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Systematic Review

Systematic review and meta-analysis: association between water and sanitation environment and maternal mortality

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Abstract

OBJECTIVE To assess whether the lack of water or the lack of sanitation facilities in either the home or in health facilities is associated with an increased risk of maternal mortality and to quantify the effect sizes.

METHODS Systematic review of published literature in Medline, Embase, Popline and Africa Wide EBSCO since 1980.

RESULTS Fourteen articles were found. Four of five ecological studies that considered sanitation found that poor sanitation was associated with higher maternal mortality. Meta-analysis of adjusted estimates in individual-level studies indicated that women in households with poor sanitation had 3.07 (95% CI 1.72–5.49) higher odds of maternal mortality. Four of six ecological studies assessing water environment found that poor water environment was associated with higher maternal mortality. The only individual-level study looking at the adjusted effect of water showed a significant association with maternal mortality (OR = 1.50, 95% CI 1.10–2.10). Two ecological and one facility-based study found an association between a combined measure of water and sanitation environment and maternal mortality.

CONCLUSIONS There is evidence of association between sanitation and maternal mortality and between water and maternal mortality. Both associations are of substantial magnitude and are maintained after adjusting for confounders. However, these conclusions are based on a very small number of studies, few of which set out to examine sanitation or water as risk factors, and only some of which adjusted for potential confounders. Nevertheless, there are plausible pathways through which such associations may operate.

keywords systematic review, water, sanitation, maternal mortality, effect size, Africa

Introduction

Numerous studies link poor water and sanitation to adverse child health outcomes, including mortality (Fink *et al.* 2011). These adverse outcomes can stem from contaminated water sources alone, but are often mediated via poor hand-hygiene, exacerbated by limited access to water (Brown *et al.* 2013). Work by Gordon, Holmes and Semmelweis as early as the end of the 18th century showed that puerperal sepsis, an important cause of maternal mortality, was contagious and linked to poor hand-hygiene in delivery facilities (Semmelweis 1983; Gould 2010). However, we have little information on the extent to which poor water or sanitation environments, in either facilities or homes, currently contribute to maternal mortality. Improved understanding of this relationship can enhance our ability to respond to the problem of maternal mortality and help identify and coordinate appropriate responses.

It seems plausible that poor water or poor sanitation could cause maternal death, as there are numerous direct and indirect mechanisms through which poor water or sanitation may lead to ill health in women. One accepted mechanism is through poor hygiene at the time of delivery, whereby infection may be introduced to the genital tract either via poor hand-hygiene or contaminated surfaces. This can lead to death from sepsis. Recent global estimates suggest 8% of all maternal deaths are due to sepsis (World Health Organization, UNICEF 2012).

There are alternative infectious mechanisms. Infections during pregnancy (e.g. hepatitis E) can be waterborne and are associated with a high risk of death (Emerson &

Purcell 2004). Poor sanitation can lead to hookworm infestation which causes anaemia and may thus increase the risk of maternal death (Brooker *et al.* 2008). Water storage may encourage mosquitoes carrying malaria and dengue to breed; both diseases pose high risks to pregnant women (Heymann 2008; Mota *et al.* 2012). Studies from Mozambique and Zambia have shown that infectious diseases such as HIV, malaria, respiratory infections and septicaemia account for more than half of maternal deaths in tertiary-level facilities (Ahmed *et al.* 1999; Menéndez *et al.* 2008). Other potential mechanisms include the life-course effect of childhood infection (repeated early childhood infections resulting in stunting, short stature in adulthood, cephalopelvic disproportion in pregnancy and increased risk of obstructed labour), (Konje & Ladipo 2000; Neilson *et al.* 2003; Toh-Adam *et al.* 2012) or the effect of harmful behaviours related to real or perceived lack of adequate water and sanitation (e.g. women not seeking institutional delivery care because of lack of toilets) (Adugna *et al.* 2001).

This study systematically reviews existing published literature to assess whether the lack of water or the lack of sanitation facilities in either the home or in health facilities is associated with an increased risk of maternal mortality and to quantify the effect sizes.

Methods

The review protocol was not registered. Medline, Embase, Popline and Africa Wide EBSCO databases were searched in September 2013. MeSH and free-text terms for maternal mortality were combined with MeSH and free-text terms for water or sanitation, in English (see Table 1 for the complete electronic search strategy). All studies, in all languages, published between 1980 and the day of the search in all settings were eligible, provided they considered water, sanitation or both as risk factors for maternal or pregnancy-related mortality. The review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline (online-only Table S1) (Moher *et al.* 2009).

Titles and abstracts were screened by one of the authors (LB). Once full-text articles were obtained, they were abstracted by two independent abstractors (LB and OMRC) using a structured form. Information abstracted from ecological studies included the study sample, definition of the water or sanitation exposures, definition and level of maternal or pregnancy-related mortality, crude and adjusted associations, and confounding variables. Information abstracted from individual-level studies included study design, study population, definition of water exposure, definition of sanitation exposure, maternal or pregnancy-related mortality definition and level, crude and adjusted estimates of association, confounding variables used in adjusted analyses (if available) and their definition. Differences between abstractors were reconciled.

The ecological studies were described in a narrative format as we could not combine estimates. All individual-level studies that provided effect estimates were included in the meta-analysis using the best available (most fully adjusted) estimate of effect and a sensitivity analysis was conducted by excluding estimates which did not adequately control for confounding. In our study, we use the term poor water and poor sanitation to reflect the worst exposure category in each study. Investigators were not contacted, but some crude estimates were recalculated based on reported data.

The Newcastle Ottawa case–control quality assessment scale was used to assess the risk of bias in individual-level studies, applied at the study level (Wells *et al.* 2006). This information was used to interpret the findings. The main summary measure was the odds ratio (OR). Meta-analysis was conducted in Stata/SE v.12 (Stata Corporation, College Station, TX, USA) using a random effects model. Heterogeneity was assessed using the Higgins and Thompson's I^2 value and its confidence interval (Higgins *et al.* 2003; Ioannidis *et al.* 2007).

Results

We identified 4162 unique papers. Figure 1 provides a flow diagram of the number of studies screened, assessed for eligibility and included in the review, with reasons for exclusion at each stage. Table 2 presents the citation, definitions and characteristics of each included study. Among the 14 identified articles, nine studies assessed the association between sanitation and maternal mortality (three individual-level, one individual-level sibling exposure and five ecological), 11 assessed the association between water and maternal mortality (four individual-level, one individual-level sibling exposure and six ecological), and three studies combined sanitation and water in score with other factors (two ecological, one facility level).

