

Commentary

Commentaries on ‘Hand washing for preventing diarrhoea’, with a response from the review authors

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Further information for this Cochrane review is available in this issue of EBCH in the accompanying Summary article.

Commentary by Diana Pinto-Masis

Diarrheal disease (DD) is among the leading causes of mortality and morbidity in children under 5 in the developing world. The toll is particularly high in Africa and Asia, where DD could account for 22% of all deaths in this age group (1). DD is also an important factor in the pathways to child malnutrition and higher vulnerability to infectious disease, and to growth and development problems. Reduction of DD is a global health priority and is specially relevant to achieve the Millennium Development Goal of reducing the under-5 child mortality rate by two-thirds (2).

The current armamentarium to combat DD consists of child health interventions, such as immunization, breastfeeding, oral rehydration therapy and micronutrient supplementation, and environmental health interventions that interrupt diarrheal disease transmission, which include improved water supply, sanitation and health behaviour changes. There is a good body of evidence on the effectiveness and cost effectiveness of large scale implementation of child health interventions in reducing the burden of DD (3), and it is likely that further expansions can save additional millions of lives.

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However, with respect to environmental health interventions, a recent critical review of the existing research on the prevention and treatment of diarrheal diseases in rural areas of developing countries finds a weak evidence base for recommendations about the extent to which further investments in the prevention of DD should emphasize environmental health interventions (4). Much more research is needed to minimize the knowledge gaps on the impact and cost effectiveness of several environmental health interventions that can complement existing child health programs. One such intervention is hand washing with soap.

Poor hand hygiene is a major risk factor for transmission of DD, and it has been demonstrated that proper hand hygiene measures are a first step towards reducing the risk of contagion (5–7). Several reviews of observational studies of hand washing and hygiene interventions in community and school settings, both in developed and developing countries have consistently found dramatic impacts in DD morbidity in children, in the magnitude of 44–47% (6, 8, 9). The current review by Ejemot *et al.* calibrates previous estimates of the effectiveness of hand washing with soap with evidence coming solely from randomized controlled intervention trials where specific hand washing interventions were tested (with or without additional hygiene promotion), conducted both in communities and in educational institutions in countries of any income level.

Utilizing a comprehensive search strategy, 37 trials were identified, of which 14 met the inclusion criteria. Eight trials were institution-based (day-care centres or primary schools), and all took place in industrialized countries (except for one trial which

was conducted in China), in settings with adequate water availability. Participants were mainly day-care providers or educators, and children aged less than 7, who were exposed to multiple hygiene interventions with the aim of providing education about personal hygiene, diarrhea transmission, treatment, and prevention, and the importance of and techniques for hand washing with soap. Five of the included trials evaluated community-based interventions conducted in low- and middle-income countries in Africa. Three of these evaluated only hand washing with soap interventions and two included hand washing with soap and proper disposal of feces interventions. Participants were mainly mothers or caregivers as well as children with ages ranging up to 15 years of age, who were provided with hand washing materials and involved in large-group hygiene education training. All trials assessed episodes of diarrhea in the children and three assessed changes in hand washing behaviour. Follow-up periods in all trials ranged from 4–12 months. This review also examined a trial in a high risk group (AIDS patients in the USA), in which patients received intensive hand washing promotion delivered by specialist nurses during 1 year, and outcomes were measured as mean episodes of DD in each group and number of hand washing episodes per day.

Given the differences between interventions in the trial settings, the results are analyzed separately. The outcomes and methods of measuring behaviour changes were too variable to make meta-analysis meaningful. The pooled estimates from the included trials show a 29% reduction in DD morbidity for the institution based trials [95% Confidence Intervals (CI) 0.60 to 0.84] and 31% for the community based trials (95% CI 0.55 to 0.87). The hand washing intervention in the high risk group achieved a reduction of 1.68 episodes (95% CI –1.93 to –1.43).

The magnitude of the effect for the institution and community based trials is about 15% less than that reported by the earlier reviews of hand washing and hygiene interventions mentioned above and by a more recent review (10). Even though the effect size is still substantial, the authors identify several methodological limitations in the reviewed studies that do not allow one to rule out that this effect could be over-estimated. The shortcomings include unclear methods of randomization, inadequate reporting and accounting for attrition and differences in baseline characteristics between the study arms, short-term follow-up, and the inability to separate impacts of different hygiene components used in the interventions. The authors also highlight that the observed level of effectiveness might not be replicated in the day-to-day world or in a larger scale application of the interventions, given that compliance in most trials could be artificially high as a result of intense follow-up and monitoring and guaranteed availability of resources for hand washing.

