Health risk assessment along wastewater recovery and reuse systems in Kampala, Uganda and Hanoi, Vietnam

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Summary

Background: Reuse and recovery of wastewater in agriculture and aquaculture has gained traction in the new millennium. In view of continued population growth, increasing scarcity of freshwater and other natural resources, the demand to boost food production and efforts to enhance wastewater reuse will increase in the years to come. Indeed, wastewater reuse and the recovery of water, nutrients and energy can generate promising business opportunities and support livelihoods in poor communities, particularly in urban and peri-urban areas in low- and middle-income countries (LMICs). Contact with untreated wastewater is associated with microbial and chemical hazards and thus might negatively affect human health. Standardised, quality-controlled methods to assess and manage health risks are available, such as those described in the World Health Organization (WHO) guidelines for the safe use of wastewater, excreta and greywater. However, the practicability and uptake of these methods have proved difficult in LMICs. There is a paucity of context-specific, quality-based environmental pollution data, epidemiological data and accurate disease burden estimates for highly dynamic environments along wastewater recovery and reuse systems in major urban settings, especially in Africa, Asia and Latin America. Moreover, discharge thresholds and health-based targets need to be reviewed to match the realities of LMICs.

Objectives: This PhD research aimed to generate evidence of health risks among people living and working along wastewater and faecal sludge management and reuse systems in Kampala, Uganda (a low-income African city) and in Hanoi, Vietnam (a lower-middle-income Asian city). By comparing relevant conditions in these two systems, the thesis seeks to: (i) generate evidence of microbial and chemical contamination and treatment capacities along wastewater management systems; (ii) assess prevalence and risk factors of intestinal parasitic infections in different population groups exposed to wastewater and faecal sludge; (iii) estimate the burden of gastrointestinal infections due to exposure to wastewater; and (iv) discuss and compare risk assessment approaches and their potential for application along wastewater recovery reuse systems in selected LMICs.

Research partnership: This PhD thesis is embedded in the “Resource Recovery and Reuse” (RRR) project, funded by the Swiss Agency for Development and Cooperation (SDC). Our main partner in this collaborating endeavour is WHO, while other international partners include the International Water Management Institute, the International Centre for Water Management Services, and the Department of Water and Sanitation in Developing Countries, Swiss Federal

Institute of Aquatic Science and Technology. In Uganda, we closely work with the Makerere School of Public Health, the Vector Control Division of the Ministry of Health and the National Water and Sewerage Corporation. In Hanoi, our main partner is the Center for Public Health and Ecosystem Research at Hanoi School of Public Health. Moreover, we closely work with the Department of Parasitology at the National Institute of Malaria, Parasitology and Entomology, the National Institute of Hygiene and Epidemiology, and the National Institute of Veterinary Research.

Methods: Two accordant case studies were carried out along the major wastewater recovery and reuse systems in Kampala (along the Nakivubo channel) between September and December 2013 and in Hanoi (along the To Lich River) between April and June 2014. A methodological triangulation was performed, including (i) an environmental assessment; (ii) a cross-sectional survey; and (iii) a quantitative microbial risk assessment (QMRA). In brief, the environmental assessment entailed different standard analyses to observe the variance of microbial contamination (thermotolerant coliforms (TTC), *Escherichia coli*, *Salmonella* spp. and helminths (e.g. *Ascaris* and hookworm eggs) in water at critical control points over a period of two months. In addition, in Kampala, a range of physico-chemical parameters and heavy metal contamination in sediment, soil and plants were measured. Cross-sectional parasitological surveys were conducted to assess intestinal parasitic infections in different population groups (aged ≥18 years) exposed to wastewater and faecal sludge such as sanitation workers, urban farmers and community members living in proximity to wastewater channels. Moreover, comparison groups without exposure to wastewater were included. Stool samples were subjected to the Kato-Katz and formalin-ether concentration methods for the diagnosis of helminth and intestinal protozoa infections. A questionnaire was administered to all participants to identify self-reported signs and symptoms and risk factors for intestinal parasite infections. The QMRA methodology was applied to different scenarios of exposure to wastewater (e.g. farming, flooding of living area, living in informal communities and swimming). Pathogenic strains of norovirus, rotavirus, *Campylobacter* spp., pathogenic *E. coli*, pathogenic *Salmonella* spp., *Cryptosporidium* spp. and *Ascaris lumbricoides* were used to estimate annual incidence of gastrointestinal illness and the resulting disease burden.

Results: The environmental assessment revealed high concentrations of bacteria along the major wastewater channels in Kampala and Hanoi (e.g. between 10^5 and 10^7 colony forming unit (CFU) per 100 mL). In Kampala, along the Nakivubo channel, the concentration of TTC,

biological oxygen demand$_5$ (BOD$_5$), chemical oxygen demand (COD) and total suspended solids (TSS) were 2- to 3-fold higher, when compared with data reported in 2008. Moreover, contamination of bacteria measured in water of the Nakivubo wetland, where urban farming takes place, was above national discharge standards and WHO's tolerable safety limits for unrestricted irrigation. In Hanoi, the To Lich River water used in wastewater-fed agriculture fields in peri-urban areas showed (beside applied treatment in retention ponds) mean contamination with total coliforms (TC), *E. coli* and *Salmonella* spp. of 1.3×10^7, 1.1×10^6 CFU/100 mL and 108 most probable number (MPN)/100 mL, respectively. These values are 110-fold above the Vietnam discharge limits for agriculture reuse and even 260-fold above WHO's tolerable safety limits for unrestricted irrigation. In both cities, the issue of faecal sludge collection is challenged by the provision of formal and adequate collection services, disposal and reuse solutions. Moreover, industrial pollution is a major issue, while registration and the source control of industries and effluents is lacking, leading to elevated concentration of various heavy metals in the environment.

The cross-sectional survey in Kampala included 915 individuals and revealed that the highest point-prevalence of intestinal parasite infections was found among urban farmers (75.9%), whereas the lowest point-prevalence was found among workers collecting faecal sludge (35.8%). Hookworm was the predominant helminth species (27.8%). *Trichuris trichiura*, *Schistosoma mansoni, A. lumbricoides*, and *Entamoeba histolytica/E. dispar* showed prevalence rates of 15% and above among urban farmers. For all investigated parasite infections, we found significantly higher odds for urban farmers than for the other groups (adjusted odds ratios ranging between 1.6 and 12.9). In Hanoi, the cross-sectional survey included 681 individuals and showed lower point-prevalence rates of intestinal parasite infections than in Kampala. The highest point-prevalence rate of parasitic infection was found among rural farmers (30.2%), with hookworm and *T. trichiura* being the predominant helminth species (24.8% and 5.4%, respectively). For intestinal parasite infections, we found significantly higher odds for rural farmers than for other groups (adjusted odds ratios 5.8, 95% confidence interval 2.5 to 13.7).

For Kampala, the QMRA estimated an annual disease burden across all 18,204 exposed people of 304,3 disability-adjusted life years (DALYs). Disease burden per person per year (pppy) was highest among urban farmers, sanitation workers and children in slum communities (0.073, 0.040 and 0.017 DALYs, respectively). For Hanoi, QMRA estimated an annual disease burden across 7,125 exposed people of 62.7 DALYs. Disease burden pppy was highest in urban farmers

(0.0122 DALYs pppy), followed by sanitation workers (0.006 DALYs pppy) and rural farmers (0.0004 DALYs pppy).

Conclusions: The findings from this 3-year PhD thesis make an important contribution for a deeper understanding of the nexus of urban wastewater recovery and reuse systems, wastewater pollution and their implications for public health in the context of a major East African and Southeast Asian city. In both cities, and besides considerable differences in applied infrastructures, wastewater treatment capacities are insufficient for reducing the levels of microbial and chemical contamination to tolerable levels that would allow for safe reuse in agriculture. Major health risks were observed along both wastewater recovery and reuse systems. Children living in informal communities in Kampala are at very high risk of gastrointestinal diseases, especially due to rotavirus, and pathogenic *E. coli* and *Salmonella* spp. Epidemiological survey estimates revealed that urban farmers using wastewater were especially vulnerable for schistosomiasis and soil-transmitted helminthiasis in Kampala, whereas the high risk for urban farmers in Hanoi was only evident by means of QMRA. Indeed, for urban farmers, QMRA estimates were as high as 0.073 and 0.011 DALYs pppy in Kampala and Hanoi, respectively. These estimates are several thousand-fold above the revised WHO health-based targets and 7 and 6 times higher than the estimates made by the Global Burden of Disease study 2010 for an average Ugandan and Vietnamese, respectively. It is argued that the current health-based targets should be set according to local reference levels (e.g. to estimates made by the Global Burden of Disease study 2010). Promoting sanitation safety planning while combining evidence generated from environmental surveys, epidemiological surveys and QMRA can contribute to the understanding of existing systems and hazards along critical control points to better evaluate further investments in infrastructure and coordinate actions to protect public health. Considering the increasing attention to wastewater in the framework of the sustainable development goals (SDGs), more integrated studies using sanitation safety planning approaches are needed to generate sufficient understanding of reuse situations in rapidly changing urban contexts to minimise detrimental health effects and maximise gains from the recovered water, nutrients and energy in urban areas of LMICs.

Zusammenfassung

Hintergrund: Die Wiederverwendung und die Verwertung von Abwasser in der Landwirtschaft und der Fischzucht hat im neuen Jahrtausend an Wichtigkeit gewonnen. In Anbetracht des anhaltenden Bevölkerungswachstums, einer zunehmenden Verknappung von Süsswasser sowie anderen natürlichen Ressourcen und der steigenden Nachfrage in der Nahrungsmittelproduktion wird die Wiederverwendung von Abwasser in Zukunft weitersteigen. Die Verwertung der daraus gewonnenen Ressourcen Wasser, Nährstoffe und Energie generiert vielversprechende Geschäftsmöglichkeiten und kann insbesondere in städtischen und stadtnahen Gebieten einkommensschwacher Länder und in Ländern mittleren Einkommens (LMICs) ein Mittel gegen dort vorherrschende Armut sein. Der Kontakt mit unbehandeltem Abwasser ist jedoch mit mikrobiellen und chemischen Risikofaktoren verbunden, weshalb Menschen, die in Kontakt mit Abwasser treten, potentiell negativen Auswirkungen auf ihre Gesundheit ausgesetzt sind. Für die Messung und den Umgang mit diesen Gesundheitsrisiken wurden standardisierte Methoden entwickelt. Ein Beispiel dafür sind die Leitlinien für die sichere Verwendung von Abwasser, Fäkalien und Grauwasser der Weltgesundheitsorganisation (WHO). Allerdings hat sich gezeigt, dass Umsetzung und Akzeptanz dieser Konzepte in LMICs schwierig sind. Tatsächlich ist ein Mangel an kontextspezifischen und qualitätsorientierten Daten zur Umweltbelastung und zur Epidemiologie sowie an verlässlichen Schätzungen zur Krankheitsbelastung festzustellen, zumal für die sich schnell verändernden Umgebungen um die Systeme von Abwasserrückgewinnung und -verwendung, gerade in afrikanischen, asiatischen und lateinamerikanischen Städten. Darüber hinaus sind die heute geltenden abwasser- und gesundheitsspezifischen Grenzwerte im Lichte der Realitäten in LMICs zu überprüfen und gegebenenfalls anzupassen.

Ziele: Das Ziel der vorliegenden Doktorarbeit ist es, Hinweise auf die Gesundheitsrisiken für Menschen zu finden, die durch ihre Arbeit oder ihren Wohnort mit Abwasser bzw. den Produkten aus der Abwasserbehandlung (z.B. Fäkalschlamm) in Berührung kommen. Die Untersuchung zu diesen Risiken wurde in einer Stadt in einem einkommensschwachen Land (Kampala in Uganda (Afrika)) und einer Stadt mittleren Einkommens (Hanoi in Vietnam (Asien)) durchgeführt. Durch den Vergleich relevanter gesundheitsspezifischer Daten in diesen beiden Systemen strebt die Arbeit folgende Ziele an: (i) Bestimmung der mikrobiellen und chemischen Verunreinigungen sowie der Behandlungskapazitäten entlang

Abwassermanagementsystemen; (ii) Beurteilung der Prävalenz und der Risikofaktoren von Darmparasiteninfektionen in verschiedenen Bevölkerungsgruppen, die Abwasser und Fäkalschlamm ausgesetzt sind; (iii) Schätzung der Belastung von abwasserverursachten Magen-Darm-Infektionen auf betroffene Risikogruppen; und (iv) Diskussion und Vergleich von Risikobewertungskonzepten und deren Anwendungspotenzial in Abwasserrückgewinnungssystemen in LMIC.

Forschungspartnerschaft: Diese Dissertation findet im Rahmen des "Resource Recovery and Reuse" Projekt (RRR) statt und wird von der Schweizerischen Direktion für Entwicklung und Zusammenarbeit (DEZA) finanziert. Das Projekt wurde in enger Zusammenarbeit mit der WHO und folgenden nationalen und internationalen Projektpartnern durchgeführt, das „International Water Management Institute“, das „International Centre for Water Management Services“, and dem „Department of Water and Sanitation in Developing Countries, Swiss Federal Institute of Aquatic Science and Technology“. In Uganda, arbeiten wir mit der “Makerere School of Public Health”, der “Vector Control Division of the Ministry of Health” und dem “National Water and Sewerage Corporation”. In Hanoi ist unserer wichtigster Partner das “Center for Public Health and Ecosystem Research at Hanoi School of Public Health”. Zudem haben wir eine Zusammenarbeit mit dem “Department of Parasitology” an der “National Institute of Malaria, Parasitology and Entomology”, dem “National Institute of Hygiene and Epidemiology”, und dem “National Institute of Veterinary Research”.

Methoden: Die zwei Studien wurden entlang der bedeutendsten Abwasserrückgewinnungs- und Wiederverwendungssysteme von Kampala (Nakivubo-Kanal), zwischen September und Dezember 2013, sowie von Hanoi (To Lich River), zwischen April und Juni 2014, durchgeführt. Für die Untersuchung wurden drei Methoden mit den entsprechenden Fallstudien angewendet: (i) Eine Umweltprüfung; (ii) eine quantitative mikrobielle Risikobewertung (QMRA); und (iii) eine epidemiologische Querschnittsbefragung. Für die Umweltprüfung wurden über einen Zeitraum von zwei Monaten entlang kritischer Kontrollpunkte verschiedene Standardanalysen vorgenommen, um die Varianz der mikrobiellen Parameter (coliforme Bakterien, *E coli, Salmonella* spp und Wurmeier, z.B. von Spul- und Hakenwürmern) im Wasser zu ermitteln. Darüber hinaus wurden in Kampala eine Reihe von physikalisch-chemischen Parametern und Schwermetallen in Flusssediment, Böden und Pflanzen gemessen. Zur Beurteilung der Darmparasiteninfektionen durch Parasiten wurde eine Querschnittsstudie mit verschiedenen Bevölkerungsgruppen (Alter ≥18 Jahre) durchgeführt. Dafür wurden

Arbeiter, die für den Unterhalt der sanitären Anlagen verantwortlich waren, sowie in der Nähe von Abwasserkanälen lebende städtische Bauern und Community-Mitglieder berücksichtigt. Außerdem wurden Vergleichsgruppen, die keiner direkten Einwirkung von Abwasser ausgesetzt waren, eingeschlossen. Die Stuhlproben der Studienteilnehmer wurden mittels Kato-Katz und Formalin-Ether-Konzentrationsverfahren auf Infektionen durch Würmer und Darmprotozoen getestet. Eine Befragung aller Teilnehmer wurde durchgeführt, um selbstberichtete Symptome und Risikofaktoren für Darmparasiteninfektionen zu identifizieren. Die QMRA-Methode wurde angewandt, um verschiedene Szenarien der Exposition gegenüber Abwasser zu simulieren (z.B. urbane Landwirtschaft, Überschwemmung der Wohngebiete, Leben in Slum-Gegenden oder Schwimmen). Die Stämme der Pathogene Norovirus, Rotavirus, *Campylobacter* spp., Pathogene *E. coli*, pathogene *Salmonella* spp., *Cryptosporidium* spp. und Ascaris wurden verwendet, um die jährliche Inzidenz von Magendarmkrankheiten und der daraus resultierenden Krankheitslast zu schätzen.

Ergebnisse: Die Umweltprüfung ergab eine Belastung durch hohe Konzentrationen von Bakterien (zwischen 10^5 und 10^7 CFU/100 ml) entlang der Hauptabwasserkanäle in Kampala und Hanoi. Entlang des Nakivubo-Kanals in Kampala waren die Konzentrationen der coliformen Bakterien, des biochemischen Sauerstoffbedarfes (BSB_5), des chemisches Sauerstoffbedarfes (CSB) und der gesamten ungelösten Stoffe (GUS) im Vergleich zum Jahr 2008 um 200% bis 300% erhöht. Diese Resultate weisen darauf hin, dass im angrenzenden Nakivubo-Sumpfgebiete, wo das Abwasser indirekt wiederverwendet wird und die dort angesiedelten Slums häufig überflutet werden, die Bakterienkonzentrationen im Wasser über den nationales Standards und über der tolerierbaren Sicherheitsgrenze der WHO für die uneingeschränkte Nutzung des Wassers zur Bewässerung liegen. Das Wasser des To Lich River in Hanoi, das zur Bewässerung der Felder in Stadtrandgebieten genutzt wird, zeigte am Entnahmeort bei einer Anlage zur Abwasserbehandlung mittlere Kontaminationen mit TC, *E. coli* und *Salmonella* spp. von $1{,}3 \times 10^7$, $1{,}1 \times 10^6$ CFU/100 ml bzw. 108 MPN/100 ml. Diese Werte sind 110-mal höher als die in Vietnam geltenden Abwasserableitungsgrenzwerte zur Wiederverwendung in der Landwirtschaft und sogar 260-mal höher als die tolerierbare Sicherheitsgrenze der WHO für die uneingeschränkte Nutzung des Wassers zur Bewässerung. In beiden Städten sind die für Sammlung, Entsorgung und Wiederverwendung des Fäkalschlamms zuständigen Dienste nicht ausreichend organisiert. Darüber hinaus ist die Umweltverschmutzung durch die Industrie ein wichtiges Thema. Es fehlt ein Instrument zur

Überwachung und Prüfung der Verursacher von Industrieabfällen und -abwässern, was zu erhöhten Konzentrationen verschiedener Schwermetalle in der Umwelt führt.
Die Querschnittsstudie in Kampala umfasste 915 Personen und ergab, dass die höchste Punktprävalenz von Darm-Infektionen durch Parasiten bei städtischen Landwirten (75.9%) vorkommt, während sich die tiefste Punktprävalenz bei den fäkalschlammsammelnden Arbeitern (35.8%) zeigt. Der Hakenwurm war die vorherrschende Helminthenart (27.8%). *Trichuris trichiura*, *Schistosoma mansoni, Ascaris lumbricoides*, and *Entamoeba histolytica/E. dispar* zeigten Prävalenzraten von 15% und mehr unter den städtischen Bauern. Für alle untersuchten Parasiteninfektionen fanden wir eine gegenüber den anderen Gruppen signifikant höhere Quote bei städtischen Bauern (bereinigte Odds Ratio zwischen 1.6 und 12.9).
In Hanoi umfasste die Querschnittsbefragung 681 Personen und zeigte niedrigere Punktprävalenzen von Darminfektionen durch Parasiten als in Kampala. Die höchste Punktprävalenz wurde bei ruralen Landwirten (30.2%) gemessen, mit dem Hakenwurm und *T. trichiura* als häufigsten Wurmarten (24.8% bzw. 5.4%,). Für Darminfektionen durch Parasiten fanden wir eine signifikant höhere Quote als bei den anderen Gruppen bei ländlichen Bauern (bereinigte Odds Ratio 5.8; 95%-Konfidenzintervall 2.5-13.7).
Für Kampala schätzte die QMRA für alle 18‘204 Personen, die den Risiken durch das verschmutzte Wasser ausgesetzt sind, eine jährliche Krankheitsbelastung von 304.3 DALYs (disability-adjusted life years). Die Krankheitslast pro Person und Jahr (pppy) war am höchsten unter den städtischen Bauern, den Arbeitern der Abwasserentsorgung und den Kindern in Slums (0.073, 0.040 bzw. 0.017 DALYs). Für Hanoi schätzte die QMRA für die 7'125 exponierten Personen eine jährliche Krankheitbeslastung von 62.7 DALYs. Die Krankheitslast pppy war am höchsten bei den städtischen Bauern (0.0122 DALYs pppy), gefolgt von den Arbeitern der Abwasserentsorgung und den ruralen Bauern (0.006 bzw. 0.0004 DALYs pppy).

Schlussfolgerungen: Die Ergebnisse der vorliegenden 3-jährigen Doktorarbeit leisten einen wichtigen Beitrag zum Verständnis des Zusammenspiels von städtischen Systemen zur Abwasserrückgewinnung und –wiederverwendung, Schadstoffen im Abwasser und deren Auswirkungen auf die öffentliche Gesundheit im Kontext einer ostafrikanischen und einer südostasiatischen Stadt. In beiden Städten sind, trotz beträchtlicher Unterschiede in den verfügbaren Infrastrukturen, die Abwasserbehandlungskapazitäten nicht ausreichend, um die Höhe der mikrobiellen und chemischen Kontaminationen auf ein tolerierbares und den Richtlinien entsprechendes Level zu senken, das eine sichere Wiederverwendung des Abwassers für die Landwirtschaft ermöglichen würde. Die grössten Gesundheitsrisiken wurden entlang der Systeme zur Abwasserrückgewinnung und –wiederverwendung identifiziert: Kinder, die in informellen Gemeinschaften in Kampala leben, sind einem hohen Risiko für gastrointestinale Erkrankungen ausgesetzt (v.a. Rotavirus, *E. coli* und *Salmonella* spp.). Die Resultate der epidemiologischen Untersuchung in Kampala ergaben, dass städtische Bauern, die Abwasser nutzen, besonders anfällig sind für Schistosomiasis und über den Boden übertragene Helminthiasis, während ein hohes Risiko für städtische Bauern in Hanoi nur in der QMRA für Infektionen mit Bakterien und Viren evident war. Die QMRA Schätzungen für städtische Bauern betragen in Kampala 0.073 Dalys pppy und in Hanoi 0.011 Dalys pppy. Diese Ergebnisse liegen um mehrere Tausendfache über den revidierten WHO gesundheitsbasierten Zielen und für Uganda 7-mal bzw. für Vietnam 6-mal höher als die Schätzungen der Global Burden of Disease-Studie aus dem Jahr 2010. Es wird diskutiert, die aktuellen gesundheitsbasierten Ziele gemäss einer lokalen Referenz festzulegen (z.B. gemäss den Erhebungen der Global Burden of Disease study 2010). Im Rahmen einer sicheren Abwassersystemplanung (i.e. Sanitation safety planning) kann die Kombination von Umweltprüfung, epidemiologischen Studien und QMRA einen Beitrag für das Verständnis der bestehenden Systeme und den Risiken entlang der kritischen Kontrollpunkte leisten. Dies ermöglicht eine bessere Beurteilung weiterer Investitionen in die Infrastruktur und die Koordination zukünftiger Massnahmen zum Schutz der Gesundheit. Die zunehmende Bedeutung der Abwasserproblematik im Rahmen nachhaltiger Entwicklungsziele (sustainable development goals) erfordert mehr Studien zu einer sicheren Abwassersystemplanung, um hinreichend Verständnis für die Problematik der Wiederverwendung von Abwasser im sich schnell verändernden Umfeld von Städten in einkommensschwachen Ländern und Ländern mittleren Einkommens zu entwickeln, nachteilige Gesundheitseffekte zu minimieren und die Vorteile aus der Wiederverwendung von Produkten wie Wasser, Nährstoffe und Energie in städtischen Gebieten von LMICs zu maximieren.

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Samuel Fuhrimann

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BOD_5	Biological oxygen demand$_5$
BSTW	Bugolobi sewage treatment works
CCP	Critical control point
Cd	Cadmium
CFU	Colony forming unit
COD	Chemical oxygen demand
Cr	chromium
Cu	Copper
DALY	Disability-adjusted life year
e.g.	exempli gratia
etc.	et cetera
Fe	Iron
GBD	Global burden of disease
HACCP	Hazard analysis and critical control point
HIA	Health impact assessment
HSDC	Hanoi sewerage and drainage company
i.e.	id est
LMIC	Low- and middle-income country
MDG	Millennium development goal
MPN	Most probable number
ODK	Open data kit
Pb	Lead
pppy	per person per year
QMRA	Quantitative microbial risk assessment
RRR	Resource recovery and reuse
SDC	Swiss agency for development and cooperation
SDG	Sustainable development goal
SSP	Sanitation safety plan
SSWM	Sustainable sanitation and water management
Swiss TPH	Swiss tropical and public health institute
TAS	Transmission assessment
TTC	Thermotolerant coliforms

TSS	Total suspended solids
UN	United nations
WASH	Water sanitation and hygiene programs
WHO	World health organization
WHO guidelines	WHO guidelines for the safe use of wastewater, excreta and greywater
WSP	Water and sanitation program
YLD	Years lived with disability
YLL	Years of life lost
Zn	Zinc

1. Thesis outline

This PhD thesis aims to generate evidence on health risks along urban and peri-urban wastewater recovery and reuse systems in low- and middle-income countries (LMICs) (Figure 1.1). The health consequences are visible among people living and working along wastewater and faecal sludge management and reuse systems near a low-income African city (Kampala, Uganda) and a lower-middle-income Asian city (Hanoi, Vietnam).

The thesis starts with an introduction (chapter 2), including a literature review to show the importance of waste recovery and reuse in regard to the post-millennium development goals (MDGs) agenda and its sustainable development goals (SDGs), to describe more explicit on existing wastewater management and reuse schemes and to summarize potential hazards, risks and health outcomes in relation to exposure pathways and exposed population groups. Subsequently, an overview of existing risk analysis frameworks with a focus on assessment and management of risks is given.

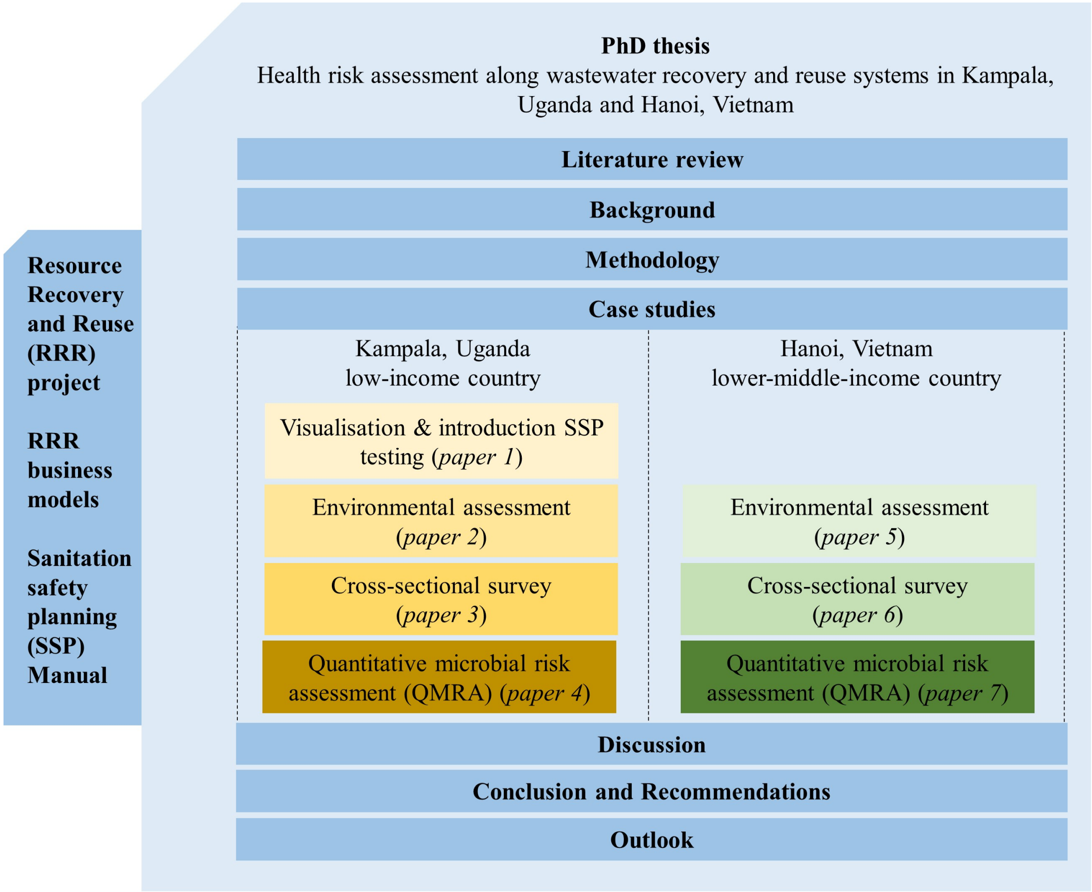

Figure 1.1 Schematic PhD thesis outline

The third chapter outlines the background of the thesis starting with the identified research needs, the PhD study specific objectives, and the collaborative framework of the "Resource Recovery and Reuse" project (RRR). This is followed by a short chapter on the methodology used, including descriptions of the study sites and the applied methods (chapter 4).

From the fifth to the eleventh chapter seven manuscripts, which are published in peer-reviewed journals, describe the findings from case studies in two major urban environments; one in a low-income African country (Kampala, Uganda) and one in a lower-middle-income Asian country (Hanoi, Vietnam). In both study sites, three approaches were applied, namely: environmental assessment, epidemiological survey and quantitative microbial risk assessment (QMRA) to assess health risks of exposure to wastewater and faecal sludge. First, this PhD study visualises in an accessible and innovative video the study framework, including the practical application of the health risk assessment approaches and the pre-testing of the sanitation safety planning (SSP) manual in Kampala (chapter 5). Second, the results of environmental assessments indicated microbial and chemical contamination of urban environments along the wastewater conveyance and treatment systems (chapters 6 and 9). Third, epidemiological cross-sectional studies were used to determine the difference in intestinal parasitic infections and associated risk factors among population groups exposed to wastewater and faecal sludge (chapters 7 and 10). Finally, QMRA was used to estimate the disease burden of gastrointestinal infections pertaining to different wastewater exposure scenarios (chapters 8 and 11).

Chapter 12 starts with an overview on the main results and how they fit into the Swiss Tropical and Public Health Institute (Swiss TPH) nexus of innovation, validation and application. Further, the main findings will be discussed in accordance with the PhD study objectives (outlined in chapter 3.2), beginning of how wastewater recovery and reuse systems are affected by rapid population growth and urbanisation (objective 1). What follows is a discussion of intestinal parasitic infections among different urban population groups exposed to wastewater and faecal sludge (objective 2) and the global burden of disease related to gastrointestinal infections in LMICs (objective 3). Subsequently, the practical relevance of the risk estimates for Kampala and Hanoi is highlighted. Hence, the promotion of risk assessment and the way into practice in LMICs is discussed (objective 4). Finally, chapter 13 will provide conclusions and specific recommendation to the broader international community.

2. Introduction including literature review

2.1. Waste recovery and reuses

2.1.1. Trends in urban waste recovery and reuse

Currently, in high-income and low-income countries, 350-400 L and 40-100 L of water is used per person each day, respectively (AQUASTAT 2015; Mara 2004). Moreover, world cities generate about 1.3 billion tonnes of solid waste per year. The world population —which currently stands at 7.3 billion (July 2015 estimate)— is expected to grow to about 9.5 billion by 2050. Over this period, urban areas will expand, the volume of water used and waste generated will increase and even more than double in LMICs (Drechsel et al. 2015; Hoornweg and Bhada-Tata 2012). Hence, the recovery and reuse of waste resources is of growing importance for urban planning (Drechsel et al. 2015; Grant et al. 2012). The relevance of the reuse will gain additional importance, when considering that half of the world's population is predicted to live in water-stressed areas, with further enhanced competition for clean water, nutrients and energy by 2025 (Dalsgaard 2007; Jiménez et al. 2010). There are simple, low-cost procedures and technologies, to collect, separate and process waste resources and transform them into valuable goods (Grant et al. 2012; Qadir et al. 2010). Most of them work on a small-scale and require minimal training (e.g. wastewater reuse in agriculture and aquaculture or processing of organic solid waste and faecal sludge through anaerobic biogas production and aerobic co-composting) (Mok et al. 2014; Tilley et al. 2014). There is growing consensus that resource recovery and reuse projects —when implemented at large scale— can fundamentally safeguard human and environment health and promote food security, cost recovery in the sanitation sector, and livelihood opportunities in urban and peri-urban areas of LMICs (Drechsel et al. 2015; Qadir et al. 2010; Raschid-sally and Jayakody 2008).

Thus, many LMICs lack formal and efficient waste management systems. There, waste recovery and reuse usually occurs in an unplanned way and is facing various economic, social, environmental and health challenges (Hoornweg and Bhada-Tata 2012; Qadir et al. 2010). For example, uncollected liquid and solid waste is a leading cause of soil, air and water pollution and acts as a source for the spreading of infectious diseases (Mara et al. 2010; WHO 2006a). Thus, waste streams can contain different kinds of waste from different origin, which need specific management strategies (e.g. wastewater, faecal sludge, municipal solid waste, hospital waste, industrial waste and agro-industrial waste) (Strande et al. 2014; Tilley et al. 2014). Hence, functional waste management systems from the point of waste generation to the point of its disposal or reuse are needed to protect human and environmental health. Provision of hygienic conditions for the safe management of human, animal and industrial wastes to prevent exposures to hazards are therefore of high importance (WHO 2010; Stenström et al. 2011).

2.1.2. Waste management systems and sustainable development goals

The ancient Romans had previously recognised waste management as key to improve public health and the development of functional waste management systems was crucial for the growing cities in Europe and America in the late 19th and early 20th centuries (Bradley 2012; Schmidt 2014). Thus, waste management has considerably added to the increase in human life expectancy in the past decades, especially while contributing to the decrease in mortality from diarrhoeal disease from 2.5 to 1.4 million between 1990 and 2010 (Lozano et al. 2012). Hence, waste management can be seen as a key element of sustainable development, which considerably impacts people's health and wellbeing worldwide (Tilley et al. 2014).

The current development agenda and its millennium development goals (MDGs) focused on sanitation in the sense of the provision of facilities and services for the safe disposal of human urine and faeces (United Nations 2015). 79 LMICs out of the total 185 participating countries had insufficient progress or could not meet the specific MDG 7c to reduce the number of people who had no access to improved sanitation —provision of safe, hygienic, and accessible sanitation— by half between 1990 and 2015 (UNICEF 2005; WHO and UNICEF 2014). As of today, about 2.5 billion people lack access to improved sanitation (Cross and Coombes 2014). This in addition to 1 billion people still practising open defecation worldwide, with highest rates in Africa and Asia (30% and 50% people affected, respectively) (WHO and UNICEF 2014).

In LMICs considerable inequalities in access to improved sanitation and waste management services exist. Inequalities are most prominent for people living in rural or urban slums areas as well as between social groups (e.g. people of different ethnicity or religion), wealth, and gender (Utzinger and Keiser 2006). By providing improved sanitation together with safe drinking water and appropriate hygiene, approximately 2.4 million mostly diarrhoeal-related deaths could be prevented annually in LMICs (Bartram and Cairncross 2010; Prüss-Ustün et al. 2014). Therefore, measures and systems solutions are needed to reduce the impact of poor sanitation and protect the health of these often marginalised population groups in LMICs (Ziegelbauer et al. 2012; Wolf et al. 2014; Burki 2015). As per 2015, the post-MDG agenda will be defined and its sustainable development goals (SDGs) are likely to focus on ensuring sustainable management of water and sanitation systems (goal 6) to protect vulnerable populations groups and effectively promote sustainable development all around the world until 2050 (WHO and UNICEF 2012; Dora et al. 2014).

2.2. Wastewater recovery and reuse

2.2.1. The increasing potentials for wastewater reuse

Wastewater can be defined as *"used water that contains waste substances from homes, factories and farms"* (Oxford Dictionaries). Its reuse has gained traction in the 21st century in LMICs (Grant et al. 2012). Wastewater is available throughout the year and has a high load of nutrients (e.g. phosphorus and nitrogen). Thus, reuse is especially attractive for agriculture or aquaculture around urban centres (Raschid-sally and Jayakody 2008). Further, business opportunities can be generated, while wastewater is used for ground water recharge, to replace chemical fertilizer (e.g. drying or co-composting of sludge can produce high quality fertilizer) or to produce electricity (e.g. anaerobic digestion of wastewater sludge, combustion of waste pellets) (Drechsel et al. 2015).

Planned reuse of treated wastewater in agriculture is projected to increase by 271%, from about 7 km^3 per year in 2011 to 26 km^3 per year in 2030 (Global Water Intelligence 2014; AQUASTAT 2015). Considerably larger volumes of untreated or partially treated wastewater are used in unplanned and indirect ways in agriculture (i.e. through diversion of water from wastewater receiving surface water bodies) (Cissé 1997; Cissé et al. 2002). In LMICs, irrigation with wastewater is often strongly linked to long local reuse traditions and found around 4 out of 5 the cities, on 6 to 20 million ha (Raschid-sally and Jayakody 2008). For example, in Hanoi indirect reuse of wastewater for vegetable, rice and fish production is conducted by as many as 658,000 farmers on an area of approximately 43,778 ha (Raschid-sally and Jayakody 2008) or in Accra where more than 200,000 people eat vegetables produced in urban wastewater-fed agriculture on a daily basis (Amoah et al. 2007).

2.2.2. Wastewater reuse and its potential for urban communities

Urban wastewater reuse is providing fresh and high-quality food for urban dwellers, at low cost and minimal logistics, while saving cost for fertilizer and irrigation water (Hamilton et al. 2013). Often entire households are engaged in the labour-intensive production and the selling of the produce on the market (Barker et al. 2007). This in turn can alleviate poverty and mitigate vulnerability of poor urban households by the creation of employment and livelihood opportunities (Cole et al. 2008). Practices require no or very limited training and rely on indigenous resources and skills, while technologies are labour-intensive, adaptive and require only little farming space (Cissé et al. 2002; Drechsel et al. 2006). Moreover, the reuse of wastewater is specific economic importance for poor urban-migrants, as it represents one way of inserting into the urban economy (Matthys 2006). Consequently, such informal irrigation schemes are increasingly recognized as an engine of growth, especially in peri-urban areas of LMICs (Drechsel et al. 2015).

However, reuse of wastewater in urban agriculture is often not permitted by law and supportive/protective regulations for the handling of wastewater are missing (Drechsel et al. 2010). Moreover, farming spots around cities often increase in value and access to land becomes a source of corruption and conflict (Matthys 2006). Thus, only limited service on safe reuse practices and institutional support is provided for urban agriculture, which in many cases impacts on the health of urban farmers and indirectly on the consumers of wastewater-fed produce (WHO 2006a).

2.3. Wastewater management

2.3.1. Contemporary challenges of urban wastewater management systems

Since 2008, more than 50% of the world's population live in urban areas. An increase of 16% in the urban population is expected by 2050, with African and Asian regions urbanising fastest (United Nations 2012). This rapid urbanisation process is posing challenges on the often aging, overloaded wastewater treatment facilities serving small proportions of the population, coupled with limited faecal sludge collection and treatment from onsite facilities (Strande et al. 2014; WHO 2015). Additionally, often lacking are basic infrastructures to supply the growing city populations with piped water and electricity or adequate disposal options for solid waste (Hunter et al. 2010; Ezeah et al. 2013).

Urbanization, driven by population growth and rural-urban migration, is also transforming the social and environmental characteristics of whole regions (Rydin et al. 2012). The result is often a highly heterogenic population with considerable differences in access to adequate infrastructures to compete with waste products (Utzinger and Keiser 2006). As a consequence, storm and wastewater channels generally carry faecal and chemical contamination from a number of sources, including treatment plant effluents, leakage or illegal discharge of faecal sludge, industrial sewage and open defecation within catchments (WHO 2006a). Further, increasing quantities and changing qualities of waste products due to changing lifestyles and industrialisation pose an ultimate risk for public health and the environment (Drechsel et al. 2015). Climate change and resulting extreme events such as seasonal flooding might exacerbate the unfavourable conditions of existing sanitation systems and lead to water-related health risks for the populations (Cissé et al. 2011; Sherpa et al. 2014). Hence, safe wastewater and faecal sludge management and reuse strategies are of pivotal importance for a healthy life in urban settings (Rydin et al. 2012; Cissé 2013).

2.3.2. Wastewater management solutions and realities

To safely manage wastewater and sanitation systems various waste products and inflows have to be considered i.e. from households (e.g. domestic wastewater, faeces, black water, faecal sludge and greywater) as well as from industries and storm water (Figure 2.1) (Schmidt 2014; Strunz et al. 2014). Multiple steps and technologies need to assess the system from the point of generation of the waste product, to collection, storage, conveyance, treatment or recovery of valuable products and finally to disposal and reuse opportunities (Tilley et al. 2014). If applied in a contextually sensitive way, procedures and technologies are able to treat and even enhance the quality and safety of the recovered products (WHO 2006a).

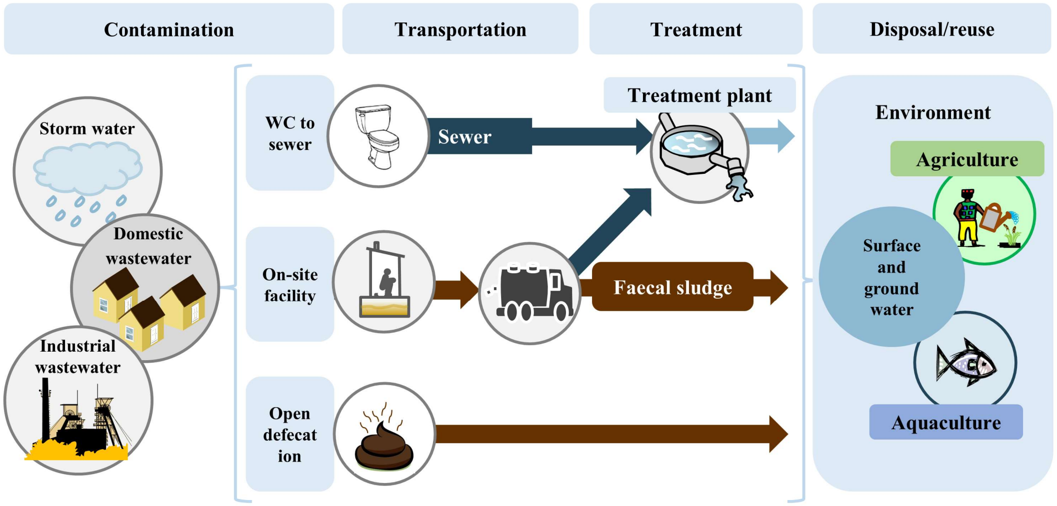

Figure 2.1 Simplified wastewater recovery and reuse system with its various components and inflows, from generation to disposal and reuse of wastewater and faecal sludge.

Globally, 10 to 20% of the generated wastewater reach a treatment facility. Thus, only about 4% of the wastewater is treated by advanced and safe levels (USEPA 2012). Most of the advanced treatment occurs in high income countries, where centralised, waterborne, sewerbased systems are the norm. Such systems are considered as the most viable, long-term solution to fulfil sanitation needs (Mara 2004). However, centralised wastewater systems proved to be not sustainable and economically feasible in LMICs. This can also be underlined by the fact that the sanitation needs of 2.7 billion people worldwide —with one billion in living urban areas— are served by onsite sanitation technologies. This number of people served by onsite sanitation systems is even expected to grow to 5 billion by 2030 (Strande et al. 2014). Irrespectively of the importance of onsite sanitation technologies in LMICs, management strategies have been neglected as such technologies were foreseen as temporary solutions only (Bassan et al. 2015). Consequently, faecal sludge deriving from onsite sanitation technologies is in many cases inappropriately treated and disposed into the environment. The importance of appropriate management solutions can be further underlined that one truck load of faecal sludge disposed untreated in the environment accounts for about 5,000 people practising open defecation (Strande et al. 2014).

The industrialisation of urban areas in LMICs has also increased the problems of industrial and agro-industrial effluents introduced into waste management systems (Winkler et al. 2012). Most of the wastewater channels receive domestic and industrial effluents (i.e. are combined) and it is therefore a challenge to keep out heavy metals, pharmaceutical, pesticides or fertilizers (Barakat 2011; Ackah et al. 2013). Furthermore, there is a paucity of context-specific laws and effective registration processes for industries discharging effluents into the environment, while enforcement mechanisms of existing environmental laws are often missing (WHO 2006a). Therefore, when assessing and planning wastewater management systems in LMICs, it is crucial to acknowledge the diversity and limitations of the different systems in place. Hence, it is pivotal importance to develop wastewater management solutions, including onsite sanitation technologies and addressing the contamination with industrial and agro-industrial effluents (Mara 2004; Tilley et al. 2014).

2.4. Hazards along wastewater recovery and reuse systems

2.4.1. Hazards and resulting risks

Exposure to wastewater bears increased health risks due to a broad range of potential health hazards (i.e. biological, chemical or physical constituents that can cause harm to human health) (WHO 2006a; Keraita and Dávila 2015). Increasing volumes and the changing quality of wastewater results in high microbial and chemical contaminations along urban wastewater systems (Hoornweg and Bhada-Tata 2012). Ill health and loss in economic productivity are often a consequence of this environmental pollution. Meanwhile, increasing incidences of water-borne and water-washed diseases, injuries and poisoning through toxic chemicals are observed (Keraita and Dávila 2015). However, the transmission of microbial hazards depends on hazard-specific and environmental factors such as the infective dose and the ability to induce immunity of pathogens or the persistence of microbial and chemical hazards in the environment over time (Stenström et al. 2011). Hence, the amount of hazards along wastewater systems is dependent on the number of infected individuals and discharge rates of industries and therefore highly variable (Barker et al. 2014; Mara 2004).

2.4.2. Wastewater-borne pathogens

Environmental contamination with viruses (e.g. norovirus and rotavirus), bacteria (e.g. *Campylobacter* spp. and *Salmonella* spp.), intestinal protozoa cysts and oocysts (e.g. *Cryptosporidium* spp. and *Giardia intestinalis*) and helminth eggs and larvae (e.g. *Ascaris lumbricoides*, hookworm and *Schistosoma* spp.) are the leading cause of gastroenteritis (i.e. diarrhoea, vomiting or stomach cramps) or intestinal parasitic infections (Becker et al. 2013). Several, of these pathogens may also lead to sequelae such as anaemia, Gullain-Barré syndrome, reactive arthritis or reduced cognitive development. In severe cases they may even lead to organ failure and death (Lamberti et al. 2012). Most of these pathogens are distributed with the faeces and urine of infected humans and animals. Positive association between diarrhoea, soil-transmitted helminths and *Schistosoma mansoni* and sanitation have been established in many studies (Ziegelbauer et al. 2012; Strunz et al. 2014). Moreover, around urban centres in Africa and Asia increased odds for infections with hookworm, *S. mansoni* or intestinal protozoa for urban farming families using wastewater compared to farmers not using wastewater have been shown (Ensink 2006; Matthys 2006; Pham-Duc et al. 2011).

The global burden of diarrhoeal diseases is estimated to be between 77 and 99 million disability-adjusted life years (DALYs, combining years of life lost (YLLs) and years lived with disability (YLDs)) (Institute for Health Metrics and Evaluation 2015). In LMICs, burden due to diarrheal disease is ranked as the 2nd most important disease outcome, just behind lower-respiratory infections (Murray et al. 2012). A considerable share of this burden is caused by pathogens transmitted due to inadequate sanitation (i.e. 280,000 deaths and 19-21 million DALYs) (Prüss-Ustün et al. 2014; Schmidt 2014). Moreover, in LMICs a broad range of these diseases belong to the neglected tropical diseases and their control, treatment and diagnosis are limited

(Utzinger et al. 2012). About 10 million DALYs are estimated to be lost due to soil-transmitted helminthiasis, schistosomiasis, and food-borne trematodiasis together (50%, 32% and 18%, respectively) (Hotez et al. 2014). Thus, there is considerable uncertainty on the prevalence and magnitude of the disease burden caused by these pathogenic organisms and the share which is associated to risk factors such as exposure to wastewater and the lack of improved sanitation (Murray et al. 2012; Institute for Health Metrics and Evaluation 2015).

2.4.3. Toxic chemicals

Heavy metals, pharmaceutical, pesticides or fertilizers discharged into the environment are likely to cause health issues for exposed people (FAO and WHO 2007). In Europe and the USA several incidences of industrial pollution of water bodies have been reported, which severely impacted on public health and the environment (Merrill 2008). However, in LMICs most often the capacity to measure specific chemicals is not given. Consequently, the impact of chemicals on health is largely unknown as people are often exposed to a “cocktail” of different substances and different concentrations (FAO and WHO 2007; Holm et al. 2010). Moreover, most of the related diseases are chronic and their signs and symptoms may only appear sometime after the initial exposure (e.g. chronic respiratory diseases, diabetes, neurological disorders and cancer) (Azandjeme et al. 2013). Thus, especially in high- and middle-income countries there is an observed shift from acute communicable diseases to chronic non-communicable diseases (i.e. epidemiological transition) (Utzinger and Keiser 2006).

2.5. Exposure routes and possible risk mitigation strategies

2.5.1. Exposure routes

Exposure to wastewater related hazards and resulting transmission of potentially harmful diseases can occur over various routes and affect different exposure groups (Figure 2.2) (Nguyen-Viet et al. 2009; Stenström et al. 2011). Direct exposure to wastewater (i.e. through accidental ingestion, inhalation or dermal contact) can take place in different contexts: (i) during working procedures (e.g. while emptying on-site sanitation facilities, managing wastewater treatment processes or reusing wastewater for irrigation purposes); (ii) during flooding events (e.g. caused by heavy rains) (Barker 2014; WHO 2015a). Indirect exposure to wastewater might occur: (i) when swimming, bathing or using water for washing dishes and clothes from wastewater receiving river or lakes (Ferrer et al. 2012); (ii) through consumption of contaminated drinking water or wastewater-fed crops and fish; and (iii) disease-vectors which breed along wastewater systems (e.g. mosquitos and animal bites) (Machdar et al. 2013; Mok and Hamilton 2014).

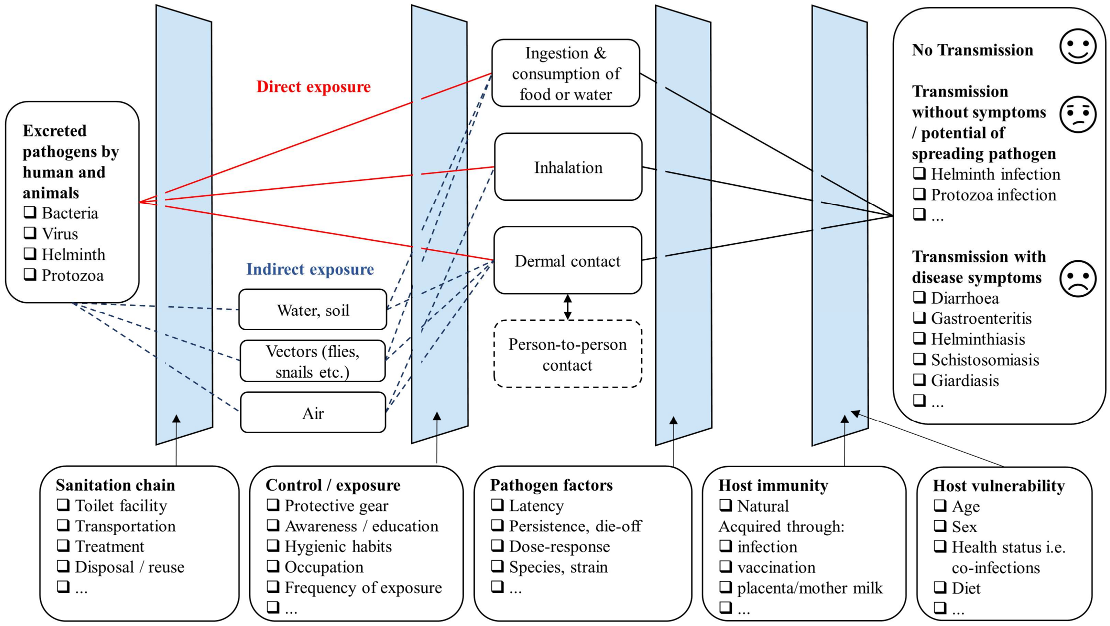

Figure 2.2 Example of potential pathogen transmission routes along wastewater and sanitation systems (adapted from Carr & Strauss 2001)

2.5.2. *Mitigation and integrated control strategies*

To prevent exposures to hazards and plan efficient mitigation strategies resulting risks, one needs to identify critical control points (CCP) (i.e. any step at which control can be applied and it is essential to prevent, eliminate or reduce a hazard to an acceptable level (Stenström et al. 2011). To do so, a detailed understanding of the sources of contamination, technological and non-technological mitigation measures and adequate morbidity control along a wastewater recovery and reuse systems is needed (Carr and Strauss 2001; Keraita and Dávila 2015).

Technological measures can be implemented through different removal or inactivation processes of microbial and chemical pollutants. There are a huge varieties of physical and chemical processes which can be applied to treat wastewater and it's by-products such as filtration, coagulation, aerobic composting, anaerobic digestion, and drying. Of note, the treatment function for microbial pollutants is usually expressed in $\log_{10}$-terms, where one and two log reduction means a reduction of microbes by 90% and 99%, respectively (WHO 2006b; Stenström et al. 2011; Tilley et al. 2014).

Non-technological barriers focus on behaviours which can lead to exposure to hazards and are involving the handling and processing of waste and its products (e.g. use of personal protective equipment, processing of food) (Ekane 2009). Such hygienic behaviours are highly context-specific and vary according to individual responsibility and acceptability (WHO 2006a). Moreover, morbidity control, particularly the prevention of infectious diseases, the WHO recommends for example the administration of anthelminthic drugs to high-risk groups such as school-aged children and directly exposed farming communities (WHO 2011). However, in case of helminth infections it has been shown that preventive chemotherapy alone fails to address the root causes of infection and reinfection (Ziegelbauer et al. 2012). Moreover, preventive action such as vaccination of children with, for example rota virus vaccines, proved to be cost-effective (Rheingans et al. 2014; Sigei et al. 2015).

There are concepts combining technological and non-technological measures (i.e. multiple-barrier approach) (WHO 2006a). For example, while considering low-cost options for reducing consumer health risks from “farm to fork” for wastewater-fed crops (Ilic et al. 2010). Other concepts integrate diseases control for several diseases (e.g. school-based hygienic education and farmer-field school) and targeting high risk groups such as school-aged children and farmers (Van Den Berg and Takken 2007; Singer and de Castro 2007; Utzinger et al. 2009). The selection of the best control strategy is context-specific and should focus on hazards and hazardous events in an integrated way. Hence, it is of pivotal importance to consider CCPs, local health-based targets, discharge standards, environment conditions (e.g. temperature, rainfall, moisture), culture aspects and available resources (e.g. human behaviour and resources and input material) (WHO 2006a; Tilley et al. 2014). Thus, to find the best strategy to mitigate health risks, risk analysis frameworks are needed, which integrate assessment, management and communication of risks (WHO 2006c).

2.6. Risk analysis frameworks along wastewater systems

2.6.1. Concepts to assess and manage health risks

Recognising the growing use of wastewater and the related health risks, the WHO published guidelines for the safe use of wastewater in 1973. The guidelines were subsequently updated, resulting in the 3rd edition of the “WHO guidelines for the safe use of wastewater, excreta and greywater” (WHO guidelines) published in 2006 (WHO 2006c). Their primary aim is to maximise public health protection and the beneficial use of important resources. The WHO guidelines integrate several approaches and tools to assess, manage and communicate health risks, including environmental assessments, epidemiological surveys and QMRA (WHO 2006a).

An important feature of the WHO guidelines is the "Stockholm Framework", which is used as a backbone to set health-based targets (e.g. performance target of 6–7 log units of pathogen reduction by employing a multiple-barrier approach) (Fewtrell and Bartram 2001). To verify these health-based targets, concentrations of *E coli* and helminth eggs in treated wastewater are provided in relation to the reuse scheme. For this purpose, a broad set of technical and non-technical control options are proposed that can be tailored to the different stages of wastewater reuse systems. Health-based targets should be set at the national level and might be based on well-defined health metrics, e.g. 10^{-4} to 10^{-6} DALYs per person per year (pppy) (Mara et al. 2010).

2.6.2. Risk assessment and sanitation safety planning

So far the up-take of the of the rich evidence base of the WHO guidelines proved difficult (Ensink and van der Hoek 2009; Mara and Bos 2010; Breitenmoser and Winkler 2012). It has been recognised that enforcing strict standards may not be sustainable, which can even lead to reduced health protection. They may be viewed as unachievable under local circumstances and thus ignored. Therefore, proposed standards and health-based targets should be adapted to local context, while bearing in mind cultural, social, environmental and economic aspects. Relevant local regulations, laws and policies should be considered to develop approaches towards safe and beneficial reuse of wastewater, excreta and greywater in agriculture and aquaculture (WHO 2006a).

To overcome this lack in up-take of the WHO guidelines the SSP manual was published in 2015. The manual provides a step-by-step guidance on how to implement the WHO guidelines (WHO 2015). The SSP approach should ensure that control measures target the greatest health risks and emphasises incremental improvement over time. The concept of the SSP manual is closely linked to already successfully implemented water safety plan (WSP) manual (Davison et al. 2006). Hence, the SSP manual was developed and tested in different countries with stakeholders from various sectors (agriculture, environment, health and water). The SSP manual can be used at planning stage for new sanitation schemes, next to the improvement of the performance of existing systems. The manual considers therefore six working steps, namely (i) prepare for SSP, describe the sanitation system; (ii) identify hazardous events; (iii) assess existing control measures and exposure risks; (iv) develop and implement an incremental improvement plan; (v) monitor control measures and verify performance; and (vi) develop supporting programmes and review plans. However, the challenge remains that often context-specify data on health risks and outcomes are missing, especially in LMICs. This paucity in data creates a challenge to scale-up SSP to bring stakeholders together in joint working groups, which address health risks due to exposure to wastewater (WHO 2015).

3. Background of the PhD thesis

3.1. Identified research needs

Increasing amounts and changing qualities of generated wastewater, presents huge challenges to management existing wastewater recovery and reuse systems (WHO 2006a; Mara et al. 2010). Pollution of the environment due to inadequate wastewater systems and disposal or reuse of wastewater and faecal sludge is a major public health issue for people living in LMICs. The problematic is greatest around their newly emerging or rapidly expanding urban centres (Rydin et al. 2012; Utzinger and Keiser 2006). For people whose livelihoods depend on the collection, sorting and reusing of wastewater and faecal sludge, and on population groups with poor access to improved sanitation and living in frequently flooded areas or consuming wastewater-fed crops and fish, measures to assess risks and reduce exposures are urgently needed (WHO 2006a, 2015; WHO and UNICEF 2012).

As outlined in the WHO guidelines environmental assessments, epidemiological surveys and QMRA can provide valuable information about health risks. Thus, practical examples to apply and make use of the generated data are needed to safely manage and reuse wastewater and faecal sludge in LMICs (Ensink and van der Hoek 2009; Nguyen-Viet et al. 2009). The risk analysis framework of the WHO guidelines was often poorly understood. Moreover, verification standardises and health-based targets were considered not feasible according to local wastewater recovery and reuse practices (WHO 2006a; Ferrer et al. 2012; Barker 2014).

Indeed, there is a paucity of quality-based environmental pollution and epidemiological data as well as accurate disease burden estimates for rapidly changing environments of cities, especially in Africa, Asia and Latin America (WHO 2006d). Moreover, discharge thresholds, verification limits and health-based targets need to be reviewed on the level of different LMICs to match their realities. For these reasons, there is an urgent need for practical examples on how to apply and make best use of riche evidence base of the WHO guidelines and apply different risk assessment approaches in LMICs (Fewtrell and Bartram 2001; WHO 2006a). The evidence obtained in a timely manner could inspire inter-sector collaboration (e.g. between urban planning, health, environment, agriculture and water sectors) and guide appropriate management and communication of risks to protect the health of vulnerable population groups around rapidly growing cities in LMICs (WHO 2006a; Mara et al. 2010; Pradyumna et al. 2015).

3.2. Goals and objectives

This PhD thesis aims to generate evidence on health risks along urban and peri-urban wastewater recovery and reuse systems in LMICs. The health consequences are visible among people living and working along wastewater and faecal sludge management and reuse systems near a low-income African city (Kampala, Uganda) and a lower-middle-income Asian city (Hanoi, Vietnam).

The study addresses the following four objectives for Kampala and Hanoi in a comparative manner. Specifically, we will:

1) generate evidence on microbial and chemical contamination and treatment capacities along the wastewater management systems;
2) assess prevalence and risk factors of intestinal parasitic infections in different population groups exposed to wastewater and faecal sludge;
3) estimate the burden of gastrointestinal infections due to the exposure to wastewater; and
4) discuss and compare risk assessment approaches and their potential for application along wastewater recovery reuse systems in LMICs.

3.3. Collaborative framework, the "Resource Recovery and Reuse project"

This PhD thesis contributes to the larger framework of a project funded by the Swiss Agency for Development and Cooperation (SDS) entitled "Resource Recovery and Reuse" (RRR). The project started in 2012 with the two aims (i) to increase the scale and viability of productive reuse of water, nutrients, organic matter and energy from municipal solid waste, faecal sludge, wastewater and agro-industrial waste streams through the analysis, promotion and implementation of economically viable business models; and (ii) to safeguard public health in the context of the rapidly expanding use of wastewater, excreta and grey water in agriculture and aquaculture, and to protect vulnerable groups from specific health risks through health risks assessment and mitigation and sanitation safety planning (SSP).

The RRR project is designed to run over a period of six years (from 2012 to 2018) in two distinct phases in the context of four selected cities Kampala (Uganda), Hanoi (Vietnam), Bangalore (India) and Lima (Peru). The first research-oriented phase (from 2012 to 2015) intended to test the feasibility and assess the enabling environment of 21 waste recovery and reuse business models and the SSP manual. The aim of the second RRR project phase is to scale-up the SSP manual in different cities around the world and implement the most feasible business models at the city level of Kampala and one other city.

Our main partner in this collaborating endeavour is WHO, while other international partners include the International Water Management Institute, the International Centre for Water Management Services, and the Department of Water and Sanitation in Developing Countries, Swiss Federal Institute of Aquatic Science and Technology. In Uganda, we closely work with the Makerere School of Public Health, the Vector Control Division of the Ministry of Health and the National Water and Sewerage Corporation. In Hanoi our main partner is the Center for Public Health and Ecosystem Research at Hanoi School of Public Health. Moreover, we closely work with the Department of Parasitology at the National Institute of Malaria, Parasitology and Entomology, the National Institute of Hygiene and Epidemiology, and the National Institute of Veterinary Research.

4. Methodology

4.1. Study sites

For the purpose of the current PhD study, it was of greatest interest to assess and compare health risks along wastewater recovery and reuse systems between two settings, which experienced rapid urbanisation but differ in wastewater management systems and reuse practices. This follows the objective to adapted and apply risk assessment tools for a broader context of cities in LMICs. Hence, from the RRR project sites, a city in a low-income country in East-Africa (Kampala, the capital of Uganda) and a city in a lower-middle-income country in Southeast Asia (Hanoi, the capital of Vietnam) were chosen.

4.1.1. Kampala, Uganda

Uganda is a land-locked country, which obtained independence from Great Britain in 1962. Afterwards, several power struggles impacted the country. The most severe struggle occurred between 1971 and 1979 during the regime of Idi Amine, where an estimated 300,000 people were killed. Since 1986, the start of the regime of the current president Yoweri Museveni, Uganda became more stable. Currently 38 million people live in the country (Cole et al. 2008). Eventhough the country is classified as a low-income country, the economy is growing, especially due to the occurrence of natural resources (e.g. copper, gold and oil). However, the average life expectancy remains low at 55 years and the majority of the disease burden is caused by communicable diseases (Institute for Health Metrics and Evaluation 2015).

Kampala, is located on the northern shore of Lake Victoria at an altitude of 1,140 m above the mean sea level at latitude 0° 18' 49.18" N and longitude 32° 36' 43.86" E. The city grew rapidly over the past decades, to 1.8 million people, largely due to migration of people of different ethnicities or nationalities from rural areas (Katukiza et al. 2010). This population growth led to elevated poverty rates alongside the establishment and extensions of informal slum settlements all over the city. Further, due to newly established factories, industrial pollution was increasing (Mbabazi et al. 2010). As in many African cities, Kampala's sewage system is constrained and covers currently less than 10% of the households (Beller Consult et al. 2004). Hence, the large majority of the population relies on local sanitation facilities such as pit latrines and septic tanks. Open defecation is still commonly practiced (Fichtner Water 2008).

The PhD study focused on the major wastewater system which can be divided into four areas: (i) the Nakivubo channel with the wastewater treatment plant "Bugolobi Sewage Treatment

Works" (BSTW); (ii) the Nakivubo wetland, which is extensively cultivated with yams and sugar cane; (iii) community areas bordering the wetlands, which are often affected by flooding events; and (iv) the Inner Murchison Bay within Lake Victoria which supplies Kampala with drinking water pumped and treated only 4 km away from the outlet of the Nakivubo channel. Moreover, the lake is economically important for fishery (Birungi et al. 2007; Kayima et al. 2008).

4.1.2. Hanoi, Vietnam

Vietnam was unified under a communist government after the Vietnam War in 1975. Since 1986, the start of the initiation of a series of economic and political reforms, Vietnam slowly opened to the world economy (van Horen 2005). This resulted in high economic growth rates and an increase in living standards. Vietnam has the status of a middle-income country and the population tripled since the Vietnam War to 90.5 million inhabitants in 2014 (GSO 2011a). The average life expectancy increased since 1990 to 72 years and the majority of the disease burden shifted from communicable diseases to non-communicable diseases (Jürg Utzinger et al. 2015).

Hanoi is located in the north of Vietnam and is situated at the Red River delta (geographical coordinates: 21° 01' 42.5" N latitude and 105° 51' 15.0" E longitude). The urban area has been constantly expanding over the past two decades (Lan et al. 2012). The average population growth rate of 3.5% has resulted in a resident population of 6.7 million people living on an area of 3,329 km^2 in 2011 (GSO 2011a). The majority of households (94%) in Hanoi relies on flush toilets connected to septic tanks from where the effluent is discharged into a wide network of drainage channels which also receive industrial effluents. Thus, faecal sludge from the septic tanks is often informally discarded into the environment, in many cases directly into peri-urban agricultural fields or ponds used for aquaculture (GSO 2011b; Schoebitz et al. 2014). Large open storm water and drainage channels convey the wastewater out of the city, controlled by water gates, pumps and artificial lakes to regulate the water level and prevent flooding events and serve as sedimentation ponds (Kuroda et al. 2015). Along Hanoi's wastewater conveyance and treatment systems, as many as 658,000 farmers are estimated to reuse wastewater on an area of approximately 43,778 ha (Raschid-sally and Jayakody 2008). Hence, in the peri-urban and rural areas around Hanoi agriculture and aquaculture creates important livelihood opportunities and is a valuable source of fresh vegetables, livestock and fish for the people living in Hanoi (Lan et al. 2012).

The PhD study focused on three elements of Hanoi's wastewater systems, namely: (i) the urban wastewater conveyance and treatment systems (operated by the Hanoi Sewerage and Drainage Company (HSDC)); (ii) the peri-urban wastewater conveyance, treatment and reuse system in the districts of Hoang Mai and Thanh Tri; and (iii) a comparison site in a rural area of Thanh Tri district, where Red River water is used for aquaculture and agriculture (World Bank 2013).

4.2. Methods

4.2.1. Study framework and applied methods

We applied risk assessment as an integral part of a step-wise health impact assessment (HIA) approach. The assessment of health risks was the central point after a screening and a scoping study to further guide mitigation and monitoring strategies (Winkler et al. 2013). The initial start of our assessment was done by conducting a scoping study (Mirko S. Winkler et al. 2011). Within this step, we could review the availability and quality of different data sources and characterize the wastewater recovery and reuse system. This scoping provided the initial sanitation system characterisation and an overview on available data, which could be used for in-depth risk assessment approaches. Moreover, our tools were also linked and generated data for the SSP manual testing phase in both cities. The results were used for semi-quantitative risk assessments and finally to develop incremental improvement plans (WHO 2015). A methodological triangulation was administrated, including (i) an environmental assessment; (ii) a QMRA; and (iii) a cross-sectional survey. Two case studies were carried out between September and December 2013 and April and June 2014 in Kampala and Hanoi, respectively (Figure 4.1).

