohani, H., Amann, M., Anderson, H.R., Andrews, K.G., Aryee, M., 2012. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 380, 2224–2260.
Luby, S.P., Rahman, M., Arnold, B.F., Unicomb, L., Ashraf, S., Winch, P.J., Stewart, C.P., Begum, F., Hussain, F., Benjamin-Chung, J., Leontsini, E., Naser, A.M., Parvez, S.M., Hubbard, A.E., Lin, A., Nizame, F.A., Jannat, K., Ercumen, A., Ram, P.K., Das, K.K., Abedin, J., Clasen, T.F., Dewey, K.G., Fernald, L.C., Null, C., Ahmed, T., Colford, J.M., 2018. Effects of water quality, sanitation, handwashing, and nutritional interventions on diarrhoea and child growth in rural Bangladesh: a cluster randomised controlled trial. Lancet Glob. Health 6, e302–e315. https://doi.org/10.1016/S2214-109X(17)30490-4.
MAL-ED Network Investigators, 2017. Relationship between growth and illness, enteropathogens and dietary intakes in the first 2 years of life: findings from the MAL-ED birth cohort study. BMJ Glob. Health 2, e000370. https://doi.org/10.1136/bmjgh-2017-000370.
Mbakaya, B.C., Lee, P.H., Lee, R.L., 2017. Hand hygiene intervention strategies to reduce diarrhoea and respiratory infections among schoolchildren in developing countries: a systematic review. Int. J. Environ. Res. Public Health 14, 371.
Mohammadpour, M., Abrishami, M., Masoumi, A., Hashemi, H., 2016. Trachoma: past, present and future. J. Curr. Ophthalmol. 28, 165–169. https://doi.org/10.1016/j.joco.2016.08.011.
Murray, C.J.L., Lopez, A.D., 1996. The Global Burden of Disease. World Health Organization. Harvard School of Public Health, World Bank, Geneva.
Murray, C.J.L., Lopez, A.D., 2013. Measuring the global burden of disease. N. Engl. J. Med. 369, 448–457. https://doi.org/10.1056/NEJMra1201534.
Murray, C.J., Ezzati, M., Lopez, A.D., Rodgers, A., Vander Hoorn, S., 2003. Comparative quantification of health risks: conceptual framework and methodological issues. Popul. Health Metrics 1, 1.
Myatt, M., Khara, T., Schoenbuchner, S., Pietzsch, S., Dolan, C., Lelijveld, N., Briend, A., 2018. Children who are both wasted and stunted are also underweight and have a high risk of death: a descriptive epidemiology of multiple anthropometric deficits using data from 51 countries. Arch. Public Health 76. https://doi.org/10.1186/s13690-018-0277-1.
Null, C., Stewart, C.P., Pickering, A.J., Dentz, H.N., Arnold, B.F., Arnold, C.D., Benjamin-Chung, J., Clasen, T., Dewey, K.G., Fernald, L.C., 2018. Effects of water quality, sanitation, handwashing, and nutritional interventions on diarrhoea and child growth in rural Kenya: a cluster-randomised controlled trial. Lancet Glob. Health 6, e316–e329.
O'Neill, J., 2016. Tackling Drug-Resistant Infections Globally: Final Report and Recommendations, the Review on Antimicrobial Resistance. Wellcome Trust. HM Government.
Prüss-Ustün, A., Bos, R., Gore, F., Bartram, J., 2008. Safer Water, Better Health. World Health Organization, Geneva.
Prüss-Ustün, A., Bartram, J., Clasen, T., Colford Jr., J.M., Cumming, O., Curtis, V., Bonjour, S., Dangour, A.D., De France, J., Fewtrell, L., Freeman, M.C., Gordon, B., Hunter, P.R., Johnston, R.B., Mathers, C., Mäusezahl, D., Medlicott, K., Neira, M., Stocks, M., Wolf, J., Cairncross, S., 2014. Burden of disease from inadequate water, sanitation and hygiene in low- and middle-income settings: a retrospective analysis of data from 145 countries. Trop. Med. Int. Health 19, 894–905. https://doi.org/10.1111/tmi.12329.
