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Getting the basic rights – the role of water, sanitation and hygiene in maternal and reproductive health: a conceptual framework

Oona M. R. Campbell[1], Lenka Benova[1], Giorgia Gon[1], Kaosar Afsana[2] and Oliver Cumming[3]

1 *Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK*
2 *BRAC, Health, Nutrition and Population and BRAC University, James P Grant School of Public Health, Dhaka, Bangladesh*
3 *Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK*

Abstract

OBJECTIVE To explore linkages between water, sanitation and hygiene (WASH) and maternal and perinatal health via a conceptual approach and a scoping review.

METHODS We developed a conceptual framework iteratively, amalgamating three literature-based lenses. We then searched literature and identified risk factors potentially linked to maternal and perinatal health. We conducted a systematic scoping review for all chemical and biological WASH risk factors identified using text and MeSH terms, limiting results to systematic reviews or meta-analyses. The remaining 10 complex behavioural associations were not reviewed systematically.

RESULTS The main ways poor WASH could lead to adverse outcomes are via two non-exclusive categories: 1. 'In-water' associations: (a) Inorganic contaminants, and (b) 'water-system' related infections, (c) 'water-based' infections, and (d) 'water borne' infections. 2. 'Behaviour' associations: (e) Behaviours leading to water-washed infections, (f) Water-related insect-vector infections, and (g-i) Behaviours leading to non-infectious diseases/conditions. We added a gender inequality and a life course lens to the above framework to identify whether WASH affected health of mothers in particular, and acted beyond the immediate effects. This framework led us to identifying 77 risk mechanisms (67 chemical or biological factors and 10 complex behavioural factors) linking WASH to maternal and perinatal health outcomes.

CONCLUSION WASH affects the risk of adverse maternal and perinatal health outcomes; these exposures are multiple and overlapping and may be distant from the immediate health outcome. Much of the evidence is weak, based on observational studies and anecdotal evidence, with relatively few systematic reviews. New systematic reviews are required to assess the quality of existing evidence more rigorously, and primary research is required to investigate the magnitude of effects of particular WASH exposures on specific maternal and perinatal outcomes. Whilst major gaps exist, the evidence strongly suggests that poor WASH influences maternal and reproductive health outcomes to the extent that it should be considered in global and national strategies.

keywords water, sanitation, hygiene, maternal health, reproductive health, perinatal health, life course

Introduction

As 2015 draws closer, there is much debate at an international level as to what will follow the Millennium Development Goals (MDGs) (Horton 2012). The unfinished MDG agenda has been discussed and a desire to complete work on current MDGs stated (The United Nations 2012). Yet it has also been argued that the sector-specific goals and targets embodied in the MDGs resulted in missed opportunities in terms of potential implementation synergies (Waage *et al.* 2010). Elsewhere, the limited progress on reducing the 'equity gap' under the MDGs has been raised as a major concern (Chopra *et al.* 2012). This article focuses directly on the potential synergies and links between improving maternal, newborn and reproductive health and safe water, sanitation and hygiene (WASH) and proposes a conceptual framework for understanding them.

The MDG7 target for water and sanitation calls for the 'halving of the proportion of the population without

sustainable access to safe drinking water and basic sanitation' by 2015 (United Nations General Assembly 2000). The water target was declared as met in 2010, although 780 million people remain without safe water, whilst the sanitation target is seriously off track and unlikely to be met by 2015, with 2.5 billion people still lacking access (UNICEF, WHO 2012). Coverage of these services is lowest in the poorest regions and countries of the world, and most acute among the poorest populations in these settings (UNICEF, WHO 2011). There was no target for hygiene in MDG7, nor it is consistently measured in global or national WASH monitoring systems.

Assessments of the disease burden associated with poor WASH are dominated by diarrhoeal disease mortality and acute morbidity (Guerrant *et al.* 2002). Whilst diarrhoeal mortality is reducing, it still accounts for 10% of all child deaths (Liu *et al.* 2012) and morbidity has declined only slightly since 1990 (Fischer Walker *et al.* 2012). There is good evidence for the effect of WASH on a range of other health outcomes, including acute respiratory infections (Rabie & Curtis 2006), soil-transmitted helminth infections (Ziegelbauer *et al.* 2012) and diseases associated with chemical contamination of water (Fewtrell *et al.* 2005). Combining multiple health effects, WHO estimates that unsafe WASH is responsible for almost one-tenth of the global disease burden (Prüss-Üstün *et al.* 2008). To date however, we are unaware of any quantification of the effects of poor WASH on maternal and perinatal health.

Under MDG5, target 5a is 'to reduce maternal mortality by three-quarters by 2015' (United Nations General Assembly 2000). Influential frameworks for improving maternal mortality – such as the 'Three Delays' (Thaddeus & Maine 1994) and the 'Continuum of Care' (Partnership for Maternal Newborn & Child Health 2011) models – focus almost exclusively on improving access to, and the quality of, maternal health services, with little focus on the wider social and environmental determinants. This emphasis on health services recurs for the MDG5b targets, which address contraceptive coverage and antenatal care services.

In this study, we explore tentative and confirmed linkages between WASH and maternal and perinatal health using scoping review methods and present a conceptual approach for systematically describing these. Our aim is to provide a broad-ranging conceptualisation that may then be used to guide a process of gathering epidemiologic data on the potential impact of the various risk factors on the ill health of mothers and foetuses/newborns. Although beyond the scope of this study, estimating the contribution of these risk factors to ill health at the population level (population attributable fractions) could then form the basis for identifying and harnessing policy, advocacy and programming synergies that will lead to more effective, efficient and equitable investments in both sectors. We end by identifying research gaps, which, if addressed, would strengthen this framework and lead to greater policy coherence and more effective interventions.

Methods

Miles and Huberman (1994) state that a conceptual framework 'lays out the key factors, constructs or variables, and presumes relationships among them'. Methods for developing frameworks vary, but ours was developed iteratively, using our experiential knowledge (including our technical knowledge and research background) and our literature review that included previous related theory and research, and concepts that had been used to represent similar problems (Novak & Canas 2008). The aim of the framework was to classify and organise the concepts and emphasise connections between them. Our conceptual framework amalgamated three main perspectives: a gender-based lens focusing on health inequalities (Kirschstein 1991), the classification of WASH-related health outcomes (White *et al.* 1972) and the longer-term perspective afforded by a life course approach (Kuh *et al.* 2003; Mishra *et al.* 2010). We applied these perspectives to information extracted from an exploratory literature review that, whilst not systematic, included electronic searches of PubMed and Google Scholar among others, and manual searching of references within key articles. We also searched all the 'mode of transmission' and 'susceptibility' headings in the Control of Communicable Disease Manual, 19th edition (Heymann 2008), to assess whether transmission for each infectious disease was WASH-related and whether women (or pregnant women and their foetuses/newborns) were at particular risk. We ended by further refining the framework in the light of this targeted search. Through these searches, we identified 77 potential factors that we categorised within our framework.

We followed with a more targeted scoping with the objective of providing an overview of the existing evidence linking the identified 77 exposures to reproductive and maternal health outcomes, whilst recognising evidence gaps (Arksey & O'Malley 2005; Levac *et al.* 2010). We systematically searched Medline and Embase databases, combining text and MeSH terms for maternal and newborn health among humans with text and MeSH terms for identified 67 chemical and biological mechanisms of exposure. We limited the results of each search to references containing text or MeSH terms for systematic reviews or meta-analyses. We placed no limitations on the date of publication or the language of manuscript.

All search results were exported to an EndNote database and screened by one co-author (LB or GG). Systematic reviews that considered the association between any aspect of reproductive or maternal health and the presence or prevention of any of the 67 exposures were identified. The remaining ten behavioural exposures are complex phenomena and would require collaboration with experts from fields beyond public health, such as anthropology, economics and sociology to identify target search terms, databases and grey literature. We did not do a systematic scoping review for these exposures as it was beyond our resources. However, we present individual studies and reports linking reproductive and maternal health to these ten exposures. Webtable S1 presents the complete listing of the 77 identified mechanisms and indicates availability of systematic reviews and other evidence based on our searches. Only the mechanisms for which links (systematic or other) with reproductive and maternal health were identified are presented in Webtable S2, along with a brief summary of the findings.

We first present the lens or framework (gender lens, WASH transmission framework and the life course perspective) and then the evidence to support posited effects.

Results

Gender inequalities

Much of the debate in recent decades around the need for epidemiological theory has been in relation to understanding and addressing health inequalities (Krieger & Zierler 1996; Susser & Susser 1996). Our first lens is explicitly gender inequality, although we refer to other inequalities such as poverty or urban/rural divides where they have been described.

Both biology and gendered behaviour contribute to differences in men's and women's health (Kirschstein 1991; Weisman 1997). The National Institutes of Health (NIH) distinguishes women's health as diseases or conditions 'unique to women or some subgroup of women; more prevalent in women; more serious among women or some subgroup of women; for which the risk factors are different for women or some subgroup of women; and for which the interventions are different for women or some subgroup of women' (Kirschstein 1991). As most WASH-related diseases or conditions affect both men and women, we used this definition to highlight those particularly relevant to women in general and to mothers more specifically. If pregnant women were not particularly susceptible, exposed, or affected, but their exposure to WASH-related hazards affected the foetus or newborn, we also highlighted such effects (Kourtis *et al.* 2014).

WASH impacts

Figure 1 summarises the main ways in which water or sanitation or hygiene can plausibly lead to ill health, distress, harmful behaviours or other adverse outcomes, grouped in two main dimensions: (i) 'in water' – microorganisms or chemicals in water and (ii) 'behaviour' – actions or cultural aspects related to WASH, including aspects relating to the location of the water point or sanitation facility. We sought to understand how WASH affects health in general and where women, pregnant women, foetuses or newborns are particularly affected.

