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What are the effects of different models of delivery for improving maternal and infant health outcomes for poor people in urban areas in low income and lower middle income countries?

Report

Systematic review

What are the effects of different models of delivery for improving maternal and infant health outcomes for poor people in urban areas in low income and lower middle income countries?

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Contents

List of abbreviations

AIDS	Acquired immunodeficiency syndrome
ANC	Antenatal care
APHRC	African Population and Health Research Center
BCG	Bacillus Calmette-Guerin
CS	Caesarean section
DALY	Disability-Adjusted Life Year
DHS	Demographic and Health Survey
DSS	Demographic Surveillance System
DTP	Diphtheria-Tetanus-Pertussis
EmOC	Emergency obstetric care
ENC	Essential newborn care
EPI	Expanded Programme on Immunization
EPPI	Evidence for Policy and Practice Information
EV	External validity
FP	Family planning
HAART	Highly active antiretroviral treatment
HBV	Hepatitis B vaccine
HIV	Human immunodeficiency virus
IMR	Infant mortality rate
IV	Internal validity
JSY	Janani Suraksha Yojana
KMC	Kangaroo mother care
LBW	Low birthweight
LIC	Low income country
LMC	Lower middle income country
MCH	Maternal and child health
MDG	Millennium Development Goal
MDR	Maternal death review
MeSH	Medical subject headings
MICS	Multiple Indicator Cluster Survey
MMR	Maternal mortality ratio
MR	Mortality rate
MTCT	Mother to child transmission

NASG	Non-pneumatic anti-shock garment
NFHS	National Family Health Survey
NGO	Non-governmental organisation
NMMS	National Maternal Mortality Study
NPI	National Programme on Immunization
NSCU	Neonatal special care unit
OPV	Oral polio vaccination
ORS	Oral rehydration salts
PMTCT	Prevention of mother-to-child transmission
RCT	Randomised controlled trial
RPR	Rapid plasma reagin
SAMM	Severe acute maternal morbidity
SBA	Skilled birth attendance
SSA	sub-Saharan Africa
SFH	Symphyseal-fundal height
TBA	Traditional birth attendant
UCP	Umbilical cord prolapse
VAS	Vitamin A supplementation
VBAC	Vaginal birth after Caesarean
VLBW	Very low birthweight
WB	World Bank
WHO	World Health Organization

Executive summary

Background

The burden of maternal and infant deaths falls disproportionately on low income countries (LICs) and lower middle income countries (LMCs[1]) and among the poorest within these countries. The causes of maternal and infant mortality and morbidity are well established, yet knowledge on effective management of conditions has not been translated into significantly improved outcomes because of a lack of resources and effective models of service delivery. Urban populations are often assumed to have better access to health care than those living in rural areas. However, urban health systems in many LICs and LMCs have a weak to non-existent public health structure and lack uniform implementation of strategies and necessary infrastructures. Given rapid urbanisation in many LICs and LMCs it is now crucial to establish evidence-based approaches to improving access to and uptake of maternal and infant care models in urban areas and improving quality of services in order to improve maternal and child outcomes. Whilst the medical solutions for preventing maternal and infant mortality are known, delivering these solutions is a considerable challenge in proximity to urban slums.

Objectives

This systematic review addresses the question:

> *What are the effects of different models of delivery for improving maternal and infant health outcomes for poor people in urban areas in low income and lower middle income countries?'*

Methods

Our systematic review focused on explicit evaluations of interventions aimed at improving health outcomes for poor people in urban areas. The review focused on maternal, infant, neonatal, perinatal and post-neonatal mortality outcomes, but also included maternal and infant health outcomes. Our review team, including information scientists and information retrieval experts, developed a search protocol and search terms that were subject to external peer review. Our search includes major databases that cover literature on this topic; these cover both English and non-English language material, including specialist health and development databases, as well as those focusing on specific geographical areas. A comprehensive search was conducted of published and unpublished materials. The search followed the study protocol, which set out the search strategy and selection methods. The study used multiple approaches to data analysis (including: narrative; cost-effectiveness; understanding links between the cause, approaches, outcomes and sustainability of change as part of a causal chain analysis) to assess not only which interventions are effective (or not), but how and under what circumstances. Quantitative and qualitative data were collected from and coded for included items, and each item was coded for a range of variables. Interventions were grouped into clinical and non-clinical categories. We collected qualitative evidence on contextual factors and causal pathways that may help to explain why interventions were (in)effective.

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[1] We used the World Bank classification: http://data.worldbank.org/about/country-classifications (accessed 10 March 2011).

Details of included studies

The searches returned 9,025 potentially relevant items of evidence, including 9,010 from database searches and 15 from handsearches. Of these papers, 98% were excluded after reviewing titles; the abstracts of the remaining 114 studies date from 1989 to 2010. Our search strategy was limited to LICs and LMCs, and certain countries were prominent in the resulting database of evidence. A quality assessment was made on all items including the evaluation of both internal and external validity by means of standard tools. Internal validity concerns the accuracy of results; for example results could be inaccurate if samples were not selected randomly. External validity concerns the generalisability of the findings to the population.

Synthesis results

There are few published studies looking at interventions that specifically target the urban poor's access to and use of maternal and child health (MCH) services, and even fewer that use mortality indicators as one of their outcomes. No items were found that explicitly assessed the effectiveness of different models of service delivery to reduce maternal and infant mortality among poor urban populations. However it should also be acknowledged that studies that have been excluded from this analysis because they do not specifically focus on urban, poor populations will contain evidence on the effectiveness of different intervention models that could potentially be targeted at the urban poor. It is important to consider the extent to which these interventions could be applied to our target population.

Of the items returned, 56% were classified as individual clinical interventions, leaving 44% in the non-clinical category. Of the 'non-clinical' interventions, most consisted of systemic interventions such as provider models, information, audits, investment and scaling up, and financial protection. Of the non-clinical items, 26% included established groups of non-clinical interventions such as Kangaroo Mother Care and nutrition approaches such as breastfeeding promotion. Most of the studies that concerned purely clinical interventions – although pertaining to urban populations – are applicable in rural areas. Interest in our review focused mainly on the non-clinical findings – as these are judged to be closer to the wider conceptualisation of 'models of delivery' which has been key to implementation but less of a focus among researchers.

Conclusions and recommendations

Our analyses form a convincing case that there is a need for high-quality evidence on maternal and infant interventions that specifically target the urban poor. The existing evidence base is minuscule compared to the rapidly growing and large urban poor population. Much of the existing evidence is of poor quality, with little emphasis on baselines and follow-up studies, and almost no qualitative (how? why?) evidence to complement the limited quantitative (what?) data. This small evidence base is out of step with the growing interest in urban poor people and the size of this population. Interventions supported by the review are already present in existing WHO guidelines. However, there is a need for research that specifically addresses the effectiveness of different models of service delivery, including how sub-populations (e.g., urban poor) are targeted.

Although the evidence base appears limited, there are in fact a number of ways in which it might be strengthened in the short term. We suggest one way of strengthening the evidence base on the cost-effectiveness of different strategies to promote better access and use of maternal and infant health services. This would

be to retrospectively make use of data looking at the uptake and effectiveness of actions that help increase uptake from papers identified in this review, then estimate the costs of implementation, including their impact on the future use of health services or on other economic costs if mortality (and morbidity) were avoided.

1. Background

Summary

The global burden of maternal and infant deaths falls disproportionately on low income countries (LICs) and lower middle income countries (LMCs) and among the poorest within these countries.

Urban growth is changing population health, particularly among the urban poor.

The number of births taking place in urban areas in LICs and LMCs is increasing; services must accommodate thisbecause large populations and high population density in urban areas influence options for service organisation.

It is crucial to establish evidence-based ways of improving models of service delivery and access to and uptake of maternal and infant care.

This systematic review addresses the question:

'What are the effects of different models of delivery for improving maternal and infant health outcomes for poor people in urban areas in low income and lower middle income countries?'

1.1 Aims and rationale for the review

The Millennium Development Goals (MDGs) have focused global attention on significantly improving maternal and infant health. In 2008, 70 percent of around 8.8 million under-five deaths occurred during the first year of life (World Health Organization, 2010). Estimates suggest that there are around 350,000-500,000 maternal deaths per year (Ban Ki-moon, 2010) with 15 million more women suffering long-lasting injury or illness from preventable pregnancy-related causes (Ban Ki-moon, 2010) and many more suffering related mental morbidities. These figures represent improvements over the last two decades in some countries but further significant mortality reductions will be required to meet the MDGs' targets of reducing under-five mortality by two-thirds from 1990-2015 and reducing maternal deaths by three-quarters (United Nations, 2009) in the same timeframe.

The burden of maternal and infant deaths falls disproportionately on low income countries and lower middle income countries and among the poorest within these countries. The causes of maternal and infant mortality and morbidity are well established (Ronsmans and Graham, 2006) yet knowledge on effective management of conditions has not been translated into significantly improved outcomes because of a lack of resources and effective models of service delivery (Campbell and Graham, 2006; Filippi *et al.*, 2006). Urban populations are often assumed to have better access to health care than those living in rural areas. However, urban health systems in many LICs and LMCs have a weak to non-existent public health structure and lack uniform implementation of strategies and necessary infrastructures.

Sub-optimal health outcomes are evident among the urban poor with the lowest access to and use of health care facilities. With respect to maternity services, urban women tend to be more likely than rural women to give birth in health facilities. However, urban inequalities in maternal-newborn health care are huge in many poor countries (Matthews *et al.*, 2010). Poor quality of care in many urban facilities plays a significant role in counteracting the positive effects of skilled birth attendance (SBA) (More *et al.*, 2009a, 2009b). Given rapid urbanisation in

many LICs and LMCs, it is now crucial to establish evidence-based ways of improving models of service delivery and access to and uptake of maternal and infant care in order to improve maternal and child outcomes.

Levels of infant mortality are often lower in urban areas than in rural at the aggregate level (UNSD, 2008). However recent trends have shown mortality improvements in the rural areas and increases in the urban areas with the exception of a few South Asian countries (UNSD, 2008). Central American and central Asian countries often show a higher level of mortality in urban areas than rural. This is possibly due to the rapid urbanisation, which often occurs without appropriate planning for infrastructure and health services. The differences become even more striking when we consider the gap between the poor and the rich. While we have a more even distribution in rural areas, the inequality within urban areas is often striking. A recent study in sub-Saharan African (SSA) countries (Anyamele, 2011) showed a considerably higher level of infant mortality in rural areas, but also a high level of variation within urban areas when considering level of wealth. However, data on maternal mortality by residence is very hard to estimate due to the small numbers. One recent study by Matthews *et al.* (2010) shows how the urban advantage is almost non-existent when we account for wealth levels within areas. In urban areas, they remark that this is mainly due to poverty marginalisation, which prevents access to care.

Despite growing evidence of poor maternal and infant health outcomes and inequalities within urban areas of low income countries, a systematic analysis and synthesis of evidence as to effective models of service delivery is lacking. The aim of our study was to conduct a robust systematic review to address the question:

> *What are the effects of different models of delivery for improving maternal and infant health outcomes for poor people in urban areas in low income and lower middle income countries?*

Through the systematic review we aim to provide important information and draw out key recommendations for policy makers at international, national and sub-national levels.

1.2 Definitional and conceptual issues

1.2.1 The urban poor: who and where?[2]

Urban growth – including the absolute and relative number of urban dwellers and the physical expansion of urban areas – is 'reshaping' population health, particularly among the urban poor (Commission on Social Determinants of Health, 2008, p.4). By 2050, there will be an estimated 6.4 billion urban dwellers, compared to 3.4 billion in 2009 (UNHABITAT, 2010), and the global future has been described as a 'planet of cities' (Angel *et al.*, 2011).

By 2050 it is estimated that seven out of every ten people will live in a city, with almost all of this growth taking place in developing countries. It is estimated that one in three urban dwellers lives in a slum, meaning that an estimated 828 million people are currently living in informal settlements, producing so-called 'hidden cities' (UNHABITAT, 2010). More than 90 percent of slums are located in cities in developing countries, and those cities that are the fastest growing are most likely to have informal settlements. In sub-Saharan Africa, it is estimated that more than 60 percent of city dwellers inhabit slums (UNHABITAT, 2010).

2 Unless stated otherwise, all data are drawn from United Nations Department of Economic and Social Affairs (2010) and UNHABITAT (2010).

An estimated one-third of all urban residents are poor, representing one-quarter of the world's total poor (Baker, 2008; Ravallion *et al.*, 2007). Poverty is multidimensional and complex; its conceptualisation and measurement is beyond the scope of this review. Related debates accompany the conceptualisation and measurement of urban poverty (Baker, 2008), for example, discussions around how to account for the higher cost of living in urban areas in national-level poverty estimates. Evidence suggests that current poverty levels might underestimate the levels of urban poverty in low and middle income countries (Satterthwaite, 2004). Debates about the definition of what is 'urban' also affect estimates of urban poverty (Satterthwaite, 2007).

We know that there are fuzzy boundaries between urban and rural, boundaries that continually evolve – both planned and unplanned. Rates of expansion of urban land cover in LICs and LMCs are high, although the absolute amount of land cover accounted for by urban areas remains low. Whilst it is beyond the scope of this review to debate what is meant by urban, and our methodology takes an inclusive approach, the issues around types of urban setting are important, and reflected not only in the substantive findings, but also the volume of published work on different sorts of urban settings.

Concern is increasingly expressed about the low levels of research and policy attention to smaller cities (> 1 million and <10 million inhabitants), of which it is estimated there are 500 globally (Commission on Social Determinants of Health, 2008, p.60; Montgomery, 2008). Analyses suggest that smaller cities, despite the research focus on mega-cities (>10 million inhabitants), might have even higher rates of poverty (Baker, 2008; National Research Council, 2003).

The urban poor as a population sub-group are spatially and temporally heterogeneous (Mabogunje, 2007), even when fairly straightforward sub-groups are identified, such as urban natives or migrants (rural-urban and urban-urban). The characteristics of where the urban poor live are equally heterogeneous – neighbourhoods are not necessarily consistently poor (Montgomery and Hewett, 2005). Slum residents are not the only urban poor, although they do represent a spatial clustering of living conditions within any single city. As projected rates of urbanisation continue, even if the relative levels of urban poor remain constant, the absolute numbers will rise, making poverty an increasingly urban phenomenon.

1.2.2 Data on the health of the urban poor

Rapid urban growth in developing countries – both in terms of population and land coverage – places increased demands on already overstretched agencies to collect data from and about the urban poor. Even aggregate 'headcount' data can fail to keep up with the speed and location of population growth in many settings. In addition, we know that slum residents tend to be less likely to be included in censuses and surveys; they might want to remain hidden if their residence is illegal; slums are difficult places to send enumerators to work in; and slum households tend to be less likely to be included in routine mapping and listing exercises (World Health Organization, 2008; Shetty, 2011). Many urban poor can be characterised as 'hard to reach' populations from the perspectives of censuses and surveys.

Routine data dealing with the health of the urban poor, where they exist, tend to be aggregated, ignoring differentials within cities and between neighbourhoods. There are increasing calls for disaggregated data to be available (Harpham, 2009; UNHABITAT, 2010, p.xiii). Similarly, health information that is produced tends to be aggregated, ignoring health and wealth differentials within cities and between neighbourhoods.

Cross-sectional surveys such as the Demographic and Health Surveys (DHS), National Family Health Survey (NFHS) in India, and Multiple Indicator Cluster Surveys (MICS) are an important source of data that allow disaggregation, for example, by wealth quintile of urban populations. These sorts of analyses have driven much of the bulk of descriptive evidence that exists about the health of the urban poor (Hazarika, 2009; Antai and Morad, 2010; Matthews *et al.*, 2010).

Whilst an important source of disaggregated information for those settings where there are no other data sources, this sort of approach is not without its critics. Montgomery (2009) outlines three major shortcomings of reliance on these sorts of datasets and analyses: low reliability of estimates of health among the poor in any given city; insufficient spatial information to identify small- and medium-sized cities; and, over-reliance on proxy variables to construct measures of living standards due to the absence of information on income or consumption expenditures.