Prüss-Ustün, A., Wolf, J., Corvalán, C., Bos, R., Neira, M., 2016. Preventing Disease through Healthy Environments: A Global Assessment of the Environmental Burden of Disease from Environmental Risks. World Health Organization.
Rabie, T., Curtis, V., 2006. Handwashing and risk of respiratory infections: a quantitative systematic review. Trop. Med. Int. Health TM IH 11, 258–267. https://doi.org/10.1111/j.1365-3156.2006.01568.x.
Reese, H., Routray, P., Torondel, B., Sclar, G.D., Delea, M., Sinharoy, S., Zambrano, L., Caruso, B., Suar, M., Clasen, T., 2018. Effect of a Combined Household-Level Piped Water and Sanitation Intervention in Rural Odisha, India on Diarrheal Diseases, Respiratory Infection. soil-transmitted helminth infection, and undernutrition.
RISK, (n.d.), https://www.palisade.com/risk/de/.
Rockhill, B., Newman, B., Weinberg, C., 1998. Use and misuse of population attributable fractions. Am. J. Public Health 88, 15–19.
Rogawski, E.T., Guerrant, R.L., 2017. The burden of enteropathy and "subclinical" infections. Pediatr. Clin. 64, 815–836. https://doi.org/10.1016/j.pcl.2017.03.003.
Savović, J., Jones, H.E., Altman, D.G., Harris, R.J., Jüni, P., Pildal, J., Als-Nielsen, B., Balk, E.M., Gluud, C., Gluud, L.L., 2012. Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. Ann. Intern. Med. 157, 429–438.
Schnee, A.E., Haque, R., Taniuchi, M., Uddin, M.J., Alam, M.M., Liu, J., Rogawski, E.T., Kirkpatrick, B., Houpt, E.R., Petri Jr., W.A., 2018. Identification of etiology-specific diarrhea associated with linear growth faltering in Bangladeshi infants. Am. J. Epidemiol. 187, 2210–2218.
Setty, K.E., Kayser, G.L., Bowling, M., Enault, J., Loret, J.-F., Serra, C.P., Alonso, J.M., Mateu, A.P., Bartram, J., 2017. Water quality, compliance, and health outcomes among utilities implementing water safety plans in France and Spain. Int. J. Hyg. Environ. Health, special issue: eighth PhD students workshop: water and health –. Cannes 220, 513–530. 2016. https://doi.org/10.1016/j.ijheh.2017.02.004.
Sima, L.C., Desai, M.M., McCarty, K.M., Elimelech, M., 2012. Relationship between use of water from community-scale water treatment refill kiosks and childhood diarrhea in jakarta. Am. J. Trop. Med. Hyg. 87, 979–984. https://doi.org/10.4269/ajtmh.2012.12-0224.
Stanaway, J.D., Afshin, A., Gakidou, E., Lim, S.S., Abate, D., Abate, K.H., Abbafati, C., Abbasi, N., Abbastabar, H., Abd-Allah, F., 2018. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 392, 1923–1994.
statista, 2016. Bottled Water Consumption Worldwide from 2007 to 2017 (In Billion Liters). [WWW Document]. Statista. http://www.statista.com/statistics/387255/global-bottled-water-consumption/ accessed 7.28.16.
Steenland, K., Armstrong, B., 2006. An overview of methods for calculating the burden of disease due to specific risk factors. Epidemiology 512–519.
Stevens, G.A., Alkema, L., Black, R.E., Boerma, J.T., Collins, G.S., Ezzati, M., Grove, J.T., Hogan, D.R., Hogan, M.C., Horton, R., 2016. Guidelines for accurate and transparent health estimates reporting: the GATHER statement. PLoS Med. 13, e1002056.
Stocks, M.E., Ogden, S., Haddad, D., Addiss, D.G., McGuire, C., Freeman, M.C., 2014. Effect of water, sanitation, and hygiene on the prevention of trachoma: a systematic review and meta-analysis. PLoS Med. 11, e1001605.