The Figure 1 framework builds on the Bradley classification which identified four principal pathways of water-related disease transmission: 'water-based', 'water-borne', 'water-washed' and 'water-related' (White *et al.* 1972). The first two categories are grouped in the 'in-water' dimension, which also incorporates subsequent adaptations (Kistemann 2004) to allow for aerosol transmission (Bartram *et al.* 2007), chemical contaminants (Dar & Khan 2011) and chemicals deliberately added to maintain water systems or as public health measures (Ashbolt 2004). The third and fourth Bradley categories are grouped under our 'behaviour' dimension, combining 'water-washed' and 'water-related' with three more 'behaviour' categories related to the hazards of location, distance and perceptions of availability or stigma. Our categorisation is influenced by Cairncross and Feachem's (1993) observation that most faecal–oral infections can be water-washed and that behaviours linked to scarce water, poor sanitation and hygiene can affect these (Wagner & Lanoix 1958). The location and nature of water supply also affects water-related insect vector transmission. For example, wastewater stabilisation ponds can increase mosquito breeding sites (Cairncross & Feachem 1993; Mukhtar *et al.* 2006). Below, we give evidence for these associations grouped by the two dimensions of 'in water' and 'behaviour' in the order shown in Figure 1. Webtable S1 presents a detailed list of various transmission routes or mechanisms that may potentially affect health or well-being and summarises the availability of evidence of their impact on women, foetuses or newborns (systematic reviews, other evidence or no evidence). We were able to identify evidence of association for 47 of the 77 identified exposure mechanisms and found at least one systematic review for 30 of the 67 mechanisms for which we conducted a search for systematic reviews.

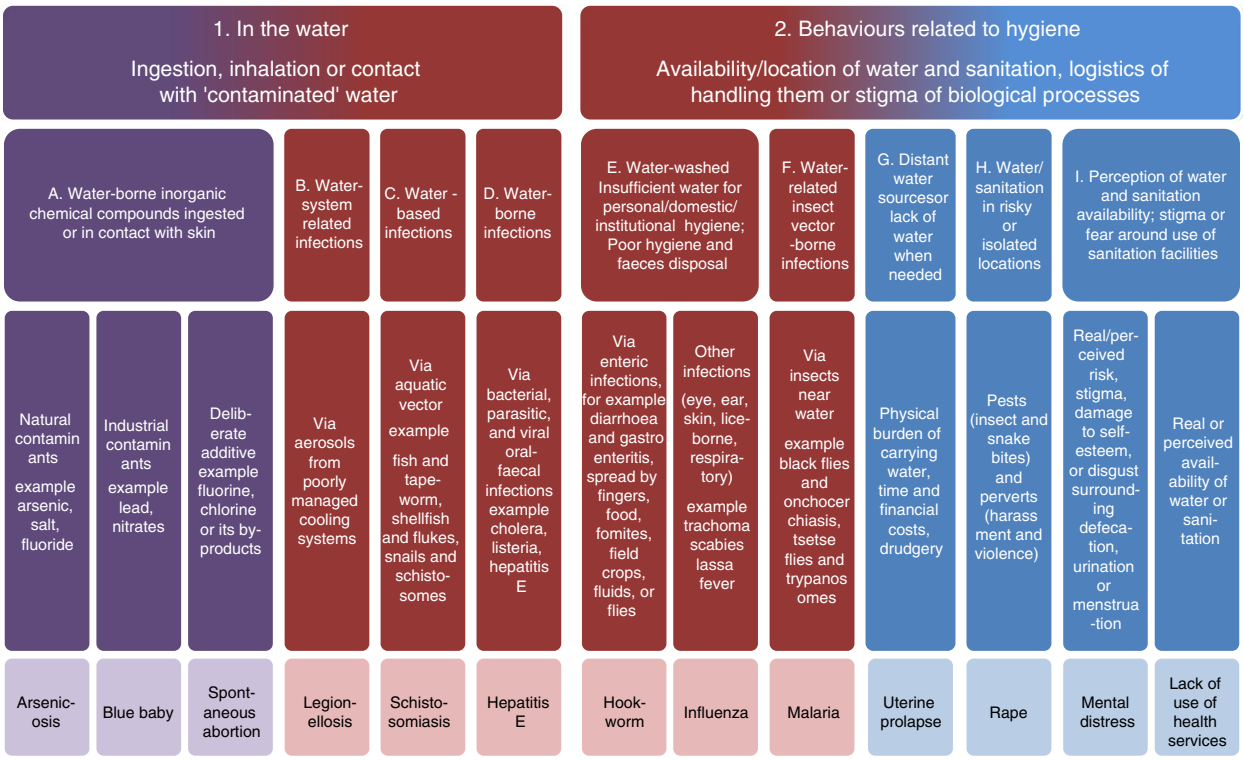

Figure 1 Dimensions, components and examples of health effects in conceptual framework linking water, sanitation and hygiene (WASH) with maternal and reproductive health.

Pathways linked to agents in water

Inorganic contaminants. The 'in-water' associations relate to two main areas: (i) inorganic contaminants and (ii) infectious agents. Many settings have high naturally occurring levels of arsenic and fluoride in groundwater. Studies have linked exposure to arsenic in drinking water with higher risks of spontaneous abortion (Milton *et al.* 2005; Rahman *et al.* 2007), stillbirth (Cherry *et al.* 2008) and infant mortality (Rahman *et al.* 2010), and fluoride has been associated with low birthweight (Diouf *et al.* 2012) and skeletal fluorosis (Bo *et al.* 2003). It has been estimated that in the coastal areas of Bangladesh, increasing saline intrusion during the dry season results in people consuming 2.5–8 times the recommended salt intake, potentially leading to hypertensive disorders of pregnancy (HDP) (Khan *et al.* 2011).

Industrial contaminants, particularly metals, in drinking water raise concerns for pregnant women, with a systematic review showing adverse effects of metal exposure on placental function and foetal development (Caserta *et al.* 2013), as well as neurodevelopment and other effects in children (Pocock *et al.* 1994; Ferris *et al.* 2008). Exposure to mercury, potassium or lead, for example, is associated with spontaneous abortion (Aschengrau *et al.* 1989) and congenital malformations (Vahter *et al.* 2002; Bellinger 2005). Lead is nephrotoxic and can progressively lead to renal failure, gout and hypertension, all risk factors for HDP (Nolan & Shaikh 1992; Ekong *et al.* 2006). Prenatal exposure resulting in maternal blood lead levels of >10 μg/dl can adversely affect fertility, hypertension, infant neurodevelopment and foetal growth (Bellinger 2005).

Systematic reviews of exposure to agricultural pesticides and herbicides – that may be consumed via contaminated surface or groundwater – have shown that whilst there is inconclusive evidence for an association between residential proximity to agricultural pesticides and adverse pregnancy outcomes (Shirangi *et al.* 2011), systematic reviews of parental exposure to specific pesticides show these to be associated with specific cancers and other adverse outcomes among children (Lopez Duenas *et al.* 2012; Nicolle-Mir 2012). Some studies have shown that pregnant women and their foetuses are particularly susceptible to effects of nitrates (Calderon 2000), including spontaneous abortions, intrauterine growth

restriction, congenital malformations and methaemoglobinaemia (blue baby syndrome), although a systematic review suggests these links are inconclusive (Manassaram *et al.* 2006). Endocrine-disrupting compounds mimic and/or block effects of endogenous hormones and have been associated with earlier age at menarche in a systematic review (Yermachenko & Dvornyk 2013). Early age at menarche is associated with earlier age at first sex, and earlier pregnancy, which in turn, is associated with worse pregnancy outcomes. Endocrine disrupters have also been linked to altered ovarian function, impaired fertility and changed placental function (Balabanič *et al.* 2011; Buttke *et al.* 2012; Fowler *et al.* 2012) and to a higher risk of spontaneous abortions and low birthweight (Calderon 2000; Balabanič *et al.* 2011), although systematic review results of these are inconclusive (Peters *et al.* 2010; Caserta *et al.* 2011). It is generally agreed that disinfection by-products may potentially cause spontaneous abortions (Waller *et al.* 1998), stillbirths (King *et al.* 2000), birth defects (Cedergren *et al.* 2002) and small-for-gestational-age infants (Grellier *et al.* 2010). Some of these associations are supported by systematic reviews.

Water-system-related infections. The second subgroup within the 'in-water' dimension concerns infectious agents in the water, grouped in the additional 'water-systems' category and Bradley's 'water-based' and 'water-borne' categories (Categories C and D in Figure 1). Whilst water systems can spread infection via poorly maintained air-cooling systems and cause Legionnaires' disease, this is uncommon and affects the general population without posing particular risks to women (Heymann 2008), so are not considered here, although the category is included in Figure 1 for completeness.

Water-based infections. Water-based infections are transmitted via aquatic vectors, such as snails, fish or crustaceans, in which part of the life cycle of the infective agent occurs. Schistosomiasis is notable from a maternal/reproductive health perspective as genital schistosomiasis is associated with cervical cancer (Feldmeier *et al.* 1995; Moubayed *et al.* 1995), ectopic pregnancy and infertility (Swai *et al.* 2006); and in pregnant women, it is associated with anaemia (Abdelgadir *et al.* 2012), undernutrition (King *et al.* 2005) and inflammation (Kurtis *et al.* 2011). It can also affect foetal immune response (Seydel *et al.* 2012), leading to foetal inflammation (Kurtis *et al.* 2011) and low birthweight (Siegrist & Siegrist-Obimpeh 1992; Qunhua *et al.* 2000). However, there are no systematic reviews. Other water-based infections, such as dracunculiasis (guinea worm) or diphyllobothriasis (tapeworm), are not known to pose specific risks to women, although pregnant or lactating women may be excluded from treatments if drugs had not been tested in pregnant women and are thus contraindicated (Gyapong *et al.* 2003). Exclusion from treatment because of pregnancy or breastfeeding applies also to other WASH-related diseases and conditions (Maduka *et al.* 2004).