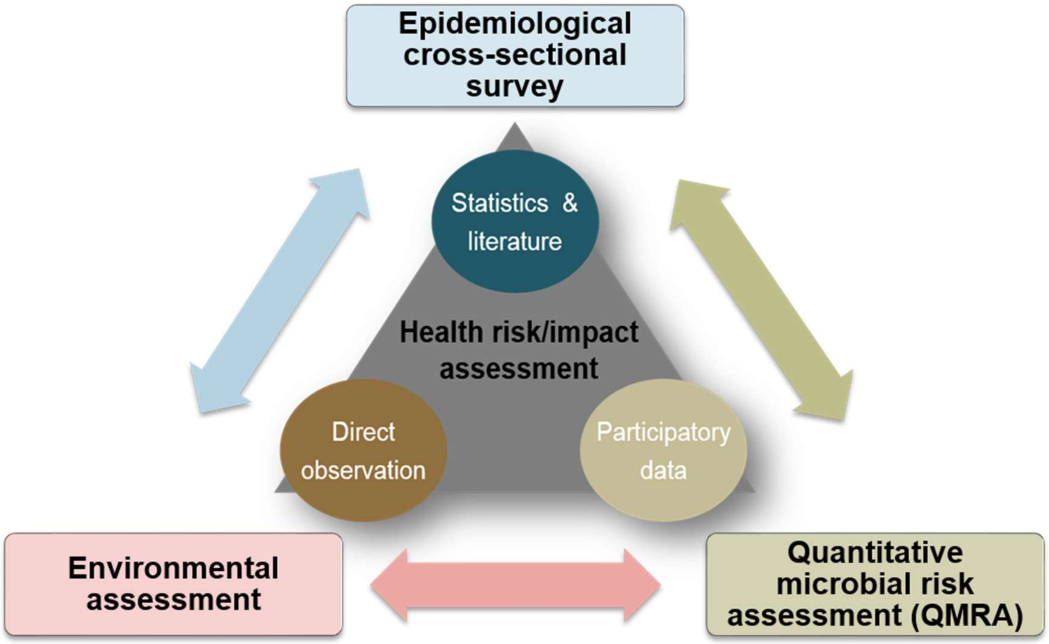

Figure 4.1 Conceptual framework of the PhD study along the wastewater recovery and reuse systems in Kampala and Hanoi. The study builds on a baseline health risk and impact assessment and sanitation safety plan manual testing. This study applies a triangular approach to better understand the related health risks and disease outcomes: 2. an environmental assessment; (ii) a cross-sectional epidemiological survey with different exposure groups; and (iii) a quantitative microbial risk assessment to simulate the health risks for various exposure groups.

4.2.2. Environmental assessment

In the environmental assessment we focused on chemical and microbial pollutants in different sentinel sites. Water samples were examined for bacteria (thermotolerant coliforms (TTC), *Escherichia coli* and *Salmonella* spp.) and helminth eggs in water. Specifically, for Kampala physico-chemical parameters and heavy metals (cadmium (Cd), chromium (Cr), copper (Cu), lead (Pb), iron (Fe) and zinc (Zn)) were analysed in water, sediment, soil and edible plants (yam and sugar cane) samples.

The environmental assessment was used to identify relevant microbial and chemical pollutants, while quantifying concentrations, reduction, inactivation or increase along the wastewater systems. First, published peer-reviewed and grey literature as well as routine monitoring data was used to get a understanding of the system. Second, and in accordance to the obtained data, we built-up relevant laboratory capacities and established collaboration between institutions to measure bacteria, helminth and heavy metals in water, sediment, soil and plants at CCPs. Third, the data collected over a period of two months helped to have context-specific information of contamination and treatment functions at CCPs. Finally, we could compare obtained data with local and international discharge or reuse standards and verification limits for tolerable concentrations of bacteria, helminth or heavy metal to come up with risk profiles for different CCPs (WHO 2006a).

4.2.3. Epidemiological surveys

Cross-sectional parasitological surveys were conducted to assess intestinal parasitic infections, their self-reported signs and symptoms and risk factors in different population groups exposed to wastewater and faecal sludge. The focus was on adult (aged ≥18 years) sanitation workers, urban farmers, community members living along wastewater streams and comparison groups without exposure to wastewater. We developed a study protocol with our local health partners and applied for ethical clearance. This process enabled us to engage with local stakeholders at an early stage of the study (e.g. with village chiefs, Ministry of Health and the president's office) and ensured that our study was scientifically sound and acceptable in the local context. Stool samples were collected and subjected to the Kato-Katz and formalin-ether concentration methods for diagnosing helminth and intestinal protozoa infections (Katz et al. 1972; Utzinger et al. 1999). A questionnaire was administered to identify self-reported signs and symptoms and risk factors for intestinal parasite infections. Questionnaire interviews were conducted with tablet computers using Open Data Kit (ODK) software. Using tablet computers decreased the time of the interview and for data processing and helped to collection spatial information of the place of the interview. Finally, results were communicated back to the concerned groups and people infected with intestinal parasitic infection received treatment according to national standards.

4.2.4. Quantitative microbial risk assessment (QMRA)

We applied QMRA to estimate incidence and disease burden of gastrointestinal diseases due to the exposure to wastewater. QMRA comes with the advantage to estimate low level of risks and to compare different exposure scenarios with each other and set priorities according to model-based predictions (Haas et al. 2014). In four working steps we considered: (i) hazard identification; (ii) exposure assessment; (iii) dose-response assessment; and (vi) risk characterisation (Haas et al. 2014). The hazards considered for the QMRA included seven pathogenic organisms: two viruses (norovirus and rotavirus), three bacteria (*Campylobacter* spp., pathogenic *Salmonella* spp. and *E. coli*), one intestinal protozoon (*Cryptosporidium* spp.) and one soil-transmitted helminth species (*A. lumbricoides*). The QMRA framework was employed as described by the WHO 2006 guidelines and complemented with the Karavarsamis-Hamilton method (Karavarsamis and Hamilton 2010; Mara et al. 2010). In addition, the following three adaptations were made. First, we applied quantitative data on *E. coli* and *Salmonella* spp. obtained in the research area and fitted them to lognormal distribution, while for *Ascaris* eggs, prevalence estimates were used. Second, the mean risk of illness was calculated over one year, while assuming that each individual can get infected with each exposure event (without considering immunity) (Haas et al. 2014). Third, the corresponding disease burden for each of the seven selected pathogens was calculated according to a recently published burden estimate for gastroenteritis and fatality rates (Gibney et al. 2014) and severity estimates for mild, moderate and severe diarrhoea episodes (Salomon et al. 2012).

5. ARTICLE 1: Health risk assessment along the wastewater management and reuse chain of Kampala, Uganda: a visualization

Photo: Nakivubo channel and bordering slum communities at risk of flooding events in Kampala, Uganda (©S. Fuhrimann, 2013)

vHEALTH

Video

https://www.youtube.com/watch?v=CQEC3d4iE_A&spfreload=10

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Health risk assessment along the wastewater and faecal sludge management and reuse chain of Kampala, Uganda: a visualization

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Abstract. Reuse of wastewater in agriculture is a common feature in the developing world. While this strategy might contribute to the livelihood of farming communities, there are health risks associated with the management and reuse of wastewater and faecal sludge. We visualise here an assessment of health risks along the major wastewater channel in Kampala, Uganda. The visualization brings to bear the context of wastewater reuse activities in the Nakivubo wetlands and emphasises interconnections to disease transmission pathways. The contextual features are complemented with findings from environmental sampling and a cross-sectional epidemiological survey in selected exposure groups. Our documentation can serve as a case study for a step-by-step implementation of risk assessment and management as described in the World Health Organization's 2006 guidelines for the safe use of wastewater, greywater and excreta in light of the forthcoming sanitation safety planning approach.

Keywords: wastewater reuse, faecal sludge, sanitation safety planning, health risk assessment, visualization, Uganda.

Link: http://www.geospatialhealth.unina.it/vHealth/gh-v9i1-fuhrimann-01

Background

Reuse of wastewater and faecal sludge is commonly practised in many parts of the world, as it generates livelihood opportunities, especially in urban settings of low- and middle-income countries (Drechsel et al., 2010). However, direct or indirect contact to wastewater and faecal sludge is associated with microbial and chemical hazards, which frequently result in adverse health outcomes as mentioned in specific guidelines issued by the World Health Organization (WHO) (WHO, 2006). Indeed, various pathogenic bacterial and viral strains can cause ill-health, such as diarrhoea, respiratory tract infection and skin disease (WHO, 2006). Environmental contamination with helminth eggs and larvae (e.g. *Ascaris lumbricoides*, hookworm and *Trichuris trichiura*) and intestinal protozoa cysts and oocysts (e.g. *Entamoeba histolytica* and *Giardia intestinalis*) can lead to intestinal parasitic infections in animals and humans (Becker et al., 2013; Strunz et al., 2014). Toxic chemical compounds, such as heavy metals discharged in industrial effluents, can lead to chronic disease and cancer (Ackah et al., 2013).

Urbanisation continues at a rapid pace, particularly in low- and middle-income countries posing challenges for the sanitation infrastructure with regard to operation and maintenance of wastewater and faecal sludge treatment plants (Rydin et al., 2012). Rapidly growing cities, such as Kampala in Uganda, are characterised by aging, overloaded wastewater treatment facilities serving a small proportion of the population, which is coupled with limited faecal sludge collection and treat-

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ment from on-site facilities. This is a scenario the majority of the population commonly has to face in densely populated, unplanned, low-lying parts of such cities. As a result, water used for irrigation generally carries faecal and chemical contamination from a number of sources, including treatment plant effluent, leakage or illegal discharge of faecal sludge, industrial sewage and open defecation within catchments. Limiting this exposure requires a better understanding of the sources of contamination and barriers that can be applied at various stages (WHO and UNICEF, 2014). Achieving targeted levels of service for wastewater and faecal sludge collection and treatment is extremely challenging in the context of rapid growth and limited funding for capital investment, operation and maintenance. There is thus a need for risk assessment and management approaches to identify and mitigate health risks especially for the most vulnerable populations. This can be done by a combination of treatment and cost-effective non-treatment measures and by mobilising a wide group of stakeholders to implement and monitor such risk assessment approaches (WHO, 2006).

Recognising the growing use of wastewater and faecal sludge, WHO has published guidelines for the safe use of wastewater, excreta and greywater (i.e. water generated from washing food, clothes and dishware, as well as from bathing, but not from toilets) (WHO, 2006). These guidelines provide a detailed methodology on how to assess and mitigate health risks in connection with the reuse of wastewater, excreta and greywater in agriculture and aquaculture. An important feature of the guidelines is that health-based targets are set out (e.g. maximum contamination of *Escherichia coli* and helminth eggs in treated wastewater in relation to the reuse scheme) by employing a multiple barrier approach. For this purpose, a broad set of technical and non-technical control options are proposed that are tailored for the different stages of a reuse system. Health-based targets should be set at the national level and might be based on well-defined health metrics, e.g. 10^{-6} disability-adjusted life years (DALYs) per person per year. While the WHO guidelines are valuable, their practicability and uptake in low- and middle-income countries proved difficult (Mara et al., 2010).

Against this background, WHO initiated the development of a sanitation safety planning (SSP) manual with the aim of providing a simple, step-by-step guidance on how to use and apply these guidelines. The approach takes users through the process of risk assessment, management and monitoring that comprises six distinct steps that include definition of the sanitation system, hazard identification and development of monitoring plans and supporting programmes. Importantly, the development of the SSP manual includes an extensive pre-testing phase in various settings across the world.

The motivation of the current visualization is to explain and feature the risk assessment and management concept covered by the SSP using the experience from Kampala as an example. The following questions guided the script:

(i) How can the rich evidence-base of the WHO guidelines be encapsulated in a simple and accessible format to trigger a step-by-step implementation of the SSP approach?

(ii) What are the lessons learned from validating the SSP approach in Kampala?

(iii) How can we visualise an in-depth assessment and mapping of health risks related to different exposure groups along the wastewater and faecal sludge reuse chain in the Nakivubo wetlands?

Our visualization is structured as follows. First, we provide a general introduction to the concepts and challenges of wastewater and faecal sludge management and reuse in low- and middle-income countries. Second, we demonstrate the application of risk assessment, management and monitoring as described in the WHO guidelines. Third, we show how our work and experience in Kampala can contribute to a step-by-step implementation of the six SSP steps.

The SSP validation in Kampala was focused on the major wastewater system in this city of 1.8 million people, the capital of Uganda, which is located on the northern shores of Lake Victoria at an altitude of 1,140 m above the mean sea level at latitude 0° 18' 49.18" N and longitude 32° 36' 43.86" E. Like the case in many African cities, Kampala's sewage system is constrained with less than 10% of the population currently covered. Hence, the large majority of the population relies on local sanitation facilities such as pit latrines and septic tanks. Open defecation is still commonly practiced (Uganda Bureau of Statistics, 2013). For the SSP manual validation, the wastewater chain was divided into four study areas: (i) the Nakivubo channel with its wastewater treatment plant "Bugolobi Sewage Treatment Works" (BSTW); (ii) the Nakivubo wetlands; (iii) community areas bordering the wetlands, which are often affected by flooding events; and (iv) the Inner Murchison Bay within Lake Victoria (Fig. 1). The Nakivubo channel is 12.3 km long and transports wastewater from the communities, markets, industries and the treated

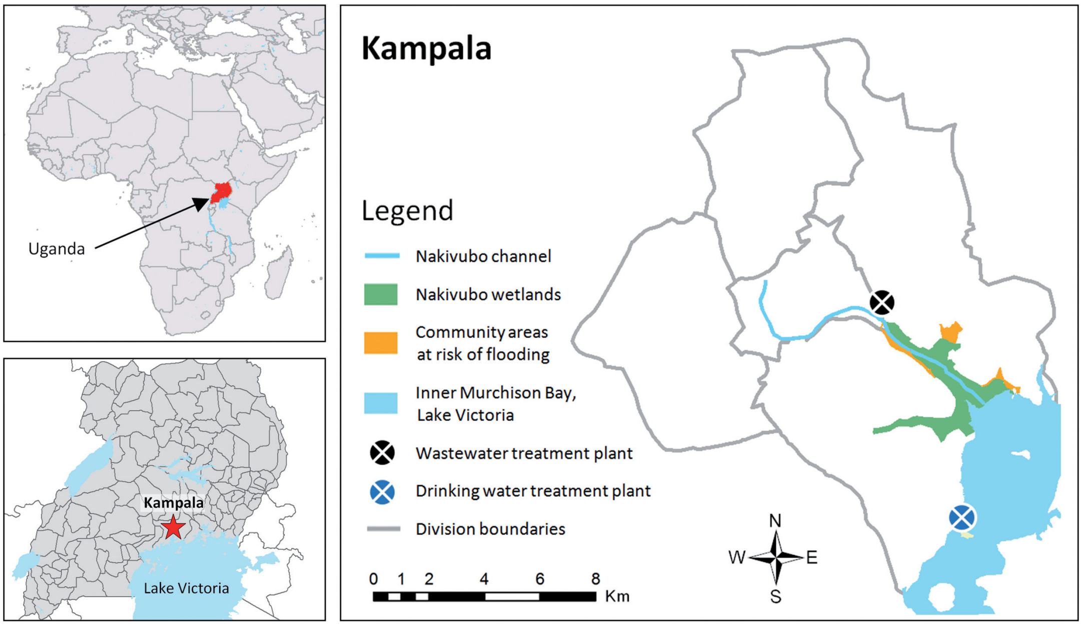

Fig. 1. Map of Kampala, the capital of Uganda, showing the study areas from the wastewater treatment to the drinking water treatment plant, highlighting the four specific study sites (Nakivubo channel, Nakivubo wetlands, community areas and the Inner Murchison Bay in Lake Victoria).

effluent of the BSTW. The final stretch of the channel comprises 4.5 km through the Nakivubo wetlands before reaching the Inner Murchison Bay within Lake Victoria. The Nakivubo wetlands cover approximately 5.3 km^2 and have a total catchment area of approximately 40 km^2. The whole wetland area is divided into a northern and a southern part separated by a railway. North of the railway is mainly drained farmland, while the South consists mainly of wetlands with floating "vegetational islands". Both areas are extensively cultivated with yams and sugar cane. Informal communities that are at highest risk of flooding events are situated along both sides of the wetlands (approximate population: 12,000 people). The Inner Murchison Bay also supplies Kampala with drinking water which is pumped and treated only 4 km away from the outlet of the Nakivubo channel. Moreover, the lake is economically important for fishery (Mbabazi et al., 2010).

The case study involved an in-depth characterisation of the wastewater and faecal sludge reuse system and specific risk assessments in different exposure groups. Since major data gaps on water- and soil-related diseases and chemical pollutants were identified, a cross-sectional survey and an environmental sampling were carried out in late 2013. In short, a total of 915 participants were enrolled and stratified into five groups according to their exposure risk to wastewater: (i) wastewater treatment plant workers; (ii) faecal sludge collectors; (iii) farmers; (iv) exposed community members who are at risk of flooding; and (v) non-exposed community members who are not directly exposed to wastewater within the Nakivubo area. Particular emphasis was placed on intestinal parasitic infections, skin disease, eye disease and diarrhoea. The survey comprised two components: (i) a questionnaire study to obtain health risk and health outcomes related to the exposure to wastewater; and (ii) collection of stool samples to determine the prevalence and intensity of helminths using the Kato-Katz method (Katz et al., 1972) and intestinal protozoa infections using the formalin-ether concentration technique (Utzinger et al., 2010). For the environmental sampling, water, sediment, soil and plants were collected for 8 weeks in the rainy season from October to December 2013. A broad range of microbial and chemical pollutants were investigated, such as thermo-tolerant coliforms, *E. coli*, *Salmonella* spp., helminth eggs and heavy metals (cadmium, copper, iron, lead, chromium and zinc) to deepen the understanding of the contamination of different environments and hence, better characterise risk profiles of the different exposure groups.

Results from the cross-sectional survey revealed that, in terms of intestinal parasitic infections, farmers were at highest risk (prevalence of infection: 75.9%), followed by exposed community members (53.2%), non-exposed community members (44.7%), wastewater treatment plant workers (41.9%) and faecal sludge collectors (35.8%). Our results from the environmental sampling showed that in water of the

Nakivubo channel and the Nakivubo wetlands, mean concentrations of thermo-tolerant coliforms (4.3 x 10^6 and 10^5 CUF/100 ml, respectively) exceeded the national standards. Moreover, mean *E. coli* concentrations (3.8 x 10^5 and 9.9 x 10^4 CUF/100 ml, respectively) were in excess of thresholds put forth in the WHO guidelines for the safe use of wastewater in agriculture. A fifth of the water samples were found positive for hookworm eggs. Copper, iron and cadmium with 3.3, 21.5 and 0.14 ppm in water, lead with 132.7 ppm in soil and lead, cadmium and chromium in plant samples (yams 0.2, 4.0 and 4.4 ppm; sugar cane 0.2, 4.3, 8.4 ppm) were above international safety standards.

Outlook

We visualise a health risk assessment along a wastewater and faecal sludge management and reuse system in the context of a major East African city, reporting applications of risk assessment, management and monitoring along the sanitation chain as described in the 2006 WHO guidelines and the SSP manual. We believe that our contribution further underscores the value and potential of visualizing complex health issues in the form of a short video that is readily accessible by multiple stakeholders and local communities (Krieger et al., 2012; Winkler et al., 2012). Hence, our visualization can serve as a case study to be used as a part of the training material to facilitate SSP and support a step-by-step implementation of the WHO guidelines for the safe use of wastewater, excreta and greywater in agriculture and aquaculture in other cities across the developing world.

Box 1. Overall aim.

- A visual tool to characterise a major wastewater and faecal sludge management and reuse system in a major East African city context that could reach a broad range of stakeholders.
- An educational tool to facilitate sanitation safety planning and the step-wise implementation of the WHO guidelines on the safe use of wastewater, greywater and excreta reuse in agriculture and aquaculture.

Box 2. Applied software.

- Content visualization, including geospatial components: Microsoft Power Point 2013 (Microsoft Corporation; Edmond; WA, USA)
- Production of video for Internet streaming: Camtasia Studio 8 (TechSmith Corporation, Okemos, MI, USA)
- Three-dimensional fly-through visuals: Google Earth Pro (Google Earth Pro version 7.1.2.2041; Google, Inc., Mountain View, CA, USA)

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Disclaimer

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6. ARTICLE 2: Microbial and chemical contamination of water, sediment and soil in the Nakivubo wetland area in Kampala, Uganda

Photo: Typical situation in an urban slum bordering the Nakivubo channel in Kampala, Uganda (©S. Fuhrimann, 2013)

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Microbial and chemical contamination of water, sediment and soil in the Nakivubo wetland area in Kampala, Uganda

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Abstract The reuse of domestic and industrial wastewater in urban settings of the developing world may harm the health of people through direct contact or via contaminated urban agricultural products and drinking water. We assessed chemical and microbial pollutants in 23 sentinel sites along the wastewater and faecal sludge management and reuse chain of Kampala, Uganda. Water samples were examined for bacteria (thermotolerant coliforms (TTCs), *Escherichia coli* and *Salmonella* spp.) and helminth eggs. Physico-chemical parameters were determined. Water, sediment and soil samples and edible plants (yams and sugar cane) were tested for heavy metals. Water samples derived from the Nakivubo wetland showed mean concentrations of TTCs of 2.9×10^5 colony-forming units (CFU)/100 mL. Mean *E. coli* was 9.9×10^4 CFU/100 mL. Hookworm eggs were found in 13.5 % of the water samples. Mean concentrations of iron (Fe), copper (Cu) and cadmium (Cd) were 21.5, 3.3 and 0.14 mg/L, respectively. In soil samples, we found a mean lead (Pb) concentration of 132.7 mg/L. In yams, concentrations of Cd, chromium (Cr) and Pb were 4.4, 4.0 and 0.2 mg/L,

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Samuel Fuhrimann and Michelle Stalder contributed equally to this work.

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while the respective concentrations in sugar cane were 8.4, 4.3 and 0.2 mg/L. TTCs and *E. coli* in the water, Pb in soil, and Cd, Cr and Pb in the plants were above national thresholds. We conclude that there is considerable environmental pollution in the Nakivubo wetland and the Lake Victoria ecosystem in Kampala. Our findings have important public health implications, and we suggest that a system of sentinel surveillance is being implemented that, in turn, can guide adequate responses.

Keywords Bacteria · Heavy metals · Helminths · Uganda · Wastewater reuse · Wetland

Introduction

For centuries, humans have reused wastewater to enhance agricultural production (Drechsel et al. 2010). In view of population growth, increasing scarcity of fresh water and the demand to boost food production, reuse of wastewater in agriculture and aquaculture has gained traction in the 21st century (WHO 2006). Particularly in urban and peri-urban areas of low- and middle-income countries, wastewater reuse can support livelihoods of poor communities (Scott et al. 2004). However, contact with untreated wastewater is associated with microbial and chemical hazards and thus can negatively impact human health (Cissé et al. 2002; Matthys et al. 2006). Indeed, pathogenic bacterial and viral organisms can cause diarrhoea, respiratory tract infections, skin and eye diseases and epidemic disease outbreaks such as cholera and typhoid fever (Blumenthal and Peasey 2002; Ensink 2006; Drechsel et al. 2010; Stenström et al. 2011; Becker et al. 2013). Environmental contamination with helminth eggs and intestinal protozoa cyst can drive transmission of intestinal parasitic infections (Matthys et al. 2006, 2007; Ziegelbauer et al. 2012; Pham-Duc et al. 2013; Strunz et al. 2014). Additionally, chronic diseases and cancer are associated with the ingestion and bioaccumulation of heavy metals such as cadmium (Cd) and lead (Pb) or toxic chemicals (e.g. pesticides) discharged in industrial effluents (Jarup 2003; Marcussen et al. 2008; Ackah et al. 2013).

Standardised methods are available to assess and mitigate health risks in connection with the reuse of wastewater, excreta and greywater in agriculture and aquaculture (WHO 2006). However, the practicability and uptake of these methods in low- and middle-income countries proved difficult. Indeed, there is a paucity of quality data that are obtained in a timely manner to guide adequate responses. There is a need for case studies that will deepen our understanding of the level of contamination in wastewater systems, including specific health risks in different exposure groups (Ensink and van der Hoek 2009; Mara et al. 2010; Keraita and Dávila 2015).

In Kampala, Uganda, reuse of wastewater in urban agriculture is commonly practiced, generating important livelihood opportunities for local dwellers in wetland areas (Cole et al. 2008). Approximately 31 km^2 of the city is classified as wetlands that have an important economic and environmental value for wastewater purification and nutrient retention (Emerton 1998). The largest wetland in Kampala is the Nakivubo system. This wetland is fed from the Nakivubo channel, an open waste and storm water channel, transporting most of the domestic and industrial wastewater of the central division of Kampala (Matagi 2002). The channel also receives secondary treatment effluent from the Bugolobi Sewage Treatment Works (BSTW) and is fed with untreated sewage from informal settlements along the wetland. During the rainy season, the channel and parts of the wetland are often flooded, exposing local residents to raw wastewater (Kayima et al. 2008).

Previous studies reported high concentrations of microbes (thermotolerant coliforms (TTCs)) and toxic chemicals (heavy metals) in the Nakivubo channel, thus posing a risk for deterioration of the surrounding natural ecosystems; namely, the Nakivubo wetland and Lake Victoria (Emerton 1998; Kansiime and Nalubega 1999; Huising 2002; Kayima et al. 2008; Mbabazi et al. 2010). It has been speculated that the natural treatment capacity of the wetland is insufficient for the amount of wastewater, which might be explained by the channelisation of the flow and the reduction of the natural wetland flora as a result of farming activities (Mbabazi et al. 2010). Workers at the wastewater treatment plant, farmers and local communities are at risk of adverse health effects linked to exposure to wastewater and faecal sludge (Nabulo et al. 2006; Katukiza et al. 2014). Additionally, the discharge of contaminated wastewater into the Inner Murchison Bay of Lake Victoria threatens the fishery industry (Birungi et al. 2007) and the drinking water supply of Kampala (Beller et al. 2004; Howard et al. 2006). The intake point of the drinking water supply system for Kampala is located in Ggaba, which is only 4 km from where the Nakivubo channel discharges into Lake Victoria. Moreover, the lake itself is under threat from eutrophication (Focardi et al. 2006).

The Nakivubo area is under considerable pressure due to profound demographic and ecological transformations, including rapid urbanisation, industrial developments and the establishment of informal settlement alongside the Nakivubo wetland (Kayima et al. 2008; Mbabazi et al. 2010). These contextual factors have led to increased volumes of wastewater, putting additional strains on an insufficiently equipped sanitary infrastructure (Beller et al. 2004; Fuhrimann et al. 2014). Hence, there is a need for a sound assessment of relevant environmental, chemical and microbiological parameters along the entire chain from the wastewater treatment plant to Lake Victoria, to enhance evidence-based decision-making for protecting ecosystems and the services that they provide and people's health and well-being (WHO 2006).

Within the frame of a larger project (Fuhrimann et al. 2014), the objective of the study presented here was to assess faecal and industrial contamination along the major wastewater system in Kampala to identify potential health risks for specific population groups that show different exposures. Thus, physico-chemical parameters, bacterial and helminth contamination and levels of heavy metals were determined in water, sediment, soil and plant samples at 23 sentinel sites.

Materials and methods

Ethics statement

The study protocol was approved by the institutional research commission of the Swiss Tropical and Public Health Institute (Swiss TPH; Basel, Switzerland; reference no. FK 106) and the Uganda National Council for Science and Technology (UNCST; Kampala, Uganda; reference no. HS 1487). Ethical approval was obtained from the ethics committee in Basel (EKBB; Basel, Switzerland;reference no. 137/13) and Higher Degrees Research and Ethics Committee of Makerere University School of Public Health (Kampala, Uganda; reference no. IRBOOO11353). This study is registered with the clinical trial registry ISRCTN (identifier: ISRCT N13601686).

Study area

Kampala is the capital of Uganda with a resident population of about 1.8 million people. The city is located at the northern shores of Lake Victoria at an altitude of 1140 m above mean sea level (geographical coordinates 0° 18′ 49.18″ N latitude and 32° 36′ 43.86″ E longitude) (UBOS 2013). Kampala's climate is tropical with precipitation throughout the year, mainly concentrated during two rainy seasons: the main one occurring between March and May and the second one in October and November. The driest month is July, which nevertheless receives an average of 62 mm precipitation (Climate-Data.org 2013).

The study area and the sampling scheme are shown in Fig. 1. For further details and a short video publication, the reader is referred elsewhere (Fuhrimann et al. 2014). In brief, the study area was divided into four sampling systems along the main wastewater chain of Kampala in the divisions Makindye and Nakawa; namely (i) the Nakivubo channel, (ii) the Nakivubo wetland, (iii) community areas bordering the wetland and (iv) the Inner Murchison Bay within Lake Victoria. The Nakivubo channel is 12.3 km long and transports wastewater from the communities, markets, industries and the secondary treated effluent from the BSTW until it drains into the Nakivubo wetland and, after another 4.5 km, reaches the Inner Murchison Bay of Lake Victoria. The Nakivubo wetland covers approximately 5.29 km^2 and has a total catchment area of over 40 km^2 (Emerton 1998). An old railway line divides the wetland into a northern and a southern part. North of the railway line is mainly drained farmland and the southern part is a floating wetland. Both areas are cultivated for yams and sugar cane. Informal communities that are at high risk of flooding are situated on both sides of the wetland (approximate population 12,000 people) (Kayima et al. 2008; Mbabazi et al. 2010). The Inner Murchison Bay is economically important for fish production and supplies Kampala with drinking water, which is pumped from about 4 km from the outlet of the Nakivubo channel.

Sampling strategy

A cross-sectional survey was conducted between October and December 2013. As shown in Fig. 1, a total of 23 sentinel sites were selected, as follows:

- Nakivubo channel: five sampling points (C1–C5) spread over a distance of 4.5 km, starting above the inflow of the BSTW until Inner Murchison Bay. Water samples were taken at 16 time points, twice a week, whereas sediment samples were taken

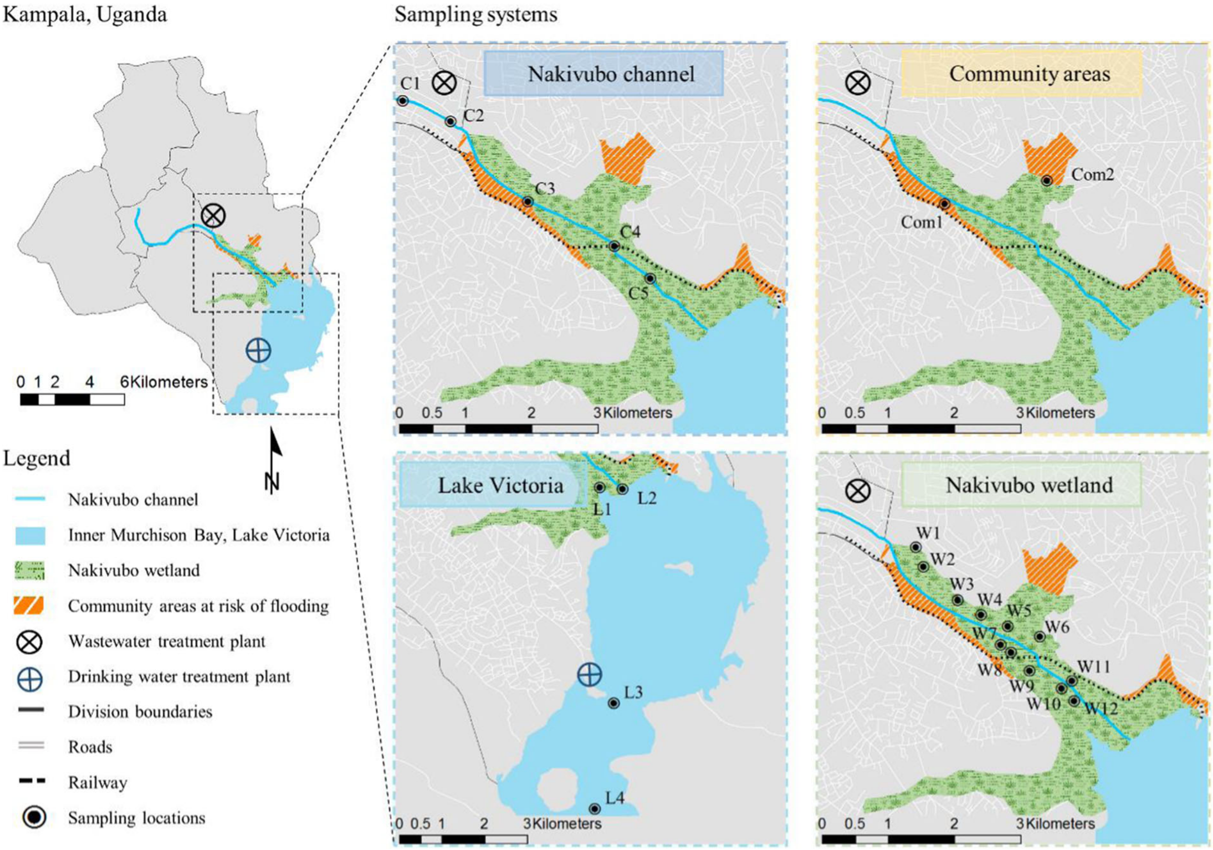

Fig. 1 Map of Kampala showing the study area, including detailed maps of the four sampling systems with the specific sampling points (Nakivubo channel, Nakivubo wetland, community areas and Inner Murchison Bay in Lake Victoria)

at two time points early and late during the study period.

- Nakivubo wetland: 12 sampling points (W1–W12) in four clusters where urban farming activities are pursued. Within the clusters, a stratified random sampling procedure was applied using a grid of 50×50 m (Webster and Lark 2013). Water, soil, and plant samples were taken at four time points, every second week.
- Community areas at risk of flooding: two sampling points (Co1 and Co2). Water and soil samples were collected at four time points, every second week.
- Shores of Lake Victoria: four sampling points (sampling at surface (*s*) and bottom (*b*)) within the Inner Murchison Bay (L1*s* and L2*s* and L1*b* and L2*b*), outlet of the Nakivubo channel; L3*s* and L3*b* in close proximity to drinking water treatment plant Ggaba II; and L4*s* and L4*b* reference point in the Inner Murchison Bay. Water samples were collected at eight time points, weekly, whereas sediment samples were taken at two time points at the beginning and towards the end of the study period.

Sample collection

Water and sediment samples were collected in sterile wide mouth, screw-capped 1 L plastic bottles. Soil samples were collected in 2 L polyethylene bags. Plant (sugar cane and yams) samples were collected as whole plants. Samples were collected in the morning hours and transferred to a nearby laboratory in a cool box at a temperature of 4 °C.

Physico-chemical analysis

While collecting the water samples, temperature, pH and electrical conductivity (EC) were measured in situ in the field using a Mettler-Toledo pH and EC meter (Mettler-Toledo International, Inc.; Greifensee, Switzerland). The following physico-chemical parameters were determined, adhering to standard methods (APHA, AWWA and WEF 2005): alkalinity (titrimetric method), total phosphate (persulphate method), orthophosphate (ascorbic method), ammonia-N (nesslerisation), nitrate-N (cadmium reduction spectrophotometric method), total solid suspended (TSS; photometric method), biochemical oxygen demand (BOD$_5$; azide modification of the Winkler method; oxygen by the electrode method) and chemical oxygen demand (COD; closed reflux colorimetric method).

Microbial analysis

All water samples were examined for TTC bacteria, *Escherichia coli*, *Salmonella* spp. and helminth eggs (*Ascaris lumbricoides*, hookworm and *Trichuris trichiura*), using standard protocols recommended by the World Health Organization (WHO) (Mara and Horan 2003; WHO 2004). For bacteria examination, a membrane filtration method was applied. Briefly, sample dilutions ranging from 10- to 100-fold were prepared and inoculated on membrane lauryl sulphate broth to count TTCs and *E. coli* and on xylose lysine deoxycholate (XLD) agar for *Salmonella* spp. Incubation temperatures and times were as follows: (i) TTCs 12–18 h at 44 °C, (ii) *E. coli* 18–22 h at 37 °C and (iii) *Salmonella* spp. 12–72 h at 37 °C (Ayres and Mara 1996). For the detection of helminth eggs, a modified Bailenger method was applied. The water or sediment samples (1 L each) were allowed to settle for a period of 12–15 h before the supernatant was drained off. Soil samples (250 g) were first diluted with 10 L of distilled water. Subsequently, the preparations were filtered for removing larger particles and then settled for 12–15 h. Water, sediment and soil samples were further analysed for helminth eggs with the McMaster method using acetoacetic buffer (pH 4.5) and zinc sulphate solution (specific density 1.18) (Ayres and Mara 1996; WHO 2004; Ensink 2006).

Heavy metal analysis

Heavy metals were only measured at one time point during the assessment at all sentinel sites. In water, soil, sediment and eatable parts of plant samples, we analysed Cd, chromium (Cr), copper (Cu), Pb, iron (Fe) and zinc (Zn) by atomic absorption spectrophotometry (PerkinElmer2380, PerkinElmer Corporation; Norwalk, USA). For analysis of water samples, 100 mL of acid-preserved samples were processed using nitric acid digestion before carrying out spectrometric measurements. At least three calibrations with different dilutions of the relevant standard solutions were done beforehand (APHA, AWWA and WEF 2005). Soil, sediment and plant samples were dried for 24 h at 105 °C, ground to fine powder and digested with mineral acids and the resultant solutions analysed by atomic absorption spectrophotometry as detailed in Mbabazi et al. (2010).

Statistical analysis

The software R, version 3.0.2, was used for statistical analyses (The R Foundation for Statistical Computing; Vienna, Austria). A log-normal probability density function was applied for characterisation of pathogen concentrations in water. Geometric mean concentrations, including 95 % confidence intervals (CIs) were calculated using a Student's *t* test. Data on the contamination of the Nakivubo wetland were compared with WHO guidelines for the safe use of wastewater in agriculture (WHO 2006) and with standards for the discharge of effluents into water or on land developed by the Ugandan National Environmental Management Authority (NEMA) (NEMA 1999).

Results and discussion

Physico-chemical parameters in water

Table 1 summarises the physico-chemical parameters of water samples, including temperature, pH, EC, total alkalinity, TSS, BOD$_5$, COD, total phosphate, orthophosphate, ammonia-N and nitrate-N. As expected, the highest values of the investigated physico-chemical parameters were found in the Nakivubo channel, while the lowest values were obtained from the samples taken in the Inner Murchison Bay. Figure 2 shows BOD$_5$, COD, TSS and ammonia-N for each sampling point, presented as box plots. For BOD$_5$, there was a decrease along the Nakivubo channel from a median value of 156.7 mg/L (C1—furthest from Lake Victoria) to about 75.9 mg/L (C5—nearest to the lake). The values for the other parameters only decreased minimally.

The physico-chemical parameters of the water samples showed large spatial heterogeneity. The lower

Table 1 Physico-chemical parameters of water samples in the four sampling systems along the Nakivubo channel in Kampala (sampling period: 15 October to 5 December 2013)

Physico-chemical parameter	Min	Max	Mean	Lower 95 % CI	Upper 95 % CI	NEMA standards
Temperature (°C)	18.1	34.3	26.4	26.1	26.8	20.0–35.0
pH	5.9	9.3[a]	7.2	7.1	7.3	6.0–8.0
EC (μS/cm)	104.7	1320.0	574.6	538.1	611.2	1500.0
Total alkalinity (mg/L)	28.0	556.0	240.5	225.1	255.8	800.0
TSS (mg/L)	6.0	5100	198.7[a]	140.8[a]	256.7[a]	100.0
BOD_5 (mg/L)	2.0	425.7	91.4[a]	82.7[a]	100.0[a]	50.0
COD (mg/L)	5.0	3231[a]	257.4[a]	211.3[a]	303.5[a]	100.0
Total phosphate (mg/L)	0.01	84.1[a]	11.5[a]	9.7	13.3[a]	10.0
Orthophosphate (mg/L)	0.0	26.2[a]	5.2[a]	4.5	5.9	5.0
Ammonia-N (mg/L)	0.0	52.8[a]	21.2[a]	19.6[a]	22.8[a]	10.0
Nitrate-N (mg/L)	0.0	2.5	0.2	0.15	0.25	10.0

The minimum and maximum concentration, geometric mean and 95 % confidence intervals (CIs) for Student's *t* test are indicated

[a] Concentrations exceeding maximum acceptable concentrations (NEMA 1999)

levels in the Inner Murchison Bay can be explained by dilution after discharge into Lake Victoria (Kansiime and Nalubega 1999). The comparison of the geometric means with standard values set by NEMA revealed biogenic pollution; the mean values for BOD_5, COD, TSS, ammonia-N and total phosphate all exceeded the national standards for the discharge of effluents into the environment. When compared with data published in 2008 for the Nakivubo channel (Kayima et al. 2008), our results suggest an increase of up to 200–300 %. In view of these findings, control measures, such as the channelisation of the Nakivubo channel that was done in 2008, seem to have failed to reduce environmental pollution (Beller et al. 2004).

Bacterial parameters in water

The results of TTCs, *E. coli* and *Salmonella* spp. in water samples obtained from the four sampling systems are displayed in Table 2. TTC and *E. coli* concentrations were highest in the samples taken within the community areas and ranged from 4.0×10^2 to 2.2×10^8 and from 1.0×10^2 to 7.9×10^7 colony-forming units (CFU)/100 mL, respectively. *Salmonella* spp. was found in all sampling points with a mean concentration of 3.8×10^2 CFU/100 mL in the Nakivubo channel and 1.3 CFU/100 mL in Lake Victoria. Figure 3 shows that there was a decrease in bacteria concentrations along the channel with increasing distance from Kampala city, both for TTCs and *E. coli*. However, this trend was interrupted by an increase in bacteria concentrations between the sampling point just before and after the inlet of BSTW's effluent, which indicates additional contamination by the treatment plant. The natural treatment function of the wetland was only obvious for *E. coli*; from the beginning of the floating wetland (C4) to the discharge of the Nakivubo channel in Lake Victoria (L1*s*/*b* and L2*s*/*b*), the mean concentration decreased by 1.56 log CFU.

Our findings show much higher microbial contamination than previously reported for Kampala (Kayima et al. 2008) and might underline a decrease in the natural treatment function of the Nakivubo wetland (Kansiime and Nalubega 1999). Flooding events of the Nakivubo channel and wetland may also contribute to the pollution of protected springs, as indicated by Nsubuga et al. (2004). Hence, our results are in line with results recently reported for open storm drainage channels and the Bwaise III slums areas in Kampala (Katukiza et al. 2014). They even showed for open drainage channels mean values for CFU *E. coli* and *Salmonella* spp. per 100 mL of up to 7.9×10^6 and 2.0×10^5, respectively. Mean concentrations for TTCs of up to 1.5×10^7 CFU/100 mL in the two sampling points close to the community areas exceeded the national thresholds for wastewater discharge of 5.0×10^3 CFU/100 mL by more than 4 log. When comparing the mean TTC concentration at railway bridge (C4) with results published for the wet season in 2008 (Kayima et al. 2008), we found 3.1

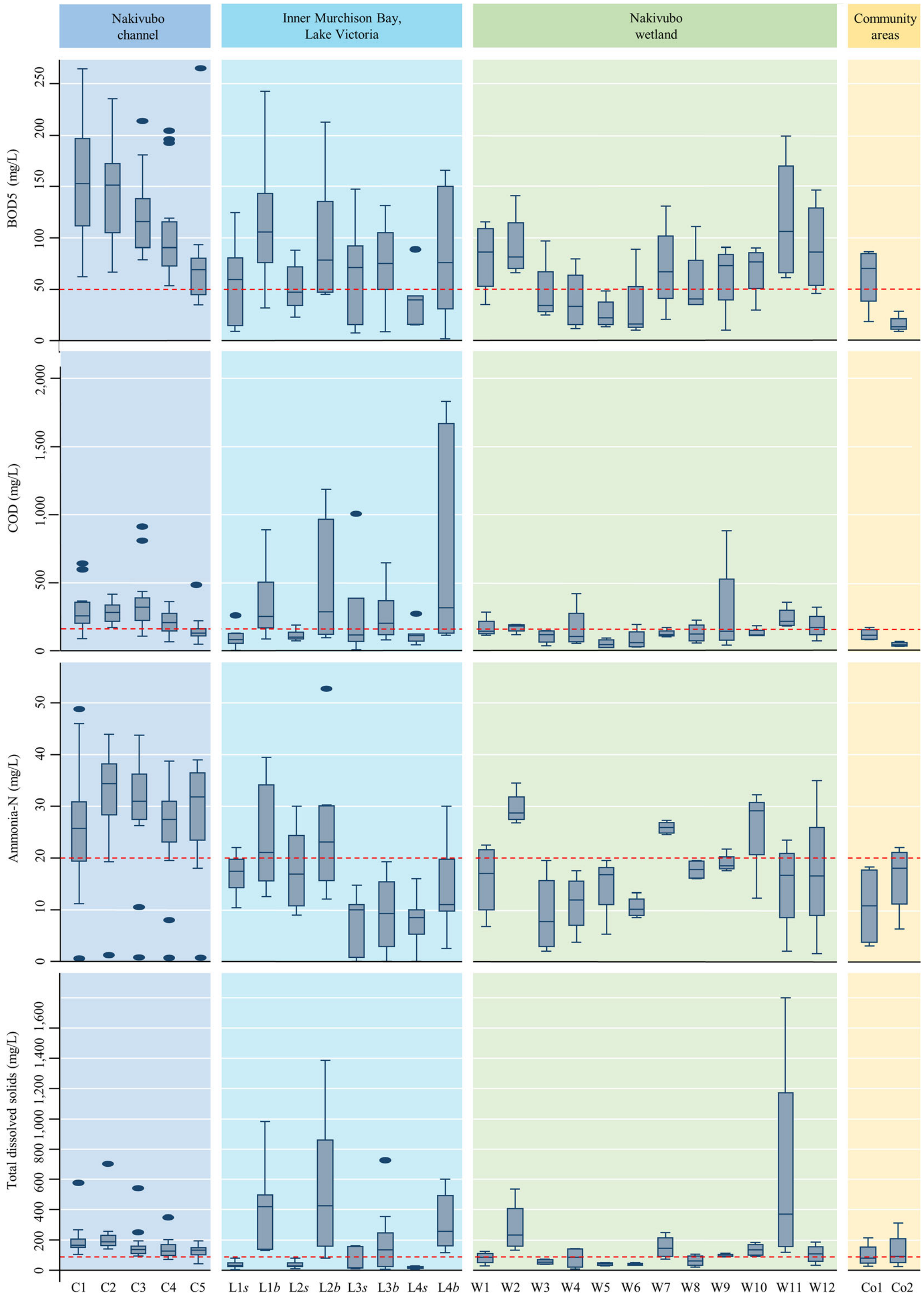

Fig. 2 Box-and-whisker plot of the concentration of BOD_5, COD, ammonia-N and total solid suspended in the four sampling systems along the Nakivubo channel, in Kampala, Uganda (sampling period: 15 October to 5 December 2013). *Red line*: maximum acceptable concentrations of TTCs (NEMA 1999) and *E. coli* (WHO 2006). L*s* surface and L*b* bottom samples taken within the Inner Murchison Bay of Lake Victoria

Table 2 Thermotolerant coliforms, *E. coli* and *Salmonella* spp. concentrations in the four sampling systems along the Nakivubo channel in Kampala (sampling period: 15 October to 5 December 2013)

Sampling system	Counts in CFU/100 mL				
Bacteria in water	Min	Max	Mean	Lower 95 % CI	Upper 95 % CI
Nakivubo channel (n=112)					
Thermotolerant coliforms	1.2×10^3	1.8×10^8	4.3×10^{6a}	2.7×10^{6a}	6.9×10^{6a}
E. coli	8.4×10^2	9.0×10^7	3.8×10^{5a}	2.3×10^{5a}	6.4×10^{5a}
Salmonella spp.	0.0	2.0×10^5	3.8×10^2	2.5×10^2	5.7×10^2
Nakivubo wetland (n=48)					
Thermotolerant coliforms	4.0×10^2	2.2×10^8	2.9×10^{5a}	1.0×10^{5a}	8.0×10^{5a}
E. coli	1.0×10^2	7.9×10^7	9.9×10^{4a}	3.6×10^{4a}	2.7×10^{5a}
Salmonella spp.	0.0	1.2×10^5	1.4×10^2	63.0	3.2×10^2
Community areas (n=8)					
Thermotolerant coliforms	4.2×10^3	3.1×10^9	1.5×10^{7a}	8.4×10^4	2.9×10^{9a}
E. coli	1.9×10^3	6.0×10^7	7.3×10^{5a}	1.8×10^4	2.9×10^{7a}
Salmonella spp.	36.0	6.0×10^2	99.0	35.0	2.8×10^2
Lake Victoria (n=32)					
Thermotolerant coliforms	0.0	40.0	3.7	2.3	6.0
E. coli	0.0	11.0	1.3	1.1	1.7
Salmonella spp.	0.0	8.0	1.3	1.0	1.6

The minimum and maximum concentration, geometric mean and 95 % confidence intervals (CIs) for Student's t test are indicated

[a] Concentrations exceeding maximum acceptable concentrations for faecal coliforms (NEMA 1999) and *E. coli* (WHO 2006)

log higher concentrations. Only TTC concentrations in water from Lake Victoria were below the current effluent discharge standards. Results of our study also found mean concentrations of up to 3.8×10^5 and 7.3×10^5 CFU *E. coli*/100 mL in the water of the Nakivubo channel. In the Nakivubo wetland, WHO thresholds for unrestricted irrigation were exceeded, as we found that values were above the recommended verification limits of 10^3–10^4 CFU *E. coli*/100 mL (Table 2, Fig. 3). Such high concentrations of these bacteria may result in adverse health impacts among farmers and community members, who are directly or indirectly exposed to these waters. For the safety of these population groups, additional control measures are required (WHO 2006). The fact that we measured low concentration of TTCs, *E. coli* and *Salmonella* spp. at L3 and L4 in the Murchison Bay of Lake Victoria should be considered for future monitoring of drinking water quality. As these bacteria mainly serve as indicator organisms for faecal pollution, the source for drinking water in Kampala is likely to be polluted by pathogenic bacteria, viruses and protozoa organism, which may survive the treatment processes (Ayres and Mara 1996; Howard et al. 2006; WHO 2011).

Contamination of water, sediment and soil with helminth eggs

Table 3 shows that 15.5 % of all water samples were positive for helminth eggs; 13.5 % for hookworm and 2.0 % for *A. lumbricoides*, whilst no *T. trichiura* eggs were detected. In eight sediment samples along the Nakivubo channel, hookworm and *A. lumbricoides* eggs were found (12.5 %) in the 28 soil samples collected in the Nakivubo wetland. Hookworm eggs were recovered in 14.3 % of the samples, while neither *A. lumbricoides* nor *T. trichiura* eggs were found.

Overall, the mean concentration of helminth eggs in water samples was between 1.3 and 2 eggs per L and therefore exceeds the WHO guidelines for the safe use of wastewater (<1 egg per L). It follows that additional control measures are required to protect people who are in frequent contact with this water (WHO 2006). The highest mean helminth egg counts were found in water

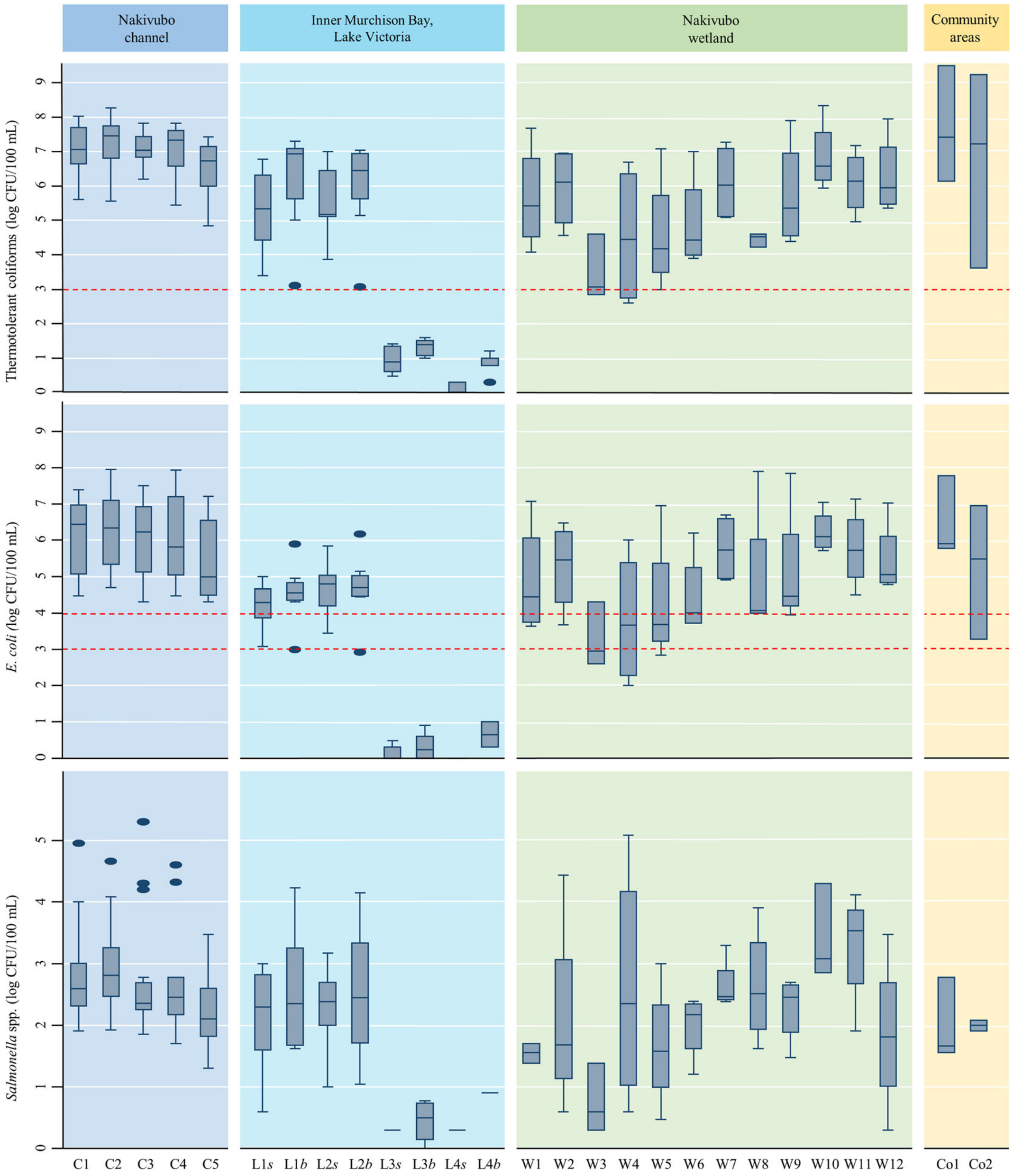

Fig. 3 Box-and-whisker plot of the concentration of thermotolerant coliforms (TTCs), *E. coli* and *Salmonella* spp. in the four sampling systems along the Nakivubo channel, in Kampala (sampling period: 15 October to 5 December 2013). *Red line*: maximum acceptable concentrations of TTCs (NEMA 1999) and *E. coli* (WHO 2006). L*s* surface and L*b* bottom samples taken within the Inner Murchison Bay of Lake Victoria

samples in the Nakivubo channel. *A. lumbricoides* eggs were detected in water samples obtained from the Nakivubo channel, but not from the Nakivubo wetland, suggesting a natural treatment function of the wetland (Jimenez-Cisneros 2006). It is conceivable that this treatment function also applies to hookworm eggs (Stott et al. 2003). However, as hookworm eggs were found in the wetland, we speculate that there is continuous contamination of the wetland with hookworm eggs. As our study was conducted during the second, short rain season of 2013 (between October and December), different prevalence rates for the first and longer rainy season (March–May) might be expected (Motazedian et al. 2006).

Table 3 Helminth egg counts (hookworm and *Ascaris lumbricoides*) and prevalence in the four sampling systems in Kampala obtained from water samples (sampling period: 15 October to 5 December 2013)

Sampling system	Egg counts (/L)					No. positive	Prevalence rates		
Helminth egg in water	Min	Max	Mean	Lower 95 % CI	Upper 95 % CI		% positive	Lower 95 % CI	Upper 95 % CI
Nakivubo channel (n=112)									
Hookworm	0	160	2.0	1.5	2.6	23	20.5	13.0	28.0
Ascaris lumbricoides	0	10	1.1	1.0	1.1	3	2.7	–	–
Nakivubo wetland (n=48)									
Hookworm	0	933	1.3	0.9	1.8	3	6.3	–	–
Ascaris lumbricoides	0	0	–	–	–	0	0	–	–
Community areas (n=8)									
Hookworm	0	0	–	–	–	0	0	–	–
Ascaris lumbricoides	0	40	1.6	0.5	4.7	1	12.5	–	–
Lake Victoria (n=32)									
Hookworm	0	40	1.3	0.8	2.2	1	3.1	–	–
Ascaris lumbricoides	0	0	–	–	–	0	0	–	–
Total (n=200)									
Hookworm						27	13.5	8.8	18.2
Ascaris lumbricoides						4	2.0	0.1	3.9
Total helminth eggs						31	15.5	10.5	20.5

For egg counts, the minimum and maximum, geometric mean and 95 % confidence intervals (CIs) for Student's *t* test are indicated. For the prevalence, CIs are indicated

Contamination of water, sediments, soils and plants with heavy metals

As shown in Table 4, highest heavy metal contaminations were found in water sampled in the Nakivubo channel and within the community areas. Data presented in Table 5 summarise the heavy metal concentration in sediment of the Nakivubo channel and in soil and plant samples taken from the Nakivubo wetland. In the Nakivubo channel, the geometric means for Fe, Cu and Cd in water samples were 21.5, 3.3 and 0.14 mg/L, respectively, and exceeded the effluent discharge standards by NEMA. Regarding Cr, the upper 95 % CI of the concentration in water from the wetland area was above the maximum acceptable concentrations (MACs).

Our findings for Cu, Cd, Pb and Zn measured in the Nakivubo wetland and Lake Victoria are in line with previous studies conducted in the same area (Barifaijo et al. 2009; Mbabazi et al. 2010). However, the present study shows considerably lower heavy metal concentrations at the beginning of the Nakivubo channel. This observation might be explained by temporal variation (Mbabazi et al. 2010). It should also be noted that the sample size was small (one sample per sampling point), and hence, care is indicated while interpreting our findings.

In soil and sediment samples, only the mean concentration of Pb exceeded the MAC. Taking the lower 95 % CI into account, values for Fe, Cd and Zn exceeded the standards. Nevertheless, the levels are well below the stated intervention levels by FAO (2004). In the examined plant samples (yams and sugar cane), mean concentrations of Cd, Cr and Pb (yams 4.4, 4.0 and 0.2 mg/L; sugar cane 8.4, 4.3 and 0.2 mg/L, respectively) exceeded thresholds put forth by NEMA (1999). The upper 95 % CI of Zn levels in yams showed an elevated concentration of 120.5 mg/L (Table 5) (FAO/WHO 2001).

Table 4 Concentration of heavy metals (copper (Cu), zinc (Zn), iron (Fe), cadmium (Cd), lead (Pb) and chromium (Cr)) in water in the four sampling systems along the Nakivubo channel in Kampala (sampling period: 18 and 19 November 2013).

Sampling system	Concentration in mg/L					
Heavy metals	Min	Max	Mean	Lower 95 % CI	Upper 95 % CI	Guideline values
Nakivubo channel (*n*=5)						
Cu	0.90	6.30	3.30[a]	1.60[a]	5.00[a]	1.00
Zn	0.20	3.00	1.40	0.70	2.00	5.00
Fe	8.10	38.10[a]	21.50[a]	13.90[a]	29.00[a]	10.00
Cd	0.05	0.31[a]	0.14[a]	0.07[a]	0.22[a]	0.10
Pb	0.09	3.00[a]	1.60[a]	0.94[a]	2.26[a]	0.10
Cr	0.01	0.01	0.06	0.03	0.08	1.00
Nakivubo wetland (*n*=12)						
Cu	0.90	4.00[a]	2.30[a]	1.70[a]	3.00[a]	1.00
Zn	0.01	1.10	0.30	0.10	0.60	5.00
Fe	10.90[a]	33.50[a]	18.60[a]	14.10[a]	23.10[a]	10.00
Cd	0.01	0.31[a]	0.13[a]	0.07	0.19[a]	0.10
Pb	0.10	2.60[a]	1.02[a]	0.56[a]	1.49[a]	0.10
Cr	0.003	0.21	0.06	0.01	0.10	1.00
Community areas (*n*=2)						
Cu	1.70[a]	4.20[a]	3.00[a]	–	–	1.00
Zn	0.17	0.20	0.19	–	–	5.00
Fe	18.20[a]	27.60[a]	22.90[a]	–	–	10.00
Cd	0.14[a]	0.26[a]	0.20[a]	–	–	0.10
Pb	1.30[a]	3.80[a]	2.50[a]	–	–	0.10
Cr	0.01	0.02	0.02	–	–	1.00
Lake Victoria (*n*=4)						
Cu	1.00	2.10[a]	1.40[a]	0.60[a]	2.20[a]	1.00
Zn	0.20	0.50	0.30	0.10	0.50	5.00
Fe	15.00[a]	21.10[a]	17.70[a]	12.70[a]	22.70[a]	10.00
Cd	0.09	0.11[a]	0.10	0.09[a]	0.11[a]	0.10
Pb	0.91[a]	1.64[a]	1.25[a]	0.76[a]	1.73[a]	0.10
Cr	0.01	0.02	0.014	0.004	0.023	1.00

Geometric means and 95 % confidence intervals (CIs) are indicated

[a] Concentrations exceeding maximum acceptable concentrations (MACs) as per Ugandan guidelines (NEMA 1999)

Soil and plant samples showed similar results to those obtained in the Nakivubo wetland by Sekabira et al. (2011). In comparison with a recent study conducted in Accra, Ghana, which focused on wastewater-irrigated vegetables (Ackah et al. 2013), the heavy metal levels in our soil and sediment samples were considerably higher. Particularly, the high values of Pb and Cd in the plant samples are of public health concern as they may accumulate in body tissue and cause adverse chronic health effects (Mwegoha and Kihampa 2010; Abaidoo et al. 2010). The tracing of heavy metals throughout the food chain, including other food crops, vegetables and also fish in Lake Victoria should be considered, to assess the related public health burden (Birungi et al. 2007; Ackah et al. 2013). Hence, to obtain a more complete picture of chemical pollution in Kampala's wastewater, studies—including other hazardous chemicals such as pesticides, pharmaceuticals, endocrine disruptors and illicit drugs— are needed (Belgiorno et al. 2007; Fatta-Kassinos et al. 2011).

Table 5 Concentration of heavy metals (copper (Cu), zinc (Zn), iron (Fe), cadmium (Cd), lead (Pb), and chromium (Cr)) in sediment, soil and plants (yam and sugar cane) in along the Nakivubo channel, in Kampala (sampling period: 18 and 19 November 2013)

Sample type	Concentration in mg/L					
Heavy metals	Min	Max	Mean	Lower 95 % CI	Upper 95 % CI	Guideline values
Sediment from the Nakivubo channel and Lake Victoria (*n*=8)						a
Cu	12.80	78.30	35.80	16.90	54.80	100.00
Zn	37.00	351.30	134.90	35.40	234.40	300.00
Fe	15,000	28,000	25,000	20,000	30,000	50,000
Cd	0.50	5.30[a]	2.10	0.90	3.30[a]	3.00
Pb	2.50	90.00	25.60	2.20	49.00	100.00
Cr	29.00	103.00[a]	49.80	30.70	68.90	100.00
Soil form the Nakivubo wetland and community areas (*n*=28)						a
Cu	18.30	98.30	53.10	44.30	61.80	100.00
Zn	32.00	742.50[a]	293.00	218.00	368.00[a]	300.00
Fe	15,000	80,000[a]	47,000	40,000	54,000[a]	50,000
Cd	0.30	3.50	1.80	1.50	2.10	3.00
Pb	20.00	427.50[a]	132.70[a]	98.40[a]	167.00[a]	100.00
Cr	24.50	105.30[a]	49.40	41.20	57.50	100.00
Yam (*n*=15)						b
Cu	0.00	11.90	2.60	0.70	4.50	73.00
Zn	0.00	387.50[a]	62.80	5.10	120.50[a]	100.00
Fe	0.00	87.50	42.10	23.70	60.50	425.00
Cd	0.00	0.50[a]	0.20[a]	0.10	0.30[a]	0.10
Pb	0.00	8.80[a]	4.00[a]	2.20[a]	6.00[a]	0.30
Cr	0.00	13.90[a]	4.40[a]	30.70[a]	7.10[a]	2.30
Sugarcane (*n*=13)						b
Cu	0.00	9.00	2.40	0.80	4.00	73.00
Zn	0.00	553.80	67.10	–	–	100.00
Fe	26.30	92.50	59.00	47.20	70.70	425.00
Cd	0.00	0.50[a]	0.20[a]	0.10	0.30[a]	0.10
Pb	0.00	17.50[a]	4.30[a]	1.20[a]	7.50[a]	0.30
Cr	1.00	14.30[a]	8.40[a]	5.40[a]	11.50[a]	2.30

Geometric means and 95 % confidence intervals (CIs) are indicated

[a] Concentrations exceeding maximum acceptable concentrations (MACs) as per guideline values (a, FAO (2004) and b, FAO/WHO (2001))

Potential and effective health risks for exposed groups along the wastewater chain

This environmental sampling was part of a larger study, comprising of a cross-sectional parasitological survey in selected population groups, a quantitative microbial risk assessment to determine the health risks related to microbial contamination, and the development and validation of a sanitation safety planning (SSP) manual (Fuhrimann et al. 2014). The results of our environmental monitoring (particularly contamination of water, sediment and soil with helminth eggs) are particularly interesting when juxtaposed with results obtained from a cross-sectional parasitological survey conducted in the Nakivubo area, which focused on five different population groups. With regard to intestinal parasitic infections (helminths and intestinal protozoa), farmers were found at the highest risk (overall prevalence of infection

75.9 %), followed by exposed community members (53.2 %), non-exposed community members (44.7 %), wastewater treatment plant workers (41.9 %) and faecal sludge collectors (35.8 %) (Fuhrimann et al. 2014).

Conclusions

This study revealed considerable microbial and chemical contamination of the Nakivubo wetland and Lake Victoria ecosystem due to domestic and industrial wastewater flows through Kampala City. A decrease in bacteria concentrations along the wetland was observed only for *E. coli* and BOD_5. Our sampling took place over an 8-week period between October and December 2013, corresponding to the rainy season. Therefore, our findings represent a snapshot of microbial and chemical contamination in the rainy season along the wastewater chain.

Our findings make an important contribution to the understanding of the nexus of wastewater pollution and its direct implications for public health in the context of a major East African city in the Great Lake region. We propose that a system of sentinel monitoring is established that will inform evidence-based decision-making and responses that are readily tailored to this social-ecological system. Our study suggests that farmers, consumers of plants grown in the Nakivubo wetland and communities living in close proximity to areas prone to flooding are exposed not only to high loads of pathogenic bacteria but also to helminth eggs (mainly hookworm) and heavy metals. Efforts should therefore be made by local authorities to minimise risks for these population groups by applying control measures (both technical and non-technical).

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7. ARTICLE 3: Risk of intestinal parasitic infections in communities exposed to wastewater and faecal sludge in Kampala, Uganda: a cross-sectional study

Photo: Sanitation worker emitting a faecal sludge truck in Kampala, Uganda (©S. Fuhrimann, 2013)

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RESEARCH ARTICLE

Risk of Intestinal Parasitic Infections in People with Different Exposures to Wastewater and Fecal Sludge in Kampala, Uganda: A Cross-Sectional Study

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Abstract

Background

There are health risks associated with wastewater and fecal sludge management and use, but little is known about the magnitude, particularly in rapidly growing urban settings of low- and middle-income countries. We assessed the point-prevalence and risk factors of intestinal parasite infections in people with different exposures to wastewater and fecal sludge in Kampala, Uganda.

Methodology

A cross-sectional survey was carried out in September and October 2013, enrolling 915 adults from five distinct population groups: workers maintaining wastewater facilities; workers managing fecal sludge; urban farmers; slum dwellers at risk of flooding; and slum dwellers without risk of flooding. Stool samples were subjected to the Kato-Katz method and a formalin-ether concentration technique for the diagnosis of helminth and intestinal protozoa infections. A questionnaire was administered to determine self-reported signs and symptoms, and risk factors for intestinal parasite infections. Univariate and multivariate analyses, adjusted for sex, age, education, socioeconomic status, water, sanitation, and hygiene behaviors, were conducted to estimate the risk of infection with intestinal parasites and self-reported health outcomes, stratified by population group.