Strunz, E.C., Addiss, D.G., Stocks, M.E., Ogden, S., Utzinger, J., Freeman, M.C., 2014. Water, sanitation, hygiene, and soil-transmitted helminth infection: a systematic review and meta-analysis. PLoS Med. 11, e1001620.

UNICEF, WHO, 2015. 25 Years Progress on Sanitation and Drinking Water, 2015 Update and MDG Assessment. UNICEF and World Health Organization, Geneva, Switzerland.

United Nations, 2018. UN Stats - SDG Indicators. [WWW Document]. https://unstats.un.org/sdgs/metadata/ accessed 6.25.18.

Vander Hoorn, S., Ezzati, M., Rodgers, A., Lopez, A.D., Murray, C.J.L., 2004. Chapter 25: estimating attributable burden of disease from exposure and hazard data. In: Comparative Quantification of Health Risks. World Health Organization, Geneva, pp. 2129–2140.

Warren-Gash, C., Fragaszy, E., Hayward, A.C., 2013. Hand hygiene to reduce community transmission of influenza and acute respiratory tract infection: a systematic review. Influenza Other Respir. Viruses 7, 738–749. https://doi.org/10.1111/irv.12015.

White, C.G., Shinder, F.S., Shinder, A.L., Dyer, D.L., 2001. Reduction of illness absenteeism in elementary schools using an alcohol-free instant hand sanitizer. J. Sch. Nurs. 17, 248–265.

WHO, 2002. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. World Health Organization, Geneva, Switzerland.

WHO, 2004. Comparative Quantification of Health Risks. World Health Organization, Geneva.

WHO, 2014. Antimicrobial Resistance: an Emerging Water, Sanitation and Hygiene Issue (Briefing Note). World Health Organization.

WHO, 2017a. WHO regional groupings. In: World Health Statistics 2017: Monitoring Health for the SDGs. Sustainable Development Goals, pp. 103.

WHO, 2017b. Diarrhoeal Disease: Fact Sheet. [WWW Document]. https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease accessed 4.29.19.

WHO, 2018a. Global Health Observatory (GHO) Data. WHO [WWW Document]. http://www.who.int/gho/en/ accessed 6.25.18.

WHO, 2018b. Disease Burden and Mortality Estimates. WHO [WWW Document]. http://www.who.int/healthinfo/global_burden_disease/estimates/en/ accessed 11.21.18.

WHO, 2018c. Schistosomiasis: Fact Sheet. [WWW Document]. http://www.who.int/news-room/fact-sheets/detail/schistosomiasis accessed 7.24.18.

WHO, 2018d. Soil-transmitted Helminth Infections: Fact Sheet. [WWW Document]. http://www.who.int/news-room/fact-sheets/detail/soil-transmitted-helminth-infections accessed 7.24.18.

WHO, 2018e. Trachoma: Fact Sheet. [WWW Document]. http://www.who.int/news-room/fact-sheets/detail/trachoma accessed 7.24.18.

WHO, 2018f. Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. World Health Organization, Geneva.

WHO, 2018g. Antimicrobial Resistance: Fact Sheet. World Health Organ [WWW Document]. http://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance accessed 8.29.18.

WHO, 2018h. Malnutrition: Fact Sheet. World Health Organ [WWW Document]. http://www.who.int/news-room/fact-sheets/detail/malnutrition accessed 9.14.18.

WHO, 2018i. WHO Methods and Data Sources for Country-Level Causes of Death 2000-2016 (No. WHO/HIS/IER/GHE/2018.3), Global Health Estimates Technical Paper. World Health Organization, Geneva.

WHO, IWA, 2017. Global Status Report on Water Safety Plans: A Review of Proactive Risk Assessment and Risk Management Practices to Ensure the Safety of Drinking-Water. World Health Organization, International Water Association.

WHOUNICEF Undated. Home | JMP. [WWW Document]. https://washdata.org/ accessed 6.3.18.