Water-borne infections. Water-borne infections are directly transmitted by micro-organisms in water, the classic example being cholera. Here, we consider those that differentially affect women, such as Hepatitis E, with higher incidence, greater severity of symptoms and elevated mortality rates among pregnant women (Emerson & Purcell 2004; Heymann 2008; Aggarwal & Naik 2009). It is also associated with a greater risk of stillbirth (Rein *et al.* 2012).

Pathways linked to behaviour

Most water-borne infections are faecal–oral and overlap with the water-washed category and so are captured in the second dimension of 'behaviour'. This dimension concerns the health effects posed by behaviour relating to WASH. Cairncross and Feachem's redefinition of the water-washed category included infections spread by behaviours stemming from a lack of water or from poor hygiene, including personal and domestic hygiene, and hygiene in the public domain such as in educational establishments and workplaces, including health facilities (Cairncross *et al.* 1996).

Water-washed infections. There are many examples of water-washed infections. Evidence in this area can be dated at least as far back as the elegant work of Gordon (1795) and Semmelweis (1983) demonstrating the association between puerperal sepsis and poor hygiene of birth attendants, a theory later strengthened by the discovery that the causal agent was Streptococcus A, a water-washed infection. Sepsis in pregnancy or the puerperium is mainly caused by unhygienic practices and poor infection control, including lack of hand-washing, unclean surfaces and unhygienic vaginal examination or cord-cutting in health facilities or in the home (Ali *et al.* 2006; Darmstadt *et al.* 2009). Tetanus is another important contributor to mortality of mothers and newborns, and tetanus toxoid vaccination among pregnant women reduces neonatal death and morbidity (Fauveau *et al.* 1993; Demicheli *et al.* 2005; Roper *et al.* 2007; Kourtis *et al.* 2014). Staphylococcus can be another common cause of puerperal or newborn infection (Heymann 2008).

Some intestinal worm infections can also be classified as water-washed. An estimated 6.9 million pregnant women in sub-Saharan Africa are infected with hookworm, and systematic reviews show they are at risk of hookworm-related anaemia (Brooker *et al.* 2008). Hookworm infestation in pregnancy is associated with decreased infant birthweight and intrauterine growth retardation (Christian *et al.* 2004), and a systematic review indicated that maternal antihelminthic treatment reduced stillbirths (Menezes *et al.* 2009). Systematic reviews of ascariasis and trichuriasis showed them to be associated with maternal anaemia (Noronha *et al.* 2012) and with stunting and cognitive deficits, respectively (Ruma *et al.* 2008). Helminth infections are also associated with increased susceptibility to HIV/AIDS, malaria and tuberculosis (Fincham *et al.* 2003; Le Hesran *et al.* 2004; Elias *et al.* 2007).

Systematic reviews indicated that the most common non-malaria bloodstream infection among pregnant women admitted to hospital in reviews of studies from both Africa (Reddy *et al.* 2010) and Asia (Deen *et al.* 2012) is *Salmonella enterica*, to which pregnant women have greater susceptibility (Smith 1999). *Salmonella* can result in spontaneous abortion (Smith 1999). Listeria, another water-borne/water-washed infection, has an annual infection rate over 17 times higher among pregnant women (Southwick & Purich 1996), who account for 27% of all listerial infections (Janakiraman 2008). Exposure in pregnancy is associated with spontaneous abortion (Heymann 2008), stillbirth and preterm delivery (Goldenberg & Thompson 2003). The latter association is confirmed in systematic reviews (Lamont *et al.* 2011; Semedo Leite *et al.* 2012). A systematic review of neonatal melioidosis suggested that vertical transmission exists (Thatrimontrichai & Maneenil 2012), whilst a systematic review of Yersinia infection showed it to be associated with adverse pregnancy outcomes (Semedo Leite *et al.* 2012). The only study found by a systematic review of antenatal genital tract screening and treatment for lower genital tract infection (GTI) showed a reduced risk of preterm birth and preterm low birthweight (Xiong *et al.* 2006). Pregnant women face increased susceptibility to influenza, with increased severity of illness (Jamieson *et al.* 2006). A systematic review showed higher rates of hospitalisation, ICU admission and death among pregnant women during the 2009 A(H1N1) flu pandemic (Mosby *et al.* 2011).

Water-related insect vector-borne infections. Numerous water-related insect vector infections are transmitted via mosquitoes (malaria, dengue, lymphatic filariasis and yellow fever), tsetse flies (trypanosomiasis) and black flies (onchocerciasis) that live or bite near water. Some of these, namely malaria and dengue, pose specific risks related to women. Pregnant and post-partum women, particularly primi- and secundi-gravidae, are more susceptible to malaria (Boel *et al.* 2012; Chico *et al.* 2012), whereas more subclinical presentation obscures detection and treatment (Desai *et al.* 2007). Malaria in pregnant women is associated with an increased risk of anaemia and severe anaemia (Shulman *et al.* 2002). An estimated 0.5–23.0% of maternal deaths in high transmission areas and 0.6–12.5% in low transmission areas are caused by malaria (Brabin & Verhoeff 2002). Infection with malaria also increases risk of spontaneous abortion (McGready *et al.* 2012), stillbirth (Goldenberg & Thompson 2003) and intrauterine growth retardation (Steketee *et al.* 2001) and leads to anaemia in newborns (van Eijk *et al.* 2002). Systematic reviews of malaria prevention show significant reductions in severe maternal anaemia, low birthweight, perinatal mortality (Desai *et al.* 2007) and stillbirth (Menezes *et al.* 2009; Barros *et al.* 2010; Ishaque *et al.* 2011). Mosquitoes that transmit dengue breed in water-storage containers. General symptoms include internal bleeding, shock and death, but in pregnant women, dengue has been associated with higher maternal mortality (Mota *et al.* 2012) and spontaneous abortion (Tan *et al.* 2012). A systematic review showed conclusive evidence of dengue vertical transmission but inconclusive evidence on adverse pregnancy outcomes (Pouliot *et al.* 2010). Another systematic review showed evidence of vertical transmission of trypanosomiasis, although the absolute risk is unknown (Lindner & Priotto 2010).

Distant water sources or lack of water when needed. The 'behaviour' dimension also includes WASH-related behaviours that lead to non-infectious diseases or conditions. These include physical aspects of carrying heavy water loads or disposing of faeces, time or money spent on these activities, risks associated with the location of water or sanitation points, and behaviours related to the actual or perceived availability of WASH or to the real or perceived risk of stigma/disgust around the biological processes of defecation, urination or menstruation.

Data from households in 45 countries show two-thirds of drinking water is collected by women (UNICEF, WHO 2011). Carrying heavy loads is associated with spinal compression, injuries to the spinal column and increased risks of degenerative rheumatism (Dufaut 1988). It can also cause hernia and genital prolapse (Jorgensen *et al.* 1994) and may increase the risk of spontaneous abortion (Florack *et al.* 1993; Figà-Talamanca

2006). Sub-Saharan African studies estimated that an average of 10% of the carrier's daily calorie intake was spent carrying water (Rosen & Vincent 1999). Handling child faeces and socialising children into using sanitation facilities can also expose individuals to risk; women and girls are much more likely to perform these roles (Hannan & Andersson 2002; Gil *et al.* 2004).

The financial and opportunity costs of obtaining and treating water, doing laundry, managing menstruation and treating WASH-related illnesses can consume a significant share of poor families' resources. In Africa, it is estimated that water collection accounts for 40 billion hours a year, and the potential reduction in time-lost, poverty and drudgery through better access to water is substantial (Bardasi & Wodon 2006; Lawson 2007). In Pakistan, greater distances from water sources led to reduced participation in income-generating activities for women (Ilahi & Grimard 2000). Households often pay unofficial suppliers of water (often of substandard quality) (Semba *et al.* 2009), and prices charged are typically >10 times the formal water supply tariff (Cairncross & Kinnear 1992). Studies show that reduction in time spent on water-related chores translates into improved school attendance among girls (Koolwal & van de Walle 2010; Nauges & Strand 2011).

Water and sanitation in isolated locations. Distant locations of water and sanitation pose other risks, such as snakebites associated with open defecation in fields (Singh *et al.* 2008), and it is known that flies, mosquitoes and cockroaches are common in humid and dark latrines, posing a nuisance, and an occasional risk of harm to health (Curtis & Minjas 1985). Because women take longer to use sanitation points and pregnant women urinate more frequently, they may be exposed to these risks for longer. Other dangers are men taking advantage of the isolated location of latrines to harass, or sexually assault women (Cairncross 2003) – rape and violence against women on the way to or from public toilets and open defecation sites have been widely reported (Amnesty International 2010; Lennon 2011; Massey 2011).

Perception of water and sanitation availability. The actual or perceived absence of WASH can lead individuals to adopt harmful behaviours, such as reductions in water use and food consumption (Cairncross & Cliff 1987; Gadgil 1998) and substitution with alcohol (Mamman *et al.* 2002; Potukuchi & Rao 2010). Optimal hydration is necessary for health and cognitive functioning; fluid restriction and inadequate personal hygiene may lead to GTI or urinary tract infections (UTI) (Bledsoe *et al.* 1994; Nygaard & Linder 1997; Amiri *et al.* 2009), which in turn are associated with preterm birth, low birthweight, pre-eclampsia and anaemia (Lettieri *et al.* 1993; Schieve *et al.* 1994; Conde-Agudelo *et al.* 2008; Mazor-Dray *et al.* 2009; Minassian *et al.* 2013).