Principal Findings

The highest point-prevalence of intestinal parasite infections was found in urban farmers (75.9%), whereas lowest point-prevalence was found in workers managing fecal sludge (35.8%). Hookworm was the predominant helminth species (27.8%). In urban farmers, the prevalence of *Trichuris trichiura*, *Schistosoma mansoni*, *Ascaris lumbricoides*, and *Entamoeba histolytica*/*E*. *dispar* was 15% and above. For all investigated parasites, we found significantly higher odds of infection among urban farmers compared to the other groups (adjusted odds ratios ranging between 1.6 and 12.9). In general, female participants had significantly lower odds of infection with soil-transmitted helminths and *S*. *mansoni* compared to males. Higher educational attainment was negatively associated with the risk of intestinal protozoa infections, while socioeconomic status did not emerge as a significant risk factor for any tested health outcome.

Conclusions/Significance

Urban farmers are particularly vulnerable to infections with soil-transmitted helminths, *S*. *mansoni*, and intestinal protozoa. Hence, our findings call for public health protection measures for urban farmers and marginalized communities, going hand-in-hand with integrated sanitation safety planning at city level.

Author Summary

Urban wastewater and fecal sludge use is of growing importance all over the world. However, unsafe management and inappropriate use might exacerbate the transmission of infectious diseases, including those caused by intestinal protozoa (e.g., amebiasis and giardiasis) and parasitic worms (e.g., soil-transmitted helminthiasis and schistosomiasis). People living and working in densely populated and rapidly transforming cities in Africa and Asia are especially vulnerable. We conducted a cross-sectional survey and assessed people's risk of intestinal parasitic infections due to exposure to wastewater and fecal sludge management and use in Kampala, the capital of Uganda. We collected data on the prevalence, intensity, and risk factors of infections with parasitic worms and intestinal protozoa among slum dwellers, urban farmers, and workers maintaining the sanitation system. We found high infection prevalence of *Schistosoma mansoni* and soil-transmitted helminths in urban farmers and slum dwellers after adjusting for age, sex, and educational attainment. Our data suggest that urban farmers are especially vulnerable to infections with intestinal parasites, which may play an important role in the transmission through contamination of their living and working environments. In view of our results, the control of schistosomiasis and soil-transmitted helminthiasis should be accelerated in Kampala.

Introduction

Africa and Asia are urbanizing faster than any other region of the world and an increase of 16% of the urban population is predicted for 2050 [1]. With such a demographic expansion, safe wastewater and fecal sludge management and use strategies are of pivotal importance for a healthy life in urban settings [2,3]. In the surroundings of densely populated urban centers of low- and middle-income countries (LMIC), inappropriate wastewater management is common [4,5]. Sanitation infrastructures often struggle to keep abreast of rapid population growth and increasing discharge of wastewater flows, including industrial effluents [6]. Consequently, people living and working in close proximity to wastewater management chains in urban settings of LMIC are frequently exposed to a broad range of pathogenic organisms and toxic chemicals

[7,8]. Water-borne, water-related, water-washed, and water-based diseases (e.g., intestinal parasitic infections, diarrheal diseases, skin, and eye infections) are associated with a lack of safe sanitation practices [9–11]. Moreover, occupational exposure to wastewater and fecal sludge was reported to be associated to intestinal parasite infections [12]. For example, an association between infection with hookworm and *Schistosoma mansoni* was found with specific farming activities in a medium-sized town in Côte d'Ivoire [13]. Additionally, increased risk of intestinal nematode infection and hookworm infection, in particular, could be shown among farmers using wastewater in Pakistan and Vietnam [14,15].

For prevention and control of these infectious diseases, the provision of basic sanitation infrastructure, coupled with education and promotion in hygiene practices, and targeted drug administration proofed effective [9,16,17]. To design interventions, one needs to understand disease transmission in the public domain (under control of a household) and domestic domain (such as public places of work and recreational sites) [18]. Indeed, measures to prevent and control infections that give rise to diarrheal diseases need to be tailored to specific urban risks factors and exposure groups [19,20].

In Kampala, the capital of Uganda, more than 90% of the 1.8 million inhabitants rely on onsite sanitation facilities, such as pit latrines and septic tanks. A small portion of wastewater is conveyed to treatment plants, while most of the generated wastewater and fecal sludge is discharged, without treatment, in open storm water channels [21,22]. Along the channel from the wastewater treatment plant to the Lake Victoria, there are three major categories of workers exposed to wastewater along this system: (i) those maintaining the sanitation systems; (ii) those at the wastewater treatment plants; and (iii) farmers using the wastewater downstream in the Nakivubo wetland. Furthermore, flooding events are spreading the wastewater flows in the poor low-laying settlements, putting the concerned communities under risk of contaminations [23]. In these marginalized settlements, seasonal flooding events might exacerbate the unfavorable conditions of existing sanitation systems and water-related health risks [24,25]. Hence, direct contact to wastewater and contamination of food crops grown in the wetlands, fish, and drinking water in Lake Victoria are putting thousands of slum dwellers, urban farmers, and workers maintaining the system at risk of ill-health [26].

Infections with soil-transmitted helminths and *Schistosoma* spp. are of particular concern, as Kampala is endemic for both soil-transmitted helminthiasis and schistosomiasis [27,28]. Recent studies from rural and peri-urban areas around Kampala revealed *S. mansoni* and hookworm prevalence of 89% and 43%, respectively [29]. The prevalence of two of the most important intestinal protozoa *Giardia intestinalis* and *Entamoeba histolytica*/*E. dispar* was 12% and 10%, respectively [30]. At the onset of our study, the city authorities did not consider intestinal parasitic infections as an issue in these urban areas. However, there is a paucity of recent epidemiologic data [31,32]. Hence, there is a need for epidemiologic studies conducted in these heterogeneous urban communities to develop an evidence-base of risk factors related to wastewater use in different population groups in order to guide preventive measures [20,33]. Population groups to be targeted include marginalized slum dwellers, urban farmers, and workers managing the sanitation system [19].

We report findings from a cross-sectional parasitologic survey in selected population groups (farmers, workers, and local communities) exposed to wastewater and fecal sludge management and use activities in the Nakivubo area in Kampala. We aimed to determine the prevalence rates of intestinal parasitic infections and to assess the associations of disease risks with socioeconomic, environmental, and lifestyle factors in the different population groups. Our investigation is part of a larger study, comprising of an environmental assessment, a quantitative microbial risk assessment to determine the health risks related to microbial contamination, and the development and validation of a sanitation safety planning manual [20,21,26].

Methods

Ethics Statement

This manuscript has been developed according to the consolidated standards of reporting trials (CONSORT). The study protocol was approved by the institutional research commission of the Swiss Tropical and Public Health Institute (Swiss TPH; Basel, Switzerland; reference no. FK 106) and the Uganda National Council for Science and Technology (UNCST; Kampala, Uganda; reference no. HS 1487). Ethical approval was obtained from the ethics committee of the cantons of Basel-Stadt and Basel-Landschaft (EKBB; reference no. 137/13) and the Higher Degrees Research and Ethics Committee of Makerere University School of Public Health (Kampala, Uganda; reference no. IRBOOO11353). This study is registered with the clinical trial registry ISRCTN (identifier: ISRCTN13601686).

The following enrolment procedures were approved by the ethical committees: all participants were informed about the purpose and procedures of the study and they were invited to sign a written informed consent. In case of illiteracy, thumb-print and signature of a witness was requested. Those with informed consent were assigned a unique identifier. Results were communicated to participants and those found infected with any kind of helminth were treated according to national guidelines (e.g., a single 400 mg oral dose of albendazole against soil-transmitted helminth infection and a single 40 mg/kg oral dose of praziquantel against schistosomiasis).

Study Design and Participants

We conducted a cross-sectional survey in September and October 2013 in Kampala. The study was undertaken in the Nakivubo area (Nakawa and Makindye divisions), which receives most of Kampala's wastewater. The area is located at an altitude of 1,140 m above the mean sea level at latitude 0° 18' 48.1" N and longitude 32° 36' 43.86" E. Domestic and industrial wastewater is derived from the central division, while the treated effluent of the Bugolobi Sewage Treatment Works (BSTW) is collected in the Nakivubo channel, a 12.3 km long open storm water channel. This channel enters into the Nakivubo wetland (5.3 km^2), where approximately 600 farmers pursue urban farming for their livelihood. Informal slum communities are at highest risk of flooding events, as they live along both sides of the wetland (approximate population size is 12,000 people). The water from the Nakivubo wetland is ultimately discharged into the Inner Murchison Bay at the shores of Lake Victoria, some 4 km ahead of where the water is pumped and treated to supply Kampala city with drinking water (Fig 1). The study area has been described in detail elsewhere, including a short video that provides additional contextual features [21].

Exposure Groups

We focused on adults (aged ≥18 years) living and working in the Nakivubo area. According to the level of exposure to wastewater, the study participants were stratified into five groups, as follows:

1. "*com* $_{exposed}$", slum dwellers at risk of flooding living along the Nakivubo wetland at altitudes ranging between 1,140 m and 1,160 m above mean sea level (AMSL). The communities are characterized by poor housing and unimproved sanitation and unsafe water supply;
2. "*com* $_{comparison}$", slum dwellers living in similar communities as *com* $_{exposed}$ without risk of flooding (comparison group) living at least 2 km away from the Nakivubo wetland at altitudes between 1,160 and 1,201 m AMSL;

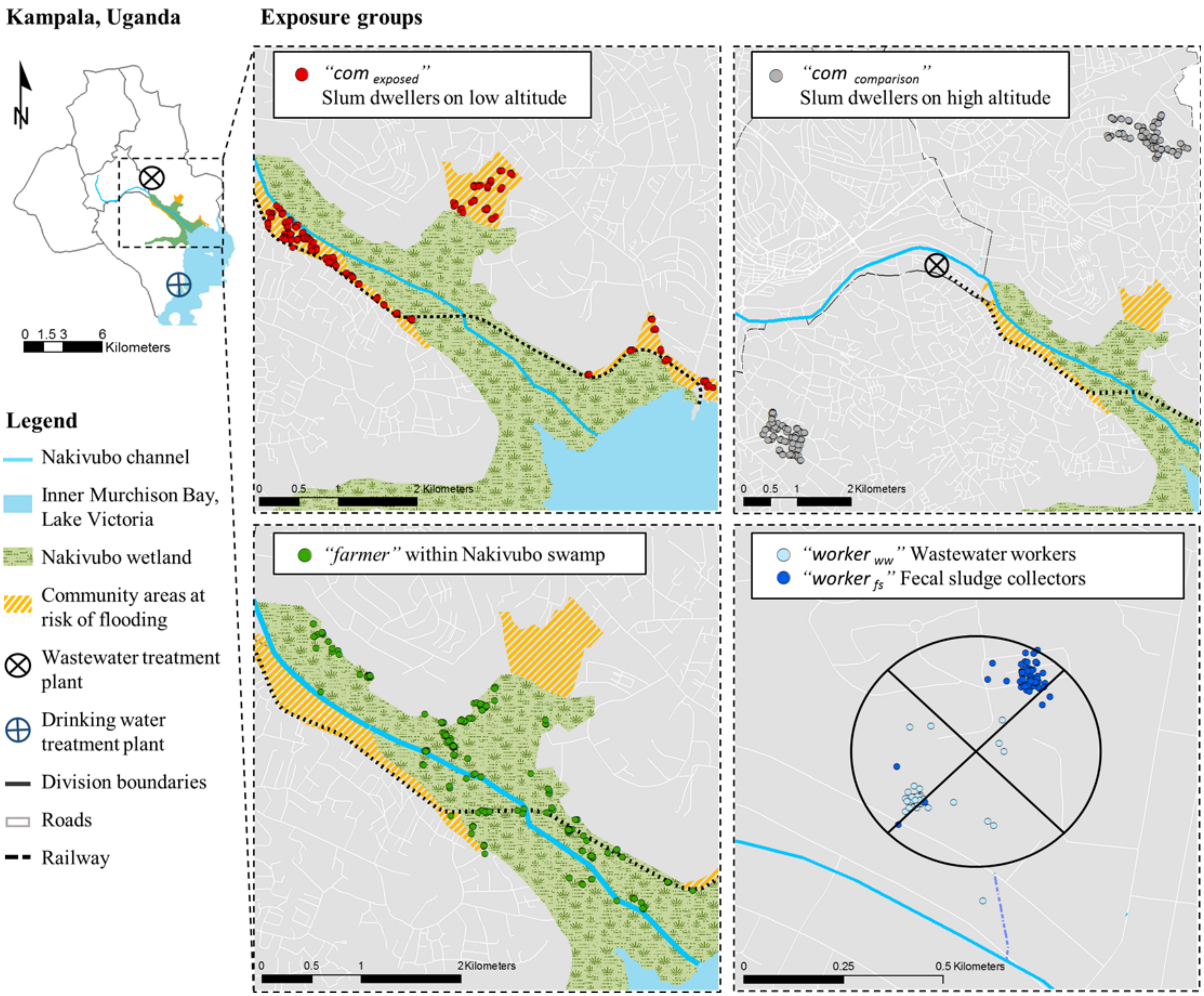

Fig 1. Map of Kampala showing the study area in the Nakivubo area. The exact geographic locations of all participants in the five exposure groups are indicated as follow: (i) red dots: "*com* $_{exposed}$", slum dwellers at risk of flooding along the Nakivubo wetland between altitudes 1,140 m and 1,160 m above mean sea level (AMSL); (ii) grey dots: "*com* $_{comparison}$", slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland and located between 1,160 and 1,201 m AMSL; (iii) green dots: "*farmer*", urban farmers using wastewater within the Nakivubo wetland; (vi) dark blue dots: "*worker* $_{ww}$", workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; and (v) light blue: "*worker* $_{fs}$", workers collecting fecal sludge at household level by means of vacuum trucks.

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3. "*farmer*", urban farmers using informally and indirectly wastewater to grow sugar cane, yams, and maize within the Nakivubo wetland and living in the same communities as *com* $_{exposed}$;
4. "*worker* $_{ww}$", workers employed by NWSC who maintain the drainage channels and operate the BSTW; and
5. "*worker* $_{fs}$", workers organised under the pit emptier association managing fecal sludge (e.g., collection at households by means of vacuum trucks).

Sample Size and Inclusion Criteria

Our intended sample size was 1,000 participants (“*com* $_{comparison}$” = 350, “*com* $_{exposed}$” = 250, “*farmer*” = 275, “*worker* $_{ww}$” = 50, and “*worker* $_{fs}$” = 100). We aimed at a power of 95%, to ensure that a reduction in effective exposure variance by 35% following confounder adjustment would still leave 80% power. Our assumptions were that the prevalence rate of intestinal parasitic infections is at least 20% in “*com* $_{comparison}$” and the difference in odds ratio (OR) to “*farmer*”, “*worker* $_{ww}$”, and “*worker* $_{fs}$” is at least 2.5. We also assumed that the final sample size would be reduced by 15% due to non-response and missing data.

The following inclusion and exclusion criteria were applied. “*com* $_{comparison}$” and “*com* $_{exposed}$” were selected proportionally to the projected number of individuals living in each village in 2013 [34]. Briefly, we applied a grid of 25 x 25 m over each village and randomly selected coordinates. At each cross point of the grid, we selected the closest four households. We used a Kish Grid to choose the participant at the unit of the household [35]. To select “*farmer*”, we mapped the on-going farming activities and estimated the number of farmers with the help of farmer chair persons. Our research team enrolled all farmers they encountered while visiting the farms between 7 a.m. and 6 p.m. over a 10-day period. To select “*worker* $_{ww}$” and “*worker* $_{fs}$”, we mobilized and informed the workers via the chair persons. All workers who showed up at their specific work sites over a period of 2 weeks were registered and invited to participate.

Procedures

We used a questionnaire to determine exposure pathways to wastewater and fecal sludge, potential confounding factors (e.g., demographic and socioeconomic), risk variables (e.g., water, sanitation, hygiene, and occupation) and self-reported health outcomes. Study participants were asked about signs and symptoms experienced over the past 2 weeks before the interview took place, using a pre-tested questionnaire [36]. Diarrheal episodes were defined according to WHO as ‘the passage of three or more loose or liquid stools per day and assessed if the participant experienced an episode within the past 1, 7, or 14 days [37]. The questionnaire was developed in English, translated into the local language Luganda, and pre-tested with five farmers and five workers. Research assistants entered data directly into tablet computers (Samsung Galaxy note 10.1 N8010) via a data entry mask using Open Data Kit (http://opendatakit.org).

Participants were invited to provide a fresh morning stool that was subject to the Kato-Katz technique (duplicate thick smears, using standard 41.7 mg templates) [38] and a formalin-ether concentration technique (FECT) [39] for the diagnosis of helminths (*Ascaris lumbricoides*, hookworm, *Trichuris trichiura*, *S. mansoni*, and other helminths) and intestinal protozoa (*Blastocystis hominis*, *Chilomastix mesnili*, *Endolimax nana*, *Entamoeba coli*, *E. histolytica*/*E. dispar*, *Entamoeba hartmanni*, *G. intestinalis*, and *Iodamoeba bütschlii*).

Statistical Analysis

Helminth- and intestinal protozoa-specific proportions between the five exposure groups were compared with Pearson’s χ^2 test. Univariate logistic regression was applied to investigate the potential association between dependent (namely, infections with (i) any intestinal parasite, (ii) intestinal helminth, (iii) soil-transmitted helminth, (iv) intestinal protozoa, (v) *A. lumbricoides*, (vi) hookworm, (vii) *T. trichiura*, (viii) *S. mansoni*, (ix) 14-day diarrhoea, (x) skin problems, and (xi) eye problems) and 49 independent variables (e.g., sex and age). People’s socioeconomic status was determined using principal component analysis and participants were grouped into three categories, as indicated in Table 1 (most poor, poor, and less poor) [40].

Table 1. Demographic and socioeconomic characteristics of the participants enrolled in a cross-sectional survey conducted in late 2013 in Kampala, stratified by exposure group.

Demographic and socio-economic characteristics	*com* $_{comparison}$ *		*com* $_{exposed}$ *		*farmer**		*worker* $_{fs}$ *		*worker* $_{ww}$ *	
	n = 331		n = 229		n = 245		n = 67		n = 43	
	n	%	n	%	n	%	n	%	n	%
Sex										
Female	233	70.4	171	74.7	110	44.9	0	0	4	9.3
Male	98	29.6	58	25.3	135	55.1	67	100	39	90.7
Age range (years)										
18–24	94	28.4	63	27.5	32	13.1	13	19.4	5	11.6
25–39	176	53.2	131	57.2	126	51.4	32	47.8	18	41.9
≥40	61	18.4	35	15.3	87	35.5	22	32.8	20	46.5
Level of education										
Never went to school	33	10.0	37	16.2	45	18.4	5	7.5	0	0
Primary school	103	31.1	102	44.5	144	58.8	15	22.4	4	9.3
'O' level	143	43.2	62	27.1	49	20.0	32	47.8	11	25.6
'A' level	29	8.8	21	9.2	4	1.6	11	16.4	7	16.3
Tertiary	20	6.0	7	3.1	2	0.8	4	6.0	13	30.2
University degree	3	0.9	0	0	1	0.4	0	0	8	18.6
Socioeconomic status (principal component analysis (PCA))[1]										
Most poor	99	29.9	87	38.0	112	45.7	0	0	1	2.3
Poor	127	38.4	73	31.9	88	35.9	17	25.4	6	14.0
Less poor	105	31.7	69	30.1	45	18.4	50	74.6	36	83.7
Residential area (division)										
Central	0	0	0	0	1	0.4	1	1.5	4	9.3
Nakawa	140	42.3	79	34.5	112	45.7	9	13.4	11	25.6
Kawempe	0	0	0	0	0	0	9	13.4	4	9.3
Rubaga	0	0	0	0	0	0	6	9.0	2	4.7
Makindye	191	57.7	150	65.5	132	53.9	16	23.9	13	30.2
of Kampala	0	0	0	0	0	0	26	38.8	9	20.9

[1] Principal component analysis (PCA) based on the possession of the following 11 items: radio, TV, mobile phone, fridge, computer, bicycle, motorbike, car, electricity, running water, and latrine. Categories of socioeconomic status were obtained by dividing the first principal component into tertiles.

* *"com* $_{exposed}$*"*, slum dwellers at risk of flooding along the Nakivubo wetland; *"com* $_{comparison}$*"*, slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *"farmer"*, urban farmers reusing wastewater within the Nakivubo wetland; *"worker* $_{ww}$*"*, workers maintaining drainage channels and operate the Bugolobi Sewage Treatment Works; *"worker* $_{fs}$*"*, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

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Our multivariate core model included the categorical exposure variable, sex, age, level of education, and socioeconomic status [9,10]. We then added risk factors that had a p-value below 0.2 (using likelihood ratio test) in the univariate analyses.

Odds ratios are reported to compare risks, while differences and associations are considered as statistically significant if p-values are below 0.05, and indicating a trend if p-values are between 0.05 and 0.1. Statistical analyses were done using STATA version 12.0 (Stata Corporation; College Station, United States of America). Maps, including geographic coordinates of the interviews, were established in ArcMap version 10 (Environmental System Research Institute; Redlands, United States of America). Kato-Katz thick smear and FECT readings were double-entered and validated.

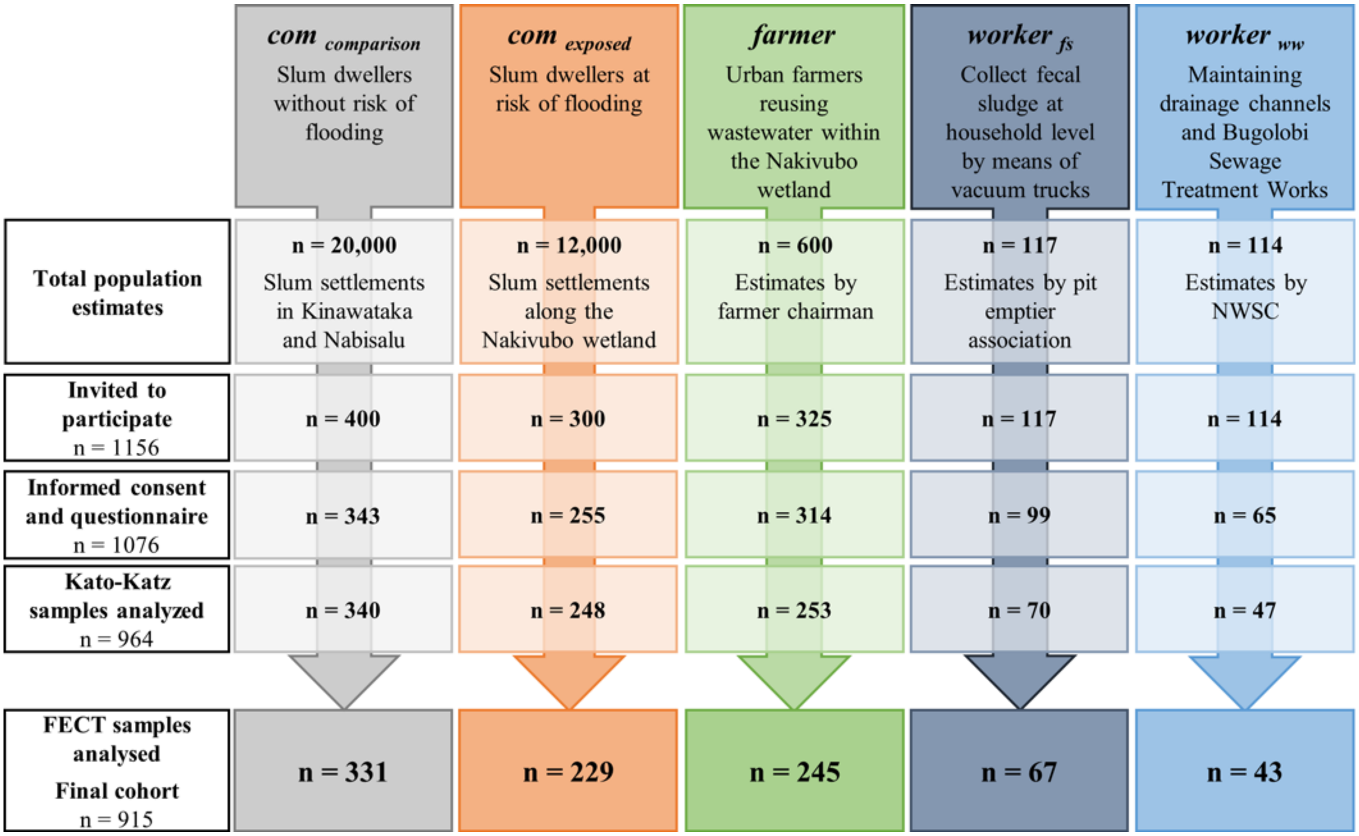

Fig 2. CONSORT flowchart showing study participation and compliance of the five specific exposure groups from October-November 2013. Flowchart shows the number of people who were invited, those who participated, and those with complete data records included in the final statistical analyses.

doi:10.1371/journal.pntd.0004469.g002

Results

Participant Enrolment

Among the 1,156 people invited, 1,076 fulfilled inclusion criteria, had written informed consent, and completed the questionnaire interview (Fig 2). Stool samples were provided by 964 individuals and subjected to Kato-Katz. Due to insufficient volumes of stool provided, only 915 of the samples were subjected to FECT, thus defining the final study cohort. As shown in Fig 2, the final cohort consisted of 229 "*com* $_{exposed}$", 331 "*com* $_{comparison}$", 245 "*farmer*", 43, "*worker* $_{ww}$", and 67 "*worker* $_{fs}$".

Study Population Characteristic

Table 1 shows the demographic (sex, age, educational attainment, religion, ethnicity, and division of living) and socioeconomic characteristics of the participants. Women accounted for 74%, 70%, 45% and 9% in "*com* $_{exposed}$", "*com* $_{comparison}$", "*farmer*", and "*worker* $_{ww}$", respectively, whereas no woman was in the "*worker* $_{fs}$" group. Socioeconomic status was highest in "*worker* $_{fs}$" and "*worker* $_{ww}$" with 83% and 74%, respectively, classified as less poor. The lowest socioeconomic status was observed in "*com* $_{comparison}$", "*com* $_{exposed}$", and "*farmer*" with 30%, 38%, and 45% classified as most poor, respectively.

Parameters for exposure to wastewater, access to drinking water, sanitation, and hygienic behaviors are summarized in S1A Table. Flooding events of the household occurred most often

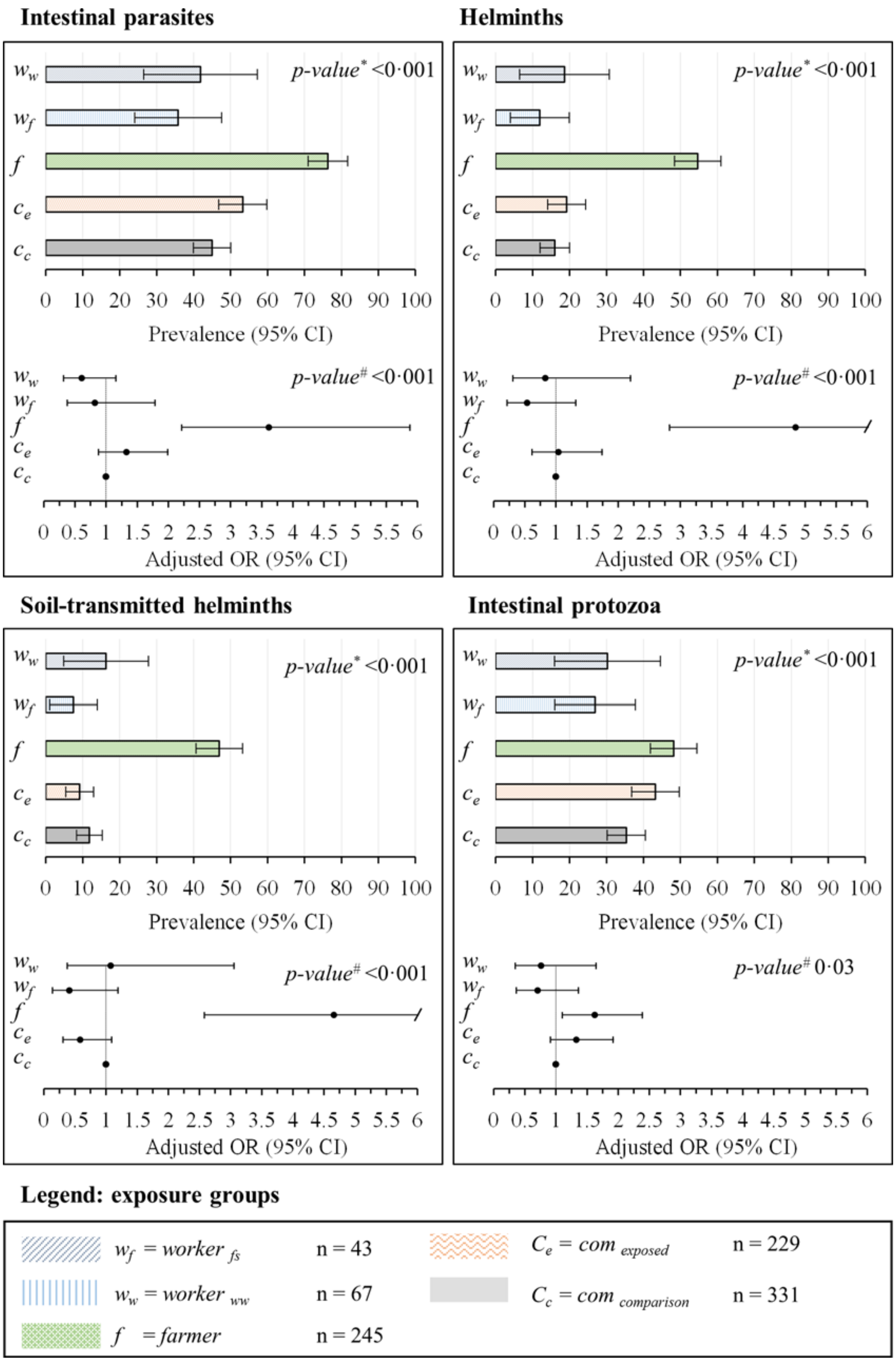
Intestinal parasites
Helminths
Soil-transmitted helminths
Intestinal protozoa
w_w
w_f
f
c_e
c_c
p-value* <0·001
p-value# <0·001
p-value# 0·03
0 10 20 30 40 50 60 70 80 90 100
Prevalence (95% CI)
0 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5 5.5 6
Adjusted OR (95% CI)
Legend: exposure groups
w_f = worker $_{fs}$ n = 43
w_w = worker $_{ww}$ n = 67
f = farmer n = 245
C_e = com $_{exposed}$ n = 229
C_c = com $_{comparison}$ n = 331

Fig 3. Prevalence rates and adjusted odds ratio (OR) and 95% confidence intervals (CIs). Values are indicated for “$com_{exposed}$”, “$com_{comparison}$”, “*farmer*”, “$worker_{ww}$”, and “$worker_{fs}$”for intestinal parasitic infections, intestinal helminth infections, soil-transmitted helminth infections, and intestinal protozoa infection. *p-value based on χ^2 test. $^{\#}$p-value based on multivariate regression using likelihood ratio test.

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in households of “*farmer*”, and “$com_{exposed}$” (64% and 47%, respectively). 65%, 49%, and 56% of the participants from “$com_{exposed}$”, “*farmer*”, and “$com_{comparison}$” had a toilet at home. Overall, 29% of all participants reported having taken a deworming drug within the past 6 months with the highest proportions reported by “$worker_{fs}$” (61%).

S1B Table shows occupational conditions and risk factors for “*farmer*”, “$worker_{ww}$”, and “$worker_{fs}$”. While most of the workers are officially contracted (97%), the opposite is seen among “*farmer*”, as most lack an official employment status (95%). 81%, 63%, and 49% of “$worker_{ww}$”, “$worker_{fs}$”, and “*farmer*” wear boots, respectively. Only 4% of “*farmer*” use gloves, whilst over 80% of the workers use them.

Prevalence and Intensity of Intestinal Parasitic Infections, Self-Reported Signs and Symptoms

The prevalence and intensity of parasitic infections, stratified by exposure group, are summarized in Figs 3 and 4 and Table 2. The overall prevalence of infection with any intestinal parasite was (from highest to lowest) 76%, 53%, 44%, 42%, and 35% in “*farmer*”, “$com_{exposed}$”, “$com_{comparison}$”, “$worker_{ww}$”, and “$worker_{fs}$”, respectively. One quarter (25%) of all participants was found infected with at least two species of intestinal parasites. The highest prevalence of soil-transmitted helminth infection was found in “*farmer*” (hookworm, *T*. *trichiura*, and *A*. *lumbricoides* prevalence of 28%, 26%, and 18%, respectively). *S*. *mansoni* was detected in all exposure groups with prevalences of 5% and above; while the highest prevalence was found in “*farmer*” (23%). Nine participants were infected with *Hymenolepis nana* (six cases occurred in “*farmer*”), two with *Taenia* spp., and one with *Strongyloides* spp. Overall, 11 participants were found with heavy *S*. *mansoni* infection (≥400 eggs per gram of stool). Forty percent of all participants were infected with intestinal protozoa; the highest prevalence rates occurred in “*farmer*” and “$com_{exposed}$” (48% and 43%, respectively). We found a prevalence of *E*. *histolytica*/*E*. *dispar* of 15%, 12%, and 7% in “*farmer*”, “$worker_{ww}$”, and “$worker_{fs}$”, respectively. Nine people had an infection with *G*. *intestinalis*, five of them in “$com_{comparison}$”.

Self-reported signs and symptoms are summarized in Fig 4 and Table 3. The prevalence of diarrhea (recall period: 2 weeks) was not significantly different between study groups; we found prevalence of 21% in “$com_{comparison}$”, 25% in “*farmer*”, and 33% in “$worker_{fs}$”. General skin problems were reported by between 28% (“$com_{exposed}$” and “$com_{comparison}$”) and 39% ($worker_{fs}$). More specific skin irritation was reported by 19%, 16%, 13%, and 12% in “$worker_{fs}$”, “$worker_{ww}$”, “$com_{exposed}$”, and “*farmer*”, whereas a considerable lower rate of 4% was found in “$com_{comparison}$”. Eye problems were most frequently reported by “*farmer*” (37%), followed by “$worker_{ww}$” and “$worker_{fs}$” (33% each).

Associations between Risk/Confounding Factors and Health Outcomes of Interest

Figs 3 and 4 provide an overview of adjusted associations of all measured helminth and intestinal protozoa infections, 14-day diarrhea prevalence, and skin and eye problems among different exposure groups, as revealed by the multivariate regression analyses. “*farmer*” had a higher odds of all measured helminth and intestinal protozoa infections, compared to the other groups (adjusted OR between 1.6 and 12.9). Workers (both “$worker_{ww}$”, and “$worker_{fs}$”) had lower adjusted odds compared to “$com_{comparison}$” for intestinal parasite infections, except for

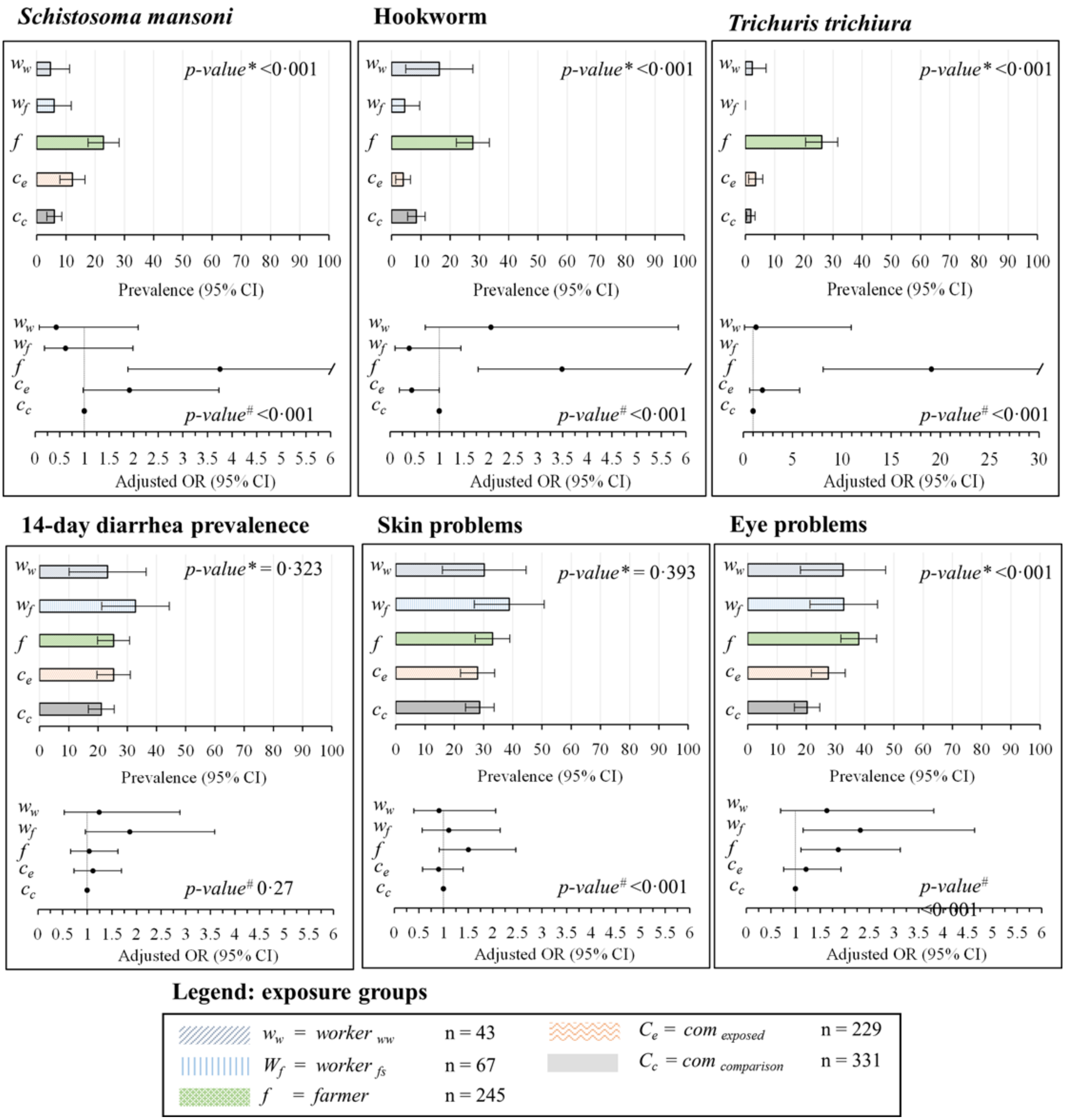

Fig 4. Prevalence rates and adjusted odds ratio (OR) and 95% confidence intervals (CIs). Values are indicated for "*com* $_{exposed}$", "*com* $_{comparison}$", "*farmer*", "*worker* $_{ww}$", and "*worker* $_{fs}$" for *Schistosoma mansoni*, hookworm, *Trichuris trichiura*, self-reported diarrhea, skin problems, and eye problems. *p-value based on χ^2 test. $^\#$p-value based on multivariate regression using likelihood ratio test.

doi:10.1371/journal.pntd.0004469.g004

Table 2. Prevalence and intensity of parasitic infections of the participants enrolled in a cross-sectional survey conducted in late 2013 in Kampala, stratified by exposure groups.

Prevalence of infection[#]	*com* $_{comparison}$ [*]		*com* $_{exposed}$ [*]		*farmer* [*]		*worker* $_{fs}$ [*]		*worker* $_{ww}$ [*]		Difference (χ^2)
	n = 331		n = 229		n = 245		n = 67		n = 43		
	n	%	n	%	n	%	n	%	n	%	p-value
Intestinal parasite	148	44.7	122	53.3	186	75.9	24	35.8	18	41.9	<0.001
Helminth	52	15.7	44	19.2	134	54.7	8	12.0	8	18.6	<0.001
Soil-transmitted helminth	39	11.8	21	9.2	115	46.9	5	7.5	7	16.3	<0.001
Intestinal protozoa	117	35.4	99	43.2	118	48.2	18	26.9	13	30.2	<0.001
Hookworm	28	8.5	9	3.9	68	27.8	3	4.5	7	16.3	<0.001
Light infection	28	8.5	8	3.5	64	26.1	2	3.0	7	16.3	
Moderate infection	0	0	1	0.4	4	1.6	1	1.5	0	0	<0.001
Trichuris trichiura	6	1.8	8	3.5	64	26.1	0	0	1	2.3	<0.001
Light infection	6	1.8	8	3.5	61	24.9	0	0	1	2.3	
Moderate infection	0	0	2	0.9	10	4.1	0	0	0	0	<0.001
Ascaris lumbricoides	0	0	7	3.1	45	18.4	0	0	1	2.3	<0.001
Light infection	0	0	5	2.2	35	14.3	0	0	1	2.3	
Moderate infection	0	0	2	0.9	10	4.1	0	0	0	0	<0.001
Schistosoma mansoni	20	6.0	28	12.2	56	22.9	4	6.0	2	4.7	<0.001
Light infection	11	3.3	21	9.2	37	15.1	2	3.0	1	2.3	
Moderate infection	7	2.1	3	1.3	15	6.1	1	1.5	1	2.3	
Heavy infection	2	0.6	4	1.8	4	1.6	1	1.5	0	0	<0.001
***Taenia* spp.**	2	0.6	0	0	0	0	0	0	0	0	0.472
Hymenolepis nana	2	0.6	0	0	6	2.5	1	1.5	0	0	0.067
***Strongyloides* spp.**	0	0	0	0	0	0	1	1.5	0	0	0.013
Entamoeba histolytica/ E. dispar	20	6.0	9	3.9	37	15.1	5	7.5	5	11.6	<0.001
Entamoeba coli	92	27.8	83	36.2	94	38.4	13	19.4	8	18.6	<0.001
Giardia intestinalis	5	1.5	1	0.4	2	0.8	1	1.5	0	0	0.677
Balantidium coli	1	0.3	0		1	0.4	0	0	0	0	0.869
Chilomastix mesnili	1	0.3	1	0.4	1	0.4	0	0	1	2.3	0.411
Entamoeba hartmanni	12	3.6	16	7.0	1	0.4	0	0	0	0	<0.001
Iodamoeba bütschlii	13	3.9	10	4.4	11	4.5	1	1.5	0	0	0.527

[*] *"com* $_{exposed}$*"*, slum dwellers at risk of flooding along the Nakivubo wetland; *"com* $_{comparison}$*"*, slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *"farmer"*, urban farmers reusing wastewater within the Nakivubo wetland; *"worker* $_{ww}$*"*, workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; *"worker* $_{fs}$*"*, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

[#] Prevalence is calculated out of the results of the examination of a single stool sample by means of duplicate Kato-Katz thick smears and the formalin-ether concentration method. Infection intensity is based on the examination of duplicate Kato-Katz thick smears.

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hookworm, where "*worker* $_{fs}$" had increased risk (OR 2.8, 95% CI 0.9 to 1.9). However, for 14-day diarrhea prevalence, skin and eye problems, workers had similar or higher risks. For soil-transmitted helminth "*com* $_{exposed}$" showed lower infection risks compared to "*com* $_{comparison}$" (OR 0.6, 95% CI 0.3 to 1.1), while the risk of intestinal protozoa infection was elevated (OR 1.3, 95% CI 0.9 to 1.9). Compared to "*com* $_{comparison}$", "*com* $_{exposed}$" were at higher risk of *S. mansoni* infection (OR 1.9, 95% CI 1.0 to 3.7), but at lower risk of hookworm infection (OR 0.4, 95% CI 0.2 and 1.0). Moreover, 14-day prevalence rates of diarrhea and skin symptoms according to self-reports were higher among "*worker* $_{fs}$" and "*farmer*" compared to the other groups.

Table 4 summarizes associations of "any parasitic infection" and S2A–S2I Table of all measured helminth and intestinal protozoa infections, 14-day diarrhea prevalence, skin, and eye

Table 3. Self-reported health outcomes experienced in the last 2 weeks before the interview among participants enrolled in a cross-sectional survey carried out in late 2013 in Kampala, stratified by exposure groups.

Self-reported health problems over the past 2 weeks	*com* $_{comparison}$*		*com* $_{exposed}$*		*farmer**		*worker* $_{fs}$*		*worker* $_{ww}$*		Difference (χ^2)
	n = 331		n = 229		n = 245		n = 67		n = 43		
	n	%	n	%	n	%	n	%	n	%	p-value
Diarrhea											
14-day prevalence	70	21.2	58	25.3	62	25.3	22	32.8	10	23.3	0.323
Blood in stool	8	2.4	5	2.2	8	3.3	3	4.5	1	2.3	0.837
Number of episodes											
1	50	15.1	49	21.4	40	16.3	10	14.9	4	9.3	
2	15	4.5	4	1.8	14	5.7	9	13.4	3	7.0	
3	2	0.6	4	1.8	5	2.0	2	3.0	0	0	
4	3	0.9	0	0	2	0.8	0	0	3	7.0	<0.001
Eye issues											
Eye problems	67	20.2	63	27.5	93	38.0	22	32.8	14	32.6	<0.001
Eye irritation	29	8.8	38	16.6	42	17.1	12	17.9	11	25.6	<0.001
Sensitivity to light	35	10.6	24	10.5	54	22.0	10	14.9	8	18.6	0.001
Other eye problems	7	2.1	6	2.6	13	5.3	6	9.0	0	0.0	0.016
Skin issues											
Skin problems	95	28.7	64	28.0	81	33.1	26	38.8	13	30.2	0.393
Skin irritation	14	4.2	29	12.7	29	11.8	13	19.4	7	16.3	<0.001
Itching	65	19.6	46	20.1	52	21.2	16	23.9	11	25.6	0.853
Sores on skin	0	0.0	2	0.9	14	5.7	4	6.0	3	7.0	0.020
Ulcer on skin	4	1.2	3	1.3	5	2.0	4	6.0	0	0.0	0.070
Other skin problems	9	2.7	4	1.8	8	3.3	1	1.5	0	0.0	0.621

*"*com* $_{exposed}$", slum dwellers at risk of flooding along the Nakivubo wetland; "*com* $_{comparison}$", slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; "*farmer*", urban farmers reusing wastewater within the Nakivubo wetland; "*worker* $_{ww}$", workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; "*worker* $_{fs}$", workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

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problems with risk and confounding factors observed in univariate and multivariate regression analyses. Significantly increased risks were observed among male participants for total intestinal parasite, helminth, soil-transmitted helminth, and *S. mansoni* infections. Relying on pit latrines or having no toilet facility was associated with significantly increased risk of "any parasitic infection", soil-transmitted helminth, and *T. trichiura* infections. Moreover, hand washing after defecation and work was negatively associated with *T. trichiura* infections (OR 0.4, 95% CI 0.2 to 0.8 and OR 0.6, 95% CI 0.3 to 1.1, respectively). Higher level of education was negatively associated with intestinal protozoa infections (OR 0.6, 95% CI 0.4 to 1.0). On the other hand, 14-day prevalence rates of diarrhea and skin symptoms according to self-reports were higher among participants with higher socioeconomic status.

Discussion

We report data on prevalence and risk factors for intestinal parasitic infections in exposed adult population groups along the major wastewater and fecal sludge use system in Kampala, Uganda. Urban farmers had the highest prevalence rate and higher ORs compared to the other exposure groups for the majority of measured health outcomes. Indeed, urban farmers had a point-prevalence of intestinal parasites of 76%. Hookworm and *S. mansoni* were the predominant infections; 28% and 23%, respectively. We found significantly higher odds of infection,

Table 4. Results of univariate and the multivariate logistic regression analysis for parasitic infection in a cross-sectional survey done in late 2013 in Kampala§.

Intestinal parasitic infection			**Univariate logistic regression***				**Multivariate logistic regression****			
N = 915 / N(cases) = 530			**OR**	**95% CI**		**p-value**	**aOR**	**95% CI**		**p-value**
Exposure group***		$com_{comparison}$	1.00			**<0.001**				**<0.001**
		$com_{exposed}$	1.39	0.99	1.96	0.061	1.33	0.88	2.01	0.173
		farmer	3.88	2.69	5.62	<0.001	3.61	2.22	5.88	<0.001
		$worker_{fs}$	0.68	0.39	1.16	0.163	0.61	0.32	1.16	0.131
		$worker_{ww}$	0.87	0.46	1.66	0.672	0.82	0.38	1.79	0.624
Sex		Male	1.00							
		Female	0.79	0.61	1.03	**0.081**	0.75	0.53	1.06	0.101
Age			1.01	1.00	1.02	**0.126**	1.00	0.98	1.01	0.741
Education		Never went to school	1.00			**0.023**				
		Primary	0.19	1.33		0.576	0.76	0.48	1.22	0.262
		Higher education	0.64	0.42	0.96	0.031	0.87	0.54	1.41	0.587
Socioeconomic status		Most poor	1.00			**<0.001**				
		Poor	0.61	0.44	0.84	<0.001	0.76	0.53	1.09	0.139
		Less poor	0.59	0.43	0.82	<0.001	0.95	0.63	1.43	0.813
Number of people per household		Single	1.00			**0.097**				
		2–4	1.28	0.85	1.93	0.245	1.33	0.83	2.05	0.252
		> 4	1.55	1.01	2.39	0.051	1.43	0.87	2.35	0.161
Toilet facility		Flush toilet	1.00			**0.010**				
		Pit latrine	1.61	0.91	2.85	0.112	1.79	0.93	3.43	0.082
		No facility	2.61	1.32	5.18	<0.001	1.43	0.63	3.23	0.394
Toilet sharing		Private toilet	1.00			**0.012**				
		2 and 3 households	0.77	0.55	1.07	0.121	0.87	0.64	1.27	0.481
		≥ 4 households	1.19	0.85	1.67	0.314	1.14	0.75	1.74	0.542
Flooding of living area		No	1.00							
		Yes	1.99	1.49	2.66	**<0.001**	1.02	0.68	1.53	0.911
Source of drinking water		Bottle, tap, rain water	1.00			**0.101**				
		Spring	1.33	1.00	1.76	0.055	0.25	0.12	1.61	0.611
		Other	1.30	0.77	2.23	0.322	0.95	0.48	1.86	0.884
Source of bath water		Tap, rain water	1.00			**0.053**				
		Spring	1.35	1.02	1.82	0.041	1.06	0.65	1.73	0.817
		Unprotected	1.44	0.91	2.29	0.121	1.16	0.64	2.09	0.632
Bathing per week		< 7	1.00			**0.062**				
		7–13	0.86	0.48	1.56	0.626	1.22	0.62	2.31	0.613
		≥ 14	0.65	0.36	1.16	0.151	1.05	0.53	2.09	0.892
Hand washing	After defecation	No	1.00							
		Yes	0.92	0.69	1.22	**0.562**				
	After work	No	1.00							
		Yes	1.22	0.94	1.59	**0.133**	1.02	0.75	1.38	0.921
	Before eating	No	1.00							
		Yes	1.29	0.92	1.83	**0.141**	1.25	0.86	1.82	0.253
Hand washing per week		< 4	1.00			**0.045**				
		4–7	0.87	0.63	1.19	0.383	0.91	0.64	1.28	0.582
		≥ 8	0.62	0.42	0.93	0.010	0.75	0.49	1.16	0.212
Use soap to wash your hand		No	1.00							
		Yes	0.96	0.70	1.31	**0.715**	0.91	0.65	1.33	0.711

(*Continued*)

Table 4. (*Continued*)

Intestinal parasitic infection		**Univariate logistic regression***				**Multivariate logistic regression****			
N = 915 / N(cases) = 530		**OR**	**95% CI**		**p-value**	**aOR**	**95% CI**		**p-value**
Deworming (month)	< 6	1.00			**0.991**				
	6–12	1.05	0.70	1.59	0.832				
	> 12	1.00	0.74	1.34	0.982				

§Parasitic infection include: *Ascaris lumbricoides*, *Trichuris trichiura*, hookworm, *Schistosoma mansoni*, and any intestinal protozoa.

*p-value and odds ratio (OR) based on likelihood ratio test of univariate logistic regression, overall p-value of the models are indicated in bold letters.

** p-value and adjusted

(a) OR based on likelihood ratio test of the multivariate regression model. The multivariate model was defined including exposure groups, sex, age, educational attainment, socioeconomic status, and number of people per household. In addition, all risk factors that had a p-value lower than 0.2 in the univariate analyses were included into the multivariate regression analysis (as indicated in the table).

*** exposure groups: *com* $_{exposed}$, slum dwellers at risk of flooding along the Nakivubo wetland; *com* $_{comparison}$, slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *farmer*, urban farmers reusing wastewater within the Nakivubo wetland; *worker* $_{ww}$, workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; *worker* $_{fs}$, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

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regardless of the parasite species for urban farmers compared to other population groups (adjusted OR between 1.6 and 12.9).

The high hookworm and *S. mansoni* prevalence in urban farmers are in line with previous reports from other studies in Africa and elsewhere in the tropics [12,13,15,41]. In addition to this already established relationship, we could show that there are considerable differences in prevalence of specific intestinal parasites between the five exposure groups. Hence, the comparison between farming and non-farming household, which has been done in previous studies, may not be sufficient to understand the occurrence of intestinal parasite infection in an urban context. Our results suggest that it is important to also take into account different occupational and non-occupational exposure groups along wastewater and fecal sludge management and use systems [19,20]. The high prevalence of hookworm in urban farmers can be explained, at least partially, with concentration of hookworm eggs (2.0 eggs/l) found in water around the Nakivubo wetland. However, low concentration of *A. lumbricoides* (0.2 eggs/l) and the absence of *T. trichiura* eggs do not correlate with the respective prevalence in the exposure groups [26]. Comparing our results with model-based prevalence predictions, we found significantly lower prevalence of soil-transmitted helminths and *S. mansoni* in slum dwellers. However, prevalence obtained in farmers match the model-based predictions for soil-transmitted helminths and *S. mansoni* and are even exceeding predicted values up to a factor five for *T. trichiura* and *A. lumbricoides* [27,28]. Hence, our findings corroborate the concept that model-based prediction for urban areas should account for environmental factors (e.g., altitude), occupation, and socioeconomic status [3]. The overall prevalence of *E. histolytica/E. dispar* and *G. intestinalis* among all study participants was considerably lower than in a study of rural communities along Lake Victoria[30]. Multivariate regression analyses revealed lower odds for participants who went to school and attained at least primary level. Altogether, and in contrast to recent risk assessments by means of quantitative microbial risk assessment [33], our results showed that helminth and intestinal protozoa infections are relevant and important factors to consider for further risk assessments and burden estimates.

Our study has five main limitations. First, due to its cross-sectional design, this study only reflects one point in time, i.e., the rainy season, and thus, we may underestimate seasonal patterns of intestinal parasite infections and other diseases that may give rise to diarrhea such as seasonal outbreaks of cholera and typhoid [42–44]. Second, a single stool sample was examined. The reported point-prevalence of helminth and intestinal protozoa infections are thus underestimated [45]. In order to increase the sensitivity and deepen our understanding of the diversity of pathogenic organisms, other methods (e.g., polymerase chain reaction or metagenomics) need to be considered in future investigations [46]. Third, due to the relatively low number of workers included, the observed OR between intestinal parasitic infection and exposure variables for workers have to be interpreted with caution. Fourth, it has been shown that self-reported disease outcomes are prone to reporting bias. Hence, longitudinal monitoring of diarrhea incidence is warranted to get a more comprehensive understanding [37]. Fifth, it is widely acknowledged that school-aged children are at highest risk of soil-transmitted helminths and intestinal protozoa infection, hence, there is a need to further investigate school-aged children in this settings [47].

Despite these limitations, our findings raise a number of important issues. First, urban farmers, living within marginalized slum communities, appear to be most exposed and vulnerable for intestinal parasites and might contribute to their transmission in urban environments. Second, we did not find any significant positive association between current deworming practices and intestinal parasitic infection. However, our findings with hookworm and *S. mansoni* prevalence rates in excess of 20% in urban farmers call for preventive chemotherapy, at least in this population group. Third, we observed differences between self-reported signs and symptoms and actual prevalence of intestinal parasitic infections measured in the different exposure groups, and hence other factors (e.g., toxic chemicals, pantothenic viruses, and bacteria) might have considerable implications in these exposure groups.

Taken together, our results show that urban farmers are especially vulnerable and may play an important role in the transmission of soil-transmitted helminths and *S. mansoni*, most likely through contamination of their living and working environment. We recommend longitudinal monitoring of parasitic infections and diarrhea alongside with targeted interventions in exposed population groups. Altogether, this calls for increased public health protection measures for urban farmers and marginalized communities and integrated sanitation safety planning at city level.

Supporting Information

S1 Checklist. CONSORT checklist.
(DOCX)

S2 Checklist. STROBE checklist.
(DOC)

S1 Table. Water, sanitation, and hygiene (WASH) specific risk factors and risk factors related to the occupation of workers and farmers.
(DOCX)

S2 Table. Univariate and multivariate regression models determining association between health outcomes of interest and risk/confounding factors.
(DOCX)

S1 Protocol. Study protocol.
(DOCX)

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Disclaimer

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Author Contributions

Conceived and designed the experiments: SF MSW NBK EMT AAH ER KM CS JU GC. Performed the experiments: SF NBK AAH. Analyzed the data: SF CS. Contributed reagents/materials/analysis tools: SF NBK EMT AAH ER. Wrote the paper: SF MSW NBK EMT AAH ER KM CS JU GC.

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8. ARTICLE 4: Disease burden due to gastrointestinal pathogens in wastewater along the major wastewater system in Kampala, Uganda

Photo: Children playing along the Nakivubo channel in Kampala, Uganda (©S. Fuhrimann, 2013)

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Disease burden due to gastrointestinal pathogens in a wastewater system in Kampala, Uganda

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ABSTRACT

In wastewater systems in Kampala, Uganda, microbial contamination has increased over the past two decades. Those people who live or work along the Nakivubo channel and wetland and those who use the recreational areas along the shores of Lake Victoria are at an elevated risk of gastrointestinal infections. A quantitative microbial risk assessment (QMRA) was applied for five population groups, characterised by different levels of exposure to wastewater in the Nakivubo area, namely: (i) slum dwellers at risk of flooding; (ii) children living in these slum settlements; (iii) workers maintaining the drainage system or managing faecal sludge (sanitation workers); (iv) urban farmers; and (v) swimmers in Lake Victoria. The QMRA was based on measured concentrations of *Escherichia coli*, *Salmonella* spp. and *Ascaris* spp. eggs in wastewater samples. Published ratios between measured organism and pathogenic strains of norovirus, rotavirus, *Campylobacter* spp., pathogenic *E. coli*, pathogenic *Salmonella* spp., *Cryptosporidium* spp. and *Ascaris lumbricoides* were used to estimate annual incidence of gastrointestinal illness and the resulting disease burden. The QMRA estimated a total of 59,493 disease episodes per year across all 18,204 exposed people and an annual disease burden of 304.3 disability-adjusted life years (DALYs). Incidence estimates of gastrointestinal disease episodes per year were highest for urban farmers (10.9) and children living in slum communities (8.3), whilst other exposed groups showed lower incidence (<4.3). Disease burden per person per year was highest in urban farmers (0.073 DALYs) followed by sanitation workers (0.040 DALYs) and children in slum communities (0.017 DALYs). Our findings suggest that the exposure to wastewater is associated with public health problems, particularly children and adults living and working along the major wastewater and reuse system in Kampala. Our findings call for specific interventions to reduce the disease burden due to exposure to wastewater.

1. Introduction

Urban wastewater is often contaminated with pathogenic organisms, and thus puts people at risk of ill-health (Blumenthal and Peasey, 2002; McBride et al., 2013; Barker, 2014). Untreated wastewater of domestic and industrial origins is of particular concern (Fuhrimann et al., 2015; WHO, 2015). It follows that in urban centres of low- and middle-income countries (LMICs), characterised by the lack of improved sanitation, high prevalence and outbreaks of gastrointestinal diseases caused by bacteria, viruses, intestinal protozoa or helminths are common (Matthys et al., 2007; Pham-Duc et al., 2014). However, there is a paucity of disease burden estimates caused by these pathogenic organisms in LMICs (Labite et al., 2010; Katukiza et al., 2013; Machdar et al., 2013).

Exposure to urban wastewater is multifaceted (Stenström et al., 2011; Keraita and Dávila, 2015). Direct exposure occurs through accidental ingestion, inhalation or dermal contact in different

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contexts: (i) during working procedures (e.g. while emptying on-site sanitation facilities, managing wastewater treatment processes or reusing wastewater for irrigation purposes); (ii) while using wastewater for domestic activities (e.g. for cleaning dishes or washing clothes); (iii) during flooding events caused by heavy rains (Cissé, 2013); and (iv) due to recreational activities (e.g. swimming or bathing in lakes or rivers fed by wastewater) (Ferrer et al., 2012; Katukiza et al., 2013; Yapo et al., 2013). Indirect exposure occurs through consumption of contaminated drinking water or wastewater-fed crops and fish (Machdar et al., 2013; Mok and Hamilton, 2014). Reducing exposures to wastewater is therefore a critical inter-sectoral responsibility for protecting public health (Amoah et al., 2011; Keraita and Dávila, 2015). Guidelines published by the World Health Organization (WHO) propose control measures to safely manage and reuse wastewater, excreta and greywater, and to protect recreational and drinking water systems (WHO, 2003, 2006, 2011a). These guidelines are built around the concept of health-based targets that are grounded on well-defined health metrics (e.g. disability-adjusted life years (DALYs)) and a level of tolerable health burden (Mara et al., 2010). Even though this health-based target was recently revised, allowing for a tolerable additional disease burden of 0.0001 DALYs per person per year (pppy), it is still out of reach in many LMICs (Ensink and van der Hoek, 2009; Mara et al., 2010; WHO, 2015).

Disease burden of pathogenic organisms can be estimated by quantitative microbial risk assessment (QMRA) (Haas et al., 2014; Ichida et al., 2015). QMRA commonly follows four working steps: (i) hazard identification; (ii) exposure assessment; (iii) dose-response assessment; and (vi) risk characterisation (Haas et al., 2014). For water-borne hazards, QMRA is widely used in industrialised countries to estimate health risks for drinking water supply systems (Hunter et al., 2000; WHO, 2011a), flood water events (de Man et al., 2014), wastewater management and reuse (Westrell et al., 2004; Ashbolt et al., 2006), storm water discharge (McBride et al., 2013) or recreational water (Soller et al., 2015). It is also widely used for food-borne hazards, based on principles and guidelines defined by Codex Alimentarius (Anonymous, 1995; Havelaar et al., 2008). In LMIC settings, QMRA is becoming increasingly popular and has been successfully applied for the identification of effective control measures for wastewater reuse in urban agriculture systems in Accra and Bangkok (Seidu et al., 2008; Ferrer et al., 2012; Barker et al., 2014) and for risk profiling along drainage channels in Abidjan and Kampala (Katukiza et al., 2013; Yapo et al., 2013). QMRA has also been used to guide cost-effective interventions for drinking water supply systems in Accra and Kampala (Howard et al., 2006; Machdar et al., 2013). It must be noted, however, that these QMRAs suffer from a lack of data on source contamination with pathogens, setting-specific dose-response relationships and validation of the estimated risks with epidemiological data (WHO, 2006; Barker et al., 2014).

To fill some of the aforementioned gaps, this paper presents a QMRA case study for Kampala, the capital of Uganda. Of note, Kampala has undergone rapid population growth and there are large volumes of wastewater in face of insufficiently equipped sanitary infrastructures (Fuhrimann et al., 2015). Microbial and chemical contamination has increased over the past two decades along the major wastewater system (Kansiime and Nalubega, 1999; Kayima et al., 2008; Fuhrimann et al., 2015). For example, concentrations of *Escherichia coli* in wastewater samples are exceeding WHO thresholds of 10^3–10^4 colony forming units (CFU) *E. coli*/100 mL by magnitude of at least 10 (Fuhrimann et al., 2015). Hence, these waters should not be reused without considering additional control measures (WHO, 2006). The mean concentration of *Ascaris lumbricoides* eggs in wastewater and soil samples in slum community areas were above WHO safety standards of $\leq$1 egg/L (WHO, 2006; Fuhrimann et al., 2015). Using a QMRA approach, the goal of the present study was to estimate the disease burden resulting from exposure to water-borne pathogens causing gastroenteritis along the major wastewater system in Kampala. By comparing the model estimates with findings from epidemiological surveys, advantages and limitations of the QMRA methodology are discussed.

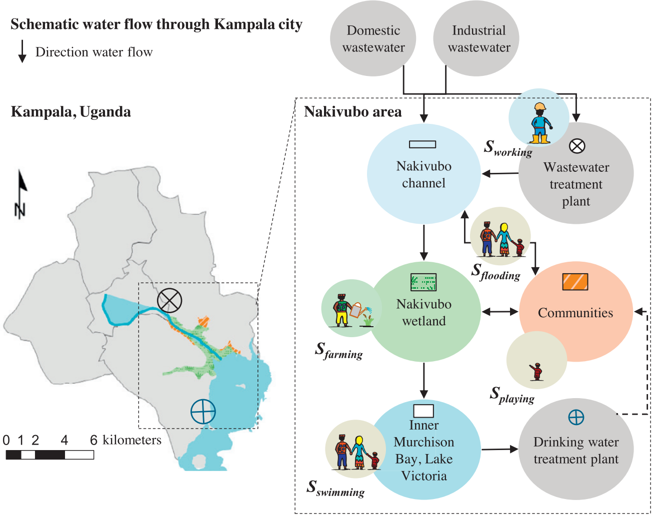

Fig. 1. Schematic flow of Kampala's main wastewater system along the Nakivubo channel, Nakivubo wetland and Lake Victoria with indication of the five exposure scenarios ($S_{flooding}$, $S_{working}$, $S_{farming}$, $S_{playing}$ and $S_{swimming}$).

2. Materials and methods

2.1. Study area

Detailed information and a short video introducing the study area and the sampling scheme have been published elsewhere (Fuhrimann et al., 2014). In brief, Kampala is located at latitude 0° 18′ 49.18″ N and longitude 32° 36′ 43.86″ E at an altitude of 1140 m above the mean sea level. The study area includes the Nakivubo channel in Kampala city (Fig. 1), which is an open storm water channel transporting most of the city's wastewater from the central division (approximately 13,928 m^3/day), comprised of wastewater from households (23%) and industries (77%). Further, the channel receives partially treated effluent from the Bugolobi Sewage Treatment Works (BSTW) (up to 12,000 m^3/day) (Beller Consult et al., 2004). Downstream of the treatment plant, the wastewater enters into the Nakivubo wetland, where it is reused for urban agriculture (main crops: sugar cane, yams and maize). Alongside the Nakivubo wetland, there are informal slum communities prone to flooding events (Fuhrimann et al., 2016). The water is finally discharged into the Inner Murchison Bay in Lake Victoria, a popular recreational area for Kampala's inhabitants, especially along its shores. In addition, only 4 km away from the discharge point, the lake water is pumped and treated to supply Kampala with drinking water (Howard et al., 2006).

2.2. Hazard identification

The hazards considered for the QMRA are seven pathogenic organisms, for which the incidence and disease burden of gastroenteritis due to exposure to wastewater are estimated: two viruses (norovirus and rotavirus), three bacteria (*Campylobacter* spp., pathogenic *Salmonella* spp. and *E. coli*), one intestinal protozoon (*Cryptosporidium* spp.) and one soil-transmitted helminth species (*A. lumbricoides*). All of these pathogens are characterised by the faecal-oral transmission route, can persist for weeks or months in the environment and are difficult to inactivate with conventional wastewater treatment processes (WHO, 2006; Machdar et al., 2013; Fuhrimann et al., 2015).

Hazard selection was motivated by findings from an environmental assessment and a cross-sectional survey conducted in the study area between October and December 2013 during the short rainy season (Fuhrimann et al., 2015, 2016), along with previous studies about major pathogens giving rise to gastroenteritis in Uganda and elsewhere in the world (Becker et al., 2013; Katukiza et al., 2013; Barker et al., 2014; Gibney et al., 2014). Our selection is further justified on the following grounds:

- Rotavirus is one of the leading causes of childhood diarrhoea, responsible for about 7.3% of deaths among children below the age of 5 years in Uganda and is considered to account for most of the disease burden in slums in Kampala (Katukiza et al., 2013; Sigei et al., 2015).
- Norovirus is the major cause of diarrhoeal disease in adults and its secondary attack rate is known to be high causing epidemic situations, especially in densely populated slum areas (Teunis et al., 2008; Katukiza et al., 2013).
- *Campylobacter* spp. are zoonotic bacteria that cause campylobacteriosis, with *Campylobacter jejuni* being a common cause of diarrhoea in LMICs (Kaakoush et al., 2015).
- *E. coli* bacteria are part of the normal gastrointestinal microflora of warm-blooded animals and humans, whilst enterohemorrhagic *E. coli* (EHEC) is considered pathogenic, with the serotype *E. coli* O157:H7 responsible for the largest public health impact (Okeke, 2009; Hynds et al., 2014).
- *Salmonella* spp. have more than 2000 sero-groups, with only a few being of concern for human health (*S. typhi* and *S. paratyphi* A, B and C, and the enteric salmonella strains) (Kariuki et al., 2015).
- *Cryptosporidium* spp. is a zoonotic intestinal protozoon that can result in severe health implications in children and immunocompromised individuals e.g. for HIV-positive people. As the HIV prevalence in Uganda is estimated to be 7.4% – the 10th highest in the world –, *Cryptosporidium* spp. are likely to be of higher public health relevance than, for example, other intestinal protozoa such as *Giardia intestinalis* and *Entamoeba histolytica* (Kaijuka et al., 2011).
- Helminth infections are endemic in the Great Lake region (Karagiannis-Voules et al., 2015; Lai et al., 2015). Prevalence rates for hookworm, *Trichuris trichiura, Schistosoma mansoni* and *A. lumbricoides* in urban farmers in the Nakivubo area were found at 28%, 26%, 23% and 18%, respectively (Fuhrimann et al., 2015). For the current QMRA, the commonly used reference organism *A. lumbricoides* is considered as its eggs are known to persist in the environment longer than any of the other helminth species (Stott et al., 2003).