There are calls (Harpham, 2009) for greater investment in longitudinal, prospective studies that deal specifically with the urban poor. Demographic Surveillance Systems (DSS) such as those covered by the In-Depth network[3] are one such source, and in Africa include sites such as the Nairobi Urban Health and Demographic Surveillance System[4] in Kenya and Bandim Health Project[5] in Guinea Bissau, which are fully established and producing data and research. A new DSS site in Ouagadougou[6] has started to collect data which are not yet available for analyses. Emergent research agendas focusing on health in LICs include the Urban Health Resource Centre in India[7] (Urban Health Resource Centre, 2006). Specific online foci for gathering relevant research have recently been developed, including the Measurement, Learning and Evaluation Project for the Urban Reproductive Health Initiative.[8]

1.3 Policy and practice background

1.3.1 What are models of service delivery?

Models of service delivery are concerned with how interventions are delivered. They specify the component intervention package, target groups and means of distribution (Campbell and Graham 2006). Their impact depends not only on the effectiveness of the package of interventions, but also on the coverage achieved by the means of distribution, its uptake by the target population, and quality (Campbell and Graham 2006). Furthermore, models of service delivery are influenced enormously by context and must consider the local epidemiology; economic, geographical and cultural barriers; and the local health system's infrastructural and human resource capacity (Lawn *et al.*, 2009).

Whilst the medical solutions for preventing maternal and infant mortality are known, delivering these solutions is a considerable challenge. Despite variation across regions, most maternal deaths in LICs and LMCs are due to a handful of causes, including haemorrhage, hypertensive disorders, sepsis/infections,

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[3] http://www.indepth-network.org/ (accessed 17 January 2012)

[4] http://www.aphrc.org/insidepage/?articleid=470 (accessed 17 January 2012)

[5] http://www.bandim.org/ (accessed 17 January 2012)

[6] http://www.issp.bf/OPO/ (accessed 17 January 2012)

[7] http://www.uhrc.in/ (accessed 17 January 2012)

[8] http://www.urbanreproductivehealth.org/ (accessed 17 January 2012)

obstructed labour, and in certain regions, unsafe abortion and HIV/AIDS (Khan *et al.,* 2006). Maternal deaths are clustered in the period during labour, delivery and the immediate postpartum period because complications arise in around 15 percent of births in any context, which are largely unpredictable and can rapidly become life-threatening (Ronsmans and Graham 2006; White Ribbon Alliance, 2010).

Maternal and infant outcomes are closely connected. A substantial proportion of infant deaths are clustered in the early neonatal period, particularly in the first 24 hours (Lawn *et al.,* 2005). Causes of death include obstetric complications before or during the birth and their management, preterm births and congenital abnormalities. Harmful practices after birth can also lead to severe infections in the neonatal period (World Health Organization, 2006). The epidemiology of infant deaths is different after the first month of life, however, when pneumonia, diarrhoea, malaria and vaccine-preventable conditions become the main causes (Lawn *et al.,* 2005; World Health Organization, 2006).

Clearly, major reductions in maternal and neonatal deaths depend on the functioning of the whole health system because no single intervention can address the diverse range of causes, and many causes have medical solutions that require prompt and skilled action (Koblinsky *et al.,* 1999). In contrast, many infant deaths in the post-neonatal period can be prevented through public health or vertical programmes, along with clinical case management for episodes of illness (Lawn *et al.,* 2005). Models of service delivery for reduction in maternal and infant mortality are thus complex and vary across several dimensions.

There is a general consensus that care during the intrapartum period is of key importance given the epidemiology of maternal and early neonatal deaths, but antenatal care, postnatal care, newborn baby and child care, and reproductive health care may also contribute to mortality reductions (Ronsmans and Graham, 2006; Kerber *et al.,* 2007). Types of intervention may be clinical and/or non-clinical in focus and packages may include information, financial assistance, community mobilisation, commodities, drugs or health care. Models also differ according to the means of distribution: where the service is provided and by whom. For example, services may be delivered to individuals at home, at primary health care facilities or at hospitals by various health professionals or non-professionals, or to whole communities through mass media. The level of involvement of public, private and non-governmental sectors in distribution will vary between countries (Baqui *et al.,* 2008; Bhattacharyya *et al.,* 2010). However, there is interdependence between the means of distribution and the content of intervention packages (Campbell and Graham, 2006). Finally, subgroups of the population may be targeted or the aim may be to reach the whole population.

1.3.2 Models of service delivery and the urban poor

A review focusing on the urban poor population is necessary because, despite difficulties in generalising across settings, there are specific characteristics of the urban environment, population and health system that have potential implications for models of service delivery. Rapid urban population growth means that the number of births taking place in urban areas in LICs and LMCs is increasing, and services must accommodate this. Furthermore, large populations and high population density in urban areas influence options for service organisation. Many of these births are among the urban poor, a large proportion of whom live in slum areas that have tended to be underserved by public services (Matthews *et al.,* 2010). Given the considerable inequality in urban areas in many regions, decisions need to be made on how services can best be prioritised to reach the poorest and most vulnerable segments of the population to reduce maternal and infant deaths.

For some causes of maternal and infant deaths, the urban environment poses specific risks. For example, the distribution of factors linked with maternal mortality, such as malnutrition, obesity, age at first birth and fertility, may differ in urban areas. Certainly, HIV/AIDS, which makes a substantial contribution to both maternal and infant mortality in SSA, disproportionately affects urban areas (Khan *et al.*, 2006; UNAIDS and World Health Organization, 2009). For infants in particular, the pollution in many cities, and the lack of sanitation and overcrowding in slum areas, also raise certain health risks (Hardoy *et al.*, 2001). These epidemiological considerations need to be addressed in the development of intervention packages.

Demand may also differ in urban areas. Urban living is perceived to be associated with modernity; levels of education tend to be higher; and urban areas may provide greater opportunities for exposure to health-related information (More *et al.*, 2009a, 2009b). Nonetheless, the 'urban poor' are heterogeneous both within and across urban areas. Alongside socio-economic inequalities, people from diverse cultural backgrounds live in proximity, with potential implications for both health-related needs, expectations and demands. In particular, rural-urban migrants may be influenced by their present context whilst also retaining influences from their previous context. Traditional social connections may be broken and new ones formed when an individual or group migrates, which may have positive or negative effects on health risks, health-related attitudes and behaviour, and health-related support (Harpham, 2009). This diversity in urban areas must be addressed in the development of models of service delivery.

Whilst the environment and characteristics of the population in urban areas have implications for models of service delivery, implications also arise from the existing health system. Urban areas tend to be served by a wide range of providers (Parkhurst and Rahman, 2007; More *et al.*, 2009a, 2009b). In particular, private health services are prominent in many LICs and LMCs, which are even used by the poor when circumstances allow (Matthews *et al.*, 2010; Bhattacharyya *et al.*, 2010). In these settings, public sector provision increasingly deals with the poorest and most vulnerable urban residents (Matthews *et al.*, 2010).

1.4 Research background

1.4.1 What is different about the health of the urban poor?

Much is known about the descriptive differences between urban poor health (versus urban non-poor or rural) in developing countries, and reviews include: Ruel *et al.*, 1999; McMichael, 2000; Harpham and Molyneux, 2001; Galea and Vlahov, 2005; Montgomery and Ezeh, 2005; Harpham, 2009. Debates continue about the characteristics of urban health: advantages, disadvantages, penalties, urban sprawl, and double burden of communicable and non-communicable diseases (Agyei-Mensah and Aikins, 2010).

Within an individual country, maternal and infant survival is generally better on average in urban than in rural areas (Dye, 2008; Matthews *et al.*, 2010), although the National Research Council (2003) shows that aggregate urban-rural differences in health outcomes can diminish once wealth is controlled for. Indeed, with the exception of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), 'in most low- and middle-income countries, the urban advantage in terms of average health levels is too well documented to dispute' (Montgomery, 2009, p.5).

The comparison of urban with rural is a crude one – and masks potentially different urban (dis)advantages dependent on what is being studied (Harpham, 2009). The

heterogeneity of urban areas and populations means that averages based on the aggregate of rural-urban can disguise broad variations, not just in terms of health outcomes, but also in terms of health systems and services. Recent analyses suggest that changing urban populations are eroding any urban health advantage and replacing it with an 'urban penalty' (Matthews *et al.*, 2010). Cities can raise some health risks, not least because rapid urban growth in many LICs and LMCs has exceeded the capacity of health systems to serve rapidly growing urban populations. It could also potentially mask a service located in an urban agglomerate but used by a large rural population, hence not specifically targeted at urban populations.

Rice and Rice's (2009) analyses of aggregate national-level data show crude but statistically significant relationships between the infant mortality rate (IMR) and maternal mortality ratio (MMR) and the level of urban slum prevalence for 99 countries. They point out that 'urban slum prevalence exhibits moderately strong and statistically significant deleterious associations with the mortality indicators, net the influence of level of economic development and pace of urbanization', and conclude that their findings support the existence of an urban penalty for slum population, especially women.

1.4.2 Poor urban women and infants: lower chances of survival?

Comparing urban and rural populations

- When compared with their rural counterparts in the aggregate, urban dwellers tend to have, on average, better access to health care services. This can be reflected in lower levels of maternal and infant mortality for urban compared with rural settings in many countries.
- Analysis of 90 DHS showed lower levels of child mortality in urban than rural populations, with similar differences by residence for several health indicators (National Research Council, 2003).
- In Latin America and the Caribbean, infant mortality is about the same among the rural and urban poor (Fay, 2005).
- The poorest migrants from rural areas and slum dwellers may have maternal, newborn and child mortality rates as high as or even higher than the rural poor (Madise et al., 2003; Madise and Diamond, 1995; Van de Poel et al., 2007).
- Much of the aggregate difference in maternal and infant mortality between urban and rural areas is attributable to greater access to health care services available to urban residents.

Comparing within urban areas by wealth status

- World Health Organization (WHO) analyses of DHS data for 2000-7 show a clear gradient in the rate of under-five mortality by wealth quintile for Africa, Asia, and the Americas, with highest risks for the poorest urban wealth quintile and lowest risk for the wealthiest quintile (UNHABITAT, 2010, Figure ES.2, p.xiv).
- Analyses of the Indian National Family and Health Survey (UNHABITAT, 2010, Box 7.1, p.84) show that the poorest urban wealth quartile has an IMR of 54.6/1,000 compared with 35.5/1,000 among urban non-poor.
- Work by the African Population and Health Research Centre (APHRC) (2002a, 2002b) estimates IMR to range from 164/1,000 in Embakasi slum, to 91/1,000 in

informal settlements on average, to <10/1,000 in high-income areas of Nairobi. The nationally comparable urban (excluding Nairobi) and rural IMR are 57/1,000 and 76/1,000, respectively.

- Slum dwellers compare unfavourably with other urban sub-groups with respect to mortality in both Nairobi and Mumbai.
- The disaggregation – usually based on availability of DHS or MICS data – of analysis by wealth status in urban areas in developing countries tends to be unable to incorporate data that show the complexities of the implications of who is 'poor' and 'non-poor'. Montgomery (2009) gives this useful example: non-poor households in urban neighbourhoods that lack drinking water and sanitation face a daily assault of health threats that household income alone cannot always fend off. Even those who can pay for health care may receive services of such low quality that they do little to restore health.

Comparing urban and rural and wealth status

Fewer studies include analysis which compares urban-rural and rich-poor status:

- Garenne's (2006) analysis of 47 DHS surveys (1986-2000) shows disaggregated early age (before fifth birthday) mortality by urban-rural and rich-poor status. The highest rates of mortality aggregated across countries were found in the poorer rural grouping, followed by the poorer urban grouping.

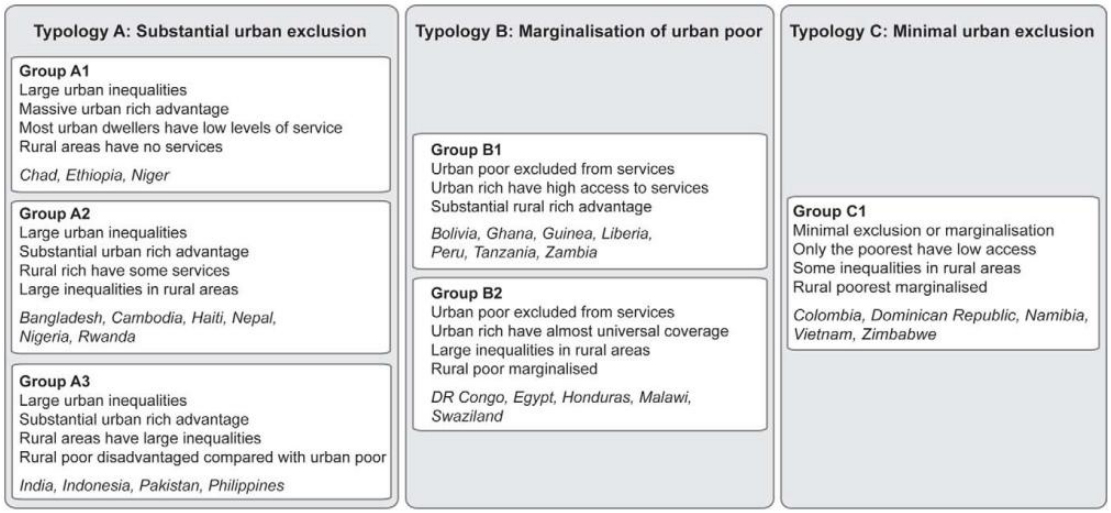
Why are poor urban women and infants disadvantaged in terms of risk of dying?

- Explanations for between- and within-place of residence differentials in maternal and infant mortality outcomes are complex. For example, the mortality risk of a poor individual living in an urban slum is likely to be attributable to both household-level poverty and the community-level spatial concentration of poverty in the slum itself. The urban poor are likely to be least well served in terms of access to health services, but the absence of disaggregated data means that relatively little is known about differentials in accessing services by neighbourhood, the effectiveness and quality of those services notwithstanding.
- Health and social services in urban areas have not kept pace with urban population growth (Montgomery, 2009; Fotso *et al.*, 2007; Ziraba *et al.*, 2009a, 2009b).
- WHO calculations (2010, p.63 Figures 5.6-5.7) of projected trends towards achieving MDG5 (SBA) disaggregated by urban wealth quintile for Bolivia and India show the least progress to date, and therefore the most rapid improvement required, for the poorest urban wealth quintile.
- Poor urban women are more likely to have a SBA than poor rural women, although there is not much difference between the percentage of women with SBA in the richer strata (Channon *et al.*, 2010, p.83).
- Wang'ombe (1995) suggests that the unavailability and inaccessibility of maternal and child health (MCH) services in unplanned urban slums in rapidly growing cities has resulted in poor child health in these settlements.
- Despite good geographic access, slum residents can be unable to access nearby health services. Women in slum communities can find care difficult to access even though a well-functioning health infrastructure is located nearby, and in

some cases the urban poor have less access to services than people who live in rural areas (Gupta *et al.*, 2008; African Population and Health Research Center, 2002a, 2002b; UNHABITAT, 2006). In some cities, this inaccessibility might be explained by the poor urbanites' spatial concentration in areas outside 'official' city zones or limits.

- In a sample survey of poor urban street and slum dwellers in Calcutta, Ray *et al.* (2001) found that of 108 mothers who gave birth in the previous year, 40 percent received three or more antenatal checkups, and only 16 percent received postnatal care. The authors of the study suggest that urban health programmes are inaccessible to poor migrants as they are not recognised as residents of Calcutta (Channon *et al.*, 2010, citing Ray *et al.*, 2001).
- Cities create an especially complex range of factors that can influence health outcomes (KNUS, 2008, Fig 5, p.9). Matthews *et al.* (2010) develop a typology – based on analyses of DHS – of urban coverage of maternal and newborn services (Figure 1.1). This typology begins to unpack some of the heterogeneity in the experience of poor urban populations in accessing services at the national level.