Defecation, menstruation and urination can be associated with stigma and consequently damage self-esteem. These biological processes are considered private, if not shameful, in most societies, and a lack of WASH facilities may result in individuals experiencing fear and significant psychological distress. Inadequate toilet provision, especially in low-income urban areas, leads to women's concerns that they cannot maintain their self-respect and social reputation, poses physical safety risks to themselves and their children, increases financial costs and leads to social stigma for living without adequate services (Amnesty International 2010). Women report feeling pressure to use sanitation facilities only at certain times (Massey 2011). The principal benefits from completed water supply projects were identified as less tension/conflict, improved self-esteem, women's empowerment, women's hygiene (e.g. menstrual), improved school attendance and teachers accepting village postings (Cairncross & Valdmanis 2006).

Menstrual hygiene and hygiene after delivery to manage lochia require water and clean, private toilets and either reusing cloths that have been adequately cleaned and dried, menstrual cups or using single-use pads. Women feel a strong pressure to hide signs of menstruation and resort to reuse of unhygienic moist menstrual rags. Studies link poor menstrual hygiene to urinary or reproductive tract infections and other illnesses (Wasserheit *et al.* 1989; Younis *et al.* 1993), including toxic shock (Heymann 2008), subsequent pelvis inflammatory disease, infertility and pelvic pain (Ahmed & Yesmin 2008).

Lastly, the availability of WASH is also important in making education establishments and health facilities acceptable to both employees and users. Improvements in water supply were associated with increased uptake of teaching posts in Ghana (Adugna *et al.* 2001). Many have posited that a lack of sanitation and hygiene contribute to truancy, failing classes, absenteeism and drop out, particularly in the transition from primary to secondary schools (Fakeye & Adegoke 1994; Abioye-Kuteyi 2000; Jones & Finlay 2001), although a systematic review of the evidence on the benefits of same-sex toilets in schools for retention of adolescent girls is inconclusive (Birdthistle *et al.* 2011). Healthcare providers ranked lack of water and sanitation points as important reasons for refusing to accept rural postings (Henderson & Tulloch 2008).

Gender inequalities

The final lens, that of the life course, examines impacts at these different time points, seeking to understand how effects at one age impact across the lifespan, including via intergenerational influences on foetal development and growth (Ben-Shlomo & Kuh 2002). Adopting the life course approach and adding it to the modified WASH framework and to the lens of gender inequality helps identify whether WASH impacts health beyond its immediate effects and presents longer-term consequences, perhaps at a later life stage or intergenerationally.

In its simplest form, life course theory allows for an effect at one age to act at a later age. For example, infection with *Escherichia coli* has been associated with pregnancy-related hypertension 5 years after infection (Moist *et al.* 2009). Many WASH-related hazards have intergenerational effects; either because contaminants or infectious agents pass through the placenta and affect the foetus, or because they have systemic effects on the mother, such as fever, an altered immune response including inflammation, low weight gain, absorption into bone or anaemia. The consequences for the foetus include spontaneous abortion and stillbirth, but also malformations, infections, anaemia, preterm birth or low birthweight in the newborn. For example, hookworm infection in young women may lead to anaemia, including in pregnancy, which is associated with low birthweight. Low birthweight in turn is associated with cognitive impairment, learning disability and behavioural problems among children; poor anthropometric status in childhood; higher risk of delivering a low birthweight baby in reproductive age; higher arterial blood pressure, chronic kidney disease, ischaemic cardiomyopathy, stroke, diabetes and respiratory disease in adulthood (Rich-Edwards *et al.* 1997; Barker *et al.* 2002; Whincup *et al.* 2008).

Many risks resulting from disadvantage or poor WASH accumulate. Gender discrimination against girls and women, in terms of access to food, care, education and work, begins in infancy and can determine later life outcomes. Chronic and recurring hookworm infection throughout childbearing age, when women are menstruating, can have a chronic effect on women's iron levels, with iron-deficiency anaemia being especially common in adolescent girls and women of childbearing age (Brooker *et al.* 2008). Hookworm and schistosoma infections are associated with increased incidence of malaria (Adegnika & Kremsner 2012), and malaria itself can also cause severe anaemia. WASH-related pathogens (especially those causing diarrhoea) lead to reduced food intake and the malabsorption of nutrients causing undernutrition, which makes repeat infections more likely (Brown 2003), by increasing the susceptibility to diarrhoea and severity of diarrhoeal episodes (Lima *et al.* 2000; Checkley *et al.* 2008).

The critical window within the life course approach is illustrated by the 0–2-year age group. Repeated infection with excreta-related pathogens, including worms, in early life leads to growth faltering and stunting (Guerrant *et al.* 2012). Stunted children have little opportunity to catch up later and grow to be short adults. Short women face an increased risk of cephalo-pelvic disproportion, obstructed labour and death and are more likely to have a Caesarean section and low birthweight infant (Song *et al.* 2009; Tsvieli *et al.* 2012). Repeated Caesarean section increases the likelihood of ruptured uterus and placenta praevia, both of which are risk factors for death (Rossi & D'Addario 2008; Main *et al.* 2012).

Discussion

The conceptual approach taken here brings together three requisite components for understanding the potential linkages between WASH and maternal and perinatal health: gendered health effects, WASH-related disease transmission and the longer-run life course risks. The framework suggests that WASH affects the risk of adverse maternal health outcomes but that these exposures are multiple and overlapping and may be distant from the immediate health outcome. Our conceptual framework reflects this by taking a life course approach, allowing for risk accumulation and intergenerational effects combined with an equity or gender lens, then linked to the more traditional classification of diseases by transmission.

Much of the evidence underpinning this framework is surprisingly weak, based on biological plausibility, observational studies and in some cases anecdotal or circumstantial evidence. We found relatively few systematic reviews addressing these topics. For example, despite numerous advocacy claims, the evidence that lack of school sanitation leads girls to dropout or that poor menstrual hygiene causes reproductive tract infections is almost non-existent. However, where direct evidence exists, it confirms the view that adequate WASH may confer substantial benefits to maternal health. Further strengthening of this evidence base is critical and the conceptual framework presented here offers a basis for identifying major research gaps. In particular, systematic reviews are required to more rigorously assess the current quality of evidence for the various exposure/outcome relationships included. Primary research is required to investigate the nature and magnitude of effects for particular WASH exposures (such as improved hygiene practice

in birth settings, sustained and heavy water collection and unsanitary menstrual cloths) on specific maternal and reproductive as well as neonatal and child health outcomes.

Additional work is also required to quantify the population-level impact (population attributable fraction) in relation to maternal and reproductive health outcomes across different settings to assess where WASH may have greater or lesser importance. Finally, in the light of the recent publication of the Global Burden of Disease 2010 estimates (Murray *et al.* 2012), risk factor analyses for WASH may need to be expanded for the outcomes, such as and maternal morbidity, not currently included in these reference models which tend to focus primarily on childhood diseases (Ezzati *et al.* 2005). Once these WASH and maternal and reproductive health relationships are quantified, the scope needs to be widened to include these elements in the disease burden and take account of the complex ways in which factors interact and produce a range of direct and indirect risks (Watts & Cairncross 2012).

Whilst major gaps exist, the evidence is strongly suggestive of poor WASH influencing maternal and perinatal health outcomes to the extent that it should be considered in global strategies and national policy (Benova *et al.* 2014a; Gon *et al.* 2014). Current evidence precludes reliable estimates of the magnitude and potential of any impact, so that the degree of priority against other critical interventions or services – for example births with skilled attendance, emergency obstetric care, female education – is not clear. However, improved WASH is a human right, and a health and development priority in its own right, irrespective of its role in improving maternal and reproductive health. As a cost-effective and proven public health intervention, WASH services should be scaled up as a matter of urgency and the evidence for links to maternal and reproductive health only reinforces this case (Bartram & Cairncross 2010).

More pertinent here is whether either sector – maternal and reproductive health or WASH – should adjust its approach to harness the potential synergies suggested by the framework. In this area, we feel justified in suggesting options for consideration and discussion by governments, technical experts and civil society. To simplify these recommendations, we consider two domains: home births and facility births. In the case of domestic births, which account for 54% of births in sub-Saharan Africa (UNICEF 2012), joint planning in providing and targeting services would enable better coordination of resources towards reaching those most at risk. Within a broader strategy to have all births taking place in adequately equipped facilities, improving the environmental conditions for pregnancy, delivery and neonatal care for populations with poor access to health facilities is critical, even if this is an interim measure as part of longer-term strategy. Targeting these high-risk populations for improved WASH should also generate other gains for women and girls, via avoidance of all the other potential WASH-related harms. Sufficient routine surveillance and household survey data are available in almost all countries to characterise WASH-related risk of domestic births but this evidence is not jointly owned, used or tracked by the two sectors. Bringing existing data together and creating incentives for coordination will help target efforts towards the areas of greatest need, thereby addressing disparities or inequities (Benova *et al.* 2014b).

The second domain of WASH in facility birth settings is critical but less well documented. Data, such as the Service Provision Assessment surveys (SPA), World Health Organization Service Availability and Readiness Assessments (SARA) and Averting Maternal Death and Disability EmONC Needs Assessments, are collected in many settings – albeit with variable quality – but are under-utilised by the WASH sector. Although the most recent WHO Global Annual Assessment of Sanitation and Drinking Water (GLAAS) exercise included questions for governments on access to WASH in health facilities, few responded and the findings were not cross-validated with other available survey data (World Health Organization 2012). The Joint Monitoring Programme of the UN which tracks progress on the MDG water and sanitation target does not report data for WASH in health facilities because the MDG target did not include healthcare facilities and because such data are not routinely captured in the surveys and censuses that it uses to develop its reports (UNICEF, WHO 2012). Better collection and use of this data by the WASH sector, incentivised with national and global targets, may enhance efforts to improve WASH in facility birth settings (Velleman *et al.* 2014).