WHO, UNICEF, 2017. Progress on Drinking Water, Sanitation and Hygiene: 2017 Update and SDG Baselines. WHO, UNICEF, Geneva.

WHO, UNICEF, 2018a. Monitoring: Hygiene. JMP [WWW Document]. https://washdata.org/monitoring/hygiene accessed 6.7.18.

WHO, UNICEF, 2018b. Data. JMP [WWW Document]. https://washdata.org/data accessed 5.18.18.

Williams, A.R., Bain, R.E.S., Fisher, M.B., Cronk, R., Kelly, E.R., Bartram, J., 2015. A systematic review and meta-analysis of fecal contamination and inadequate treatment of packaged water. PLoS One 10, e0140899. https://doi.org/10.1371/journal.pone.0140899.

Wolf, J., Bonjour, S., Prüss-Ustün, A., 2013. An exploration of multilevel modeling for estimating access to drinking-water and sanitation. J. Water Health 11, 64. https://doi.org/10.2166/wh.2012.107.

Wolf, J., Prüss-Ustün, A., Cumming, O., Bartram, J., Bonjour, S., Cairncross, S., Clasen, T., Colford Jr., J.M., Curtis, V., De France, J., Fewtrell, L., Freeman, M.C., Gordon, B., Hunter, P.R., Jeandron, A., Johnston, R.B., Mäusezahl, D., Mathers, C., Neira, M., Higgins, J., 2014. Assessing the impact of drinking-water and sanitation on diarrhoeal disease in low-and middle-income settings: a systematic review and meta-regression. Trop. Med. Int. Health 19, 928–942. https://doi.org/0.1111/tmi.12331.

Wolf, J., Hunter, P.R., Freeman, M.C., Cumming, O., Clasen, T., Bartram, J., Higgins, J.P.T., Johnston, R., Medlicott, K., Boisson, S., Prüss-Ustün, A., 2018a. Impact of drinking water, sanitation and hand washing with soap on childhood diarrhoeal disease: updated meta-analysis and –regression. Trop. Med. Int. Health 23. https://doi.org/10.1111/tmi.13051.

Wolf, J., Johnston, R., Freeman, M.C., Ram, P.K., Slaymaker, T., Laurenz, E., Prüss-Ustün, A., 2018b. Handwashing with soap after potential faecal contact: global, regional and country estimates for handwashing with soap after potential faecal contact. Int. J. Epidemiol. https://doi.org/dyy253.

Wolf, J., Johnston, R., Hunter, P.R., Gordon, B., Medlicott, K.O., Prüss-Ustün, A., 2018c. A Faecal Contamination Index for interpreting heterogeneous diarrhoea impacts of water, sanitation and hygiene interventions and overall, regional and country estimates of community sanitation coverage with a focus on low- and middle-income countries. Int. J. Hyg Environ. Health (in press), corrected proof.

Wood, L., Egger, M., Gluud, L.L., Schulz, K.F., Jüni, P., Altman, D.G., Gluud, C., Martin, R.M., Wood, A.J., Sterne, J.A., 2008. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. BMJ 336, 601.

World Bank, 2016. New Country Classifications by Income Level: 2016-2017. Data Blog [WWW Document]. http://blogs.worldbank.org/opendata/miga/new-country-classifications-2016 accessed 8.27.18.

Wright, J., Dzodzomenyo, M., Wardrop, N.A., Johnston, R., Hill, A., Aryeetey, G., Adanu, R., 2016. Effects of sachet water consumption on exposure to microbe-contaminated drinking water: household survey evidence from Ghana. Int. J. Environ. Res. Public Health 13, 303. https://doi.org/10.3390/ijerph13030303.

A2.2 Confirmation of my contributions to the included publications

The following two letters confirm my specific contributions to the eleven peer-reviewed publications that are included as main research in this critical analysis (sections 2.2-2.12).