Definitions of the exposures and outcome used in the literature are also presented in Table 2. In terms of maternal mortality definitions used by individual-level studies, one study used the ICD pregnancy-related mortality definition, one used the ICD late pregnancy-related mortality definition, two used the ICD maternal mortality definition (one of these studies reduced the post-partum period to 40 rather than 42 days), and one study did not define the maternal mortality measure (World Health Organization 2004). The facility-level study defined maternal mortality as death of mother after admission in

Table 1 MeSH and text search terms used in databases searched

Database *Search Concept*	Text search terms	MeSH terms (Medline and Embase only)
Medline Search (1 AND (2 OR 3))		
1. Maternal Mortality	(Mortality or death or fatal*) ADJ3 (Maternal or obstetric or pregnan* or postpartum or delivery or labo?r or prenatal or antenatal or postnatal or childbirth or puerper* or abortion or miscarriage)	Maternal mortality
2. Water	Water ADJ3 (drinking OR household OR domestic OR tap? Or piped or source or supply or improved or protected or borehole or quality or treatment or contaminat* or point? of?use or pump or connection or location or distance or amenit* or access or provision or safe or clean)OR Soap or hand?washing	Drinking water, water pollution, water purification, water quality, water supply, water wells, soaps, handwashing
3. Sanitation	Sanitation or toilet or latrine or flush* or sewer or sewage or septic or hygiene or clean* or ((treatment OR disposal) ADJ3 (faec* OR excreta))	Toilet facilities, sanitation, hygiene, sewage
Embase (1 AND (2 OR 3))		
1. Maternal Mortality	(Mortality or death or fatal*) ADJ3 (Maternal or obstetric or pregnan* or postpartum or delivery or labo?r or prenatal or antenatal or postnatal or childbirth or puerper* or abortion or miscarriage)	Maternal mortality
2. Water	Water ADJ3 (drinking OR household OR domestic OR tap? Or piped or source or supply or improved or protected or borehole or quality or treatment or contaminat* or point? of?use or pump or connection or location or distance or amenit* or access or provision or safe or clean) OR Soap or hand?washing	Drinking water, tap water, water contamination, water pollution, water quality, water supply, water treatment, water well, soap, handwashing
3. Sanitation	Sanitation or toilet or latrine or flush* or sewer or sewage or septic or hygiene or clean* or ((treatment OR disposal) ADJ3 (faec* OR excreta))	Sanitation, sewage disposal, hygiene
Popline and African Index Medicus through Africa Wide EBSCO (1 AND 2)		
1. Maternal Mortality	(Mortality OR death OR fatal OR fatality) AND (Maternal OR obstetric OR pregnant OR pregnancy OR postpartum OR delivery OR labor OR labour OR prenatal OR antenatal OR postnatal OR childbirth OR puerperal OR abortion OR miscarriage)	
2. Water or Sanitation	Water AND (drinking OR household OR domestic OR tap OR piped OR source OR supply OR improved OR protected OR borehole OR quality OR treatment OR contaminated OR contamination OR use OR pump OR connection OR location OR distance OR access OR provision OR safe OR clean) OR Soap OR handwashing OR handwashing OR sanitation OR toilet OR latrine OR flush OR sewer OR sewage OR septic OR hygiene OR faeces OR excreta	

pregnancy, labour or after delivery, but before discharge from the hospital. All eight ecological studies reported using 100 000 live births as denominator. However, three of these studies did not provide a definition of maternal mortality for their numerator.

In the individual-level studies, the exposure variable for water was binary in three studies and categorical in two studies. No two studies used the same definition to capture poor water. In the binary classification, water was described by source (tap or not, potable or not) or quality (clean or not), although no further rationale or clarification was provided. The two studies with categorical groups used water source alone (piped, standpipe, unprotected, open source) or in combination with access (in dwelling, yard or public). In the ecological studies, the proportion of the population with poor water (described in a binary fashion) was used. Water was characterised as being safe or not; clean or not; an adequate amount of safe water or not; or protected or improved or not. The latter two are nearly identical and very similar to the WHO/UNICEF Joint Monitoring Programme (JMP) for water supply and sanitation classification which defines an improved water source as one which is either piped, from a tube well/borehole, protected dug well, protected spring or rainwater (World Health Organization 2013).

The four individual-level studies examining sanitation used binary variables (flush toilet or not, available sanitation or not) or categories based on either type of facility

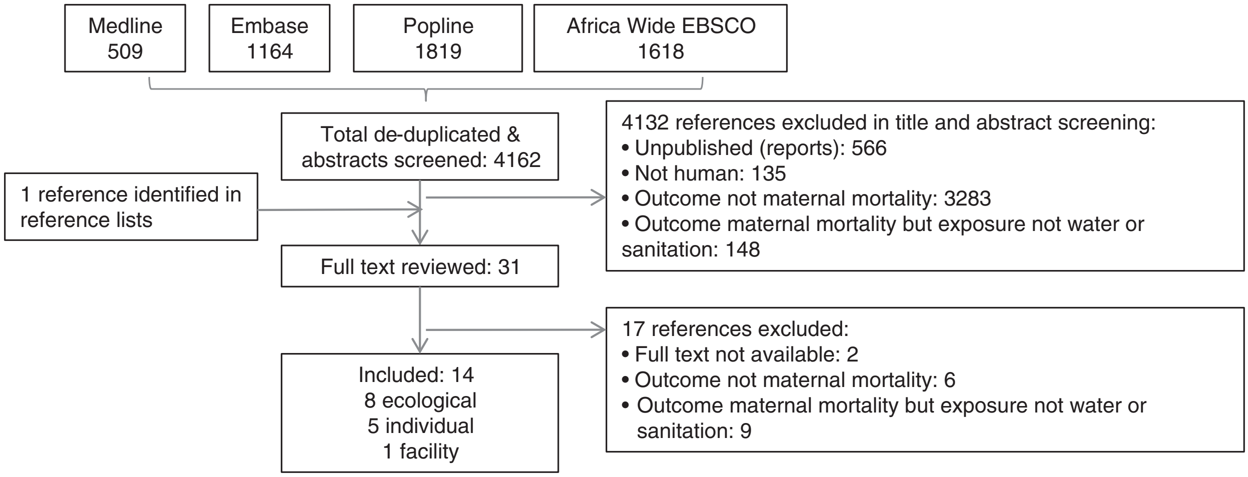

Figure 1 Flow diagram of studies included in the systematic review.

(flush, pit latrine or no facility) or access to it (private, shared, pit or bush). Among ecological studies, two defined sanitation environments in terms of the proportion of population with access to excreta disposal facilities or not; one study assessed access to a sanitary sewer or not. The remaining two ecological studies specified exposure as proportion of population with access to improved sanitation or not, which according to the JMP definition of improved sanitation includes flush or pour-flush systems connected to a piped sewer, septic tank or pit latrine; ventilated improved pit latrine; pit latrine with slab or a composting toilet, if such facilities are private.