2.3. Exposure assessment

The exposure scenarios for the QMRA are based on information derived from a survey of 915 people in the Nakivubo area. The findings of this survey have been reported elsewhere (Fuhrimann et al., 2015). Overall, the QMRA only included accidental ingestion of contaminated water and the following exposure pathways were excluded based on the given context: (i) ingestion of contaminated soil, dermal contact, inhalation and drinking of potentially contaminated water (due to lack of data); (ii) consumption of contaminated food crops (not in direct contact with wastewater (sugar cane and maize) or sufficiently cooked (yams)); and (iii) exposure to contaminated water used for bathing or washing clothes (uncommon local practice).

Five exposure scenarios in four study areas (Nakivubo channel, Nakivubo wetland, community areas and shores of Lake Victoria) were developed and assumptions about exposure groups, number of people exposed, exposure frequency and volume of ingested water are made (Fig. 2).

- **Scenario 1 ($S_{flooding}$):** Slum dwellers (all age groups) living in close proximity to the Nakivubo wetland are located on low altitude and, hence, were prone to flooding events. Almost half (47%) of the people living in these communities reported having been exposed to flooding events in the previous year (i.e. 5640 out of 12,000 people) (Fuhrimann et al., 2016). According to Lwasa and colleagues (2010), six flooding events may occur during the two rainy seasons (March to May and September to November) in one year. During a flooding event, ingestion of water due to unintentional immersion is assumed to be between 10 and 30 mL (Katukiza et al., 2013).
- **Scenario 2 ($S_{working}$):** There are 231 registered sanitation workers. 90 workers are employed by the National Water and Sewerage Corporation (NWSC) and responsible for the maintenance of the drainage system and the operation of the BSTW. Those working for the Pit Emptier Association (PEA) ($n = 141$), are responsible for emptying of on-site toilet facilities and transfer of the faecal sludge to BSTW (Fuhrimann et al., 2016). Their working practices expose workers to wastewater and faecal sludge (Stenström et al., 2011). On average, workers report 312 days on duty per year, with 70% of the workers regularly wearing boots and gloves. An accidental ingestion between 1 and 5 mL per working day is assumed (10-times less compared to workers without protective equipment) (WHO, 2006; Labite et al., 2010; Mara and Bos, 2010).
- **Scenario 3 ($S_{farming}$):** The farming areas in the Nakivubo wetland are frequently flooded with polluted water from Nakivubo channel, combined with effluent from BSTW, and the area bordering Lake Victoria is defined as floating wetland (Kansiime and Nalubega, 1999). Thus, the likelihood of accidental ingestion of wastewater is considerable. Overall, approximately 650 urban farmers (>15 years of age) reported working within the Nakivubo wetland. On average, farmers reported to work 297 days per year and only 3% of them regularly wear boots and gloves (Fuhrimann et al., 2016). An accidental ingestion between 10 and 50 mL per working day is assumed (WHO, 2006; Labite et al., 2010; Mara and Bos, 2010).
- **Scenario 4 ($S_{playing}$):** Children living in slum communities are at an elevated risk of daily accidental ingestion of water (Katukiza et al., 2010). Due to flooding events and poor sanitation infrastructures, slum environments are constantly contaminated (Fuhrimann et al., 2016) and children aged <15 years are considered at risk when playing (49.4%, 5,880 children out of 12,000 people) (UBOS, 2013). Exposure is assumed to be daily (365 days per year) with an accidental ingestion rate between 1 and 5 mL per day (Labite et al., 2010; Katukiza et al., 2013).
- **Scenario 5 ($S_{swimming}$):** Several studies found adverse health outcomes associated with exposure to contaminated recreational water (WHO, 2003; Schets et al., 2011; Yapo et al., 2013). In Kampala, swimming at the local beaches along the Inner Murchison Bay (e.g. Miami Beach, Ggaba Beach, KK Beach) is popular (Beller Consult et al., 2004). However, in our previous study, only three out of 915 individuals interviewed (0.32%) reported to have swum in Lake Victoria in the year preceding the survey (Fuhrimann et al., 2016). This is likely to be an underestimate as only people from lower socioeconomic strata were included in the survey and may not be able to access the private beaches. Still, when extrapolating this to the 1.8 million inhabitants of Kampala, 5760 people can be estimated to be swimming in the Inner Murchison Bay of Lake Victoria. It is assumed

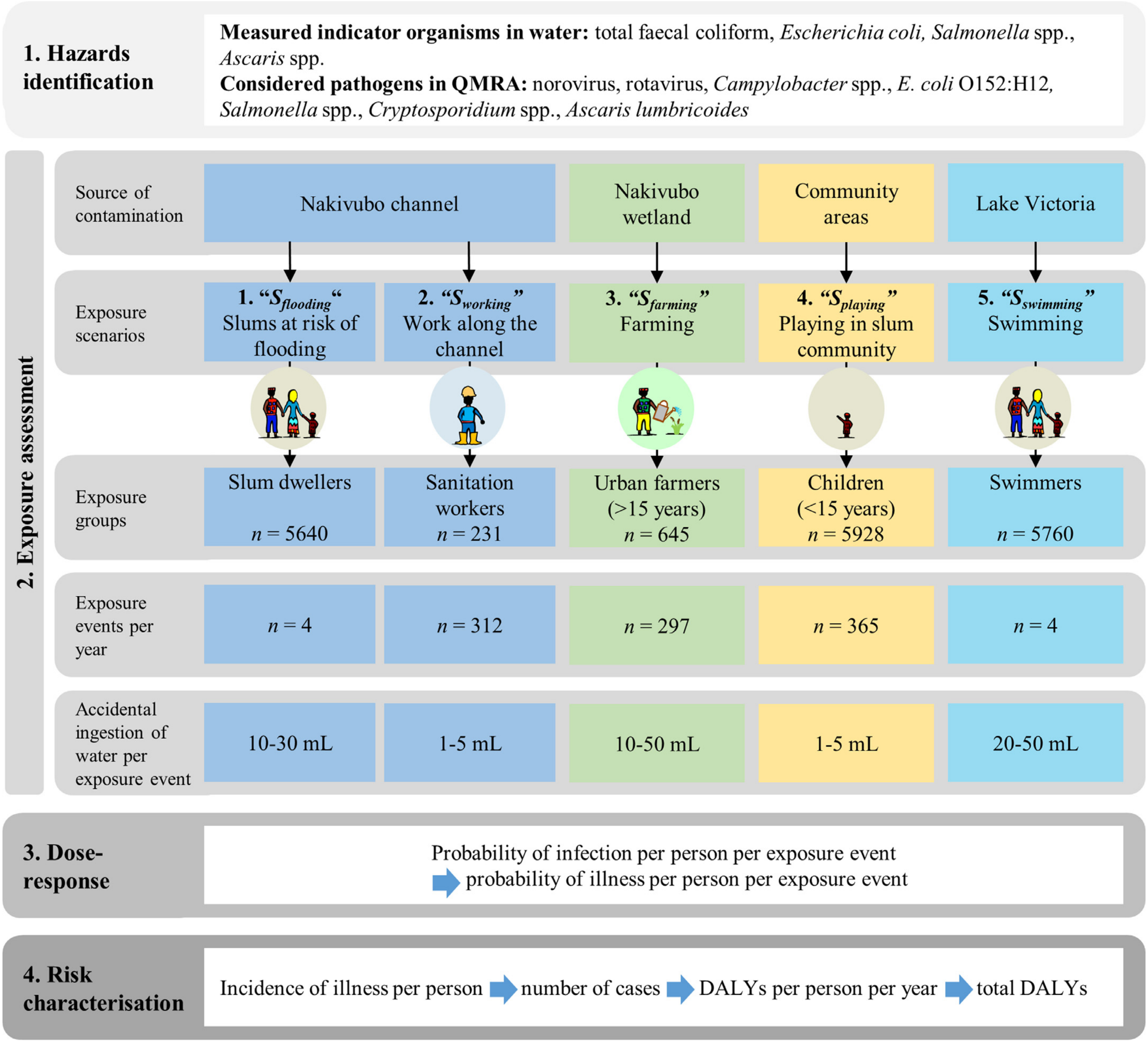

Fig. 2. Exposure scenarios ($S_{flooding}$, $S_{working}$, $S_{farming}$, $S_{playing}$ and $S_{swimming}$) considered in the quantitative microbial risk assessment (QMRA) to estimate the burden of *Campylobacter* spp., *Escherichia coli* O157:H7, *Salmonella* spp., norovirus, rotavirus, *Cryptosporidium* spp. and *Ascaris lumbricoides* along the major wastewater system in Kampala.

these people swim six times per year in the Lake, ingesting 20 to 50 mL per swimming event (WHO, 2003; Schets et al., 2011; Fuhrimann et al., 2016).

2.4. Measurements of pathogenic organisms along the wastewater system

Between October and December 2013, wastewater samples were collected at 23 sentinel sites along the Nakivubo channel (five points) and wetland (12 points), community areas bordering the Nakivubo wetland (two points) and within the Inner Murchison Bay in Lake Victoria (four points). The samples were tested for *E. coli*, thermotolerant coliforms (TTC), *Salmonella* spp. and helminth eggs. Details of the methodology and sampling strategy, including measurements of heavy metals and physicochemical parameters, have been published elsewhere (Fuhrimann et al., 2015). According to guidance documents put forth by WHO, the ratio between measured *E. coli* and the pathogens (p_{path}) can be simplified and therefore assumed to vary between 10^{-6}–10^{-5} (rotavirus, norovirus and *Campylobacter* spp.) and 10^{-7}–10^{-6} (*Cryptosporidium* spp.) (Haas et al., 1999). The ratio between pathogenic and non-pathogenic strains of *E. coli* (p_{path}) was set to vary between 7.6×10^{-4} and 1×10^{-2} (Shere et al., 2002; Soller et al., 2010; Hynds et al., 2014). In the absence of data, the same ratio was assumed for *Salmonella*. For *Ascaris* spp. it was assumed that each egg detected represents *A. lumbricoides* ($p_{\text{path}} = 1$, not considering the occurrence of other species such as *A. suum*) (Mara and Sleigh, 2010).

2.5. QMRA structure, implementation and analysis

2.5.1. QMRA structure

In most points, our QMRA approach follows the descriptions of the WHO 2006 guidelines and Karavarsamis and Hamilton (WHO, 2006; Karavarsamis and Hamilton, 2010; Mara et al., 2010).

However, we purposely do not adopt the entire approach, because we do not aim to study the overall infection risk but the disease burden, which needs estimates of the number of cases for each of the hazards separately. Hence, in addition, three adjustments were made. First, we used quantitative data on *E. coli*, *Salmonella* spp. and *Ascaris* spp. eggs obtained in the research area and fitted them to log-normal distribution, while prevalence estimates were used for *Ascaris* eggs (Fuhrimann et al., 2015). Second, our QMRA allows people to get ill from more than one hazard at the same time and the mean risk of illness was calculated over the duration of one year for each person, while assuming that each individual can become infected with each exposure event (without considering immunity) (Haas et al., 2014). Third, the corresponding disease burden for each of the seven selected pathogens was calculated according to published probability estimates for mild, moderate, severe and fatal gastroenteritis (Havelaar et al., 2000; Brooker, 2010; Katukiza et al., 2013; Gibney et al., 2014). Note that probability estimates for the severity grade were taken from other countries than Uganda, as no local estimates exist. Burden estimates for mild, moderate and severe diarrhoea episodes were taken from the Global Burden of Disease Study 2010 (Salomon et al., 2012). Mortality was calculated according to the average life expectancy at birth in Uganda of 54.20 years from 2008 (World Bank, 2016). Finally, sequelae such as Guillain–Barré syndrome, reactive arthritis or irritable bowel syndrome are not considered in the model.

2.5.2. QMRA implementation and analysis

As summarised in Table 1, spatial and temporal variability of the number of CFU of *E. coli*, *Salmonella* spp. and number of eggs of *Ascaris* spp. were measured from October to December 2013 during the short rainy season at 23 sampling points over the four study areas. For *E. coli* and *Salmonella* spp., we fitted normal distributions to the log-transformed enumeration data on concentration in the water (C_{water}), using a maximum likelihood estimation (MLE) method, allowing inclusion of censored data and accounting for the abundance, while considering the measured prevalence of the indicator bacteria in the water along the four systems (Lorimer and Kiermeier, 2007), in Excel 2013 (Microsoft Corporation, Redmond; WA, USA). As a result, the data fitting provided estimates for the true prevalence of contaminated water samples, and the distribution of concentrations in these contaminated samples. For *Ascaris* spp. eggs, this approach was not possible as only four out of 168 (excluding Lake Victoria) samples were positive. Hence, with a value of 0.024, a positive count is expected, between 1 and 100 eggs/L, which is included with uniform distribution on a log-scale (Fuhrimann et al., 2015). Project evaluation and review techniques (PERT) distributions are fitted to minimum, most likely and maximum ratio of pathogen concentration per *E. coli* (p_{path}) for rotavirus, norovirus, *Campylobacter* spp. and *Cryptosporidium* spp. Uniform distribution were fitted to *E. coli* and *Salmonella* spp. ratio of pathogen concentration per measured *E. coli* and *Salmonella* spp. (WHO, 2006; Katukiza et al., 2013). This is implemented in the model by assuming that a fraction p_{path} of the ingested volumes of water consists of a pathogenic strain of the bacterial species. PERT distributions are also fitted to assumed minimum, most likely and maximum ingestion rates (volume (V) in mL water) per exposure event. In a Monte Carlo simulation, values are sampled for these three variables and the ingested amount of pathogens (dose; d) is calculated as:

$$d = C_{water} \times \ p_{path} \times \ V \tag{1}$$

The variation in C_{water} is implemented as variability per exposure event, the variation in p_{path} and V is implemented as variability per person (i.e. for practical reasons it had the same value for all exposure events for one person in one iteration of the Monte Carlo simulation). As ingested bacteria are discrete units, assumed to be homogeneously distributed in the water, ingested doses are assumed to be Poisson distributed (d ~Poisson (d) as e.g. in (Nauta et al., 2012).

Doses (d) are used as input in the dose-response relations to obtain the probability of illness $P_I(d)$ (Eqs. (1)–(3)). Monte Carlo simulations are performed for 100,000 iterations using @Risk, version 6 (Palisade Corporation; Newfield, NY, USA), where one iteration simulates all the n exposure events and associated $P_{ill}(d)$ of one person in a year. Based on this, the expected frequency of illness for this person per year (which, in our approach, can be more than one) can be calculated as the sum of the n values of $P_{ill}(d)$ obtained. Model outputs are presented as number of cases per year, DALYs pppy and total DALYs per year (see Eqs. (6), (9) and (10)).

2.6. Dose-response models

Well-established dose-response models for the various pathogens were used to determine the relationship between quantity of exposure (i.e. number of organism ingested) and the effective health outcome (i.e. infection and illness) (Haas et al., 2014). For the QMRA, the simplified Beta-Poisson dose-response models for rotavirus, *Campylobacter* spp., *E. coli* O157:H7, pathogenic *Salmonella* spp. and *A. lumbricoides* were employed (Teunis and Havelaar, 2000; McBride et al., 2013; Haas et al., 2014), as defined as

$$P_I(d) = 1 - \left[1 + \left(\frac{d}{\beta}\right)\right]^{-\alpha} \tag{2}$$

with a median infectious dose defined as

$$N_{50} = \beta\left(2^{1/\alpha} - 1\right) \tag{3}$$

For norovirus, a hypergeometric function is presented by Teunis et al. (2008), which is fit to run with the @Risk software, version 6 (Palisade Corporation; Newfield, NY, USA) and to include the uncertainty about the dose-response. We used an approximation for the mean probability of infection (Haas, 2002) of the Beta-Poisson dose-response model:

$$P_I(d) = 1 - \frac{\Gamma(\alpha+\beta)\Gamma(\mathrm{d}+\beta)}{\Gamma(\alpha+\beta+d)\Gamma(\beta)} \tag{4}$$

where Γ(.) represents Eulers gamma function. For *Cryptosporidium* spp., an exponential model was used (Westrell et al., 2004; de Man et al., 2014; McBride et al., 2013):

$$P_I(d) = 1 - (1 - r)^d \tag{5}$$

In brief, $P_I(d)$ represents the probability of infection, d is a single dose of the pathogen, whereas the pathogen infectivity constants α, β and r characterise the dose-response relationship. To account for the proportion of infections that turn into symptomatic gastroenteritis cases ($P_{ill}(d)$), we used for each pathogen a constant value (λ) (i.e. illness to infection ratio):

$$P_{ill}(d) = P_I(d) \times \lambda \tag{6}$$

Table 1 provides the parameter values used in the QMRA for each pathogen. Moreover, for $P_{ill}(d)$ we use the probability of a symptomatic gastroenteritis for each of the seven pathogens (or hazards) h, $P_{ill,h}(d_i)$, which is a function of the ingested dose d_i at exposure event i (Haas et al., 2014).

2.7. Risk characterisation

2.7.1. Incidence: the number of cases per year

Our model assumed that each exposure event i is independent and that there is no immunity after a previous infection (no dose-response available for the context of LMICs and, hence, it is not possible to include immunity status of exposed population groups

Table 1
QMRA model parameter, distributions and assumptions.

Description	Units	Distribution and/or values	Reference(s)
(C_{water}) Concentrations: water Nakivubo channel			Fuhrimann et al., 2015
Escherichia coli	$\log_{10}$ (CFU/100 mL)	Normal(6.0;1.1)[a]; prevalence = 1	
Salmonella spp.	$\log_{10}$ (CFU/100 mL)	Normal(2.7;0.8)[a]; prevalence = 1	
Ascaris spp.	$\log_{10}$ Eggs/1 L	Uniform(0;2)[b]; prevalence = 0.024	
(C_{water}) Concentrations: water Nakivubo wetland			
E. coli	$\log_{10}$ (CFU/100 mL)	Normal(5.0;1.5)[a]; prevalence = 1	
Salmonella spp.	$\log_{10}$ (CFU/100 mL)	Normal(2.1;1.3)[a]; prevalence = 0.95	
Ascaris spp.	$\log_{10}$ Eggs/1 L	Uniform(0;2)[b]; prevalence = 0.024	
(C_{water}) Concentrations: water community areas			
E. coli	$\log_{10}$ (CFU/100 mL)	Normal(5.9;1.4)[a]; prevalence = 1	
Salmonella spp.	$\log_{10}$ (CFU/100 mL)	Normal(2.1;1.3)[a]; prevalence = 1	
Ascaris spp.	$\log_{10}$ Eggs/1 L	Uniform(0;2)[b]; prevalence = 0.024	
(C_{water}) Concentrations: water Lake Victoria			
E. coli	$\log_{10}$ (CFU/100 mL)	Normal(1.8;3.0)[a]; prevalence = 0.69	
Salmonella spp.	$\log_{10}$ (CFU/100 mL)	Normal(0.6;2.0)[a]; prevalence = 0.50	
Ascaris spp.	$\log_{10}$ Eggs/1 L	Uniform(0;2)[b]; prevalence = 0.024	
(p_{path}) Ratio between indicator and pathogenic organisms			
A. lumbricoides to *Ascaris* spp.		Point estimate: $p_{path} = 1$	Mara et al., 2010
Campylobacter spp. to *E. coli*		PERT(0.1;0.55;1)[c] per 10^5 *E. coli*	WHO, 2006
Cryptosporidium spp. to *E. coli*		PERT(0.01;0.055;0.1)[c] per 10^5 *E. coli*	WHO, 2006
Pathogenic *E. coli:* O157:H7 to *E. coli*		Uniform (7.6×10^{-4};1×10^{-2})[b]	Shere et al., 2002; Soller et al., 2010; Hynds et al., 2014
Norovirus to *E. coli*		PERT(0.1;0.55;1)[c] per 10^5 *E. coli*	WHO, 2006
Rotavirus to *E. coli*		PERT(0.1;0.55;1)[c] per 10^5 *E. coli*	Katukiza et al., 2013
Pathogenic *Salmonella* to *Salmonella* spp.		Uniform (7.6×10^{-4};1×10^{-2})[b]	Shere et al., 2002; Soller et al., 2010; Hynds et al., 2014
(V) Volume ingested per exposure event for each scenario			
$S_{flooding}$	mL	PERT(10;20;30)[c]	Katukiza et al., 2013
$S_{working}$	mL	PERT(1;3;5)[c]	WHO, 2006; Labite et al., 2010
$S_{farming}$	mL	PERT(10;35;50)[c]	WHO, 2006; Labite et al., 2010
$S_{playing}$	mL	PERT(1;3;5)[c]	Katukiza et al., 2013
$S_{swimming}$	mL	PERT(20;35;50)[c]	Schets et al., 2011; Yapo et al., 2013
Dose-response models			
A. lumbricoides		Point estimate: α = 0.0104; N_{50} = 859	Mara et al., 2010
Campylobacter spp.		Point estimate: α = 0.145; N_{50} = 896	Medema et al., 1996
Cryptosporidium spp.		Point estimate: r = 0.0042	Haas et al., 1999
E. coli O157:H7		Point estimate: α = 0.49; N_{50} = 596,000	Teunis et al., 2008
Norovirus		Point estimate: α = 0.04; β = 0.055;	Teunis et al., 2008
Rotavirus		Point estimate: α = 0.253; N_{50} = 6	Teunis and Havelaar, 2000
Pathogenic *Salmonella* spp.		Point estimate: α = 0.3126; N_{50} = 23,600	Haas et al., 1999
(λ) Illness to infection ratio			
A. lumbricoides		Point estimate: 0.39	Mara et al., 2010
Campylobacter jejuni		Point estimate: 0.3	Machdar et al., 2013
Cryptosporidium		Point estimate: 0.79	Machdar et al., 2013
Pathogenic E. coli		Point estimate: 0.35	Machdar et al., 2013
Norovirus		Point estimate: eta = 0.00255; r = 0.086	Teunis et al., 2008
Rotavirus		Point estimate: 0.5	Barker et al., 2014
Pathogenic *Salmonella* spp.		Point estimate: 1	McBride et al., 2013
(n) number of exposure events per year			Fuhrimann et al., 2016; UBOS, 2013
$S_{flooding}$		Point estimate: 6	
$S_{working}$		Point estimate: 312	
$S_{farming}$		Point estimate: 297	
$S_{playing}$		Point estimate: 365	
$S_{swimming}$		Point estimate: 6	
(Pop_E) population at risk per exposure scenario			Fuhrimann et al., 2016
$S_{flooding}$	People at risk of flooding	Point estimate: 5640	
$S_{working}$	Workers	Point estimate: 231	
$S_{farming}$	Urban farmers	Point estimate: 645	
$S_{playing}$	Children in slum communities	Point estimate: 5928	
$S_{swimming}$	People swimming in Lake Victoria	Point estimate: 5760	
($DALY_h$) disease burden per pathogenic organisms (disability-adjusted life years (DALYs) calculation is indicated in Table 2)			
A. lumbricoides	DALYs/case	Point estimate: 0.0029	
Campylobacter spp.	DALYs/case	Point estimate: 0.0053	
Cryptosporidium spp.	DALYs/case	Point estimate: 0.0022	
Pathogenic *E. coli*	DALYs/case	Point estimate: 0.0013	
Norovirus	DALYs/case	Point estimate: 0.0008	
Rotavirus	DALYs/case	Point estimate: 0.0032	
Pathogenic *Salmonella* spp.	DALYs/case	Point estimate: 0.0719	

[a] Normal distribution (mean; standard deviation).
[b] Uniform distribution (min; max).
[c] Project evaluation and review techniques (PERT) (min; most likely; max).

Table 2
Disease burden due to gastroenteritis expressed in disability-adjusted life years (DALYs) calculated by means of severity (mild, moderate, severe and fatality), probability, and duration of the respective severity grade per pathogen.

Gastroenteritis		Severity weights					Reference(s)
		Mild	Moderate	Severe	Fatal	Total DALYs	
DALYs per severity grade of gastroenteritis		0.06	0.20	0.28	1.00		Salomon et al., 2012
Norovirus	Probability	0.92	0.07	0.01	7.80×10^{-6}		Gibney et al., 2014
	Duration (days)	2.10	2.40	7.20	-		
	Duration (years)	0.01	0.01	0.02	54.20[a]		
	DALYs	3.24×10^{-4}	9.56×10^{-5}	3.33×10^{-5}	4.23×10^{-4}	8.75×10^{-4}	
Rotavirus	Probability	0.85	0.10	0.05	3.37×10^{-5}		Gibney et al., 2014
	Duration (days)	4.90	7.10	7.70	-		
	Duration (years)	0.01	0.02	0.02	54.20[a]		
	DALYs	6.94×10^{-4}	4.01×10^{-4}	2.96×10^{-4}	1.83×10^{-3}	3.22×10^{-3}	
Cryptosporidium spp.	Probability	0.86	0.12	0.02	-		Gibney et al., 2014
	Duration (days)	5.00	15.00	33.00	-		
	Duration (years)	0.01	0.04	0.09	-		
	DALYs	7.19×10^{-4}	1.02×10^{-3}	4.32×10^{-4}	-	2.17×10^{-3}	
Campylobacter spp.	Probability	0.80	0.18	0.02	6.72×10^{-5}		Havelaar et al., 2000
	Duration (days)	3.50	9.70	14.40	-		Gibney et al., 2014
	Duration (years)	0.01	0.03	0.04	54.20[a]		
	DALYs	4.70×10^{-4}	9.72×10^{-4}	1.77×10^{-4}	3.64×10^{-3}	5.26×10^{-3}	
Pathogenic *Salmonella* spp.	Probability	0.21	0.66	0.14	1.26×10^{-3}		Gibney et al., 2014
	Duration (days)	2.50	6.00	12.00	-		
	Duration (years)	0.01	0.02	0.03	54.20[a]		
	DALYs	8.61×10^{-5}	2.18×10^{-3}	1.27×10^{-3}	6.85×10^{-2}	7.20×10^{-2}	
Pathogenic *Escherichia coli*	Probability	0.94	0.06	0.09	2.00×10^{-4}		Katukiza et al., 2013
	Duration (days)	5.60	10.70	16.20	1.00		
	Duration (years)	0.02	0.03	0.04	54.20[a]		
	DALYs	8.80×10^{-4}	3.55×10^{-4}	1.12×10^{-3}	1.08×10^{-2}	1.13×10^{-2}	
Ascaris lumbricoides	Probability	0.95	0.05	-	-		Brooker, 2010
	Duration (days)	35.0	28.0	-	-		
	Duration (years)	0.05	0.01	-	-		
	DALYs	2.90×10^{-3}	1.83×10^{-5}	-	-	2.92×10^{-3}	

[a] Average life expectancy at birth in Uganda from 2008 (World Bank, 2016).

in this model). For an average of n_h exposures to the hazard per person per year, with population size Pop_E, the expected number of cases in the population is:

$$Cases_h = \sum_{i=1}^{n_h \times Pop_E} P_{ill,\ h}(d_i) \tag{7}$$

The incidence estimate for pathogen h is:

$$Inc_h = \frac{Cases_h}{Pop_E} \tag{8}$$

The combined incidence estimate, Inc_{comb} (episodes of gastroenteritis per year), for all seven pathogens h is defined as:

$$Inc_{comb} = \sum_{all\ h} \frac{Cases_h}{Pop_E} \tag{9}$$

2.7.2. Estimation of disease burden

The disease burden was expressed by the DALY metric. This metric combines morbidity (years lived with disability) and premature death (years of life lost) (Murray et al., 2012). For each pathogen h, DALY per case of gastrointestinal illness (DALY_h) was estimated as the sum of the product of the probability of developing disease symptom j (i.e. $j =$ mild, moderate and severe diarrhoea or death) given a case of gastroenteritis, relative frequency of the symptom (f_j), duration of the developed symptom in years (D_j) and the respective severity factor (Sj) (Table 2) (Salomon et al., 2012):

$$\text{DALY}_h = \sum_j \left(f_j \times D_j \ \times \ S_j \right) \tag{10}$$

The total disease burden ($Total_{\text{DALYs},h}$) per hazard was the product of cases ($Cases_h$) and DALYs per pathogen:

$$Total_{\text{DALYs},h} = Cases_h \ \times \ \text{DALY}_h \tag{11}$$

2.8. Sensitivity analysis to detect uncertainty and effect of potential interventions

To explore the uncertainty around the model outputs in DALYs, a nominal range sensitivity analysis (NRSA) was done. The NRSA was employed for scenario $S_{playing}$ only to exemplify the impact of small changes in some of the model parameters used. Selected individual inputs were varied over a certain range, while holding all other inputs at their nominal values (Table 3). The following five parameter groups were investigated to obtain information about their uncertainty and effect of a potential intervention: (i) (V) volume ingested per exposure event were based on assumptions and, hence, values were multiplied by 0.1 and 10; (ii) (p_{path}) ratio between indicator and pathogenic organisms vary considerably between different contexts and, hence, values were multiplied by 0.1 and 10; (iii) (C_{water}) water contamination in community areas and the potential effect of treatment while varying the concentration with 1 log; (iv) (n) number of exposure events per year vary according to implemented health education programmes and, hence, we simulated a reduction by half (153 events) and to one event per year; and (v) (Pop_E) population at risk per exposure scenario may also vary according to the exposure event, we multiplied the population by 0.1 and 10.

2.9. Ethical considerations

The study protocol was approved by the institutional research commission of the Swiss Tropical and Public Health Institute (Swiss TPH; Basel, Switzerland; reference no. FK 106) and the Uganda National Council for Science and Technology (UNCST; Kampala, Uganda; reference no. HS 1487). Ethical approval was obtained from the ethics committee in Basel (EKBB; reference no. 137/13) and the Higher Degrees Research and Ethics Committee

Table 3
Sensitivity analysis of input parameters of the model indicated for scenario $S_{playing}$.

Scenarios		Description	Units	Distribution	Estimates	
					Upper	Lower
Uncertainty (V)						
Volume ingested per exposure event	*1*		mL	PERT(1;3;5)[a]	10;30;50	0.1;0.3;0.5
(p_{path}) Ratio between indicator and pathogenic organisms	*2.1*	Norovirus to *E. coli*		PERT(0.1;0.55;1)[a] per 10^5 *E. coli*	10;55;100	0.01;0.055;0.1
	2.2	Rotavirus to *E. coli*		PERT(0.1;0.55;1)[a] per 10^5 *E. coli*	10;55;100	0.01;0.055;0.1
	2.2	*Campylobacter* spp. to *E. coli*		PERT(0.1;0.55;1)[a] per 10^5 *E. coli*	1;5.5;10	0.01;0.055;0.1
	2.3	Pathogenic *E. coli* to *E. coli*		Uniform(7.6×10^{-4};1×10^{-2})[b]	0.1–7.6×10^{-3}	1×10^{-3}–7.6×10^{-5}
	2.4	Pathogenic *Salmonella* to *Salmonella* spp.		Uniform(7.6×10^{-4};1×10^{-2})[b]	1–7.6×10^{-2}	1×10^{-3}–7.6×10^{-5}
	2.5	*Cryptosporidium* spp. to *E. coli*		PERT(0.01;0.055;0.1)[a] per 10^5 *E. coli*	0.1;0.5.5;1	0.001;0.0055;0.01
Interventions						
(C_{water}) Water contamination in community areas	*3.1*	*Escherichia coli*	$\log_{10}$ (CFU/100 mL)	Normal(5.9;1.4)[c]	6.9	4.9
	3.2	*Salmonella* spp.	$\log_{10}$ (CFU/100 mL)	Normal(2.1;1.3)[c]	3.1	2.1
	3.3	*Ascaris* spp.	$\log_{10}$ eggs/1 L	Uniform(0;2)[b]	0–3	0–1
(n) Number of exposure events per year	*4*	Children in slum communities	Events	Point estimate: 365	1	153
(Pop_E) Population at risk per exposure scenario	*5*	Number of children	Children	Point estimate: 5928	592	59,280

[a] Project evaluation and review techniques (PERT) (min; most likely; max).
[b] Uniform distribution (min; max).
[c] Normal distribution (mean; standard deviation).

of Makerere University, School of Public Health (Kampala, Uganda; reference no. IRBOOO11353). This study is registered with the clinical trial registry ISRCTN (identifier: ISRCTN13601686).

3. Results

3.1. Incidence of gastroenteritis per year

The combined estimated incidence (Inc_{comb}) was highest for urban farmers ($S_{farming}$), children living in slum communities ($S_{playing}$) and sanitation workers ($S_{working}$) who suffer from 10.9, 8.3 and 4.3 gastroenteritis episodes per person per year (mean values; Fig. 3 and Table 4). The lowest risk was estimated for people swimming in Lake Victoria ($S_{swimming}$) who suffer from 0.18 gastroenteritis episodes per year. With regard to the individual pathogens, the risk of gastrointestinal infection was highest for children ($S_{playing}$) and urban farmers ($S_{playing}$) for rotavirus (4.4 and 3.9 episodes per year, respectively) and *E. coli* (2.7 and 1.7 episode per year, respectively). Considerably lower incidences were estimated for the same scenarios for *A. lumbricoides* (0.062 and 0.001 episode per year, respectively) and norovirus (between 0.46 and 0.34 episode per year, respectively).

Among the overall 18,204 exposed people in the Nakivubo area, 59,493 cases of gastroenteritis were estimated due to any of the seven pathogens, five scenarios and over the duration of one year (Fig. 3 and Table 4). Gastrointestinal infection due to rotavirus, *E. coli* and *Cryptosporidium* contributed most to the total cases (46%, 21% and 17%, respectively), followed by *Campylobacter* spp. (12%) and norovirus (4%). Together, 82% of all cases were concentrated in the 5,928 children living in slum communities ($S_{playing}$: 48,882 cases) and 650 urban farmers ($S_{farming}$: 7111 cases).

3.3. Total disease burden per year

Across all five scenarios, the model estimated a burden of 304.3 DALYs per year due to exposure to wastewater in the Nakivubo area among 18,204 exposed people, for all seven pathogens together (Fig. 3 and Table 4). The main responsible pathogens were *E. coli*, rotavirus and *Campylobacter*, accounting for 46%, 29% and 12% of DALYs, respectively. Children living in slum communities ($S_{playing}$; $n = 5928$) and urban farmers ($S_{farming}$; $n = 645$) were most vulnerable with burdens of 236.8 and 47.8 DALYs, respectively.

3.4. Disease burden per person per year

Combined DALYs pppy for all scenarios (summed-up for the seven pathogens and all exposed individuals) were far above the revised WHO reference level of 0.0001 DALYs pppy (Fig. 3 and Table 4). The highest impact was estimated for urban farmers in the Nakivubo wetland ($S_{farming}$), children living in slum communities ($S_{playing}$) and workers maintaining sanitation infrastructures ($S_{working}$), with DALYs pppy of 0.074, 0.040 and 0.017, respectively. In terms of different pathogens in $S_{farming}$, *E. coli*, *Salmonella* spp. and rotavirus had the largest share with 0.031, 0.018 and 0.014 DALYs pppy, respectively.

3.5. Sensitivity analysis

The effect of the sensitivity analysis, stratified for uncertainty and intervention scenarios, is shown in Fig. 3 for total cases of gastroenteritis. Uncertainty analysis revealed the highest change when adapting the volume of water accidentally ingested (−0.69 and 0.58). The pathogen ratio showed highest variation for rotavirus, *Cryptosporidium* and *E. coli*. Intervention strategies to reduce the water contamination with *E. coli* would have an impact of 0.70 and 0.58. Reducing the number of exposure events by half or to one event per year would reduce the number of gastroenteritis episodes by 0.29 and 2.56, respectively. The change of population at risk was found to be proportional to the indicated people exposed.

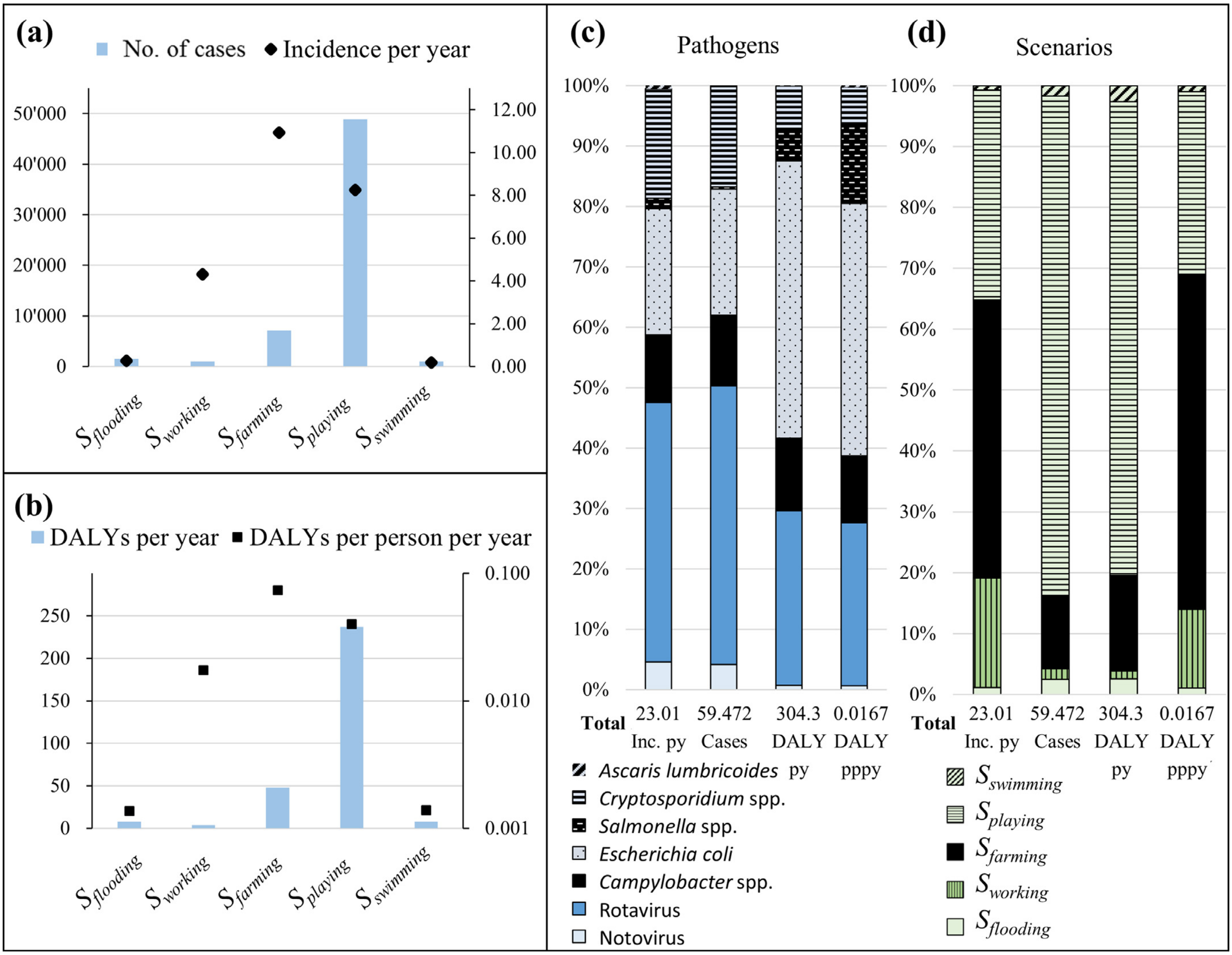

Fig. 3. Estimated gastroenteritis incidence per year (Inc. py), number of cases, disability-adjusted life years (DALYs) per year (py) and per person per year (pppy). (a) and (b) are showing estimates of the respective outcomes per $S_{flooding}$, $S_{working}$, $S_{farming}$, $S_{playing}$ and $S_{swimming}$. (c) and (d) are indicating the contribution of individual pathogens and scenarios, respectively, to the total estimated numbers per outcome along the major wastewater system in Kampala.

4. Discussion

4.1. Estimated burden due to gastroenteritis

Our estimated disease burden of 304.3 DALYs across all 18,204 exposed people per year corresponds to the estimates by the global burden of diseases study for entire Uganda of 0.017 DALYs pppy (612,202 DALYs considering a total population of Uganda of 35.4 million people) (GBD, 2010; UBOS, 2013). Broken down to the individual exposure groups in our model, urban farmers, children in slum communities and sanitation workers experience a 7, 3 and 2 times higher disease burden due to gastroenteritis than the general population in Uganda, respectively. These estimates are still lower than the disease burden estimates made for a typical slum area in Kampala of 10,172 DALYs (15,015 people) (Katukiza et al., 2013) and the 31,979 DALYs for 286,833 people being exposed to the urban wastewater systems in Accra (Labite et al., 2010). This large discrepancy between the QMRA estimates can partly be explained by different pathogens used for the QMRA, applied DALY estimates per pathogens (e.g. we excluded sequelae) and methodological differences (e.g. in the calculation of risk of illness). A common finding of QMRA studies in Africa is that *E. coli* and rotavirus together cause more than half of the disease burden (Katukiza et al., 2013; Machdar et al., 2013). The relatively high model-based estimate for pathogenic *E. coli* is supported by a recent case-control study in Côte d'Ivoire, which found that enterotoxigenic *E. coli* is indeed one of the most prevalent pathogens, being the causative agent in 32% of all participants with persistent diarrhoea (≥2 weeks) (Becker et al., 2015). The importance of rotavirus infection was demonstrated in an investigation at the Mulago Hospital in Kampala, where the rotavirus was detected in 177 out of 390 children aged 3 to 59 months (45.4%) presenting with acute diarrhoea (Nakawesi et al., 2010). Accordingly, the WHO reports that rotavirus is the main diarrhoea-causing agent in this age group, causing 7.3% of all deaths in children aged under 5 years in Uganda (Sigei et al., 2015).

4.2. Estimated incidence of gastroenteritis

Few papers have compared or even validated QMRA estimates with diarrhoea episodes assessed by epidemiological studies (Bouwknegt et al., 2014; Haas et al., 2014). In conjunction with the environmental assessment carried out for the QMRA, we have implemented a cross-sectional epidemiological survey in slum dwellers at risk of flooding events, urban farmers and sanitation workers (Fuhrimann et al., 2016). In this survey the self-reported

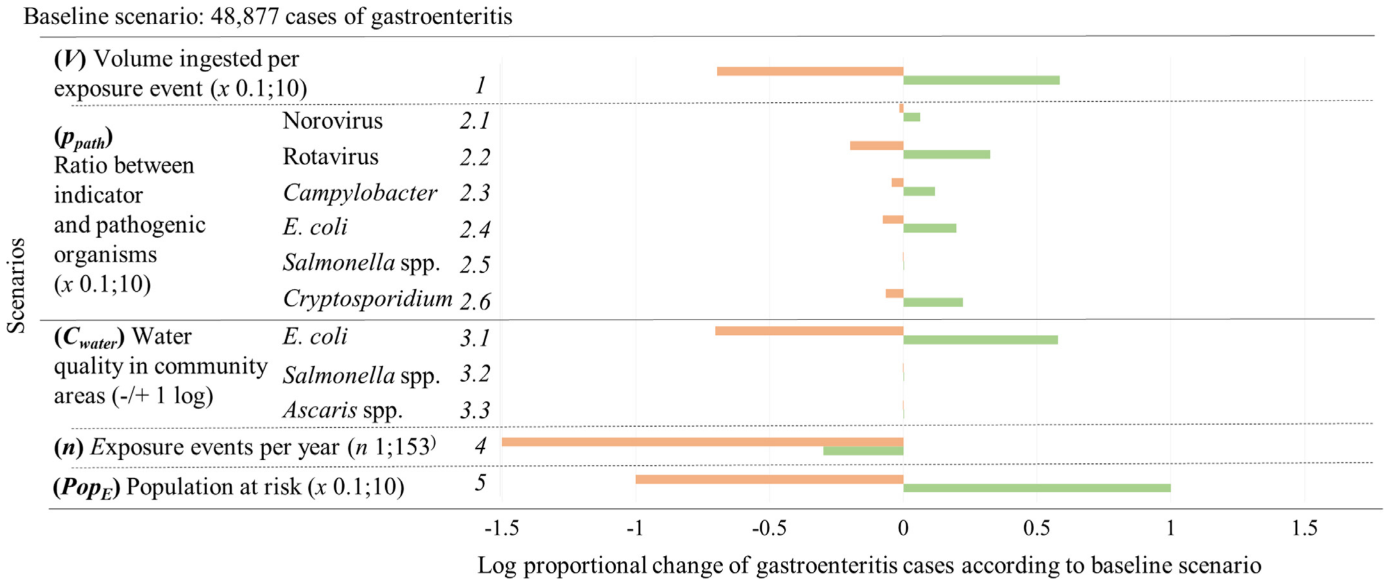

Fig. 4. Sensitivity analysis showing change in log(proportion) of gastroenteritis cases according to the baseline scenario ($S_{playing}$, children in slum communities) and stratified in uncertainty and intervention scenarios. Green line = upper estimates; red line = lower estimates. *indicating change in parameter values (upper; lower estimates). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 4
QMRA estimates for annual incidence of illness, number of cases per year, total DALYs per year, DALYs per person per year across all five exposure scenarios ($S_{flooding}$, $S_{working}$, $S_{farming}$, $S_{playing}$ and $S_{swimming}$) and seven pathogens along the major wastewater system in Kampala.

Exposure scenario (n = exposed population)	$S_{flooding}$ ($n = 5640$)	$S_{working}$ ($n = 231$)	$S_{farming}$ ($n = 645$)	$S_{playing}$ ($n = 5928$)	$S_{swimming}$ ($n = 5760$)	Total ($n = 18{,}204$)
Incidence of gastroenteritis per year (Inc_h)						
Norovirus	0.010	0.106	0.459	0.342	0.012	0.93
Rotavirus	0.127	1.812	4.402	3.880	0.055	10.28
Campylobacter	0.032	0.425	1.158	0.985	0.018	2.62
E. coli	0.053	0.675	2.697	1.679	0.032	5.14
Salmonella spp.	0.001	0.010	0.251	0.001	0.009	0.27
Cryptosporidium	0.039	0.371	1.893	1.355	0.050	3.71
A. lumbricoides	0.001	0.003	0.062	0.003	0.001	0.07
Total number	0.26	3.31	10.92	8.25	0.18	23.01
No. cases per year (Cases_h)						
Norovirus	57	25	299	2′030	70	2′480
Rotavirus	719	419	2′861	23′000	319	27′317
Campylobacter	178	98	753	5′837	101	6′966
E. coli	300	156	1′753	9′955	182	12′345
Salmonella spp.	7	2	163	4	51	227
Cryptosporidium	218	86	1′230	8′035	287	9′856
A. lumbricoides	5	1	40	17	8	71
Total number	1483	996	7099	48,877	1017	59,472
DALYs per year ($\text{Total}_{\text{DALYs,h}}$)						
Norovirus	0.0	0.0	0.3	1.8	0.1	2
Rotavirus	2.3	1.3	9.2	74.1	1.0	88
Campylobacter	0.9	0.5	4.0	30.7	0.5	37
E. coli	3.4	1.8	19.8	112.5	2.1	139
Salmonella spp.	0.5	0.2	11.7	0.3	3.6	16
Cryptosporidium	0.5	0.2	2.7	17.4	0.6	21
A. lumbricoides	0.0	0.0	0.1	0.1	0.0	0
Combined DALYs	7.7	4.0	47.8	236.8	8.0	304.3
DALYs per person per year ($\text{DALY}_{\text{pppy,h}}$)						
Norovirus	0.0000	0.0001	0.0004	0.0003	0.0000	0.0001
Rotavirus	0.0004	0.0058	0.0142	0.0125	0.0002	0.0048
Campylobacter	0.0002	0.0022	0.0061	0.0052	0.0001	0.0020
E. coli	0.0006	0.0076	0.0305	0.0190	0.0004	0.0076
Salmonella spp.	0.0001	0.0007	0.0181	0.0000	0.0006	0.0009
Cryptosporidium	0.0001	0.0008	0.0041	0.0029	0.0001	0.0012
A. lumbricoides	0.0000	0.0000	0.0002	0.0000	0.0000	0.0000
Combined DALYs	0.0014	0.0172	0.0741	0.0400	0.0014	0.0167

14-day incidence of diarrhoea episodes ranged from 0.25 in slum dwellers and urban farmers to 0.29 in workers along the sanitation system. When extrapolating this 14-day incidence to 1 year (52 weeks, without considering seasonality), the annual incidence would range between 6.6 and 7.6 episodes pppy. The comparison of the incidence estimate from the cross-sectional survey with the combined incidence of all seven pathogens used for the QMRA reveals that estimates are similar (i.e. 10.9 *versus* 6.6 in urban farmers and 4.3 *versus* 7.6 in sanitation workers, 0.3 *versus* 6.6 in community members). Hence, the estimates might match even more had the QMRA included the level of immunity (reduction in estimates) and additional exposures adding to diarrhoea incidence such as human to human transmission or consumption of contaminated water and food (Machdar et al., 2013; Barker, 2014). Further, when focusing on helminth infections, the QMRA estimated 92 people to be infected with *A. lumbricoides* over the course of a year, with 52 cases occurring in urban farmers (8% of the total number). The incidence estimate is in contrast to findings from our cross-sectional survey, which showed high prevalence in adult urban farmers: *A. lumbricoides:* 18.4%; *T. trichiura:* 26.1%; hookworm: 27.8%; and *S. mansoni* 22.9%, respectively (Fuhrimann et al., 2016). The comparatively low model-based estimates can be explained by the low prevalence and concentration of helminth eggs measured in wastewater samples. Indeed, only four samples were positive for *Ascaris* spp. eggs out of 168 (Fuhrimann et al., 2015). On the other hand, the high prevalence in urban farmers may result from accumulation of worms over time as deworming was reported not to be done on a regular basis (Fuhrimann et al., 2016). Similar tendencies, i.e. higher risk estimates by the QMRA than suggested by epidemiological surveys while predicting a lower number of infection, have also been shown by other studies (Havelaar et al., 2008). This points at the need for further cross-comparison between epidemiological surveys and QMRA with the ultimate goal to develop a standardised procedures to assess incidence and burden of diarrhoeal episodes and intestinal parasitic infections to make use of both tools.

4.3. QMRA limitations

Our model framework entails several limitations. The model relies on a range of assumptions pertaining to the volume of ingested water, the indicator to pathogen ratio and the number of exposure events, which were addressed in the uncertainty analysis and may lead to overestimation of the results. Especially the use of pathogen ratios is a key limitation, as *E. coli* counts may not reflect the densities of enteric virus in water bodies accurately (O'Toole et al., 2014). The dose-response models applied in this model are based on feeding studies (e.g. norovirus) or rely on epidemiological evidence (e.g. *Ascaris* spp.) conducted with healthy individuals in high income countries. Thus, dose-response may be considerably different due to acquired immunity related to exposure history or vaccination (Haas et al., 2014; Havelaar and Swart, 2014). The simplification of allowing no immunity after an exposure event in the QMRA may result in an overestimation of the disease burden (Haas et al., 2014). Certain pathogens, such as rotavirus, may have considerable different health impact in different age classes, which have not be taken it to account in this QMRA (Sigei et al., 2015). The helminth eggs in water can vary greatly as seasonal and clustered transmission of helminths is common (Cairncross et al., 1996). The model excluded exposure pathways such as dermal contact and inhalation and people living in a slum-like environment may also be exposed to contaminated drinking water and greywater, which should be taken into account in future QMRAs (Howard et al., 2006; Machdar et al., 2013). Further, it is known that in Kampala other pathogens such as adenoviruses, hepatitis A virus, *Vibrio cholerae*, hookworm and *S. mansoni* are present in the environment (Bwire et al., 2013; Katukiza et al., 2013); these were not included in the model although they can cause diarrhoea and other adverse health effects (Karagiannis-Voules et al., 2015; Fuhrimann et al., 2016).

4.4. Sensitivity analysis

In the sensitivity analysis we showed a considerable effect of different volume of water accidentally ingested. These values might, however, not be very accurate as exposure to wastewater very much depends on individual behaviours in the given environment and is also influenced by age, sex, level of education and socio-economic status (WHO, 2006; Haas et al., 2014). Clearly, there is a need to generate specific estimates for accidental ingestion of water during different exposures in low-income countries in the global South. In absence of valid information on the pathogenic strains, assumptions were drawn based on published ratios between *E. coli* and the pathogenic strain. We showed that especially values for rotavirus, *E. coli* and *Campylobacter* have a considerable effect on the total number of gastroenteritis cases. Studies have reported that temporal and spatial variation of environmental pollution is common in urban wastewater systems (Ensink, 2006; Katukiza et al., 2013; Fuhrimann et al., 2015). Furthermore, the *E. coli* to pathogen ratio might change over time as *E. coli* is secreted by humans and animals continuously, whereas pathogens are secreted only by a proportion of infected people over a short period of a few days (Mara, 2004).

4.5. Proposed mitigation strategies for exposure scenarios

In view of our findings, and acknowledging inherent limitations, a set of options for reducing disease burden for each of the five exposure groups are proposed (from highest burden to lowest burden). Importantly, the choice of the appropriate mitigation strategy needs to take into account cost-effectiveness as well as acceptability in concerned population groups (Machdar et al., 2013).

- $S_{playing}$: in order to protect children (<15 years) living in slum communities, oral rotavirus vaccination could be added to the Ugandan immunisation schedule and given to children at the age of >6 weeks (The Republic of Uganda, 2012; UNAS, 2014). This may be supplemented with bi-annual hygienic and deworming campaigns at schools, as well as at the level of households for targeting women of childbearing age (WHO, 2011b; Sigei et al., 2015).
- $S_{farming}$: the health of farmers working in the Nakivubo wetland can be promoted by means of farmer field schools. For example, in workshops on occupational health risks the value of personal protective equipment and the importance of sanitation and personal hygiene can be introduced (Van Den Berg and Takken, 2007).
- $S_{working}$: sanitation workers employed by the NWSC and those working for the PEA could be trained on the recognition of health risks and effective use of personal protective equipment. Moreover, bi-annual hygienic and deworming campaigns could be implemented (Van Den Berg and Takken, 2007; Strande et al., 2014).
- $S_{flooding}$: slum dwellers living in close proximity to the Nakivubo wetland could be protected against flooding events through the construction of small dams and drainage systems. In addition, access to frequently flooded areas along the Nakivubo channel might be restricted via perimeter fences (Katukiza et al., 2010).
- $S_{swimming}$: swimmers at the local beaches along the Inner Murchison Bay (e.g. Miami Beach, Ggaba Beach, KK Beach) could be informed about the risks involved with swimming in Lake Victoria (e.g. warning signs at unsafe places). Regulations

to restrict swimming at certain commercial beaches close to the discharge point of the Nakivubo Channel could be introduced and the beach water quality could be monitored on an ongoing basis (Soller et al., 2015).

Some general recommendations to reduce the exposure of the population to pathogens in contaminated water, proposed by others, are (i) re-establish the Nakivubo wetland flora to reclaim its function as a natural maturation pond and retention pool to protect the Murchison Bay in Lake Victoria (Mbabazi et al., 2010; Fuhrimann et al., 2015); (ii) fight faecal contamination of slum areas by promoting sanitation coverage in combination with safe collection, treatment or disposal of faecal sludge (Fuhrimann et al., 2016); and (iii) in the longer term, increase wastewater treatment and reuse capacity of Kampala city (Strande et al., 2014; Fuhrimann et al., 2015).

5. Conclusions

By using a QMRA approach, we estimated high risk, and considerable burden, due to water-borne pathogens among different population groups being exposed to wastewater in Kampala. Disease burden was estimated to be highest in children living in slum communities and in urban farmers with 0.199 and 0.06 DALYs pppy, respectively. Indeed, the DALYs pppy for these two population groups were several thousand fold above the revised WHO tolerable level of 0.0001 DALYs pppy. Hence, exposure to wastewater is anticipated to have considerable public health implications, calling for action to reduce *E. coli* and rotavirus infection, which were found to be of major concern. The presented QMRA provides a case study on how the risk assessment framework of the WHO guidelines for the safe use of wastewater, greywater and excreta can be applied to fit an urban low-income setting. The QMRA framework was built on context specific data of indicator microorganism and recent burden estimates for the most common water-borne pathogens resulting in gastroenteritis in Uganda. We showed the need to further link QMRA and epidemiological studies and to elaborate on how to assess the number of exposure events, the indicator organism to pathogen ratio and the dose-response relationship. Such risk assessment frameworks can make an important contribution to our understanding of health impacts in different population groups related to specific exposures, and thus promote the development of targeted mitigation strategies in resource-constrained settings.

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9. ARTICLE 5: Microbial contamination along wastewater conveyance and treatment systems: health risks for agriculture and aquaculture in Hanoi, Vietnam

Photo: Wastewater of the To Lich River discharging into Red River in Hanoi, Vietnam
(©S. Fuhrimann, 2014)

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Microbial contamination along the main open wastewater and storm water channel of Hanoi, Vietnam, and potential health risks for urban farmers

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HIGHLIGHTS

- We assessed the wastewater systems in reducing microbial contamination in Hanoi, Vietnam.
- We found that bacterial contamination in water used in agricultural field exceeds safety limits.
- We propose a series of control measures that would allow reducing microbial contamination.
- This paper can guide cities in Asia on how to work towards the Sustainable Development Goal 6.3 linked to safe use of wastewater.

GRAPHICAL ABSTRACT

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ABSTRACT

The use of wastewater in agriculture and aquaculture has a long tradition throughout Asia. For example, in Hanoi, it creates important livelihood opportunities for >500,000 farmers in peri-urban communities. Discharge of domestic effluents pollute the water streams with potential pathogenic organisms posing a public health threat to farmers and consumers of wastewater-fed foodstuff. We determined the effectiveness of Hanoi's wastewater conveyance system, placing particular emphasis on the quality of wastewater used in agriculture and

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Abbreviations: CFU, colony forming unit; HSDC, Hanoi Sewerage and Drainage Company; MPN, most probable number; NIHE, National Institute for Hygiene and Epidemiology; QMRA, quantitative microbial risk assessment; SDG, Sustainable Development Goal; SSP, sanitation safety planning; Swiss TPH, Swiss Tropical and Public Health Institute; TC, total coliforms; WHO, World Health Organization.

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aquaculture. Between April and June 2014, a total of 216 water samples were obtained from 24 sampling points and the concentrations of total coliforms (TC), *Escherichia coli*, *Salmonella* spp. and helminth eggs determined. Despite applied wastewater treatment, agricultural field irrigation water was heavily contaminated with TC (1.3×10^7 colony forming unit (CFU)/100 mL), *E. coli* (1.1×10^6 CFU/100 mL) and *Salmonella* spp. (108 most probable number (MPN)/100 mL). These values are 110-fold above Vietnamese discharge limits for restricted agriculture and 260-fold above the World Health Organization (WHO)'s tolerable safety limits for unrestricted agriculture. Mean helminth egg concentrations were below WHO tolerable levels in all study systems (<1 egg/L). Hence, elevated levels of bacterial contamination, but not helminth infections, pose a major health risk for farmers and consumers of wastewater fed-products. We propose a set of control measures that might protect the health of exposed population groups without compromising current urban farming activities. This study presents an important example for sanitation safety planning in a rapidly expanding Asian city and can guide public and private entities working towards Sustainable Development Goal target 6.3, that is to improve water quality by reducing pollution, halving the proportion of untreated wastewater and increasing recycling and safe reuse globally.

1. Introduction

Asia has a long tradition in the use of wastewater in agriculture and aquaculture (Qadir et al., 2010). Particularly, in peri-urban areas of large urban centres, farmers benefit from the all-year-round availability of wastewater and its high nutrient content (Drechsel et al., 2015). However, as Asian cities have grown rapidly, and continue to do so, appropriate infrastructures to collect and treat wastewater are often lacking, and hence, there are high levels of environmental pollution (Evans et al., 2012). Moreover, sewerage usually receive combined effluents from households, hospitals and industries, which in turn can contaminate the environment with a diffuse mix of pathogenic organisms and toxic chemicals (Phung et al., 2015). Consequently, safe wastewater management is of considerable public health relevance for people living along wastewater channels, farmers using wastewater, as well as consumers of wastewater irrigated crops and wastewater-fed fish (Hanjra et al., 2011; Utzinger et al., 2015). Safe wastewater management and use is also prominently featured in the Sustainable Development Goal (SDG) target 6.3, which was put forth by the United Nations and aims at improving water quality by reducing pollution, eliminating dumping and minimising release of hazardous chemicals and materials, halving the proportion of untreated wastewater and increasing recycling and safe reuse globally (UN, 2015).

A prominent example is Hanoi, the capital city of Vietnam. Over the past 20 years, the urban area has expanded, the population grew at an annual rate of 3.5%, resulting in 6.7 million people living on an area of 3329 km^2 in 2011 (GSO, 2011). More than 90% of the households in Hanoi rely on flush toilets that are connected to septic tanks, from where effluents are informally discarded into a wide network of drainage channels. In addition, these channels receive industrial effluents. In response to these challenges, the system was expanded in recent years to control the water flow out of the city and treat the wastewater with conventional treatment plants and decentralised water management systems (Kuroda et al., 2015). The latter should prevent flooding events, while regulating the water flow with water gates and a series of artificial ponds. In these artificial ponds, the wastewater is partially treated through sedimentation in combination with oxygenation. As a common practice, this partially treated wastewater is used in aquaculture and agriculture (Lan et al., 2012). Indeed, an estimated 658,000 farmers use wastewater on an area of approximately 43,778 ha in Hanoi (Raschid-sally and Jayakody, 2008). It must be noted that the use of wastewater creates important livelihood opportunities, as its high nutrient load is valuable for growing fresh vegetables and farm livestock and fish (Lan et al., 2012).

Several studies have reported high levels of microbial and chemical pollution in river sediments, irrigation water, splashing water used on markets and wastewater-fed foodstuff in Hanoi (Ingvertsen et al., 2013; Nguyen and Dalsgaard, 2014; Kuroda et al., 2015). Adverse health outcomes, such as diarrhoeal diseases, helminth infections and dermatitis, due to exposure to wastewater are well documented (Anh et al., 2007; Do et al., 2007a; Hien et al., 2007; Pham-Duc et al., 2013). Of note, as far as 60 km downstream of Hanoi, in Hanam province, adverse health conditions were associated to the city's wastewater (Pham-Duc et al., 2013, 2014). Additionally, flooding events exacerbated negative health impacts with considerable burden for public health such as drowning of people and cholera epidemics (Bich et al., 2011). While the current evidence suggests multiple environmental and health issues, a systematic assessment of the effectiveness of the different components of Hanoi's wastewater conveyance and treatment system that might reduce microbial contamination is currently lacking. This includes the identification of targeted mitigation strategies for improving the quality of products from urban farming in Hanoi (Fuhrimann et al., 2014; WHO, 2015).

The objectives of the present study were: (i) to assess whether the existing treatment scheme is effective in reducing microbial (bacteria and helminth) contamination along the main wastewater channels and retention drainages prior to the use of water in aquaculture ponds and agricultural fields; and (ii) suggest control measures that might provide a safe management and use of wastewater in agriculture and aquaculture in Hanoi. This environmental assessment was part of a larger study, comprising of a cross-sectional parasitological survey in selected population groups exposed to wastewater and a quantitative microbial risk assessment (QMRA) to determine disease burden related to microbial contamination (Fuhrimann et al., in press). Moreover, the data contributed to the development of the sanitation safety planning (SSP) manual that has recently been published by the World Health Organization (WHO) (WHO, 2015).

2. Materials and methods

2.1. Study area

Hanoi is located in the north of Vietnam, situated in the Red River delta (geographical coordinates: 21° 01′ 42.5″ N latitude and 105° 51′ 15.0″ E longitude). Hanoi's climate is sub-tropical. The main rainy season occurs from April to September. There is year-round high humidity ranging from 80% to 90% (Climate-Data.org, 2015). The wastewater flows from north to south, along a topographic gradient from 20 m to 5 m above mean sea level in four main rivers, namely To Lich River, Nhue River, Kim Nguu River and Red River (Nguyen and Parkinson, 2005; Kuroda et al., 2015).

2.2. Sampling sites and procedure

A cross-sectional survey was conducted between April and June 2014. The present study focused on three parts of Hanoi's wastewater system, namely (i) the urban wastewater conveyance and treatment system (operated by the Hanoi Sewerage and Drainage Company

(HSDC)); (ii) the peri-urban wastewater conveyance, treatment and reuse system in the districts of Hoang Mai and Thanh Tri; and (iii) a comparison site in a rural area of Thanh Tri district, where Red River water (not considered as wastewater) is used for aquaculture and agriculture. As shown in Fig. 1, 24 sampling points were selected and a total of 216 samples obtained over the whole study period (a total of nine samples per sampling point were taken, one every week) in the three study systems. At each sampling point, three separate water samples (2 × 100 mL and 1 L) were collected approximately 10 cm below the surface of the respective water body in sterile wide mouth glass bottles. Samples were collected between 08:00 and 12:00 h each Monday (T_{R1-5}, R_{R1}, $N_{R1/2}$, WW_{D1-3} and WW_{F1-3}) or Tuesday (R_{R2}, C_{D1-3}, WW_{D1-3} and WW_{F1-3}). Upon collection, samples were transferred within 4 h to a nearby laboratory in a cool box (temperature 4 °C).

2.2.1. Sampling sites in the urban wastewater system

To Lich River (T_R) is the main open storm water and drainage channel of the city. It is 14 km long, starts at West Lake and is draining into Nhue River and Red River. The river arm flowing towards Red River drains into a series of artificial lakes, where it is partially treated through primary sedimentation ponds and sequential batch reactors at the Yen So wastewater treatment plant. Subsequently, the wastewater is screened and actively pumped into a drainage channel (3 km) that discharges into Red River. The arm flowing into Nhue River is controlled by a water gate that releases the raw wastewater without treatment into Nhue River (Duc et al., 2007; Kuroda et al., 2015). In To Lich River, five sampling points (T_{R1} to T_{R5}) spread over a distance of 9 km, starting from one at the Bang B pagoda just before the water is partly flowing into the Nhue River (T_{R1}), two in Bang B village and Tam Hiep commune (T_{R2} and T_{R3}), one just before the Yen Son lake system (T_{R4}) and one just before the water drains into Red River (T_{R5}).

Nhue River (N_R) originates from Red River in the north of Hanoi and flows south along the peri-urban area, where it receives domestic, hospital and industrial effluents (Duc et al., 2006). In Nhue River two sampling points were chosen (N_{R1} and N_{R2}), one just before the To Lich River drains into Nhue River (N_{R1}) and one 500 m downstream after the two rivers join (N_{R2}).

Red River (R_R) has its source in China and is draining in the Gulf of Tonkin. The Red River delta is the second most important rice growing area in Vietnam, and also known as an intensive pig production system (Nguyen et al., 2014). In Red River, two sampling points were chosen (R_{R1} and R_{R2}), one at 150 m before To Lich River drains into Red River (R_{R1}) and the second at 3 km downstream, where water is pumped for agricultural purposes in Duyen Ha commune (R_{R2}).

2.2.2. Sampling sites in the peri-urban wastewater system

Bang B village and Tam Hiep commune, representing typical peri-urban communities pumping wastewater from To Lich River into local drainage channels (W_D) for use in agricultural fields (W_F), were selected as peri-urban sampling sites. The communities are located in Hoang Mai and Thanh Tri district, respectively (geographical coordinates: 20° 57′ 17.54″ N latitude and 105° 49′ 42.48″ E longitude) and are prone to rapid demographic transition, industrial development and land use change. A large part (33%) of the community members are involved in agriculture (*e.g.* rice, morning glory, neptunia and watercress) or aquaculture (Lan et al., 2012). Water was sampled at six sites in the drainage and pond systems (W_{D1} to W_{D6}), which connect and retain the water pumped from To Lich River to aquaculture ponds and agricultural fields. Another six sites (W_{F1} to W_{F3}) were selected in agricultural fields (primarily vegetables and rice) fed with water from the local drains and ponds.