Figure 1.1: Typologies for urban coverage of maternal-newborn services



Source: Fig 2, Matthews *et al.*, 2010.

1.5 Objectives

Before presenting the methodology and results of our systematic review, it is important to consider the focus and scope of our research question, 'What are the effects of different models of delivery for improving maternal and infant health outcomes for poor people in urban areas in low income and lower middle income countries?' Addressing this question provides useful lessons for decision makers as both positive and negative effects are considered. Previous knowledge of this area led us to conclude that a systematic review focusing on effective models would provide a tighter and narrower review but with less useful findings from which to draw policy recommendations. Our protocol based on this revised question was agreed by the funding body, DFID, and reviewed by two external expert reviewers.

Maternal and infant health of poor people in urban areas may be improved through many different mechanisms. Evidence pertaining to different 'models of service delivery' is vital but, based on previous knowledge, also likely to be scarce. Our

review focused on explicit evaluations of interventions aimed at improving health outcomes for poor people in urban areas. We did not seek to exclude any particular types of intervention and as such our review was designed to identify evaluation of models of delivery but also discrete interventions that might be part of a wider model of delivery. These could include clinical or non-clinical interventions, such as changes in financing, regulation and service organisation. They might also range in focus from the individual to health systems reform. The review aimed not only to draw lessons from the stated effect of interventions, but to provide causal chain analysis for these effects as well as to draw lessons from how, where, and why different models of delivery showed effects.

Given the likely paucity of evidence from urban areas in LICs we also aimed to include LMCs and to be non-restrictive in defining poor and urban populations. The methodology and appendices set out exact definitions, but 'urban' was essentially defined as 'non-rural'. With regard to poverty, we sought to include any study making explicit reference to models of delivery for identified poor or socio-economically disadvantaged groups at the sub-national level, irrespective of the definition of poverty. We feel that our inclusive approach is most appropriate as a first measure in establishing the evidence base for the effects of interventions aimed at improving maternal and infant outcomes in poor urban populations.

2. Methods used in the review

Summary

The types of studies, interventions, outcomes and participants for inclusion are described.

Our review team, including information scientists and information retrieval experts, developed a search protocol that was subject to external peer review. Our search strategy was limited to LICs and LMCs, and certain countries were prominent in the resulting database of evidence.

Quality checks – both in terms of internal quality assurance processes and the assessment of the quality of included studies – are described.The synthesis of evidence includes both a wider narrative synthesis and a detailed causal chain analysis of high-quality items. Decisions about what the results meant for policy, practice and research were based on discussions within the review team, set against the wider knowledge base.

2.1 User involvement

2.1.1 Approach and rationale

The protocol was finalised following review from the DFID and two additional experts in field.

In order to engage a wide range of stakeholders, the following methods were/will be used:

- Online publishing of: the protocol; the final report; a research brief; and a web summary.
- To maximise exposure, links to the published report will be established with major e-lists and websites
- Publication of articles in peer-reviewed journals
- Presentation and networking of findings at academic conferences

2.2 Identifying and describing studies

2.2.1 Defining relevant studies: inclusion and exclusion criteria

Types of study
The following types of intervention study were included in the analysis:

- Randomised controlled trials
- Non-randomised controlled trials
- Observational studies with control groups
- Longitudinal time series studies
- Systematic reviews of these interventions
- Economic evaluations and modelling studies of relevant interventions
- Qualitative evaluations looking at implementation of relevant interventions

Types of intervention
Interventions were broadly defined as actions concerned with improving the access, utilisation or effectiveness of maternal and infant health services in areas serving urban poor populations. These interventions could be concerned either with clinical or non clinical services. Studies that did not clearly distinguish effects from other non-targeted health interventions, such as the provision of potable water, were excluded.

Types of participant
Mothers and infants up to the age of 24 months. Studies had to address specific poor populations in urban, semi-urban or peri-urban settings. Studies that estimated only maternal morbidity (other than sever acute maternal morbidity – SAMM) or only infant morbidity were excluded. While it should be acknowledged that studies set in rural areas may well be transferable to urban-poor settings, in this review we excluded these studies that only dealt with this population from our analysis. Studies that dealt only with non-poor urban populations were also excluded from the analysis.

The World Bank definition of low income and lower middle income countries was used, with the additional restriction that countries in Europe were excluded from the analysis (World Bank, 2011). It should however be acknowledged that there may be interventions in upper middle income countries, particularly those that have high levels of income inequality that could be used in low and middle income country settings.

2.2.2 Identification of potential studies: search strategy

Our review team, including information scientists and information retrieval experts, developed a search protocol that was subject to external peer review and agreement of the study funders for approval. Our search includes major databases that cover literature on this topic; these cover both English and non-English language material, including specialist health and development databases, as well as those focusing on specific geographical (Box 2.1).

Box 2.1: Electronic databases searched

African Index Medicus

African Journals On-Line

ASSIA (Applied Social Sciences Index and Abstracts)

Campbell Collaboration

Cochrane

Database of Abstracts of Reviews of Effectiveness (University of York)

Office of Health Economics, Health Economic Evaluation Database

NHS Economic Evaluation Database (University of York)

Econlit

EMBASE

Geobase

Global Health

Health evidence.ca

IBSS
LILACS
Pubmed/Medline
PAIS
POPLINE
PsychINFO
R4D
Western Pacific Region Index Medicus

In addition to the databases included in our search protocol, a number of additional databases were examined and were excluded on the basis of lack of functionality, country or topic coverage, and in a few cases because of a lack of access (Appendix 2.9). Relevant studies were identified by searching electronic databases, combining terms for (1) included maternal and infant health outcomes and (2) included countries. We decided not to narrow down by urban terms, but instead to determine whether studies took place in an urban environment through analysis of abstracts and the keywords used. A full detailed list of terms used is provided in Appendix 2.2. Editorials, letters, commentaries, book reviews and non-systematic literature reviews were excluded from the analysis.

Given the very broad nature of this review, we relied on a wide range of appropriate keywords, descriptors and indexing terms, e.g. the medical subjects headings (MeSH) keywords for the US National of Library PubMed/Medline database, and descriptors, where these we available. In databases where such terms were limited we had to rely on a broad range of free text terms. Relevant search terms were identified both from the expert input of members of the research team, analysis of terms used in papers identified in handsearches and pilot database searches, as well as analysis of keyword and indexing hierarchies where available in the different databases searched. Details of the databases searched and the search strategies used, specifying keywords, descriptors and free text terms are in Appendix 2.2.

One limitation of our search however, was that we did not replicate our search strategy in terms other than English, which potentially could have increased the number of relevant papers found in some databases that carry more non-English language journals. We did not conduct a specific search for conference proceedings, theses or other dissertations.

Google Advanced Search[9] was used to search organisation websites (Appendix 2.3). These included some government websites for overseas development aid departments, as well as international agencies (Box 2.2). The search strings were 'infant mortality' and/or 'maternal mortality'. Only items in English were sought, and the first 20 items were reviewed for relevance. All of the websites that were searched have been tagged as *LSEDFID_SysRev2011* in Diigo[10] to facilitate sharing.

[9] http://www.google.co.uk/advanced_search

[10] http://www.diigo.com/user/LSE_DFID

Box 2.2: Websites searched

AFD (Agence Française de Développement)

APHRC (African Population and Health Research Center)

Center for International Health and Development

Cochrane LMIC

COOPITA (Cooperazione Italiana allo Sviluppo)

DFID (UK Department for International Development)

EADI (European Association of Development Research and Training Institutes)

ELDIS

EU Development (European Commission Development and Relations with African Caribbean and Pacific States)

EU Humanitarian Aid and Civil Protection (European Commission Humanitarian Aid and Civil Protection)

EuropeAid (European Commission Cooperation Office)

Family Care International

Irish Aid

London School of Hygiene and Tropical Medicine library

Measurement, Learning and Evaluation Project for the Urban Reproductive Health Initiative

NORAD (Norwegian Agency for Development Cooperation)

Pan American Health Organisation Library

PMNCH (Partnership for Maternal, Newborn and Child Health)

R4D (Research 4 Development)

SDC (Swiss Agency for Development and Cooperation)

SIDA (Swedish International Development Cooperation Agency)

UNDP (United Nations Development Programme)

UNFPA (United Nations Population Fund)

UNHCR (United Nations High Commissioner for Refugees)

UNICEF (United Nations Children's Fund)

Urban Health Resource Centre

USAID (United States Agency for International Development)

WB (World Bank)

WHO (World Health Organization)

MLE Programme

Open SIGLE

WHO International Trial registry portal

A handsearch of 11 journals was performed from 2008, electronically where possible, so as to include papers accepted and available online pre-publication but not yet in print (Appendix 2.4). When the electronic version was not available, relevant shelves at the British Library of Political and Economic Science were handsearched.

Due to time constraints, we restricted studies to those published from 1987 onwards, the year of the Nairobi Conference on Safe Motherhood (Cohen, 1987).

References produced by electronic database searches were stored into a first EndNote bibliographic database and duplicate records were discarded. The approach designed by the Evidence for Policy and Practice Information Co-ordinating Centre (EPPI-Centre), Social Science Research Unit, Institute of Education, University of London (Gough and Elbourne, 2002) and its program EPPI-Reviewer 4 were used to record extracted data from eligible articles and make them available for analysis.

2.2.3 Screening studies: applying inclusion and exclusion criteria

In the first stage, titles and abstracts were screened for inclusion, using four short questions on key inclusion criteria (country, urbanity, evaluation of maternal and infant interventions) (Box 2.3).

Box 2.3: Screening questions

Questions	**Answers**
Is it a study in a country in the list of WB LICs and LMCs (from Africa, Asia, Latin America and the Caribbean)?	Yes/no/unclear
Does the study include poor, urban populations?	Yes/no/unclear
Is it a study dealing with evaluation of MCH interventions?	Yes/no/unclear
Do the data deal with access to, utilisation of, or effectiveness of MCH interventions?	Yes/no/unclear

Full texts were obtained for studies screened for inclusion and stored in a second EndNote bibliographic database. In the second stage, full texts were screened for inclusion, using all inclusion and exclusion criteria (Appendix 2.1). References meeting all inclusion criteria were imported into EPPI-Reviewer 4[11] for coding. Excluded references were stored in a third EndNote bibliographic database. Interesting references excluded during the first or second stage were stored in a separate EndNote bibliographic library for discussion. References with full text in foreign languages (other than English, French, Spanish or Italian) were stored into a separate EndNote bibliographic library for record keeping.

References from websites searches were managed using the bookmarking tool Diigo.[12] The first 20 items of each website search were compared with records stored in the first EndNote bibliographic database. Records not already found through electronic database searches were screened for inclusion following the first and the

[11] http://eppi.ioe.ac.uk/cms/Default.aspx?alias=eppi.ioe.ac.uk/cms/er4

[12] http://www.diigo.com/user/LSE_DFID

second stage previously described for electronic databases. References from handsearching were compared with records stored in the first EndNote bibliographic database and screened for inclusion, as for references from websites searches.

2.2.4 Characterising included studies

We first created and entered into EPPI-Reviewer 4 a coding tool to extract and record information on generalities, context, intervention, study design, outcomes, findings, comments, quality assessment and meta-analysis inclusion (Appendix 2.5).

2.2.5 Identifying and describing studies: quality assurance process

Two reviewers screened the results of searches independently. Before starting screening, a cross-check on a sample of 100 references was conducted to test for inter-reviewer variability, and where there was disagreement on inclusion, reviewers consulted with each other until consensus was reached. When consensus could not be reached, a decision was made after discussion by the team as a whole.

Included studies stored in EPPI-Reviewer4 were randomly allocated to reviewers for coding. Reviewers coded the results of searches independently. A cross-check on coding was conducted to test for inter-reviewer variability, and where there was disagreement on inclusion, reviewers consulted with each other until consensus was reached. When consensus could not be reached, a decision was made after discussion within the team.

2.3 Methods for synthesis

2.3.1 Assessing the quality of studies

We reviewed the quality for quantitative and qualitative studies making use of new revised guidelines for both quantitative and qualitative studies published by the National Institute for Health and Clinical Excellence's Centre for Public Health (2009). In the case of quantitative studies, these checklists (Appendix 2.6) allowed us to separately make an assessment of internal and external validity using objective criteria. In terms of external validity, we assessed whether the source population or study area was well described, whether the eligible study population was representative of the study population or study area and finally whether the actual participants were representative of the study population. We evaluated, for example, whether studies used theoretical perspectives, had clear aims and discussed the limitations and possible biases. Most of the evaluation of the methods concerned: whether the randomised controlled trial or the baseline of quantitative or review methodologies were laid out clearly, for instance, the methods of randomisation, participant blinding, sample size based on power calculations to detect significant effects; and whether the conclusions were appropriately justified by the methods and data. If most of these criteria were fulfilled, then the analysis would be judged to have a high degree of internal validity (++); if some of the criteria had been fulfilled, then it would be coded as (+), whilst those studies where few criteria were met would be coded as (-).

In the case of qualitative studies, the focus was on whether a theoretical approach could be identified, and whether a clear explanation and justification for the study design, and information on data collection methods, contexts and discussion of conclusions and findings were provided, using NICE (2009) guidelines (Appendix 2.7). Studies would be rated as (++) if they fulfilled most criteria appropriately, (+) for some criteria and (-) if few criteria were met. In addition, we made use of a combination of criteria from two different economic evaluation checklists for economic studies conducted prospectively or retrospectively alongside effectiveness studies (Drummond and Jefferson, 1996; Evers *et al.*, 2005). A separate checklist

(Philips *et al.*, 2004) was available to assess the quality of economic evaluations based on a synthesis of effectiveness data from a range of papers and the construction of different forms of economic evaluation (Appendix 2.8).

2.3.2 Overall approach to and process of synthesis

The approach to synthesis was driven by the research question, the types and quality of studies and the data included in the review. Heterogeneity of study design, population and intervention precluded statistical meta-analysis. The most appropriate approach – a textual narrative synthesis – was conducted. Because our review question involves two linked but distinct populations – mothers and infants – we have structured our review accordingly. For a subset of high-quality items, we conducted a causal chain analysis, also separated according to whether the outcome was maternal or infant mortality.

2.3.3 Selection of studies for synthesis

The narrative synthesis includes all eligible studies on the basis of the inclusion/exclusion criteria. The causal change analyses are restricted to studies identified as high quality.

2.3.4 Selection of outcome data for synthesis

Outcomes included maternal and infant health outcomes: maternal, infant, neonatal, perinatal, post-neonatal mortality, and still-birth; and severe acute maternal morbidity (SAMM) (haemorrhage, dystocia, hypertension, sepsis, incomplete abortion, Caesarean section (CS), hysterectomy and blood transfusion) (World Health Organization, 2011b).

This review focuses on maternal and infant mortality outcomes. Process indicators, such as skilled care at birth, are often used as substitutes for mortality outcomes whose measurement poses considerable challenges. However, mortality outcomes are not necessarily improved where gains in individual process indicators are not accompanied by broader changes (Koblinsky *et al.*, 1999). A focus on mortality outcomes is thus crucial, particularly in areas where the mortality burden is high (Campbell and Graham, 2006; Bhutta *et al.*, 2008; Lawn *et al.*, 2009).

2.3.5 Synthesis of evidence

All eligible studies were included within the qualitative analysis to establish a detailed picture of the available evidence. We first analysed the data using EPPI-Reviewer 4 and generated comprehensive tables for each code. All tables were then exported and merged in Excel[13] to produce a unique results table.

Narrative synthesis was the principal approach used. Eligible studies were grouped into type of interventions – broadly grouped into clinical and non-clinical – as described later on in the report. Findings were analysed within each category for the two main target populations: mothers and infants, including neonates. While most systematic reviews focus on synthesising evidence on effectiveness from quantitative research, we wanted to develop the contribution that can be made by different types of evidence, including that involving qualitative data.