In synthesis, the results of the review by Ejemot *et al.* confirm that hand washing with soap is efficacious in reducing the incidence of DD in different

settings, although to a lesser degree than previously shown. Nonetheless, the demonstrated benefits in morbidity reduction are far from trivial, and promotion of hand washing continues to be an important tool in the arsenal for preventing DD.

For further investments in promotion of hand washing with soap to be successful much more research is needed about the factors influencing the adoption of hand hygiene procedures in different settings and about the cost effectiveness of ways to facilitate long-term behaviour change and technology adoption in diverse cultural contexts. Although hand washing in itself is apparently simple and the rationale behind it can be well understood, inducing behavioural changes to ensure its adoption and compliance can be quite complex and may need to be tailored to different target populations. For example, even in the health care community, where hand hygiene is recognized as an essential procedure for the prevention of infection, failure to adhere to hand washing guidelines is common and a wide array of strategies may need to be adopted to consistently improve compliance with hand hygiene practice (11).

The practicality of hand washing with soap in high-demand situations such as in health care settings and schools is questionable and can certainly become a barrier for adherence. The Centers for Disease Control recommends the following routine (<http://www.cdc.gov/cleanhands/>):

- Wet your hands with clean running water and apply soap. Use warm water if it is available.
- Rub hands together to make a lather and scrub all surfaces.
- Continue rubbing hands for 20 seconds. Need a timer? Imagine singing 'Happy Birthday' twice through to a friend!
- Rinse hands well under running water
- Dry your hands using a paper towel or air dryer. If possible, use your paper towel to turn off the faucet

This procedure could take about 2 minutes. It is not hard to picture a typical situation in a day care centre where there is one sink and a class of 15 children lined up for hand washing. If the kids are rigorous, the time required for the entire class to wash their hands could be around half an hour, at the expense of pedagogical or leisure activities. Situations like these have prompted research on more convenient alternatives to hand disinfection such as alcohol-based hand rubs. Although the available evidence on the effectiveness of alcohol-based hand sanitizers in reducing gastrointestinal illness suggests an effect of similar magnitude to hand washing with soap, methodological shortcomings prevent reaching any conclusion (7).

As a final thought, we should not forget the fact that a large proportion of the population burdened by DD lives in places where water is a scarce resource. Of the 1069 million people in the world that lack

potable water services, 50% live in South-Eastern Asia and 30% in Africa (12). Furthermore, there is a great concern regarding a future global water crisis and 'By 2025 more than 3 billion people could be living in water-stressed countries – and 14 countries will slip from water stress to water scarcity' (13). Therefore, identifying and testing hand hygiene alternatives for populations with limited or no possibilities of hand washing with soap and water is another priority line of research.

International advocacy for hand washing with soap and water as a strategy to reduce infectious disease has been growing. A noteworthy and recent example of global efforts to promote the hand washing cause was the organization of the Global Hand washing Day held on October 15 2008, which mobilized activities to motivate people in more than 20 countries across all five continents to wash their hands with soap. The initiative was led by the Public-Private Partnership for Hand Washing with Soap-PPPHW (<http://www.globalhandwashing.org>), which seeks to increase rates of hand washing with soap in developing countries. Better evidence on what works in hand hygiene interventions will allow the international community to obtain higher returns on investments in the prevention of DD.

Declarations of Interest

None.