Conclusion

There is a body of evidence, supported by biological plausibility, that poor WASH negatively influences maternal and reproductive health outcomes, and foetal and neonatal outcomes, in a multitude of ways. This study presents a framework that builds on and combines existing approaches to identify gender inequalities in health, to classify WASH-related diseases and to delineate a life course approach. We identified a number of systematic reviews reporting associations between WASH and these outcomes that confirm that these

linkages are complex and long term, but nonetheless important. Within the conceptual framework presented here, we also elucidate that there are many gaps requiring both primary research to investigate specific exposure–outcome relationships, and additional systematic reviews of existing evidence. Whilst more evidence is needed, this work suggests there is sufficient evidence for greater consideration of WASH in closing the gap on maternal and perinatal health.

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Supporting Information

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

Webtable S1. Overview of identified mechanisms linking reproductive and maternal health to WASH exposures and types of evidence identified.

Webtable S2. WASH mechanisms linked with reproductive and maternal health for which we identified systematic or other evidence.

Corresponding Author Oona M. R. Campbell, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. Tel.: +44 (0)20 7927 2210; E-mail: Oona.Campbell@lshtm.ac.uk

Webtable 1. Overview of identified mechanisms linking reproductive and maternal health to WASH exposures and types of evidence identified

#	Mechanism	Agent(s)	Evidence from systematic reviews		Other evidence		No evidence
			Reproductive and Maternal	*Foetus and Neonate*	*Reproductive and Maternal*	*Foetus and Neonate*	
	A. Water-borne chemical compounds: Chemical elements/compounds contaminate water and are ingested or contact skin						
	1. Natural contaminants						
1	Arsenicosis	Arsenic					
2	Fluorosis	Fluoride					
3	Salinity	Salt (NaCl)					
4	Water hardness	Calcium and magnesium levels					
	2. Industrial, agricultural and human-produced contaminants						
5	Metal poisoning	Aluminium, lead, manganese, mercury, potassium, silver, thallium, zinc, etc.					
6	Other inorganic compounds	Asbestos, cyanide, selenium, sulphate					
7	Nitrate/nitrite poisoning	Fertiliser and human waste					
8	Pesticides and herbicides	Agricultural runoff					
9	Pharmaceuticals and personal care products	Anthropogenic chemical contaminants in freshwaters and wastewaters					
	3. Deliberate additives (substances added to water for public health purposes and their by-products)						
10	Disinfectants and disinfection by-products	Chloroform, bromoform, bromodichloromethane and chlorodibromomethane					
	B. Water-systems related: Poorly managed water-systems spread contaminated aerosols (air conditioning systems)						
11	Legionellosis	Legionellae bacilli					
	C. Water-based: Life-cycle of infective agent requires an aquatic vector and infection is transmitted through dermal contact with or ingestion of contaminated water						
	1. Crustaceans						
12	Dracunculiasis	Dracunculus medinensis - guinea worm					
	2. Fish						
13	Diphyllobothriasis	Diphyllobothrium - tapeworm					
	3. Shellfish						
14	Flukes	Clonorchiasis, Opisthorchis viverrini					
	4. Snails						
15	Schistosomiasis	Schistosoma mansoni and others					
16	Fasciopsiasis	Fasciolopsis buski					
	D. Water-borne infections: Water is passive vehicle for infective agent. Transmission by consuming contaminated water or by faecal-oral route						
	1. Bacterial infections						
17	Salmonellosis	Salmonella enterica					
18	Listeriosis	Listeria monocytogenes					
19	Typhoid fever	Salmonella typhi					
20	Campylobacter enteritis	Campylobacter jejuni					
21	Cholera	Vibrio cholera					
22	Melioidosis	Burkholderia pseudomallei					
23	Acute (bloody) diarrhoea	Escherichia coli					
24	Shigellosis	Shigella					
25	Yersiniosis	Yersinia					
	2.Viral infections						
26	Hepatitis E	Hepatitis E virus					
27	Hepatitis A	Hepatitis A virus					
28	Gastroenteritis	Rotavirus					
29	Gastroenteropathy	Norwalk-like viruses					
30	Poliomyelitis	Poliovirus					
31	Myalgia	Group B coxsackie viruses					

	3. Parasitic infections						
32	Hookworm disease	Ancylostoma duodenale, A. Ceylanicum and others					
33	Toxoplasmosis	Toxoplasma gondii					
34	Amebiasis	Entamoeba histolytica					
35	Ascariasis	Ascaris lumbricoides, roundworm					
36	Cryptosporidiosis	Cryptosporidium hominis, C.parvum, other intestinal protozoa					
37	Giardiasis	Giardia lamblia					
38	Hymenolepiasis	Hymenolepis nana, dwarf tapeworm					
39	Naegleriasis, Acanthamebiasis and Balamuthiasis	Naegleria fowleri, Acanthameba, Balamuthia mandrillaris					
40	Trichuriasis	Trichuris trichuria, whipworm					
	4. Fungal infections						
41	Candidiasis	Candida species					
	5. Chemical contaminants produced by living organisms						
42	Cyanotoxins	Cyanobacteria, bluegreen algae					
	E. Water-washed (also water-scarce): Insufficient quantities of water for personal or domestic hygiene or institutional/occupational hygiene leads to infections						
	1. Wound infections						
43	Tetanus	Clostridium tetani					
	2. Enteric infections causing diarrhoea and dysentery						
44	Enterobiasis	Enterobius vermicularis, pinworm					
45	Gastritis	Helicobacter pylori					
	3. Respiratory infections						
46	Influenza	Influenza viruses					
	4. Skin infections						
47	Boils	Staphylococcus aureus					
48	Scabies	Sarcoptes scabiei					
49	Cellulitis	Streptococcus					
50	Leprosy	Mycobacterium leprae					
	5. Eye and Ear infections						
51	Otitis	Streptococcus pneumonia					
52	Conjunctivitis	Haemophilus influenzae, Streptococcus pneumoniae and others					
53	Trachoma	Chlamydia trachomatis					
	6. Lice- and Flea-borne Infections						
54	Typhus fever	Rickettsia prowazekii, Rickettsia typhi					
55	Plague	Yersinia pestis					
56	Relapsing fever	Borrelia recurrentis					
	7. Nosocomial infections						
57	Puerperal sepsis	Staphylococcus aureus and Streptococcus spp					
	8. Rodent transmitted infections						
58	Lassa fever	Lassa virus					
59	Hantaviral diseases	Hantaviruses					
60	Lymphocytic choriomeningitis	Lymphocytic choriomengitis virus					
	F. Water-related (vector borne): Insects that breed in water or bite near it spread infections						
	1. Mosquitoes						
61	Malaria	Plasmodium falciparum, P.vivax, P. ovale and P.malariae					
62	Dengue fever	Dengue virus					
63	Filariasis (lymphatic)	Wuchereria bancrofti, Brugia malayi, B. Timori					
64	Yellow fever	Yellow fever virus					
65	Mosquito borne viral encephalitides	Japanese encephalitis virus and others					
	2. Tsetse flies						
66	Trypanosomiasis	Trypanosoma brucei					
	3. Black flies						
67	Onchocerchiasis	Onchocerca volvulus					
	G. Distant water sources or lack of water when needed						

	1. Physical burden					
68	Carrying heavy loads of water	n/a	n/a			
69	Exposure to faeces during disposal	n/a	n/a			
	2. Costs					
70	Opportunity costs	n/a	n/a			
71	Financial costs	n/a	n/a			
	H. Water/sanitation in risky or isolated locations					
	1. Natural risks associated with isolated water and sanitation facilities					
72	Insects/pests	n/a	n/a			
73	Risk of drowning	n/a	n/a			
	2. Social risks associated with remote and isolated water and sanitation facilities					
74	Harassment, bullying and rape	n/a	n/a			
	I. Perception of water and sanitation availability and consequent behaviours					
	1. Behaviours due to real or perceived risk, stigma, damage to self-esteem, or disgust surrounding biological processes of defecation, urination and/or menstruation					
75	Fear, social isolation and mental distress	n/a	n/a			
	2. Behaviours due to real or perceived availability of WASH					
76	Reduction in water use, substitution in drinking, prolonged periods without urination and defecation	n/a	n/a			
77	Reduced use of health and educational institutions	n/a	n/a			

Shading indicates availability of evidence, which is further presented in Webtable 2. n/a – not applicable, searches for systematic reviews not conducted for domains G, H and I.

Webtable 2. WASH mechanisms linked with reproductive and maternal health for which systematic or other evidence was identified