In addition, causal chain analysis was performed on included studies identified as high quality to allow the extraction and illustration of the casual path emerging from our review, linking reasoning for intervention, with experience, implementation and sustainability. We used an approach based on White's (2009) theory-based impact evaluation, and drawing on the realist review approach of Pawson *et al.* (2005),

[13] http://office.microsoft.com/en-us/excel/

using qualitative analysis to attempt to provide an analysis of how and why complex interventions can work (Lewin *et al.,* 2009). For each item included in the causal chain analysis, we identify the root causes of the issue, the intervention, the final outcome(s) and the intervention sustainability.

2.4 Deriving conclusions and implications

Decisions about what the results meant for policy, practice and research were based on discussions within the review team, set against the wider knowledge base.

3. Search results

Summary

The searches returned 9,025 potentially relevant items of evidence, 98% of which were excluded after reviewing titles and abstracts.

We did not identify a single item that both had a qualitative focus and also had a discussion of change in mortality outcomes

31 per cent of the included quantitative studies were identified as 'low quality'.

Our causal chain analyses are restricted to medium- and high-quality items only. We assessed item quality after completion of the searches, and to avoid exclusion of potentially valid items, quality was not part of the inclusion criteria.

Of particular note was the lack of clarity or depth surrounding the ethical conduct of research that involved human subjects.

Electronic databases searches produced over 9,000 potentially relevant papers. All searches were downloaded into EndNote[14] and duplicates were excluded. This left 7,324 records to be examined. Two reviewers systematically screened all references by title/abstract using the screening short questions: the majority of papers were discarded and the remaining 703 references were downloaded into another EndNote library and full text obtained. After multiple searches, we were unable to locate 16 references (Appendix 3.3).

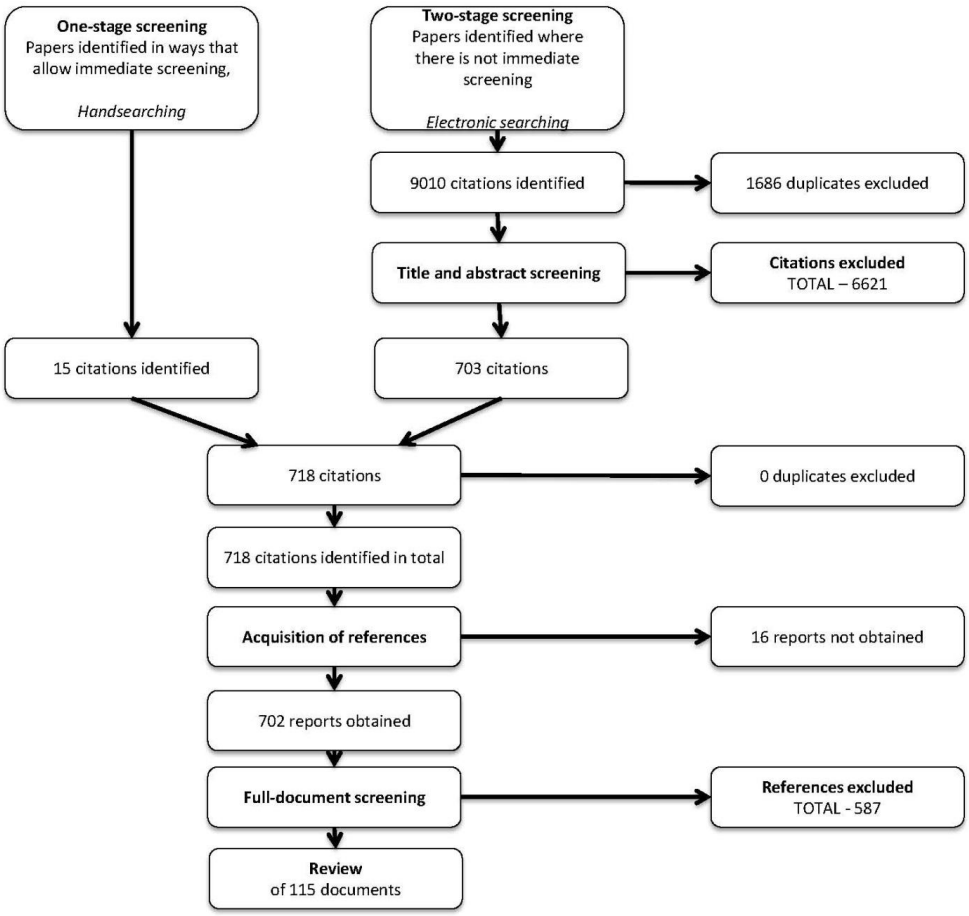
3.1 Studies included from searching and screening

Full-text references were screened for inclusion/exclusion criteria: 114 were included in the final review and downloaded into EPPI-Reviewer 4 for coding. Articles were excluded because they were published in a foreign language other than English, French, Spanish or Italian, they did not present separate outcomes for urban and rural populations, were editorials/commentaries/book reviews/literature reviews, or did not present data on our outcomes of interest (Appendix 3.2). Searches of websites did not lead to new references. Handsearching journals produced 15 new references, all successively discarded during the full-text screening. The screening cross-check, to test for inter-reviewer variability, resulted in final agreement rates between 82 and 92 percent.

Figure 3.1 provides a detailed representation of the search strategy and review process. Separate appendices (3.1 and 3.2) detail included and those excluded after full-text screening, respectively. Additional appendices (3.4 and 3.5) list interesting references excluded during the first or the second stage and references with full text in languages other than English, French, Spanish or Italian.

[14] http://www.endnote.com

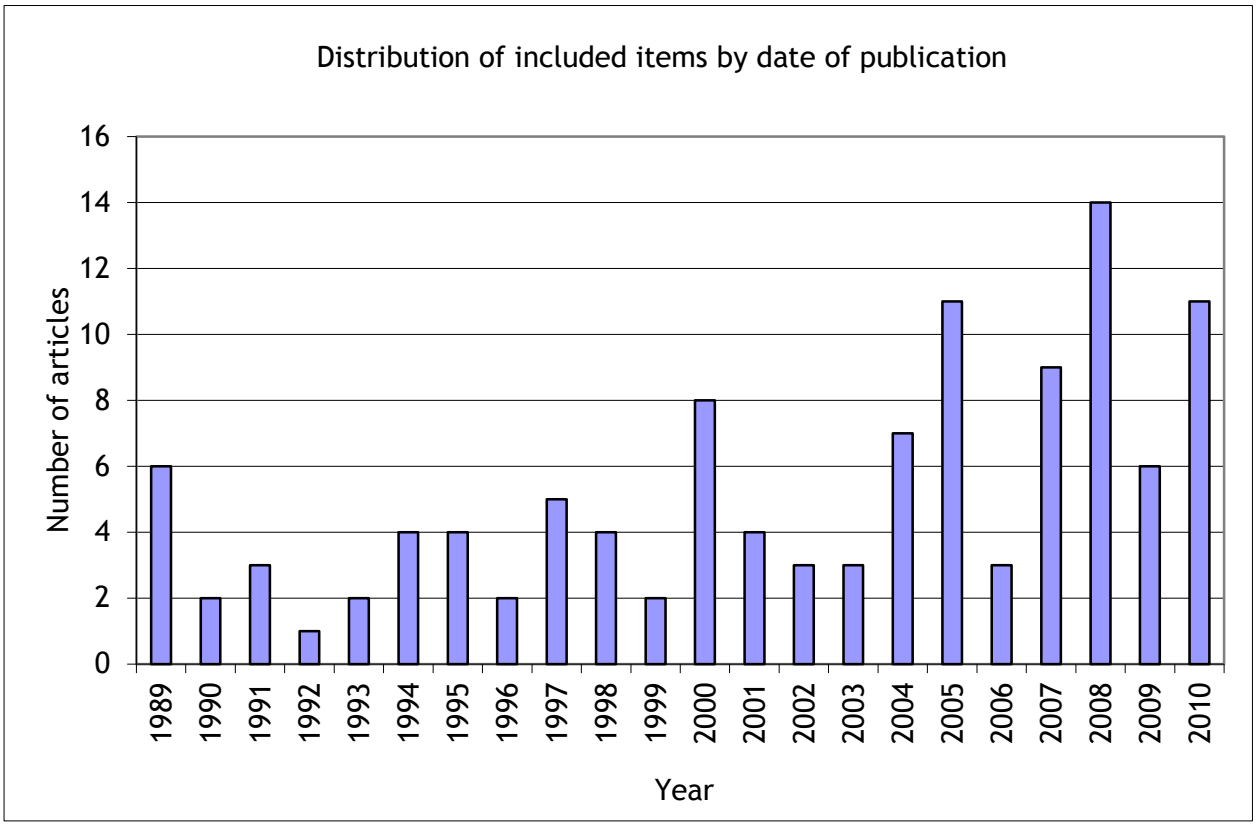
Figure 3.1: Filtering of papers from searching to map to synthesis



3.2 Details of included studies

The searches returned 9,025 potentially relevant items, including 9,010 from database searches and 15 from handsearches. The majority (98 percent) of papers were excluded after reviewing titles, and the abstracts of the remaining 114 items were downloaded into EndNote. All included studies date from 1989 (Figure 3.2).

Figure 3.2: Distribution of included studies by publication date



Our search strategy was limited to LICs and LMCs, and the distribution of items included in the review reflects clustering of evidence at the country level. For example, 56 percent of the included items from sub-Saharan Africa are accounted for by items from just two countries, Nigeria and Guinea Bissau (Table 3.1).

Table 3.1: Country distribution of included items

Region	**Country**	**N***
East Asia and Pacific (10%)	China	5
	Indonesia	3
	Papua New Guinea	1
	Thailand	3
Latin America and Caribbean (2%)	Guatemala	1
	Haiti	1
	Nicaragua	1

Middle East and North Africa (8%)	Egypt	6
	Jordan	3
	Tunisia	1
South Asia (24%)	Bangladesh	6
	India	15
	Pakistan	7
	Sri Lanka	1
Sub-Saharan Africa (56%)	Angola	1
	Burkina Faso	2
	Central African Republic	0
	Cote d'Ivoire	3
	Ethiopia	2
	Ghana	1
	Guinea-Bissau	11
	Kenya	2
	Madagascar	1
	Malawi	6
	Mozambique	6
	Nigeria	14
	Senegal	3
	Sierra Leone	1
	Sudan	1
	Tanzania	5
	Uganda	2
	Zambia	4
	Zimbabwe	4

Notes: % refers to the regional distribution of all included items. *Number of studies not mutually exclusive.

The types of study designs included in the review were highly variable, ranging from randomised controlled trials (RCTs) (e.g., Malaba *et al.*, 2005 (++)/(++);[15] Kuhn *et al.*, 2008 (++)/(++)) to observational studies (e.g., Colonna *et al.*, 1990 (-)/(-); Campbell *et al.*, 2005 (+)/(+)). Of the 11 included studies, 34 were RCTs.

[15] The two symbols relate to internal and external validity respectively.

Included items were coded on the basis of whether they reported on interventions that dealt with the supply and/or demand side, and on the basis of the main focus of that intervention (multiple responses allowed) to reduce maternal and/or child mortality in poor, urban populations (Table 3.2). Just two items included in our review (Orji and Ajenifuja, 2003 (-)/(-); Padmanaban *et al.*, 2009 (-)/(+)) did not report on specific interventions, but reviewed intervention strategies and lessons learned. The majority (55 percent) of included items dealt with supply-side interventions.

Table 3.2: Distribution of included items by intervention focus

Intervention	N (%)
Clinical	
Surgical/instrumental procedure	6
Drug treatments (including micronutrient supplementation)	30
Vaccination	11
Other clinical management	17
Non-clinical	
Training and audits	12
Provider models	1
Financing	4
Investment and scaling up	3
Discharge and admissions policies	5
Kangaroo Mother Care	6
Nutrition (including breastfeeding)	6
Service organisation	1
Complex interventions	12

All of the included items directly addressed maternal and/or infant (including neonate) mortality, and seven items dealt with interventions that explicitly focused on both maternal and infant mortality outcomes (de Muylder and Thiery, 1989 (-)/(-); Bugalho and Bergstrom, 1993 (-)/(-); Shihadeh and Najdawi, 2001 (-)/(+); Bakr and Karkour, 2005 (+)/(-); Abdul *et al.*, 2007 (-)/(+); Saleem *et al.*, 2007 (+)/(+); Deschamps *et al.*, 2009 (+)/(-)).

Typically in order to run a meta-analysis we should have been able to say whether the population from which the sample was drawn was clearly defined; whether (and how) the sample was representative of the population, whether the participants who agreed to participate were different from those who refused and whether the response rate was adequate; and whether the methods were standardised and the statistical methods adequate.

When analysing our results, we did not identify a single paper that both had a qualitative focus and also had a discussion of change in outcomes, although many qualitative papers that looked at impacts on process (e.g. perceptions of barriers to

access or satisfaction with services) were identified but excluded from our review. All included studies in the review were therefore assessed using quantitative checklist criteria (in the case of two economic evaluations, we were able to assess the quality of the empirical trial and separately use economic evaluation checklists).

Almost a third (31 percent) of the included quantitative studies were identified as 'low quality' by the team which meant both external and internal validity were scored as (-) low. Our causal chain analyses are restricted to medium- and high-quality items only. We assessed item quality after completion of the searches, and to avoid exclusion of potentially valid items, quality was not part of the inclusion criteria. Of particular note was the lack of clarity or depth surrounding the ethical conduct of research that involved human subjects.

Out of 114 studies, 21 were identified as high quality (++/++) and 14 medium quality (either ++/+ or +/++). For those high- or medium-quality studies which included specific interventions with clearly identified outcomes, we considered whether the study could be potentially included for meta-analysis. We obtained nine items of high quality and 8 of medium quality that met these criteria.

Meta-analysis is particularly common in the analysis of studies which include clinical trials when the samples and results of individual studies are not conclusive enough to be able to generalise the overall results. It is also commonly used to remove bias from the conclusions as it combines the results of many trials and allows more transparency in the interpretation of the results. Despite the many advantages, it needs careful coding of the studies as well a careful evaluation of the quality of the papers. One of the key requirements above all for meta-analysis is a complete, unbiased collection of all the original studies of acceptable quality that examine the same therapeutic question (Crombie and Davies, 2009). This systematic review aimed for breadth rather than depth, given the lack of studies in the field.

In Table 3.3, we show the distribution of the high-quality papers which were suitable for meta-analysis. The overall number of studies was nine, although in a few instances more than one outcome was included in the analysis.

Table 3.3: Distribution of items coded as 'high quality' and suitable for metadata by outcome and focus

Intervention outcome	**Clinical**	**Non-clinical**
Maternal mortality		Dumont *et al.* (2005) Dumont *et al.* (2006)
Neonatal mortality	Darmstadt *et al.* (2008) Kaestel *et al.* (2005)	
Infant mortality	Darmstadt *et al.* (2008) Kuhn *et al.* (2008) Martins *et al.* (2008)	Jakobsen *et al.* (2008) Mbori-Ngacha *et al.* (2001)

Given the heterogeneity of the populations, interventions and sample selection, meta-analysis was not deemed feasible. If we consider the cell with the highest number of studies (infant health with clinical intervention), the range of types of interventions was too high and the number of studies too small to derive a significant statistical analysis. In addition most of the clinical interventions related to urban hospitals and not necessarily to urban poor populations. When looking at the second-highest frequency (neonatal health with clinical interventions), no two interventions related to the same type (e.g., vitamin intake, vaccination, skin emollient). In general, the studies differed in interventions, approach, population, and outcome. If we cross-tabulated all those variables, we would end up with a level of heterogeneity that would invalidate any type of meta regression. It is for this reason that this review includes narrative only.

4. Synthesis results

Summary

No items were found that specifically tested the effectiveness of different models of service delivery to reduce maternal and infant mortality among poor urban populations.

Items relevant to interventions targeting poor urban women and infants were heterogeneous in their focus and study design.