2.2.3. Comparison site: rural non-wastewater system

Duyen Ha commune was selected as a comparison site (C_D) to represent a typical farming community relying on irrigation water from Red River. About 38% of the people work in agriculture (Fuhrimann et al., in press). The commune belongs to Thanh Tri district and is about 5 km from the outskirts of Hanoi (geographical coordinates: 20° 55′ 42.37″ N latitude and 105° 52′ 23.32″ E longitude). Water samples were collected at three sites (C_{D1} to C_{D3}), which transport the water from Red River to the agricultural fields. It is important to note that

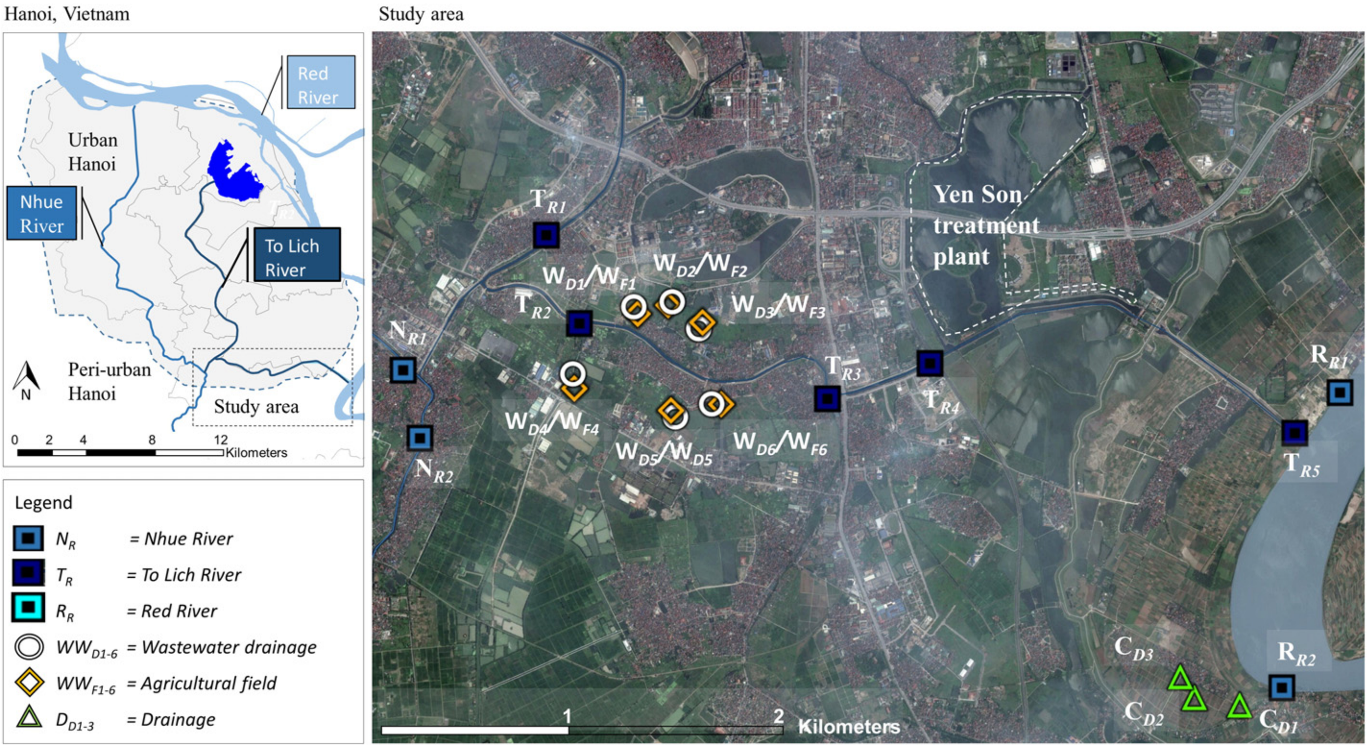

Fig. 1. Map of Hanoi showing the study area and respective sampling points (Google Earth, 2010).

these local drainage channels are potentially contaminated with household effluents but do not contain wastewater from Hanoi city.

2.3. Microbial analysis

2.3.1. Total coliforms and Escherichia coli analysis

TC and *E. coli* enumeration was performed by the National Institute for Hygiene and Epidemiology (NIHE), on Brilliance *E. coli*/coliform Selective Agar (CM1046, Oxoid) following incubation at 37 °C for 24 h. One milliliter of the water sample was aseptically transferred to a sterile tube containing 9 mL peptone saline broth (1:10). The sample was mixed well and 10-fold and 100-fold dilutions were prepared. 100 μL of each dilution was surface-spread onto duplicate agar plates. Agar plates showing growth of dark purple to indigo blue colonies were designated as *E. coli*, while pink colonies were considered TC. *E. coli* and TC counts were calculated using the standard formula and are expressed as CFU per 100 mL (Nguyen and Dalsgaard, 2014).

2.3.2. Salmonella spp. analysis

Salmonella spp. enumeration was conducted by the National Institute of Veterinary Research (NIVR) using the most probable number (MPN) technique (ISO 6579, 2002). Briefly, a series of 10-fold dilution sample with Buffer Peptone Water (BPW-Merk, Germany) was prepared; 2.5 mL of each dilution was transferred into a 12-well microtiter plate and incubated at 37 °C for 18 h. After incubation, 20 μL of incubated suspension was transferred into another 12-well microtiter plate, where each well contained 2 mL Modified Solid Rappaport Vassiliadis (MSRV-Merck; Darmstadt, Germany) and incubated at 41.5 °C for 24 h. Results were read after 24 h of incubation. Subsequently, 1 μL loop of the suspected MSRV (grey-white, turbid zone extending out from the inoculated drop) was sub-cultured on Xylose Lactose Tergitol TM4 (XLT4-Merck; Darmstadt, Germany) agar plate and invert incubated on XLT4 plate at 37 °C for 24 h. After 24 h of incubation, the typical colonies of *Salmonella* spp. grown on XLT4 (with black centre) were isolated to perform the confirmation test by biochemical (lysine, urease, citrate utilize and indole) and serological (poly OH) tests. The number of wells giving a positive confirmed reaction was counted for each dilution and the MPN were calculated from the number of positive confirmed wells (EPA, 2012).

2.3.3. Helminth egg analysis

Helminth egg detection was done by National Institute of Malaria, Parasitology, and Entomology by means of the Romanenko technique (WHO, 2004; NIMPE, 2013). In brief, the water samples (1 L each) were allowed to settle for a period of 10 to 15 h before approximately 90% of the supernatant was removed using a siphon. The sediment was moved into a tube, and the bottles were rinsed with detergent Tween 80 (0.1%). Next, the tube was centrifuged at 1000*g* for 15 min, the supernatant discarded. Flotation solution was added to the tube (saturated $NaNO_3$) and centrifuged at 1000*g* for 15 min. The floatation solution above was discharged and new floatation solution added (up to 40 mL), stirred with a glass chopstick and centrifuged at 1000*g* for 5 min. Subsequently, flotation solution was added until it reached the top of the tube. A slide was placed on top of the tube for 20 min and replaced by a second slide for another 10 min. Finally, glycerine was added to cover the slides and helminth eggs were counted under a microscope (10×, and 40× magnification) and reported as numbers of eggs/L.

2.4. Statistical analysis

Statistical analysis were done using STATA version 12.0 (Stata Corporation; College Station, USA). Geometric means with 95% confidence intervals (CIs) and minima and maxima of bacteria and helminth egg concentrations and prevalence rates were calculated as the proportion of positive sample in each sampling system. Distribution and change in bacteria concentration were calculated at the log10-scale, where 1 unit reduction is equivalent with 90% and 2 units with 99% reduction on the original scale. Gradients between neighbouring sampling points were assessed by means of non-parametric Wilcoxon rank-sum tests. Level of water contamination was compared with WHO Guidelines for the Safe Use of Wastewater in Agriculture (WHO, 2006) and the National Technical Regulation on Domestic Wastewater (QCVN 14: 2008/BTNMT) and Industrial Water (QCVN 24: 2009/BTNMT) of Vietnam (MONRE, 2008, 2009). Maps, including geographical coordinates of the sampling points, were established in ArcMap version 10 (Environmental System Research Institute; Redlands, USA).

2.5. Ethics statement

The study protocol was approved by the institutional research commission of the Swiss Tropical and Public Health Institute (Swiss TPH; Basel, Switzerland; reference no. FK 106). Ethical approval was obtained from the ethics committee in Basel (EKBB; reference no. 137/13) and the Hanoi School of Public Health (Hanoi, Vietnam; reference no. 010/2014/YTCC-HD3). This study is registered with the clinical trial registry ISRCTN (identifier: ISRCTN13601686).

3. Results

3.1. Bacteria and helminth egg contamination

Fig. 2 and Table 1 summarise concentrations and prevalence rates of TC, *E. coli* and *Salmonella* spp. in the study systems. Highest mean concentrations of TC, *E. coli* and *Salmonella* spp. were obtained in the water from To Lich River (5.6×10^7 and 4.2×10^6 CFU/100 mL and 1044 MPN/100 mL, respectively). The lowest concentrations of TC and *E. coli* were measured (1.1×10^6 and 1.7×10^4 CFU/100 mL, respectively) in Red River, where no *Salmonella* spp. was detected. In agricultural fields of Bang B and Tam Hiep, where wastewater is reused, mean concentrations of *E. coli* were approximately four times higher than the mean concentrations measured in Duyen Ha commune where Red River water is used (1.1×10^6 CFU/100 mL *vs.* 2.5×10^5 CFU/100 mL, respectively). *Salmonella* spp. counts were approximately four times higher in Duyen Ha than in Bang B and Tam Hiep (108 MPN/100 mL *vs.* 455 MPN/100 mL, respectively), while prevalence of *Salmonella* spp. was 1.7 times higher (21.7% *vs.* 12.5%, respectively).

Table 2 summarises egg counts and prevalence rates of helminths. Helminth eggs were obtained in 12% of all the samples, 8% were positive for *A. lumbricoides* eggs and 6% for *T. trichiura* eggs. No hookworm eggs or any other helminth eggs were detected. Overall, the mean concentration of helminth eggs in water samples was 0.22 eggs/L. Highest mean concentration of 0.59 eggs/L (0.17 and 0.43 eggs/L for *A. lumbricoides* and *T. trichiura*) could be detected in agricultural fields in Bang B village and Tam Hiep commune, with maximum egg counts of 22 eggs/L.

3.2. Microbial reduction along the different study systems

3.2.1. Urban wastewater system

Fig. 3 shows that there were only marginal differences of all three measured bacteria groups along the To Lich River with increasing distance from Hanoi city (between point T_{R1} and T_{R4}). Further, the wastewater treatment through the Yen So stabilisation pond and treatment systems significantly reduced the TC, *E. coli* and *Salmonella* spp. counts concentration by 0.5, 0.7 and 0.8, respectively, on the log10-scale ($p \leq 0.03$) (T_{R4} to T_{R5}). Significant log reductions were also determined for TC, *E. coli* and *Salmonella* spp. (1.0, 1.9 and 2.1, respectively) in Red River (R_{R2}) 5 km downstream of the discharge point of To Lich River. Moreover, the water from Red River showed no significant difference in pollution after discharge of To Lich River between R_{R1} and R_{R2}. Nhue River showed a similar high level of contamination as To Lich River

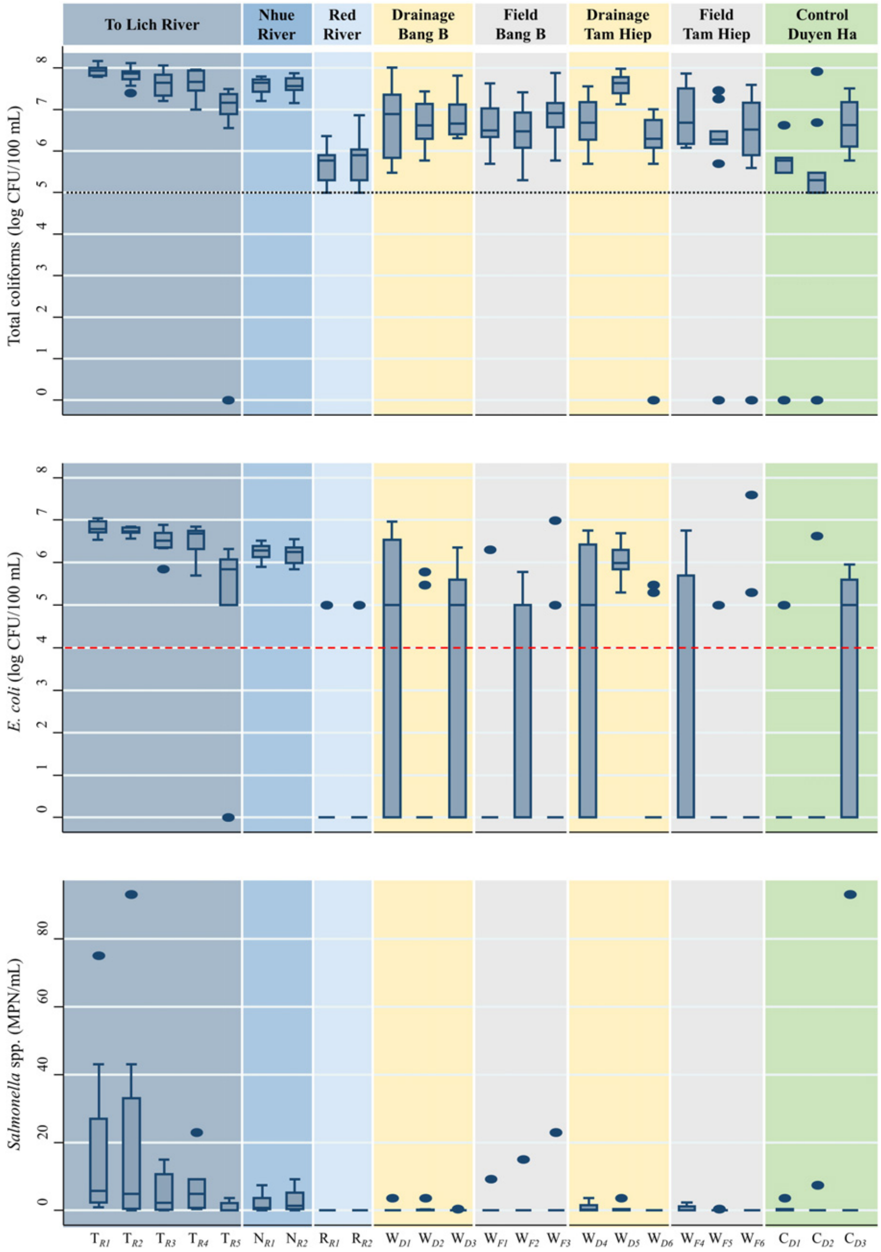

Fig. 2. Box-and-whisker plots of the log concentration of colony forming unit (CFU) total coliforms (TC) and *E. coli* per 100 mL, and MPN *Salmonella* spp. per mL. For each sampling point, a total of nine samples were collected along the wastewater systems in Hanoi, Vietnam (sampling period: 4 April to 6 June 2014). Black-dotted line maximum acceptable concentrations of TCs (MONRE, 2008) and red-dashed line: maximum acceptable concentrations of *E. coli* (WHO, 2006).

and no significant difference after To Lich discharges between N_{R1} and N_{R2}.

3.2.2. Peri-urban wastewater system

We observed significant higher concentration of TC, *E. coli* and *Salmonella* spp. between To Lich River (T_{R2} and T_{R3}) and the pond and drainage systems in Bang B village and Tam Hiep commune (WW_{D1} to WW_{D6}) of 0.5, 0.7 and 1.5, respectively ($p < 0.01$) on the log10-scale (Fig. 3). Between the drainage and ponds and the agricultural fields (WW_{F1} to WW_{F6}), no significant difference in bacteria concentration could be observed. For *E. coli*, there was even a significant higher contamination measured (by 0.1 on the log10-scale, $p < 0.01$).

3.2.3. Comparison site: rural non-wastewater system

The lowest concentration with bacteria could be measured in water pumped at R_{R2} from Red River (Fig. 3). The three sampling points along the drainage of Duyen Ha commune (D_{D1-3}) showed a significantly higher concentration with TC, *E. coli* and *Salmonella* spp. of 0.6, 1.6 and 2.8 log ($p < 0.01$), respectively, when compared water samples obtained from Red River (R_{R2}).

4. Discussion

4.1. Microbial contamination along the wastewater system

Wastewater used in aquaculture ponds and agriculture fields of Hanoi is heavily contaminated with TC, *E. coli* and *Salmonella* spp. (on average 1.3×10^7 CFU/100 mL, 1.1×10^6 CFU/100 mL and 108 MPN/100 mL, respectively). These values are 110-fold above the Vietnam discharge limits of 5000 CFU TC/100 mL in wastewater for agriculture reuse (MONRE, 2008) and 260-fold above WHO tolerable safety limits for unrestricted irrigation (10^3–10^4 CFU *E. coli*/100 mL) (WHO, 2006).

Table 1
Total coliforms, *E. coli* and *Salmonella* spp. concentrations and prevalence along the wastewater systems in Hanoi, Vietnam (sampling period: 4 April to 6 June 2014). Geometric mean, standard deviation (SD), minimum and maximum concentration, and 95% confidence intervals (CIs) are indicated.

Sampling system	Counts for total coliforms and *E. coli* in CFU/100 mL or *Salmonella* spp. in MPN/100 mL						Prevalence rates
Bacteria in water	Mean	SD	Min.	Max.	Lower 95% CI	Upper 95% CI	%
To Lich River (n = 45)							
Total coliforms	5.6×10^7	3.70×10^7	0	1.5×10^8	4.4×10^7	6.6×10^7	98.3
E. coli	4.2×10^6	2.8×10^6	0	1.1×10^7	1	5.1×10^6	96.2
Salmonella spp.	1044	2007	0	9300	402	1685	77.5
Nhue River (n = 18)							
Total coliforms	4.2×10^7	1.7×10^7	1.4×10^7	7.4×10^7	3.3×10^7	5.1×10^7	100
E. coli	1.9×10^6	8.8×10^5	6.9×10^5	3.6×10^6	1.4×10^6	2.3×10^6	100
Salmonella spp.	251	308	0	920	80	422	87.7
Red River (n = 18)							
Total coliforms	1.1×10^6	1.7×10^6	9.9×10^4	7.3×10^6	2.5×10^5	1.9×10^6	100
E. coli	1.7×10^4	3.8×10^4	0	9.9×10^4	0	3.5×10^4	17.1
Salmonella spp.	0	0	0	0	0	0	0
Urban drainage: Bang B and Tam Hiep (n = 54)							
Total coliforms	1.8×10^7	2.6×10^7	0	1.0×10^8	1.1×10^7	2.5×10^7	98.2
E. coli	8.9×10^5	1.8×10^6	0	9.1×10^6	4.1×10^5	1.4×10^6	52.4
Salmonella spp.	41	104	0	360	10	72	23.4
Urban agriculture fields: Bang B and Tam Hiep (n = 54)							
Total coliforms	1.3×10^7	1.9×10^7	0	7.7×10^7	7.7×10^6	1.8×10^7	96.5
E. coli	1.1×10^6	5.5×10^6	0	3.9×10^7	0	2.6×10^6	24.4
Salmonella spp.	108	410	0	2300	11	228	12.5
Peri-urban drainage: Duyen Ha (n = 27)							
Total coliforms	6.4×10^6	1.7×10^7	0	8.3×10^7	0	1.3×10^7	85.6
E. coli	2.5×10^5	8.1×10^5	0	4.2×10^6	0	5.7×10^5	30.6
Salmonella spp.	455	1935	0	9300	0	1292	21.7

Our findings confirm results from a previous study reporting that water bodies in urban and peri-urban areas of Hanoi are contaminated with faecal matter (Kuroda et al., 2015). The average treatment of 0.5 and 0.7 log CFU for TC and *E. coli* due to drainage and retention ponds is not sufficient to comply with safety thresholds. In addition, bacteria contamination was higher in the agriculture field compared to drainage and retention ponds, most probably due to local defecation or even illegal discharge of faecal sludge (Fuhrimann et al., in press). Clearly, high charges with human, and potentially animal waste, in combination with the insufficient treatment of bacterial contamination along Hanoi's wastewater conveyance system, represent a public health concern for people living along wastewater channels, farmers using wastewater, and consumers of wastewater irrigated crops and wastewater-fed fish (WHO, 2006; MONRE, 2008).

4.2. Potential implication for public health

The association between health risks and the high level of bacterial contamination is further underpinned by studies that have shown significant associations between diarrhoeal diseases and use of wastewater in children in peri-urban and rural communities around Hanoi (Hien et al., 2007; Pham-Duc et al., 2014). With regard to helminth egg concentrations along the wastewater system, our findings are in line with studies by Do et al. (2007b), who showed no significant association between peri-urban wastewater use and helminth infections in Hanoi. However, other studies reported that the use of wastewater from Nhue River was significantly associated with helminth and intestinal protozoa infections as well as self-reported diarrhoea (Pham-Duc et al., 2013, 2014). In order to better understand the risk of the specific causative agents, a context-specific QMRA is required (Mok and Hamilton, 2014). For example, as shown by Pham-Duc (2012), the estimated risk of diarrhoeal diseases due to the exposure to wastewater reused for rural agriculture across communities in Hanam was 100-fold greater than the acceptable risks (Pham-Duc, 2012). Other hazards and pollutants such as antibiotic-resistant bacteria, heavy metals and toxic chemicals were observed by other studies in the wastewater and sediment of Hanoi city (Ingvertsen et al., 2013; Pham et al., 2015). These findings point to a challenge when aiming at the safe use of wastewater and sediments for any kind of land application. In combination with the reported microbial pollution, this also poses a serious risk of groundwater and drinking water pollution (Holm et al., 2010; Sanders et al., 2014; Kuroda et al., 2015).

4.3. Proposed control measures along the wastewater systems

Our observation suggest that the current configuration of the conveyance and treatment system in Hanoi fails in reducing bacterial contamination for safe use of wastewater in agriculture and aquaculture (WHO, 2006). In view of the scale of wastewater use in Hanoi, improvement of the current conveyance and treatment is warranted, as urban farming practices represent an important livelihood strategy (Drechsel et al., 2015). Improvements of the current system will probably require both technical and non-technical measures. In the following paragraph we describe such control measures, however, it is important to note, that they should be further assessed for their cost-effectiveness and their impact in reducing disease burden in the local context (Hanjra et al., 2011; Drechsel et al., 2015).

With regard to technical control measures, a series of options are available at different stages of the wastewater system. First, the total amount of human waste ending up in Hanoi's wastewater should be reduced. This can be achieved by improving the treatment efficiency of septic tanks through regular empting and the establishment of decentralised treatment systems such as anaerobic baffled reactors (Tilley et al., 2014). Moreover, the practice of informal disposal of faecal sludge into the wastewater conveyance system could be transformed into a more sustainable form of human waste treatment. Indeed, faecal sludge is rich in nutrients and calorific value, clearly presenting a business opportunity for waste recovery and reuse businesses (Strande et al., 2014; Bassan et al., 2015). A prominent example of faecal sludge reuse is the 'honeysuckers' in Bangalore, which earn a livelihood by collecting the sludge and selling it to farmers for field application after prior treatment of the material in drying beds (Kvarnström, 2012). However, to induce transformation in faecal sludge disposal and reuse practices, there is a need for a dialogue at community and policy levels (Strande et al., 2014). Second, the existing ponds could be upgraded to waste stabilisation ponds with controlled retention times (Tilley et al., 2014). Functional anaerobic, facultative and aerobic maturation ponds were able to reduce bacteria contamination by up to 6 log, which

Table 2
Helminth egg counts (*Ascaris lumbricoides* and *Trichuris trichiura*) and prevalence along the wastewater conveyance and treatment systems in Hanoi, Vietnam (sampling period: 4 April to 6 June 2014). For egg counts, geometric mean, standard deviation (SD), minimum and maximum concentration are indicated.

Sampling system	Egg counts/L				Prevalence rates
Helminth egg in water	Mean	SD	Min.	Max.	%
To Lich River (n = 45)					
Ascaris lumbricoides	0.07	0.33	0	2	4.4
Trichuris trichiura	0.04	0.21	0	1	4.4
Nhue River (n = 18)					
Ascaris lumbricoides	0.12	0.49	0	2	5.9
Trichuris trichiura	0	–	–	–	0
Red River (n = 18)					
Ascaris lumbricoides	0	–	–	–	0
Trichuris trichiura	0	–	–	–	0
Urban drainage: Bang B and Tam Hiep (n = 54)					
Ascaris lumbricoides	0.13	0.73	0	5	3.7
Trichuris trichiura	0.02	0.14	0	1	1.9
Urban agriculture fields: Bang B and Tam Hiep (n = 54)					
Ascaris lumbricoides	0.17	0.97	0	7	5.6
Trichuris trichiura	0.43	2.99	0	22	3.7
Peri-urban drainage: Duyen Ha (n = 27)					
Ascaris lumbricoides	0	–	–	–	0
Trichuris trichiura	0.04	0.19	0	1	1.2
Total (n = 216)					
Ascaris lumbricoides	0.10	0.64	0	7	8.3
Trichuris trichiura	0.13	1.51	0	22	6.4
Total helminth eggs (n = 216)	0.22	1.64	0	22	12.4

would allow for safe use in aquaculture and agriculture (Stenström et al., 2011). Hence, aquaculture practice could be maintained by having a final pond that is specifically assigned for this purpose. Third, regular desludging and basic screening of Nhue River should be implemented to protect downstream communities by reducing the risk of flooding events and thus avoiding dispersion of highly contaminated water and sediments (Tilley et al., 2014). This is already practiced in To Lich River and has proven feasible (World Bank, 2013). Of note, the sludge from river and drainage systems is not recommended for use because of likely contamination with heavy metals and potentially other contaminates (Ingvertsen et al., 2013).

With regard to non-technical control measures, a multi-barrier approach is recommend (Ilic et al., 2010). In practice this means that integrated disease control, including the provision of vaccination (*e.g.* for rotavirus) and preventive chemotherapy (for soil-transmitted helminthiasis), should be pursued at the level of farmers, as well as the use of personal protective equipment and health education programmes (Utzinger et al., 2009). At the level of markets, awareness on safe processing of produce is necessary to avoid cross-contamination (Nguyen et al., 2008). At consumer level, information campaigns can promote safe storage and processing of wastewater-fed products (WHO, 2006; Drechsel et al., 2015). Finally, the existing sentinel wastewater monitoring system operated by the Vietnam Environment Administration should be upgraded to a surveillance and response system (Vietnam Environment Administration, 2015). Such a system ideally includes both microbial and chemical indicators and is coupled to a pre-defined response for the event that parameter values are above set limits. Such an early warning system would not only allow to recognise trends and seasonal variability of specific health hazards but also enhance a more proactive protection of urban farming communities and consumers of their produce (WHO, 2006; Fuhrimann et al., 2015).

4.4. Limitations

Our sampling took place over an 8-week period between April and June 2014, corresponding to the main rainy season. Therefore, our findings represent a snapshot of microbial contamination along the wastewater system in the rainy season and do not allow for generalization to other seasons (Nguyen et al., 2008). As the dilution of wastewater with storm water is high during the rainy season, larger sampled quantities of wastewater could have improved the detection rate (Ayres and Mara, 1996). Moreover, it is anticipated that helminth eggs may be retained in sludge of septic tanks, soil or river sediments, which may result in underestimating the true prevalence of helminth eggs in wastewater (Strande et al., 2014). It should also be noted that other hazards, such as specific pathogens, antibiotic-resistant bacteria, heavy metals and toxic chemicals should be investigated in future studies to deepen our understanding of the overall risk for people exposed to wastewater in Hanoi.

5. Conclusions

Our results suggest that the wastewater conveyance system linked to To Lich and Nhue River fails to reduce bacterial contamination to safe levels for wastewater use in aquaculture and agriculture. This represents a public health threat for large numbers of farmers and consumers of wastewater fed-products in Hanoi. Yet, control measures at multiple stages of the wastewater system are available. Priorities should be set to improve current faecal sludge management and treatment of wastewater in existing pond systems in the peri-urban areas of Hanoi. Moreover, to protect urban farming communities downstream of Hanoi, the water quality of Nhue River needs to be improved considerably. Thus, such control measures would allow to maximise the gains from wastewater use. Our study has direct implications for sanitation safety planning approaches in rapidly expanding Asian cities and is relevant for SDG target 6.3 that seeks to ensure safe wastewater management and use in agriculture and aquaculture by 2030.

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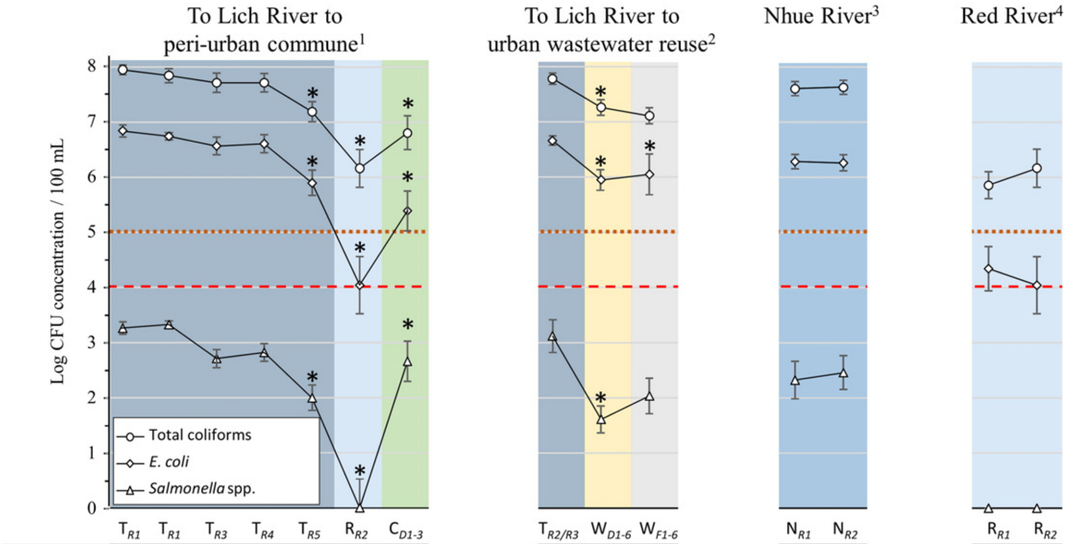

	T_{R1}	T_{R1}	T_{R3}	T_{R4}	T_{R5}	R_{R2}	C_{D1-3}	$T_{R2/R3}$	W_{D1-6}	W_{F1-6}	N_{R1}	N_{R2}	R_{R1}	R_{R2}
Total coliforms		-0.1	-0.1	<0.1	-0.5	-1.0	0.6		-0.5	-0.2		0.1		0.3
E. coli		-0.1	-0.2	0.1	-0.7	-1.9	1.4		-0.7	0.1		-0.1		-0.3
Salmonella spp.		0.1	-0.62	0.1	-0.8	-2.8	2.7		-1.5	0.4		0.1		0.1

Fig. 3. Mean log concentration of colony forming unit (CFU) total coliforms (TC) and *E. coli* and most probable number (MPN) *Salmonella* spp. and 95% confidence intervals (CIs) along the wastewater system in Hanoi, Vietnam. [1]Along To Lich River ($T_{R1–5}$) to Red River (R_{R1}) to drainage channels in Duyen Ha; [2]along To Lich River ($T_{R2/3}$) to the peri-urban wastewater conveyance, treatment and reuse system in the districts of Hoang Mai and Thanh Tri ($W_{D1–6}$ and $W_{F1–6}$); [3]along Nhue River ($N_{R1–2}$); and [4]along Red River ($R_{R1–2}$). Sampling period: 4 April to 6 June 2014. *p-values* are given for the changes in mean log concentration from the preceding to the given measuring site were assessed using the Wilcoxon rank sum test. Orange-dotted line indicating discharge limits of TC of domestic wastewater provided by the Vietnam Ministry of Natural Resources and Environment. Red-dashed line indicating verification limit for *E. coli* of the World Health Organization for safe use in unrestricted agriculture. *Significant change (<0.05) between two sampling points.

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10. ARTICLE 6: Intestinal parasitic infections and associated risk factors in communities exposed to wastewater in rural urban transition zones in Hanoi, Vietnam

Photo: To Lich River, Hanoi's main drainage channel (©S. Fuhrimann, 2014)

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RESEARCH Open Access

Intestinal parasite infections and associated risk factors in communities exposed to wastewater in urban and peri-urban transition zones in Hanoi, Vietnam

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Abstract

Background: Infections with intestinal parasites (helminths and intestinal protozoa) are endemic in Southeast Asia and inappropriate management and reuse of wastewater might exacerbate the risk of human infections. In rapidly growing urban settings, little is known about the extent of intestinal parasite infections. We assessed the point-prevalence and risk factors of intestinal parasite infections in population groups differently exposed to wastewater in urban and peri-urban transition zones in Hanoi, the capital of Vietnam.

Methods: A cross-sectional survey was carried out between April and June 2014 in people aged ≥ 18 years at risk of wastewater exposure from To Lich River: workers maintaining wastewater treatment facilities; urban farmers reusing wastewater; and urban dwellers at risk of flooding events. For comparison, two peri-urban population groups living in close proximity to the Red River were chosen: farmers using river water for irrigation purposes; and people living in the same communities. A single stool sample was subjected to Kato-Katz and formalin-ether concentration methods for the diagnosis of helminth and intestinal protozoa infections. A questionnaire was administered to determine risk factors and self-reported signs and symptoms.

Results: A total of 681 individuals had complete data records. Highest point-prevalence rates of intestinal parasite infections were observed for peri-urban farmers (30 %). Hookworm and *Trichuris trichiura* were the predominant helminth species (25 % and 5 %, respectively). Peri-urban farmers were at higher odds of infection with intestinal parasites than any other groups (adjusted odds ratio 5.8, 95 % confidence interval 2.5 to 13.7). Lack of access to improved sanitation and not receiving deworming within the past 12 months were associated with higher infection risk, while higher educational attainment and socioeconomic status were negatively associated with intestinal parasite infections.

Conclusions: Our results suggest that exposure to wastewater was not directly associated with infection with helminths and intestinal protozoa in different population groups in Hanoi. These findings might be explained by a high level of awareness of health risks and access to safe sanitary infrastructure in urban areas. The high prevalence rates observed in peri-urban farmers call for specific interventions targeting this population group.

Keywords: Helminth, Intestinal protozoa, Peri-urban farming, Urban farming, Vietnam, Wastewater

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Background

In Southeast Asia, infections with intestinal parasites (e.g. helminths and intestinal protozoa) cause a considerable public health burden [1, 2]. Despite efforts to control morbidity and interrupt transmission, infection with soil-transmitted helminths (*Ascaris lumbricoides*, hookworm, *Strongyloides stercoralis* and *Trichuris trichiura*) are common and show geographic, demographic, socioeconomic and cultural differences within and across countries of Cambodia, Lao People's Democratic Republic (PDR) and Vietnam [3–5]. In urban areas, socioeconomic development, including improvements in sanitation and water infrastructures are thought to be associated with a decline in the prevalence and intensity of intestinal parasites over the past decades [6–8]. However, in rural areas and deprived urban and peri-urban settings, access to clean water and improved sanitation remains insufficient and is an important risk factor for infections with helminth and intestinal protozoa [9, 10]. Additionally, reuse of wastewater and faeces in agriculture and aquaculture might contribute to the transmission of intestinal parasites [2, 11].

Hanoi, the capital of Vietnam, has undergone considerable economic growth since the end of the Vietnam War in 1975, resulting in a change in lifestyles and increased living standards. Moreover, population growth and rural-urban migration led to an expansion of the city boundaries [12]. Due to rapid urbanization, improved access to health care and awareness campaigns are available (i.e. yearly deworming of school-aged children and hygiene campaigns such as "eating cooked food and drinking boiled water"), which decreased prevalence of intestinal parasitic infections [13]. However, increasing volumes of domestic waste, mixed with chemical and microbial pollutants, have increased the heterogeneity in exposure to such pollutants and pathogens [14, 15]. Especially for urban and peri-urban transition zones around Hanoi, it is crucial to ensure access to basic water and sanitation infrastructures. Moreover, guidance on safe management and reuse of wastewater is needed [6, 7, 16]. It is conceivable that increasing volumes of wastewater might exacerbate the spread of intestinal parasites, enteric bacteria and viruses [16, 17]. Moreover, past extreme weather events, such as heavy rains, jeopardized the proper functionality of Hanoi's sanitation systems, with likely adverse health outcomes [18].

In urban and peri-urban areas of Hanoi, an estimated 650,000 farmers reuse wastewater in agriculture and aquaculture to supply the 6.7 million people living in the city with fresh vegetables and fish [19]. Use of wastewater comes at low cost for water and nutrients, and hence provides an important livelihood opportunity for farming communities [20]. Of note, lack of sanitation facilities and use of human excreta in such communities were shown to be a major risk factor for intestinal parasite infections. Moreover, diarrhoeal and skin diseases have been associated to occupational contact with wastewater [13, 21–24]. In more rural communities, the occupational exposure to Hanoi's reused wastewater has also been associated with *A. lumbricoides* and *T. trichiura* infections [2]. Thus, it is commonly observed in urban communities that the prevalence rates of intestinal parasitic infections are lower than in peri-urban and rural areas [1]. Over the past decade, a number of studies indicated levels of microbial and chemical pollution above national and international safety standards in the environment [15, 25–28]. Thus, pollution reduction may not be sufficient to allow for safe reuse of wastewater for agriculture and aquaculture [29].

As the city of Hanoi expanded rapidly, with annual population growth rates of up to 3.5 %, timely data on prevalence and risk factors of infection with helminths and intestinal protozoa are needed to understand the effect of urbanization in urban and peri-urban transition zones [12]. Surveys investigating prevalence rates and risk factors for parasitic diseases, diarrhoea, skin and eye infections in the urban and peri-urban environment around Hanoi are dating back to 2005 [13, 21–24]. Such data will help to effectively plan public health interventions and justify investments in sanitary infrastructures [16, 30]. The objective of the present study was to assess the prevalence rates and risks factors for intestinal parasite infections in different population groups exposed to wastewater reuse activities in Hanoi.

Methods

Study design and participants

A cross-sectional survey was conducted between April and June 2014. The study was undertaken in the southern part of Hanoi, along To Lich River (main open storm water and drainage channel of the city) and Red River (natural river stemming from the People's Republic of China that is discharged in the Gulf of Tonkin). These rivers receive most of the city's wastewater, managed by Hanoi Sewerage and Drainage Company (HSDC). However, water quality differs considerably: while water of the To Lich River is not allowing for the safe reuse of wastewater in agriculture and aquaculture according the World Health Organization (WHO) guidelines, the Red River water quality is within tolerable limits colony forming unit (CFU) total coliforms and *Escherichia coli* (4.2×10^6 CFU/100 ml and 1.7×10^4 CFU/100 ml, respectively). Helminth eggs were only found in To Lich River (0.1 egg/l), which however is still within the WHO tolerable concentration for safe reuse [16, 29]. Particular emphasis was placed to the wastewater reuse in agriculture and aquaculture in urban and peri-urban transition zones of the districts Hoang Mai and Thanh Tri (geographical coordinates: 21°01'42.5"N, 105°51'15.0"E)

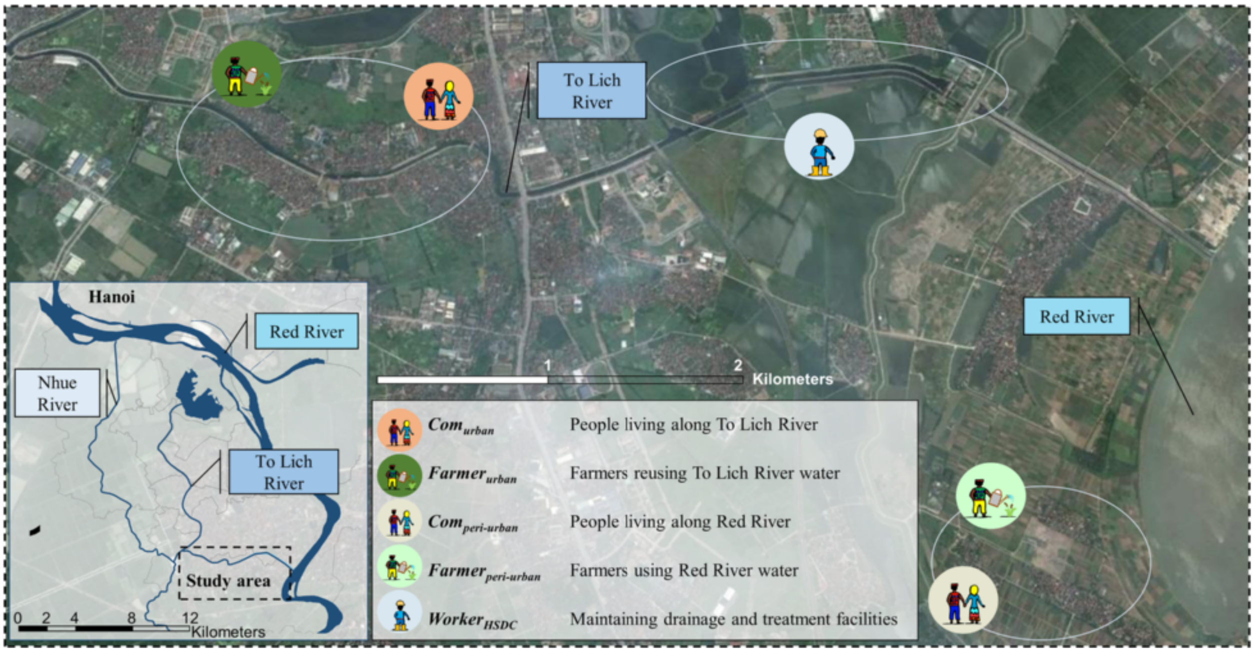


Fig. 1 Map of Hanoi showing the study area and the five exposure groups in the Than Tri district. (Map data ©2015 Google)

(Fig. 1). A detailed description of the study system and water quality of the rivers is published elsewhere [29].

The study enrolled adults (aged ≥ 18 years) living and working in urban or peri-urban areas in the two districts. According to the level of exposure to wastewater, the study participants were stratified into five population groups: three exposed to wastewater from To Lich River (i-iii); and two comparison groups living along Red River without direct exposure to urban wastewater (iv and v):

(i) “Com_{urban}”, people living in the urban to peri-urban transition zone of Hanoi, in Bang B village or Tam Hiep commune along To Lich River who are potentially exposed to wastewater while flooding events occur during the rainy season. The communities are located in Hoang Mai and Thanh Tri district, respectively (geographical coordinates: 20°57'17.54"N, 105°49'42.48"E), and are prone to rapid demographic transition, industrial development and land use change.

(ii) “$Farmer_{urban}$”, urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River. A large part of the community members (33 %) are involved in agriculture (e.g. rice, morning glory, neptunia and watercress mainly) or aquaculture activities [31].

(iii) “$Worker_{HSDC}$”, workers from HSDC maintaining drainage channels and operating the Yen So treatment plants along To Lich River.

(iv) “$Com_{peri\text{-}urban}$”, people living in Duyen Ha commune (comparison group). The commune represents a typical peri-urban community along Red River with poor sanitation and drinking water systems. The commune belongs to Thanh Tri district and is located approximately 5 km from the outskirt of Hanoi (geographical coordinates: 20° 55'42.37"N, 105°52'23.32"E).

(v) “$Farmer_{peri\text{-}urban}$”, farmers living in Duyen Ha commune using the irrigation water from Red River (comparison group). About 38 % of the people work in agriculture.

Sample size was calculated by aiming at a power of 95 %, to ensure that a reduction in effective exposure variance by 35 % following confounder adjustment would still leave 80 % power. Our assumptions were that the prevalence of intestinal parasite infections is at least 20 % in $Com_{peri\text{-}urban}$ and the odds ratio (OR) of $Farmer_{urban}$, and $Worker_{HSDC}$ to $Com_{peri\text{-}urban}$ is at least 2.5. We also assumed that the final sample size might be reduced by 15 % due to loss to follow-up. Hence, our intended sample size was 1,025 (Com_{urban}, $n = 250$; $Farmer_{urban}$, $n = 250$; $Com_{peri\text{-}urban}$, $n = 175$; $Farmer_{peri\text{-}urban}$, $n = 175$; and $Worker_{HSDC}$, $n = 150$).

The following inclusion and exclusion criteria were applied. First, households were randomly selected from two separate lists (one for farming and one for all non-farming households in the community) readily available from the communal people committees. All listed households were numbered and the appropriate number selected using a random number list from Excel. All individuals in the selected households were invited to participate in the survey. If they were willing to participate, one person per household (household heads or adults living permanently in the household) was selected for a questionnaire interview at a convenient time at the community health station. Participants were provided with a stool container and asked to return a filled container the day of the interview with her or his own morning stool sample. To select members of $Worker_{HSDC}$, the HSDC headquarter mobilized and informed the workers and randomly selected them from the existing staff list. $Worker_{HSDC}$ were then invited to come on a fixed day for the interview along with a fresh morning stool sample to the health station of the HSDC the day after the interview.

Procedures

We employed a questionnaire to determine exposure pathways to wastewater, potential confounding factors (e.g. demographic and socioeconomic), risk variables (e.g. water, sanitation, hygiene and occupation) and self-reported signs and symptoms. Our questionnaire had previously been validated in a study in Uganda [32]. The questionnaire was translated into Vietnamese, and further adapted to the Hanoi context and pre-tested among five farmers and five community members not otherwise involved in the current study. Research assistants entered data directly into tablet computers (Samsung Galaxy note 10.1 N8010) via a data entry mask using Open Data Kit (http://opendatakit.org).

Participants were invited to provide a fresh morning stool that was subjected to the Kato-Katz technique (duplicate thick smears, using standard 41.7 mg template) [33] and a formalin-ether concentration technique (FECT) [34] for the diagnosis of helminths (*A. lumbricoides*, hookworm, *T. trichiura* and other helminths) and intestinal protozoa (*Blastocystis hominis*, *Chilomastix mesnili*, *Endolimax nana*, *Entamoeba coli*, *Entamoeba histolytica*/*E. dispar*, *Entamoeba hartmanni*, *Giardia intestinalis* and *Iodamoeba bütschlii*). Kato-Katz thick smear and FECT readings were double-entered and cross-checked.

Table 1 Demographic and socioeconomic characteristics of the participants enrolled in the cross-sectional survey, stratified by five exposure groups in the Than Tri district, Hanoi, between April and June 2014

Demographic and socioeconomic characteristics/ Exposure groups[a]	$Com_{peri\text{-}urban}$		Com_{urban}		$Farmer_{peri\text{-}urban}$		$Farmer_{urban}$		$Worker_{HSDC}$	
	N = 101		*N* = 170		*N* = 129		*N* = 153		*N* = 128	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Sex										
Female	85	84.2	134	78.8	105	81.4	132	86.3	58	45.3
Male	16	15.8	36	21.2	24	18.6	21	13.7	70	54.7
Age categories (years) (mean ± SD)	50.0 ± 15.6		45.7 ± 14.5		48.7 ± 11.1		52.6 ± 10.6		41.2 ± 10.7	
Educational attainment										
Never went to school	3	3.0	7	4.1	0	0.0	5	3.3	0	0.0
Primary school	13	12.9	16	9.4	19	14.7	42	27.5	2	1.6
Secondary school	47	46.5	70	41.2	76	58.9	76	49.7	37	28.9
Tertiary school	15	14.9	59	34.7	31	24.0	27	17.6	73	57.0
University degree	23	22.8	18	10.6	3	2.3	3	2.0	16	12.5
Socioeconomic status[b]										
Most poor	28	27.7	31	18.2	51	39.5	33	21.6	12	9.4
Poor	22	21.8	49	28.8	42	32.6	48	31.4	17	13.3
Less poor	17	16.8	41	24.1	25	19.4	34	22.2	56	43.8
Least poor	34	33.7	49	28.8	11	8.5	38	24.8	43	33.6
How many people live in your household (mean ± SD)	4.7 ± 2.0		4.6 ± 1.7		4.3 ± 1.9		5.1 ± 2.6		5.3 ± 8.5	
Living at the same place (years) (mean ± SD)	34.4 ± 21.3		37.7 ± 19.8		37.8 ± 19.5		53.3 ± 56.3		34.0 ± 14.5	

[a] Exposure groups: $Com_{peri\text{-}urban}$: people living in the peri-urban commune Duyen Ha, 5 km away from the city along the Red River; Com_{urban}: people living in the urban area of Hanoi, in Bang B village or Tam Hiep commune along the To Lich River and potential exposed to wastewater; $Farmer_{peri\text{-}urban}$: peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater; $Farmer_{urban}$: urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and $Worker_{HSDC}$: workers from Hanoi Sewerage and Drainage Company (HSDC) maintaining drainage channels and operating the Yen So treatment plants

[b] Derived using principal components analysis (PCA) of the following 11 ownership items: radio, TV, mobile phone, fridge, computer, bicycle, motorbike, car, electricity, running water and latrine

Statistical analysis

Helminth- and intestinal protozo-specific proportions were compared between the five exposure groups, using Pearson's χ^2 test. Univariate logistic regression was applied to investigate for potential associations between nine dependent variables, i.e. infections with (i) any intestinal parasite; (ii) soil-transmitted helminth; (iii) intestinal protozo; (iv) *A. lumbricoides*; (v) hookworm; (vi) *T. trichiura*; (vii) 14-day diarrhoea prevalence; (viii) skin problems; and (ix) eye problems), and 20 independent variables (e.g. exposure groups, sex and age). A measure of socioeconomic status was derived, based on an asset index using principal components analysis (PCA), with participants grouped into four categories, as summarised in Table 1 (most poor, poor, less poor and least poor) [35]. Our multivariate core model included the categorical exposure variables sex, age, educational attainment and socioeconomic status [9, 36]. We then added risk factors that had a *P*-value lower than 0.2 (using likelihood ratio test) in the univariate analyses. Of note, a univariate or multivariate analysis was only conducted if the number of respective cases was above 50 or 70, respectively.

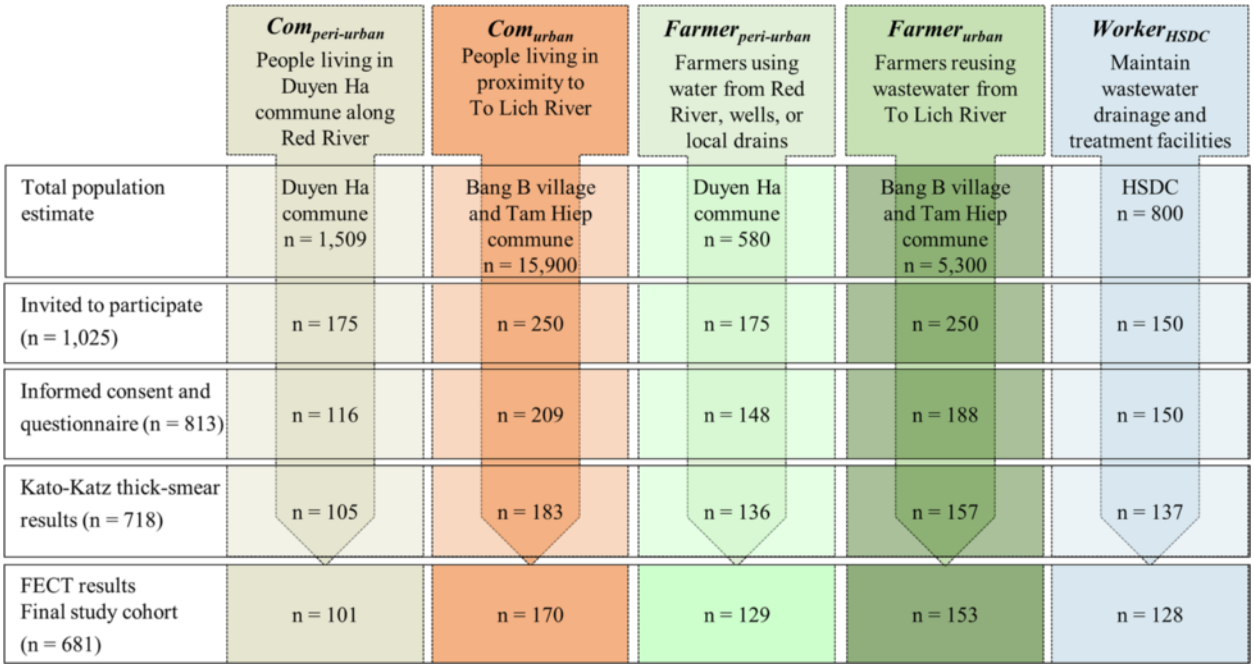
ORs were reported to compare risks. Differences and associations were considered as statistically significant if their *P*-values were below 0.05 and as indicating a trend if *P*-values were between 0.05 and 0.1. Statistical analyses were done using STATA version 12.0 (Stata Corporation; College Station, USA).

Results

Among 1,025 people invited, 813 fulfilled our inclusion criteria, provided written informed consent and completed the questionnaire interview (Fig. 2). Stool samples were provided by 718 individuals that were subjected to Kato-Katz thick smear examination. Due to insufficient volumes of stool provided, only 681 of the samples were subjected to FECT. These 681 individuals were considered as the final study cohort, composed of 170 Com_{urban}, 153 $Farmer_{urban}$, 129, $Farmer_{peri\text{-}urban}$, 128 $Worker_{HSDC}$ and 101 $Com_{peri\text{-}urban}$.

Table 1 summarises the demographic (sex, age, educational attainment, people per household, living duration at the same place) and socioeconomic characteristics, stratified by the five population groups. In brief, females accounted for 79 % and more in all exposure groups, expect for $Worker_{HSDC}$ (45 %). Most of the participants (>60 %) were aged above 40 years and attended in minimum secondary school. Socioeconomic status was highest in $Worker_{HSDC}$ and $Com_{peri\text{-}urban}$ with 34 % classified as "least poor" in both groups. The lowest socioeconomic status was observed in $Farmer_{peri\text{-}urban}$ with 40 % classified as "most poor". On average, between 4.3 and 5.3 people live in a household. Two-thirds of the participants (65 %) reported that they lived in the study area for at least ten years.

Risk factors for intestinal parasite infections, such as perceived exposure to wastewater, access to sanitation, drinking water and bath water and deworming practise



	$Com_{peri\text{-}urban}$ People living in Duyen Ha commune along Red River	Com_{urban} People living in proximity to To Lich River	$Farmer_{peri\text{-}urban}$ Farmers using water from Red River, wells, or local drains	$Farmer_{urban}$ Farmers reusing wastewater from To Lich River	$Worker_{HSDC}$ Maintain wastewater drainage and treatment facilities
Total population estimate	Duyen Ha commune n = 1,509	Bang B village and Tam Hiep commune n = 15,900	Duyen Ha commune n = 580	Bang B village and Tam Hiep commune n = 5,300	HSDC n = 800
Invited to participate (n = 1,025)	n = 175	n = 250	n = 175	n = 250	n = 150
Informed consent and questionnaire (n = 813)	n = 116	n = 209	n = 148	n = 188	n = 150
Kato-Katz thick-smear results (n = 718)	n = 105	n = 183	n = 136	n = 157	n = 137
FECT results Final study cohort (n = 681)	n = 101	n = 170	n = 129	n = 153	n = 128

Fig. 2 Flow chart indicating the enrolment of study participants and compliance, stratified into exposure groups in the cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014

Table 2 Water, sanitation and hygiene (WASH) specific risk factors of the participants enrolled in a cross-sectional survey, stratified by the five exposure groups in the Than Tri district, Hanoi, between April and June 2014

Risk factors related to water, sanitation and hygiene/ Exposure groups[a]	$Com_{peri\text{-}urban}$		Com_{urban}		$Farmer_{peri\text{-}urban}$		$Farmer_{urban}$		$Worker_{HSDC}$	
	$N = 101$		$N = 170$		$N = 129$		$N = 153$		$N = 128$	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Wastewater is …										
polluted water	87	86.1	162	95.3	111	86.0	143	93.5	126	98.4
causing health issues	83	82.2	149	87.6	96	74.4	141	92.2	126	98.4
causing environmental issues	83	82.2	149	87.6	93	72.1	135	88.2	127	99.2
Exposure to wastewater (water from rivers or lakes around Hanoi) while …										
flooding of living area	0	0.0	5	2.9	3	2.3	2	1.3	17	13.3
flooding of working area	1	1.0	9	5.3	21	16.3	59	38.6	53	41.4
washing clothes	0	0.0	0	0.0	0	0.0	1	0.7	2	1.6
cleaning of a fish pond	0	0.0	1	0.6	0	0.0	5	3.3	15	11.7
fishing	3	3.0	7	4.1	3	2.3	6	3.9	13	10.2
swimming	1	1.0	3	1.8	2	1.6	0	0.0	6	4.7
Toilet facility at household										
Flush toilet	94	93.1	167	98.2	108	83.7	147	96.1	127	99.2
Pit latrine	6	5.9	6	3.5	2	1.6	6	3.9	0	0.0
No facility (defecation in the open)	1	1.0	1	0.6	19	14.7	1	0.7	1	0.8
Toilet facility at work										
Flush toilet	91	90.1	150	88.2	61	47.3	47	30.7	39	30.5
Pit latrine	6	5.9	14	8.3	4	3.1	4	2.6	68	53.1
No facility (defecation in the open)	4	4.0	6	3.5	64	49.6	102	66.7	21	16.4
Household with tap water	82	81.2	164	96.5	102	79.1	148	96.7	126	98.4
Source of drinking water (multiple answers possible)										
Bottled water	40	39.6	65	38.2	36	27.9	41	26.8	61	47.7
Tap water	60	59.4	149	87.6	73	56.6	136	88.9	113	88.3
Rain water	14	13.9	5	2.9	18	14.0	9	5.9	7	5.5
Bore hole water	31	30.7	7	4.1	43	33.3	4	2.6	1	0.8
Source of bathing water (multiple answers possible)										
Tap water	73	72.3	150	88.2	55	42.6	70	45.8	123	96.1
Rain water	6	5.9	2	1.2	11	8.5	18	11.8	8	6.3
Bore hole water	42	41.6	16	9.4	76	58.9	9	5.9	12	9.4
Well water	2	2.0	0	0.0	4	3.1	0	0.0	2	1.6
Water from lakes or rivers	0	0.0	1	0.6	5	3.9	48	31.4	19	14.8
Preventive chemotherapy received in the past										
< 6 months	13	12.9	15	8.8	15	11.6	11	7.2	15	11.7
6 to < 12 months	9	14.1	24	14,1	12	9.3	12	7.8	20	15.6
> 12 months	75	71.2	121	71.2	96	74.4	114	74.5	87	68.0
Never took deworming	4	4.0	10	5.9	6	5.7	16	10.5	6	4.7

[a] Exposure groups: $Com_{peri\text{-}urban}$: people living in the peri-urban commune Duyen Ha, 5 km away from the city along the Red River; Com_{urban}: people living in the urban area of Hanoi, in Bang B village or Tam Hiep commune along the To Lich River and potential exposed to wastewater; $Farmer_{peri\text{-}urban}$: peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater; $Farmer_{urban}$: urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and $Worker_{HSDC}$: workers from Hanoi Sewerage and Drainage Company (HSDC) maintaining drainage channels and operating the Yen So treatment plants

are shown in Table 2. Almost 90 % of the participants exposed to wastewater perceived wastewater as polluted water, which causes ill-health and environmental risks (Com_{urban}, $Farmer_{urban}$ and $Worker_{HSDC}$), while 26 to 28 % $Farmer_{peri\text{-}urban}$ perceived no health and environmental risks due to wastewater. Past flooding of the working area was most frequently reported among $Farmer_{urban}$ (39 %) and $Worker_{HSDC}$ (41 %). Overall, 96 % of participants reported to have a toilet at home, whereas 15 % of the $Farmer_{peri\text{-}urban}$ had no accesses to sanitation and thus perform open defecation. Self-reported deworming drugs within the past six months ranged between 7 % ($Farmer_{urban}$) and 13 % ($Com_{peri\text{-}urban}$).

Table 3 shows occupational conditions (employment status, working hours, etc.) and protective factors (personal protective equipment) for $Farmer_{peri\text{-}urban}$, $Farmer_{urban}$ and $Worker_{HSDC}$. While all $Worker_{HSDC}$ reported to be officially contracted, 90 % and 91 % of the $Farmer_{peri\text{-}urban}$ and $Farmer_{urban}$ lacked an official employment status, respectively. More than 90 % of all $Worker_{HSDC}$ used different personal equipment (e.g. gloves, boots, uniform) for self-protection against wastewater exposure, while approximately 80 % farmers owned boots and gloves.

The prevalence of infection with any intestinal parasite among $Farmer_{peri\text{-}urban}$, $Farmer_{urban}$, Com_{urban}, $Worker_{HSDC}$ and $Com_{peri\text{-}urban}$ was 30 %, 11 %, 10 %, 10 % and 7 %, respectively (Table 4 and Fig. 3). Only 1 % of the participants was found with multiple intestinal parasitic infections. The highest prevalence of soil-transmitted helminths was found in $Farmer_{peri\text{-}urban}$ (25 % for hookworm and 5 % for *T. trichiura*). *Ascaris lumbricoides* was only detected in Com_{urban} and $Worker_{HSDC}$; a prevalence of 2 % and 1 %, respectively. Infections with soil-transmitted helminths were of light intensity [37]. The prevalence of intestinal protozoa was low; only nine infections with *B. coli*, *E. coli* and *G. intestinalis* were found, resulting to an overall prevalence of 1.2 %.

The prevalence of self-reported 14-day diarrhoea was not significantly different between study groups and ranged between 12 % ($Com_{peri\text{-}urban}$) and 4 % ($Farmer_{urban}$) (Table 5, Fig. 3). However, self-reported rates of skin and eye problems were significantly different between the five exposure groups. General skin problems ranged between

Table 3 Risk factors related to the occupation of workers and farmers enrolled in the cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014

Risk factors related to occupation/ Exposure groups[a]	$Farmer_{peri\text{-}urban}$		$Farmer_{urban}$		$Worker_{HSDC}$	
	N = 129		N = 153		N = 128	
	n	%	*n*	%	*n*	%
Employed	13	10.1	13	8.5	128	100
Retired	11	8.5	16	10.5	0	0
Duration worked in the current job (mean ± SD)	30.3 ± 12.9		36.9 ± 13.5		15.3 ± 9.1	
Days worked per week (mean ± SD)	6.5 ± 1.2		5.5 ± 2.1		6.2 ± 0.6	
Hours worked per week (mean ± SD)	39.8 ± 17.3		35.9 ± 23.2		50.0 ± 4.0	
Possession of personal protective equipment						
Gloves	106	82.2	113	73.9	117	91.4
Boots	107	82.9	131	85.6	110	85.9
Uniform/cotton overall	28	21.7	11	7.2	120	93.8
Rain coat with boots	29	22.5	48	31.4	120	93.8
Rain coat without boots	36	27.9	58	37.9	84	65.6
Long sleeves	97	75.2	137	89.5	48	37.5
Helmet	3	2.3	1	0.7	117	91.4
Soft hat (baseball cap)	24	18.6	37	24.2	7	5.5
Vietnamese hat	111	86.0	141	92.2	4	3.1
Face mask	110	85.3	105	68.6	121	94.5
Application of...						
Pesticides	113	87.6	117	76.5	na[b]	
Fertilizer	122	94.6	146	95.4	na	

[a] Exposure groups: $Farmer_{peri\text{-}urban}$: peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater; $Farmer_{urban}$: urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and $Worker_{HSDC}$: workers from Hanoi Sewerage and Drainage Company (HSDC) maintaining drainage channels and operating the Yen So treatment plants

[b] na, not applicable for sanitation workers

Table 4 Prevalence and intensity of parasite infections among the participants enrolled in the cross-sectional survey in Hanoi, stratified by five exposure groups in the Than Tri district, Hanoi, between April and June 2014

Prevalence of infection/ Exposure groups[a]	$Com_{peri-urban}$		Com_{urban}		$Farmer_{peri-urban}$		$Farmer_{urban}$		$Worker_{HSDC}$		Chi-square test
	N = 101		*N* = 170		*N* = 129		*N* = 153		*N* = 128		
	n	%[d]	*n*	%[c]	*n*	%[c]	*n*	%[c]	*n*	%[c]	*P*-value
Intestinal parasite[b]	7	6.9	17	10.0	39	30.2	17	11.1	13	10.2	< 0.001
Soil-transmitted helminth[c]	6	5.9	16	9.4	39	30.2	15	9.8	11	8.6	< 0.001
Intestinal protozoa	1	1.0	1	0.6	2	1.6	2	1.3	2	1.6	0.932
Hookworm	4	4.0	6	3.5	32	24.8	11	7.2	5	3.9	< 0.001
Light infection (1–1,999 epg)	4	4.0	6	3.5	32	24.8	11	7.2	4	3.1	< 0.001
Moderate infection (2,000–3,999 epg)	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8	
Trichuris trichiura	2	2.0	9	5.3	7	5.4	4	2.6	9	7.0	0.281
Light infection (1–999 EPG)	2	2.0	9	5.3	7	5.4	4	2.6	8	6.3	0.384
Moderate infection (1,000–9,999 epg)	0	0.0	0	0.0	0	0	0	0	1	0.8	
Ascaris lumbricoides	0	0.0	2	1.2	0	0	0	0	2	1.6	0.252
Light infection (1–4,999 epg)	0	0.0	2	1.2	0	0	0	0	1	0.8	< 0.001
Moderate infection (5,000–49,999 epg)	0	0.0	0	0.0	0	0	0	0	0	0.0	< 0.001
Giardia intestinalis	0	0.0	1	0.6	0	0	0	0	1	0.8	0.612
Entamoeba coli	0	0.0	1	0.6	1	0.8	2	1.3	1	0.8	0.833
Entamoeba histolytica/E. dispar	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	na
Balantidium coli	1	1.0	0	0.0	1	0.8	0	0.0	0	0.0	0.403

[a] Exposure groups: $Com_{peri-urban}$: people living in the peri-urban commune Duyen Ha, 5 km away from the city along the Red River; Com_{urban}: people living in the urban area of Hanoi, in Bang B village or Tam Hiep commune along the To Lich River and potential exposed to wastewater; $Farmer_{peri-urban}$: peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater; $Farmer_{urban}$: urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and $Worker_{HSDC}$: workers from Hanoi Sewerage and Drainage Company (HSDC) maintaining drainage channels and operating the Yen So treatment plants

[b] Intestinal parasitic infection includes: *Ascaris lumbricoides*, *Trichuris trichiura*, hookworm and any intestinal protozoa

[c] Soil-transmitted helminth infection includes: *Ascaris lumbricoides*, *Trichuris trichiura*, hookworm

[d] Prevalence rate is calculated out of the results of the examination of a single stool sample by means of duplicate Kato-Katz and the formalin-ether concentration method, infection intensity by the examination via duplicate Kato-Katz

Abbreviation: *epg*, eggs per gram; *na*, not applicable

27 % ($Farmer_{peri-urban}$) and 12 % ($Farmer_{urban}$). Eye problems were most frequently reported in $Farmer_{urban}$ (38 %), followed by $Worker_{HSDC}$ (34 %) and Com_{urban} (29 %), whereas considerably lower rates of 22 % and 21 % were found in $Farmer_{peri-urban}$ and $Com_{peri-urban}$.

$Farmer_{peri-urban}$ had the highest adjusted odds of intestinal parasitic infection compared to the other groups (aOR 5.3, 95 % CI: 2.1–13.7) (Table 6 and Fig. 3). Higher educational attainment and socioeconomic status were negatively associated with parasitic infections, though without statistical significance. Lack of access to toilet at home and not being dewormed for more than 12 months showed an almost significant positive association with intestinal parasitic infection (aOR 3.1, 95 % CI: 0.9–11.0 and aOR 2.5, 95 % CI: 0.9–7.0, respectively). By means of univariate regression analysis, higher odds for intestinal parasite infections were observed by at least a factor of 1.7 for all exposure groups when compared to $Farmer_{peri-urban}$ (Fig. 3 and Additional file 1: Tables S1-S6). For hookworm infections, increased risks were observed among $Farmer_{peri-urban}$ and $Farmer_{urban}$ (OR 8.0, 95 % CI: 2.7–23.5 and 1.9, 95 % CI: 2.7–6.1, respectively). For *T. trichiura* infection, highest risks were observed in $Worker_{HSDC}$ (OR 3.7, 95 % CI: 0.8–17.7). Risks for eye problems were highest in participants with exposure to wastewater; $Farmer_{urban}$, Com_{urban} and $Worker_{HSDC}$ (OR of 2.3, 95 % CI: 1.5–1.9, respectively). No trend for a difference in risk between the exposure groups was observed for 14-day diarrhoea prevalence.