References

- Morris SS, Black RE, Tomaskovic L. Predicting the distribution of under-five deaths by cause in countries without adequate vital registration systems. *Int J Epidemiol* 2003; **32**(6): 1041–1051.
- Lenton R, Wright AM, Lewis K. Health, dignity, and development: what will it take? Task Force on Water and Sanitation. In: *United Nations Development Program* (Eds.); 2005; Available from <http://www.unmillenniumproject.org/documents/WaterComplete-lowres.pdf>.
- Keusch GT, Fontaine O, Bhargava A, Boschi-Pinto C, Bhutta ZA, Gottuzzo E, Rivera JA, Chow J, Shahid-Salles SA, Laxminarayan R. Diarrheal diseases. In: *Disease Control Priorities in Developing Countries*, 2nd edn, pp. 371–388. New York: Oxford University Press; 2006.
- Zwane AP, Kremer M. *What Works in Fighting Diarrheal Diseases in Developing Countries? A Critical Review*. NBER Working Paper No. 12987; 2007.
- Larson E. A causal link between handwashing and risk of infection? Examination of the evidence. *Infection Control* 1988; **9**(1): 28–36.
- Fewtrell L, Colford JM. *Water, Sanitation and Hygiene: Interventions and Diarrhoea: A Systematic Review and Meta-Analysis [Report No 34960]*. Washington DC: The International Bank for Reconstruction and Development/The World Bank; 2004.
- Bloomfield SF, Aiello AE, Cookson B, O'Boyle C, Larson EL. The effectiveness of hand hygiene procedures, including handwashing and alcohol-based hand sanitizers, in reducing the risks of infections in home and community settings. IFH Expert Report; 2007; Available from: www.ifh-homehygiene.org.
- Curtis V, Cairncross S. Effect of washing hands with soap on diarrhoea risk in the community: a systematic review. *Lancet Infect Dis* 2003; **3**(5): 275–281.
- Fewtrell L, Kaufmann RB, Kay D, Enanoria W, Haller L, Colford JM Jr. Water, sanitation, and hygiene interventions to reduce diarrhoea in less developed countries: a systematic review and meta-analysis. *Lancet Infect Dis* 2005; **5**(1): 42–52.
- Aiello AE, Coulborn RM, Perez V, Larson E. Effect of hand hygiene on infectious disease risk in the community setting: a meta-analysis. *Am J Public Health* 2008; **98**: 1372–1381.
- Pittet D. Improving adherence to hand hygiene practice: a multidisciplinary approach. *Emerging Infect Dis* 2001; **7**(2): 234–240.
- World Health Organization & UNICEF Joint Monitoring Programme (JMP) for water supply and sanitation; 2006; Available from: <http://www.wssinfo.org/en/welcome.html> (accessed 16 May 2007).
- United Nations Development Programme. Human Development Report. Beyond Scarcity: Power, Poverty and the Global Water Crisis; 2006; Retrieved 6 March 2009. Available from: <http://hdr.undp.org/en/media/HDR06-complete.pdf>.

Commentary by Yanina Sguassero

Poor access to safe water is directly linked with water-borne and faecal-oral diseases, especially diarrhoea. According to UNICEF, a child born in Europe or the United States is 520 times less likely to die from diarrhoeal disease than an infant born in sub-Saharan Africa, where only 36% of the population can access hygienic sanitation (1). Over 90% of deaths from diarrhoeal diseases due to unsafe water and sanitation in the developing world occur in children under 5 years old (2). Diarrhoea is transmitted by ingesting contaminated food or drink, by direct person-to-person contact, or from contaminated hands. Thus, the main causes are the use of contaminated water, unhygienic practices in food preparation and excreta disposal.

Hand washing is the act of cleansing the hands with water or another liquid, with or without the use of soap or other detergents, for the sanitary purpose of removing soil and/or microorganisms. In this scenario, hand washing is a possible beneficial intervention to interrupt the transmission of diarrhoea-causing pathogens. Nevertheless, like many other hygiene promotion interventions, hand washing entails clean water supply and adequate sanitation at the household and community level.

This systematic review of RCTs aimed to estimate an effect size of interventions to promote hand washing on diarrhoeal episodes in children and adults. In addition, these interventions (using educational programs, leaflets, and discussions) had to be compared with other hygiene promotion interventions that could include hand washing but no specific activities to promote hand washing. In other words, controls did not receive hand washing promotion. The criteria for considering studies for the review were clearly stated. Observational, case-control, and controlled before-and-after studies were excluded. Participants were adults and children in institutional settings, communities, or households. A large spectrum of activities to promote hand washing was considered (e.g. small group discussions, meetings, posters, radio and television shows, etc.), hence; high levels of heterogeneity

among trials were expected. Primary outcomes were acute primary diarrhoea defined as three or more loose or watery stools in a 24-hour period, persistent diarrhoea lasting 14 or more days, and dysentery defined as bloody diarrhoea. Secondary outcomes were diarrhoea-related death, behavioural changes, and changes in knowledge and attitudes toward hand washing. A comprehensive literature search was conducted on multiple databases; researchers, international organizations, and the Grey Literature were consulted. No language restriction was applied.

Of 37 potentially eligible trials, 14 met inclusion criteria, of which eight were institution-based RCTs (by clusters with use of classrooms or day-care centres), five were community-based trials, and one examined an at-risk population with AIDS. The potentially eligible studies were assessed independently by two review authors. Excluded studies were listed and the reasons for exclusion were provided. Whenever it was feasible, the generic inverse variance method and random-effects model with 95% Confidence Intervals (CI) were used to pool Incidence Rate Ratios (IRRs).