World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Tel. direct: +41 22 791 3584
Fax direct: +41 22 791
E-mail : pruessa@who.int

In reply please
refer to:

Your reference:

To whom it may concern

Geneva, 12 June 2019

I hereby confirm that Ms Jennyfer Wolf, born 24 March1980, is a co-author of each of the listed below papers (Annex 1). Additionally, I have listed her specific contributions to each of the individual papers (Annex 2).

Dr Annette Pruss-Ustun
Senior Scientist
Public Health, Environmental and
Social Determinants of Health
Division of Healthier Populations

منظمة الصحة العالمية • 世界卫生组织
Organisation mondiale de la Santé • Всемирная организация здравоохранения • Organización Mundial de la Salud

ANNEX 1. List of publication of Ms J. Wolf as a co-author.

1. Prüss-Ustün A, **Wolf J**, Bartram J, Clasen T, Cumming O, Freeman MC, Gordon B, Hunter PR, Medlicott K, Johnston R (2019) Burden of disease from inadequate water, sanitation and hygiene for selected adverse health outcomes: an updated analysis with a focus on low- and middle-income countries, Int J Hyg Environ Health. 2019, doi: 10.1016/j.ijheh.2019.05.004
2. **Wolf J**, Johnston R, Hunter PR, Gordon B, Medlicott K, Prüss-Ustün A (2018) A Faecal Contamination Index for interpreting heterogeneous diarrhoea impacts of water, sanitation and hygiene interventions and overall, regional and country estimates of community sanitation coverage with a focus on low- and middle-income countries. Int J Hyg Environ Health. doi: 10.1016/j.ijheh.2018.11.005.
3. **Wolf J**, Johnston R, Freeman MC, Ram PK, Slaymaker T, Laurenz E, Prüss-Ustün A (2018) Handwashing with soap after potential faecal contact: Global, regional and country estimates. Int J Epidemiol, doi: 10.1093/ije/dyy253.
4. **Wolf J**, Hunter PR, Freeman MC, Cumming O, Clasen T, Bartram J, Higgins JPT, Johnston R, Medlicott K, Boisson S, Prüss-Ustün A. (2018) Impact of Drinking Water, Sanitation and Hand Washing with Soap on Childhood Diarrhoeal Disease:
   Updated Meta-Analysis and meta-regression. Trop Med Int Health, Volume 23, Issue 5, March 2018 doi: 10.1111/tmi.13051.
5. Prüss-Ustün A, **Wolf J**, Corvalán C, Neville T, Bos R, Neira M. (2016) Diseases due to unhealthy environments: an updated estimate of the global burden of disease attributable to environmental determinants of health. J Public Health, doi: 10.1093/pubmed/fdw085
6. **Wolf J**, Prüss-Ustün A, Cumming O, Bartram J, Bonjour S, Cairncross S, Clasen T, Colford JM Jr, Curtis V, De France J, Fewtrell L, Freeman MC, Gordon B, Hunter PR, Jeandron A, Johnston RB, Mäusezahl D, Mathers C, Neira M, Higgins JP. (2014) Assessing the impact of drinking water and sanitation on diarrhoeal disease in low- and middle-income settings: systematic review and meta-regression. Trop Med Int Health, Volume 19, Issue 8, pages 928–942, August 2014 doi: 10.1111/tmi.12331

7. Prüss-Ustün A, Bartram J, Clasen T, Colford JM Jr, Cumming O, Curtis V, Bonjour S, Dangour AD, De France J, Fewtrell L, Freeman MC, Gordon B, Hunter PR, Johnston RB, Mathers C, Mäusezahl D, Medlicott K, Neira M, Stocks M, **Wolf J**, Cairncross S. (2014) Burden of disease from inadequate water, sanitation and hygiene in low- and middle-income settings: a retrospective analysis of data from 145 countries. Trop Med Int Health, Volume 19, Issue 8, pages 894–905, August 2014. doi: 10.1111/tmi.12329.

8. Freeman MC, Stocks ME, Cumming O, Jeandron A, Higgins JP, **Wolf J**, Prüss-Ustün A, Bonjour S, Hunter PR, Fewtrell L, Curtis V. (2014) Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. Trop Med Int Health, Volume 19, Issue 8, pages 906–916, August 2014. doi: 10.1111/tmi.12339.