Mechanisms linked to WASH	Effects on health in adults; particularly women in reproductive age	Effects on the foetus, neonate and child
A. Water-borne chemical compounds: Chemical elements/compounds contaminate water and are ingested or contact skin		
1. Natural contaminants		
Arsenicosis	**Other:** Arsenic exposure was found to be associated with cancer,[1-4] metabolic disease,[5,6] cerebrovascular illness[7-9] as well as with long-term memory loss,[10] anaemia,[11] and morbidity and mortality in the general population.[12-15] Women may metabolize arsenic more efficiently than men,[16] but were more sensitive to certain arsenic-related toxic effects.[17] Increased age at menarche was found among girls exposed to arsenic in drinking water.[18,19] Exposure to arsenic may be associated with anaemia during pregnancy[20,21] and increased systolic blood pressure during the postpartum period.[22] Arsenic can pass the placenta.[23-25]	**Systematic:** Prenatal exposure to arsenic was associated with mental retardation in children.[26] Among children aged 5-15 years, an increase of arsenic levels in urine was associated with a decrease in IQ.[27] Arsenic may be associated with paediatric hepatic malignancies,[28] another review found no conclusive evidence to support the broader association between childhood cancers and arsenic exposure based on six studies.[29] No consistent evidence was found for an association between individual chemical exposures and preterm birth.[30] **Other:** Arsenic exposure may be associated with spontaneous abortion,[31,32] congenital malformations,[33] stillbirth,[34] preterm birth,[10] low birth weight,[10,35] and increased infant mortality[32,36,37] (most likely due to prenatal exposure, because arsenic levels in breast milk tend to be low).[25] Later life effects of gestational and early-life exposure to arsenic appear to be associated with an increase in liver cancer, lung cancer, and bronchiectasis mortality in adulthood.[38] Epigenetic effects may occur even at low exposure levels and impact long-term foetal programming.[25]
Fluorosis	**Other:** Fluoride toxicity appears to be associated with skeletal fluorosis,[39-41] thyroid changes, growth retardation, kidney changes and urolithiasis;[42] neurological effects (radiculopathy, myelopathy);[43] cardiovascular disease;[44] and poor nutritional status.[45] An interaction between fluorosis and arsenicosis may exist.[46]	**Systematic:** Based on 27 studies, a systematic review found that children in high-fluoride areas had lower IQ scores than those who lived in low-fluoride areas.[47] **Other:** Fluoride is detected in foetus[48] and may be associated with low birth weight.[49] Infants and children were particularly susceptible to toxic effects of fluoride on liver and kidney function[50] and skeletal fluorosis.[41] Dental fluorosis only occurs with exposure to fluoride when enamel is developing, is irreversible,[51] and has been associated with lower IQ in children.[52]
Salinity	**Other:** Exposure to salinity in drinking water may be associated with pre-eclampsia, eclampsia, and hypertension in pregnancy.[53,54]	
Water hardness	**Systematic:** Three systematic reviews assessing the effect of water hardness on chronic degenerative diseases have been identified, but full text versions were not available at the time of writing.[55-57]	**Other:** Exposure to water hardness may be associated with spontaneous abortion.[58]
2. Industrial, agricultural and human-produced contaminants		
Metal poisoning	**Systematic:** Exposure to metals can adversely affect placental functions and foetal development.[26] **Other:** Exposure to aluminium may be associated with Alzheimer's disease.[59]	**Systematic:** *Metals:* A review of environmental risk factors for paediatric hepatic malignancies found they were associated with metals.[28] A systematic review found no consistent evidence for the association between metals and metalloids exposures and preterm birth.[30] *Lead:* Meta-analysis of 5 prospective studies found strong evidence of a negative association between blood lead levels and IQ in children below 2 years.[60] Exposure to lead appeared to be associated negatively with general brain development. [61,62] Foetal and postnatal exposure to elevated levels of lead were associated with attention deficit, below average school performance, increased impulsiveness, aggressiveness and delinquent behaviour among children.[63] Parental occupational exposure lead and lead compounds was associated with later development of leukaemia and lymphoma in children.[64] A systematic review aimed at reviewing the potential risks associated with exposure to lead from breast milk found too few studies to make any conclusions.[65] *Mercury:* Foetal exposure to high-dose of mercury was associated with mental retardation, gait, visual disturbances[63] and general brain development.[61] The evidence of risk of neurodevelopmental disabilities from low-level exposure to mercury was inconclusive.[62,66] *Manganese:* Exposure to manganese was negatively associated with IQ among children aged 6-13 years,[27] and with hyperactivity and learning disabilities in children.[63] *Cadmium:* Exposure to cadmium in children was found to be associated with neurodevelopmental and behavioural disorders[27] and with hyperactivity and lower verbal and performance IQ.[63] **Other:** Lead passes through placenta[67] and can be present in breast milk.[68] Pregnancy exposure to metals may be associated with spontaneous abortion (mercury and potassium[58]), congenital malformations (lead,[69] mercury,[70] potassium[71]) and neurocognitive development and functioning (lead,[72,73] mercury,[70] manganese[74,75]). Pregnant women and young children living close to informal electronic waste recycling sites may be at risk of perturbations of foetus and child neurodevelopment.[76]

Nitrate or nitrite poisoning	**Systematic:** The epidemiologic evidence of a direct exposure-response relationship between drinking water nitrate level and adverse reproductive effect was inconclusive.[77] **Other:** Nitrates may be associated with an increased risk of cancers;[39] pregnant women and infants may be particularly susceptible to its effects.[59]	**Other:** Nitrates in drinking water was associated with intrauterine growth restriction, congenital malformations, spontaneous abortions, and methaemoglobinaemia (blue baby syndrome).[77]
Pesticides and herbicides	**Other:** Adverse reproductive outcomes were found among women working in Colombian floriculture.[78] Pesticides were linked to endometriosis.[79]	**Systematic:** The evidence of an association between residential proximity to agricultural pesticide and stillbirth, intrauterine growth retardation, low birthweight, preterm birth and miscarriage was inconclusive.[80] Good evidence exists for the association between leukemia and lymphoma and exposure to general pesticides,[81] paternal/maternal occupational exposure to pesticides,[64] maternal prenatal exposure[82,83] and residential exposure during pregnancy.[84] Children's exposure to herbicides were not significantly associated with childhood leukaemia.[84] Brain tumours in children were associated with exposure to pesticides,[81] paternal exposure (before or after birth) to pesticides[82] and with parents potentially exposed to pesticides in occupational settings.[85] Maternal exposure to pesticides prior to the child's birth was associated with an increased risk of Wilms' tumour.[86] A meta-analysis of the three cohort studies did not find evidence of an association between parental pesticide exposure and general childhood cancer incidence.[82] A systematic review of female workers founds that women's exposure to pesticides was negatively associated with their children's neurodevelopment.[87] General exposure to pesticides did not appear to cause adverse neurodevelopmental outcomes in infants and children.[88] The evidence for the link between exposure to pesticides and preterm birth was inconclusive.[30] There may be an association between residential proximity to agricultural pesticide and congenital malformations, but the evidence was inconclusive.[80] Exposure to Agent Orange was found to be associated with birth defects and spina bifida, maternal; paternal exposure to pesticides were found to be associated with congenital anomalies; maternal exposure to pesticides is associated with oral clefts.[89] Maternal exposure to environmental pesticides was found to be associated with urinary malformation.[90] **Other:** Exposure to pesticides has been linked to congenital malformations[91] and foetal death.[92]
Pharmaceuticals and personal care products Endocrine-disrupting compounds (EDCs)	**Systematic:** There were inconsistent results for the association between EDCs exposure and women's reproductive health,[93] fertility disorders and pregnancy complications.[94] Estrogen-like EDCs appear to affect the age at menarche and intrauterine exposure to EDCs can lead to premature puberty.[95] Exogenous EDCs have the potential to induce hypospadias but it is unclear whether human exposure is high enough to exert this effect.[96] **Other:** Estrogens and androgens were found in drinking water,[97] and human and animal antibiotics introduce antibiotic resistance genes to drinking water.[98] EDCs were shown to mimic and/or block effects of endogenous hormones and were associated with neurological, cardiovascular, metabolic and immune effects;[99] urogenital malformations (cryptorchidism and/or hypospadias) in male offspring, with links to infertility in later life;[100] decrease in sperm count and quality;[101] endometriosis, impaired fertility and infertility;[101] and earlier age at menarche.[102]	**Other:** Exposure to EDCs during gestation may be associated with placental function, onset of puberty and adult ovarian function;[103] low birth weight[59] and spontaneous abortion.[101] Children were more sensitive to the carcinogenic effects of EDCs.[104] EDCs such as bisphenol A and phthalates were linked to development of childhood obesity.[105]
3. Deliberate additives (substances added to water for public health purposes and their by-products)		
Disinfectants and disinfection by-products, chlorine by-products	**Systematic:** An association between formaldehyde exposure in women and adverse pregnancy outcomes was found.[106]	**Systematic:** Evidence was found for an association between third trimester residential total trihalomethane exposure and small size for gestational age.[107] There was an association between disinfection by-products and stillbirths.[89,108] High exposure to water chlorination or third trimester residential total trihalomethane appeared to be associated with an increased risk of congenital anomalies.[89] **Other:** Exposure to disinfection by-products in pregnancy may be associated with spontaneous abortion,[109] low birthweight,[59] congenital malformations,[110-112] and preterm birth.[113]
B. Water-systems related: Poorly managed water-systems spread contaminated aerosols (air conditioning systems)		
C. Water-based: Life-cycle of infective agent requires an aquatic vector and infection is transmitted through dermal contact with or ingestion of contaminated water		
Schistosomiasis	**Other:** Schistosomiasis in pregnant women was associated with anaemia,[114] diarrhoea and undernutrition,[115]and maternal and placental inflammation.[116] Female genital schistosomiasis[117] was associated with cervical cancer,[118] ectopic pregnancy, infertility, and cervical lesions.[119]	**Other:** Maternal infection with schistosomiasis was associated with foetal immune response,[120] foetal inflammation,[116] and reduced birthweight.[121,122]
D. Water-borne infections: Water is passive vehicle for infective agent. Transmission by consuming contaminated water or by faecal-oral route		
1. Bacterial infections		