Based on the review findings, interventions promoting hand washing among children were associated with a decrease in diarrhoeal episodes of 29% in institutions in high-income countries (IRR, 0.71; 95% CI, 0.60–0.84; $I^2 = 57.2%$) and 31% in communities in low- or middle-income countries (IRR, 0.69; 95% CI, 0.55–0.87; $I^2 = 86.7%$). This positive effect was greater in the three trials that provided soap and promoted hand washing only (IRR 0.57, 95% CI 0.44–0.75; $I^2 = 55.6%$) than in the two trials that did not provide soap and promoted multiple hygiene interventions (IRR 0.84, 95% CI 0.67–1.05; $I^2 = 87.4%$). A positive behavioural change was also found in children receiving the intervention at day care centres compared to the control group (IRR of 0.34, 95% CI 0.17–0.65).

Despite these benefits, the data should be interpreted with caution because of the limited quality of available RCTs (e.g. the method of concealment allocation was unclear, the concealment allocation was not stated, and the blinding of outcomes assessors was not used in the majority of the included trials). Furthermore, comparability between the intervention and control groups with respect to diarrhoea incidence and socio-demographic characteristics at baseline was not always reported and this may have introduced some bias. As the reviewers rightly note, most of the trials should be regarded as ‘efficacy’ trials (rather than ‘effectiveness’ trials) in the sense that they include intense follow-up and monitoring (all contacted intervention communities at least fortnightly to collect data on diarrhoea episodes), and many also provided hand washing materials regularly. So, while the review itself is robust, it is unclear if the level of effectiveness reported would be maintained in other resource-limited regions with less intensive monitoring. The short length of follow-up of the included studies (4–12 months) precluded assessing relevant long-term outcomes such as child growth and

nutritional status. Diarrhoea-related deaths were not reported.

In terms of applicability of the review findings, the institutional-based studies were conducted in high-income countries such as Australia, Canada, Denmark and USA. Their results cannot be applied to poor communities. On the other hand, the five community-based trials included entire communities (villages or neighbourhoods) in low- and middle-income countries in Africa and Asia. Likewise, it would be difficult to extrapolate these results to other developing countries given that hygienic habits are closely related to cultural, social, and religious factors. Participants of included studies were predominantly younger than 7 years old, so, it is not known the extent to which they were representative of older children who are able to make their own behavioural decisions.

In agreement with a previous review (4), the authors concluded that “hand washing interventions are efficacious in reducing diarrhoeal episodes and should be promoted”. Yet, regardless of its lifesaving potential, educating families on the importance of good hand washing technique (i.e. when, how often, and in what manner hands should be washed) is but one obstacle to overcome. The barriers and key motivators for hand washing behaviour change should be explored thoroughly before the implementation of large-scale hand washing initiatives at a community level.

The limited number of included reviews in low and middle income countries highlights the need for new, better-designed studies aimed to measure the effect of hand washing on child morbidity and mortality in developing countries. Meanwhile, alliances between governments, NGOs, the private sector and communities themselves are vital to raise the world’s awareness about the lack of clean water in poor rural areas. Without such partnerships, the likelihood of reaching the Millennium Development Goal 7 (i.e. to cut in half the proportion of people without access to safe water and basic sanitation between 1990 and 2015) (4) will not be reached. This is of paramount importance and should be considered an urgent and universal child health matter.

Declaration of Interest

None.

References

1. UNICEF. Available from: http://www.unicef.org/wes/index_31600.html (accessed 18 February, 2009).
2. World Health Organization. The world health report 2002: Reducing risks, promoting healthy life [WHO/WHR/02.1]. Geneva: World Health Organization; 2002.
3. Curtis Val, Cairncross S. Effect of washing hands with soap on diarrhoea risk in the community: a systematic review. *Lancet Infect Dis* 2003; **3**: 275–281.

4. UNICEF. Available from: <http://www.unicef.org/wes/files/CWWFGlobalWaterSanitationData.doc> (accessed 18 February, 2009).