One of the two ecological studies to look at exposure in terms of a combined water and sanitation environment used the proportion of population with sustainable access to water and sanitation or not, with no further description. The other study constructed a sanitation factor including proportion of rural and urban populations with access to sanitation and to safe water based on World Bank definitions. The facility-based study incorporated descriptions of sanitation and water environment in delivery facilities into a score with other aspects of facility hygiene. If all else was equal, facilities with better water and sanitation would score lower.

The individual and facility-level studies all examined the association of interest in low- and middle-income countries (World Bank classification). Four of the eight ecological studies examined the whole spectrum of high-, middle- and low-income countries, three focused specifically on African countries, and one study conducted a time-series analysis for Chile. The maternal mortality ratios in the contexts analysed by the 14 studies varied from three to 2000 per 100 000 live births. Likewise, the proportion of study population with poor sanitation (worst category if categorical) ranged from 0% to 99% and with poor water from 0% to 87%. Table 3 shows the results of the studies with crude and adjusted effect estimates and confidence intervals, and a list of confounders adjusted for in final analysis (if provided). Table 4 includes our assessment of the risk of bias among individual-level studies included in meta-analysis.

Sanitation

Four of the five ecological studies considering sanitation found that poor sanitation was associated with higher maternal mortality, with the remaining study showing a borderline association ($P = 0.09$). Three of these studies adjusted for potential confounders (shown in Table 3 section A). All three individual-level studies found a crude association with sanitation and two found an association after adjusting for confounders. Table 3 section B shows the individual-level studies (with their potential confounders where studied). Figure 2 presents the meta-analysis for the effect of sanitation on maternal mortality using the best available estimates from the three individual-level studies included. The pooled odds ratio for the effect of poor home sanitation on maternal mortality was 3.14 (95% CI 1.98–4.99). The I^2 value indicated low heterogeneity (<0.01%; 95% CI 0–90%), suggesting the variation in effect sizes estimated by the various studies may be compatible with chance alone. However, the confidence interval was very wide, reflecting the small number of studies. A sensitivity analysis conducted by excluding crude estimates of effect removed the study by Urassa *et al.* from the analysis, resulting in a pooled odds ratio

Table 2 Descriptive characteristics of 14 included studies

#	Author, Year	Study sample	Exposure Definition and proportions among controls	Outcome Definition, level
A. Study design: Ecological, country level				
1	Paul, 1993(Paul 1993)	36 African countries. Data from UNICEF, WHO and UN sources, period between 1980 and 1987.	**Water**: % of population with access to safe water (data from 1990, reference year 1985–7) Level(s) not shown.	Maternal deaths (death during pregnancy, delivery or up to 42 days post-partum, excluding accidents or incidental causes of death). Range: 40–2000/100 000 live births.
2	Hertz *et al*., 1994 (Hertz *et al*. 1994)	66 countries, 55 with MMR available, 35 in final model. Indicators from World Bank, WHO and FAO, FAO nutritional data from 1979–81, no info on time frame of remaining indicators, sources from 1980s.	**Water**: % population without safe water. Mean: 15.4% (IQR: 0–25%). **Sanitation**: % population without excreta disposal facilities. Mean: 18.9% (IQR: 0–31%). Both indicators obtained from WHO.	MMR (not further defined). (The denominator is erroneously listed as per 100 000 population in the original study.) Mean MMR (n = 55): 123.2 (IQR: 17.5–108) per 100 000 live births.
3	Herrera *et al*., 2001 (Herrera & Kakehashi 2001)	Final model with 89 countries. Data: World Development Indicators 1998, started with n = 210 countries in four groups (high, lower middle, upper middle and low income). Definitions of variables not provided.	**Water**: % population with access to adequate amount of safe water, 20 litres/day, SAFEW: 70.5%; SAFEWAR: 60.5%; SAFEWAU: 78.3%. **Sanitation**: % of population with adequate excreta disposal, SANIA: 75.7%; SANIAU: 76.0%.	MMR (not further defined).
4	Andoh *et al*., 2006 (Andoh *et al*. 2006)	53 African countries, models for 1990 (average of 1990, 1991 and 1992) and 2000 (average of 1998, 1999 and 2000). Data from the World Bank, UNAIDS/WHO global HIV/AIDS online database, web pages of Le Monde Diplomatique, Freedom House and World Audit.	Used principal component analysis factor for 'sanitation' with 16 component variables, the highest loading was contributed by four variables capturing access to safe water and sanitation: Definitions and coverage levels for all four indicators based on World Bank data. **Water: %** of urban/rural population with access to safe water. Mean (min, max) levels in 53 countries 1990: urban: 83% (34–100), rural: 51% (13–100); 2000: urban: 78% (23–100), rural: 54% (13–100). **Sanitation:%** of urban/rural population with access to sanitation. Mean (min, max) levels in 53 countries 1990: urban: 78% (23–100), rural: 46% (4–100); 2000: urban: 76% (12–100), rural: 44% (1–99).	Maternal mortality rate per 100 000 live births. Level among 53 countries (mean, min, max). - 1990: 742, 112, 1600 - 2000: 733, 55, 1500.

(continued)

Table 2 (*Continued*)

#	Author, Year	Study sample	Exposure Definition and proportions among controls	Outcome Definition, level
5	Alvarez *et al.*, 2009 (Alvarez *et al.* 2009)	45 Sub-Saharan African countries, grouped as high, medium and low HDI (UNDP methodology). Data from WHO, UNICEF, UNDP and World Bank between 1997 and 2006.	**Water**: % population with access to protected sources of water (piped, public tap, borehole or pump, protected well, protected spring or rainwater). Mean: 56%, SD 17, range 22–100. **Sanitation**: % population with access to improved sanitation (sewers or septic tanks, pour-flush latrines and simple pit or VIP latrines were improved if not public). Mean: 37%, SD 15, range 9–65.	MMR per 100 000 live births (death during pregnancy, delivery or up to 42 days post-partum, excluding accidents or incidental causes of death). Overall (45 countries): 885/ 100 000 live births (95% CI: 300–1400), SD 321, range 15–2100.
6	Muldoon *et al.*, 2011(Muldoon *et al.* 2011)	136 countries, data form GAIA (Globally Accumulated Health Indicator Archive), UN, WHO and Transparency International. MMR from 2008, explanatory from 2001 to 2008.	**Water** & **Sanitation**: % of population with sustainable access to water and sanitation (no further definition). Mean: 87.5% (range: 24–100%). eight high-income countries with missing water access modelled.	MMR (not further defined). Median 81.5/100 000 live births (IQR 26–350), range 3–1400.
7	Cheng *et al.*, 2012 (Cheng *et al.* 2012)	193 countries, data from WHO, UNICEF and World Bank. MMR from World Health Survey 2010, other indicators from 2008 to 2010.	**Water**: % with access to improved water source (piped household water connection, public standpipe, borehole, protected dug well, protected spring or rainwater). Mean: 85.99%, SD: 17.0, range 30–100%. **Sanitation**: % with access to improved sanitation (sewer connections, septic system connections, pour-flush latrines, ventilated improved pit latrines and pit latrines with a slab or covered pit; shared facilities were not considered improved). Mean: 71.14, SD: 30.18, range 9–100.	MMR – number of maternal deaths per 100 000 live births. Mean: 206.60, SD: 307.66.
8	Koch *et al.*, 2012 (Koch *et al.* 2012)	Time-series analysis between 1957 and 2007 in Chile. Data on MMR from Chilean National Institutes of Statistics, data on water and sanitation coverage from Central Bank of Chile (1963–1999) and from the Chilean Superintendence of Sanitary Services (SISS) for periods 1965–2009.	**Water:%** of population with clean water supply Level: 25.5% in 1957, 99.9% in 2007. **Sanitation: %** of population with sanitary sewer access Level: 12.1% in 1957, 95.2% in 2007.	MMR per 100 000 live births. Maternal deaths classified according to ICD7 (1958–1967), ICD8 (1968–1979), ICD9 (1980–1996) and ICD10 (1997–2007). Level: 270.7 in 1957, 18.2 in 2007.