Discussion

We report prevalence rates of, and risk factors for, intestinal parasite infections in urban and peri-urban communities that are at different levels of exposure to the wastewater reuse system in Hanoi, Vietnam. The highest prevalence of intestinal parasite infections was observed in peri-urban farmers (30 %), whereas lower prevalences (< 11 %) were found in urban farmers reusing wastewater, workers who maintain the wastewater channels and common urban and peri-urban community members. Hookworm was the predominate soil-transmitted helminth with an overall prevalence of 25 % in peri-urban farmers. Peri-urban farmers were at a significantly higher

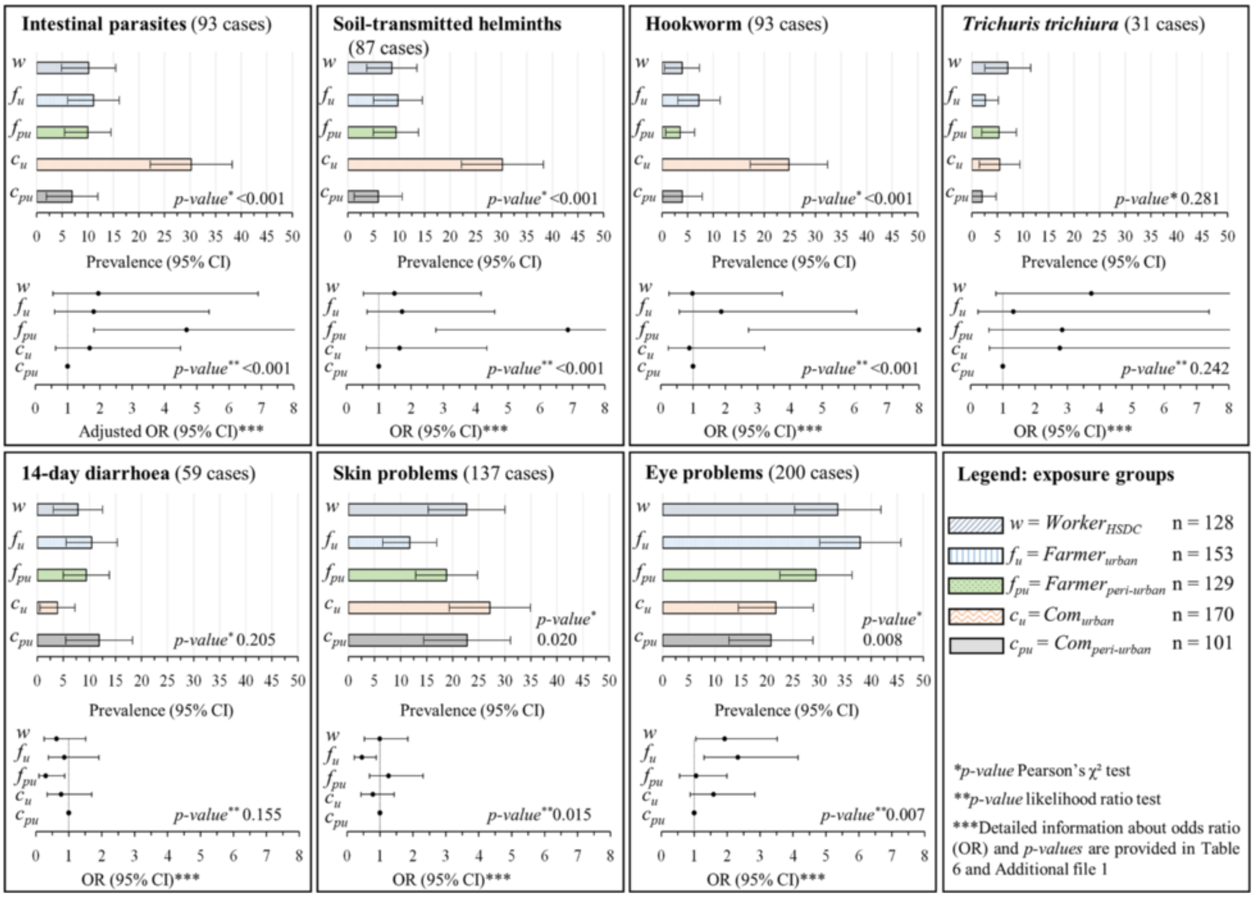


Fig. 3 Prevalence rates and adjusted odds ratios (OR) with 95 % confidence intervals (CIs) for infection with any intestinal parasite, soil-transmitted helminth, hookworm, *Trichuris trichiura* and self-reported diarrhoea, skin problems and eye problems in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014. Data for (i)"$Com_{peri\text{-}urban}$" = people living in the peri-urban commune Duyen Ha 5 km away from the city along the Red River; (ii) "Com_{urban}" = people living in the urban area of Hanoi, in Bang B village or Tam Hiep commune along the To Lich River and potential exposed to wastewater; (iii) "$Farmer_{peri\text{-}urban}$" = peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater; (iv) "$Farmer_{urban}$" = urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and (v) "$Worker_{HSDC}$" = workers from Hanoi Sewerage and Drainage Company (HSDC) maintaining drainage channels and operating the Yen So treatment plants

odds of intestinal parasite infection compared to other groups (aOR 5.3, 95 % CI: 2.1–13.7). The considerable risk for intestinal parasite infection in this group might be explained, at least partially, by a reported lack of access to toilet facility at home and a general lack of awareness towards the health risk in regard to wastewater among peri-urban farmers. Moreover, it was striking that 72 % of all participants reported to not having received deworming within the past 12 months before the study.

The observed differences between rural and peri-urban communities, especially in farmers, are in line with previous reports from studies in Asia and other parts of the world, indicating that urbanization is related to a decline of intestinal parasites [1, 6]. We found that at least one third of the peri-urban inhabitants rely on bore hole water as source for drinking or bathing and that 15 % of the peri-urban inhabitants had no access to toilet facilities at their home. Our findings support the conclusions of Do and colleagues who conducted a cross-sectional survey in Yen So commune in Hanoi in 2002 that revealed similar risk of intestinal parasite infections among urban farmers handling wastewater compared to peri-urban farmers [38]. However, prevalence rates of species-specific soil-transmitted helminths were considerably higher across all participants [*A. lumbricoides* (21.6 %), *T. trichiura* (9.8 %) and hookworm (21.8 %)] in [38], as compared to prevalences of 0.4 %, 4.4 % and 8.4 %, respectively, observed in our study. These considerably lower rates might suggest that the various improvements due to education and socioeconomic development in face of urbanization helped to bring down the prevalence of intestinal parasites over the last decade. Another reason is that people in many parts of

Table 5 Self-reported health outcomes experienced in the last two weeks before the interview among the participants enrolled in a cross-sectional survey stratified by five exposure groups in the Than Tri district, Hanoi, between April and June 2014

Self-reported health issues over the past 2 weeks/ Exposure group[a]	$Com_{peri-urban}$		Com_{urban}		$Farmer_{peri-urban}$		$Farmer_{urban}$		$Worker_{HSDC}$		Chi-square test
	N = 101		N = 170		N = 129		N = 153		N = 128		
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*P*-value
Diarrhoea											
14-day prevalence	12	11.9	16	9.4	5	3.9	16	10.5	10	7.8	0.205
7-day prevalence	10	9.9	11	6.5	4	3.1	12	7.8	7	5.5	0.279
Number of episodes (14 days)											
1	9	8.9	12	7.1	5	3.9	12	7.8	6	4.7	0.411
2	0	0.0	3	1.8	0	0.0	1	0.7	3	2.3	
3	2	2.0	0	0.0	0	0.0	2	1.3	1	0.8	
4	1	1.0	1	0.6	0	0.0	0	0.0	0	0.0	
Eye problems (one or more symptoms)	21	20.8	50	29.4	28	21.7	58	37.9	43	33.6	0.008
Eye irritation	8	7.9	6	3.5	10	7.7	23	15.0	32	25.0	< 0.001
Sensitivity to light	2	2.0	1	0.6	0	0.0	5	3.3	3	2.3	0.172
Other eye problems	11	10.9	45	26.4	18	14.0	41	26.8	13	10.2	0.352
Skin problems (one or more symptoms)	23	22.8	32	18.8	35	27.1	18	11.8	29	22.7	0.024
Skin irritation	3	3.0	5	2.9	6	4.7	2	1.3	13	10.2	0.004
Itching	21	20.8	22	12.9	29	22.5	10	6.5	18	14.1	0.001
Other skin problems	0	0.0	10	5.9	3	2.3	10	6.5	5	4.7	0.402
Other self-reported signs and symptoms											
Headache	38	37.6	69	40.6	68	52.7	84	54.9	50	39.1	0.006
Fever	7	6.9	8	4.7	9	7.0	10	6.5	4	3.1	0.591
Abdominal pain	27	26.7	40	23.5	39	30.2	42	27.5	26	20.3	0.398
Acute coughing	25	24.8	46	27.1	39	30.2	44	28.8	40	31.3	0.822
Chronic coughing	5	5.0	15	8.8	1	0.8	14	9.2	2	1.6	0.002
Chest pain	13	12.9	30	17.6	23	17.8	30	19.6	18	14.1	0.582
Loss of weight	14	13.9	16	9.4	14	10.9	17	11.1	5	3.9	0.113
Nausea	12	11.9	16	9.4	7	5.4	15	9.8	5	3.9	0.125
Vomiting	2	2.0	3	1.8	2	1.6	3	2.0	1	0.8	0.941
Vomiting of blood	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0.485
Muscle pain	19	18.8	43	25.3	32	24.8	52	34.0	33	25.8	0.097
Back pain	48	47.5	80	47.1	77	59.7	102	66.7	45	35.2	< 0.001
Joint pain	30	29.7	74	43.5	68	52.7	91	59.5	29	22.7	< 0.001
Injuries	3	3.0	8	4.7	5	3.9	8	5.2	5	3.9	0.922

[a] Exposure groups: $Com_{peri-urban}$: people living in the peri-urban commune Duyen Ha, 5 km away from the city along the Red River; Com_{urban}: people living in the urban area of Hanoi, in Bang B village or Tam Hiep commune along the To Lich River and potential exposed to wastewater; $Farmer_{peri-urban}$: peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater; $Farmer_{urban}$: urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and $Worker_{HSDC}$: workers from Hanoi Sewerage and Drainage Company (HSDC) maintaining drainage channels and operating the Yen So treatment plants

Southeast Asia are being targeted by preventive chemotherapy against soil-transmitted helminthiasis and other neglected tropical diseases [39, 40]. The low prevalence of *A. lumbricoides* and *T. trichiura* infections correlates with concentrations of < 1 egg/l found in the environment and the presumed low infection risk of *A. lumbricoides* and *T. trichiura* [29]. However, the absence of hookworm eggs does not correlate with the respective prevalence in the exposure groups, especially in peri-urban farmers [29]. This may be explained by the fact that only hookworm eggs in water were assessed, while larval stages and eggs in soil or sediments were not [41]. Another reason for hookworm transmission could be open defecation, which is mainly practised

Table 6 Results of univariate and multivariate logistic regression analysis for total parasitic infections (*Ascaris lumbricoides*, *Trichuris trichiura*, hookworm and intestinal protozoa) in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014

Intestinal parasitic infection[a] (total population, $N = 681$; infections 13.6 %, $n = 93$)		Infections		Univariate logistic regression[c]				Multivariate logistic regression[c]			
		n	%	OR	95 % CI		*P*-value[d]	aOR	95 % CI		*P*-value[d]
Exposure group[b]	$Com_{\mathbf{peri\text{-}urban}}$	101	6.9	1.00			< 0.001	1.00			
	$Com_{\mathbf{urban}}$	170	10.0	1.49	0.60	3.73	0.392	1.61	0.61	4.22	0.333
	$Farmer_{\mathbf{peri\text{-}urban}}$	129	30.3	5.82	2.48	13.68	< 0.001	5.30	2.05	13.69	0.001
	$Farmer_{\mathbf{urban}}$	153	11.1	1.68	0.67	4.21	0.269	1.72	0.60	4.91	0.314
	$Worker_{HSDC}$	128	10.2	1.52	0.58	3.96	0.393	2.11	0.71	6.24	0.179
Sex	Male	166	12.1	1.00							
	Female	512	14.6	0.84	0.49	1.42	0.511	0.77	0.42	1.41	0.395
Age				1.02	1.01	1.04	0.001	1.01	1.00	1.03	0.122
Educational attainment	Never went to school	15	20.0	1.00			0.035				
	Primary school	92	16.3	0.78	0.20	3.10	0.723	0.67	0.15	3.03	0.604
	Secondary school	306	17.0	0.82	0.22	3.00	0.763	0.68	0.16	2.96	0.605
	Tertiary school	205	8.8	0.39	0.10	1.49	0.167	0.33	0.07	1.62	0.173
	Higher education	63	7.9	0.34	0.07	1.64	0.181	0.51	0.09	3.01	0.459
Socioeconomic status	Most poor	155	18.6	1.00			0.114				
	Poor	178	11.8	0.61	0.33	1.12	0.110	0.89	0.44	1.82	0.754
	Less poor	173	15.6	0.84	0.47	1.50	0.552	1.80	0.86	3.74	0.116
	Least poor	175	9.7	0.49	0.26	0.93	0.030	1.07	0.48	2.39	0.868
Number of people per household				0.90	0.79	1.01	0.067	0.93	0.82	1.05	0.250
Toilet facility at home	Yes	661	12.9	1.00							
	No	20	40.0	5.14	2.10	12.57	< 0.001	3.12	0.88	11.03	0.078
Toilet facility at work	Yes	458	12.1	1.00							
	No	195	17.4	1.54	0.96	2.48	0.076	0.87	0.47	1.60	0.653
Wastewater cause health issues	No	86	22.1	1.00							
	Yes	595	12.4	0.50	0.28	0.88	0.016	0.74	0.39	1.40	0.352
Flooding of living area	No	654	13.9	1.00							
	Yes	27	7.4	0.49	0.12	2.13	0.344				
Flooding of working area	No	538	13.4	1.00							
	Yes	143	14.7	1.11	0.66	1.88	0.687				
Drinking tap water	No	150	14.0	1.00							
	Yes	531	13.6	0.96	0.57	1.63	0.890				
Drinking rain water	No	628	13.4	1.00							
	Yes	53	17.0	1.32	0.62	2.81	0.464				
Drinking bore hole water	No	595	12.9	1.00							
	Yes	86	18.6	1.54	0.85	2.78	0.155	0.91	0.41	2.01	0.808
Bathing with tap water	No	90	16.7	1.00							
	Yes	591	13.2	1.69	0.71	4.00	0.232				
Bathing with rain water	No	647	13.3	1.00							
	Yes	34	20.6	1.31	0.80	2.13	0.278				
Bathing with bore hole water	No	514	12.8	1.00							

Table 6 Results of univariate and multivariate logistic regression analysis for total parasitic infections (*Ascaris lumbricoides*, *Trichuris trichiura*, hookworm and intestinal protozoa) in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014 *(Continued)*

	Yes	167	16.2	1.27	0.15	10.97	0.830				
Preventive chemotherapy received in the past	< 6 months	69	7.2	1.00			*0.038*				
	6 to <12 months	77	6.5	0.89	0.25	3.21	0.857	0.83	0.20	3.42	0.798
	<12 months	493	15.6	2.37	0.92	6.08	0.073	2.53	0.92	6.95	0.072
	Never took deworming	42	14.3	2.13	0.61	7.48	0.237	1.87	0.48	7.25	0.363

[a] Intestinal parasitic infection includes: *Ascaris lumbricoides*, *Trichuris trichiura*, hookworm and any intestinal protozoa

[b] Exposure groups: $Com_{peri\text{-}urban}$: people living in the peri-urban commune Duyen Ha, 5 km away from the city along the Red River; Com_{urban}: people living in the urban area of Hanoi, in Bang B village or Tam Hiep commune along the To Lich River and potential exposed to wastewater; $Farmer_{peri\text{-}urban}$: peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater; $Farmer_{urban}$: urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and $Worker_{HSDC}$: workers from Hanoi Sewerage and Drainage Company (HSDC) maintaining drainage channels and operating the Yen So treatment plants

[c] *P*-values were obtained from likelihood ratio tests. The core of the multivariate model included exposure group, sex, age, educational attainment, socioeconomic status and number of people per household. In addition, all risk factors with a *P*-value < 0.2 in the univariate analyses were included into the multivariate regression analysis (as indicated in the table)

[d] *P*-values were obtained from likelihood ratio tests overall *P*-value of the respective categorical variable are indicated in italic letters

by peri-urban farmers, due to a lack of access to toilet facilities at home and at work [9]. Overall, the prevalence of intestinal protozoa detected in the current study (< 2 %) was considerably lower than what has been reported from rural communities along Nhue River in Hanam province [11]. However, other intestinal protozoa species that were not detected by our diagnostic approach, such as *Cryptosporidium* spp. and *Cyclospora* spp., may be of importance [42]. The higher prevalence of diarrhoea, skin and eye diseases in farmers and workers exposed to wastewater compared to other groups is in line with reports from other studies conducted around Hanoi and along sanitation chains of urban and peri-urban settings [23, 24, 32]. Hence, further risk profiling such as quantitative microbial risk assessment (QMRA) or chemical risk assessments should be pursued for specific causative hazards (i.e. pathogenic bacteria, viruses and toxic chemicals, such as heavy metals, pesticides and fertilizers).

Our study has several limitations. First, the general attendance was lower than anticipated, and hence, we did not achieve the intended sample size. Results must be interpreted with caution. Secondly, most of the participants were females aged 40 years and above. Hence, our sample is not representative of the general population. However, it is representative for Hanoi's farmers as farming activities in urban and peri-urban communities are indeed mostly carried out by older women [43]. Thirdly, a single stool sample was examined, and hence, the point-prevalence rates of helminth and intestinal protozoa infections were underestimated [44]. In order to increase the sensitivity and to have a more precise understanding of the diversity of pathogenic organisms, multiple stool samples and a suite of highly sensitive diagnostic approaches such as polymerase chain reaction (PCR) or a metagenomics approach should be considered [45, 46]. Fourthly, since this study only reflects one point in time, i.e. the rainy season, we may have missed seasonal outbreaks of typhoid, cholera and other diseases. More generally, there might be seasonal patterns of intestinal parasite infections, not captured by our study design [47–49]. Finally, it has been shown that self-reported disease outcomes (e.g. diarrhoea, skin and eye problems) are prone to reporting bias. Hence, longitudinal monitoring of diarrhoea incidence by well-trained health personnel are warranted to obtain a more accurate understanding [50].

Despite these limitations, our findings raise a number of important issues. First, even though the risk of parasite infection was relatively low, other pathogenic organisms such as viruses or bacteria may be transmitted directly or indirectly via the crops and fish produced with wastewater, which may give rise to diarrhoea, skin and eye diseases as reported by the participants of our study [16]. Secondly, even though we found low prevalence in adults, intestinal parasite infections may be a health issue in school-aged children in these settings, as children may play in agriculture fields or swim in ponds fed with wastewater. This is underlined by a study published in 2004, which detected a high prevalence rate in schoolchildren (77 %), particularly *T. trichiura* (67 %) and *A. lumbricoides* (34 %), in the area around Hanoi [51]. Thirdly, integrated strategies to control or eliminate intestinal parasitic infections in such urban and peri-urban transition zones are needed [52, 53]. For example, adapted risk analysis frameworks and transmission assessment surveys of intestinal parasitic infections to break transmission cycles and approach local elimination of intestinal parasitic infections [54].

Conclusions

Taken together, our results suggest that peri-urban farmers are at higher risk of intestinal parasitic infections than their urban counterparts, even though exposure to highly contaminated wastewater is less common. Peri-urban communities, located only 5 km away from the urban area have limited access to improved sanitation and lack awareness towards health risks of exposure to contained water, which is associated with a high prevalence of intestinal parasitic infections. We recommend further quantitative risk assessments of microbial and chemical hazards and transmission assessment surveys of intestinal parasite infections, diarrhoeal, skin and eye diseases. Hence, there is a need for the implementation of control strategies to break transmission cycles, approach local elimination of parasitic infections and reduce risk for diarrhoea in urban and peri-urban transition zones in Hanoi and other cities in Southeast Asia.

Additional file

Additional file 1: Univariate logistic regression models for intestinal parasitic infections and self-reported signs. **Table S1.** Results of univariate logistic regression analysis for soil-transmitted helminth infections (*Ascaris lumbricoides*, *Trichuris trichiura* and hookworm) in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014. **Table S2.** Results of univariate logistic regression analysis for *Trichuris trichiura* infections in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014. **Table S3.** Results of univariate logistic regression analysis for hookworm infections in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014. **Table S4.** Results of univariate logistic regression analysis for self-reported 14-days diarrhoea in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014. **Table S5.** Results of univariate logistic regression analysis for self-reported skin problems in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014. **Table S6.** Results of univariate logistic regression analysis for self-reported eye problems in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014. (DOCX 106 kb)

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Authors' contributions

All authors contributed to the study design. SF and PPD managed the study. SF and MSW drafted the manuscript. All authors contributed to redrafting the paper. All authors read and approved the final version of the manuscript.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The study protocol was approved by the institutional research commission of the Swiss Tropical and Public Health Institute (Swiss TPH; Basel, Switzerland; reference no. FK#106). Ethical approval was obtained from the ethics committee of the cantons of Basel-Stadt and Basel-Landschaft (EKBB; reference no. 137/13) and the Hanoi School of Public Health (Hanoi, Vietnam; reference no. 010/2014/YTCC-HD3). This study is registered with the clinical trial registry ISRCTN (identifier: ISRCTN13601686).

All participants were informed about the purpose, procedures, and the potential risk and benefits of the study and they were invited to sign a written informed consent. Those with informed consent were assigned a unique identifier. In case of illiteracy, thumb-print and signature of a witness was requested. Results were communicated to participants and those found infected with soil-transmitted helminths were treated according to national guidelines with a single oral dose of albendazole (400 mg). Participants found infected with intestinal protozoa were referred to a local health centre.

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11. ARTICLE 7: Disease burden due to gastrointestinal pathogens in wastewater along the major wastewater system in Hanoi, Vietnam

Photo: Urban farmer using water from To Lich River in Hanoi, Vietnam (©S. Fuhrimann, 2014)

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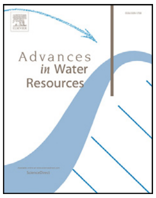

Disease burden due to gastrointestinal infections among people living along the major wastewater system in Hanoi, Vietnam

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ABSTRACT

Background: Despite recent improvements of wastewater treatment capacities in urban areas of Hanoi, Vietnam, microbial pollution is still considerable. There is a paucity of burden estimates due to gastrointestinal infection in people living along the wastewater system, and among people who are in direct contact with the wastewater, such as farmers using wastewater in agriculture and aquaculture.
Methods: A quantitative microbial risk assessment (QMRA) was pursued focussing on four population groups characterised by different levels of exposure to wastewater: (i) workers maintaining the wastewater conveyance and treatment systems; (ii) urban farmers using wastewater from To Lich River; (iii) community members in urban areas exposed to flooding events in the districts of Hoang Mai and Thanh Tri; and (iv) peri-urban farmers in Thanh Tri district, where Red River water is used for agriculture and aquaculture. The QMRA was developed on the basis of measured concentration of *Escherichia coli* and *Salmonella* spp. and *Ascaris* spp. eggs in water samples. Published ratios between measured organisms and pathogenic strains of norovirus, rotavirus, *Campylobacter* spp., pathogenic *E. coli*, pathogenic *Salmonella* spp., *Cryptosporidium* spp. and *Ascaris lumbricoides* were employed to estimate annual risk of gastrointestinal infection and disease burden.
Results: The QMRA estimated a disease burden of 0.011 disability-adjusted life years (DALYs) per person per year in urban farmers, 0.006 DALYs for sanitation workers, 0.0005 DALYs for urban communities at risk of flooding events and 0.0004 DALYs for peri-urban farmers. Urban farmers had considerably higher incidence estimates for gastrointestinal disease episodes per year (2.0) compared to the other exposure groups (≤ 1.0).
Conclusions: Urban farmers using wastewater from To Lich River have a high gastrointestinal disease burden, which is about 100 times larger than the health-based targets for wastewater use set by the World Health Organization. These findings are of direct public health relevance and call for upgrading Hanoi's wastewater system to reduce microbial contamination. Finally, this study presents a first example on how to link QMRA to a sanitation safety planning (SSP) approach in an Asian context and its findings are interesting in the frame of Sustainable Development Goal (SDGs) #6.

1. Introduction

In many urban centres in low- and middle-income countries (LMICs) large quantities of untreated or partially treated wastewater are discharged into the environment (Evans et al., 2012; Drechsel et al., 2015). At the same time, there is an increasing demand of nutrients and energy in these contexts. This renders untreated wastewater – a resource that is rich in nutrients (e.g. nitrogen and phosphorus) – attractive for use in urban agriculture and aquaculture (Qadir et al., 2010; Hamilton et al., 2013). Indeed, planned use of treated wastewater in agriculture is projected to more than triple globally, from about 7 km^3 in 2011 to 26 km^3 in 2030 (Global Water Intelligence, 2014; AQUASTAT, 2015). Considerably larger volumes of only partially treated or untreated wastewater are used in agriculture (e.g. through diversion of

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water from wastewater receiving surface water bodies) (Fuhrimann et al., 2014, 2015; WHO, 2015). In Hanoi, for example, an estimated 660,000 farmers use wastewater for vegetable and rice farming and aquaculture on a surface area of approximately 44,000 ha (Raschid-Sally and Jayakody, 2008).

While the use of wastewater is an important livelihood strategy for poor urban farmers, there are important public health concerns (Winkler et al., 2016). In Southeast Asian cities, such as Hanoi, large quantities of insufficiently treated effluents contaminate surface waters and soils, resulting in high concentrations of pathogenic organisms and toxic chemicals (Kuroda et al., 2015; Fuhrimann et al., 2016a). This is explained by the fact that most of the 6.7 million people living in Hanoi rely on flush toilets directly connected to septic tanks from where the partially treated effluents are discharged into a complex network of drainage channels, which additionally receive effluents from industries (Fuhrimann et al., 2016b). Of note, faecal sludge from septic tanks is often informally discarded into the environment; in many cases directly into agricultural fields or ponds used for aquaculture (Bassan et al., 2015). In response, wastewater flows have been largely controlled by channelization of the main urban rivers, water gates and sedimentation pond systems to prevent flooding and to treat wastewater before use in agriculture and aquaculture (Nguyen and Parkinson, 2005; World Bank, 2013).

In a recent water quality assessment we found that, despite efforts to improve Hanoi's wastewater conveyance and treatment systems, water deriving from the wastewater channels being used in agricultural fields for irrigation is heavily contaminated with total coliforms (TC), *Escherichia coli* and *Salmonella* spp. (Fuhrimann et al., 2016a). Observed values were up to 110-fold above Vietnamese discharge limits for restricted agriculture and up to 260-fold above the World Health Organization (WHO)'s tolerable safety limits for unrestricted agriculture (Fuhrimann et al., 2016a). Additionally, a cross-sectional epidemiological survey revealed high prevalence of intestinal parasite infections in peri-urban and urban farmers (up to 30%), general communities (up to 10%) and workers maintaining the wastewater channels (10%) (Fuhrimann et al., 2016b). In the aforementioned study, the prevalence of self-reported diarrhoea episodes (recall period: 2 weeks) in adults in peri-urban communities, urban farmers and sanitation workers was 8–12%. These observations suggest that treatment efficacy of Hanoi's wastewater management system is insufficient in preventing microbial contamination. Consequently, people exposed to wastewater are at risk of gastrointestinal infection. However, prior research does not provide an estimate of the magnitude of the disease burden caused by specific pathogenic organisms (Katukiza et al., 2013; Machdar et al., 2013). The 2010 Global Burden of Disease (GBD) study estimated the burden caused by diarrhoeal diseases at 0.002 disability-adjusted life years (DALYs) per person per year (pppy) for an average Vietnamese, which is considerably higher than the WHO's health-based target for the exposure to wastewater (a tolerable additional burden between $10^{-6}$and 0.0001 DALYs pppy is suggested) (WHO, 2006; Mara et al., 2010; Institute for Health Metrics and Evaluation, 2015). Context-specific disease burden estimates are, however, relevant to compare the impact of individual pathogens for different population groups, and to govern control measures in the wastewater system (Drechsel and Seidu, 2011).

Here we present a quantitative microbial risk assessment (QMRA), which is linked a sanitation safety planning (SSP) approach (WHO, 2015) with three specific objectives: (i) to estimate the disease burden due to gastroenteritis resulting from exposure to water-borne pathogens along the major wastewater system in Hanoi (Fuhrimann et al., 2016a); (ii) to validate model estimates with findings obtained from a cross-sectional epidemiological survey (Fuhrimann et al., 2016b, 2016c); and (iii) to compare disease burden estimates with national and international standards and estimates (Institute for Health Metrics and Evaluation, 2015; Fuhrimann et al., 2016d).

2.1. Ethical considerations

The study protocol was approved by the institutional research commission of the Swiss Tropical and Public Health Institute (Swiss TPH; Basel, Switzerland; reference no. FK #106). Ethical approval was obtained from the ethics committee in Basel, Switzerland (EKBB; reference no. 137/13) and the Hanoi School of Public Health (HSPH; Hanoi, Vietnam; reference no. 010/2014/YTCC–HD3). This study is registered with the clinical trial registry ISRCTN (identifier: ISRCTN13601686).

2.2. Study area

Hanoi is located in the north of Vietnam, situated at the Red River delta (geographical coordinates: 21°01′42.5″ N latitude and 105°51′15.0″ E longitude). The climate is sub-tropical with the main rainy season occurring from April to September and a year-round humidity of 80–90% (Climate-Data.org, 2015). The wastewater flows through the city, from north to south, along a topographic gradient of 20 m to 5 m above mean sea level in three main rivers: To Lich, Nhue and Red (Nguyen and Parkinson, 2005; Kuroda et al., 2015) (Fig. 1).

Our study focussed on three specific parts of Hanoi's wastewater system: (i) the To Lich River, which receives most of Hanoi's storm- and wastewater and the Yen Son treatment plant (operated by the Hanoi Sewerage and Drainage Company (HSDC)); (ii) two typical urban communes (Bang B and Tam Hiep) where wastewater from To Lich River is used for agriculture and aquaculture; and (iii) the peri-urban commune Duyen Ha where Red River water (considered as clean) is used in agriculture and aquaculture (Fuhrimann et al., 2016a, 2016b).

2.3. Hazard identification

The hazards considered for the QMRA are seven pathogenic organisms giving rise to gastroenteritis in Vietnam and elsewhere: two types of viruses (norovirus and rotavirus), three different bacteria (*Campylobacter* spp., *Salmonella* spp. and *E. coli*), one intestinal protozoon (*Cryptosporidium* spp.) and one species of soil-transmitted helminths (*Ascaris lumbricoides*) (Becker et al., 2013; Katukiza et al., 2013; Barker et al., 2014; Gibney et al., 2014; Fuhrimann et al., 2016d). These pathogens are characterised by faecal-oral transmission, can persist for weeks or months in the environment and are difficult to inactivate with conventional wastewater treatment processes such as those applied in Hanoi (Kuroda et al., 2015; Fuhrimann et al., 2016a). Our selection is further justified on the following grounds:

- Rotavirus is one of the leading cause of childhood diarrhoea (Bodhidatta et al., 2007).
- Norovirus is the major cause of diarrhoeal disease in adults and its secondary attack rate is known to be high causing epidemic situation (Barker, 2014; Mok et al., 2014).
- *Campylobacter* spp. are zoonotic bacteria that cause campylobacteriosis, with *Campylobacter jejuni* being a common cause of diarrhoea in LMICs (Kaakoush et al., 2015).
- *E. coli* belongs to the normal gastrointestinal microflora of warm-blooded animals and humans, whilst different types of *E. coli* (e.g. enterotoxigenic *E. coli*, enteroinvasive *E. coli* and enterohemorrhaghic *E. coli*) have been associated with diarrhoeal

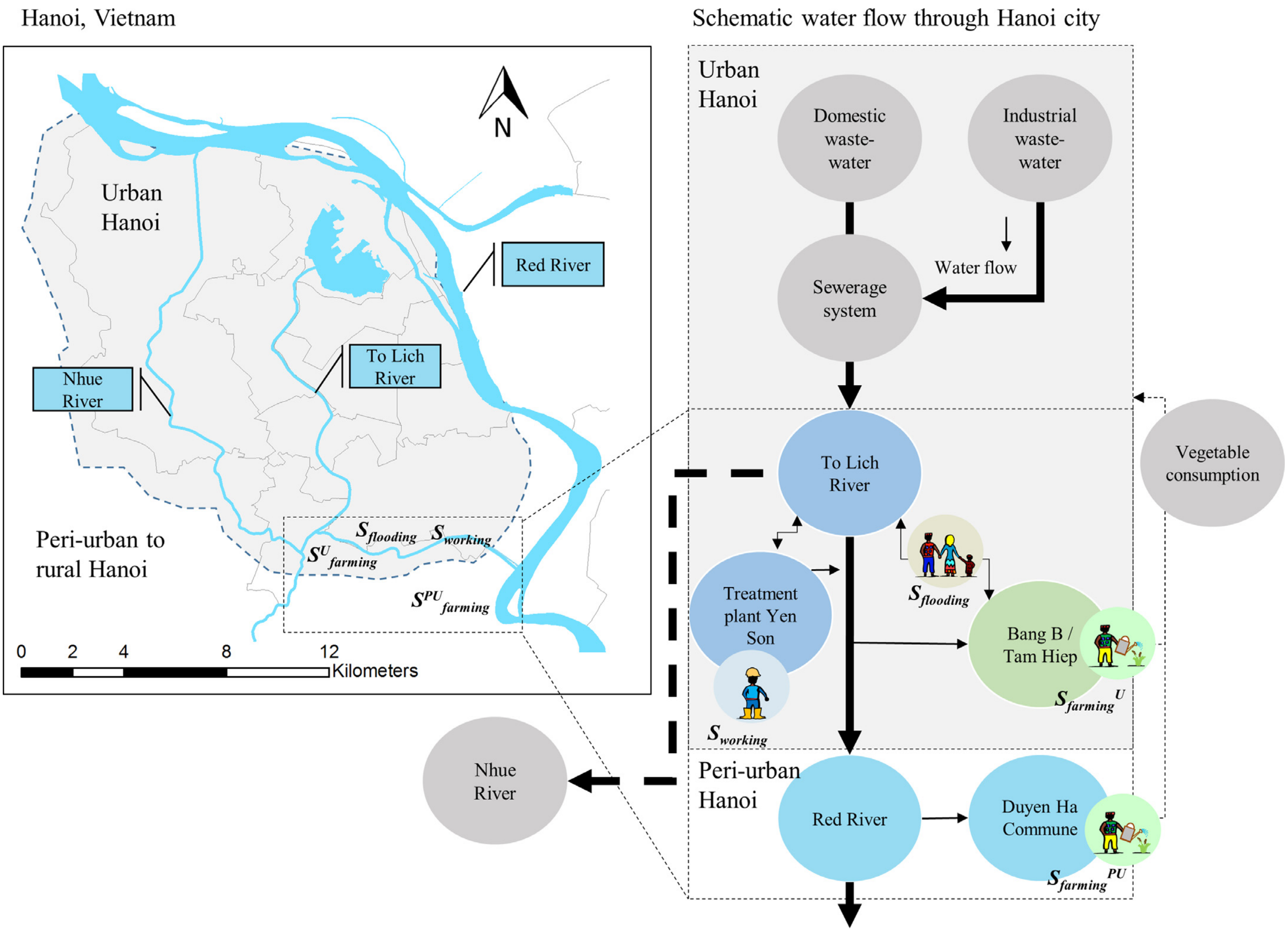

Fig. 1. Schematic flow of Hanoi's main wastewater system, with indication of the four exposure scenarios within the study areas ($S_{flooding}$, $S_{working}$, $S_{farming^U}$ and $S_{farming}{}^{PU}$) and potential exposure outside the scope of this study (i.e. contact to Nhue River water and vegetable consumption).

disease or even worse public health impact such as hemolytic uremic syndrome (HUS) (Okeke, 2009). As a simplification for the current QMRA, we refer to pathogenic *E. coli* that sums up all diarrhoea causing *E. coli*, whilst using the dose-response relation for probability of illness as derived for *E coli* O157:H7.

- *Salmonella* spp. have more than 2,500 sero-groups; yet, of concern for human health are only *S. typhi* and *S. para-typhi* A, B and C, and the enteric *Salmonella* strains (Kariuki et al., 2015). As a simplification for the current QMRA, we refer to pathogenic *Salmonella* spp., which includes the diarrhoea causing *Salmonella* spp. *S. typhi, S. para-typhi* A, B and C, *S. Enteritidis* and *S. Typhimurium.*
- *Cryptosporidium* spp. is a zoonotic intestinal protozoon that can result in severe health implication in children and immunocompromised individuals (e.g. HIV-positive people).
- *A. lumbricoides* is the most widespread soil-transmitted helminth and is highly endemic in Vietnam. Parasite eggs are known to persist in the environment longer than any of the other soil-transmitted helminth species (Brooker et al., 2009).

The exposure scenarios for the QMRA are based on information derived from a cross-sectional survey, consisting of a questionnaire survey and examination of stool samples from 618 people in the districts of Hoang Mai and Thanh Tri (Fuhrimann et al., 2016b). The results of the cross-sectional survey were used to obtain mode and frequency of exposure to wastewater and compare prevalence of parasitic infections and self-reported diarrhoea (recall period: 2 weeks) with estimates taking from the QMRA. As the focus of the model was to determine direct contact to contaminated water (considering all modes of pathogen transmission where contaminated water can be swallowed in the respective exposure scenario), the QMRA only included accidental ingestion of contaminated water as an exposure pathway. Other potential exposure pathways were excluded, such as: (i) ingestion of contaminated soil, dermal contact, inhalation and drinking of potentially contaminated water (lack of data); (ii) consumption of contaminated food crops (no data on degree of contamination of food crops); and (iii) exposure to contaminated water used for bathing or washing clothes (uncommon local practice).

Four exposure scenarios along the three selected study areas (To Lich River, wastewater use and Red River) were developed and assumptions about exposure groups, number of people exposed, exposure frequency and volume of ingested water were made (Figs. 1 and 2).

Exposure to water from To Lich River:

- **Scenario 1 ($S_{flooding}$):** Urban communities (all age groups) in Bang B and Tam Hiep living in close proximity to the To Lich River are prone to flooding events. For instance, 5% of the people living in these communities reported to be at risk of

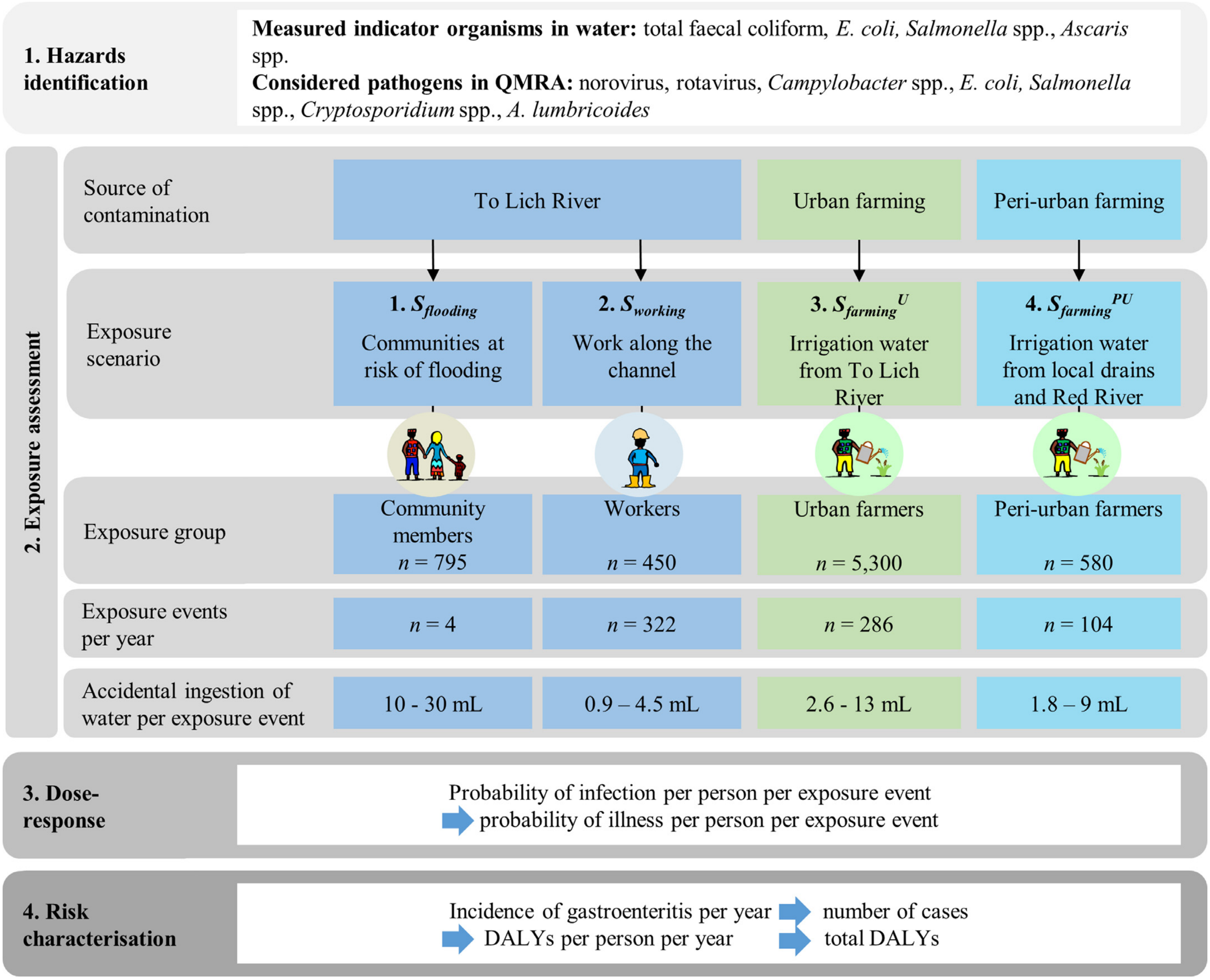

Fig. 2. Exposure scenarios ($S_{flooding}$, $S_{working}$, $S_{farming}{}^{U}$ and $S_{farming}{}^{PU}$) considered in the quantitative microbial risk assessment (QMRA) to estimate the burden of norovirus, rotavirus, *Campylobacter* spp., *Escherichia coli* 0157:H7, *Salmonella* spp., *Cryptosporidium* spp. and *Ascaris lumbricoides* along the major wastewater system in Hanoi.

flooding events (i.e. 795 out of 15,900 people) (Fuhrimann et al., 2016b). According to HSDC, four flooding events occurred during the rainy season in 2013; the year before our epidemiological survey (Fuhrimann et al., 2016b). During a flooding event, ingestion of water due to unintentional immersion is assumed to range between 10 and 30 mL (McBride et al., 2013).

- **Scenario 2 ($S_{working}$):** There are 450 registered workers employed by the HSDC who are in charge of the maintenance of the To Lich River and the operation of the wastewater treatment plants (Yen Son). On average, a worker is on duty 322 days per year. Most of the workers wear gloves (91%), which we considered as a proxy for the level of awareness and preparedness to avoid accidental ingestion of contaminated water (WHO, 2006; Fuhrimann et al., 2016d). It was assumed that the worst case scenario (an accidental ingestion of 10–50 mL of wastewater per working day) was reduced to ingestion of 0.9–4.5 mL per working day (WHO, 2006; Labite et al., 2010; Mara and Bos, 2010).

Exposure to water use from To Lich River in agriculture fields of urban farming communes in Hanoi:

- **Scenario 3 ($S_{farming}{}^{U}$):** Urban farmers living in Bang B village or Tam Hiep commune using wastewater from To Lich River were selected for the model. One third of the community (an estimated 5,300) are involved in urban farming (mainly rice, morning glory, neptunia and watercress) or aquaculture. Thus, the likelihood of accidental ingestion of water is considerable. On average, farmers in Bang B village and Tam Hiep commune reported to work 338 days per year in flooded agricultural fields and they are in contact with irrigation water on a daily basis. Three out of four workers (74%) wear gloves, which we considered as a proxy for the level of awareness and preparedness to avoid accidental ingestion of contaminated water (WHO, 2006; Fuhrimann et al., 2016d). It was assumed that the worst case scenario (an accidental ingestion of 10–50 mL of wastewater per working day) was reduced to ingestions between 2.6 mL and 13 mL per working day (WHO, 2006; Labite et al., 2010; Mara and Bos, 2010).

Exposure to water used from Red River in agriculture fields of peri-urban farming communes in Hanoi:

- **Scenario 4 ($S_{farming}^{PU}$):** A typical peri-urban farming community living in Duyen Ha commune, 10 km away from the outskirts of Hanoi. Farmers using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater but contaminated with household effluents. About 38% of the people work in agriculture (i.e. 580 urban famers). On average, farmers reported to work 338 days per year, though, fields are irrigated only every second day. 82% of the workers wear gloves, which we considered as a proxy for the level of awareness and preparedness to avoid accidental ingestion of contaminated water (WHO, 2006; Fuhrimann et al., 2016d). It was assumed that the worst case scenario (an accidental ingestion of 10–50 mL of wastewater per working day) was reduced to ingestions between 1.8 mL and 9 mL per working day (WHO, 2006; Labite et al., 2010; Mara and Bos, 2010).

2.5. Measurements of pathogens along the wastewater system

Water quality was tested for *E. coli*, TC, *Salmonella* spp. and helminth eggs between April and June 2014 (Fuhrimann et al., 2016a). The ratio between measured pathogens (p_{path}) and *E. coli* is assumed to vary between 10^{-6} and 10^{-5} (rotavirus, norovirus and *Campylobacter* spp.) or between 10^{-7} and 10^{-6} (*Cryptosporidium* spp.). The ratio between pathogenic and non-pathogenic strains of *E. coli* and *Salmonella* spp. (p_{path}) is assumed to vary between 7.6×10^{-4} and 1×10^{-2} (Shere et al., 2002; WHO, 2006; Soller et al., 2010; Barker et al., 2014; Hynds et al., 2014). For *Ascaris* spp. it is assumed that each egg detected represents an *A. lumbricoides* ($p_{path} = 1$, not considering the occurrence of other helminth species such as, for example, *A. suum*) (Mara and Sleigh, 2010).

Our QMRA approach has been described elsewhere (Fuhrimann et al., 2016d). We adhered to the WHO 2006 guidelines and the improved Karavarsamis–Hamilton method to determine annual disease and infection risks (WHO 2006; Karavarsamis and Hamilton 2010; Mara et al., 2010). As summarised in Table 1, spatial and temporal variability of the number of colony forming unit (CFU) *E. coli* and *Salmonella* spp., we fitted normal distributions to the log-transformed enumeration data on concentration in the water (C_{water}) (Fuhrimann et al., 2016a). A maximum likelihood estimation (MLE) method was used, allowing inclusion of censored data and accounting for the abundance, while considering the measured prevalence of the indicator bacteria in the water along the four systems (Lorimer and Kiermeier, 2007), in Excel 2013 (Microsoft Corporation, Redmond; WA, USA). As a result, the data fitting provided estimates for the true prevalence of contaminated water samples, and the distribution of concentrations in these contaminated samples. For *Ascaris* spp. eggs, this approach is not possible as only 17 out of 216 samples were positive. Hence, with $p = 0.08$ a positive count is expected, between 1 and 100 eggs/L, which is included with uniform distribution on a log scale (Fuhrimann et al., 2016a). Project evaluation and review techniques (PERT) distributions are fitted to minimum, most likely and maximum ratio of pathogen concentration per *E. coli* (p_{path}) for rotavirus, norovirus, *Campylobacter* spp. and *Cryptosporidium* spp. Uniform distribution were fitted to *E. coli* and *Salmonella* spp. ratio of pathogen concentration per measured *E. coli* and *Salmonella* spp. (WHO, 2006; Katukiza et al., 2013). This is implemented in the model by assuming that a fraction p_{path} of the ingested volumes of water consists of a pathogenic strain of the bacterial species. PERT distributions are also fitted to assumed minimum, most likely and maximum ingestion rates (volume (V) in mL water) per exposure event. In a Monte Carlo simulation, values are sampled for these three variables and the ingested amount of pathogens (dose; d) is calculated as:

$$d = C_{water} \times \ p_{path}\ V \tag{1}$$

The variation in C_{water} is implemented as variability per exposure event, the variation in p_{path} and V is implemented as variability per person (i.e. for practical reasons it had the same value for all exposure events for one person in one iteration of the Monte Carlo simulation). As ingested bacteria are discrete units, assumed to be homogeneously distributed in the water, ingested doses are assumed to be Poisson distributed (d ∼ Poisson (d) as e.g. in Nauta et al. (2012).

Doses (d) are used as input in the dose-response relations to obtain the probability of illness $P_{ill}(d)$ (Eqs. 1 to 6). Monte Carlo simulations are performed for 100,000 iterations using @Risk, version 6 (Palisade Corporation; Newfield, NY, USA), where one iteration simulates all the n exposure events (n different doses d) and associated $P_{ill}(d)$ of one person in a year. The expected frequency of illness for a person per year (which, in our approach, might be above one) can be calculated as the sum of the n values of $P_{ill}(d)$ obtained (without considering immunity) (Haas et al., 2014). Model outputs are presented as number of cases per year, DALYs pppy and total DALYs per year (according to published burden estimate for gastroenteritis and fatality rates and adapted to the average life expectancy of 72 years in Vietnam (Salomon et al., 2012; Gibney et al., 2014).

2.7. Dose-response models

The same dose-response models for the various pathogens are used as described elsewhere (Fuhrimann et al., 2016d) to determine the relationship between quantity of exposure (i.e. number of organism ingested) and the effective health outcome (i.e. infection and illness) (Haas et al., 2014). For the QMRA, Beta-Poisson dose-response models for rotavirus, *Campylobacter* spp., pathogenic *E. coli*, pathogenic *Salmonella* spp. and *A. lumbricoides* were employed (Haas et al., 1999, 2014; Teunis and Havelaar, 2000; Teunis et al., 2008a; McBride et al., 2013), as follows:

$$P_I(d) = 1 - \left[1 + \left(\frac{d}{\beta}\right)\right]^{-\alpha} \tag{2}$$

With a median infectious dose defined as

$$N_{50} = \beta\left(2^{1/\alpha} - 1\right) \tag{3}$$

For norovirus, a hypergeometric function was used (Teunis et al., 2008b). We employed an approximation for the mean probability of infection (Haas, 2002) of the Beta-Poisson dose-response model:

$$P_I(d) = 1 - \frac{\Gamma(\alpha+\beta)\Gamma(\mathrm{d}+\beta)}{\Gamma(\alpha+\beta+d)\Gamma(\beta)} \tag{4}$$

where Γ(.) represents Eulers gamma function (McBride et al., 2013). For *Cryptosporidium* spp., an exponential model was used (Westrell et al., 2004; de Man et al., 2013; McBride et al., 2013).

$$P_I(d) = 1 - (1 - r)^d \tag{5}$$

In brief, $P_I(d)$ represents the probability of infection, d is a single dose of the pathogen, whereas the pathogen infectivity constants α, β and r characterise the dose-response relationship. To account for the proportion of infections that turn into symptomatic cases ($P_{ill}(d)$), we used for each pathogen a constant value (λ) (i.e. illness to infection ratio):

$$P_{ill}(d) = P_I(d)\ x\ \lambda \tag{6}$$

Table 1 (see also Section 2.8) provides values used in the QMRA for each pathogen.

Table 1
QMRA model assumptions used to estimate the burden of gastrointestinal infections among people living along the major wastewater system in Hanoi, Vietnam.

Description	Unit	Distribution and/or value(s)	Reference(s)
(C_{water}) Concentrations in water To Lich River			(Fuhrimann et al., 2016a)
Escherichia coli	$\log_{10}$ (CFU/100 mL)	Normal (6.6;0.18)*	
Salmonella spp.	$\log_{10}$ (CFU/100 mL)	Normal (3.0;0.2)*	
Ascaris spp.	$\log_{10}$ eggs/1 L	Uniform (0;1.4)**, prevalence = 0.08	
(C_{water}) Wastewater-fed agricultural fields in Bang B and Tam Hieap			
Escherichia coli	$\log_{10}$ (CFU/100 mL)	Normal (6.0;0.7)*	
Salmonella spp.	$\log_{10}$ (CFU/100 mL)	Normal (2.0;0.6)*	
Ascaris spp.	$\log_{10}$ eggs/1 L	Uniform (0;1.4)**; prevalence = 0.08	
(C_{water}) Drainage system Duyen HA			
Escherichia coli	$\log_{10}$ (CFU/100 mL)	Normal (5.4;0.5)*	
Salmonella spp.	$\log_{10}$ (CFU/100 mL)	Normal (2.6;0.6)*	
Ascaris spp.	$\log_{10}$ eggs/1 L	Uniform (0;1.4)**, prevalence = 0.08	
(p_{path}) Ratio between indicator and pathogenic organisms			
A. lumbricoides to *Ascaris* spp.	Eggs/Eggs	Point estimate = 1	(Mara and Sleigh, 2010)
Campylobacter spp. to *E. coli*	CFU/CFU	PERT (0.1;0.55;1)*** per 10^5 *E. coli*	(WHO, 2006)
Cryptosporidium spp. to *E. coli*	CFU/CFU	PERT (0.01;0.055;0.1)*** per 10^5 *E. coli*	
Pathogenic *E. coli* O157:H7 to *E. coli*	CFU/CFU	Uniform (7.6×10^{-4}; 1×10^{-2})**	Shere et al., 2002; Soller et al., 2010; Hynds et al., 2014
Norovirus to *E. coli*	CFU/CFU	PERT (0.1;0.55;1)*** per 10^5 *E. coli*	(WHO, 2006)
Rotavirus to *E. coli*	CFU/CFU	PERT (0.1;0.55;1)*** per 10^5 *E. coli*	(Fuhrimann et al., 2016d; Katukiza et al., 2013)
Pathogenic *Salmonella* to *Salmonella* spp.	CFU/CFU	Uniform (7.6×10^{-4};1×10^{-2})**	(Shere et al., 2002; Soller et al., 2010; Hynds et al., 2014)
(V) Volume ingested per exposure event for each scenario			
$S_{flooding}$	mL	PERT (10;20;30)***	(Katukiza et al., 2013; Fuhrimann et al., 2016d)
$S_{working}$	mL	PERT (0.9;2.7;4.5)***	(Labite et al., 2010)
$S_{farming}{}^{U}$	mL	PERT (2.6;7.8;13)***	(Labite et al., 2010)
$S_{farming}{}^{PU}$	mL	PERT (1.8;5.4;9)***	(Katukiza et al., 2013; Fuhrimann et al., 2016d)
Dose-response models			
A. lumbricoides		Point estimate: α = 0.0104; N_{50} = 859	(Mara and Sleigh, 2010)
Campylobacter spp.		Point estimate: α = 0.145; N_{50} = 896	(Medema et al., 1996)
Cryptosporidium spp.		Point estimate: r = 0.0042	(Haas et al., 1999)
E. coli O157:H7		Point estimate: α = 0.49; N_{50} = 596,000	(Teunis et al., 2008a)
Norovirus		Point estimate: α = 0.04; β = 0.055;	(Teunis et al., 2008b)
Rotavirus		Point estimate: α = 0.253; N_{50} = 6	(Teunis and Havelaar, 2000)
Salmonella spp.		Point estimate: α = 0.3126; N_{50} = 23,600	(Haas et al., 1999)
(λ) Illness to infection ratio			
A. lumbricoides		Point estimate: 0.39	(Mara and Sleigh, 2010)
Campylobacter spp.		Point estimate: 0.3	(Machdar et al., 2013)
Cryptosporidium spp.		Point estimate: 0.79	(Machdar et al., 2013)
Pathogenic *E. coli*		Point estimate: 0.35	(Machdar et al., 2013)
Norovirus		Point estimate: eta = 0.00255; r = 0.086	(Teunis et al., 2008b)
Rotavirus		Point estimate: 0.5	(Barker, 2014)
Pathogenic *Salmonella* spp.		Point estimate: 1	(Amha et al., 2015)
(n) Number of exposure events per year			(Fuhrimann et al., 2016b)
$S_{flooding}$		Point estimate: 4	
$S_{working}$		Point estimate: 322	
$S_{farming}{}^{U}$		Point estimate: 286	
$S_{farming}{}^{PU}$		Point estimate: 104	
(Pop_E) Population at risk per exposure scenario			(Fuhrimann et al., 2016b)
$S_{flooding}$	People	Point estimate: 795	
$S_{working}$	People	Point estimate: 450	
$S_{farming}{}^{U}$	People	Point estimate: 5,300	
$S_{farming}{}^{PU}$	People	Point estimate: 580	
($DALYs_h$) Disease burden per pathogenic organisms; disability-adjusted life years (DALYs) calculation is indicated in Table 2			
A. lumbricoides	DALYs/case	Point estimate: 0.0029	
Campylobacter spp.	DALYs/case	Point estimate: 0.0053	
Cryptosporidium spp.	DALYs/case	Point estimate: 0.0022	
Pathogenic *E. coli*	DALYs/case	Point estimate: 0.0013	
Norovirus	DALYs/case	Point estimate: 0.0008	
Rotavirus	DALYs/case	Point estimate: 0.0032	
Pathogenic *Salmonella* spp.	DALYs/case	Point estimate: 0.0719	

* Normal distribution (mean; standard deviation); **Uniform distribution (min; max); ***Project evaluation and review techniques (PERT) (min; most likely; max)

2.8. Risk characterisation

2.8.1. Incidence: the number of cases per year

Risk characterisation was done as described elsewhere (Fuhrimann et al., 2016d). When assuming that each exposure event i is independent and that there is no acquired immunity after an infection, with $P_{ill/h}(d_i)$ representing the probability of illness, which is a function of the ingested dose d_i at exposure event i for each of the seven pathogens (or hazards) h (Eq. 6), then for an average of n_h exposures to the hazard per person per year, with population size Pop_E, the expected number of cases is

$$Cases_h = \sum_{i=1}^{n_h \times Pop_E} P_{ill,\ h}(d_i) \tag{7}$$

The incidence estimate for pathogen h is

$$Inc_h = \frac{Cases_h}{n_h \times Pop_E} \qquad (8)$$

The combined incidence estimate, Inc_{comb} (episodes of gastroenteritis per year), for all seven pathogens h is defined as

$$Inc_{comb} = \underset{all\ h}{} \frac{Cases_h}{n_h \times Pop_E} \qquad (9)$$

2.8.2. Estimation of disease burden

The disease burden due to human exposure is expressed in DALYs. This metric combines morbidity (years lived with disability) and premature death (years of life lost) (Murray et al., 2012). For each pathogen h, DALYs per case of gastrointestinal illness ($DALY_h$) are calculated as the sum of the product of the probability of developing disease symptom j (i.e. $j =$ mild, moderate and severe diarrhoea or death) given the illness occurs, relative frequency of the symptom (f_j), duration of the developed symptom in years (D_j) and the respective severity factor (S_j) (Salomon et al., 2012):

$$DALY_h = \underset{j}{} f_j \times D_j \times S_j \qquad (10)$$

Mortality is calculated according to the average life expectancy at birth in Vietnam of 72 years (Katukiza et al., 2013). Note that sequelae such as HUS, Guillain-Barré syndrome, reactive arthritis or irritable bowel syndrome are not considered in the model. The total disease burden ($Total_{DALYs,h}$) per hazard is the product of cases ($Cases_h$) and DALYs per pathogen:

$$DALYs_h = Cases_h\ x\ DALY_h \qquad (11)$$

The total disease burden for all hazards together is

$$Total_{DALYs} = \underset{h}{} Cases_h\ x\ DALY_h \qquad (12)$$

3. Results

3.1. Incidence of gastroenteritis

The combined estimated incidence (Inc_{comb}) for gastroenteritis episodes per year due to the exposure to contaminated water was highest for urban farmers ($S_{farming}{}^{U}$), and sanitation workers ($S_{working}$) who suffer, on average, 2.0 and 1.0 gastroenteritis episodes per person per year (Fig. 3, Table 3). Incidence estimates were considerably lower for people exposed to flooding events ($S_{flooding}$) and peri-urban farmers ($S_{farming}{}^{PU}$) (> 0.1 episodes per person per year for both groups) (Table 3). Most episodes were caused by rotavirus (1.5 episode per year), *E. coli* (0.6 episodes per year), *Campylobacter* spp. (0.4 episodes per year) and *Cryptosporidium* spp. (0.4 episodes per year). Considerably fewer episodes were caused by any of the other pathogens (< 0.1 episodes per year).

3.2. Number of gastroenteritis cases per year

Among the 7,125 exposed people in the districts of Hoang Mai and Thanh Tri, a total of 11,073 cases of gastroenteritis caused by any of the seven pathogens were estimated due to exposure to wastewater for the four scenarios and the duration of one year (Fig. 3, Table 2). Gastrointestinal infection due to rotavirus, *E. coli* and *Campylobacter* spp. contributed most to the total cases (59%, 18% and 13%, respectively). Taken together, 95.0% of all cases were concentrated in the 5,300 urban farmers ($S_{farming}{}^{U}$: 10,511 cases).

3.3. Total disease burden per year

Across all 7,125 exposed people and four scenarios, our model estimated a burden of 62.6 DALYs per year due to exposure to wastewater in Hoang Mai and Thanh Tri district. The main responsible pathogens were *E. coli*, rotavirus and *Campylobacter* spp., accounting for 42%, 39% and 14% of the burden, respectively. Urban farmers ($S_{farming}{}^{U}$) were most vulnerable with a burden of 59.5 DALYs.

3.4. Disease burden per person per year

Combined DALYs pppy for all scenarios (summed-up for the seven pathogen and all exposed individuals) were far above the revised WHO reference level of 0.0001 DALYs pppy (Table 1). The highest disease burden was estimated at 0.011 DALYs pppy in urban farmers ($S_{farming}{}^{U}$), followed by sanitation workers ($S_{working} =$ 0.0057 DALYs pppy), urban communities at risk of flooding events ($S_{flooding} =$ 0.0005 DALYs pppy) and peri-urban farmers ($S_{farming}{}^{PU} =$ 0.0004 DALYs pppy). In terms of different pathogens, *E. coli*, rotavirus and *Campylobacter* spp. had the largest share with 0.0037, 0.0035 and 0.0013 DALYs pppy, respectively.

4. Discussion

4.1. Disease burden estimates and comparison with standards

Our estimated gastrointestinal disease burden among urban farmers and sanitation workers who are exposed to wastewater are 5.6- and 2.8-fold higher than the diarrhoea burden estimates for the average Vietnam citizen (0.002 DALYs pppy) (Institute for Health Metrics and Evaluation, 2015). The high number of cases and the resulting burden due to *E. coli*, rotavirus and *Campylobacter* spp. together cause most of the disease burden (88%), which is in line with prior QMRA investigations in Asia and Africa (Pham-Duc, 2012; Katukiza et al., 2013; Machdar et al., 2013; Fuhrimann et al., 2016d). To our knowledge, we present the first specific QMRA to estimate disease burden due to exposure to wastewater for high-risk groups in Southeast Asia. Compared to a prior study conducted in Kampala, Uganda, using the same methodology as presented here, the current estimates are considerably lower (e.g. the estimated burden for urban farmers in Hanoi was 0.011 DALYs pppy compared to 0.073 DALYs pppy in Kampala) (Fuhrimann et al., 2016d). Very high estimates were obtained by QMRA models with regard to people exposed to wastewater in a typical slum area in Kampala (15,015 people; burden 10,172 DALYs) (Katukiza et al., 2013) and an urban wastewater systems in Accra (286,833 people; burden 31,979 DALYs) (Labite et al., 2010). These differences might, at least partially, be explained by specific social-ecological contexts, pathogen spectrum, DALY estimates per pathogens (e.g. we excluded sequelae) and methodological differences (e.g. calculation of risk of illness).

4.2. Comparison of QMRA estimates with epidemiological survey data

Only few studies have compared QMRA estimates with diarrhoea episodes assessed in epidemiological surveys (Bouwknegt et al., 2014; Haas et al., 2014). We aimed to fill this gap, and hence, conducted a cross-sectional survey, assessed water quality and obtained data on self-reported diarrhoeal episodes with a recall period of 2 weeks (Fuhrimann et al., 2016b). Extrapolating the self-reported 2-week diarrhoeal prevalence rate to 1 year (52 weeks, considering no seasonality), the annual incidence would be slightly higher compared to the combined incidence rates of all seven pathogens estimated in the QMRA (i.e. 2.6 versus 2.0 in urban farmers; 2.3 versus 0.09 in urban community members at

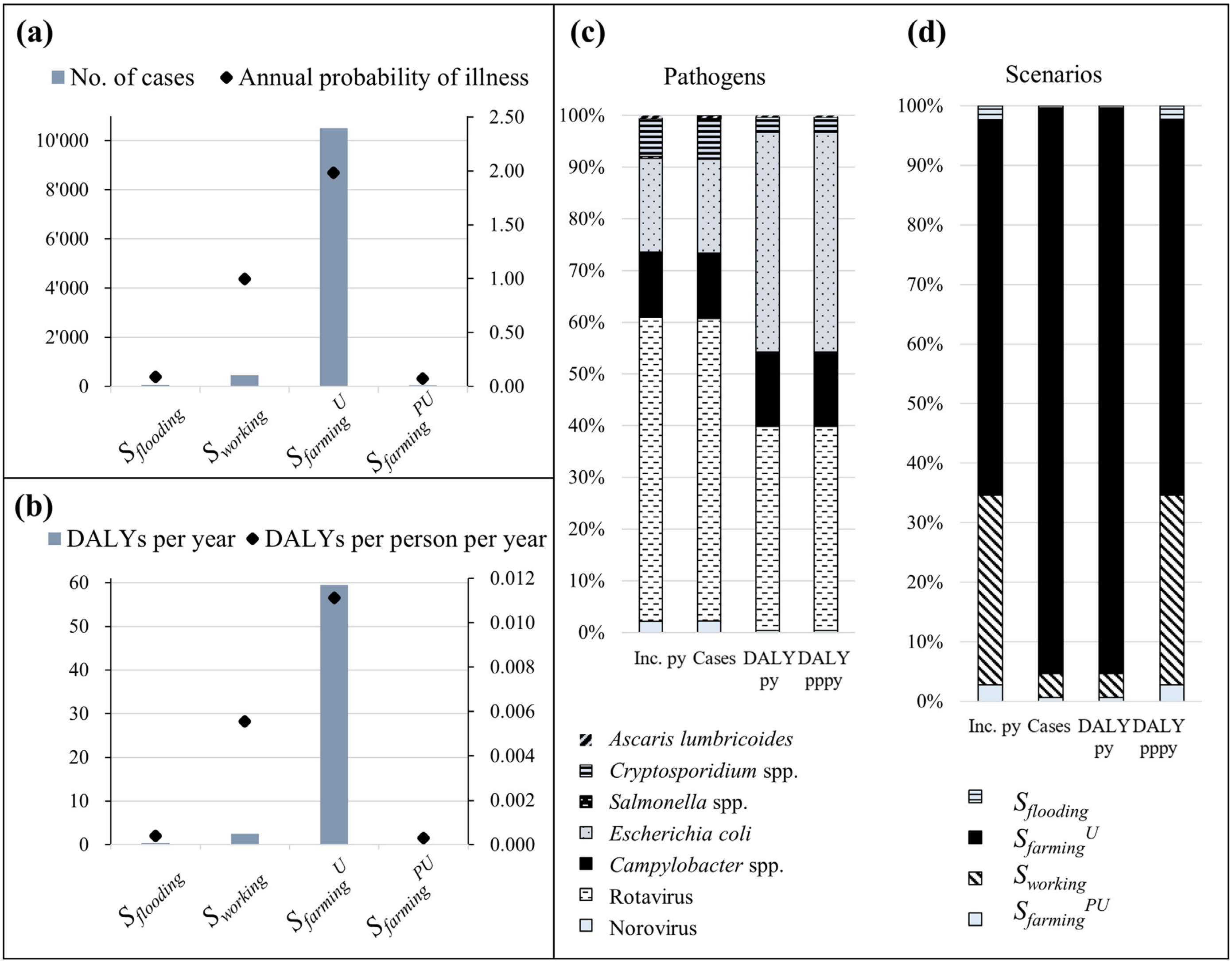

Fig. 3. Estimated number of cases, annual incidence of gastroenteritis per year (Inc py), disability-adjusted life years (DALYs) per year (py) and per person per year (pppy); (a) and (b) showing estimates of the respective outcomes per $S_{flooding}$, $S_{working}$, $S_{farming}{}^{U}$ and $S_{farming}{}^{PU}$; (c) and (d) are indicating the contribution of individual pathogens and scenarios, respectively, to the total estimated numbers per outcome along the major wastewater system in Hanoi, Vietnam.

risk of flooding events; 2.1 versus 1.0 in sanitation workers; and 1.0 versus 0.07 in peri-urban farmers). These obtained differences for urban farmers, communities and sanitation workers might be explained by additional risk factors for diarrhoeal disease, which drive the higher estimate (e.g. contaminated food crops, drinking water, human-to-human transmission, heavy metals or pesticides). Hence, future QMRA or chemical risk assessment should account for such factors, along with the potential effect of vulnerability and potentially acquired immunity to infectious agents within the exposed population groups in LMICs (Minh et al., 2004; Holm et al., 2010; Mok et al., 2014).