Response from the Review Authors

We thank Drs Pinto-Masis and Sguassero for their excellent commentaries on our review and for their suggestions on strategies to optimize the benefits of hand washing for the improvement of child health in less developed countries. In responding to the commentary by Dr Pinto-Masis, we submit that diseases underpinned by poor environmental and social condition and by human behaviour can be sustainably controlled by interventions that target their environmental, social, and behavioural root causes. Childhood diarrhea is a typical example. Diarrheal disease control efforts of the 1980s targeted the reduction of mortality from dehydration by promoting the use of Oral Rehydration Solution (ORS) during diarrheal episodes. Increased intake of fluids, supplemented by ORS together with continued feeding, has proven to be a powerful intervention for the prevention of childhood deaths from diarrhea (1). Estimates have shown a steady decline ever since: almost 5 million deaths in the 1980s (2), 3.3 million in the 1990s (3), and 2.5 million in 2000 (4). In spite of these declines, diarrhea is still the second leading cause of under-5 mortality globally. The key lesson in this is that disease focused child health interventions may reduce mortality, but because they do not modify the 'environmental' conditions that make children sick, their effectiveness in reducing the overall burden of childhood disease is limited (5).

Dr Pinto-Masis raised a number of important questions regarding barriers in promoting hand washing in resource-poor settings. First, she noted the difficulty in getting large groups of children in places such as schools and day care centres to wash their hands and how time and efforts expended on hand washing could detract from pedagogical and leisure activities. While the typical scenario in developed countries is that hands are washed in sinks under tap water, there are alternative appropriate technologies that serve the same purpose, and which can be further developed and used to scale in resource-poor settings. Figure 1 provides an example of such technology, which if placed at three or more strategic locations in a school or day care centre, could reduce long waiting time to use the facility.

Second, she questioned whether to invest in environmental approaches for diarrheal disease control, including provision of soap and water, or in other technologically driven approaches such as use of hand sanitizers. It is unlikely that marketed technologies such as hand sanitizers will have any discernible effect on hand washing, and therefore on childhood diarrhea, as only well-to-do families are likely to afford them. Also, experience of the past two decades has shown that sustainable improvements will not occur



Source: Southern Institute for Appropriate Technology (<http://www.sifat.org>) (Photo taken by Dr John Ehiri, October 2007)

Figure 1. Alternative technology to promote hand washing

through therapeutic or high-tech interventions, but by environmental interventions, of which provision of potable water and hand hygiene are key elements. It is known that over 90% of diarrhea mortality among children under 5 occurs in less developed countries. Why is this? We submit that differences in environmental and social infrastructures account for this. While equally important, immunization, zinc supplementation, and related therapeutic interventions will not sustainably reduce this disparity if the underlying environmental root causes of childhood diarrhea are not addressed.

In considering the best options for child health promotion in less developed countries, it is important to analyze and draw parallels with factors that contributed to population health improvements in high income countries over the past century. This parallel is not unreasonable given that many less developed countries are, more or less, currently at the level of health and social economic development that many high income countries were at several decades ago. In his analysis of factors that contributed to improvements in

health and growth of the population of England and Wales, McKeown (6) showed that the high death rates of the past were largely attributable to a combination of infectious diseases, nutritional, and environmental factors. He estimated that from the beginning of the 18th century to the mid 1970s, 80–90% of the total reduction in death rate in England and Wales was as a result of the decline in deaths caused by infections and water- and food-borne diarrheal diseases. He noted that with the exception of vaccination against smallpox (associated with less than 2% of the decline in the death rate from 1848–1871), it was unlikely that immunization or therapy had any significant effect on infectious diseases before the 20th century given that much of the reduction in mortality from tuberculosis, respiratory, water- and food-borne diseases had already occurred before effective immunization or treatment was available. In conclusion, he asserted that these improvements in health had resulted more from 'environmental public health', political, economic, and social measures than from specific medical or therapeutic interventions.

Several other analyses (7, 8) have yielded similar conclusions. Box 1 presents a summary of the factors that contributed to early reductions in mortality in Europe and North America. While it is important to question the validity of these retrospective reviews, it is interesting to note the consensus among many authors regarding the importance of social and environmental factors. Beaver (9) noted that in the second half of the 18th century, infant mortality fell in England and Wales when supplies of cheap cow's milk became generally available throughout the year. With regard to smallpox for example, Razzell (10) stressed the huge influence of improved hygiene, including the use of soap and washable cotton clothes in the first 40 years of the 19th century. In France, Preston and van de Walle (11) found that mortality was relatively high in three urban areas, but that after 1850, mortality in these settings declined dramatically as a result of improvements in water supply and sewage disposal. As they noted, medical improvements did not become important until diphtheria immunizations in the 1890s.