Audit (death reviews) are a low-cost non-clinical intervention that appears to have positive mortality outcomes for both women and infants.

Kangaroo Mother Care (KMC) was the most tested non-clinical intervention for infants, with cautious positive impacts on infant mortality.

Complex interventions with positive mortality impacts were localised and heterogeneous in their impact, even within the study community.

No study looked at the impact that intervention had on poverty nor at how the intervention was less or more successful because of the poor setting.

Just one study, from Senegal (de Bernis *et al.*, 2000) (+)/(+), used a comparative study design and showed lower mortality in an area where women had SBA.

4.1 Further details of studies included in the synthesis

The review did not find any items that tested the effectiveness of different models of service delivery to reduce maternal and infant mortality among poor urban populations. To the best of our knowledge, there are no studies that address this issue for this population sub-group. However, we did identify a wide range of interventions that, whilst not testing different models of service delivery, were relevant for the research question. The review found extensive heterogeneity of interventions in terms of both target population and type of intervention. In order to deal with this heterogeneity, we present our description and discussion of interventions using four headings for interventions addressing:

- Clinical interventions
    - Surgical/instrumental procedures
    - Drug treatment (including micronutrient supplementation)
    - Management of labour (and induction)
    - Vaccinations
    - Other clinical management
- Non-clinical interventions
    - Service organisation
    - Training
    - Audit
    - Provider models
    - Financing
    - Nutrition (including breastfeeding)

- Complex interventions (interventions that involved multiple components across a range of domains)
    - Cost-effectiveness.

Each of these sections deals with maternal and infant mortality separately.

In doing this, it is important to note that our focus was on the improvements in delivery and access to services for the urban poor population rather than on specific clinical interventions per se. However our review illustrates that few of the effectiveness studies that may be identified, for instance through Cochrane reviews, have focused specifically on delivering services and reducing mortality in this specific target population group.

4.1.1 Clinical interventions: maternal mortality

In total, 42 papers focused on clinical interventions as a means to reduce maternal mortality (Appendix 4.1). Clinical interventions targeted at mothers formed three main groups:

- Surgical/instrumental procedures
- Drug treatments (including micronutrient supplementation)
- Other clinical management

Surgical/instrumental procedures

Five papers focused on surgical/instrumental procedures. Four papers provide comparison of Caesarean sections and vaginal delivery. In three cases, this comparison was made in the context of optimal management of breech delivery (Malhotra *et al.*, 1994 (+/-); Ziadeh *et al.*, 1997 (-/-); Orji and Ajenifuja, 2003 (-/-)). All conclude that Caesarean section does not seem to offer advantages over vaginal delivery in terms of perinatal mortality, neonatal deaths and still births. Agarwal *et al.* (2007a) (+/++) compared outcomes from Caesarean section with those following vaginal births for women with a post-Caesarean pregnancy. In the context of Lucknow, India, vaginal birth after Caesarean (VBAC) was found to be associated with higher perinatal mortality and maternal morbidity. In a comparison of modes of instrumental delivery in Jordan, Shihadeh and Al Najdawi (2001) (-/+) found that forceps and vacuum extraction were associated with differing adverse events but that overall vacuum extraction may be preferable to forceps because of reduced birth trauma and blood loss.

Drug treatments (including micronutrient supplementation)

Twenty-four papers focused on drug treatments. Seven studies focused on anticonvulsants in the management of eclampsia. Six of these concentrated on magnesium sulphate (Chinayon, 1998 (+)/(+); Adewole *et al.*, 2000 (-)/(-); Begum *et al.*, 2000 (-)/(-); Kamilya *et al.*, 2005 (-)/(-); Naz *et al.*, 2005 (++)/(++); Tukur and Muhammad, 2010 (-)/(-)). Based on observational data, all provide favourable conclusions regarding the use of magnesium sulphate. Benefits were reported in terms of maternal mortality (Adewole *et al.*, 2000 (-)/(-); Begum *et al.*, 2000 (-)/(-); Kamilya *et al.*, 2005(-)/(-); Tukur and Muhammad, 2010 (-)/(-)) and perinatal mortality (Kamilya *et al.*, 2005 (-)/(-)). Chaudhuri *et al.* (1994) (+)/(+) studied the outcomes of babies born to eclamptic mothers in India. A comparison of three treatment regimens found that babies of mothers treated with a combination of diazepam, chlorpromazine and phenargan had the best outcomes in terms of perinatal deaths and still births. Magnesium sulphate was not considered as a treatment in this study. However, in a more recent study in Nigeria, Tukur and Muhammad (2010) (-)/(-) found that magnesium sulphate was superior to the use of diazepam in reducing maternal morbidity and mortality.

Four studies focused on the induction of labour. Two of these focused on induction for women with eclampsia (Nahar *et al.*, 2004 (-)/(-); Tukur *et al.*, 2007 (+)/(-)) by means of misoprostol (50mg). There did not appear to be any advantage of misoprostol in terms of mortality in either study, although Nahar *et al.* (2004) (-)/(-); was able to conclude that intravaginal misoprostol was well tolerated and effective in the induction of labour. The third study considered induction of labour in the context of women going beyond 42 weeks gestation (Bergsjo *et al.*, 1989) (-)/(-). Induction by stripping of membranes and intravenous oxytocin infusion in this context offered no advantage as measured by perinatal mortality. Abdul *et al.* (2007) (-)/(+) compared misoprostol to oxytocin as drugs for induction during the third stage of labour. No deaths were recorded in either group and the efficacy of misoprostol was judged to be comparable to oxytocin.

Three studies concerned the assessment of micronutrient supplements. These have been classified under 'drug treatments' as they were prescribed within a clinical setting. Fawzi *et al.* (2007) (++)/(++) compared daily multivitamins (vitamins B, C, E) with a placebo group in HIV-negative women in Tanzania. No benefits were found in terms of risk of prematurity and foetal death in the treatment group but there was significantly reduced risk of low birthweight (LBW) compared to the placebo group. Kaestel *et al.* (2005) (++)/(++) compared different levels of micronutrient supplements for pregnant women in Guinea-Bissau but found no differences in perinatal or neonatal mortality. Kupka *et al.* (2008) (++)/(-) also found no significant effect of selenium supplementation for HIV-infected pregnant women in terms of maternal or neonatal mortality.

Ndibazza *et al.* (2010) (++)/(+) and de Silva *et al.* (1999) (+)/(++) evaluated the impact of the use of anthelmintics to expel parasitic worms by women during pregnancy on perinatal mortality. In Sri Lanka, de Silva *et al.* (1999) (+)/(++) found perinatal deaths to be lower in the anthelmintic group, whereas Ndibazza *et al.* (2010) (++)/(+) found no overall effect in an area in Uganda where helminth prevalence was high but infection intensity low.

Two studies focused on the use of antiretrovirals in HIV-infected pregnant women (Ekouevi *et al.*, 2008 (+)/(-); Walter *et al.*, 2006 (+)/(+)). The use of highly active antiretroviral treatment (HAART) was found to have no benefit as measured by stillbirths among women with advanced HIV (Ekouevi *et al.*, 2008) (+)/(-) but antiretroviral treatment for HIV-infected pregnant women with low CD4 counts was found to significantly decrease neonatal mortality in a study in Zambia.

Two studies focused on the use of antibiotics, but in different contexts. Aboud *et al.* (2009) (++)/(+) assessed the effect of giving antibiotics to HIV-infected pregnant women. No benefits were found in terms of maternal morbidity or mortality. Bergstrom (1991) (+)/(+) assessed the use of antibiotics in the conservative management of women with preterm rupture of membranes. Neonatal mortality was found to be significantly lower than in a control group in which no pharmaceutical treatment was given but labour was induced.

The remaining papers involved single studies looking at different aspects of drug treatment: the use of steroids in women with high-risk premature delivery (Fekih *et al.*, 2002) (+)/(-); use of misoprostol in the active management of third stage of labour (Afolabi *et al.*, 2010) (+)/(-); use of injectable contraceptive during pregnancy (Gray and Pardthaisong, 1991) (+)/(+); and administration of the antimalarial, quinine hydrochloride, for pregnant women with malaria (Kietinun *et al.*, 1993) (-)/(-). All except Gray and Pardthaisong (1991) reported favourable outcomes for the drug treatment evaluated.

Other clinical management

Thirteen papers focused on other issues related to clinical management. Certain studies could not be classified under the three clinical categories above. Five studies (Munjanja *et al.*, 1996 (++)/(++); Etuk *et al.*, 2000a (-)/(-); Etuk *et al.*, 2000b (-)/(-); Enakpene *et al.*, 2010 (+)/(-); Fabamwo *et al.*, 2010 (-)/(-)) concerned antenatal care provision. Enakpene *et al.* (2010) (+)/(-) evaluated the effect of adequate prenatal care on perinatal outcomes for women with umbilical cord prolapse. Adequate care was defined as at least four prenatal visits in index pregnancy and/or at least one prenatal visit within the 2-4 weeks preceding the occurrence of umbilical cord prolapse. Lower perinatal death was found among women receiving adequate antenatal care compared to those without prenatal care. Focusing on pregnant women in general, Munjanja *et al.* (1996) (++)/(++) found that an antenatal care programme in Zimbabwe with fewer, more objective oriented visits and fewer interventions during visits, could be introduced without having an adverse impact on perinatal or maternal mortality. In two Nigerian studies, Etuk *et al.* (2000a and 2000b) found that there was a significant increase in both maternal and perinatal mortality for pregnancies that were booked for antenatal care but delivered outside health facilities.

Abdel *et al.* (2010) (+)/(-) assessed the effectiveness of uterine massage as a means of preventing postpartum haemorrhage in a trial set in Egypt and South Africa. The authors found that massage alone was associated with more blood loss after 30 minutes compared to treatment with oxytocin (with or without massage). Miller *et al.* (2009) (+)/(++) also looked at non-pharmaceutical management of obstetric haemorrhage through the use of non-pneumatic anti-shock garments (NASG) and concluded that it showed potential for reducing blood loss and maternal mortality. Training of doctors in dealing with emergency Caesarean section (CS) was the focus for the study by Pereira *et al.* (1996). While there were no substantial differences in the mortality outcomes, they still recommended the training of doctors in areas served by low levels of health personnel. In a Malawian study, Fenton (1999) (+)/(-) looked at women requiring Caesarean section and compared those who received a blood transfusion with those who did not. No significant difference in mortality was found between the two groups.

Antisepsis and vaginal cleansing were shown in three studies to be safe and to reduce neonatal and maternal infections (Taha *et al.*, 1997 (++)/(++); Bakr and Karkour, 2005 (+)/(-); Saleem *et al.*, 2007 (+)/(+)). In a study in squatter settlements in Karachi, Pakistan, Saleem *et al.* (2007) evaluated the use of chlorhexidine vaginal and neonatal wipes by traditional birth attendants (TBAs) at home births. The study was not powered to show differences in mortality but the use of wipes was found to be acceptable and no concerns regarding safety were found. These interventions to reduce sepsis were ultimately targeted at reducing maternal and neonatal mortality, but the studies lacked power to demonstrate this. Iqbal (2004) (+)/(-) compared strategies in a maternity hospital in Karachi, Pakistan, to manage prolonged labour. The strategy was the focus of comparison rather than the effectiveness of a particular drug. In a comparison of induction of labour at 42 weeks and expectant management (non-intervention, careful monitoring), active management resulted in lower perinatal mortality.

4.1.2 Clinical interventions: infant mortality outcomes

In total, 22 papers focused on clinical interventions as a means to reduce infant mortality (Appendix 4.2). Again, clinical interventions focused on infant mortality can be categorised into:

- Surgical/instrumental procedures

- Drug treatments (including micronutrient supplementation)
- Vaccinations
- Other clinical management

Surgical/instrumental procedures

Only one study aimed at improving infant mortality outcomes was focused on surgical intervention. In a retrospective study based in Amman, Jordan, Ziadeh (2000) (-)/(-) sought to determine the perinatal outcomes associated with triplet pregnancies and compare outcomes for Caesarean section with vaginal delivery. Caesarean section was not found to be advantageous but the sample size was very small (n=41).

Drug treatments (including micronutrient supplementation)

Six papers focused on drug treatments. One study focused on the use of drug treatments to improve infant outcomes (Kumwenda *et al.*, 2008) (++)/(++). This randomised controlled trial in Malawi evaluated extended antiretroviral prophylaxis to reduce breast-milk HIV-1 transmission. Extended prophylaxis for the first 14 weeks of life significantly reduced postnatal HIV-1 transmission at 9 months but there was not a significant difference in mortality at this stage of follow-up.

Five studies focused on micronutrient supplementation to improve infant mortality outcomes. A randomised controlled trial in urban Zimbabwe (Malaba *et al.,* 2005) (++)/(++) measured the effect on infant mortality of supplementing neonates and their HIV-negative mothers with single, large doses of vitamin A during the immediate postpartum period, but found no significant impact. A controlled experimental study located in a peri-urban Indonesian community (Cobra *et al.*, 1997) (++)/(++) showed a positive impact on infant mortality outcomes as a result of oral iodine supplementation. The study concluded that in populations at risk of iodine deficiency, oral iodized oil supplementation of infants may reduce infant mortality. Furthermore, a study from China examined the effect of water treatment with iodine on infant and neonatal mortality (de Long *et al.,* 1997) (+)/(+). The authors concluded that iodine replacement through iodination of irrigation water was possibly an important factor in the recorded decline in infant mortality in China in areas with severe iodine deficiency. Finally, in Egypt, increased availability of oral rehydration salts (ORS) was associated with an improvement in the case management of, and mortality from, diarrhoea (Miller *et al.,* 1994) (+)/(++).Finally, Joshi *et al.* (2007) (-)/(-) showed that inhalational nitric oxide (INO) can be life saving and cost-effective in a LIC setting such as India.

Vaccinations

Eleven papers focused on vaccinations. All studies on vaccinations included in this review focused on infant outcomes. Vaccination remains a key prevention tool to reduce IMR in low resource settings. This review found 10 studies looking at ways to implement vaccination programmes to improve infant and neonatal mortality. Amin *et al.* (1992) (-)/(-) looked at the impact of the Expanded Program on Immunization in Sierra Leone and found that immunisation had a dramatic effect on infant mortality declines between 1975 and 1990. A series of studies from Guinea Bissau provide evidence relating to measles and BCG vaccinations and their impact on infant mortality. Aaby *et al.* (2002) (+)/(+), working in urban, peri-urban and rural areas of Guinea Bissau, compared measles-vaccinated children with those not vaccinated, and the former showed significantly lower levels of mortality. Martins Cesario *et al.* (2008) (++)/(++) further confirmed the results, showing that outbreaks of measles can be curtailed by giving the measles vaccine as early as 4.5 months of age. Bacillus Calmette-Guerin (BCG) vaccine on the other hand does not show straightforward results. Garly *et al.* (2003) (+)/(-), also working in a peri-urban area

of Guinea Bissau, showed significantly higher levels of mortality for BCG non-vaccinated infants. The timing of vaccination was an important issue in the Roth *et al.* (2004) (+)/(+) study in urban Guinea-Bissau, where vaccination of LBW in the first week of life seemed to have a stronger protective effect in terms of mortality compared to those receiving vaccination later on..

The only paper to report a negative or no significant difference at the end of a large-scale immunisation programme is the study by Fetuga *et al.* (2010) (+)/(+) in Nigeria. The study focused on the impact of moving from an expanded programme of immunisation to a national programme that was supported solely by the Nigerian government. It hypothesised that this absence of effect was due to poor access to health facilities and to the lack of ante-natal care for mothers and that despite efforts being made in increase community participation, the delivery of tetanus vaccinations remained clinic-based. Further work by Garly *et al.* (2004) (+)/(++) in urban Guinea-Bissau showed that hepatitis B vaccine (HBV) did not have a specific impact on mortality decline, but simply changed between girl and boys' mortality. HBV-vaccinated infants 7½-12 months of age had higher mortality than cohorts who had not received HBV, the difference being particularly strong for girls. Aaby *et al.* (2005) (++)/(+) showed how national immunisation days had a positive impact, mainly if polio vaccination was conducted below 6 months of age. Overall vaccination has a positive impact on infant mortality, but the timing and mode of delivery are crucial. Three studies by Benn *et al.* (2008a (+)/(++); 2008b (++)/(++); 2010 (++)/(++)), also from Guinea-Bissau, looked at vitamin A supplementation at the time of vaccination. All three studies showed that there were no significant results and recommended against its implementation in an African setting.