9. **Wolf J**, Bonjour S, Prüss-Ustün A (2013) An exploration of multilevel modeling for estimating access to drinking-water and sanitation. J Water Health. 2013 Mar;11(1):64-77.

ANNEX 2. Specific contributions of Ms J. Wolf to each of the above listed papers

1. *Manuscript title: Burden of disease from inadequate water, sanitation and hygiene for selected adverse health outcomes: an updated analysis with a focus on low- and middle-income countries. Int J Hyg Environ Health. doi: 10.1016/j.ijheh.2019.05.004*

   Jennyfer Wolf's contributions:

   Design of the investigation:
   - Contributing to the choice of counterfactuals for disease burden estimation and setting up the analysis frameworks in collaboration with an international expert group

   Conduct of the research:
   - Delivering critical input (exposure estimates and exposure-response relationships) for burden of disease assessment

   Analysis of the outcome:
   - Contributing to calculation of disease burden estimates for various health outcomes
   - Calculating aggregated estimates at regional level and overall

   Preparation of the work for publication:
   - Contributing to the interpretation of results
   - Reviewing the published evidence
   - Drafting all sections of the manuscript, tables and figures
   - Incorporating comments received from co-authors and reviewers

2. *Wolf J, Johnston R, Hunter PR, Gordon B, Medlicott K, Prüss-Ustün A (2018) A Faecal Contamination Index for interpreting heterogeneous diarrhoea impacts of water, sanitation and hygiene interventions and overall, regional and country estimates of community sanitation coverage with a focus on low- and middle-income countries. Int J Hyg Environ Health. doi: 10.1016/j.ijheh.2018.11.005.*

   Jennyfer Wolf's contributions:

   Design of the investigation
   - Contributing to the choice of suitable water, sanitation and hygiene indicators for the development of the faecal contamination index

   Conduct of the research
   - Conducting the literature search to define health-relevant community sanitation coverage thresholds

   Analysis of the outcome
   - Cleaning and preparing data for analysis
   - Analysing the association between the level of faecal environmental contamination and diarrhoea using meta-regression
   - Analysis of household survey microdata to estimate the proportion of the population living in communities with defined sanitation coverage levels

   Preparation of the work for publication
   - Interpreting results
   - Drafting all sections of the manuscript, tables and figures
   - Incorporating comments received from co-authors and reviewers

3. *Wolf J, Johnston R, Freeman MC, Ram PK, Slaymaker T, Laurenz E, Prüss-Ustün A (2018) Handwashing with soap after potential faecal contact: Global, regional and country estimates. Int J Epidemiol, doi: 10.1093/ije/dyy253.*

   Jennyfer Wolf's contributions:

   Design of the investigation
   - Contributing to the development of the logical and analytical framework for deriving estimates for handwashing with soap using survey data on access to handwashing facilities

   Conduct of the research
   - Extracting national survey data on handwashing facility access
   - Identifying relevant epidemiological studies and datasets describing both the presence of handwashing facilities and observed handwashing with soap identified through a systematic review and through contacting subject-matter experts
   - Extracting the relevant data from handwashing observation studies identified through a systematic review

   Analysis of the outcome
   - Cleaning and preparing data for analysis
   - Modeling access to on-site handwashing facilities with soap and water using multilevel (hierarchical) modeling
   - Using multilevel Poisson modeling for assessing the association between presence of handwashing facilities and observed handwashing with soap
   - Conducting random-effects meta-analysis on handwashing observation studies from high-income countries
   - Calculating country, regional and global estimates of prevalence of handwashing with soap after potential faecal contact

   Preparation of the work for publication
   - Interpreting results
   - Drafting of all sections of the manuscript, tables and figures
   - Incorporating comments received from co-authors and reviewers