Salmonellosis	**Systematic:** Salmonella enterica was the most common non-malaria bloodstream infection among pregnant women admitted to hospital in a review of studies from both Africa[123] and Asia.[124] **Other:** Pregnant women have increased susceptibility to salmonella infection.[125]	**Systematic:** A systematic review found limited evidence of salmonella transmission from breast milk to preterm infants.[126] **Other:** Foetus may be at risk of transplacental infection of salmonella [127] and exposure was associated with spontaneous abortion.[125] Salmonella caused more severe symptoms in infants, that were not usually self-limiting[128] and associated with higher mortality among children <5 with diarrhoea.[129]
Listeriosis	**Systematic:** 16-27% of all infections with listeria occurred in pregnant women.[130] Listeria monocytogenes infection was associated with adverse pregnancy outcomes, in particular with preterm delivery.[130,131] **Other:** Listeriosis carried higher fatality rates than other bacteria that cause food-poisoning.[132] The annual rate of listeria infection was more than 17 times higher among pregnant women (12 cases per 100,000) compared with the overall annual infection rate.[133]	**Systematic:** Sporadic cases of perinatal listeriosis, as well as epidemic cases, were reported, but the evidence for an association between listeria infection and spontaneous and recurrent abortion remains inconclusive.[130] Neonatal listeriosis may be associated with meningitis.[130,134] A review of listeriosis in China found a case fatality rate of 46% among neonatal cases of listeria.[135] **Other:** Exposure to listeria infection in pregnancy may be associated with pre-term delivery,[136] spontaneous abortion,[136] and stillbirth.[137] Higher susceptibility to listeria among foetuses and newborns;[136] infection carries a 20%-30% case fatality rate among newborns.[136]
Cholera	**Other:** Severity of cholera episodes during pregnancy in Haiti was linked to risk of intrauterine fetal death.[138]	
Melioidosis		**Systematic:** A systematic review of neonatal melioidosis suggested that vertical transmission exists.[139]
Acute (bloody) diarrhoea	**Other:** Infection with E.Coli was associated with pregnancy-related hypertension five years after infection.[140]	**Systematic:** The estimated prevalence of enteropathic E. coli types of pathogens in children with persistent diarrhoea in low and middle income countries was up to 63%.[141] In India, diarrheogenic E.coli were the most common organisms underlying childhood diarrhoea.[142] **Other:** Infection with E.Coli may be associated with stillbirth.[137] Infectious diarrhoea during pregnancy appears to be associated with congenital malformations.[143] Infectious diarrhoea during infancy/childhood is associated with malnutrition ("Mills-Reincke phenomenon"), stunting,[144-146] and anaemia.[147]
Shigellosis		**Systematic:** Hand-washing with soap is associated with a 59% reduction of shigellosis.[148]
Yersiniosis	**Systematic:** Yersinia enterocolitica infections were associated with adverse pregnancy outcomes, and in particular preterm delivery.[131]	
2. Viral infections		
Hepatitis E	**Other:** Pregnant women faced higher incidence of Hepatitis E infection,[136] increased susceptibility to fulminant hepatitis in the third trimester,[149] greater severity of symptoms,[149,150] and higher mortality rates (~20%) than in the general population (0.5%-4%).[151]	**Other:** Hepatitis E in pregnancy was associated with stillbirth[152,153] and intrauterine foetal death.[154]
Gastroenteritis		**Systematic:** Community-acquired rotavirus gastroenteritis greatly affected children ages 3 months to 3 years. Attack rates of symptomatic nosocomial rotavirus illness varied between 1.4% to 56%.[155] Rotavirus accounted for 37.5% of year-round hospitalized gastroenteritis cases among children under 5 in South Asia and rotavirus was associated with approximately 145,000 deaths every year in Asia.[156] Diarrhoea accounted for 14% of the total deaths in children under-five in India and rotavirus was one of the most common organisms identified underlying diarrhoea.[142] By 3 years of age, 75% of children in the Mediterranean region experienced a documented rotavirus infection.[157]
Myalgia		**Other**: Coxsackie virus infection in pregnancy may be associated with stillbirth.[137]
3. Parasitic infections		
Hookworm disease	**Systematic:** Hookworm infection intensity was associated with lower haemoglobin levels in pregnant women in poor countries.[158] However, evidence from trials of anti-helminthic treatment, while sparse, showed no evidence of an association between anti-helminthic treatment in pregnancy and reduction in maternal anaemia. Observational studies showed an association between anti-helminthics in pregnancy and improved maternal iron status (3 studies).[159] **Other:** In Africa and Asia 30–54% of moderate to severe anaemia in pregnant women is attributable to hookworm.[160,161] [162]	**Systematic:** A review of community-level interventions in low and middle income countries concluded that although further studies are needed, maternal anti-helminthic treatment showed promising impact on reducing stillbirth rates.[163] While evidence from trials of anti-helminthic treatment showed no evidence of an association between anti-helminthics in pregnancy and low birthweight or perinatal mortality, two trials showed reduced risk of very low birthweight. Observational studies showed an association between anti-helminthics in pregnancy and improvement in birthweight (2 studies) and increased infant survival (2 studies).[159] Hookworm infection was associated with anaemia and stunting among pre-school children and soil transmitted helminths, such as hookworm, may increase the risk of infection and outcomes of other infections (malaria, tuberculosis, HIV/AIDS).[164] **Other**: Long-term infection in children was associated with hypoproteinemia, delay in cognitive and physical development;[136] moderate and severe anaemia;[165,166] and impaired learning, increased absences from school.[167] Highest intensity infections were most common in children.[168]
Toxoplasmosis	**Other:** Toxoplasma gondii can be transmitted through waterborne route.[169] The global annual	**Systematic:** Review of the long-term consequences of intrauterine and neonatal insults showed that the median

	incidence of congenital toxoplasmosis was estimated to be nearly 200,000 cases; South America, some Middle Eastern and low-income countries had high burden of congenital toxoplasmosis.[170]	risk of at least one sequela in any domain (cognitive, vision, hearing, motor, seizure disorder, behavioural) was 55.6% for toxoplasmosis, based on 5 studies.[171] There was weak evidence for an association between early treatment (within 3 weeks compared to after 8 or more weeks after seroconversion) and reduced risk of congenital toxoplasmosis. While there was no evidence that prenatal treatment significantly reduced the risk of clinical manifestations in infected liveborn infants identified by prenatal or neonatal screening, increasing gestational age at seroconversion was strongly associated with increased risk of mother-to-child transmission.[172] **Other**: Toxoplasmosis in pregnancy may be associated with stillbirth.[137]
Ascariasis	**Systematic:** Infection with ascariasis was associated with anaemia in pregnancy in a systematic review of studies from South Asia.[173]	**Systematic:** In pre-school age children, ascariasis is associated with low serum vitamin A (retinol) levels, potentially contributing to increased morbidity and mortality.[164] **Other:** Ascariasis infection in children was associated with lactose intolerance and other nutrient deficiencies[174]; one of its consequences among children under 10 years of age was intestinal obstruction.[164]
Giardiasis		**Systematic:** Meta analysis of five studies showed that giardia infections in early infancy may be associated with a three-fold increase in odds of acute or persistent diarrhoea in nonindustrialised countries.[175]
Trichuriasis		**Systematic:** Trichuriasis infection was associated with growth stunting and cognitive deficits among children.[164] **Other:** Moderate to heavy trichuriasis infections were associated with higher anaemia levels in pre-school age children, particularly in malnourished children.[176] Children enduring intense infections with whipworm missed twice as many school days as their infection-free peers.[177]
4. Fungal infections		
Candidiasis	**Systematic:** A systematic review of antenatal lower genital tract infection screening and treatment programs identified one study of antenatal lower genital tract infection screening showing that women screened and treated for lower genital tract infection before 20 weeks gestation had a reduced risk of preterm birth (<37 weeks) and preterm low birthweights compared to women in the control group (no screening).[178] **Other:** Women in third trimester were susceptible to vulvovaginal candidiasis;[136,179] the prevalence of vaginal colonization by Candida species among pregnant women may be as much as double compared to non-pregnant women.[180]	
5. Chemical contaminants produced by living organisms		
E. Water-washed (also water-scarce): Insufficient quantities of water for personal or domestic hygiene or institutional/occupational hygiene leads to infections (person-to-person, rodents, etc)		
1. Wound infections		
Tetanus	**Systematic:** Systematic review of effective preconception care aimed at decreasing maternal and foetal/neonatal morbidity and mortality showed that women should receive tetanus/diphtheria/pertussis immunisation if lacking these vaccination.[181] **Other:** Maternal tetanus infection may result from unhygienic delivery, induced abortion or any wound during pregnancy and was estimated to account for 5% of maternal mortality in early 1990s.[182], [183] Maternal tetanus has higher mortality rates than adult tetanus.[184]	**Systematic:** Birth attendant handwashing was associated with 49% (95%CI: 35-62%) reduction in neonatal tetanus (low quality evidence). Clean birth surface was associated with a 93% (95%CI: 77-100%) reduction in neonatal tetanus mortality (very low quality evidence). An expert panel involved in a Delphi process assessing the evidence estimated that neonatal tetanus mortality was reduced by clean birth practices at home by 30%, in a facility 38%, and by clean postnatal care practices 40%.[185] Vaccination of women of childbearing age or pregnant women with tetanus toxoid was identified as the key intervention to reduce neonatal tetanus deaths and neonatal mortality from neonatal tetanus in low and middle income countries.[186,187] Systematic review of the long-term consequences of intrauterine and neonatal insults based on four studies of tetanus showed that the median risk of at least one sequela in any domain (cognitive, vision, hearing, motor, seizure disorder, behavioural) was 20.8%.[171] **Other:** Neonatal tetanus was associated with inability to feed resulting in malnutrition, cognitive delay, and high fatality rates(>80%).[136]
2. Enteric infections causing diarrhoea and dysentery		
Enterobiasis		**Other:** Enterobiasis was associated with nutrient malabsorption and resulting malnutrition (tropical enteropathy).[188]
Gastritis	**Systematic:** Infection with Helicobacter pylori was associated with an increased risk of hyperemesis gravidarum.[189-191] Presence of helicobacter pylori antibodies was not associated with an increased risk of preeclampsia.[192]	