Other clinical management

Four papers focused on other aspects of clinical management. Two papers focused on clinical interventions but could not be classified as surgical interventions, drug treatments or vaccinations (Mandelbrot *et al.,* 2002 (++)/(+); Le Fevre *et al.*, 2010 (++)/(+)). The topical application of skin emollients as a skin barrier was evaluated as part of a strategy to improve survival among hospitalised infants through the prevention of infection (Darmstadt *et al.*, 2008) (++)/(++). The randomised controlled trial in Dhaka, Bangladesh found that both sesame seed oil and Aquaphor significantly reduced mortality rates among preterm hospitalised infants, compared to those receiving no topical emollient. The cost-effectiveness of this intervention was also reported in Le Fevre *et al.*, 2010) (++)/(+); (see section 4.1.8). the study by Darmstadt *et al.*, 2004 (+)/(+)in Egypt, which found good (but not significant) results for reductions in neonatal mortality due to sepsis, paved the way for the subsequent larger (and significant) study in 2008. The study by Mandelbrot *et al.* (2002) (++)/(+) drew on data from urban Cote d'Ivoire and Burkina Faso to consider the effect of vaginal cleansing with benzalkonium chloride during late pregnancy and delivery for infants born to HIV infected mothers. The intervention showed no particular benefit for infant mortality.

4.1.3 Non-clinical interventions: maternal mortality outcomes

In total, 14 papers focused on changes in aspects of service organisation as a means to reduce maternal mortality (Appendix 4.3). These could be further classified into papers dealing with:

- Training and audits
- Provider models
- Financing

No papers were found to focus on regulation, commodities or logistics.

Training and audit

Nine papers focused on training and audit. Several studies evaluated the impact of training and/or audit (or death review) on maternal and neonatal deaths. These facility-based quality improvement measures seemed to be associated with improved maternal health outcomes (Bugalho and Bergstrom, 1993 (-)/(-); Dumont *et al.*, 2005 (++)/(++); Dumont *et al.*, 2006 (++)/(++); Kongnyuy *et al.*, 2008 (+)/(+)).

Audit was the most frequently reported service intervention for reducing maternal mortality. A study by Awan *et al.* (1989) (+)/(-) in Lahore, Pakistan, evaluated a complex intervention (staff increases, peer review and feedback), and used trend analysis with before-intervention and during- and post-intervention outcomes for a range of reproductive health outcomes, including IMR and MMR. They demonstrated how audits can be used to develop professional responsibility. Comprehensive audit systems with periodical checks were also found to be significant in reducing waiting times, emergency cases and ultimately maternal mortality. A pre- and post-test study in urban Angola by Strand *et al.* (2009) (-)/(+) specifically considered the audit of obstetric emergencies. A substantial decline in the number of maternal deaths occurred alongside the use of improved partogrammes, reduced waiting times, improved vigilance and increased awareness of the birthing process, but the study design was unable to show causality. De Muylder and Thiery (1989) (-)/(-) reported time trend analyses of rates of C-section following the introduction of guidelines for the management of dystocia, previous C-section, foetal distress and breech presentation in Zimbabwe. They showed a decline in rates of C-section and maternal mortality over two years, and attributed this to implementation of the guidelines, in the absence of any new technology introduced over the same period. Bhatt (1989) (-)/(-) considered how a drop in maternal deaths from 1967-8 to 1983-4 at a teaching hospital in Baroda, India, might have been due to the initiation of medical audit and maternal death review. The paper showed a decline in maternal deaths from 43 in 1967-8 to 36 in 1983-4 despite a growing case load over that period. The audit was able to highlight problems such as lack of supervision for junior staff and high-risk times when senior staff were away at weekends and holidays. In general, audit meetings appeared to be low-cost interventions to identify avoidable deaths and gaps in the human resource performance.

A note of caution must be introduced, however, regarding the impact of audits and reviews. Although not one of our included papers, Filippi *et al.* (2004), based on a four-country study (Benin, Côte d'Ivoire, Ghana and Morocco), demonstrate the difficulties involved in sustaining this kind of initiative. The majority of papers in our review did not consider the sustainability of the intervention and we can only speculate that they would be sustainable due to the reported low cost in some studies.

Training is the focus of an intervention in Guatemala (O'Rourke, 1995) (+)/(-). The programme's goals were to institute standards of care for obstetric and neonatal patients as well as to improve relations between hospital staff and TBAs in both rural and urban areas. Despite increasing referral and improving satisfaction, the programme did not result in a statistically significant reduction in mortality.

Provider models

Only one paper (de Bernis *et al.*, 2000) (+)/(+) looked specifically at the link between service delivery and maternal mortality and morbidity in urban populations with contrasting availability of health care. This study, from Senegal, showed that an area where women were more likely to deliver in hospitals with trained midwives had lower levels of maternal mortality than an area where most women gave birth in district health centres, usually assisted by TBAs, implying that access to skilled health care is fundamental. Given that the distribution of women by socio-economic

groups was very similar in both communities, most of the effect could be attributed to these differentials in service provision.

Financing

Four papers focused on financing, which includes, among other things, cash vouchers, pumping into existing resources and lifting user fees. Financing mechanisms played a role in four studies (Bashir *et al.*, 1991 (-)/(-); Ahmed *et al.*, 2004 (-)/(-);Ronsmans *et al.*, 2001 (+)/(+); Lim *et al.*, 2010 (++)/(++)), and the scale of these financing mechanisms ranged from a single-hospital loan scheme (Ahmed *et al.*, 2004) (-)/(-) to a single city (Bashir et al., 1991) (-)/(-) to regional (Ronsmans *et al.*, 2001) (+)/(+) and national programmes (Lim *et al.*, 2010) (++)/(++). The analyses of secondary survey data in Lim *et al.* did not establish causality between India's Janani Suraksha Yojana (JSY) conditional cash transfer scheme and maternal and neonatal health outcomes, although the study design might not have been powered to detect changes in mortality. At a much smaller scale, the description by Ahmed *et al.* (2004) (-)/(-) of a hospital's short-term loan facility (financed by hospital doctors) to women presenting with a ruptured uterus in Nigeria, suggested reduced maternal and SAMM rates but, again, was unable to confirm causality due to its design. Of note was the high rate of loan payback (94 percent); in order to qualify for a loan, women undertook to repay it prior to discharge.

4.1.4 Non-clinical interventions: infant mortality outcomes

Twenty six studies deal with a wide range of interventions related to service provision aimed at improving neonatal and infant mortality (Appendix 4.4). Again, these interventions can be categorised into:

- Service organisation
- Nutrition (including breastfeeding).

Service organisation

Within service organisation, papers dealt with training and audit, increased investment and scaling up of interventions and changes in hospital admissions and discharge procedures. A distinct group of papers then looked at Kangaroo Mother Care (KMC) as an intervention to reduce infant mortality.

Only one study in urban Mozambique considered both maternal and infant health outcomes (Bugalho and Bergstrom, 1993) (-)/(-). Facility-based quality improvement measures, including the introduction of audit measures, showed a significant but transient improvement in perinatal mortality, alongside an increase in C-sections.

TRAINING AND AUDIT

Threestudies considered the impact of training and/or auditing on infant mortality outcomes. Two studies, one from Uganda and one from China, focused on evaluating the impact of training for neonatal resuscitation. In a Kampala hospital in Uganda, enhanced training in neonatal resuscitation was provided so that a specialist team could be formed which would be available at deliveries (O'Hare *et al.*, 2006) (-)/(-). The intervention led to a decrease in mortality and improved outcomes for babies weighing more than 2kg at birth. Although the authors pointed out that this type of training would be feasible only in big teaching hospitals that could justify the presence of a permanent team, this model might be replicable in similar settings. Training in the Neonatal Resuscitation Program Guidelines in a hospital in China also led to a statistically significant decline in the perinatal neonatal mortality rate (Zhu *et al.*, 1997) (-)/(-).In Nicaragua, following the introduction of a hospital-based system to register births and deaths (and cause of death) in one hospital, neonatal mortality declined from 56/1,000 live births in 1985 to 11/1,000 in 1993 (Aleman *et al.*, 1998) (-)/(-)). The authors noted, however, that the registration system, in

order to be effective, could not operate in isolation and required continued and active involvement of healthcare staff in order to review and improve neonatal care routines.

INCREASING INVESTMENT AND SCALING UP

Three studies considered the impact of increasing investment and scaling up on infant mortality outcomes. The scaling up of facility-based neonatal care in a district in southern India showed benefits in perinatal and neonatal mortality (Shantharam Baliga *et al.*, 2007) (+)/(++). Using a pre- and post-study design, the authors show a significant decline in early neonatal and perinatal mortality rates, together with a significant decline in case fatality rates for LBW, sepsis and birth asphyxia. They noted that, without sufficient community and health worker motivation, the scaling up was unlikely to have been so successful in reducing early age mortality. Similarly, Enweronu *et al.* (2008) (+)/(-) showed the benefits of investment in infrastructural and staff improvements in neonatal care for the survival of lower birthweight babies in Ghana. In urban Zambia, Essential Newborn Care training reduced early neonatal mortality (Chomba *et al.*, 2008) (+)/(++). However, there was a differential impact of improved service organisation by educational status of the mother, with the greatest impact among women with no secondary education.

DISCHARGE AND ADMISSION PROCEDURES IN NEONATAL UNITS

Five papers involved the evaluation of improved hospital discharge and admissions procedures for neonates. Three studies considered this specifically for LBW babies, albeit with different definitions of LBW. Bhakhoo *et al.* (1989) (+)/(+) in India, Bhutta *et al.* (2004) (+)/(-) in Pakistan and Blencowe *et al.* (2009) (+)/(+) in Malawi all suggested that early discharge of neonates was safe and did not lead to an increase in adverse neonatal mortality outcomes. Among these, the study by Blencowe *et al.* (2009) (+)/(+) looked at the early discharge with Kangaroo Mother Care (KMC) as an alternative to routine hospitalisation of low-birthweight babies. The study suggested that early discharge was safe and feasible and that, if rolled out to all levels of health facilities, Kangaroo Mother Care might help to overcome existing problems in access to care. Agarwal *et al.* (2007b) also looked early discharge and rational admissions among other low-cost interventions in a resource-limited teaching hospital in India. The findings of the study suggested that simple interventions such as these could result in a significant decline of neonatal mortality.

In an Indian-based study, Sasidharan *et al.* (2005) (-)/(-) looked wider than admissions and discharges and considered the impact of changed practices in terms of maternal and newborn contact for high-risk neonates in a hospital newborn unit. Prior to the intervention, mothers and their newborns were physically separated, with only occasional breastfeeding permitted. The intervention changed this regime, and permitted mothers (or their substitutes) to breastfeed on demand, alongside other service changes. This can be categorised as a low-cost intervention where increased maternal involvement in the neonatal period proved to be successful in reducing neonatal mortality.

KANGAROO MOTHER CARE

A total of six studies specifically addressed Kangaroo Mother Care (KMC), which is a method of care for preterm infants usually involving the infant being carried by the mother, with skin to skin contact (World Health Organization, 2003). The study by Colonna *et al.* (1990) (-)/(-) in urban Mozambique recommended KMC as a low-cost effective intervention. Three other papers were specifically on KMC as a method of infant care rather than simply service reorganisation. Whilst Lincetto *et al.* (2000) reported significant reductions in neonatal mortality following the introduction of KMC in a low-resource setting in Mozambique, evidence from the other studies was

less conclusive (Cattaneo *et al.*, 1998 (++)/(++) in Ethiopia, Indonesia, Mexico; Nagai *et al.*, 2010 (++)/(-) in Madagascar). Two further studies in Zimbabwe and Ethiopia (Bergman and Jurisoo, 1994 (-)/(-); Worku and Kassie, 2005 (-)/(+)) reported interventions aimed at improving infant and neonatal care which included the introduction of KMC. Both reported positive mortality outcomes, especially for LBW infants. However, both studies stressed the importance for the success and sustainability of the intervention of continued support and advice to the mother until the recommended infant weight was achieved.

Nutrition (including breastfeeding practice and guidelines)
Six studies considered the impact of nutrition interventions on infant mortality outcomes. The promotion of exclusive breastfeeding in Guinea-Bissau (Jakobsen *et al.*, 2008) (++)/(++) for the first 4-6 months of life according to WHO recommendations at the time of the study had no significant impact on infant mortality in a traditional setting which relied on exclusive breastfeeding. The final conclusion was not to discourage local practices, as long as they work.

A specific sub-group of papers dealt with the prevention of mother-to-child transmission (PMTCT), of which only one involved observation of both maternal and infant outcomes (Nduati *et al.*, 2001) (++)/(+). Four key studies looked at the ongoing debate on breastfeeding for HIV-positive mothers. Three of these (Mbori-Ngacha *et al.*, 2001 (++)/(++); Becquet *et al.*, 2007 (++)/(++)); Deschamps *et al.*, 2009 (+)/(-)) agreed that in resource-poor settings, given appropriate nutritional counselling and care, access to clean water and a supply of breastmilk substitutes, alternatives to breastfeeding could lower considerably the levels of infant mortality. Furthermore, Kuhn *et al.* (2008) (++)/(++) reported that early, abrupt cessation of breastfeeding by HIV-infected women in a low resource setting, such as Lusaka, Zambia, did not improve the rate of HIV-free survival among children born to HIV-infected mothers and was harmful to HIV-infected infants. Taken together, the results suggest that it is not only the type of feeding but the timing of feeding choices that may be important.

4.1.5 Complex interventions: maternal mortality outcomes

Complex interventions are those that include several components, and their evaluation is challenging because the different components of the intervention, and their outcomes, need to be independently and summatively evaluated (Campbell *et al.*, 2000). Methodologies for reviewing data from complex interventions are still developing (Petticrew, 2003). Few interventions are simple, and levels of complexity can vary, but the primary question is whether the intervention works in everyday practice (Haynes, 1999; Medical Research Council, 2008). A further level of complexity for this review is introduced by the fact that most of the complex interventions we identified included rural, as well as urban, populations. In the review, only one item (Borulkar *et al.*, 1998) (-)/(-) made explicit reference to replicability and sustainability. In general there was a sense of interventions being quite localised and heterogeneous in their impact, even within their community (Mirghani and Saeed, 2000) (-)/(-).

Our review identified eight interventions for maternal mortality that we coded as sufficiently complex to merit reporting separately (Appendix 4.5). In this instance, we consider complex those interventions which include more than one aspect of the overall health care process: from clinical intervention to service reorganisation to staff training, etc. In some cases, interventions were multi-sectoral, involving sectors beyond health. By considering the key themes that emerge from these interventions, we can strengthen understanding of how interventions cause change (or not). The interventions we have included were often implemented at a

government administration, regional or national levels, and as such include rural and urban populations.

One study focused entirely on an urban population (Bashir *et al.*, 1995) (-)/(-). A combination of low-cost services or free services for deserving cases, obstetric flying squad services, training for TBAs, antenatal check-ups and intensive community education had a positive impact on maternal mortality levels in a major city in Pakistan. A key to the uptake and success of services such as the flying squad was the community events and radio education campaigns highlighting their availability.