Further, when focusing on helminthiases, the QMRA estimated that 74 people would be infected with *A. lumbricoides* over the course of a year, with 71 cases among urban farmers. These low incidence rates for urban farmers (1.4% of total cases) are in line with our cross-sectional survey, which did not detect a single *A. lumbricoides* infection in famers using wastewater. As deworming is done on a regular basis and a significant protective effect was found in our cross-sectional survey, this low incidence might indeed remain undetected in epidemiological surveys (Fuhrimann et al., 2016b). In the light of our findings, for further cross-comparison between epidemiological surveys and QMRA, a standardised way to assess incidence and burden of diarrhoeal episodes and intestinal parasitic infections should be proposed and validated to make use of both tools. This statement can also be underlined by a similar comparison of QMRA estimates with findings from an epidemiological survey in Kampala (Fuhrimann et al., 2016b, 2016c).

4.3. Sensitivity analysis

A sensitivity analysis of the QMRA model employed here has been presented by Fuhrimann et al. (2016d). There is a considerable effect of different volumes of water accidentally ingested. Such accidental ingestion may not be very accurate, as it is highly dependent on individual behaviours, which are influenced by age, sex, educational attainment and socioeconomic status (WHO, 2006; Haas et al., 2014). Moreover, pathogen ratio for rotavirus, *E. coli* and *Campylobacter* have shown a considerable effect on the total number of gastroenteritis cases, as there is considerable difference in microbial contamination between seasons in urban wastewater systems this might have considerable effect on the number of cases (Ensink, 2006; Katukiza et al., 2013; Fuhrimann et al., 2015, 2016a). It is important to note that *E. coli* is secreted by humans and animals continuously, whereas pathogens

Table 2
Disease burden due to gastroenteritis expressed in disability-adjusted life years (DALYs) calculated by means of severity (mild, moderate, severe and fatal), probability and duration of the respective severity grade, stratified by pathogen.

Gastroenteritis		Severity weights					Reference
		Mild	Moderate	Severe	Fatal	Total DALYs	
DALYs per severity grade of gastroenteritis		0.06	0.20	0.28	1.00		(Salomon et al., 2012)
Norovirus	Probability	0.92	0.07	0.01	7.80×10^{-6}		(Gibney et al., 2014)
	Duration (days)	2.10	2.40	7.20			
	Duration (years)	0.01	0.01	0.02	72		
	DALYs	3.24×10^{-4}	9.56×10^{-5}	3.33×10^{-5}	4.23×10^{-4}	1.01×10^{-3}	
Rotavirus	Probability	0.85	0.10	0.05	3.37×10^{-5}		(Gibney et al., 2014)
	Duration (days)	4.90	7.10	7.70			
	Duration (years)	0.01	0.02	0.02	72		
	DALYs	6.94×10^{-4}	4.01×10^{-4}	2.96×10^{-4}	1.83×10^{-3}	3.82×10^{-3}	
Cryptosporidium spp.	Probability	0.86	0.12	0.02			(Gibney et al., 2014)
	Duration (days)	5.00	15.00	33.00			
	Duration (years)	0.01	0.04	0.09			
	DALYs	7.19×10^{-4}	1.02×10^{-3}	4.32×10^{-4}		2.17×10^{-3}	
Campylobacter spp.	Probability	0.80	0.18	0.02	6.72×10^{-5}		(Havelaar et al., 2000)
	Duration (days)	3.50	9.70	14.40			(Gibney et al., 2014)
	Duration (years)	0.01	0.03	0.04	72		
	DALYs	4.70×10^{-4}	9.72×10^{-4}	1.77×10^{-4}	3.64×10^{-3}	6.46×10^{-3}	
Pathogenic *Salmonella* spp.	Probability	0.21	0.66	0.14	1.26×10^{-3}		(Gibney et al., 2014)
	Duration (days)	2.50	6.00	12.00			
	Duration (years)	0.01	0.02	0.03	72		
	DALYs	8.61×10^{-5}	2.18×10^{-3}	1.27×10^{-3}	6.85×10^{-2}	9.43×10^{-2}	
Pathogenic *E. coli*	Probability	0.94	0.06	0.09	2.00×10^{-4}		(Katukiza et al., 2013)
	Duration (days)	5.60	10.70	16.20			
	Duration (years)	0.02	0.03	0.04	72		
	DALYs	8.80×10^{-4}	3.55×10^{-4}	1.12×10^{-3}	1.08×10^{-2}	1.32×10^{-2}	
Ascaris lumbricoides	Probability	0.95	0.05				(Barker et al., 2014)
	Duration (days)	35.0	28.0				
	Duration (years)	0.05	0.01				
	DALYs	2.90×10^{-3}	1.83×10^{-5}			2.92×10^{-3}	

are secreted only by a proportion of infected people over a short period of a few days. This might affect the *E. coli* to pathogen ratio change over time (Mara, 2004; Haas et al., 2014).

4.4. QMRA limitations

Our model framework has several limitations, which are offered for consideration. First, the estimates of the ingested volumes of water are based on literature values for certain human behaviours (Labite et al., 2010; Schets et al., 2011; Katukiza et al., 2013). Second, the dose-response models applied in our model are based on feeding studies (e.g. norovirus) or rely on epidemiological evidence (e.g. *Ascaris* spp.) collected in high-income countries (de Man et al., 2013; Barker et al., 2014). Third, in scenario 1 we do not differentiate between adults and children. Especially for rotavirus, burden is known to be substantially different between age groups (Mok and Hamilton, 2014). Fourth, the model excluded other exposure pathways such as dermal contact (e.g. hookworm and skin disease) and inhalation. It is reported that other water-borne pathogens such as hepatitis, cholera and adenoviruses occur in high prevalence and cause severe health implications (Karagiannis-Voules et al., 2015; Fuhrimann et al., 2016b). Fifth, partially acquired immunity due to exposure history or vaccination may result in lower estimates (Sunger and Haas, 2015). Sixth, the duration of a fatal case was assumed to be equal to the life expectancy at birth, which is likely to result in an overestimation of the burden estimates (Katukiza et al., 2013; Fuhrimann et al., 2016d). Finally, long-term sequelae is often contributing to a significant proportion of DALYs when assessing burden to intestinal pathogens in high-income countries, hence, for next QMRA in LMICs sequelae should be included (Havelaar et al., 2000).

5. Conclusions

Employing a QMRA approach, we found high incidence of water-borne pathogens among urban farmers in Hanoi who use wastewater in agriculture and aquaculture. The validation of the QMRA estimates with findings from epidemiological surveys showed that QMRA estimated incidence of gastroenteritis was considerably lower, which can be explained by additional transmission routes (e.g. food crops) which can result in gastroenteritis cases. The high incidence of gastrointestinal infections results in considerable disease burden, which is 5.6-fold higher in urban farmers compared to an average Vietnamese and more than hundred times above the revised WHO tolerable level of 0.0001 DALYs pppy. In turn, exposure to wastewater around Hanoi has considerable public health implications for these three population groups and call for actions, especially to bring down the burden due to *E. coli*, rotavirus and *Campylobacter* spp. infections.

Against this background, health-based targets should be set according to local idiosyncrasies after validation with epidemiological findings. For example, as a first step towards setting local targets could be the consideration of estimates provided by the Global Burden of Disease study 2010. These findings are especially interesting in the frame the Sustainable Development Goals (SDGs), as they address sustainable and safe wastewater reuse and recovery systems, from the point of generation to the point of disposal and (re)use for minimising adverse health impacts associated with water-borne disease, while maximising gains from safe wastewater use in agriculture and aquaculture in LMICs. Finally, the study provides a first example on how to link quantification of health risk using a QMRA to an SSP approach in an Asian context.

Table 3
QMRA estimates for annual probability of illness, number of cases per year, total DALYs per year, DALYs per person per year across all four exposure scenarios ($S_{flooding}$, $S_{working}$, $S_{farming}{}^{U}$ and $S_{farming}{}^{PU}$) and seven pathogens along the major wastewater system in Hanoi, Vietnam.

Exposure scenario (n = exposed population)	$S_{flooding}$ (n = 795)	$S_{working}$ (n = 450)	$S_{farming}{}^{U}$ (n = 5,300)	$S_{farming}{}^{PU}$ (n = 580)	Total (n = 7125)
Incidence of gastroenteritis per year (Inc_h)					
Norovirus	0.002	0.020	0.045	0.001	0.07
Rotavirus	0.051	0.597	1.160	0.041	1.85
Campylobacter	0.011	0.127	0.249	0.009	0.40
E. coli	0.016	0.180	0.361	0.013	0.57
Salmonella spp.	0.000	0.004	0.002	0.002	0.01
Cryptosporidium	0.006	0.069	0.153	0.005	0.23
A. lumbricoides	0.001	0.003	0.013	0.002	0.02
Total number	0.088	1.000	1.983	0.074	3.14
No. cases per year ($Cases_h$)					
Norovirus	2	9	237	1	248
Rotavirus	41	269	6,146	24	6,480
Campylobacter	9	57	1,321	5	1,392
E. coli	13	81	1,915	8	2,017
Salmonella spp.	0	2	12	1	15
Cryptosporidium	5	31	809	3	848
A. lumbricoides	1	1	71	1	74
Total number	70	450	10,511	43	11,073
DALYs per year ($Total_{DALYs,h}$)					
Norovirus	0.00	0.01	0.24	0.00	0.25
Rotavirus	0.16	1.03	23.46	0.09	24.73
Campylobacter	0.06	0.37	8.53	0.03	8.99
E. coli	0.17	1.07	25.27	0.10	26.61
Salmonella spp.	0.00	0.00	0.01	0.00	0.02
Cryptosporidium	0.01	0.07	1.76	0.01	1.84
A. lumbricoides	0.00	0.00	0.21	0.00	0.22
Combined DALYs ($Total_{DALYs}$)	0.40	2.54	59.48	0.24	62.66
DALYs per person per year ($DALY_{pppy,h}$)					
Norovirus	0.0000	0.0000	0.0000	0.0000	0.0000
Rotavirus	0.0002	0.0023	0.0044	0.0002	0.0035
Campylobacter	0.0001	0.0008	0.0016	0.0001	0.0013
E. coli	0.0002	0.0024	0.0048	0.0002	0.0037
Salmonella spp.	0.0000	0.0000	0.0000	0.0000	0.0000
Cryptosporidium	0.0000	0.0001	0.0003	0.0000	0.0003
A. lumbricoides	0.0000	0.0000	0.0000	0.0000	0.0000
Combined DALYs	0.0005	0.0057	0.0112	0.0004	0.0088

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12. Discussion

12.1. Summary of results and outline of the discussion

This PhD thesis aims to generate evidence on health risks along urban and peri-urban wastewater recovery and reuse systems in LMICs. Health risk assessment methodology was adapted and applied to contexts of LMICs and visualised in form of a short video presentation for Kampala (chapter 5). The assessment of health risks along wastewater recovery and reuse systems in Kampala and Hanoi is showcased in detail by applying a methodological triangulation, including (i) environmental assessments to measure microbial and chemical contamination (chapters 6 and 9); (ii) epidemiological cross-sectional surveys to identify existing health risks related to intestinal parasitic infections (chapters 7 and 10); and (iii) QMRAs to estimate the burden of gastrointestinal diseases in different scenarios simulating exposure to wastewater (chapters 8 and 9). The set of generated data on health risks informed local communities, stakeholders and decision makers on health risks and possible action to reduce exposures to wastewater and faecal sludge in Kampala and Hanoi. Moreover, the findings contributed to the RRR project related development of the SSP manual (WHO 2015) and to the "health and environmental risk and impact assessments of waste reuse business models" proposed for Kampala, Hanoi, Bangalore and Lima. Finally, the findings of this PhD thesis advances innovation, validation and application, the three main pillars of Swiss TPH in the field of public health (

Table 12.1).

Hence, the following discussion addresses the four PhD study objectives for Kampala and Hanoi (outlined in chapter 3.2) by comparative means, highlighting lessons learned while applying the three methods. This under the broader topics of environmental contamination along wastewater recovery and reuse systems (addressing objective 1), intestinal parasitic infections in different urban population groups (addressing objective 2) and burden of diarrhoeal disease due to exposure to wastewater in LMICs (addressing objective 3). Further, to address object 4, the limitations and the practical relevance of in-depth risk assessments and their data generated are given on the example of risk mitigation and morbidity control strategies for Kampala and Hanoi. Finally, promotion strategies for risk assessment approaches leading their way into practice are provided along with a set of concussion, recommendations and an outlook in regard to SSP scale-up and the SDG agenda in LMICs.

Table 12.1 Summary of manuscripts and their contributions to the Swiss TPH nexus of innovation, validation and application

	Innovation	Validation	Application
Chapter 4	• Visualisation of health risks along wastewater recovery and reuse systems in form of a video contribution		• Communication and training tool to create awareness and build capacity for health risk assessors and managers in LMICs
Chapter 5 & 8		• Identification of critical control points and effectiveness of treatment functions along the wastewater system	• Monitoring frameworks for wastewater recovery and reuse systems in LMICs
Chapter 6 & 9		• Comparison of risk and confounding factors for intestinal parasitic infections with previous findings in urban environments of LMICs	• Identification of high risk groups and risk factors for intestinal parasitic infections in urban environments of Kampala and Hanoi
Chapter 7 & 10	• Further development of QMRA framework to fit the context of urban wastewater recovery and reuse systems in LMICs	• Comparing incidence and burden estimates with findings from epidemiological surveys • Comparing burden estimates with WHO’s health-based targets and estimates by the global burden of disease study	• Outline high risk populations, which should be protected by additional control measures • Indication of mitigation strategies to potentially reduce the model-based health impacts

12.2. Environmental contamination along wastewater recovery and reuse systems

12.2.1. Microbial and chemical pollution in Kampala

Our environmental assessment was conducted along the major wastewater management system in Kampala, the Nakivubo channel, between October and December 2013. Measurements revealed that the environment along the Nakivubo channel was highly polluted with TTC and *E. coli*. Highest concentrations were measured in the samples taken within the community areas and ranged from 4.0×10^2 to 2.2×10^8 and from 1.0×10^2 to 7.9×10^7 CFU/100 mL, respectively. The concentration of TTC, BOD_5, COD and TSS increased in the range of 200 to 300%, when compared with data reported in 2008 (Kayima et al. 2008). Consequently, in the bordering Nakivubo wetland and the frequently flooded slum communities level of bacteria in water were above national discharge standards of 3,000 TTC (NEMA 1999) and above the WHO tolerable safety limits for unrestricted irrigation (between 10^3 and 10^4 for CFU *E. coli*/100 mL) (WHO 2006a). Moreover, in 15.5% of the total 200 water and soil samples helminth eggs could be detected (27 were positive for hookworm and four for *A. lumbricoides*). Mean concentrations of measured helminth eggs in water samples were between 1.3 and 2 eggs/L, exceeding WHO guidelines thresholds (<1 egg/L) (WHO 2006a). Finally, in the examined plant samples (yams and sugar cane), mean concentrations of Cd, Cr and Pb (yams 4.4, 4.0 and 0.2 mg/L; sugar cane 8.4, 4.3 and 0.2 mg/L, respectively) exceeded thresholds put forth by NEMA (NEMA 1999).

The high level of microbial and chemical pollution is in line with previous studies in similar urban environments of Kampala or elsewhere in Africa (Katukiza et al. 2013; Yapo et al. 2013; Kpoda et al. 2015). As previously indicated, we could confirm that it is limited to bring down the level of pollution (i.e. for *E. coli* 1.56 log CFU treatment is achieved) in regard to the natural treatment function of the Nakivubo wetland before the water was discharged into Lake Victoria (Kansiime and Nalubega 1999; Beller Consult et al. 2004). The increasing levels of pollution in the environments may be explained by three points: (i) the increasing amount of domestic and industrial wastewater, which is overwhelming the aging wastewater treatment system; (ii) the limited collection and treatment possibilities of faecal sludge; and (iii) the occupation of the wetland areas around the city by industries and informal urban farming activities (Kansiime and Nalubega 1999; Katukiza et al. 2013). High concentrations of microbes and chemicals were above national and international safety standards and are likely to impact on the health of people living (communities at risk of flooding, consuming wastewater fed-crops, fish from the Murchison Bay in Lake Victoria or polluted drinking water) and working along the system (workers maintaining the sanitation system and urban farmers) (Howard et al. 2006; Katukiza et al. 2013; Sekabira et al. 2011; WHO 2006a).

12.2.2. Microbial and chemical pollution in Hanoi

In Hanoi, the environmental assessment was conducted along the three major wastewater receiving rivers, the To Lich River, the Nhue River and the Red River, between April and June 2014. High levels of microbial contamination were measured in wastewater of the To Lich River, the Nhue River (e.g. between 10^4 and 10^6 CFU *E. coli*/100 mL), whereas considerable lower concentrations were measured in Red River (between 0 and 10^4 CFU *E. coli*/100 mL). The To Lich River water used in wastewater-fed agriculture fields in peri-urban areas of Hanoi showed —beside applied treatment in retention ponds— mean contamination with Total coliforms (TC), *E. coli* and *Salmonella* spp. of 1.3×10^7, 1.1×10^6 CFU/100 mL and 108 MPN/100 mL, respectively. These values are 110-fold above the Vietnam discharge limits for agriculture reuse (5'000 CFU TC/100 mL) (MONRE 2008) and even 260-fold above WHO tolerable safety limits for unrestricted irrigation (between 10^3 and 10^4 for CFU *E. coli*/100 mL) (WHO 2006a). High concentrations of bacteria were also measured in local drainage systems in the Duyen Ha commune, which is an area five km outside of the city ring and not connected to the city's wastewater network. Overall study areas, helminth eggs (*T. trichuris* and *A. lumbricoides*) were measured at tolerable levels in all systems of the study areas, i.e. <1 egg/L (WHO 2006a).

Our findings confirm the results of a previous study reporting that surface water bodies around Hanoi are highly contaminated with faecal matter (using tracer for faecal pollution) (Kuroda et al. 2015). Further, Pham-Duc and colleagues (2012) reported that the water from the Nhue River is still polluted with similar high concentrations of TCC and *E. coli* 60 km downstream of Hanoi in Hanam province as we reported in the presented study. However, implemented control measures likely contributed to the reduction in helminth egg concentration over the last decade, from 367-5730 egg/L reported by Do and colleagues (2007) to <1 egg/L. We did not measure chemical contamination in the Hanoi study, however, several other studies pointed out that industrial effluents pollute surface rivers and lakes. High level of various heavy metals were measured in water and sediment of To Lich River and therefore should not be used for any kind of land use application (Holm et al. 2010; H Marcussen et al. 2012). Hence, despite improvements of wastewater conveyance and treatment infrastructures, there should be further adaptation of mitigation measures to bring down the level of bacterial and chemical contamination and thereby protecting the health of urban famers, consumer of wastewater-fed vegetable and downstream rural communities (a set of different technological and non-technological option for Hanoi is offered under the chapter 12.5.2).

12.2.3. Comparison of microbial and chemical pollution between Kampala and Hanoi

There are considerable differences in wastewater systems in terms of applied infrastructure and reuse practises between Kampala and Hanoi. Kampala's wastewater management system is not yet able to compete with the wastewater generated and large volumes of wastewater are discharged into Lake Victoria each day. Moreover, informal reuse of wastewater and the occupation of natural wetland areas increasingly challenge existing treatment infrastructures (Kayima et al. 2008; Mbabazi et al. 2010). In Hanoi large investments in the infrastructures were made to convey and treat the wastewater over the last years (World Bank 2013). Despite these considerable differences in wastewater systems high concentrations of bacteria and chemicals are reported by several studies in both cities. Moreover, in both cities the issue of faecal sludge collection is challenged by the provision of formal and adequate collection services, disposal and reuse solutions (Schoebitz et al. 2014; Strande et al. 2014). Industrial pollution is a major issue, while registration and the source control of industries and effluents is lacking (Helle Marcussen et al. 2008; Tilley et al. 2014). Hence, discharge standards cannot be achieved in both settings.

Taken together, our two case studies underline the importance of a context specific understanding of microbial and chemical contamination along wastewater management and reuse systems. Such evidence can help public authorities and stakeholders to understand existing system dynamics and identify hazards along CCPs. Such a understanding would enhance evidence-based decision-making for protecting ecosystems and the services that they provide to protect people's health and well-being (Magalie Bassan et al. 2015; WHO 2015). Finally, the described environmental assessments can serve as useful examples to adapt wastewater quality monitoring strategies (i.e. designing specific operational and verification monitoring plans along wastewater recovery and reuse systems) by local authorities in Kampala and Hanoi but also other urban contexts in LMICs.

12.3. Intestinal parasitic infections in different urban population groups

12.3.1. Intestinal parasitic infections in urban population in Kampala

In Kampala, the cross-sectional survey with 915 adults showed significant differences between the five population groups in regard to intestinal parasitic infections. The highest point-prevalence of intestinal parasite infections was found in urban farmers (75.9%), whereas lowest point-prevalence was found in workers collecting faecal sludge (35.8%). Hookworm was the predominant helminth species (27.8%). *T. trichiura*, *S. mansoni*, *A. lumbricoides*, and *E. histolytica/E. dispar* showed a prevalence of 15% and above in urban farmers. The prevalence of diarrhoea (recall period: 2 weeks) was high in all study groups and ranged from 21.2% in the comparison population to 32.8% in workers collecting faecal sludge. For all investigated parasitic infections, we found significantly higher odds for urban farmers compared to the other groups (adjusted odds ratio between 1.6 and 12.9). Moreover, we found that relying on pit latrines or having no toilet facility was associated with significantly increased risk of "any parasitic infection". However, no protective effect could be found for current deworming practices and use of personal protective equipment.

The high prevalence of hookworm and *S. mansoni* in urban farmers are generally in line with previous results of other studies in Africa and elsewhere in the tropics (Blumenthal and Peasey 2002; Matthys et al. 2007). However, measured prevalence of *S. mansoni* and hookworm in urban Kampala were lower compared to prevalence measured in rural fishing communities around Lake Victoria corresponding to 88.6% and 46.1%, respectively (Tukahebwa et al. 2013). The high prevalence of hookworms in urban farmers can be explained, at least partially, with concentrations of hookworm eggs above WHO safety limits (2.0 eggs/L) found in water around the Nakivubo wetland. However, the low concentration of *A. lumbricoides* (0.2 eggs/L) and the absence of *T. trichiura* eggs do not correlate with the respective prevalence in exposure groups (Fuhrimann et al. 2015). In the overall study the participants prevalence of *E. histolytica*/*E. dispar* and *G. intestinalis* were considerably lower compared to a study of rural communities along Lake Victoria (McElligott et al. 2013). For infections with intestinal protozoa the multivariate regression analyses revealed lower odds for participants who attended school and attained at least primary level.

Comparing our results with model-based prevalence predictions, we found significantly lower prevalence of soil-transmitted helminths and *S. mansoni* in slum dwellers. However, prevalence obtained in farmers match the model-based predictions for soil-transmitted helminths and *S.*

mansoni and are even exceeding predicted values up to a factor of five for *T. trichiura* and *A. lumbricoides* (Karagiannis-Voules et al. 2015; Lai et al. 2015). Hence, our findings corroborate the concept that model-based predictions for urban areas should account for environmental factors (e.g. altitude), occupation, and socioeconomic status (Utzinger and Keiser 2006). Altogether and also in contrast to recent risk assessments by means of QMRA (Katukiza et al. 2013), our results showed that helminth and intestinal protozoa infections are relevant and important factors to consider for further risk assessments and burden estimates.

12.3.2. Intestinal parasitic infections in urban population in Hanoi

In Hanoi, the cross-sectional survey conducted with 618 adults from five groups found lower point-prevalence of intestinal parasitic infections than in Kampala, with highest rates in rural farmers (30.2%), followed by farmers reusing wastewater (11.1%), workers maintain the wastewater channels (10.2%) and peri-urban community groups (10.0%) and rural community groups (6.9%). Hookworm and *T. trichiura* represented the predominate infections overall participants with point-prevalence in rural farmers of 24.8% and 5.4%, respectively. These findings were underlined by the significantly higher odds of intestinal parasitic infection, regardless of the parasite species for rural farmers compared to other population groups (OR 5.8, 95% CI 2.5 to 13.7). Moreover, the higher risk for intestinal parasitic infection can be partially explained by the observed lack of access to improved sanitation and water among rural community groups (Ziegelbauer et al. 2012).

The observed differences between rural and peri-urban communities, especially farmers, are in line with previous reports from studies in Asia and around the world, indicating a beneficial effect of urbanization on the prevalence of intestinal parasite infections (Jex et al. 2011; Utzinger and Keiser 2006). We could not find significant association between the occupational exposure to urban wastewater and intestinal parasitic infections, which supports the findings of Do and colleagues (2006 and 2007) who conducted a cross-sectional survey in the Yen So commune in 2002 (rural at this time). However, in 2002 prevalence rates of helminth species were considerably higher across all participants (*A. lumbricoides*, *T. trichiura* and hookworm were 21.6%, 9.8% and 21.8%, respectively), suggesting that the various infrastructural improvements and strengthening of the health system helped to bring down the prevalence over the last decade. The observed protective effect among people who received deworming over the last year adds also to this improvement of people's health. The low prevalence of *A. lumbricoides and T. trichiura* infection correlates with concentrations of <1 eggs/L found in our environment assessment, which presumed low infection risk of *A. lumbricoides and T. trichiura*. However, the absence of hookworm eggs does not correlate with the respective prevalence in the exposure groups, especially in the rural farmers. This may be partially due to the fact that we were only able to measure hookworm eggs in water, while larval stages and eggs in soil or sediments were not investigated (WHO 2004). For all study participants low prevalence of intestinal protozoa were detected (<2%), which were considerably lower than the prevalence reported from rural communities along the Nhue River in Hanam province (Pham-Duc et al. 2011). However, other intestinal protozoa (for which we did not diagnose), such as *Cryptosporidium* spp and *Cyclospora* spp., may be of importance in these communities (Nguyen et al. 2008). The higher prevalence of diarrhoea episodes, skin and eye disease in farmers and workers exposed to wastewater compared to other groups is in line with reports from other studies conducted around Hanoi (Anh et al. 2007; Hien et al. 2007). Hence, further risk assessments such as QMRA or chemical risk assessments should be indicators to further examine exposures to wastewater for characterising the risks of the specific causative hazards (i.e. pathogenic bacteria, viruses or toxic chemicals such as heavy metals, pesticides or fertilizer).

12.3.3. Comparison between Hanoi and Kampala

The infection rates with intestinal parasitic infections differ considerably between exposed populations groups and also between the two cities. While, in Kampala the high prevalence was generally due to urban farmers, people living in peri-urban areas of Hanoi were at lower risk than people living in rural communities. However, around both cities farming was related to a higher prevalence and odds of infections with intestinal parasites. In Kampala urban farmers had prevalence of intestinal parasitic infections of 76%, while high infection intensity was found, depending on the helminth species, in 7% to 22% of all cases. However, in Hanoi, we could not identify a significant increase of the risks for farmers using urban wastewater, while all participants infected with intestinal parasites were found with low infection intensities. Thus, rural farmers, not using wastewater, showed the highest prevalence of intestinal parasitic infections (30%) and increased odds compared to urban farmers. Sanitation workers did not show significant increased odds compared to the other exposure groups in both cities. However, due to the generally low sample size of the workers, these results should be interpreted with caution. Moreover, in both surveys access to improved water and sanitation was found protective against infections with intestinal parasites. Hence, the situation in regards to intestinal parasitic infection is considerable different between the cities, which asks for different control strategies.

In Kampala, especially the people found with moderate to high infection intensities of *S. mansoni* and hookworm should be protected. They are likely to be impacted by severe soil-transmitted helminthiasis and schistosomiasis and related health consequences such as anaemia or organ failure (Tukahebwa et al. 2013). Moreover, farmers re-contaminate their living and working environments, which is likely playing an important role in the transmission of intestinal parasitic infections in this urban environment. In view of our results, there is an urgent need for integrated disease control strategies for urban framers and people living in informal communities (Singer and de Castro 2007; Utzinger et al. 2009). The extension of the national helminth control program should be considered to Kampala's high risk population groups (MoH Uganda 2013). In Hanoi, prevalence of intestinal parasitic infections decreased in the urban population over the past decades (Do, Mølbak, et al. 2007). Hence, one can attribute this to the local control programs for intestinal parasitic infections in these areas (Montresor et al. 2013). For Hanoi, the focus of control strategies should rather be on rural communities, while anticipating urbanization and providing specific training and education programs. The two cross-sectional survey confirmed the relevance for epidemiological case studies to identify high risk groups within heterogeneous urban communities to build on an evidence-base of a locally relevant disease to be considered (e.g. schistosomiasis) and risk factors (e.g. improved water and sanitation) related to wastewater reuse in order to guide preventive measures (Utzinger and Keiser 2006; Matthys et al. 2007). Population groups to be targeted include urban farmers and workers maintaining the sanitation system, marginalized slum dwellers along wastewater recovery and reuse systems and people living in proximity to urban centres or under similar conditions without exposure to urban wastewater streams.

12.4. Burden of diarrhoeal disease due to exposure to wastewater

12.4.1. Burden of diarrhoeal diseases related to health-based targets

This chapter outlines the situation of gastroenteritis in Kampala and Hanoi and tries to estimate the related burden due to exposure to wastewater by means of QMRA. Indeed many pathogenic viruses, bacteria, intestinal protozoa and helminths transmitted by wastewater are causing gastroenteritis (Becker et al. 2013; Pham-Duc et al. 2013). Hence, to discuss and compare burden of diseases and risk factors, DALY are gaining interest worldwide (Murray et al. 2012). For example, WHO is setting their health-based target for the exposure to wastewater according to the DALY metrics (a tolerable additional burdens between 10^{-4} and 10^{-6} DALYs pppy is suggested) (WHO 2006a; Mara et al. 2010). Thus, the health burden due to diarrhoeal diseases is estimated to be the 2nd most important disease outcome just after lower-respiratory diseases in developing countries. There, it accounts between 76.2 and 97.5 million DALYs. This is 98,3% of the global burden due to diarrhoeal disease and is mainly caused by children below the age of 5 years (Murray et al. 2012). However, model-based estimates indicate that the global burden of diarrhoeal disease was reduced by about half since 1990 together with an epidemiological transition i.e. a shift from acute communicable to non-communicable disease occurred (Utzinger and Keiser 2006; Jürg Utzinger et al. 2015).

Focusing on Uganda, one can see that the life expectancy increased by 5 years (from 50 to 55 years) between 1990 and 2010. The highest burdens were and are still caused by acute communicable diseases (Figure 12.1). Concomitant the burden of diarrhoeal diseases decreased by 3.4 times since 1990 but is still accounting for 612,306 DALYs (1,819 DALYs/100,000 people per year) (Institute for Health Metrics and Evaluation 2015). For Vietnam the change in disease pattern looks more drastic since 1990. While the life expectancy increased by 12 years (from 60 to 72 years), there was also a shift from communicable to non-communicable diseases, i.e. the country is in a epidemiological transition. In addition, considerable reduction in burden of diarrhoeal diseases by 4.6 to 186,271 DALYs (212 DALYs/100,000 people per year) were achieved. Compared to Uganda, this DALY estimates are 8.6-fold lower pppy.

Besides the vast possibilities to compare data between countries, sex and age with the data provided by the global burden of disease study, there is a lack of data on regional levels (urban vs. rural) or specific exposure groups and risk factors. Moreover, there is considerable uncertainty on the prevalence and magnitude of the disease burden caused by specific pathogenic organisms (Murray et al. 2012).

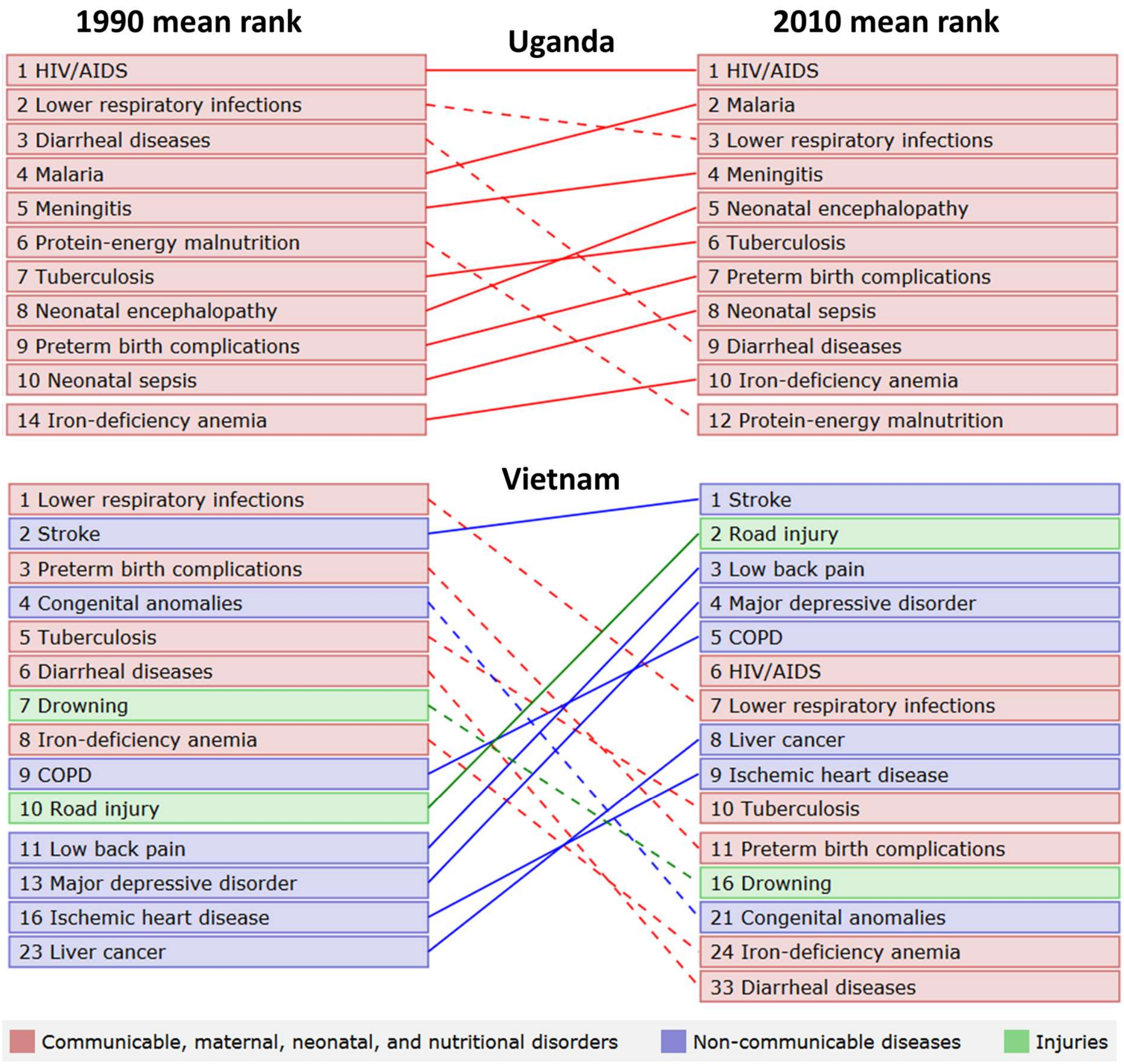

Figure 12.1 Arrow diagram of the global burden of disease study 2010 outlining the importance of disease for Uganda and Vietnam in disability-adjusted life years in 1990 and 2010.

12.4.2. Burden of diarrhoeal diseases estimated for Kampala and Hanoi

Using a QMRA approach, we estimated a considerable burden due to water-borne pathogens among different population groups who were exposed to wastewater in the Nakivubo area in Kampala. The total annual disease burden across all 18,204 exposed people was estimated to be 304.3 DALYs. Incidence estimates of gastrointestinal disease episodes per year were highest for urban farmers (10.9) and children in slum communities (8.3); estimates were lower for other exposed groups (<4.3). Disease burden pppy were highest in urban farmers, sanitation workers and children in slum communities (0.073, 0.040 and 0.017 DALYs). For our study area in peri-urban Hanoi, the QMRA estimated an annual disease burden across 7’125 people exposed to wastewater of 62.7 DALYs. Incidence estimates of gastrointestinal disease episodes per year were much higher for urban farmers (2.0) than for all the other exposed groups (≤1.0). Consequently, also disease burden per person per year (pppy) was highest in urban farmers (0.011 DALYs pppy), followed by sanitation workers and people exposed to flooding events (0.006 and 0.0005 DALYs pppy, respectively).

The QMRA estimates for both cities are considerably lower than the few attempts which have been made to estimate the exposer of wastewater in LMICs. Thus, the disease burden estimates made for a typical slum area in Kampala was 10,172 DALYs per 15,015 people (Katukiza et al. 2013) and for an urban wastewater systems in Accra 31,979 DALYs per 286,833 people (Labite et al. 2010). These large differences can partly be explained by different pathogens included, DALY estimates per pathogen (i.e. we excluded sequelae) and the methodological differences (i.e. calculation of risk of illness).

For Kampala our burden estimates for urban farmers, sanitation workers and children playing in slum communities are 7, 3 and 2 times higher, respectively, than average diarrhoeal disease burden estimate for an Ugandan of 0.018 DALYs pppy (Institute for Health Metrics and Evaluation 2015). The same conclusion can be drawn for the scenarios in Hanoi were for urban farmers, sanitation workers and rural farmers are 6 and 3 times higher than the diarrhoea burden estimates for an average Vietnamese of 0.002 DALYs pppy. The high number of cases and the resulting burden due to rotavirus, *E. coli* and *Cryptosporidium* spp. combined caused most of the disease burden (>90%) in the models. The same was also indicated by other QMRA studies in Africa (Katukiza et al. 2013; Machdar et al. 2013). However, assumptions on pathogen concentration ratios and dose-response relationships were obtained in studies in high income countries. Hence, there might be considerable differences for low-income and lower-middle income settings like Kampala and Hanoi as there is likely a different level of immunity do to more frequent exposures. Thus, there is an urgent need for further studies clarifying on pathogen concentration ratios and dose-response relationships for LMICs settings.

12.4.3. Validation of QMRA findings with epidemiological data

To further compare and validate the QMRA estimates, the self-reported 14-day incidence of diarrhoea episode obtained in our cross-sectional surveys was used. The diarrhoea incidence was estimated by asking the participants if they experienced diarrhoea (three or more liquid stools per day) today, yesterday, last week or two weeks ago. In the cross-sectional survey conducted in Kampala, self-reported 14-day incidence of diarrhoea episodes ranged from 21% in slum communities and urban farmers to 33% in workers along the sanitation system. Whereas in Hanoi self-reported 14-day incidence of diarrhoea episodes were highest in communities in Duyen Ha, followed by urban farmers, communities in Bang B and Tam Hiep, workers and rural famers 12%, 10%, 9%, 8% and 4%, respectively. When speculatively assumed that this 14-days incidence can be extrapolated to 1 year (52 weeks, considering no seasonality), the annual incidence would be between 5.5 and 8.6 episodes pppy in Kampala and between 3.1 and 1.0 in Hanoi. If we compare this with the combined incidence rates of all seven pathogens, the estimates are similar (i.e. for Kampala 10.9 in urban farmers, 8.3 in children living in slum communities and 3.3 in sanitation workers, 0.3 in community members and 0.2 in swimmers in Lake Victoria; and for Hanoi, 2.0 in urban farmers, 1 in sanitation workers, 0.1 in rural farmers and community members). Moreover, when comparing our estimates to incidence of diarrhoeal episodes obtained by cohort studies in developing countries, our estimates are in line for children in Kampala (3.0 to 7.3 for age ≤5 pppy) but appear to be too high for adults (0.1 to 0.6 for age >5 pppy) (Mara et al. 2010; Fischer Walker et al. 2012).

However, when looking at the different estimates, one has to keep in mind that with both, cohort studies and cross-sectional surveys, the accurate assessment of self-reported diarrhoea episodes is a challenge. As methodological weakness due to recall and reporting biases of diarrhoea episodes are eminent, these biases may lead to a considerable underreporting. The definition of a diarrhoea episode can be interpreted differently (three or more liquid stools per day) and people may not be willing to share this information as it is considered as a personal issue (Schmidt et al. 2011; Pham-Duc et al. 2014). Accordingly, lessons from applying QMRA to estimate risks in food safety showed a tendency to estimate higher risks than epidemiological surveys. At the same time QMRA is able to predict the often very low number of infections (Havelaar et al. 2008). For further cross-comparison between epidemiological surveys and QMRA, a standardised way to assess incidence and burden of diarrhoeal episodes but also for intestinal parasitic infections should be proposed and validated to make best use of both tools. Further QMRA should include certain exposures, which are also relevant for causing diarrhoea (e.g. drinking polluted water, eating contaminated food and human to human transmission); and for frequently exposed population groups, the likely established level of immunity should be included.

12.4.4. The context specificity of health-based targets

We presented a case study on how the risk assessment framework of the WHO guidelines for the safe use of wastewater, greywater and excreta could be applied (WHO 2006d; Mara et al. 2010). The validation of the QMRA estimates with findings from epidemiological surveys and other QMRAs showed important limitations of the estimates. Hence, results have to be interpreted with caution. To improve the QMRA, further sensitivity analyses of the effect of used parameters are needed and the uncertainty of the estimates should be analysed (Haas et al. 2014). A standardised methodology should be proposed allowing for comparison between QMRA but also with epidemiological surveys in environments of LMICs.

Indeed the DALYs pppy for these different population groups were several thousand-fold above the revised WHO tolerable level of 0.0001 DALYs pppy (Mara et al. 2010). Thus, one has to keep in mind that health-based targets are often politically driven rather than context specific (WHO 2006a). However, from my point of view of as a risk assessor, it would be advisable to set targets according to local realities and validated with epidemiological findings. For example, as a first step towards local targets, the GDB study could be a useful tool to provide such a background. In Figure 12.2, a comparison of our different QMRA-based DALYs estimates pppy compared with WHO health-based target and estimates made by the Global Burden of Disease study 2010 is shown to exemplify this statement (WHO 2006d; Mara et al. 2010; Institute for Health Metrics and Evaluation 2015).

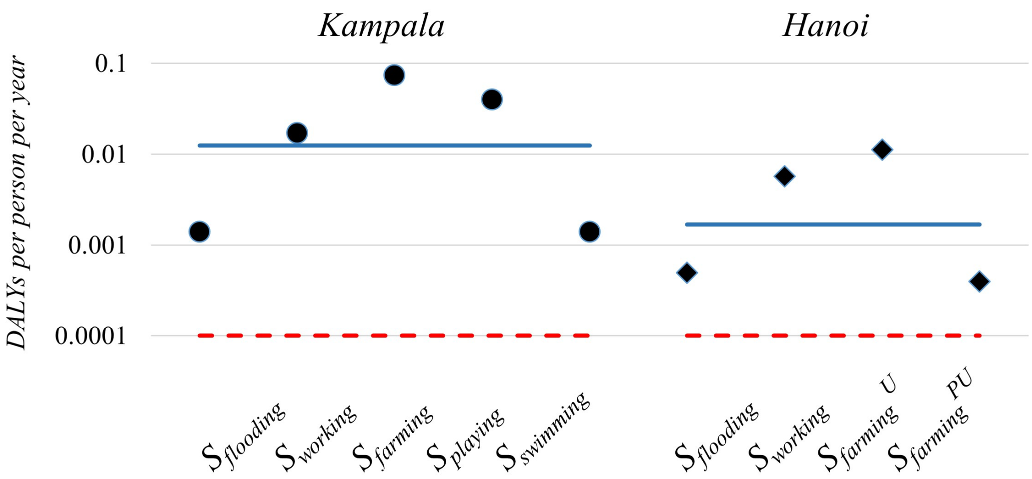

Figure 12.2 Quantitative microbial risk assessment (QMRA) for the exposre to wastewater Combined disability-adjusted life years (DALYs) for diarrhoea generated for norovirus, rotavirus, *Campylobacter* spp., pathogenic *E. coli*, pathogenic *Salmonella* spp., *Cryptosporidium* spp. and *Ascaris lumbricoides*. Black dots showing exposure scenarios in Kampala, namely: $S_{flooding}$: people at risk of flooding events; $S_{working}$: sanitation worker; $S_{farming}$: urban farmer using wastewater; $S_{playing}$: children living in slum communities; and $S_{swimming}$: people swimming in Lake Victoria. Black diamantes showing exposure scenarios in Hanoi, namely: $S_{flooding}$: people at risk of flooding events; $S_{working}$: sanitation worker; $S_{farming}^{U}$: urban farmer using wastewater; and $S_{farming}^{U}$: peri-urban farmer not using wastewater. Green line: country estimates of the Global Burden of Disease study 2010. Red dotted line: revised health-based targets of the World Health Organization.

12.5. Limitations and practical relevance of health risk estimates

12.5.1. Limitations and lessons learned

While conducting environmental assessments, cross-sectional surveys and QMRAs to determine the health risks due to the exposure to wastewater in Kampala and Hanoi, we came across different limitations and lessons for each of the applied tools, which are given in bullet-point-style below and are summarised in Table 12.2.

- For the environmental assessments five important points came up for which further research and adaptations are needed: (i) measurements over a period of two months can reveal important information on microbial and chemical pollution; (ii) building on this information, further concepts should be developed to obtain yearly variation and variation caused by extreme events, while relying on a subset of the indicator parameters (Cissé 2013); (iii) discharge standards should rely on sound assessment of locally measured chemical and microbiological parameters as current national and international discharge and reuse standards did not match the reality found with our case studies (MONRE 2008;

NEMA 1999); (iv) indicator parameters for faecal and chemical pollution cannot provide specific information on diversity or concentration of pathogens or toxic chemicals; and (v) context-specific hazards should be identified and quantified by means of, for example, PCR or metagenomics studies (Djikeng et al. 2009; Becker et al. 2015).

- While having conducted two cross-sectional surveys and enrolled about 2,000 individuals in Kampala and Hanoi together, we determined five important lessons: (i) cross-sectional design represents a good way to get an initial understanding of the situation; (ii) cross-sectional surveys are time-consuming and the process of protocol development and applying for ethical permission needs strong local partnerships and networks; (iii) to follow up on identified health issues, cohort, case-control or reinfection studies would be the method of choice (Do et al. 2007); (iv) self-reported signs and symptoms (e.g. diarrhoea episodes, skin and eye disease) are difficult to interpret as methodological weakness due to recall and reporting bias of diarrhoea episodes are eminent (Pham-Duc et al. 2014); and (v) such bias may lead to a considerable over- or underreporting, as the definition of a diarrhoea episode can be interpreted differently (three or more liquid stools per day) and the people may not be willing to share this information as it is considered as a personal issue (Schmidt et al. 2011).
- QMRA is already an established tool within risk analysis frameworks for assessing risks in the food and water sector in high-income countries (Haas et al. 2014). However, it lacks application and validation in LMICs (Barker 2014; Katukiza et al. 2013). Therefore, of highest importance to be considered in next models are context-specific: (i) estimates of ingested volumes of water; (ii) information on the ratio of pathogenic strains in accordance to indicator organism; (iii) dose-response relationships which account for acquired immunity of exposed individuals; (iv) other exposure pathways such as dermal contact and inhalation; and (v) other water-borne pathogens which occur in high prevalence and cause severe health implications such as adenoviruses, cholera, hepatitis, hookworm and *S. mansoni* (Katukiza et al. 2013; Barker 2014; Eddleston et al. 2012).

Table 12.2 Risk assessment approaches showing advantages, limitations and potential when used together.

	Environmental assessments	**Epidemiological studies**	**Quantitative microbial risk assessments (QMRA)**
Data which can be obtained	• Concentration of microbial and chemical contamination in water, soil, sediment and plants • Identification of critical control points • National and international quality standards	• Prevalence and intensity of helminth infection • Prevalence of intestinal protozoa infections • Self-reported signs and symptoms (e.g. diarrhoea, skin and eye disease) • Risk factors • Confounding factors • Spatial information • Exposure pathways	• Incidence of gastroenteritis • Number of disease episodes • Burden estimates • Health-based targets and Global burden of disease estimates
Advantage	• Determines concentrations and die-off/removal rates of indicator microorganisms in water, soil, sediment and plants • Treatment function at critical control points	• Measures actual disease in exposed population • Can be used to test different exposure hypotheses • Provides data on the effect of adjusted effects (for other risk and confounding factors) for exposures to wastewater	• Estimation of risk and disease burden at critical control points and exposure scenarios • Can estimate very low levels of risk of infectious disease • Faculties comparison of different exposure routs and with other disease burden estimates
Limitations	• Time-consuming • Need of trained staff and laboratory facilities • Obtaining laboratory results takes time • Lack of standardized procedures of the detection of pathogens in LMICs • Recovered parameters may show high variability • Some methods do not determine viability	• Time-consuming • Need of trained staff and laboratory facilities • Bias can affect results • Sample size needed to be able to measure statistical significant health outcomes (i.e. large sample size needed) • Need for ethical approval • Need to find a balance between power of the study in relation to its sensitivity	• Exposure scenarios may differ significantly • Only an assumption of the reality • Data on pathogens may not be available • No standardised way to validate model estimates with epidemiological data • Dose-response relationships, pathogen ratio, ingestion rates are missing for context of LMICs
Potential when used in combination	• Proving a first understanding of potential hazards and treatment functions along the sanitation chain. • Context specific information on microbial contamination for QMRA	• Focus on known disease and compare between exposure groups • Defines the existing relevance of measured hazards • Characterised exposure pathways can be used for QMRA (e.g. farmers, communities, workers) • Validation with QMRA findings	• Estimates risk population groups where prevalence and cause cannot easily be obtained (swimming, impact of flooding event, consumption of crops or water) • Defining health-based targets and potential for simulating cost-effective interventions

12.5.2. Mitigation strategies along wastewater recovery and reuse systems

With our two comprehensive case studies we showed a possible way to assess and interpret different environment contamination and health risks in regard to the exposure to wastewater in LMICs. Indeed, we measured typical contamination of wastewater receiving water bodies (e.g. drainage and storm water channels) between 10^6-10^8 CFU TTC/100ml and 10^6-10^7 CFU *E. coli*/100mL in Kampala and Hanoi (Mara 2004). However, many other features along wastewater recovery and reuse systems differed considerably between the two sites and did not directly respond to text-book knowledge. Starting from the complex legal reuse frameworks and the various existing reuse practice to the highly varying microbial and chemical contamination found in community areas, aquaculture ponds, agricultural fields and natural lakes, in addition to the treatment and control measures which were not operating as designed or expected (Mara 2004; Stenström et al. 2011; WHO 2006a). From the point of view of a risk assessor this underlines the importance for context-specific health risk assessments and asks for individual responses to address these health risks. Subsequently in view of our findings, and acknowledging inherent limitations, mitigation strategies are discussed for the context of Kampala and Hanoi. Of note, cost-effectiveness studies should be conducted (e.g. as part of QMRA in combination with socio-economic analysis) and the results should be independently evaluated by risk managers before communicated to stakeholders.

12.5.2.1. Public health programmes

For Kampala, based on our findings we propose the following measures to further improve public health programmes:

- protect preschool-aged children, school-aged children and women of childbearing age living in slum communities through rotavirus vaccination, and bi-annual hygienic and deworming campaigns to reduce morbidity in the population (WHO 2011; Sigei et al. 2015). The possibilities of extending the current national deworming program to Kampala should be considered based on the study findings (MoH Uganda 2013);
- educate farmer communities along the Nakivubo wetland and other wetlands around Kampala by means of integrated control and farmer field schools (Utzinger et al. 2009; Van Den Berg and Takken 2007) i.e. of regular information workshops on health risks and personal protective equipment. Provision of rotavirus vaccination, and bi-annual hygienic and deworming campaigns could also be recommended (Sigei et al. 2015); and

- teach workers at NWSC and PEA on the recognition of health risks and the use of personal protective equipment, and the provision of rotavirus vaccination, and bi-annual hygienic and deworming campaigns (WHO 2006a).

For Hanoi, based on our findings we propose the following measures to further improve public health programs:

- continue school-based helminth and education programs (Montresor et al. 2013);
- provide specific training and education programs for rural communities, while anticipating for further urbanization of the rural areas (Pham-Duc et al. 2014);
- provide vaccination of rota virus for urban farmers and children (Hien et al. 2007);
- promote non-technical control (e.g. personal protective equipment, food processing) measures along with awareness campaigns on safe work practices (farmers and workers) and processing of wastewater-fed produce to maximise the benefit from wastewater reuse and minimize public health impacts (Bassan et al. 2014; Drechsel et al. 2015); and
- evaluate and adapt integrated disease control programs to peri-urban communities, including intestinal parasitic infections, Dengue and Japanese encephalitis (Van Den Berg and Takken 2007; Cuong et al. 2011).

12.5.2.2. Infrastructural improvements

For Kampala, based on our findings, we propose the following measures to further improve wastewater management and allow for safe reuse and recovery of wastewater and faecal sludge:

- re-establish the Nakivubo wetland flora and fauna to reclaim its function as a natural maturation pond and retention pool, allowing for safe reuse and reducing costs and risks for the drinking water system in Lake Victoria (Beller Consult et al. 2004; Howard et al. 2006);
- inform people who access the recreational beaches at Lake Victoria about the risks involved in swimming in Lake Victoria;
- protect communities at risk of flooding (e.g. through the construction of small dams and drainage systems) (Cissé et al. 2011; Katukiza et al. 2013);
- improve access to improved water and sanitation in informal communities (Katukiza et al. 2010);
- restrict access to frequently flooded areas and the Nakivubo channel (e.g. via perimeter fences) (Katukiza et al. 2013);

- decrease faecal contamination of the slum areas, applying a strategic way for safe collection, treatment and disposal of faecal sludge (Schoebitz et al. 2014); and
- implement the central treatment of wastewater, however, most likely this is not feasible due to the economical and sustainable considerations in Kampala, which also applies to many other urban contexts in low- and middle-income countries (Magalie Bassan et al. 2015; Strande et al. 2014).

For Hanoi, based on our findings we propose the following measures to further improve wastewater management and allow for safe reuse and recovery of wastewater and faecal sludge:

- reduce microbial pollutions, while improving the treatment efficiency of septic tanks, e.g. through regular empting and anaerobic baffled reactor together with faecal sludge treatment through e.g. drying beds or co-composting (Schoebitz et al. 2014);
- improve and upgrade the existing sedimentations ponds to functional waste stabilisation ponds with anaerobic, facultative and aerobic treatment together with appropriate retention times (Tilley et al. 2014);
- implement wastewater treatment options for the wastewater in the To Lich River and Nhue Rivers, e.g. through regular desludging of the channels, basic screening and additional waste stabilisation ponds or constructed wetlands (Tilley et al. 2014); and
- update the existing sentinel wastewater monitoring system operated by the Vietnam Environment Administration, for the Nhue River and the Day River basin with indicators for microbial pollution (i.e. *E. coli*) to further recognise trends and seasonal variability of microbial contamination (Sherpa et al. 2014; Vietnam Environment Administration 2015).

12.6. Promotion of risk assessment and the way into practice

In this chapter the discussion addresses applied risk assessment approaches and their potential for application in the larger framework of SSP along wastewater recovery and reuse in LMICs (objective 4). As presented, each of the applied approaches can produce valuable results to interpret health risks for different population groups exposed to wastewater. Thus, it is crucial to integrate such risk assessments into a broader risk analysis framework to inform and prioritize health risks (Winkler 2011). Various different frameworks are given to integrate such tools, e.g. hazard analysis and critical control points (HACCP), life cycle assessments, the "Stockholm Framework", the "EcoHealth approach" and the SSP manual (WHO 2006a, 2015; Nguyen-Viet et al. 2009; Corominas et al. 2013). In our case, we initially applied risk assessment as an integral part of a step-wise health impact assessment approach, where the assessment of health risks is the central point after a screening and a scoping study to further guide mitigation and monitoring strategies (Winkler et al. 2013). Over the course of the RRR project the in-depth risk assessment approaches could be successfully linked to the broader risk assessment and management framework of the SSP manual and the risk and impact assessment for RRR business models in Kampala and Hanoi (WHO 2015).

We acknowledge that health risk assessment along wastewater recovery and reuse or even the wider sanitation sector is a complex issue as it is managed by different local private and public institutions, responsible for treatment (e.g. wastewater treatment companies), collection (e.g. private faecal collectors), conveyance, disposal (e.g. environmental institution) or reuse (e.g. agriculture, wetland protections agencies) (Qadir et al. 2010; Keraita and Dávila 2015). Therefore, it is not a straight forward task to address such systems, which showed to be mixed in design and different exposure groups can be affected by various diseases (WHO 2006a). Data quality and availability are often not sufficient and SSP or other risk-based frameworks have to work with assumptions on potential health risks drawn from other similar contexts (Labite et al. 2010; Katukiza et al. 2013). Without context-specific data the SSP process likely remains a theoretical exercise (WHO 2006a). Hence, collection of primary data would ensure that control measures target the greatest health risks and incremental improvement plans could be integrated into existing local master plans for the infrastructural development of the wastewater sector and public health programs (e.g. deworming or vaccination) (Bartram et al. 2015; WHO 2015).

Our studies in Kampala and Hanoi, next to a few others, showed that the combination of environmental assessments, epidemiological surveys and QMRA can address this complex wastewater recovery and reuse systems and can provide valuable and complementary information if applied in a systematic way (Nguyen-Viet et al. 2009; Pham-Duc 2012). Indeed, such information are crucial for risk managers and provide the best information on risks with often imperfect data. Overall the approach helps to engage with various local stockholders from the health sector (e.g. Ministry of Health, School of Public Health and local NGOs) (WHO 2015). Hence, bringing a public health perspective to traditional non-health sectors like sanitation engineering and urban agricultural will strengthen urban planning and can help to protect vulnerable urban population groups (Utzinger and Keiser 2006). The risk analysis should be promoted with independent risk assessment, management and communication structures (Haas et al. 2014).

We fostered our experience with the health risk assessment approaches and the SSP testing in Kampala in the form of a short paper and video (chapter 5), which can be used for training and promotion of health risk assessment and SSP along wastewater recovery and reuse systems. It is an important step to bring these tools to practise, while building on local capacities and making best use of the results. Linking such in-depth risk assessments to SSP approaches, and existing risk management and communication frameworks are crucial tasks. This would help to build-up the necessary local capacity to conduct and interpret the approaches and feed the data into the SSP process. As we learned in the two case studies additional resources are required to build and strengthen local capacities in the detection of microbial and chemical contamination in the environment, intestinal parasites in exposed population groups and QMRA approaches. Taken together, this could ensure and promote a safe recovery and reuse along wastewater systems as it is also proposed by the SSP manual to: (i) systematically identify and manage health risk at CCPs; (ii) guide investment based on actual risks, to promote health benefits and minimize adverse health impacts; and (iii) provide assurance to authorities and the public on the safety of sanitation-related products and services (WHO 2015).

13. Conclusions and recommendations

The findings from this 3-year PhD thesis study make an important contribution to understanding the nexus of urban wastewater recovery and reuse systems, wastewater pollution and their implications for public health in the context of a major East African and Southeast Asian city. While conducting these two case studies, we underlined the importance of having a detailed context-specific understanding of wastewater recovery and reuse systems. Combining evidence generated from environmental survey, epidemiological surveys and QMRA can help authorities and stakeholders to understand existing systems and hazards along critical control points, while evaluating further investments in infrastructure and actions to protect public health.

For the studies in Kampala and Hanoi the following conclusions are offered for consideration:

- in Kampala, wastewater reuse is not permitted by law and no management system is in place that can handle the amount of wastewater generated. The level of pollution has drastically increased over the past five years. Hence, large volumes of, at best, partially treated wastewater are discharged into Lake Victoria each day, which poses a threat for the drinking water supply in Kampala. Moreover, contamination of microbial and chemical pollutants in natural wetland areas were found above tolerable levels for unrestricted wastewater reuse in urban agriculture;
- in Hanoi, supportive legal frameworks for wastewater reuse are in place and large investments in infrastructure were made to convey and treat wastewater over the past decades. However, the concentration of bacteria in agricultural fields remains above tolerable levels and does not yet allow for safe reuse in agriculture. Hence, further non-technological mitigation measures are needed. Moreover, in the rural Duyen Ha commune, local drainage systems are highly polluted with bacteria, besides using water from Red River and wells;
- in both cities, the issue of faecal sludge collection is challenged by the lack of formal and adequate collection services and limited disposal and reuse solutions. Industrial pollution is a major issue, while registration and source control of industrial effluents is lacking;
- the epidemiological case study in Kampala identified high risk groups within heterogeneous urban communities with intestinal parasite infection prevalence rates in excess of 20% and considerably high intensities of soil-transmitted helminths and *S. mansoni*. Of note, *S. mansoni* was not considered as an important disease occurring in urban Kampala and only limited control and treatment was available before the study. Our findings confirm that water

and sanitation are important risk factors for infection with intestinal parasites. Moreover, current deworming practices showed no effect on intestinal parasitic infection. Especially, marginalised slum dwellers and urban farmers should be targeted with integrated control measures (deworming and awareness programs). Further research should identify the cause of the high prevalence of self-reported diarrhoea (20-40%);

- the epidemiological case study in Hanoi identified lower prevalence of intestinal parasitic infection than previously reported, leading to the conclusion that implemented hygienic and deworming programmes have had an effect. However, considerably higher prevalence rates of parasitic infection were found in rural communities (five km away from the city outskirt). These increased prevalence rates are mainly driven by limited access to improved water and sanitation. Of note, wastewater reuse had no significant association with increase in intestinal parasitic infections. We recommend to target rural population groups with integrated control measures (deworming and awareness programs);
- indeed, the DALYs pppy for these different population groups were several thousand-fold above the revised WHO tolerable levels of 0.0001 DALYs pppy. Considering the inherent limitations of QMRA in Kampala, urban farmers, sanitation workers and children playing in slum communities experience diarrhoeal burdens that are 7, 3 and 2 times higher, respectively, than the diarrhoeal burden estimates for the whole of Uganda (0.018 DALYs pppy). While in Hanoi, urban farmers, sanitation workers and rural farmers experience diarrhoeal disease burdens that are 6 to 3 times higher than the estimates for an average Vietnamese (0.002 DALYs pppy);
- high burden estimates, especially for urban farmers and workers in both cities and for children living in informal settlements in Kampala are of greatest concern. There is an urgent need to further investigate the health burden of gastroenteritis caused by pathogenic *E. coli*, *Salmonella* spp. and rotavirus and to confirm model-based estimates, which can trigger protective actions (e.g. vaccination and exposure reduction); and
- health-based targets should be set according to local realities that have been validated with epidemiological findings. For example, as a first step towards setting local targets could be the consideration of estimates provided by the Global Burden of Disease study 2010.

Following these specific conclusions we highlighted the need to integrate in-depth health risk assessments tools into the SSP concept. This would build-up the local capacity necessary for conducting and interpreting assessments and make the best use of the data to guide preventive actions. Additional resources are required to build and strengthen local capacities for detecting intestinal parasites, indicating organisms in the environment and using QMRA approaches. These findings are especially interesting for those working towards the sustainable development goals, as they address sustainable and safe wastewater reuse and recovery systems, from the point of generation to the point of disposal and reuse. Hence, expanding on sanitation safety planning approaches to include in-depth health risk assessments has great potential for minimising public health implications and could maximise gains from recovered water, nutrients and energy around urban areas in LMICs.

14. Outlook and further research needs

Over the past years there were many initiatives addressing the issue of sanitation, which led to an enormous theoretical evidence based on sanitation systems, good hygienic and safe reuse practises (Strunz et al. 2014; WHO 2014, 2015; Bartram et al. 2015). Various organisations and programs have started to address water, sanitation and hygiene within frameworks towards sustainable sanitation solutions (e.g. sustainable sanitation alliance). A world toilet day (19 November) was initiated by the United Nation (UN) and the UN General Assembly declared the year 2008 to the international year of sanitation to stress that sanitation is not only an issue of hygiene and disease but also of dignity (UN 2015). Indeed, this led to subnational improvements in access to improved wastewater and sanitation. However, the up-take of these approaches and their sustainability beyond a project period is often minimal (Dora et al. 2014; WHO 2014). In view of the rapid population growth, unplanned urbanization resulting in densely populated and poorly equipped areas, will continue in many parts in Africa and Asia and are asking for applicable solutions and local capacity to protect public health and the environment (United Nations 2014).

Therefore, joint efforts and integrated management approaches, such as SSP, are needed where local stakeholders can assess and manage recovery and reuse systems, involving local health and environment authorities (WHO 2015). "Local capacity building" and "ownership creations" are the key words and ask for a rethink of many of the current approaches. The SDG agenda should ensure that these two headlines are more than just nice buzz words. Joint efforts international institutions to streamline strategies, assessments and intervention plans, which deal with wastewater recovery and reuse issues from generation of waste to the point of disposal and reuse (WHO & UNICEF 2012; Strande et al. 2014; Bassan et al. 2015).

Thus, the following research needs were identified to assess and protect the health of people living and working along wastewater recovery and reuse systems in LMICs:

- provide more case studies on urban sanitation systems and wastewater recovery and reuse schemes in Africa and Asia but also in Latin America;
- involve health actors in SSP processes (e.g. Ministry of Health or Schools of Public Health) to apply in-depth risk assessments and fill data gaps which can be used within the SSP framework for improvement plans;

- up-date WHO guidelines with recent evidence and developments, especially around the establishment of health-based targets and QMRA approaches;
- review latest data on health risk related to exposures to wastewater;
- implement sentinel monitoring systems that will inform evidence-based decision-making and responses that are readily tailored to this social-ecological system;
- assess by longitudinal means parasitic infections and diarrhoea alongside with targeted interventions in exposed population groups;
- develop integrated control strategies specifically for urban and peri-urban farming communities;
- adapt health-based targets to reasonable levels, e.g. based on prevalence of disease or presence of contamination rather than on DALYs; and
- develop QMRA methods that can make use of the burden estimates and produce estimates which can be compared to GDB estimates and epidemiological findings;
    - identify and quantity context-specific pathogens;
    - develop context-specific dose-response relationships;
    - conduct sensitivity and uncertainty analysis of applied parameters;
    - conduct cost-effectiveness studies on feasible mitigation measures.

15. References

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16. Appendix

16.1. Chapter 7: S1 Table. Water, sanitation and hygiene (WASH) specific risk factors and risk factors related to the occupation of workers and farmers

S1A Water, sanitation and hygiene (WASH) specific risk factors of the participants enrolled in the cross-sectional survey in Kampala, stratified by five exposure groups.