3. Respiratory infections		
Influenza	**Systematic:** Systematic review of effective preconception care aimed at decreasing maternal and foetal/neonatal morbidity and mortality showed that women should receive the influenza vaccine if planning pregnancy during the flu season.[181] Women less than four weeks post partum had a significantly increased risk of death from pandemic influenza.[193] Pregnancy was associated with increased risk of hospital and intensive care unit admission and risk of death during the 2009 pandemic influenza A(H1N1).[194] **Other:** Pregnant women faced increased influenza susceptibility, increased severity of illness and higher mortality rates.[195]	**Systematic:** Vaccination of pregnant women against influenza might be beneficial for their newborns.[196]
4. Skin infections		
Leprosy	**Systematic:** Among women with leprosy, severe and recurrent reactions of erythema nodosum leprosum may occur during pregnancy and lactation.[197]	
5. Eye & Ear infections		
6. Lice- and Flea-borne Infections		
7. Nosocomial infections		
Puerperal sepsis	**Other:** Women were susceptible to puerperal sepsis during vaginal examinations.[198] A Tanzanian study found that women who bathed before delivery were almost three times less likely to develop puerperal sepsis than those who did not.[199]	**Systematic:** Based on systematically review evidence, an expert panel involved in a Delphi process assessing the evidence estimated that neonatal sepsis deaths can be reduced by clean birth practices and by clean postnatal care practices (studies identified included practices such as cord applications in the first 24 hours of life, antimicrobial cord applications and postnatal maternal handwashing).[185] Systematic review of the long-term consequences of intrauterine and neonatal insults based on five studies of sepsis showed that the median risk of at least one sequela in any domain (cognitive, vision, hearing, motor, seizure disorder, behavioural) was 48.9%.[171] A systematic review of the literature describing the aetiology of community-acquired neonatal and infant sepsis in developing countries found that among neonates, Staphylococcus aureus, Klebsiella spp. and Escherichia coli accounted for 55% (39-70%) of culture positive sepsis.[200]
8. Rodent transmitted infections		
F. Water-related (vector borne): Insects that breed in water or bite near it spread infections		
1. Mosquitoes		
Malaria	**Systematic:** Prevention of malaria infection reduced the risk of severe maternal anaemia by 38%, low birthweight by 43%, and perinatal mortality by 27% among paucigravidae.[201] Given to women in all parity groups, prophylaxis and intermittent preventive treatment (IPT) reduced antenatal malaria parasite prevalence and placental malaria.[202] While risk for malaria infection decreased after delivery, women in the postpartum period face higher susceptibility to malaria compared to pre-pregnancy levels.[203] **Other:** Pregnant women were more susceptible to malaria,[201] [204,205] particularly primi- and secundigravidae, due to lower immunity during pregnancy.[136] Increase in sub-symptomatic presentation of malaria in pregnancy may result in non-detection and lack of/delay in treatment.[201] Malaria in pregnant women was associated with increased risk of severe anaemia[206] and anti-malarial prophylaxis was found effective in reducing the risk of severe antenatal anaemia.[207] Malaria in pregnant women was found associated with increased risk of maternal death.[136] Malaria was estimated to cause between 0.5—23.0% (high transmission areas) and 0.6—12.5% (low transmission areas) of maternal deaths.[208] Pregnant HIV-positive women had a higher risk of placental malaria and HIV increased the strength of association between malaria and severe maternal anaemia, as well as low birthweight.[209] Hookworm and Schistosoma mansoni infections were associated with increased incidence of malaria.[210] Malaria was associated with increased susceptibility to HIV/AIDS and TB.[211]	**Systematic:** Placental malaria was associated with a higher risk for stillbirth, regardless of parity.[212] IPT for malaria during pregnancy and insecticide-treated mosquito nets (ITNs) reduced the risk of stillbirth.[163,213,214] The use of ITNs reduced perinatal mortality.[163] In randomized control studies conducted in Africa, use of ITNs compared to no nets reduced low birth weight by 23% miscarriages/stillbirths by a third in the first few pregnancies.[215] Malaria control measures (ITNs, antimalarial chemoprophylaxis and insecticide residual spraying) in malaria-endemic areas of Africa increased mean haemoglobin levels among children under 5 years of age.[215] Prophylaxis or intermittent treatment with antimalarial drugs among children aged one month to six years living in malaria-endemic areas resulted in fewer clinical malaria episodes, reduction in severe anaemia and fewer hospital admissions for any cause.[216] **Other:** Malaria was associated with increased risk of spontaneous abortion.[217,218] Malaria in pregnancy was associated with an increased risk of all-cause anaemia in newborn,[219] [220] low birthweight,[221,222] lower immune system response to infectious diseases,[201] and increased risk of perinatal mortality.[202],[223] One tenth of neonatal deaths in malaria-endemic areas of Africa may be caused by malaria in pregnancy-associated low birthweight.[224] A retrospective birth cohort from national cross-sectional datasets in 25 African countries from 2000-10 concluded that malaria prevention during pregnancy was associated with reductions in neonatal mortality and low birthweight.[225]
Dengue fever	**Systematic:** The existing evidence about whether maternal dengue infection was a significant risk factor for adverse pregnancy outcomes was inconclusive.[226] **Other:** Mosquito species that transmit dengue fever shown to breed in storage containers. General symptoms include internal bleeding, shock and death.[136] Dengue fever may be associated with higher maternal mortality.[227]	**Systematic:** Maternal infection with dengue was associated with vertical transmission.[226] **Other:** Maternal infection with dengue was associated with spontaneous abortion.[228] In case studies of neonates with vertically transmitted dengue, children manifested a rash, and some manifested hepatomegaly, respiratory distress, pleural infiltrates, and pleural effusion.[229]
Filariasis (lymphatic)	**Other:** Filariasis treatment was contraindicated in pregnant women and in first week of lactation due to risk to foetus.[136]	

2. Tsetse flies		
Trypanosomiasis	**Other:** People between the ages of 15-45 years and living in remote rural areas face increased vulnerability to trypanosomiasis infection,[230] especially those collecting water from unprotected water sources.[231]	**Systematic:** A systematic review concluded that although case reports and small case series describing vertical transmission of trypanosomiasis were identified, the risk of vertical transmission is unknown.[232]
3. Black flies		
Onchocerchiasis	**Other:** Women in reproductive age may miss treatment opportunities due to exclusion of pregnant and breastfeeding women in treatment campaign coverage.[233]	
G. Distant water sources or lack of water when needed		
1. Physical burdens		
Carrying heavy loads of water	**Other:** Based on data for 18 African countries, a UN report showed that women were five times more likely than men to collect drinking water for the household.[234] Carrying heavy loads is associated with limitation of flexion and increased incidence of arthrosis (degenerative rheumatism), injuries to the vertebral column,[235] and genital prolapse.[236,237] Caloric expenditure (estimated approximately 10% of daily intake)[238] may render pregnant and lactating women with dangerously low caloric reserves.[239]	**Other:** Bending and lifting heavy loads linked to spontaneous abortion[240,241] and scoliosis among children.[235]
Exposure to faeces during disposal	**Other:** Cleaning of child faeces carries a high risk of infection.[242,243]	
2. Costs		
Opportunity costs	**Other:** Opportunity costs include time spent during water collection, travel to defecation place, time spent doing laundry, menstrual rags, time out of work with illness/caring for ill family member. There is a potential for loss of future productivity due to morbidity/disability and premature mortality and lower employment skills/employability. In Pakistan, greater distance to a water source associated with lower women's participation in income-generating activities.[244]	**Other:** School attendance among children increased significantly for every hour reduction in water collection.[245]
Financial costs	**Other:** High cost of buying/boiling/treating water[246] and medical expenses during illness (e.g., visit fees, prescription fees, transportation).	
H. Water/sanitation in risky or isolated locations		
1. Natural risks associated with isolated water and sanitation facilities		
Insects/pests	**Other:** Isolated water and sanitation facilities were linked to exposure to insect and snake bites.[247]	
Risk of drowning	**Other:** Girls and women may be less likely to know how to swim.[248]	
2. Social risks associated with remote and isolated water and sanitation facilities		
Harassment, bullying , rape	**Other:** Violence against women on the way to or from public toilets or remote places of defecation.[249-252]	
I. Perception of water and sanitation availability and consequent behaviours		
1. Behaviours due to real or perceived risk, stigma, damage to self-esteem, or disgust surrounding biological processes of defecation, urination and/or menstruation		
Fear, social isolation and mental distress	**Other:** **Menstrual practice:** Reuse of menstrual absorbents/use of moist rags was linked to increased risk of infection.[253] **Defecation practices:** Unacceptability of defecating indoors can lead to nonuse of latrines.[98] **Discrimination:** Occupational sub groups (e.g., sewage workers, hospital cleaners) and vulnerable subpopulations (e.g., pregnant women, older and disabled people, women with fistula,[254] HIV-positive people, dalits, prisoners) were at risk of discrimination.[255,256]	
2. Behaviours due to real or perceived availability of WASH		
Reduced water use, substitution in drinking, long periods without urination and defecation	**Other:** Optimal hydration is essential for health and cognitive functioning. Isotonic and/or hypertonic dehydration may lead to kidney stones, renal toxicity of certain drugs and cystic fibrosis.[257] Reduction in water necessary for cooking may lead to malnutrition.[258] Dehydration and inadequate personal hygiene may lead to UTI[259] and thus to pre-eclampsia[192] and maternal anaemia.[260] Oral hygiene practices may be sub-optimal or compromised; maternal periodontal disease is associated with an increased risk of pre-eclampsia.[164,178]	**Other:** Breastfeeding women require larger quantity of water.[261] Consumption of alcohol (potentially substituting for water in instances of shortage of clean water) is linked to spontaneous abortion.[262] Prolonged exclusive breastfeeding (lack of supplementary foods) due to unavailability/ expense of clean water may have adverse effects on physical development in children.[263] Maternal UTI has been linked to preterm delivery, low birthweight and risk of cerebral palsy and mental retardation in the newborn.[183,184,260,264,265]
Use of health and educational institutions	**Other:** Lack of water and sanitation facilities in health and educational institutions may lead to a reduction in the use of health facilities (family planning, antenatal, delivery and post-natal care for women) and reduced staff retention in education and health care facilities.[266]	**Other:** The lack of adequate toilet facilities in schools contributes to absenteeism, school dropout, and failure to progress.[15,267,268]

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