(continued)

Table 2 (*Continued*)

#	Author, Year	Study sample	Exposure Definition and proportions among controls	Outcome Definition, level
B. Study design: Individual-level, case–control studies				
9	Golding *et al.*, 1989 (Golding *et al.* 1989)	Jamaica. Cases: all maternal deaths during 12 months in 1986–7 in Jamaica, n = 62 (final model n = 45) Comparisons: All women who had a live birth or stillbirth during 2 months in 1986, n = 10000 + (final model n = 10245).	**Water**: Piped into dwelling (40.7%), piped into yard (20.8%), public standpipe (20.8%) and other (17.7%). **Sanitation**: WC – flushing toilet (44.9%) or other facility (mostly pit latrines).	Women who died during pregnancy or within one year of delivery. MMR: 115/100 000 live births.
10	Urassa *et al.*, 1995 (Urassa *et al.* 1995)	Ilala district, Dar es Salaam, Tanzania; Feb 1991–Jan 1993, community-based incident case control design. All deaths to females age 12–44 identified and relative interviewed. Cases: n = 117 (76% occurred in hospital, 3.4% in clinics, remaining at home or on the way) Controls: three per case, matched by 5-year age groups in same delivery hospital, or in cases of abortion and home deaths, from nearest district hospital (not stated, but should be n = 351).	**Water**: Access to tap water (binary), yes (53.8%). **Sanitation**: Flush toilet (19.4%), pit latrine (79.1%), no facility (1.5%).	WHO definition of maternal mortality (death during pregnancy, delivery or up to 42 days post-partum, excluding accidents or incidental causes of death). MMR: 572/100 000 live births.
11	Fikree *et al.*, 1997 (Fikree *et al.* 1997)	Pakistan, three clusters (Karachi, Balochistan, Northwest Frontier). Population survey (ever married 15–54), 1989–1992. Cases: 218 (212 with non-missing values). Controls: five per case, randomly selected from 23809 currently surviving women who reported a pregnancy in preceding 5 years, n = 1090 (1043 with non-missing values).	**Water**: Potable (46.3%) or not potable. No further definition.	Death during pregnancy, delivery or up to 42 days post-partum, excluding accidents or incidental causes of death. Reduced post-partum period to 40 days (local concept of *chilla*). MMR overall: 433/100 000 live births (CI 95%: 372–494), range 281–673 by cluster.
12	Taguchi *et al.*, 2003 (Taguchi *et al.* 2003)	Surabaya (East Java), Indonesia. Cases: maternal deaths (identified at one teaching referral hospital between Jan 1996–Dec 1999), n = 59 (another 38 had missing data). Controls matched by age and gravidity from same hospital between Jan–Dec 1999, selected by systematic random sampling after matching for age and gravidity from 5697 admitted to same hospital, n = 177.	**Water**: Availability of clean water (binary), available (83%). **Sanitation**: Availability (binary), available (90%).	No definition of maternal mortality provided. MMR not estimated, only hospital-based maternal deaths.

(continued)

Table 2 (*Continued*)

#	Author, Year	Study sample	Exposure Definition and proportions among controls	Outcome Definition, level
13	Graham *et al.*, 2004 (Graham *et al.* 2004)	10 developing countries (Burkina Faso, Chad, Ethiopia, Indonesia, Kenya, Mali, Nepal, Peru, Philippines, Tanzania), 11 DHS surveys (1994–2000), which had data on >10 000 adult sisters available for analysis. Sisters of respondents: three survivor groups (living and in reproductive age 15–49, died of non-maternal cause, died of maternal cause).	**Water**: Piped, protected, unprotected or open supply. Levels not provided. **Sanitation**: Private, shared, pit or bush. Levels not provided.	Death from maternal causes; defined as pregnancy-related mortality. Range 240–1800/100 000 live births.
C. Study design: Facility-level				
14	Galadanci *et al.*, 2011(Galadanci *et al.* 2011)	Kano and Kaduna state, Nigeria. 10 rural hospitals (five from each state). Register for all deliveries n = 29833 in 2 years (2008–9).	**Water** & **Sanitation**: Score criteria for infrastructure: Water supply as one of seven components of general conditions assessment. Cleanliness of sink as one of 12 components of operating theatre hygiene. Sink hygiene and toilet hygiene as two of seven components of general hospital conditions. Hand disinfection as one of eight components of delivery room hygiene.	Maternal death: death of mother after admission in pregnancy, labour or after delivery, but before discharge from the hospital. MMR 423/100 000 deliveries.

Table 3 Summary of results from 14 included studies

#	Author, Year	Crude measure of association	Adjusted measure of association Confounders	Notes
A. Study design: Ecological, country level				
1	Paul, 1993	Not reported.	B-coefficient of stepwise linear regression model Access to safe **water**: −3.482 (partial $R^2 = 0.020$), $P > 0.05$. Model $R^2 = 0.583$, $P < 0.0001$. Confounders: population size, GNP *per capita* (USD), crude birth and death rates,% urban population, adult female literacy%, calorie supply as% of requirements.	Water may not be significant because of its high correlation with calorie supply (r = 0.66), the largest predictor.
2	Hertz *et al.*, 1994	Not reported.	Stepwise regression model ($n = 35$, model R^2: 0.54) - % households without **sanitation**: F-test: 10.54, $P = 0.002$ - % households without safe **water**: F-test: 0.65, $P = 0.43$. General linear model ($n = 36$, model R^2: 0.54) - % households without **sanitation**: Parameter estimate: 8.299, $P = 0.0003$. - % households without safe **water**: Parameter estimate: 2.717, $P = 0.24$. Confounders: total calories consumed, total fat residual, total fat calories consumed, medical personnel available per 10 000 population, hospital beds available, total literacy rate.	Samples only included countries with no missing data. Does not list countries or time frame of data (MMR, water and sanitation).
3	Herrera *et al.*, 2001	Spearman rank correlation (assessed 'high', no *P*-value reported): **Water**: SAFEWA: −0.813, SAFEWAU: −0.827, SAFEWR: −0.652 **Sanitation**: SANIA: −0.717, SANIAU: −0.677	Water and sanitation not included in the final adjusted model of MMR (only fertility rate, immunisation DPT, urban population, and females working in industry).	Assumed 'U' and 'R' variable name endings refer to urban and rural.