Water, sanitation and hygiene risk factors	$com_{comparison}^{*}$		$com_{exposed}^{*}$		$farmer^{*}$		$worker_{fs}^{*}$		$worker_{ww}^{*}$		**Difference (χ^2)**
	n=331		n=229		n=245		n=67		n=43		
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**p-value**
Exposure to potentially contaminated water while											
Flooding of living area	5	1.5	108	47.1	157	64.1	6	9.0	14	32.6	<0.001
Swimming in Lake Victoria	0	0	0	0	1	0.4	1	1.5	1	2.3	0.043
Household with latrine	214	64.7	112	48.9	137	55.9	63	94.0	41	95.4	<0.001
What kind of your toilet do you use											
Flush toilet	8	2.4	3	1.31	19	7.8	10	14.9	12	27.9	
VIP latrine	92	27.8	110	48.0	74	30.2	39	58.2	23	53.5	
Traditional pit late	222	67.1	77	33.6	100	40.8	17	25.4	7	16.3	
No facility	4	1.2	2	0.9	8	3.3	0	0	0	0	
Other places	5	1.5	37	16.1	44	18.0	1	1.5	1	2.3	<0.001
With how many households do you share your toilet											
Private toilet	84	25.4	43	18.7	76	31.0	17	25.4	20	46.5	
1-5 households	77	23.3	34	14.8	37	15.1	21	31.3	10	23.3	
5-11 households	79	23.9	20	8.7	36	14.7	19	28.4	11	25.6	
≥ 11 public toilet	91	27.5	132	55.0	96	39.2	10	14.9	2	4.7	<0.001
Handwashing											
After defecation	280	84.6	182	79.5	139	56.7	28	41.8	22	51.2	<0.001
Before starting work	32	9.7	28	12.2	15	6.1	7	10.5	9	20.9	0.025
After work	135	40.8	98	42.8	178	72.7	48	71.6	29	67.4	<0.001
Before eating	264	79.8	186	81.2	207	84.5	51	76.1	35	81.4	0.505
After eating	266	80.4	181	79.0	168	68.6	37	55.2	30	69.8	<0.001
Do you use soap to wash your hand	221	66.8	180	78.6	204	83.3	64	95.5	38	88.4	<0.001
Household with tap water	121	36.6	93	40.6	72	29.4	46	68.7	24	55.8	<0.001
Source of drinking water											
Bottled water	62	18.7	35	15.3	16	6.5	44	65.7	23	53.5	<0.001
Tap water	276	83.4	129	56.3	144	58.8	48	71.6	33	76.7	<0.001
Rain water	28	8.5	12	5.2	19	7.8	6	9.0	7	16.3	0.156
Bore whole water	4	1.2	1	0.4	5	2.0	1	1.5	0	0	0.533
Spring water	98	29.6	115	50.2	92	37.6	10	14.9	8	18.6	<0.001
Well water	6	1.8	2	0.9	19	7.8	2	2.9	5	11.6	<0.001
Water from Lake Victoria	0	0	0	0	1	0.4	1	1.5	0	0	0.152
Eating or potential contaminated food											
Vegetables	135	40.8	103	44.9	107	43.7	43	64.2	37	86.1	<0.001
Root crops	144	43.5	173	75.6	234	95.5	45	67.2	35	81.4	<0.001
Sugar cane	46	13.9	98	42.8	134	54.7	20	29.9	17	39.5	<0.001
Yam roots	68	20.5	115	50.2	189	77.1	20	29.9	16	37.2	<0.001
Cassava roots	84	25.4	95	41.5	129	52.7	36	53.7	28	65.1	<0.001
Preventive chemotherapy taken against soil transmitted helminth infections (month)											
< 3	55	16.6	38	16.6	48	19.6	31	46.3	10	23.3	<0.001
< 6	93	28.1	59	25.8	66	26.9	40	59.7	11	25.6	<0.001
< 12	135	40.8	102	44.5	101	41.2	47	70.2	24	55.8	<0.001
≥ 12	331	100	229	100	245	100	62	92.5	42	97.7	0.032

* "$com_{exposed}$", slum dwellers at risk of flooding along the Nakivubo wetland; "$com_{comparison}$", slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *"farmer"*, urban farmers reusing wastewater within the Nakivubo wetland; "$worker_{ww}$", workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; "$worker_{fs}$", workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

S1B Risk factors related to the occupation of workers and farmers enrolled in the cross-sectional survey in Kampala.

Occupational risk factors	*farmer*[*] n=245		*worker*$_{fs}$[*] n=67		*worker*$_{ww}$[*] n=43		Difference (χ^2)
	n	**%**	**n**	**%**	**n**	**%**	**p-value**
Formally employed	10	4.1	65	97.0	42	97.7	<0.001
Months worked in the current job (month)							
1-12	91	37.1	38	56.7	15	34.9	
12-36	62	25.3	18	26.9	11	25.6	
≥ 36	91	37.1	11	16.4	17	39.5	<0.001
Hours worked per week (hours)							
1-20	32	13.1	1	1.5	0	0.0	
20-40	132	54.7	2	3.0	1	2.3	
40-60	60	24.5	19	28.4	24	55.8	
≥ 60	19	32.2	64	67.2	18	41.9	<0.001
Use of personal protective equipment							
Gloves	10	4.1	59	88.1	35	81.4	<0.001
Uniform	8	3.3	39	58.2	32	74.4	<0.001
Long sleeves	61	24.9	4	6.0	8	18.6	<0.001
Rubber boots	121	49.4	42	62.7	35	81.4	<0.001
Appropriate shoes	38	15.5	24	35.8	23	53.5	<0.001
Working tools	59	24.1	2	3.0	2	3.0	<0.001

[*] *"farmer"*, urban farmers reusing wastewater within the Nakivubo wetland; *"worker*$_{ww}$*"*, workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; *"worker*$_{fs}$*"*, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

16.2. Chapter 7: S2 Table. Univariate and multivariate regression models determining association between health outcomes of interest and risk/confounding factors

S2A Results of univariate and the multivariate logistic regression analysis for helminth infection infections in a cross-sectional survey done in late 2013 in Kampala[§]

Any helminth infection N=915 / N(cases)=247			Univariate logistic regression*				Multivariate logistic regression**			
			OR	95% CI		p-value	aOR	95% CI		p-value
Exposure group***		$com_{comparison}$	1			**<0·001**	1			**<0·001**
		$com_{exposed}$	1·31	0·8	2·0	0·241	1·04	0·62	1·75	0·883
		farmer	6·48	4·4	9·6	<0·001	4·85	2·83	8·33	<0·001
		$worker_{fs}$	0·73	0·3	1·6	0·454	0·54	0·22	1·32	0·184
		$worker_{ww}$	1·24	0·5	2·8	0·614	0·83	0·31	2·20	0·711
Sex		Male	1							
		Female	0·55	0·4	0·7	**<0·001**	0·58	0·40	0·85	0·011
Age			1·02	1·0	1·0	**0·012**	1·00	0·99	1·02	0·952
Education		Never went to school	1			**<0·001**				
		Primary	1·47	0·9	2·3	0·111	1·34	0·79	2·27	0·281
		Higher education	0·75	0·5	1·2	0·248	1·15	0·65	2·03	0·632
Socio-economic status		Most poor	1			**0·032**				
		Poor	0·72	0·5	1·0	0·072	0·98	0·65	1·50	0·931
		Less poor	0·61	0·4	0·9	0·011	1·16	0·72	1·86	0·544
Number of people per household		Single	1			**0·061**				
		2 to 4	1·19	0·7	1·9	0·482	1·24	0·71	2·16	0·453
		> 4	1·59	1·0	2·6	0·071	1·36	0·75	2·46	0·322
Toilet facility		Flush toilet	1			**0·027**				
		Pit latrine	1·14	0·6	2·2	0·705	1·50	0·70	3·22	0·302
		No facility	2·15	1·0	4·6	0·057	1·39	0·55	3·52	0·492
Toilet sharing		Private toilet	1			**0·031**				
		2 and 3 households	0·68	0·5	1·0	0·051	0·82	0·53	1·27	0·376
		≥ 4 households	1·07	0·7	1·5	0·703	0·90	0·55	1·48	0·691
Flooding of living area		No	1							
		Yes	2·69	1·99	3·66	**<0·001**	1·38	0·88	2·15	0·162
Source of drinking water		Bottle, Tab, rain	1			**0·023**				
		Spring	1·53	1·12	2·09	0·012	1·12	0·62	2·01	0·714
		Other	1·23	0·7	2·2	0·481	0·62	0·28	1·37	0·245
Source of bath water		Tab, rain water	1			**<0·001**				
		Spring	1·54	1·1	2·1	0·011	1·19	0·66	2·17	0·561
		Unprotected	1·57	1·0	2·6	0·080	1·40	0·71	2·77	0·330
Bathing per week		< 7	1			**0·632**				
		≥ 7 to < 14	0·71	0·4	1·3	0·277	1·06	0·53	2·15	0·869
		> 14	0·53	0·3	1·0	0·048	1·07	0·51	2·26	0·851
Hand washing	After defecation	No	1							
		Yes	0·66	0·48	0·90	**0·010**	0·90	0·61	1·33	0.602
	After work	No	1							
		Yes	1·28	1·0	1·7	**0·101**	0·79	0·55	1·14	0.218
	Before eating	No	1							
		Yes	1·23	0·8	1·8	**0·292**				
Hand washing per week		< 4	1			**0·411**				
		< 8	0·97	0·7	1·4	0·853	1·12	0·75	1·65	0·584
		≥ 8	0·62	0·4	1·0	0·030	0·90	0·53	1·51	0·691
Use soap to wash your hand		No	1							
		Yes	0·84	0·6	1·2	**0·345**				
Deworming (month)		< 6	1			**0·692**				
		6-12	1·21	0·8	1·9	0·402				
		> 12	1·08	0·8	1·5	0·641				

[§]Helminth infection include: *Ascaris lumbricoides, Trichuris trichiura*, hookworm, *Schistosoma mansoni.* *p-value and odds ratio (OR) based on likelihood ratio test of univariate logistic regression, overall p-value of the models are indicated in bold letters. ** p-value and adjusted (a) OR based on likelihood ratio test of the multivariate regression model. The multivariate model was defined including exposure groups, sex, age, educational attainment, socioeconomic status, and number of people per household. In addition, all risk factors that had a p-value lower than 0.2 in the univariate analyses were included into the multivariate regression analysis (as indicated in the table). *** exposure groups: $com_{exposed}$, slum dwellers at risk of flooding along the Nakivubo wetland; $com_{comparison}$, slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *farmer*, urban farmers reusing wastewater within the Nakivubo wetland; $worker_{ww}$, workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; $worker_{fs}$, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

S2B Results of univariate and the multivariate logistic regression analysis for soil-transmitted helminth infection in a cross-sectional survey done in late 2013 in Kampala§

Soil-transmitted helminth infection N(total)=915 / N(cases)= 187			Univariate logistic regression*				Multivariate logistic regression**			
			OR	95% CI		p-value	aOR	95% CI		p-value
Exposure group***		$\mathit{com}_{comparison}$	1			**<0·001**	1			**<0·001**
		$\mathit{com}_{exposed}$	0·78	0·4	1·4	0·381	0·58	0·31	1·09	0·091
		farmer	6·78	4·4	10·3	<0·001	4·66	2·58	8·41	<0·001
		worker_{fs}	0·61	0·2	1·6	0·322	0·41	0·14	1·19	0·103
		worker_{ww}	1·48	0·6	3·6	0·381	1·07	0·38	3·06	0·893
Sex		Male								
		Female	0·57	0·4	0·8	**<0·001**	0·67	0·44	1·02	0·064
Age			0·02	0·0	0·0	**<0·001**	1·01	0·99	1·02	0·511
Education		Never went to school				**<0·001**				
		Primary	1·27	0·8	2·1	0·333	1·28	0·72	2·27	0·402
		Higher education	0·56	0·3	0·9	0·032	0·94	0·50	1·75	0·841
Socio-economic status		Most poor				**0·05**				
		Poor	0·69	0·5	1·0	0·061	1·01	0·63	1·61	0·985
		Less poor	0·62	0·4	0·9	0·027	1·44	0·85	2·43	0·183
Number of people per household		Single				**0·19**				
		2 to 4	1·18	0·7	2·0	0·540	1·25	0·67	2·32	0·491
		> 4	1·54	0·9	2·7	0·138	1·21	0·62	2·37	0·574
Toilet facility		Flush toilet				**<0·001**				
		Pit latrine	1·26	0·6	2·7	0·561	1·91	0·80	4·57	0·151
		No facility	3·27	1·4	7·7	0·011	3·14	1·11	8·88	0·032
Toilet sharing		Private toilet				**0·03**				
		2 and 3 households	0·70	0·5	1·1	0·101	0·91	0·56	1·49	0·721
		≥ 4 households	1·17	0·8	1·7	0·457	1·09	0·62	1·89	0·776
Flooding of living area		No								
		Yes	2·76	1·98	3·84	**<0·001**	1·27	0·76	2·13	0·367
Source of drinking water		Bottle, Tab, rain				**0·532**				
		Spring	1·20	0·85	1·69	0·302				
		Other	1·15	0·6	2·2	0·673				
Source of bath water		Tab, rain water				**0·081**				
		Spring	1·30	0·9	1·8	0·142	0·97	0·63	1·48	0·887
		Unprotected	1·70	1·0	2·9	0·053	1·29	0·72	2·31	0·403
Bathing per week		< 7				**0·04**				
		≥ 7 to < 14	0·73	0·4	1·4	0·331	1·07	0·51	2·25	0·872
		> 14	0·51	0·3	1·0	0·050	1·12	0·50	2·48	0·789
Hand washing	After defecation	No								
		Yes	0·55	0·39	0·77	**<0·001**	0·74	0·49	1·13	0.171
	After work	No								
		Yes	1·28	0·9	1·8	**0·143**	0·73	0·48	1·09	0.121
	Before eating	No								
		Yes	1·30	0·84	2·02	**0·231**				
Hand washing per week		< 4				**0·010**				
		< 8	0·95	0·7	1·4	0·802	1·23	0·80	1·89	0·341
		≥ 8	0·53	0·3	0·9	0·011	0·80	0·44	1·45	0·462
Use soap to wash your hand		No								
		Yes	0·84	0·6	1·2	**0·381**				
Deworming (month)		< 6				**0·321**				
		6-12	0·99	0·6	1·7	0·982				
		> 12	1·10	0·8	1·6	0·625				

§Soil-transmitted helminth infection include: *Ascaris lumbricoides, Trichuris trichiura* and hookworm. *p-value and odds ratio (OR) based on likelihood ratio test of univariate logistic regression, overall p-value of the models are indicated in bold letters. ** p-value and adjusted (a) OR based on likelihood ratio test of the multivariate regression model. The multivariate model was defined including exposure groups, sex, age, educational attainment, socioeconomic status, and number of people per household. In addition, all risk factors that had a p-value lower than 0.2 in the univariate analyses were included into the multivariate regression analysis (as indicated in the table). *** exposure groups: $\mathit{com}_{exposed}$, slum dwellers at risk of flooding along the Nakivubo wetland; $\mathit{com}_{comparison}$, slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *farmer*, urban farmers reusing wastewater within the Nakivubo wetland; worker_{ww}, workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; worker_{fs}, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

S2C Results of univariate and the multivariate logistic regression analysis for any intestinal protozoa infections in a cross-sectional survey done in late 2013 in Kampala

Intestinal protozoa infection N(total)=915 / N(cases)= 365			Univariate logistic regression*				Multivariate logistic regression**			
			OR	95% CI		p-value	aOR	95% CI		p-value
Exposure group***		$\textit{com}_{comparison}$	1			**<0·001**	1			**0·031**
		$\textit{com}_{exposed}$	1·39	1·0	2·0	0·061	1·33	0·92	1·92	0·132
		farmer	1·70	1·2	2·4	<0·001	1·63	1·10	2·39	0·013
		$\textit{worker}_{fs}$	0·67	0·4	1·2	0·187	0·71	0·37	1·36	0·303
		$\textit{worker}_{ww}$	0·79	0·4	1·6	0·518	0·76	0·35	1·65	0·498
Sex		Male	1							
		Female	1·19	0·9	1·6	**0·202**	1·05	0·75	1·46	0·786
Age			0·00	0·0	0·0	**0·705**	0·99	0·98	1·00	0·215
Education		Never went to school	1			**0·043**				
		Primary	0·66	0·4	1·0	0·052	0·64	0·41	0·99	0·050
		Higher education	0·59	0·4	0·9	0·010	0·69	0·44	1·09	0·114
Socio-economic status		Most poor	1			**0·074**				
		Poor	0·70	0·5	1·0	0·033	0·78	0·55	1·10	0·165
		Less poor	0·75	0·5	1·0	0·087	0·92	0·63	1·35	0·675
Number of people per household		Single	1			**0·165**				
		2 to 4	1·22	0·8	1·9	0·366	1·19	0·76	1·86	0·452
		> 4	1·49	1·0	2·3	0·087	1·43	0·88	2·32	0·151
Toilet facility		Flush toilet	1			**0·883**				
		Pit latrine	1·16	0·6	2·1	0·612				
		No facility	1·17	0·6	2·3	0·667				
Toilet sharing		Private toilet	1			**0·13**				
		2 and 3 households	0·75	0·5	1·1	0·109	0·82	0·58	1·18	0·296
		≥ 4 households	0·99	0·7	1·4	0·960	0·92	0·63	1·34	0·669
Flooding of living area		No	1							
		Yes	1·17	0·88	1·55	**0·298**				
Source of drinking water		Bottle, Tab, rain	1			**0·346**				
		Spring	1·13	0·85	1·50	0·415	0·96	0·70	1·32	0·802
		Other	1·43	0·9	2·4	0·174	1·23	0·78	1·96	0·381
Source of bath water		Tab, rain water	1			**0·323**				
		Spring	1·14	0·9	1·5	0·361	1·02	0·55	1·87	0·961
		Unprotected	1·37	0·9	2·1	0·171	0·95	0·51	1·77	0·874
Bathing per week		< 7	1			**0·820**				
		≥ 7 to < 14	0·93	0·5	1·7	0·814				
		> 14	0·87	0·5	1·6	0·642				
Hand washing	After defecation	No	1							
		Yes	1·15	0·86	1·55	**0·358**				
	After work	No	1							
		Yes	1·17	0·9	1·5	**0·264**				
	Before eating	No	1							
		Yes	1·11	0·79	1·57	**0·533**				
Hand washing per week		< 4	1			**0·634**				
		< 8	0·91	0·7	1·2	0·552				
		≥ 8	0·83	0·6	1·2	0·351				
Use soap to wash your hand		No	1							
		Yes	1·04	0·8	1·4	**0·821**				
Deworming (month)		< 6	1			**0·696**				
		6-12	0·84	0·6	1·3	0·423				
		> 12	0·90	0·7	1·2	0·522				

*p-value and odds ratio (OR) based on likelihood ratio test of univariate logistic regression, overall p-value of the models are indicated in bold letters. ** p-value and adjusted (a) OR based on likelihood ratio test of the multivariate regression model. The multivariate model was defined including exposure groups, sex, age, educational attainment, socioeconomic status, and number of people per household. In addition, all risk factors that had a p-value lower than 0.2 in the univariate analyses were included into the multivariate regression analysis (as indicated in the table). *** exposure groups: $\textit{com}_{exposed}$, slum dwellers at risk of flooding along the Nakivubo wetland; $\textit{com}_{comparison}$, slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *farmer*, urban farmers reusing wastewater within the Nakivubo wetland; $\textit{worker}_{ww}$, workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; $\textit{worker}_{fs}$, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

S2D Results of univariate and the multivariate logistic regression analysis for Schistosoma mansoni infection in a cross-sectional survey done in late 2013 in Kampala

Schistosoma mansoni infection N(total)=915 / N(cases)= 110			Univariate logistic regression*				Multivariate logistic regression**			
			OR	95% CI		p-value	aOR	95% CI		p-value
Exposure group***		*com* $_{comparison}$	1			**<0·001**	1			**<0·001**
		com $_{exposed}$	2·17	1·2	3·9	0·018	1·91	0·98	3·73	0·061
		farmer	4·61	2·7	7·9	<0·001	3·75	1·89	7·45	<0·001
		worker $_{fs}$	0·99	0·3	3·0	0·982	0·62	0·19	1·99	0·422
		worker $_{ww}$	0·76	0·2	3·4	0·721	0·43	0·09	2·09	0·304
Sex		Male	1							
		Female	0·49	0·3	0·7	**<0·001**	0·47	0·30	0·76	<0·001
Age			0·01	0·0	0·0	**0·46**	1·00	0·98	1·02	0·786
Education		Never went to school	1			**0·033**				
		Primary	2·21	1·1	4·6	0·032	1·77	0·82	3·84	0·155
		Higher education	1·45	0·7	3·1	0·332	1·93	0·85	4·40	0·120
Socio-economic status		Most poor	1			**0·341**				
		Poor	0·83	0·5	1·3	0·431	1·12	0·66	1·89	0·671
		Less poor	0·69	0·4	1·1	0·156	1·19	0·66	2·15	0·551
Number of people per household		Single	1			**0·352**				
		2 to 4	1·38	0·7	2·8	0·371	1·43	0·68	3·01	0·343
		> 4	1·65	0·8	3·4	0·188	1·53	0·70	3·34	0·298
Toilet facility		Flush toilet	1			**0·684**				
		Pit latrine	1·02	0·4	2·4	0·973				
		No facility	1·32	0·5	3·6	0·597				
Toilet sharing		Private toilet	1			**0·223**				
		2 and 3 households	0·80	0·5	1·3	0·403				
		≥ 4 households	1·20	0·7	2·0	0·468				
Flooding of living area		No	1							
		Yes	2·43	1·62	3·63	**<0·001**	1·21	0·72	2·03	0·471
Source of drinking water		Bottle, Tab, rain	1			**0·021**				
		Spring	1·71	1·13	2·58	0·010	1·36	0·63	2·92	0·431
		Other	0·73	0·3	1·9	0·510	0·56	0·18	1·78	0·332
Source of bath water		Tab, rain water	1			**0·023**				
		Spring	1·68	1·1	2·5	0·024	1·13	0·52	2·46	0·754
		Unprotected	0·85	0·4	1·9	0·682	0·82	0·32	2·13	0·681
Bathing per week		< 7	1			**0·486**				
		≥ 7 to < 14	0·61	0·3	1·3	0·214				
		> 14	0·66	0·3	1·4	0·298				
Hand washing	After defecation	No	1							
		Yes	0·99	0·64	1·53	**0·951**				
	After work	No	1							
		Yes	1·10	0·7	1·6	**0·641**				
	Before eating	No	1							
		Yes	1·05	0·63	1·75	**0·863**				
Hand washing per week		< 4	1			**0·557**				
		< 8	0·88	0·6	1·4	0·601				
		≥ 8	0·73	0·4	1·3	0·282				
Use soap to wash your hand		No	1							
		Yes	0·69	0·4	1·2	**0·165**				
Deworming		< 6 month	1			**0·575**				
		6 to < 12 month	1·28	0·7	2·3	0·412				
		> 12 month	0·95	0·6	1·5	0·840				

*p-value and odds ratio (OR) based on likelihood ratio test of univariate logistic regression, overall p-value of the models are indicated in bold letters. ** p-value and adjusted (a) OR based on likelihood ratio test of the multivariate regression model. The multivariate model was defined including exposure groups, sex, age, educational attainment, socioeconomic status, and number of people per household. In addition, all risk factors that had a p-value lower than 0.2 in the univariate analyses were included into the multivariate regression analysis (as indicated in the table). *** exposure groups: *com* $_{exposed}$, slum dwellers at risk of flooding along the Nakivubo wetland; *com* $_{comparison}$, slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *farmer*, urban farmers reusing wastewater within the Nakivubo wetland; *worker* $_{ww}$, workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; *worker* $_{fs}$, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

S2E Results of univariate and the multivariate logistic regression analysis for hookworm infection in a cross-sectional survey done in late 2013 in Kampala

Hookworm infection N(total)=915 / N(cases)= 115			Univariate logistic regression*				Multivariate logistic regression**			
			OR	95% CI		p-value	aOR	95% CI		p-value
Exposure group***		*com* $_{comparison}$	1			**<0·001**	1			**<0·001**
		com $_{exposed}$	0·44	0·2	1·0	0·042	0·44	0·19	1·00	0·052
		farmer	4·16	2·6	6·7	<0·001	3·49	1·79	6·79	<0·001
		worker $_{fs}$	0·51	0·1	1·7	0·281	0·39	0·10	1·44	0·166
		worker $_{ww}$	2·10	0·9	5·2	0·105	2·05	0·72	5·85	0·181
Sex		Male								
		Female	0·52	0·4	0·8	**<0·001**	0·67	0·42	1·08	0·101
Age			0·02	0·0	0·0	**0·021**	1·00	0·98	1·02	0·817
Education		Never went to school				**<0·001**				
		Primary	1·17	0·7	2·1	0·593	1·07	0·57	2·02	0·833
		Higher education	0·49	0·3	0·9	0·029	0·57	0·28	1·17	0·123
Socio-economic status		Most poor				**0·291**				
		Poor	0·74	0·5	1·2	0·212	0·94	0·54	1·62	0·819
		Less poor	0·71	0·4	1·1	0·163	1·20	0·65	2·20	0·561
Number of people per household		Single				**0·943**				
		2 to 4	1·00	0·5	1·9	0·991				
		> 4	1·07	0·6	2·1	0·830				
Toilet facility		Flush toilet				**0·055**				
		Pit latrine	0·83	0·4	1·9	0·668				
		No facility	1·67	0·7	4·2	0·281				
Toilet sharing		Private toilet				**0·091**				
		2 and 3 households	0·60	0·4	1·0	0·052	0·79	0·45	1·41	0·438
		≥ 4 households	0·91	0·6	1·5	0·710	1·18	0·63	2·20	0·612
Flooding of living area		No								
		Yes	1·65	1·11	2·46	**0·010**	0·73	0·40	1·35	0·315
Source of drinking water		Bottle, Tab, rain				**0·471**				
		Spring	1·25	0·83	1·90	0·292				
		Other	1·38	0·7	2·8	0·381				
Source of bath water		Tab, rain water				**<0·016**				
		Spring	1·31	0·9	2·0	0·225	1·09	0·67	1·79	0·722
		Unprotected	2·57	1·5	4·5	<0·0018	1·98	1·06	3·68	0·032
Bathing per week		< 7				**<0·012**				
		≥ 7 to < 14	0·58	0·3	1·2	0·131	0·78	0·36	1·70	0·544
		> 14	0·34	0·2	0·7	<0·001	0·62	0·27	1·41	0·251
Hand washing	After defecation	No								
		Yes	0·47	0·32	0·71	<0·001	0·75	0·47	1·20	0·233
	After work	No								
		Yes	1·36	0·9	2·0	**0·133**	0·83	0·52	1·32	0·442
	Before eating	No								
		Yes	1·11	0·67	1·86	**0·682**				
Hand washing per week		< 4				**0·193**				
		< 8	1·13	0·7	1·8	0·612				
		≥ 8	0·70	0·4	1·3	0·244				
Use soap to wash your hand		No								
		Yes	1·12	0·7	1·8	**0·642**				
Deworming		< 6 month				**0·801**				
		6 to < 12 month	1·18	0·6	2·2	0·591				
		> 12 month	1·15	0·7	1·8	0·560				

*p-value and odds ratio (OR) based on likelihood ratio test of univariate logistic regression, overall p-value of the models are indicated in bold letters. ** p-value and adjusted (a) OR based on likelihood ratio test of the multivariate regression model. The multivariate model was defined including exposure groups, sex, age, educational attainment, socioeconomic status, and number of people per household. In addition, all risk factors that had a p-value lower than 0.2 in the univariate analyses were included into the multivariate regression analysis (as indicated in the table). *** exposure groups: *com* $_{exposed}$, slum dwellers at risk of flooding along the Nakivubo wetland; *com* $_{comparison}$, slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *farmer*, urban farmers reusing wastewater within the Nakivubo wetland; *worker* $_{ww}$, workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; *worker* $_{fs}$, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

S2F Results of univariate and the multivariate logistic regression analysis for Trichuris trichiura infections in a cross-sectional survey done in late 2013 in Kampala

Trichuris trichiura infection N(total)=915 / N(cases)=79			Univariate logistic regression*				Multivariate logistic regression**			
			OR	95% CI		p-value	aOR	95% CI		p-value
Exposure group***		$com_{comparison}$	1			**<0·001**	1			**<0·001**
		$com_{exposed}$	1·96	0·67	5·73	0·221	1·64	0·52	5·14	0·403
		farmer	19·1	8·13	45·10	<0·001	12·9	4·50	37·5	<0·001
		$worker_{fs}$	-				-			
		$worker_{ww}$	1·29	0·15	10·98	0·822	0·41	0·04	4·13	0·453
Sex		Male	1							
		Female	0·44	0·27	0·70	**<0·001**	0·54	0·29	0·98	0·044
Age			0·03	0·01	0·05	**<0·001**	1·01	0·99	1·04	0·317
Education		Never went to school	1			**0·031**				
		Primary	1·00	0·52	1·95	0·991	0·86	0·39	1·90	0·715
		Higher education	0·53	0·27	1·07	0·088	1·07	0·43	2·66	0·883
Socio-economic status		Most poor	1			**0·022**				
		Poor	0·51	0·29	0·90	0·021	0·86	0·44	1·67	0·654
		Less poor	0·52	0·30	0·92	0·020	1·80	0·87	3·76	0·125
Number of people per household		Single	1			**0·045**				
		2 to 4	1·84	0·70	4·79	0·216	1·95	0·67	5·63	0·227
		> 4	2·82	1·08	7·38	0·033	2·44	0·82	7·26	0·119
Toilet facility		Flush toilet	1			**<0·001**				
		Pit latrine	2·06	0·49	8·69	0·322	4·19	0·89	19·7	0·073
		No facility	5·72	1·28	25·61	0·022	5·60	1·04	30·0	0·042
Toilet sharing		Private toilet	1			**0·09**				
		2 and 3 households	0·75	0·40	1·41	0·375				
		≥ 4 households	1·38	0·78	2·45	0·274				
Flooding of living area		No	1							
		Yes	4·84	2·97	7·89	**<0·001**	1·29	0·63	2·66	0·494
Source of drinking water		Bottle, Tab, rain	1			**0·604**				
		Spring	0·97	0·59	1·61	0·918				
		Other	1·50	0·67	3·33	0·322				
Source of bath water		Tab, rain water	1			**0·500**				
		Spring	0·93	0·56	1·55	0·782				
		Unprotected	1·46	0·72	2·96	0·293				
Bathing per week		< 7	1			**0·275**				
		≥ 7 to < 14	0·67	0·28	1·57	0·362				
		> 14	0·51	0·21	1·22	0·131				
Hand washing	After defecation	No	1							
		Yes	0·38	0·24	0·60	**<0·001**	0·43	0·23	0·77	0.014
	After work	No	1							
		Yes	1·48	0·92	2·37	**0·111**	0·59	0·32	1·09	0.103
	Before eating	No	1							
		Yes	2·17	1·02	4·59	**0·042**	1·50	0·62	3·61	0.377
Hand washing per week		< 4	1			**0·081**				
		< 8	0·78	0·47	1·31	0·354	1·06	0·58	1·92	0·863
		≥ 8	0·45	0·22	0·94	0·038	0·83	0·35	1·95	0·666
Use soap to wash your hand		No	1							
		Yes	0·59	0·31	1·11	**0·103**	0·73	0·35	1·51	0·401
Deworming		< 6 month	1			**0·747**				
		6 to < 12 month	0·77	0·36	1·66	0·516				
		> 12 month	1·01	0·60	1·70	0·973				

*p-value and odds ratio (OR) based on likelihood ratio test of univariate logistic regression, overall p-value of the models are indicated in bold letters. ** p-value and adjusted (a) OR based on likelihood ratio test of the multivariate regression model. The multivariate model was defined including exposure groups, sex, age, educational attainment, socioeconomic status, and number of people per household. In addition, all risk factors that had a p-value lower than 0.2 in the univariate analyses were included into the multivariate regression analysis (as indicated in the table). *** exposure groups: $com_{exposed}$, slum dwellers at risk of flooding along the Nakivubo wetland; $com_{comparison}$, slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *farmer*, urban farmers reusing wastewater within the Nakivubo wetland; $worker_{ww}$, workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; $worker_{fs}$, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

S2G Results of univariate and the multivariate logistic regression analysis for 14-day diarrhea prevalence in a cross-sectional survey done in late 2013 in Kampala

14-day diarrhoea prevalence			**Univariate logistic regression***				**Multivariate logistic regression****			
N(total)=915 / N(cases)= 222			OR	95% CI		p-value	aOR	95% CI		p-value
Exposure group***		*com* $_{comparison}$	1			**0·331**	1			**0·273**
		com $_{exposed}$	1·26	0·8	1·9	0·252	1·10	0·72	1·67	0·665
		farmer	1·26	0·9	1·9	0·241	1·01	0·65	1·58	0·962
		worker $_{fs}$	1·82	1·0	3·2	0·042	1·67	0·86	3·25	0·132
		worker $_{ww}$	1·13	0·5	2·4	0·751	1·25	0·53	2·92	0·616
Sex		Male	1							
		Female	0·83	0·6	1·1	**0·232**	0·87	0·61	1·24	0·445
Age			0·00	0·0	0·0	**0·531**	1·00	0·99	1·01	0·954
Education		Never went to school	1			**0·194**				
		Primary	0·94	0·6	1·5	0·815	0·92	0·56	1·49	0·725
		Higher education	0·72	0·5	1·1	0·178	0·71	0·43	1·19	0·204
Socio-economic status		Most poor	1			**0·235**				
		Poor	1·32	0·9	1·9	0·143	1·49	1·01	2·20	0·045
		Less poor	1·01	0·7	1·5	0·956	1·12	0·72	1·74	0·616
Number of people per household		Single	1			**0·906**				
		2 to 4	1·08	0·7	1·8	0·754				
		> 4	1·12	0·7	1·9	0·678				
Toilet facility		Flush toilet	1			**0·242**				
		Pit latrine	1·31	0·6	2·7	0·461	1·29	0·61	2·74	0·506
		No facility	1·83	0·8	4·1	0·147	1·72	0·71	4·16	0·236
Toilet sharing		Private toilet	1			**0·382**				
		2 and 3 households	1·03	0·7	1·5	0·903				
		≥ 4 households	1·27	0·9	1·9	0·234				
Flooding of living area		No								
		Yes	1·05	0·76	1·45	**0·795**				
Source of drinking water		Bottle, Tab, rain	1			**0·114**				
		Spring	1·39	1·01	1·91	0·053	1·33	0·77	2·28	0·312
		Other	1·35	0·8	2·4	0·313	1·19	0·58	2·44	0·643
Source of bath water		Tab, rain water	1			**0·175**				
		Spring	1·33	1·0	1·8	0·088	1·06	0·61	1·83	0·842
		Unprotected	1·34	0·8	2·2	0·265	1·24	0·66	2·34	0·511
Bathing per week		< 7	1			**0·454**				
		≥ 7 to < 14	1·10	0·5	2·2	0·795				
		> 14	1·32	0·7	2·6	0·448				
Hand washing	After defecation	No	1							
		Yes	0·84	0·61	1·17	**0·319**				
	After work	No	1							
		Yes	1·12	0·8	1·5	**0·485**				
	Before eating	No	1							
		Yes	0·92	0·63	1·34	**0·654**				
Hand washing per week		< 4	1			**0·995**				
		< 8	1·02	0·7	1·5	0·925	0·85	0·53	1·37	0·502
		≥ 8	1·00	0·7	1·5	0·996	0·58	0·40	0·83	0·001
Use soap to wash your hand		No	1							
		Yes	0·80	0·6	1·2	**0·254**				
Deworming (month)		< 6	1			**0·014**				
		6-12	0·84	0·5	1·3	0·473				
		> 12	0·60	0·4	0·8	0·001				

*p-value and odds ratio (OR) based on likelihood ratio test of univariate logistic regression, overall p-value of the models are indicated in bold letters. ** p-value and adjusted (a) OR based on likelihood ratio test of the multivariate regression model. The multivariate model was defined including exposure groups, sex, age, educational attainment, socioeconomic status, and number of people per household. In addition, all risk factors that had a p-value lower than 0.2 in the univariate analyses were included into the multivariate regression analysis (as indicated in the table). *** exposure groups: *com* $_{exposed}$, slum dwellers at risk of flooding along the Nakivubo wetland; *com* $_{comparison}$, slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *farmer*, urban farmers reusing wastewater within the Nakivubo wetland; *worker* $_{ww}$, workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; *worker* $_{fs}$, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

S2H Results of univariate and the multivariate logistic regression analysis for skin problems over the past two weeks in a cross-sectional survey done in late 2013 in Kampala

Skin problems over the past two weeks N(total)=915 / N(cases)= 279			**Univariate logistic regression***				**Multivariate logistic regression****			
			OR	95% CI		p-value	aOR	95% CI		p-value
Exposure group***		$com_{comparison}$	1			**<0·001**	1			**<0·001**
		$com_{exposed}$	0·96	0·7	1·4	0·85	0·90	0·58	1·40	0·643
		farmer	1·23	0·9	1·8	0·26	1·50	0·91	2·47	0·114
		$worker_{fs}$	1·58	0·9	2·7	0·10	1·11	0·57	2·15	0·777
		$worker_{ww}$	1·08	0·5	2·2	0·84	0·91	0·40	2·06	0·825
Sex		Male								
		Female	0·63	0·5	0·8	**<0·001**	0·60	0·42	0·86	0·011
Age			0·00	0·0	0·0	**0·48**	1·00	0·99	1·01	0·901
Education		Never went to school	1			**0·15**				
		Primary	0·85	0·5	1·3	0·45	0·75	0·47	1·20	0·242
		Higher education	0·68	0·4	1·1	0·08	0·60	0·37	0·99	0·051
Socio-economic status		Most poor	1			**<0·001**				
		Poor	0·95	0·7	1·4	0·77	1·05	0·71	1·56	0·802
		Less poor	1·67	1·2	2·4	<0·001	2·17	1·42	3·33	<0·001
Number of people per household		Single	1			**0·25**				
		2 to 4	0·94	0·6	1·5	0·79				
		> 4	0·74	0·5	1·2	0·21				
Toilet facility		Flush toilet	1			**0·13**				
		Pit latrine	1·03	0·6	1·9	0·93				
		No facility	1·59	0·8	3·3	0·21				
Toilet sharing		Private toilet	1			**0·06**				
		2 and 3 households	0·78	0·5	1·1	0·18	1·02	0·68	1·52	0·932
		≥ 4 households	1·16	0·8	1·6	0·42	1·47	0·95	2·27	0·083
Flooding of living area		No	1							
		Yes	0·80	0·58	1·08	**0·15**	0·68	0·45	1·04	0·084
Source of drinking water		Bottle, Tab, rain	1			**0·14**				
		Spring	1·31	0·97	1·77	0·07	1·08	0·64	1·81	0·783
		Other	1·10	0·6	1·9	0·74	1·12	0·56	2·25	0·756
Source of bath water		Tab, rain water	1			**0·07**				
		Spring	1·40	1·0	1·9	0·03	1·40	0·83	2·37	0·202
		Unprotected	1·02	0·6	1·7	0·94	0·87	0·46	1·64	0·661
Bathing per week		< 7	1			**0·08**				
		≥ 7 to < 14	1·99	1·0	4·1	0·06	2·12	0·98	4·58	0·067
		> 14	1·82	0·9	3·7	0·10	2·21	1·00	4·90	0·054
Hand washing	After defecation	No	1							
		Yes	0·74	0·54	1·00	**0·05**	0·73	0·52	1·04	0.092
	After work	No	1							
		Yes	0·60	0·5	0·8	**<0·001**	0·52	0·37	0·72	<0.001
	Before eating	No	1							
		Yes	0·71	0·50	1·00	**0·05**				
Hand washing per week		< 4	1			**0·04**				
		< 8	0·74	0·5	1·0	0·07	0·77	0·54	1·10	0·156
		≥ 8	0·60	0·4	0·9	0·02	0·64	0·41	1·02	0·061
Use soap to wash your hand		No	1							
		Yes	0·91	0·6	1·3	**0·59**				

*p-value and odds ratio (OR) based on likelihood ratio test of univariate logistic regression, overall p-value of the models are indicated in bold letters. ** p-value and adjusted (a) OR based on likelihood ratio test of the multivariate regression model. The multivariate model was defined including exposure groups, sex, age, educational attainment, socioeconomic status, and number of people per household. In addition, all risk factors that had a p-value lower than 0.2 in the univariate analyses were included into the multivariate regression analysis (as indicated in the table). *** exposure groups: $com_{exposed}$, slum dwellers at risk of flooding along the Nakivubo wetland; $com_{comparison}$, slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *farmer*, urban farmers reusing wastewater within the Nakivubo wetland; $worker_{ww}$, workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; $worker_{fs}$, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

S2I Results of univariate and the multivariate logistic regression analysis for eye problems over the past two weeks prevalence in a cross-sectional survey done in late 2013 in Kampala

Eye problems over the past two weeks N(total)=915 / N(cases)= 259			**Univariate logistic regression***				**Multivariate logistic regression****			
			OR	95% CI		p-value	aOR	95% CI		p-value
Exposure group***		$com_{comparison}$	1			**<0·001**	1			**<0·001**
		$com_{exposed}$	1·50	1·0	2·2	0·051	1·21	0·76	1·93	0·413
		farmer	2·41	1·7	3·5	<0·001	1·87	1·11	3·13	0·027
		$worker_{fs}$	1·93	1·1	3·4	0·033	2·32	1·16	4·64	0·024
		$worker_{ww}$	1·90	1·0	3·8	0·071	1·64	0·70	3·81	0·252
Sex		Male	1							
		Female	0·87	0·6	1·2	**0·332**	1·12	0·78	1·62	0·543
Age			0·04	0·0	0·1	**<0·001**	1·04	1·02	1·05	0·002
Education		Never went to school	1			**0·011**				
		Primary	1·04	0·7	1·6	0·851	1·44	0·88	2·36	0·152
		Higher education	0·67	0·4	1·0	0·088	1·13	0·67	1·91	0·653
Socio-economic status		Most poor	1			**0·332**				
		Poor	0·78	0·5	1·1	0·172	0·90	0·61	1·33	0·593
		Less poor	0·82	0·6	1·2	0·258	1·04	0·67	1·61	0·878
Number of people per household		Single	1			**<0·001**				
		2 to 4	1·18	0·7	1·9	0·511	1·16	0·69	1·97	0·573
		> 4	2·00	1·2	3·3	0·017	1·69	0·97	2·95	0·072
Toilet facility		Flush toilet	1			**0·033**				
		Pit latrine	1·25	0·6	2·4	0·522	1·58	0·76	3·27	0·225
		No facility	2·15	1·0	4·6	0·056	1·52	0·63	3·66	0·353
Toilet sharing		Private toilet	1			**0·171**				
		2 and 3 households	0·96	0·7	1·4	0·831	1·10	0·72	1·67	0·664
		≥ 4 households	1·30	0·9	1·9	0·171	1·32	0·83	2·11	0·243
Flooding of living area		No	1							
		Yes	1·70	1·25	2·29	**<0·001**	1·27	0·83	1·95	0·268
Source of drinking water		Bottle, Tab, rain	1			**0·187**				
		Spring	1·33	0·98	1·81	0·073	1·21	0·71	2·08	0·487
		Other	1·15	0·7	2·0	0·646	0·83	0·40	1·73	0·626
Source of bath water		Tab, rain water	1			**0·323**				
		Spring	1·23	0·9	1·7	0·194	0·87	0·50	1·51	0·621
		Unprotected	1·29	0·8	2·1	0·308	1·24	0·66	2·35	0·502
Bathing per week		< 7	1			**0·244**				
		≥ 7 to < 14	1·06	0·5	2·1	0·873				
		> 14	1·34	0·7	2·6	0·385				
Hand washing	After defecation	No	1							
		Yes	0·92	0·67	1·26	**0·601**				
	After work	No	1							
		Yes	0·77	0·6	1·0	**0·081**	0·54	0·39	0·76	<0.001
	Before eating	No	1							
		Yes	1·49	1·01	2·21	**0·056**	1·3	0·84	2·00	0.242
Hand washing per week		< 4	1			**0·544**				
		< 8	0·92	0·7	1·3	0·648				
		≥ 8	0·80	0·5	1·2	0·281				
Use soap to wash your hand		No	1							
		Yes	0·76	0·5	1·1	**0·133**	0·94	0·63	1·37	0·721

*p-value and odds ratio (OR) based on likelihood ratio test of univariate logistic regression, overall p-value of the models are indicated in bold letters. ** p-value and adjusted (a) OR based on likelihood ratio test of the multivariate regression model. The multivariate model was defined including exposure groups, sex, age, educational attainment, socioeconomic status, and number of people per household. In addition, all risk factors that had a p-value lower than 0.2 in the univariate analyses were included into the multivariate regression analysis (as indicated in the table). *** exposure groups: $com_{exposed}$, slum dwellers at risk of flooding along the Nakivubo wetland; $com_{comparison}$, slum dwellers without risk of flooding at least 2 km away from the Nakivubo wetland; *farmer*, urban farmers reusing wastewater within the Nakivubo wetland; $worker_{ww}$, workers maintaining drainage channels and operating the Bugolobi Sewage Treatment Works; $worker_{fs}$, workers managing fecal sludge (e.g., collection at households by means of vacuum trucks).

16.3. Chapter 10: Additional file 1. Univariate logistic regression models intestinal parasitic infections and self-reported signs

Table S1 Results of univariate logistic regression analysis for soil-transmitted helminth infections in a cross-sectional survey in Than Tri district, Hanoi, between April and June 2014

Soil-transmitted helminth infections (Ascaris lumbricoides, Trichuris trichiura and hookworm (total population, $N = 681$; infections $n = 87$)		Univariate logistic regression*			
		OR	95% CI		*P*-value
Exposure group**	$Com_{peri\text{-}urban}$				0.000
	Com_{urban}	1.65	0.62	4.35	0.316
	$Farmer_{peri\text{-}urban}$	6.86	2.77	16.99	<0.001
	$Farmer_{urban}$	1.72	0.64	4.60	0.279
	$Worker_{HSDC}$	1.49	0.53	4.17	0.449
Sex	Male				
	Female	0.79	0.45	1.37	0.395
Age		1.02	1.01	1.04	0.004
Educational attainment	Never went to school				0.030
	Primary	0.72	0.18	2.87	0.640
	Secondary	0.74	0.20	2.74	0.657
	Higher education	0.36	0.09	1.36	0.132
Socio-economic status	Most poor				0.181
	Poor	0.66	0.35	1.24	0.195
	Less poor	0.92	0.51	1.67	0.784
	Least poor	0.52	0.27	1.02	0.058
Number of people per household	1 to 4				0.342
	4 to 6	0.68	0.40	1.17	0.166
	> 6	0.67	0.36	1.27	0.222
Toilet facility at home	Yes				
	No	5.60	2.28	13.71	<0.001
Toilet facility at work	Yes				0.198
	No	1.54	0.96	2.47	0.102
Wastewater can cause health issues	No				
	Yes	0.46	0.26	0.80	0.073
Flooding of living area	No				
	Yes	0.54	0.12	2.30	0.401
Flooding of working area	No				
	Yes	0.98	0.56	1.70	0.940
Drinking tap water	No				
	Yes	0.94	0.55	1.60	0.817
Drinking rain water	No				
	Yes	1.44	0.68	3.07	0.342
Drinking bore hole water	No				
	Yes	1.53	0.83	2.82	0.168
Bath tap water	No				
	Yes	0.77	0.41	1.42	0.398
Bath rain water	No				
	Yes	1.84	0.77	4.36	0.167
Bath bore hole water	No				
	Yes	1.37	0.16	11.86	0.775
Preventive chemotherapy received in the past	< 6 months				0.084
	6 to <12 months	0.89	0.25	3.21	0.857
	<12 months	2.15	0.84	5.54	0.111
	Never took deworming	2.13	0.61	7.48	0.237

**P*-values were obtained from likelihood ratio tests. **(i)"$Com_{peri\text{-}urban}$" = people living in the peri-urban commune Duyen Ha, 5 km away from the city along the Red River; (ii) "Com_{urban}" = people living in the urban area of Hanoi, in Bang B village or Tam Hiep commune along the To Lich River and potential exposed to wastewater; (iii) "$Farmer_{peri\text{-}urban}$" = peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains; (iv) "$Farmer_{urban}$" = urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and (v) "$Worker_{HSDC}$" = workers from HSDC maintaining drainage channels.

Table S2 Results of univariate logistic regression analysis for *Trichuris trichiura* infections in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014

Trichuris trichiura infection (total population, $N = 681$; infections $n = 31$)		Univariate logistic regression*			
		OR	95% CI		*P*-value
Exposure group**	$Com_{peri-urban}$				0.242
	Com_{urban}	2.77	0.59	13.07	0.199
	$Farmer_{peri-urban}$	2.84	0.58	13.98	0.199
	$Farmer_{urban}$	1.33	0.24	7.39	0.745
	$Worker_{HSDC}$	3.74	0.79	17.73	0.096
Sex	Male				
	Female	1.33	0.60	2.96	0.486
Age		0.98	0.96	1.01	0.233
Educational attainment	Never went to school				
	Primary	n.a.			
	Secondary	n.a.			
	Higher education	n.a.			
Socio-economic status	Most poor				0.052
	Poor	0.87	0.21	3.53	0.843
	Less poor	3.07	0.98	9.61	0.055
	Least poor	2.29	0.70	7.45	0.169
Number of people per household	1 to 4				
	4 to 6	1.58	0.57	4.33	0.377
	> 6	1.44	0.46	4.51	0.527
Toilet facility at home	Yes				0.655
	No	1.05	0.14	8.09	0.963
Toilet facility at work	Yes				
	No	0.72	0.30	1.69	0.447
Wastewater can cause health issues	No				
	Yes	1.37	0.41	4.59	0.614
Flooding of living area	No				
	Yes	1.00			
Flooding of working area	No				
	Yes	0.90	0.36	2.23	0.818
Drinking tap water	No				
	Yes	1.49	0.56	3.96	0.420
Drinking rain water	No				
	Yes	1.29	0.38	4.38	0.688
Drinking bore hole water	No				
	Yes	0.22	0.03	1.65	0.141
Bath tap water	No				
	Yes	1.03	0.35	3.01	0.958
Bath rain water	No				
	Yes	1.33	0.30	5.83	0.704
Bath bore hole water	No				
	Yes	1.00			
Preventive chemotherapy received in the past	< 6 months				0.836
	6 to <12 months	0.89	0.21	3.70	0.873
	<12 months	0.76	0.25	2.27	0.622
	Never took deworming	0.40	0.04	3.67	0.415

* *P*-values were obtained from likelihood ratio tests. **(i)"$Com_{peri-urban}$" = people living in the peri-urban commune Duyen Ha, 5 km away from the city along the Red River; (ii) "Com_{urban}" = people living in the urban area of Hanoi, in Bang B village or Tam Hiep commune along the To Lich River and potential exposed to wastewater; (iii) "$Farmer_{peri-urban}$" = peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater; (iv) "$Farmer_{urban}$" = urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and (v) "$Worker_{HSDC}$" = workers from Hanoi Sewerage and Drainage Company (HSDC) maintaining drainage channels and operating the Yen So treatment plants.

Table S3 Results of univariate logistic regression analysis for hookworm infections in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014

hookworm infections (total population, $N = 681$; infections $n = 58$)		Univariate logistic regression*			
		OR	95% CI		P-value
Exposure group**	$Com_{peri\text{-}urban}$				0.000
	Com_{urban}	0.89	0.24	3.22	0.856
	$Farmer_{peri\text{-}urban}$	8.00	2.73	23.48	0.000
	$Farmer_{urban}$	1.88	0.58	6.07	0.292
	$Worker_{HSDC}$	0.99	0.26	3.77	0.983
Sex	Male				
	Female	0.63	0.31	1.27	0.198
Age		1.04	1.02	1.05	0.000
Educational attainment	Never went to school				0.023
	Primary	0.54	0.13	2.23	0.397
	Secondary	0.45	0.12	1.69	0.236
	Higher education	0.20	0.05	0.81	0.024
Socio-economic status	Most poor				0.019
	Poor	0.59	0.29	1.18	0.137
	Less poor	0.61	0.30	1.22	0.161
	Least poor	0.27	0.11	0.64	0.003
Number of people per household	1 to 4				0.089
	4 to 6	0.50	0.27	0.94	0.030
	> 6	0.54	0.26	1.13	0.104
Toilet facility at home	Yes				
	No	7.51	2.97	18.97	0.000
Toilet facility at work	Yes				
	No	2.18	1.26	3.77	0.005
Wastewater can cause health issues	No				
	Yes	0.33	0.18	0.62	0.001
Flooding of living area	No				
	Yes	0.85	0.20	3.70	0.833
Flooding of working area	No				
	Yes	1.22	0.65	2.29	0.540
Drinking tap water	No				
	Yes	0.79	0.43	1.47	0.462
Drinking rain water	No				
	Yes	1.41	0.58	3.46	0.448
Drinking bore hole water	No				
	Yes	2.43	1.27	4.66	0.007
Bath tap water	No				
	Yes	0.71	0.34	1.45	0.346
Bath rain water	No				
	Yes	1.93	0.72	5.20	0.192
Bath bore hole water	No				
	Yes	2.17	0.25	18.88	0.483
Preventive chemotherapy received in the past	< 6 months				0.012
	6 to <12 months	2.76	0.28	27.14	0.385
	<12 months	7.50	1.02	55.24	0.048
	Never took deworming	9.19	1.03	81.62	0.047

* P-values were obtained from likelihood ratio tests. **(i)"$Com_{peri\text{-}urban}$" = people living in the peri-urban commune Duyen Ha, 5 km away from the city along the Red River; (ii) "Com_{urban}" = people living in the urban area of Hanoi, in Bang B village or Tam Hiep commune along the To Lich River and potential exposed to wastewater; (iii) "$Farmer_{peri\text{-}urban}$" = peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater; (iv) "$Farmer_{urban}$" = urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and (v) "$Worker_{HSDC}$" = workers from Hanoi Sewerage and Drainage Company (HSDC) maintaining drainage channels and operating the Yen So treatment plants.

Table S4 Results of univariate logistic regression analysis for self-reported 14-days diarrhoea in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014

14-days diarrhoea (total population, $N = 681$; infections $n = 59$)		Univariate logistic regression*			
		OR	95% CI		*P*-value
Exposure group**	$Com_{peri\text{-}urban}$				0.156
	Com_{urban}	0.77	0.35	1.70	0.519
	$Farmer_{peri\text{-}urban}$	0.30	0.10	0.88	0.028
	$Farmer_{urban}$	0.87	0.39	1.92	0.723
	$Worker_{HSDC}$	0.63	0.26	1.52	0.303
Sex	Male				
	Female	1.51	0.85	2.69	0.160
Age		1.01	0.99	1.03	0.307
Educational attainment	Never went to school				0.174
	Primary	0.23	0.06	0.90	0.035
	Secondary	0.22	0.07	0.76	0.016
	Higher education	0.28	0.08	0.95	0.042
Socio-economic status	Most poor				0.782
	Poor	0.86	0.39	1.92	0.713
	Less poor	1.27	0.60	2.68	0.534
	Least poor	1.02	0.47	2.23	0.952
Number of people per household	1 to 4				0.965
	4 to 6	0.91	0.47	1.78	0.790
	> 6	0.95	0.44	2.04	0.892
Toilet facility at home	Yes				
	No	1.00			
Toilet facility at work	Yes				
	No	0.84	0.45	1.54	0.569
Wastewater can cause health issues	No				
	Yes	2.09	0.74	5.91	0.166
Flooding of living area	No				
	Yes	0.84	0.19	3.63	0.813
Flooding of working area	No				
	Yes	1.75	0.97	3.14	0.063
Drinking tap water	No				
	Yes	1.26	0.64	2.48	0.513
Drinking rain water	No				
	Yes	1.11	0.42	2.90	0.836
Drinking bore hole water	No				
	Yes	0.77	0.32	1.84	0.553
Bath tap water	No				
	Yes	0.97	0.44	2.11	0.935
Bath rain water	No				
	Yes	1.89	0.70	5.09	0.206
Bath bore hole water	No				
	Yes	2.13	0.24	18.52	0.494
Preventive chemotherapy received in the past	< 6 months				0.995
	6 to <12 months	1.05	0.34	3.29	0.933
	<12 months	0.98	0.40	2.39	0.961
	Never took deworming	1.11	0.29	4.17	0.883

* *P*-values were obtained from likelihood ratio tests. **(i)"$Com_{peri\text{-}urban}$" = people living in the peri-urban commune Duyen Ha, 5 km away from the city along the Red River; (ii) "Com_{urban}" = people living in the urban area of Hanoi, in Bang B village or Tam Hiep commune along the To Lich River and potential exposed to wastewater; (iii) "$Farmer_{peri\text{-}urban}$" = peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater; (iv) "$Farmer_{urban}$" = urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and (v) "$Worker_{HSDC}$" = workers from Hanoi Sewerage and Drainage Company (HSDC) maintaining drainage channels and operating the Yen So treatment plants.

Table S5 Results of univariate logistic regression analysis for self-reported skin problems in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014

Self-reported skin problems (total population, *N* = 681; infections *n* = 137)		Univariate logistic regression*			
		OR	95% CI		*P*-value
Exposure group**	$Com_{peri\text{-}urban}$				0.015
	Com_{urban}	0.79	0.43	1.44	0.435
	$Farmer_{peri\text{-}urban}$	1.26	0.69	2.31	0.450
	$Farmer_{urban}$	0.45	0.23	0.89	0.022
	$Worker_{HSDC}$	0.99	0.53	1.85	0.983
Sex	Male				
	Female	1.06	0.69	1.64	0.781
Age		0.98	0.97	1.00	0.016
Educational attainment	Never went to school				
	Primary				
	Secondary				
	Higher education				
Socio-economic status	Most poor				0.386
	Poor	0.65	0.38	1.11	0.112
	Less poor	0.81	0.48	1.36	0.423
	Least poor	0.69	0.41	1.17	0.168
Number of people per household	1 to 4				0.428
	4 to 6	0.92	0.58	1.45	0.716
	> 6	0.71	0.41	1.23	0.223
Toilet facility at home	Yes				
	No	1.25	0.45	3.47	0.669
Toilet facility at work	Yes				
	No	0.71	0.46	1.10	0.128
Wastewater can cause health issues	No				
	Yes	1.34	0.73	2.46	0.344
Flooding of living area	No				
	Yes	2.88	1.31	6.36	0.009
Flooding of working area	No				
	Yes	1.25	0.80	1.95	0.321
Bath with bore hole water	No				
	Yes	2.00	0.36	11.03	0.426

* *P*-values were obtained from likelihood ratio tests. **(i)"$Com_{peri\text{-}urban}$" = people living in the peri-urban commune Duyen Ha, 5 km away from the city along the Red River; (ii) "Com_{urban}" = people living in the urban area of Hanoi, in Bang B village or Tam Hiep commune along the To Lich River and potential exposed to wastewater; (iii) "$Farmer_{peri\text{-}urban}$" = peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater; (iv) "$Farmer_{urban}$" = urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and (v) "$Worker_{HSDC}$" = workers from Hanoi Sewerage and Drainage Company (HSDC) maintaining drainage channels and operating the Yen So treatment plants.

Table S6 Results of univariate logistic regression analysis for self-reported eye problems in a cross-sectional survey in the Than Tri district, Hanoi, between April and June 2014

Self-reported eye problems (total population, N = 681; infections n = 200)		Univariate logistic regression*			
		OR	95% CI		*P*-value
Exposure group**	$Com_{peri\text{-}urban}$				0.008
	Com_{urban}	1.59	0.89	2.84	0.120
	$Farmer_{peri\text{-}urban}$	1.06	0.56	2.00	0.867
	$Farmer_{urban}$	2.33	1.30	4.16	0.004
	$Worker_{HSDC}$	1.93	1.05	3.53	0.033
Sex	Male				
	Female	0.67	0.45	1.01	0.056
Age		1.03	1.02	1.04	0.000
Educational attainment	Never went to school				0.047
	Primary	0.34	0.11	1.04	0.058
	Secondary	0.27	0.09	0.79	0.017
	Higher education	0.24	0.08	0.70	0.009
Socio-economic status	Most poor				0.167
	Poor	0.63	0.39	1.02	0.059
	Less poor	0.97	0.61	1.54	0.908
	Least poor	0.75	0.47	1.20	0.228
Number of people per household	1 to 4				0.544
	4 to 6	0.83	0.55	1.26	0.380
	> 6	1.00	0.63	1.60	0.996
Toilet facility at home	Yes				
	No	0.39	0.11	1.34	0.136
Toilet facility at work	Yes				
	No	0.83	0.57	1.20	0.327
Wastewater can cause health issues	No				
	Yes	1.66	0.96	2.88	0.068
Flooding of living area	No				
	Yes	1.01	0.44	2.35	0.976
Flooding of working area	No				
	Yes	1.09	0.73	1.63	0.679
Bath bore with hole water	No				
	Yes	0.48	0.06	4.12	0.502

* *P*-values were obtained from likelihood ratio tests overall *P*-value. **(i)"$Com_{peri\text{-}urban}$" = people living in the peri-urban commune Duyen Ha, 5 km away from the city along the Red River; (ii) "Com_{urban}" = people living in the urban area of Hanoi, in Bang B village or Tam Hiep commune along the To Lich River and potential exposed to wastewater; (iii) "$Farmer_{peri\text{-}urban}$" = peri-urban farmers living in Duyen Ha commune using the irrigation water from Red River, wells or local drains, which are not contaminated with the city's wastewater; (iv) "$Farmer_{urban}$" = urban farmers living in Bang B village or Tam Hiep commune reusing wastewater from To Lich River; and (v) "$Worker_{HSDC}$" = workers from Hanoi Sewerage and Drainage Company (HSDC) maintaining drainage channels and operating the Yen So treatment plants.

17. Curriculum vitae

Personal data

Full name:	Samuel Fuhrimann
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Research interests

Trained in infection biology and epidemiology (MSc) and environmental epidemiology (PhD) Samuel is currently working as a Post Doc fellow at the Swiss Tropical and Public Health Institute and the University of Cape Town. His main research focus is on the link between microbial and chemical water contamination, exposure assessment and related disease burden estimation in the context of agriculture, wastewater, sanitation safety planning and urbanization. Over the past six years, Samuel has been involved in various epidemiological surveys and environmental assessments linked to risk assessments approaches in sub-Saharan Africa (South Africa, Uganda, Kenya), Asia (Vietnam, India) and Latin America (Costa Rica). Applied methods range from clinical studies, water, soil and air sampling to mathematical modelling (pesticide exposure assessment, QMRA, individual based transmission models) and interdisciplinary approaches (One-Health). Hence, he has a particular interest in visualization of environmental pollution related to health issues.

Education

8/2012 – 9/2015	PhD in Epidemiology; Swiss Tropical and Public Health Institute/University of Basel, Basel, Switzerland
9/2010 – 12/2011	MSc in Infection Biology and Epidemiology; Swiss Tropical and Public Health Institute (Swiss TPH)/University of Basel, Basel, Switzerland
9/2007 – 6/2010	BSc of Science in Biology, Major in Animal and Plant Sciences; University of Basel, Basel, Switzerland
8/2006 – 9/2007	Higher Education Entrance Qualification ‘Passerelle at Gymnasium; Kirschgarten, Basel, Switzerland
8/2002 – 6/2005	Professional Degree: Chemistry lab assistant including technical ’Berufsmaturität’; Ciba SC. AG, Basel, Switzerland

Positions and employment

09/2015 – present	Post-Doc fellow at Swiss TPH/University of Basel, Basel, Switzerland under the supervision of Prof. Dr. Guéladio, Cissé, Prof. Dr. Jürg Utzinger and Dr. Mirko Winkler
8/2012 – 9/2015	PhD fellow in epidemiology at Swiss TPH/University of Basel, Basel, Switzerland, pursuing a 3-year PhD programme under the supervision of Prof. Dr. Guéladio, Cissé, Prof. Dr. Jürg Utzinger and Dr. Mirko Winkler
1/2013 – 12/2014	PhD student representative at Swiss TPH/University of Basel, Basel, Switzerland
1/2011 – 6/2012	Research fellow at the Human and Animal Health Unit, Swiss TPH, under the supervision of Prof. Dr. Jakob Zinnstag and Dr. Esther Schelling
1/2009 – 6/2012	Part time school teacher for biology, math, German and arts at the secondary school, Basel, Switzerland
1/2009 – 1/2011	Part time employee as chemistry lab assistant in bio-analytic at Solvias AG, Basel Switzerland

Work experience in other countries

Kenya (6 month stay over three travels, longest stay 4,5 month at ILRI in Nairobi), **Uganda** (9 month stay over six travels, longest stay for 5 month at the Makarere School of Public Health in Kampala), **South Africa** (2 month stay over two visits, longest stay 1 month at UCT in Cape Town), **India** (2 month stay over three travels to Bangalore (St. John's Medical College) and Hyderabad (IWMI)**, Vietnam** (7 month stay over three travels, longest stay 5 month at Hanoi School of Public Health in Hanoi) and **Costa Rica** (5 month stay over two travels, longest stay for 4 month at IRET in Heredia and Zarcero).

Presentations at international meetings and congresses and training activities

1/9/2016	28th Annual conference international society for environmental epidemiology. **Oral presentation and session chair:** Disease burden due to gastrointestinal pathogens in wastewater along the major wastewater system in Kampala, Uganda
3/12/2015	SSP sensitisation and preparation workshop, Kampala, Uganda. **Oral presentation:** Sanitation safety planning testing in Kampala 2013-2015
21/10/2015	IWA Water and Development Congress, Amman, Jordan. **Oral presentation:** Conducting in-depth health risk assessment in developing countries: case study from Kampala, Uganda
8/9/2015	9th European Congress on Tropical Medicine and International Health, Basel, Switzerland. **Poster presentation:** Risks of helminth transmission from urban wastewater reuse systems in Kampala, Uganda and Hanoi, Vietnam
6/9/2015	9th International Symposium on Geospatial Health, Basel, Switzerland. **Oral presentation:** Wastewater recovery and reuse systems in Hanoi, Vietnam: a visualization
1/4/2015	Films for Health: an Indo-Swiss Partnership, Basel. **Oral presentation:** A visualisation of health risk assessments along wastewater and faecal sludge management and reuse systems in Kampala, Uganda
28/3/2015	Dresden Nexus Conference, Dresden. **Oral presentation:** Health risk assessment along the major wastewater reuse chain in Kampala, Uganda
31/8/2014	World Water Week, Stockholm. **Oral presentation:** Health risk and impact assessments of RRR business cases and models in Hanoi and Kampala
18/10/2012	MVVR Symposium, Nairobi. **Oral presentation:** Individual-based Rift Valley Fever transmission model for Kenyan livestock

Review activities

Review for Experimental Parasitology, Microbial Risk Analysis and Acta Tropica,
PLoS Neglected Tropical Disease

Grands and awards

1/2017 – 8/2017	**Swiss-African Research Cooperation (SARECO), visiting research fellowship at University of Cape Town, South Africa** (CHF 69’090). Pesticide pollution of water and air in different agricultural systems in the Western Cape, South Africa (career grant).
8/2016 – 12/2016	**Universität Basel, Spezialprogram Nachwuchsförderung Klinische Forschung** (CHF 61,983) Health risk assessment along water bodies contaminated with pesticides in Zarcero, Costa Rica (career grant).
11/2015 – 2/2016	**Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ** (EUR 34,973) Baseline study of the water quality at industrial hotspots in the Nakivubo Channel, Kampala (project grant).
10/2015 – 12/2015	**PhD Educational Platform for Health Sciences, University of Basel** (CHF 18,586) Award to fund extra activities that were initially not planned as part of the PhD proposal but that are fundamentally important to maximize the scientific impact and the quality of the PhD.

Student supervision

5/2016 – 11/2016	**Philipp Staudacher (Swiss)**: Health impact of pesticides application in farmworkers in Zarcero, Costa Rica (co-supervisor; principal supervisor Dr. Mirko Winkler, Swiss TPH and Prof. Dr. Christian Stamm, ETH Zurich)
1/2016 – 1/2017	**Nesre Redi (Ethiopia)**: Water quality and health in three different urban areas of Western Cape, South Africa (co-supervisor; principal supervisor Prof. Dr. Guéladio Cissé and Prof. Dr. Martin Röösli, Swiss TPH and Dr. Aqiel Dalvie, University of Cape Town, South Africa)
8/2013 – 3/2014	**Lena Breitenmoser (Swiss)**: Health protection measures in wastewater reuse systems acceptability and practicability of adoption in Devanahalli, India (co-supervisor; principal supervisor Prof. Dr. Guéladio Cissé, Swiss TPH and Prof. Dr. Kristopher McNeil, ETH Zurich)
8/2013 – 3/2014	**Michelle Stalder (Swiss)**: Microbial and Industrial Contamination Along the Major Wastewater Chain in Kampala, Uganda (co-supervisor; principal supervisor Prof. Dr. Guéladio Cissé, Swiss TPH and Prof. Dr. Kristopher McNeil, ETH Zurich)

Skills

Proficient in working with ArcGIS, Stata 12, C++, R, @risk, Open Data Kit, Mendely and MS Office programmes

Languages

German (mother tongue); English (proficient); French and Spanish (basic)

Publication published

Fuhrimann S (2017) Health risk assessment along wastewater recovery and reuse systems in Kampala, Uganda and Hanoi, Vietnam, PhD thesis, University of Basel, Switzerland

Fuhrimann S, Nauta M, Pham-Duc P, Tram NT, Nguyen-Viet H, Utzinger J, Cissé G, Winkler MS (2016). Disease burden due to gastrointestinal infections among people living along the major wastewater system in Hanoi, Vietnam. Advances in Water Resources. doi.org/10.1016/j.advwatres.2016.12.010.

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Fuhrimann S, Pham-Duc P, Cissé G, Thuy Tram N, Hoang H, Dunge DT, Ngoc P, Nguyen H, Anh T, Utzinger J, Schindler C, Winkler MS (2016). Microbial contamination along the main open wastewater and storm water channel of Hanoi, Vietnam, and potential health risks for urban farmers; Science of The Total Environment 556-567: 1014-1022.

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Fuhrimann S (2011). Rift Valley Fever in Kenyan pastoral livestock: Individual-based demographic model to analyses the impact of Rift Valley Fever on livestock, MSc thesis, University of Basel, Switzerland.

Book chapter

Zinsstag J, **Fuhrimann S**, Hattendorf J, Chitnis N (2015). One Health: the theory and practice of integrated health approaches, Edition: 1, Chapter: 9, Animal-human transmission models, CAB International, pp.122-133.