Three studies published over the last decade focused on evaluation of Safe Motherhood or Mother Care interventions as a whole. These complex programmes involved many different types of interventions which present particular challenges for evaluation. Studies in Egypt and Tanzania assessed the impact of national programmes on maternal mortality, and found that reductions in mortality over time were evident (Mbaruku and Bergstrom (1995) (-)/(-); Mswia *et al.*, 2003 (+)/(++); Alwen *et al.*, 2005 (-)/(+); Campbell *et al.*, 2005 (+)/(+)), although attributing causality was poor. In Nigeria, Okaro *et al.* (2001) (-)/(-) showed that the Safe Motherhood Initiative had not succeeded, with the MMR increasing fivefold since its start. This was attributed to a deterioration in general living standards which had wiped out any improvements due to better maternal health care. This highlights that health sector investment alone is unlikely to reduce maternal deaths.

Two further studies have considered how interventions at a national or state level may have contributed to declining maternal mortality over time. Padmanaban *et al.* (2009) (-)/(+) outlined the interventions that were judged to have contributed to the significant decrease in maternal mortality in the Indian state of Tamil Nadu. The MMR in the state reduced from 380 to 90 per 100,000 live births in the period from 1993 to 2007. The paper drew on the observations of the authors, based within the Ministry of Health and Family Welfare, as well as secondary data and literature where available. The paper described wide-ranging interventions from improvements in availability of human resources; availability of key drugs, blood and supplies; improved management capacity; and better surveillance and analysis of maternal deaths. It is not possible from the paper to quantify the effect of the interventions directly but it does highlight the importance of political will and leadership, and engagement of directorates across governments, not just health. For China, Yan (1989) (-)/(-) showed how improved training and services under a national programme had helped to reduce maternal mortality in the country since the 1950s. Starting with training of TBAs, then with referral systems in 1952, up to recruitment and training of midwives and obstetricians alongside TBAs, the Chinese MMRs declined sharply in the 1950s and 1960s. However, no specific reference is made in this study to specific interventions in poor urban areas.

4.1.6 Complex interventions: infant mortality outcomes

Only three papers focused on complex interventions for infant mortality (Appendix 4.6). Section 4.1.5 showed that the complex interventions for maternal mortality focused mainly on national or large scale programmes. Two of the complex interventions for infant mortality focused more closely on addressing a specific area of clinical care through a package of interventions. The areas of focus were special care for infants (Borulkar *et al.*, 1998) (-)/(-) and management for mothers with diabetes during pregnancy and labour (Mirghani and Saeed, 2000) (-)/(-).

The study by Borulkar *et al.* (1998) (-)/(-) in India reported on the development of a model for the special care of newborns at a community hospital in a predominantly tribal block in an urban area. The key interventions included: adequate warmth; prompt resuscitation; proper feeding; and oxygen administration when necessary.

This facility was developed with existing staff and infrastructure, and minimal material inputs, which made this intervention low cost and sustainable. The authors also suggested that this model was replicable and had the potential for developing horizontal links with perinatal care and child survival programmes to be delivered through community hospitals.

The other study, based in Sudan, focused on simplified management of mothers with diabetes during pregnancy and labour (Mirghani and Saeed, 2000) (-)/(-). There were multiple strands to the intervention. After testing for diabetes, patients were monitored during pregnancy, labour was induced at 38 weeks, basic resuscitation was carried out for all babies, and early breastfeeding was made the norm. Treatment was sought for complications immediately. This simplified management led to significant improvement in perinatal and neonatal mortality, although impact depended on the socio-economic characteristics of the patient.

Brown (1996) followed a cohort of newborn in a hospital in Papua New Guinea over a year from birth to either death or discharge. His study looked at the impact of following Paediatric Standard Treatment book guidelines, which included warming, intravenous fluids, nasopharyngeal oxygen for respiratory distress and phototherapy and/or exchange transfusion for jaundice. Despite different results for different treatments and the non-total uptake of services, he showed that simple and cheap management alone could result in higher survival rates. In his view the results were not generalisable though and possibly only feasible within the context of Papua New Guinea.

4.1.7 Complex interventions: maternal and infant mortality outcomes

Richard *et al.* (2008) (++)/(++) was the only study focused on complex interventions for maternal and infant mortality (Appendix 4.7). It was a comprehensive intervention to improve access to quality caesarean delivery in an urban district of Burkina Faso involving: staff training; equipment; internal clinical audits; implementation of a cost sharing system; and patients–providers meetings. It was an experimental study without control and represented a facility-based quality improvement intervention. It resulted in increased rates of women receiving needed CS with no negative mortality outcomes for maternal or perinatal mortality. The increased rate was as a result of different factors including improved access to CS and improved diagnosis and management. The authors underline the need for a holistic approach, involving technical, operational, socio-cultural and political components in order to achieve a successful intervention.

4.1.8 Cost-effectiveness

While it is critical to increase our knowledge about what actions and interventions can help improve access to services that will improve maternal and infant health, it is also important to identify the costs of delivering these changes. In all societies, but especially in low and middle income countries where resources for health systems are very limited, it is important to assess the cost-effectiveness of interventions, that is, identifying what level of additional resources are required to generate improvements in health outcomes. There are several different approaches to undertaking economic evaluation, all involving measuring costs in the same way, whilst outcomes may be recorded using natural measures, e.g. number of lives saved, deaths due to pregnancy complications avoided etc., as well as common metrics such as the Disability Adjusted Life Year (DALY) or the Quality Adjusted Life Year (QALY). Where evaluations make use of such common metrics, it then becomes possible to compare all potential uses of resources to improve health outcomes; thus improvements in maternal and child health can be compared with interventions to improve mental health or reduce the consequences of infectious diseases such as

HIV/AIDS and Malaria, as well as non-communicable diseases like diabetes or cardiovascular disease.

When assessing whether studies met our inclusion criteria, not only did we want therefore to identify whether some studies looked at the costs of implementing interventions, but also whether we could identify any economic evaluations synthesising cost and effects data. In doing this we were interested not only in economic evaluations linked to empirical studies, but also those studies that constructed models drawing on effectiveness and resource use data from many sources to make a judgement on potential cost-effectiveness. The quality of evaluations included in our review was assessed using both the Drummond and Jefferson (1996) and Evers *et al.* (2005) checklists as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins and Green, 2011).

Results

It is important to note that there is an ever-increasing evidence base looking at the cost-effectiveness of interventions related to maternal and infant health in low income country contexts (e.g. Jowett, 2000; Rouse, 2003; Adam *et al.*, 2005; Vos *et al.*, 2006; Darmstadt *et al.,* 2008 (++)/(++); Goldie *et al.*, 2010). For instance, Adam *et al.* (2005) drew together a range of data on the effectiveness of interventions to look at potential cost-effectiveness in sub-Saharan Africa and south-east Asia, coming to the conclusion that improving access to preventive measures and early care would all be cost effective in all settings. These would include antenatal care (tetanus toxoid, screening for pre-eclampsia, screening and treatment of asymptomatic bacteria and syphilis); skilled attendance at birth, offering first-level maternal and neonatal care around childbirth; and emergency obstetric and neonatal care.

Despite this increase in the broad cost-effectiveness evidence base, our analysis suggests that few economic evaluations that *explicitly met our inclusion criteria* have been undertaken. Little work has been undertaken to look at issues of access, uptake and use of effective interventions in our study population. As part of our review, 11 potential economic evaluations were identified by the study team. However after reading the full text, only four met our inclusion criteria (Appendix 4.8). Seven other studies were excluded because they did not have some focus on an urban poor population, although they did provide some further economic evidence for interventions to tackle maternal and infant mortality in low income country settings. For instance, Hounton *et al.* (2008) reported on the cost-effectiveness of improving access to skilled birthing care in a rural area of Burkina Faso. Meantime Hutton *et al.* (2009) reported that the administration of three sessions of sulfadoxine-pyrimethamine treatment to prevent malaria in infants up to the age of nine months in rural Tanzania and Mozambique had a cost per death averted of US $100 and US $300 respectively. Thus this intervention would be considered cost effective in these two populations. Tsu *et al.* (2009) suggested that increased use of oxytocin during the third stage of labour would be cost effective in reducing the risk of postpartum haemorrhage in rural Vietnam.

From our original set of studies, we did identify some papers that had some limited information on the costs of some services, but without any discussion of the consequences for health services and other resource use going forward. We also identified several additional economic evaluations at the abstract screening stage that all focused on rural populations. For example, Rydzak (2008) and colleagues looked at the economic case for prenatal syphilis screening in sub-Saharan Africa as a whole, suggesting overall that some screening programmes could not only reduce stillbirths and infant deaths, but also reduce costs overall. Sutherland *et al.* (2009 and 2010) modelled the potential cost-effectiveness of prenatal iron

supplementation and misoprostol use on maternal mortality rates in India, but focused solely on the rural population.

In addition, some papers, most of which did not meet the terms of our inclusion criteria, looked at the importance of financing arrangements and cost as a barrier to service access in some settings. One study that did meet these criteria looked at the Indian conditional cash transfer scheme and is discussed in detail elsewhere in this chapter (Lim *et al.*, 2010) (++)/(++). Another example is one excluded qualitative study in Bangladesh looked at the hidden costs of apparently free access to maternal services in Dhaka, including transport costs to and from hospital and additional food costs while in hospital. It explored the willingness of women to pay these costs, reporting that 21 percent were having to spend between 50 percent and 100 percent of all their monthly income on this (Nahar and Costello, 1998). Another excluded study Chiwuzie *et al.* (1997) also reported on the potential benefits of community-established and -run emergency loan funds to pay for obstetric care in Nigeria.

Analysis of specific studies

Appendix 4.8 provides a summary of key information on economic analysis in the four studies identified that met the inclusion criteria for this review. These are all now briefly discussed in turn.

MODELLING THE LONG-TERM BENEFITS OF A MICRONUTRITIONAL INTERVENTION

One of these studies (Sharieff *et al.*, 2008) (+)/(-), making use of data from two empirical studies, was able to take a modelling approach to demonstrate that there were lifetime economic benefits that could arise as a result of the avoidance of premature mortality during the first year of life of a hypothetical urban slum dwelling population in Karachi, Pakistan. In terms of the quality of the economic analysis, the study scores well on both the Drummond and Evers checklists, although evidence on effectiveness of the intervention comes from two previous studies of the authors, but is not detailed in this economic analysis.

The intervention was the use of a nutritional supplement containing iron and zinc that could be sprinkled over food in a home setting. The authors modelled the long-term payoffs over 55 years that would arise from reducing the risk of mortality in the first year of life, coupled with a lower risk of cognitive impairment. They estimated both the costs of intervention and the costs of treatment for diarrhoea in the first year of life. Their simulated study population was developed making use of local data on an urban population to determine potential mortality benefits, as well as risk of diarrhoea and cognitive impairment. Their model suggested that in nearly all scenarios, investment in home-based nutrition supplements would have long-term benefits.

It is important to recognise that these long-term benefits were not just health related, but had an impact on human resources (through better potential to benefit from education) and greater participation in employment. The study projected the impact of better health on participation in employment in adulthood and in the level of earnings achieved. In doing this the authors were able to demonstrate a long-term net return on investment to society as a whole of up to $800 per child.

While generating a positive return on investment, the model is in fact conservative as it does not take account of health-related benefits in adulthood. It is also acknowledged that these benefits would be greatest for low income individuals; those with high incomes in low income settings would be unlikely to benefit as they would not experience nutritional deficiencies. The intervention has now been rolled out throughout the country through the Lady Health Workers Scheme.

ASSESSING THE COST-EFFECTIVENESS OF SKIN BARRIER ENHANCING EMOLLIENTS

The second study looked at the cost-effectiveness of skin barrier enhancing emollients in Bangladesh (Le Fevre *et al.*, 2010) (++)/(+). Unlike the previous study, this is an economic evaluation conducted retrospectively alongside a randomised controlled trial that is also included in our systematic review (Darmstadt *et al.*, 2008) (++)/(++). It is a well-designed study, also scoring well on the two economic evaluation checklists.

The clinical trial compared the use of sunflower seed oil (SSO) or a synthetic skin emollient called Aquaphor against no treatment in order to assess impact on the risk of sepsis and mortality for low birthweight babies at a tertiary hospital in Dhaka. The study highlighted the very good cost-effectiveness of both interventions, compared to other published estimates of cost effective interventions; moreover it also looked at budgetary impact, assuming that it might be difficult for the health care system to fund these interventions.

A detailed breakdown of the costs of providing the intervention, including separate identification of start-up and implementation costs was provided. In total for a 20-bed facility at the hospital start-up and implementation costs came to $1,833.32. Costs per infant treated at the hospital by either of the two interventions or receiving standard care were also provided: on average, costs for SSO were $99.47 compared with $125.35 for Aquaphor and $93.39 for controls receiving usual care. The economic analysis then reported the incremental cost per Year of Life Lost (YLL) averted between the different intervention groups.

The study found that both sunflower seed oil and Aquaphor were highly cost effective in reducing mortality. But Aquaphor was relatively much more expensive – the cost per Year of Life Lost (YLL) averted for Aquaphor was $5.74 compared to do nothing; cost per YLL averted for SSO versus do nothing was $2.15; incremental cost per YLL using Aquaphor compared with SSO was $20.74. A similar study was conducted by the same author in Egypt (Darmstadt *et al.*, 2004) (+)/(+) which paved the way for the implementation of this larger scale cost-effectiveness study.

All of these estimates of cost-effectiveness make good comparison with other potential cost effective interventions highlighted in the World Bank's Disease Control Priorities Project (Musgrove and Fox-Rushby, 2006). Investment in these skin-barrier enhancing emollients appears more cost effective than all of the interventions in a South Asian context. They also make good comparison with the work of the WHO Choosing Interventions that are Cost Effective (WHO-CHOICE) Programme, where cost-effective interventions in South Asia range from $6 per DALY averted for support for breast feeding to reach 50 percent coverage to $16,930 per DALY averted for a comprehensive package of maternal and infant care at 95 percent coverage (World Health Organization, 2011a). It should, however, be noted that this latter analysis does not take distributional issues into account, so a direct comparison of cost-effectiveness for interventions targeted at the urban poor is not possible. Nor does it look at the impact on costs beyond the health sector.

Cost effective interventions can sometimes be expensive; importantly, this study also looks at the costs of obtaining the two interventions. Given the low likelihood of public funding in the short term in Bangladesh, the use of sunflower seed oil (albeit not as effective as Aquaphor) is likely to be more sustainable as treatments costs are at a level that is much more affordable to people in Bangladesh paying out of pocket for medicine – $1.55 per month compared with $29 per month for Aquaphor (the average monthly salary is $39). There is a strong case, however, for public funding of Aquaphor, given the highly favourable cost-effectiveness ratio.

EXAMINING THE COST-EFFECTIVENESS OF KANGAROO MOTHER CARE FOR LOW BIRTHWEIGHT INFANTS

Kangaroo Mother Care (KMC) has often been cited as a low-cost intervention from a health system perspective, particularly as much of the cost is borne by mothers (and other family members) in maintaining skin-to-skin contact with their infants. A previous systematic review looking for evidence from high-income country contexts on this intervention reported that effectiveness studies that looked at physical and mental health impacts rarely considered cost impacts; they simply assumed these to be low (McDaid and Park, 2011). The same appears to be true in the case of KMC interventions in low income country settings, although we were able to identify one randomised controlled trial of KMC versus conventional care (warm room or incubator care) that also looked at the costs associated with care (Cattaneo *et al.*, 1998) (++)/(++). This study was set in urban hospitals in three cities, but only results from Addis Ababa in Ethiopia, where it was indicated that the poor population would make use of services, were eligible for our analysis. Low birthweight infants were randomised to KMC or conventional care and monitored for up to 30 days. The study sample size was not sufficient to generate statistically significant differences in infant mortality between the two groups, but it was observed that the costs of care, both in terms of salaries and other hospital-related costs were lower in the KMC group. One limitation of this analysis however, was that only overall cost data across all three study cities, rather than data for Addis Ababa alone were presented, although the authors did not note any difference in cost trends between the three study sites.