4. *Wolf J, Hunter PR, Freeman MC, Cumming O, Clasen T, Bartram J, Higgins JPT, Johnston R, Medlicott K, Boisson S, Prüss-Ustün A. (2018) Impact of Drinking Water, Sanitation and Hand Washing with Soap on Childhood Diarrhoeal Disease: Updated Meta-Analysis and meta-regression. Trop Med Int Health, Volume 23, Issue 5, March 2018 doi: 10.1111/tmi.13051.*

   Jennyfer Wolf's contributions:

   Design of the investigation
   - Contributing to the updated analytical framework for burden of disease analysis from inadequate water, sanitation and hygiene

   Conduct of the research
   - Systematically reviewing the scientific literature and extracting the relevant data from intervention studies using a standardized form
   - Rating the quality of evidence for each included study

   Analysis of the outcome
   - Cleaning and preparing data for analysis
   - Conducting random-effects meta-analysis and meta-regression on the extracted data

Preparation of the work for publication

- Interpreting results
- Drafting of all sections of the manuscript, tables and figures and incorporating comments received from co-authors and reviewers

5. *Prüss-Ustün A, Wolf J, Corvalán C, Neville T, Bos R, Neira M. (2016) Diseases due to unhealthy environments: an updated estimate of the global burden of disease attributable to environmental determinants of health. J Public Health, doi: 10.1093/pubmed/fdw085*

   Jennyfer Wolf's contributions:

   Conduct of the research
   - Systematically reviewing the scientific literature on the links between a broad range of diseases and environmental risk factors, setting up the respective search strategies

   Preparation of the work for publication
   - Interpreting results
   - Drafting of all sections of the manuscript, tables and figures and incorporating comments received from co-authors and reviewers

6. *Wolf J, Prüss-Ustün A, Cumming O, Bartram J, Bonjour S, Cairncross S, Clasen T, Colford JM Jr, Curtis V, De France J, Fewtrell L, Freeman MC, Gordon B, Hunter PR, Jeandron A, Johnston RB, Mäusezahl D, Mathers C, Neira M, Higgins JP. (2014) Assessing the impact of drinking water and sanitation on diarrhoeal disease in low- and middle-income settings: systematic review and meta-regression. Trop Med Int Health, Volume 19, Issue 8, pages 928–942, August 2014 doi: 10.1111/tmi.12331*

   Jennyfer Wolf's contributions:

   Design of the investigation
   - Contributing to the analytical framework for burden of disease analysis from inadequate water and sanitation

   Conduct of the research
   - Extracting the relevant data from intervention studies using a standardized form

   Analysis of the outcome
   - Cleaning and preparing data for analysis
   - Conducting random-effects meta-analysis and meta-regression on the extracted data

Preparation of the work for publication

- Interpreting results
- Drafting of all sections of the manuscript, tables and figures and incorporating comments received from co-authors and reviewers

7. *Prüss-Ustün A, Bartram J, Clasen T, Colford JM Jr, Cumming O, Curtis V, Bonjour S, Dangour AD, De France J, Fewtrell L, Freeman MC, Gordon B, Hunter PR, Johnston RB, Mathers C, Mäusezahl D, Medlicott K, Neira M, Stocks M, Wolf J, Cairncross S. (2014) Burden of disease from inadequate water, sanitation and hygiene in low- and middle-income settings: a retrospective analysis of data from 145 countries. Trop Med Int Health, Volume 19, Issue 8, pages 894–905, August 2014. doi: 10.1111/tmi.12329.*

<u>Jennyfer Wolf's contributions:</u>

Design of the investigation

- Contributing to the analytical framework for burden of disease analysis from inadequate water, sanitation and hygiene

Conduct of the research

- Providing required input data for burden of disease analysis

Preparation of the work for publication

- Revising the draft manuscript and providing critical input

8. *Freeman MC, Stocks ME, Cumming O, Jeandron A, Higgins JP, Wolf J, Prüss-Ustün A, Bonjour S, Hunter PR, Fewtrell L, Curtis V. (2014) Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. Trop Med Int Health, Volume 19, Issue 8, pages 906–916, August 2014. doi: 10.1111/tmi.12339.*