(continued)

Table 3 (*Continued*)

#	Author, Year	Crude measure of association	Adjusted measure of association Confounders	Notes
4	Andoh *et al.*, 2006	Not reported.	The 'sanitation' factor included in six adjusted linear regression models predicting maternal mortality ratio in 1990 and 2000. Model 1: **Sanitation factor** was associated with MMR in 1990 (B-coefficient: −0.552, $P < 0.001$) and in 2000 (B: −0.479, $P < 0.001$) when adjusted for development and education factors. Model 2: **Sanitation factor** was associated with MMR in 1990 (B-coefficient: −0.318, $P < 0.01$) and in 2000 (B: −0.334, $P < 0.01$) when adjusted for national income *per capita* and the education factor. Model 3: **Sanitation factor** was associated with MMR in 1990 (B-coefficient: -0.410, $P < 0.01$) and in 2000 (B: -0.311, $P < 0.05$) when adjusted for debt *per capita* and the education factor. Model 4: **Sanitation factor** was associated with MMR in 1990 (B-coefficient: -0.290, $P < 0.05$) and in 2000 (B: -0.300, $P < 0.01$) when adjusted for national net income *per capita* and the education factor. Model 5: **Sanitation factor** was associated with MMR in 1990 (B-coefficient: -0.537, $P < 0.001$) and in 2000 (B: -0.426, $P < 0.001$) when adjusted for HIV/AIDS and the development factor. Model 6: **Sanitation factor** was associated with MMR in 1990 (B-coefficient: -0.474, $P < 0.001$) and in 2000 (B: -0.423, $P < 0.001$) when adjusted for political instability and the development and education factors.	

(continued)

Table 3 (*Continued*)

#	Author, Year	Crude measure of association	Adjusted measure of association Confounders	Notes
5	Alvarez *et al.*, 2009	R correlation coefficient from Pearson or Spearman tests: Access to improved **water** source(%), $n = 43$: R = −0.399 ($P = 0.008$). Access to improved **sanitation**(%), $n = 43$: R = −0.291 ($P = 0.091$).	Not reported.	
6	Muldoon *et al.*, 2011	Used linear mixed effects model. Risk ratio between MMR (10% increase in% population with sustainable access to **water and sanitation**): 0.67 (CI 95%: 0.61–0.73).	Risk ratio between MMR (10% increase in% population with sustainable access to **water and sanitation**): 0.88, CI 95%: 0.82–0.94. Confounders: total health expenditure *per capita* (USD), corruption index (log transformed), fertility rate (average number of children/woman). Not significant and not in final model: nursing/midwife density, physician density,% births attended by skilled staff,% measles immunisation coverage, out-of-pocket expenditure on health (as a% of total health expenditure), government health expenditure (USD), private share of total health expenditure (%), population growth value (annual%), urban population value (annual%), female labour force participation (%).	
7	Cheng *et al.*, 2012	Access to improved **water** source (%, divided into quartiles): OR 0.20 (95% CI: 0.14–0.28, $P < 0.001$). Access to improved **sanitation**(%, quartiles): OR 0.14 (95% CI: 0.10–0.20, $P < 0.001$).	Ordinal logistic regression. Access to improved **water** source (%, divided into quartiles): OR 0.58 (95% CI: 0.39–0.86, $P = 0.008$). Access to improved **sanitation** (%, quartiles): OR 0.52 (95% CI: 0.32–0.85, $P = 0.009$). Confounders: GNI (log transformed), fertility rate (log transformed),% births attended by skilled health personnel, world region.	Water and sanitation in separate multivariate regression models, did not explore simultaneous effect of both.

(continued)

Table 3 (*Continued*)

#	Author, Year	Crude measure of association	Adjusted measure of association Confounders	Notes
8	Koch *et al.*, 2012	Not reported.	Pathway modelling using autoregressive integrated moving average models in time series 1957–2007, showing B-coefficient values Model 1: Adjusted model with initial slope (1957) **Water**: B = −2.32, P = 0.002; **Sanitation**: B = −1.57, P = 0.196 Model 2: Adjusted model with initial slope (1957) and average years of schooling **Water**: B = −1.98, P = 0.001; **Sanitation**: B= –0.73, P = 0.319 Model 3: Adjusted model with initial slope (1957), average years of schooling and time period from 1965 **Water**: B = −2.78, P = 0.001; **Sanitation**: B = −2.16, P = 0.001 Model 4: Adjusted model with initial slope (1957), average years of schooling, and time periods from 1965 to 1981 **Water**: B = 0.24, P = 0.765; **Sanitation**: B = 0.17, P = 0.726 Confounders (all models): Total fertility rate,% primiparous women,% primiparous>29 years, delivery with skilled attendance, GDI *per capita*, % with clean water,% with access to sanitary sewer.	
B. Study design: Individual-level, case control studies				
9	Golding *et al.*, 1989	**Water** (reference piped into dwelling): - All deaths (n = 57): RR (piped into yard): 1.8, RR (public standpipe): 3.0, RR (other): 2.1, overall X^2 P-value <0.01. - Haemorrhage and infection deaths (n = 28): RR (piped into yard): 1.3, RR (public standpipe): 5.9, RR (other): 2.3, overall X^2 P-value >0.05. **Sanitation** (reference flush WC): - All deaths (n = 53): RR (other): 2.3, P < 0.05. - Haemorrhage and infection deaths (n = 16): RR (other): 5.7, P < 0.05.	No adjusted estimate for water. **Sanitation**, all deaths (n = 45 cases, 10 245 controls): (other type compared to flush WC): OR: 3.16 (CI 95%: 1.56–6.41, P < 0.001). Confounders: Maternal age (<30, 30 +), parity, household amenities, maternal education, mother as major wage earner, major wage earner in agriculture, marital status, parish (=region).	Adjusted model includes 45 of initial 62 cases. No statement whether household amenities (confounder) includes water source.