Provision of potable water and hygiene promotion, including hand washing hold the key to sustainable reduction in the burden of diarrhea morbidity and mortality in less developed countries. Experience has shown (5) that in less developed countries, there are no short cuts or magic bullets for solving health conditions that are rooted in poor environmental conditions, including lack of access to potable water and basic sanitation.

Dr Sguassero made many valuable observations. Some of the limitations she noted had already been

acknowledged in the review. We agree, as noted in the review, that the intense monitoring which was a key component of the reviewed trials may be difficult to achieve in routine field practice. However, we believe that this is an important finding from our review. Knowing that programs work or do not work is important; but knowing *why* they work or do not work is even more critical in program planning and implementation. Based on this review, we know that effective monitoring is an important element of successful hand washing promotion interventions. Thus, it is important for all programs that promote hand washing to include appropriate monitoring and follow-up procedures in order to maximize impact. This also relates to Dr Sguassero's comments regarding the extrapolation of findings from trials in high income countries to situations in low income countries. The key here again, is to critically examine correlates of successful institution-based hand washing programs in high income countries in order to identify best practices and how they can realistically replicated in settings with the greatest need.

References

1. Victora CG, Bryce J, Fontaine O, *et al.* 2000 Reducing deaths from diarrhea through oral rehydration therapy. *Bull WHO* 2000; **78**: 1246–1255.
2. Snyder JD, Merson MH. The magnitude of the global problem of acute diarrheal disease: a review of active surveillance data. *Bull WHO* 1982; **60**: 605–613.
3. Bern C, Martines J, de Zoysa I, Glass RI. The magnitude of the global problem of diarrheal disease: a ten year update. *Bull WHO* 1992; **70**: 705–714.
4. Kosek M, Bern C, Guerrant R. The global burden of diarrheal disease as estimated from studies published between 1992 and 2000. *Bulletin of the World Health Organization* 2003; **81**(3): 197–204.
5. Ehiri JE, Prowse JM. Child health promotion in developing countries: the case for integration of environmental and social interventions? *Health Policy Plan* 1999; **14**(1): 1–10.
6. McKeown T. *The Role of Medicine: Dream, Mirage, or Nemesis?* Princeton, NJ: Princeton University Press; 1979.
7. Lucas D. *World Population Growth. Beginning Australian Population Studies.* Canberra: The Australian National University; 2003; <http://adsri.anu.edu.au/pubs/BAPS/BAPSChap3.pdf> Cited March 13, 2009.
8. United Nations. *The Determinants and Consequences of Population Trends.* New York: United Nations; 1973.
9. Beaver S. Population, infant mortality and milk. *Popul Studies* 1973; **27**(2): 243–254.
10. Razzell R. An interpretation of the modern rise of population in Europe - critique. *Popul Studies* 1974; **28**(1): 5–17.
11. Preston SH, van de Walle E. Urban French mortality in the nineteenth century. *Popul Studies* 1978; **32**(2): 275–297.
12. Thomlinson R. *Population Dynamics.* New York: Random House; 1976.

Box 1. Causes of mortality decline in the 18th and 19th centuries in Europe, North America, Australia and New Zealand

Improved agriculture: increased food production and better nutrition (e.g. the Agricultural Revolution in England included better fertilizers, crop rotation, and winter crops)

Industrialization: the development of the factory system led to wider availability of manufactured goods. Factory production of machinery (e.g. iron plough, team engine, etc.) also contributed to improved agriculture

Improved transport: facilitated the distribution of food and other goods (e.g. in Europe, railways enabled food supplies to be sent rapidly from rural to urban areas)

Social reforms: various health and social welfare schemes and regulations, including the regulation of child labour in factories

Greater control of temperature and humidity: regulation of temperature and humidity in homes and at work may have contributed to the decline of some diseases

Public sanitation: including improved sewage disposal, water supplies and water purification (e.g. filters that eliminated cholera and typhoid from the water)

Improved personal hygiene: the availability of cheap and easy to wash cotton clothing, potable water supplies and soap facilitated improved personal hygiene

Asepsis and antisepsis: the exclusion and killing of disease-causing organisms was developed by Joseph Lister in the late 19th century (e.g. the sterilization of surgical instruments)

Immunology: e.g. Edward Jenner's inoculation against smallpox and discoveries by Koch and Pasteur that inoculation with a mild form of the disease will prevent a serious case

Biological factors: increased resistance to some diseases, and some diseases becoming more benign (e.g. scarlet fever)

Source: Thomlinson (12)