<u>Jennyfer's contributions:</u>

Design of the investigation

- Contributing to the analytical framework for burden of disease analysis from inadequate hygiene

Conduct of the research

- Extracting the relevant data from intervention studies using a standardized form

Analysis of the outcome

- Cleaning and preparing data for analysis
- Conducting random-effects meta-analysis and meta-regression on the extracted data

Preparation of the work for publication

- Interpreting results
- Writing relevant analysis sections for the first draft of the manuscript
- Revising the draft manuscript and providing critical input

9. *Wolf J, Bonjour S, Prüss-Ustün A (2013) An exploration of multilevel modeling for estimating access to drinking-water and sanitation. J Water Health. 2013 Mar; 11(1):64-77.*

Jennyfer Wolf's contributions:

Design of the investigation

- Contributing to the development of the analytical framework

Conduct of the research

- Exploring suitable model options

Analysis of the outcome

- Preparing and cleaning data for analysis
- Setting up the multilevel model to estimate access to drinking water and sanitation facilities including model checking

Preparation of the work for publication

- Interpreting results
- Drafting of all sections of the manuscript, tables and figures and incorporating comments received from co-authors and reviewers

Swiss TPH

Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut
Institut Tropical et de Santé Publique Suisse

Epidemiology & Public Health
Household Economics & Health Systems Research Unit

Prof. Dr. Daniel Mäusezahl
Epidemiologist (MSc PhD MPH)
Head Household Health Systems Research Group

Daniel.Maeusezahl@unibas.ch
T +41 61 284 83 15 secr.
T +41 61 284 81 78 direkt

Basel, 10.June 2019

To whom it may concern

I hereby confirm that **Jennyfer Wolf** is a coauthor on the below peer-reviewed articles.
Her specific contributions to these two papers were as follows:

Article-1: *Hartinger SM, Lanata CF, Hattendorf J, Verastegui H, Gil AI, **Wolf J**, Mäusezahl D. (2016) Improving household air, drinking water and hygiene in rural Peru: a community-randomized–controlled trial of an integrated environmental home-based intervention package to improve child health. Int J Epidemiol, doi:10.1093/ije/dyw242*

Jennyfer Wolf's contributions to this paper:

Jennyfer prepared the manuscript draft including the relevant research input and incorporated comments after peer-review. Additionally, she contributed to the design and setup of a subsequent and related trial of a similar environmental intervention package which was subsequently funded and implemented.

Article-2: *Wolf J, Mäusezahl D, Verastegui H, Hartinger SM. (2017) Adoption of Clean Cookstoves after Improved Solid Fuel Stove Programme Exposure: A Cross-Sectional Study in Three Peruvian Andean Regions. Int J Environ Res Public Health. 2017 Jul 8;14(7). doi: 10.3390/ijerph14070745.*

Jennyfer Wolf's contributions to this paper:

Jennyfer's contributions included designing and developing the questionnaire, checking the accurate completion of the questionnaire on site in Peru; cleaning, preparing and analysing the data, interpreting the results from data analysis also in the light of previous research. She wrote the first draft of the manuscript and incorporated comments from coauthors and peer-review comments

Swiss TPH, Socinstrasse 57, Postfach, CH-4002 Basel, T +41 61 284 81 11, F +41 61 284 81 01, www.swisstph.ch

Article-3: *Impact of a child stimulation intervention on early child development in rural Peru: A cluster randomised trial using a reciprocal control design. S.M. Hartinger, C.F. Lanata, J. Hattendorf,* ***J. Wolf,*** *A.I Gil, M. Ortiz Obando, M. Noblega, H. Verastegui, T Ochoa, D. Mäusezahl J Epidemiol Community Health, 2016; doi:10.1136/jech-2015-206536*

<u>Jennyfer Wolf's contributions to this paper:</u>

Jennyfer's contributions included analysing the data, interpreting the results from data analysis also in the light of previous research. She contributed to writing the first draft of the manuscript with the main authors and helped formulating the response to reviewer comments.

Daniel Mäusezahl

Basel, 10.6.2019