(continued)

Table 3 (*Continued*)

#	Author, Year	Crude measure of association	Adjusted measure of association Confounders	Notes
10	Urassa *et al*., 1995	**Water** (reference tap water): - OR (no access): 2.6 (CI 95% 1.7–4.0). **Sanitation** (reference flush toilet): - OR (pit latrine): 3.1 (CI 95% 1.5–6.6) - OR (none): 8.3 (CI 95% 2.3–30.0), X^2 test for trend: $P < 0.001$.	Not reported.	Water (no access to tap water) OR cited as 2.7 (CI 95% 1.7–4.2) in abstract.
11	Fikree *et al*., 1997	**Water** (reference potable): Cases $n = 212$, controls $n = 1019$ - OR (not potable): 1.6 (CI 95%: 1.2–2.0), $P < 0.01$.	**Water** (reference potable): OR (not potable): 1.5 (CI 95%: 1.1–2.1), $P < 0.05$. Confounders: Distance from nearest hospital (<40 miles, 40+), housing construction material, household assets, age group, gravidity group, obstetric history (live births, stillbirths/abortions).	
12	Taguchi *et al*., 2003	**Water** (reference clean water): OR (no clean water): 0.9 ($P > 0.05$). **Sanitation** (reference toilet available): OR (not available): 3.0 ($P < 0.05$).	No adjusted estimate for water. **Sanitation** (reference toilet available): OR (not available): 2.9 (CI 95%: 1.0–7.7, $P < 0.05$). Confounders: Living area (in town or outside), maternal education, maternal employment status, frequency of ANC, timing of first ANC visit.	Identified 97 maternal deaths, but missing socio-economic data for 38 (39%). Not all cases (65.3%) or all controls (87.6%) delivered at the hospital. Maternal mortality among hospital deliveries may have weaker association with home water and sanitation.
13	Graham *et al*., 2004	**Water supply:** Burkina Faso (1999): 0.8251, Chad (1996): 0.3844, Ethiopia (2000): 0.0019, Indonesia (1994): 0.033, Indonesia (2000): 0.0046, Kenya (1998): <0.0001, Mali (1996): 0.0006, Nepal (1996): 0.0001, Peru (2000): <0.0001, Philippines (1998): 0.0203, Tanzania (1996): 0.0144. **Sanitation type:** Burkina Faso (1999): 0.1809, Chad (1996): 0.0376, Ethiopia (2000): 0.0016, Indonesia (1994): <0.0001, Indonesia (2000): 0.3386, Kenya (1998): 0.8624, Mali (1996): 0.0218, Nepal (1996): 0.0002, Peru (2000):<0.0001, Philippines (1998): 0.0009, Tanzania (1996): 0.0495.	Not reported.	Reported estimates of Pearson X^2 test P-values for association between three types of survivorship among sisters and water/toilet categories, adjusted for survey design. Attributes of adult sister respondents assigned to dead sisters.

(continued)

Table 3 (*Continued*)

#	Author, Year	Crude measure of association	Adjusted measure of association Confounders	Notes
C. Study design: Facility-level				
14	Galadanci *et al.*, 2011	Association between general conditions rating (GCR) and MMR (%, 2009). $R^2 = 0.7703$, MMR(%) $=0.0502*e^{(0.1519*GCR)}$ GCR (15) = MMR (approximately 0.5%), GCR (25) = MMR (approximately 2.23%) Association between hygiene rating (HR) and MMR (%, 2009). $R^2 = 0.5335$, MMR(%) $=0.2223*e^{(0.086*HR)}$ HR (10) = MMR (approximately 0.5%), HR(25) = MMR (approximately 1.91%).	Not reported.	Toilet, water supply, sink and handwashing part of total score from five to 30. Not completely clear if regression in on general infrastructure and general hygiene or all hygiene. Cannot separate effect of water supply and toilet availability/cleanliness from other factors in the two ratings.

of 3.07 (95% CI 1.72–5.49) for the remaining two adjusted studies.

Golding *et al.* investigated cause-specific mortality and found a larger relative risk of combined infection/haemorrhage maternal mortality (5.7 times higher for women living in households with poor sanitation, $P < 0.05$), compared with the relative risk hypertensive disorders of pregnancy (1.4, $P > 0.05$), or other causes (2.1, $P > 0.05$). Urassa and colleagues also looked for and found a dose–response relationship in crude analysis between three types of sanitation facilities and maternal mortality [chi-square test for trend $P < 0.001$, comparing flush toilet OR = 1.0 (reference category), pit latrine OR = 3.1 and no facility OR = 8.3]. The individual-level study by Graham and colleagues showed a statistically significant crude correlation between the maternal death of the respondent's sibling and the respondent's own lack of toilet in eight of 11 assessed DHS surveys. This study did not present odds ratios and considered the water and sanitation situation among siblings of women who died from maternal causes; it was therefore not included in the meta-analysis for either exposure.

Water

Four ecological studies found an association between poor water availability and higher maternal mortality, two did not. Four of these six ecological studies adjusted for potential confounders (see Table 3 section A). Three of the four individual-level studies showed an association between poor water access and maternal death; one of these adjusted for potential confounders. Based on the four available estimates for water in individual-level studies, the pooled odds ratio for the effect of poor home water environment was 1.75 (95% CI 1.21–2.54), shown in Figure 2. This pooled estimate showed a medium level of heterogeneity ($I^2 = 57.5\%$; 95% CI 0–86%). As with the I^2 value for sanitation, the confidence interval was wide, partly due to the small number of studies. It is unclear whether the crude estimate by Golding *et al.* should be included in the 'best estimate' meta-analysis, as the authors conducted an adjusted analysis but did not report the effect size for water. This is most probably because the adjusted water effect was not statistically significant and may well have been reduced in size. Restricting the analysis to adjusted estimates for the effect of water left only the study by Fikree *et al.*, with its point estimate of 1.50 (95% CI 1.10–2.10).

In terms of other supportive evidence, a dose–response relationship between four types of water source and maternal mortality was seen in Golding *et al.*'s crude analysis (chi-square test for trend $P < 0.01$, comparing

Table 4 Risk of bias assessment for individual-level papers included in meta-analysis

Risk of bias category		Golding 1989		Urassa 1995		Fikree 1997		Taguchi 2003	
Selection	Adequate case definition	+		+		+		+	
	Representativeness of cases (consecutive or obviously representative)	+		+		+		+	
	Selection of controls (community best, hospital second best)	+		?		+		?	
	Definition of controls	+		+		+		+	
Comparability	Comparability of cases and controls – age	+		+		?		+	
Exposure	Exposure type	*Wat*	*San*	*Wat*	*San*	*Wat*	*San*	*Wat*	*San*
	Ascertainment of exposure	+	+	+	+	+	n/a	+	+
	Same method of ascertainment cases and controls	?	?	?	?	?		?	?
	Non-response rate same for cases and controls (missing data)	?	?	+	+	+		?	?
Control for confounding	Present an adjusted estimate of association controlled for minimum confounders (age, parity/gravidity, socio-economic status, and residence location or access to healthcare services)	–	+	–	–	+		–	?

Key: + Low risk of bias ? Potential/unclear risk of bias – High risk of bias. Wat, Water; San, Sanitation; n/a, Not analysed.

water piped into dwelling OR = 1.0 (reference category) with piped into yard OR = 1.8, public standpipe OR = 3.0 and other source OR = 2.1). Fikree *et al.* estimated the population attributable risk proportion of maternal mortality linked to the lack of access to potable water to be 21.2%. Graham *et al.* showed a statistically significant crude correlation between a sibling's maternal mortality and the respondent's lack of water in nine of 11 assessed DHS surveys.

Water and sanitation combined

Andoh *et al.* found that higher score of the 'sanitation' factor (combining the proportions of the urban and rural populations' access to sanitation and to safe water) was significantly associated with lower maternal mortality in all six adjusted models. Muldoon *et al.*'s ecological study found a significant association between having a lower proportion of population with 'sustainable access to water and sanitation combined' and a higher maternal mortality. The facility-based study by Galadanci *et al.* incorporated sanitation and water into a score with other aspects of facility hygiene and found that a high (=worse) score was associated with high in-hospital maternal mortality (Table 3).

Discussion

This systematic review showed some evidence of an association between poor sanitation and high levels of maternal mortality and of an association between inadequate water access and high maternal mortality. The meta-analysis of best estimates suggested women in households with poor sanitation had 3.14 times the odds of dying compared to women with better sanitation. The sensitivity analysis after removing a study which only adjusted for age produced a similar estimate of 3.07. The pooled estimate of association between water and maternal mortality suggested that women with poor water supply had roughly 1.75 the odds of maternal mortality compared to those with adequate water, but only one study adjusted for confounders (adjusted OR 1.5). Our confidence in the above conclusions is bolstered by the magnitude of the effect sizes, the dose–response effects seen for both exposures, the biologically plausible cause-specific effect on maternal deaths from infection and haemorrhage, and the compatible findings from the large majority of ecological studies. However, we also acknowledge that the results are based on very few studies that explicitly set out to test sanitation or water as risk factors, a small number of individual-level studies with differing definitions of exposure, and limited attention to carefully adjusting for confounding.

Strengths and limitations

In assessing data quality of each study, we considered selection bias, information bias and confounding. Most of the individual-level studies were well conducted. They

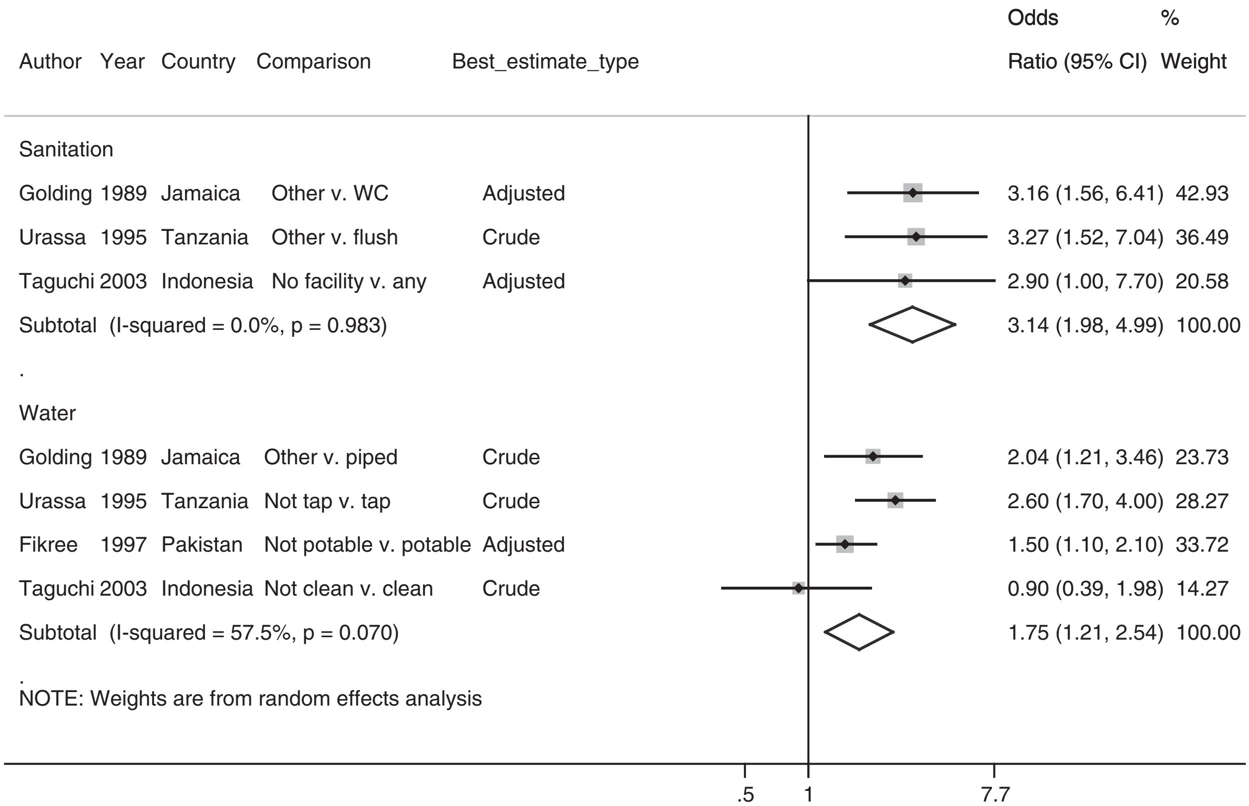

Figure 2 Meta-analysis and pooled odds ratios for the effect of toilet and water facilities on maternal mortality in individual-level studies.

did not appear to suffer from selection bias as they included all deaths in the target population with an apparently unbiased comparison group (all births or controls, nested within a population-based sample) (Table 4). In terms of information bias, outcome status was clear cut, with a remote chance that some maternal deaths might have been missed or misclassified. The sources of information for the controls came from the women themselves, while information on cases, such as water and sanitation environment, was from relatives' reports. This opens up the possibility of recall bias. Furthermore, it is unclear from the studies whether the water and sanitation status of the household was assessed at the time the cases died or at the time of interview. However, we believe that these potential sources of bias are unlikely to be important. In our judgement, the largest source of potential bias is uncontrolled or residual confounding by socioeconomic status, which may be linked with, for example, poor underlying health status, access to health services or quality of maternal care, which in turn may cause maternal mortality. New studies and analyses to explicitly test the hypothesis that either water or sanitation is risk factor for maternal mortality could resolve some of these concerns.

It was not possible to assess the data sources of the ecological studies thoroughly. Many used UN maternal mortality ratios (MMR), which mix empirical measures with estimates derived from predictive models generated using other measures of development, such as GDP *per capita*. Fortunately, none of the models used water or sanitation measures as predictors, (World Health Organization 2012) as this would have led to a spurious association and invalid findings. In comparison with MMR, more countries had empirical data on water and sanitation provision, including from DHS/MICS surveys. The years for which exposure and outcome data are available are generally aligned in rather broad bands, but not all studies provided this information.

In addition to limitations of the studies identified, we also assessed the limitations of the search strategy and potential for publication bias. We had complete retrieval of identified research. However, our search may have missed studies which reported results in the text, but where water or sanitation was not listed in the title, keywords or abstract. Studies of maternal mortality that used composite measures of socio-economic status incorporating water or sanitation may not have estimated or reported the effect of these two exposures separately. It is also possible that studies that failed to find an association did not report the crude or adjusted estimates, or were not submitted for publication or not published. All identified studies assessed a large number of general risk factors for maternal mortality, except the study by Cheng *et al.*, which looked specifically for the effect of water and sanitation on maternal, infant and child mortality. This may have led to an overrepresentation of studies that found a statistically significant association between a water exposure or a sanitation exposure and maternal mortality in the published literature.

If the effects of sanitation and water on maternal mortality are real, we need to understand the mechanisms through which they operate. The most obvious potential mechanism is puerperal sepsis introduced at the time of delivery through unhygienic environment or practices. Clinical guidelines require practice of hand-hygiene around delivery, and lack of availability of water and sanitation infrastructure in the location of delivery may inhibit or preclude consistent adherence (World Health Organization 2009). All the studies identified in this review, except Galadanci *et al.*, assessed water or sanitation in the home environment, irrespective of where the delivery took place. None of the included studies directly considered the role of water and sanitation infrastructure as determinants of hygienic practice during pregnancy and childbirth. To assess whether infection was introduced at the time of delivery, we would need to consider exposure at the place of delivery, an analysis not available in the studies identified. The Golding *et al.* study identified a larger effect size of both poor water and poor sanitation on combined infection and haemorrhage deaths compared with all deaths, suggesting this direct infection route at the time of delivery is plausible. However, this cause of death category is broad and includes causes beyond puerperal sepsis.

Other infections during pregnancy and the puerperium, such as influenza (linked to poor hand-hygiene), malaria (mosquitoes can breed in open water sites) or hookworm (common in environments with heavy faecal contamination), could also arise in poor water or sanitation environments. Looking at the time of death (i.e. deaths occurred during pregnancy, delivery or post-partum) and causes of death (e.g. severe anaemia) could elucidate whether the association is a direct effect of puerperal sepsis introduced at the time of delivery or via some other infectious mechanism. Furthermore, non-infectious routes affecting health during pregnancy could also be implicated, for instance, as a result of chemical contamination of drinking water, physical effects of carrying heavy water loads, or other harmful behaviours related to unavailability of sufficient quantities of water or conveniently located improved sanitation facilities.

Another potential mechanism includes the long-term effects of infectious and non-infectious exposures related to poor water and sanitation experienced *in utero*, during childhood or pre-pregnancy, leading to long-term harms complicating pregnancy and childbirth. For instance, repeated childhood infections may lead to stunting, short adult stature and an increased risk of obstructed labour leading to death. Graham *et al.*'s findings that a sibling's water and sanitation environment is a risk factor for maternal mortality in the majority of DHS surveys assessed may partly reflect such shared water and sanitation exposures in childhood.

To identify the mechanisms of effect implicated in these associations, further research is needed to elucidate which specific causes of maternal mortality are associated with poor water, sanitation or both. Two studies which considered the effects of different types of sanitation (Urassa *et al.*) and water access (Golding *et al.*) found a dose–response relationship, suggesting that not just access is important, but also the quality of that access. In addition to analysing the water and sanitation environment in the place of delivery to elucidate the effects of the direct infectious route, a wider approach could be adopted to assess the association of maternal mortality with water exposure and/or sanitation exposure at various points in the life course, as related to the pathway(s) under investigation. If both biological and social (behavioural) mechanisms on the individual as well as population level underpin the association between poor water or sanitation environments and maternal mortality, the strength of association and size of effect would be expected to differ in various contexts. This is especially the case in those with different attributes (prevalence, quality, quantity, distance to water or sanitation facilities) of improved water and sanitation, as well as cultural and hygienic behaviours related to water and sanitation. Studies in a variety of contexts would help clarify the potential mechanism.

In summary, there is a critical need for more research to explicitly explore water and sanitation, its characteristics and associated hygiene practices (individual as well as societal) as risk factors, as well as the multiple plausible pathways (including lifelong and intergenerational) that might explain the associations reported for a variety of cause-specific mortality outcomes. A better understanding of the mechanisms and the long-term and short-term risks that poor water and sanitation present will help identify appropriate interventions. The SHARE consortium is undertaking such analyses in three countries.

Conclusion

The importance of water and sanitation to health is well known, and the link between hand-hygiene and infection during childbirth and in the post-partum period was demonstrated over 200 years ago. However, the contributions of water and sanitation in general to maternal mortality are poorly understood, as are the direct and indirect mechanisms linking them. This systematic review identified 14 studies published since 1980 exploring links between water or sanitation or both and maternal mortality. Our meta-analysis of individual-level studies and synthesis of evidence from ecological and facility-based studies suggests evidence of an association between increased maternal mortality and poor sanitation environment, as well as an association with poor water environment.

The findings reported here are pertinent to two traditionally distant areas of public health policy: water and sanitation, and maternal health. This distance may be due in part to maternal health being largely the domain of medicine and midwifery, and water and sanitation one of infrastructure and engineers. The evidence reviewed suggests that there are potentially important linkages between the water and sanitation environment and maternal mortality, and this is relevant to all concerned with the broader public health outcome of reducing maternal mortality. It is possible to make policy recommendations even in the absence of further research, and there is room for increasing the scope of collaboration between the water and sanitation and maternal health efforts. There is an urgent and undisputable need to ensure that healthcare facilities have adequate sanitation and water availability. However, this review suggests that even if the main maternal health strategy is to increase the proportion of facility deliveries, we must also consider the water and sanitation environment in households.

Although the MDG7 water target was declared met in 2010, 780 million people remain without safe water and 2.5 billion people are estimated to live without access to improved sanitation (UNICEF 2012). If women with poor sanitation at home indeed have three times higher maternal mortality, and the relationship is causal, a sizable number of maternal deaths may be averted by improving access to water and sanitation. Finally, we must go beyond solely identifying the mechanisms and estimating of effect size and population attributable fraction of poor water and sanitation on maternal mortality. Living, working and receiving health care in poor quality water and sanitation environments is an affront to women's (and men's) dignity, human rights, as well as a preventable cause of reproductive morbidity, mortality and poor mental health. While more research on the specific links to maternal mortality will strengthen our understanding and response, efforts to improve the provision of water and sanitation should not be stopped or delayed.

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Supporting Information

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

Table S1. PRISMA guidelines checklist

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