Assessing the cost impacts of antenatal maternal corticosteroid treatment on risk of neonate mortality

One small RCT in Tunisia of 118 women (Fekih *et al.*, 2002 (+)/(-)) looked both at the effectiveness and the cost implications of targeting women at high risk of premature delivery for antenatal maternal corticosteroid treatment. The comparator group did not receive any additional intervention. Corticosteroid treatment, it was hypothesised, would reduce the respiratory distress syndrome in newborn infants which increased the risk of mortality. The economic analysis was conducted from a health system perspective; infant mortality rates were significantly lower in the intervention group, whilst costs to the health care system, despite the additional cost of corticosteroid treatment for the group (Tunisian $2,000), were Tunisian $21,000 less in the intervention group as a result of having to treat fewer neonates with symptoms of acute respiratory distress.

Strengthening the economics evidence base

Although the evidence base appears limited, there are in fact a number of ways in which it might be strengthened in the short term. For instance, one could retrospectively make use of data looking at uptake and effectiveness of actions that help increase uptake from papers identified in this review; the costs of implementation could then be estimated, including their impact on the future use of health services, or on other economic costs if mortality (and morbidity) were avoided.

Although our review recognises the very different circumstances that are to be found in urban compared to rural areas, this does not necessarily mean that some of the economic studies that we identified in rural areas cannot be adapted to urban settings. Economic models could also be used to estimate some of the longer-term costs and benefits of a reduction in maternal and/or infant mortality. These models could be subject to a series of sensitivity analyses, so as to take account of different potential levels of effectiveness and uptake in different contexts. There may also be existing data that can help with some of these analyses; for instance we identified one detailed analysis of the costs of replicating the scaling up of skilled maternal

and birthing care services, including the costs of promoting behaviour change to encourage the use of skilled care in different districts of Tanzania and Kenya (Boulenger and Dmytraczenko, 2007).

It is also possible to use economic modelling techniques to look at the economic case for scaling up access to a package of appropriate services. One excellent example of a high-quality modelling study, by Goldie *et al.* (2010), sought to look at this across rural and urban areas in India. While it does not indicate methods by which access would be increased, nor look specifically at the urban poor population, it does illustrate that scaling up services can be very cost effective. Reducing the level of unmet need for family planning services alone, or coupled with the elimination of unmet need for safe abortion services, would be very cost effective, reducing the lifetime risk of death due to maternal complications in urban India from 1 in 119 to 1 in 155 or 1 in 173 respectively. Projected costs avoided for a single cohort of 15-year-old women over their lifetimes could be as much as US$ 120 million. A package of measures to scale up fully integrated services, including intrapartum care as well as family planning and abortion services, would have an incremental cost per year of life saved of between US$200 and $900. This would be considered cost effective in an Indian context. Darmstadt *et al.* (2008) also modelled the cost-effectiveness of scaling up 16 interventions to tackle infant mortality in 60 low income countries in sub-Saharan Africa and south-east Asia. Scaling up of intrapartum care, in particular given the more limited availability of services in these countries was shown in this economic modelling exercise to be the most cost effective strategy if a step-wise approach to scaling up was required due to limited resources. Similarly Adam *et al.* (2005), in observing that there are a number of cost effective maternal and child health interventions, suggested that scaling these up to 95 percent population coverage would halve neonatal and maternal deaths.

The evidence base might also be strengthened by looking at literature from countries that were excluded on the grounds of their World Bank classification, but that nonetheless have large disparities in income and access to maternal and infant health services. For example, Horton *et al.* (1996) looked at the cost-effectiveness of breastfeeding promotion programmes in Brazil and Mexico, concluding that they are among the best value buys for policy makers who wished to reduce the incidence and number of diarrhoea-related deaths. As this study noted, 'maternity services that have already eliminated formula [through promotion of breast feeding] can, by investing from $2 to $3 per birth, prevent diarrhoea cases and deaths for $3.50 to $6.75 per case, and $550 to $800 per death respectively, with DALYs gained at $12 to $19 each'. The results of this economic analysis might be adapted to low and middle income country settings to provide further information on the potential cost-effectiveness of promotion programmes.

4.2 Synthesis of evidence: causal chain analysis

The causal chain analysis included papers of high quality only (n=21). These were studies that scored ++ in both the internal and external validity checklist. For the reasons highlighted in Section 3.2, we will only conduct a narrative causal chain analysis based on these 21 studies. They are subdivided for neonatal/infant and maternal interventions.

Table 4.1: Distribution of high-quality items included in causal chain analysis by intervention type and target group

Intervention outcome	Intervention focus	
	Clinical	**Non-clinical**
Maternal mortality	Fawzi *et al.* (2007) Kaestel *et al.* (2005) Munjanja *et al.* (1996) Naz and Mehr-un Nisa (2005) Taha *et al.* (1997)	Dumont *et al.* (2005) Dumont *et al.* (2006) Lim *et al.* (2010) Richard *et al.* (2008)
Neonatal mortality	Darmstadt *et al.* (2008) Kaestel *et al.* (2005) Taha *et al.* (1997)	Bergsjo *et al.* (1989) Cattaneo *et al.* (1998) Munjaja et al. (1996)
Infant mortality	Benn *et al.* (2008b) Benn *et al.* (2010) Cobra *et al.* (1997) Kumwenda *et al.* (2008) Martins Cesario *et al.* (2008) Malaba *et al.* (2005)	Becquet *et al.* (2007) Cattaneo *et al.* (1998) Jakobsen *et al.* (2008) Kuhn *et al.* (2008) Mbori-Ngacha *et al.* (2001)

Only seven (Bergsjo, 1989; Cobra *et al.* (1997); Taha *et al.* (1997); Dumont *et al.* (2005); Dumont *et al.* (2006); Darmstadt *et al.* (2008); Lim *et al.* (2010)) out of the 21 studies were identified as successful and four had a negative outcome (Malaba *et al.*, 2005; Jakobsen, 2008; Benn et al, 2010); the remaining 11 were either inconclusive or did not have a major swing towards positive or negative.

4.2.1 Root causes

Most maternal deaths occur during the intrapartum or a few hours after delivery; few papers explicitly discussed the root causes of the obstetric complications which had an impact on both maternal and infant outcome (these were Taha *et al.*, 1997; Darmstadt *et al.*, 2008; Richard *et al.*, 2008). Lack of staff training combined with low levels of knowledge were identified as dominant causes for the lack of implementation of protocols and obstetric care procedures. Social norms in a variety

of settings were also identified as a cause of non-implementation of breastfeeding and obstetric care. One example of this was the practice in some countries of new mothers sequestering themselves from most people during a culturally determined period after delivery, as in parts of India (Lim *et al.*, 2010). Micronutrient shortage in pregnant women in LICs linked to low birthweight for infants was associated with morbidity and mortality (Kaestel *et al.*, 2005).

Cultural barriers remain a key determinant to lack of access to services (Lim *et al.*, 2010) and to the implementation of appropriate health services/interventions (Jakobsen *et al.*, 2008). Only one study (Lim *et al.*, 2010) highlighted the inequalities in access to care to explain high rates of maternal mortality.

The root causes of infant and neonatal negative outcomes were identified as pneumonia and diarrhoea mainly because of delays in vaccination (Martins *et al.*, 2008), lack of antenatal care (Munjanja *et al.*, 1996), and general lack of guidelines in breastfeeding for HIV positive women (Becquet *et al.*, 2007; Kumwenda *et al.*, 2008). Children born prematurely had compromised barrier functions which increased their risk of infection and of hypothermia (Darmstadt *et al.*, 2008).

4.2.2 Impact on health outcomes

Only 7 out of the 21 studies reported a positive impact on health outcomes (Cobra *et al.*, 1997; Taha *et al.*, 1997; Dumont *et al.*, 2005; Dumont *et al.*, 2006; Darmstadt *et al.*, 2008; Richard *et al.*, 2008; Lim *et al.*, 2010), of which five were related to maternal outcomes and three to infant and neonatal ones. The interventions included: skin barrier methods (Darmstadt *et al,*. 2008); death reviews and financial regulations (Dumont *et al.*, 2005; Dumont *et al.*, 2006; Richard *et al.*, 2008); oral iodine supplementation for infants (Cobra *et al.*, 1997); cash transfer schemes to improve institutionalised deliveries (Lim *et al.*, 2010); and birth canal cleansing to reduce infections (Taha *et al.*, 1997). Although we consider Kumwenda *et al.* (2008) as an overall neutral study, some of the clinical interventions did result in a positive impact on postnatal mortality.

The range of interventions and specificity of the settings shows that no general conclusion can be reached on successful impact on health. Vaccination remains a key determinant of curbing infant mortality rates in resource poor settings. However what still needs to be further studied is the timing of vaccination. Martins Cesario *et al.* (2008) found no significant reduction in post-natal mortality in infants vaccinated before 9 months of age in resource-poor settings. However they suggested that an early two-dose strategy providing Edmonston-Zagreb vaccination (measles) as early as 4.5 months of age might be used in humanitarian emergencies or during outbreaks with a high risk of measles infection. A few studies suggested that there was insufficient evidence that changes in feeding practices did significantly reduce infection rates, as overall the effects might be counterbalanced (Kuhn *et al.*, 2008) . However Becquet (2008) stressed that given appropriate nutritional counselling and care, access to clean water, and a supply of breastmilk substitutes, these alternatives to prolonged breastfeeding could be safe interventions to prevent mother-to-child transmission of HIV in urban African settings.

4.2.3 Poverty and impact (sustainability)

One study looked at the sustainability of intervention in low-resource urban settings (Figures 4.1 and 4.2): one controlled trial in Bangladesh identified a low-cost intervention that could be funded if necessary through out-of-pocket payments, for emollient skin barrier therapy, although this still needs further testing (Darmstadt *et al.*, 2008). Other interventions such as vaginal wash (Taha *et al.*, 1997) were deemed to be low cost and sustainable, although this study is now over a decade old.

In general, no overall change of policy was reported. In only one study (Malaba *et al.*, 2005) was it considered that the Zimbabwean government might have started recommending postpartum vitamin supplementation as a result of the study (not confirmed though). Audit was reported to be low cost and high impact (Dumont *et al.*, 2005; Dumont *et al.*, 2006).

Kangaroo Mother Care is a feasible, low-cost and successful intervention, and sustainable in resource-poor settings (Cattaneo *et al.*, 1998). However no recent studies have been found which look at more recent initiatives. More evidence is needed to assess whether administration of micronutrients for pregnant women might be sustainable in African countries (Kaestel *et al.*, 2005) , although the approach (in a paper of medium quality) has been shown to be cost effective in a south Asian context (Karachi, Pakistan) (Sharieff *et al.,* 2008) (+)/(-).

Jakobsen *et al.* (2008) highlighted the waste of resource of policies aimed at breastfeeding-only practices in countries with strong breastfeeding practices.

Poverty and intervention causality: No study looked at the impact that an intervention had on poverty nor at how the intervention was less or more successful because of the poor setting.

Intervention because of poverty: Only one paper considered cash transfers as an intervention to decrease infant and maternal mortality (Lim *et al.*, 2010) . The paper highlighted the difficulty in reaching the most disadvantaged groups despite their being the key focus of the intervention. Infants of urban-based mothers benefited less from the scheme than mothers in rural areas; similarly, the poorest decile of the study population benefited least from the cash-transfer scheme.

4.2.4 Urbanity and impact (sustainability)

No study reported a specific intervention which was purposefully done for urban areas alone. In most cases, the key focus was the poor/low-resource setting. Urban areas were mostly identified by the location of the hospital/health centre where the study was conducted. In general there was a lack of reflection on the issues linked to urban areas and what this entailed for the type of intervention conducted. Possibly underlying all the studies was the idea that some of the interventions were only feasible in urban settings. Lim *et al.* (2010) highlighted the relative lack of progress in Indian urban areas where it should be easier to get access to services because of the big investments made through the cash-transfer scheme. Disadvantaged groups are hard to reach despite regardless of the residence.

Overall the responses seemed to be focused on the short-term impact of the trials on the key outcomes. Even studies that looked at the impact that audit might have in the long term did not specifically report on changes in policy. The range of studies we have considered highlight the need for more long-term evaluations as well as analysis of the potential effectiveness of interventions that have been evaluated in low income country settings, but not specifically considered in the context of urban, poor populations.

Figure 4.1: Causal chain for maternal health

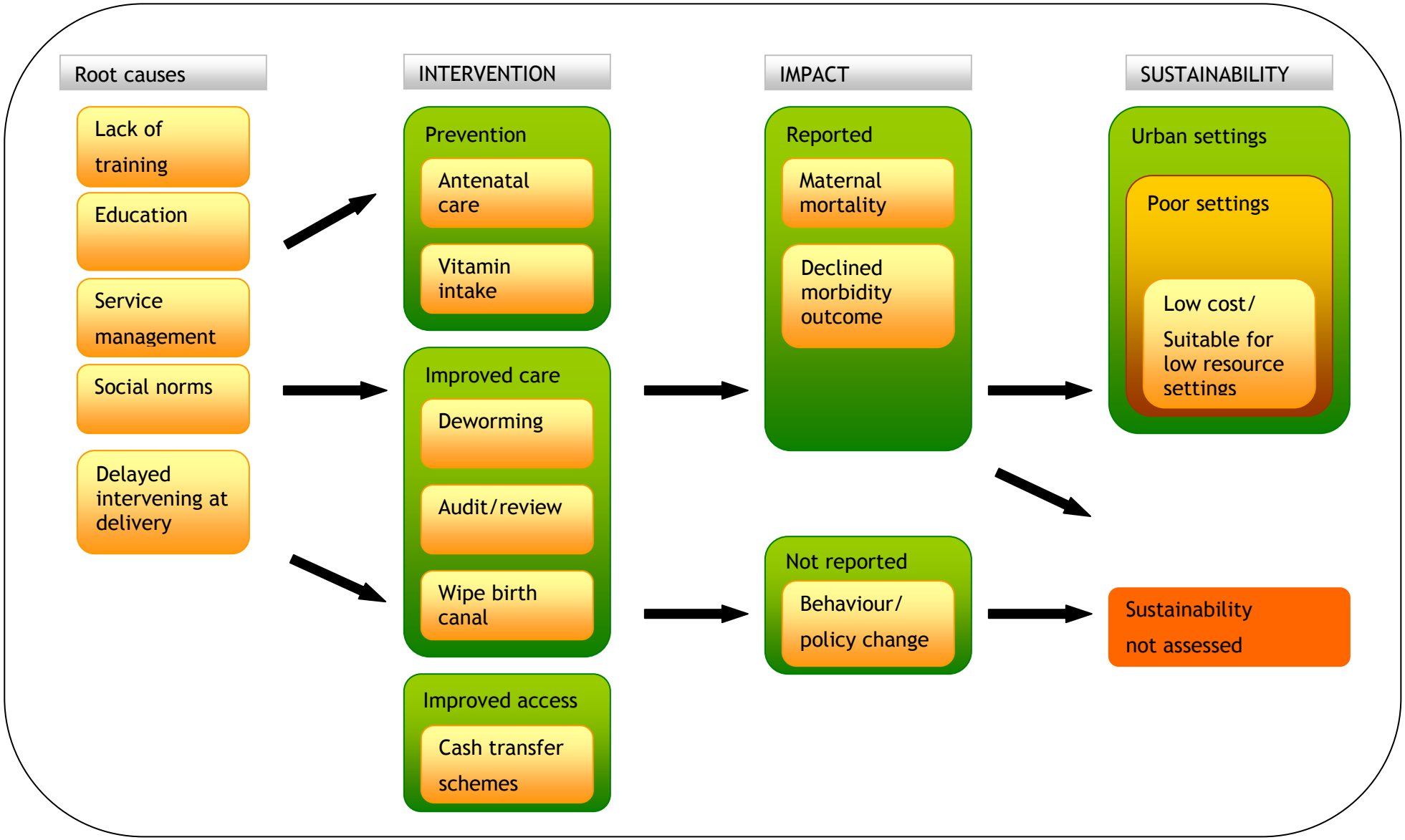
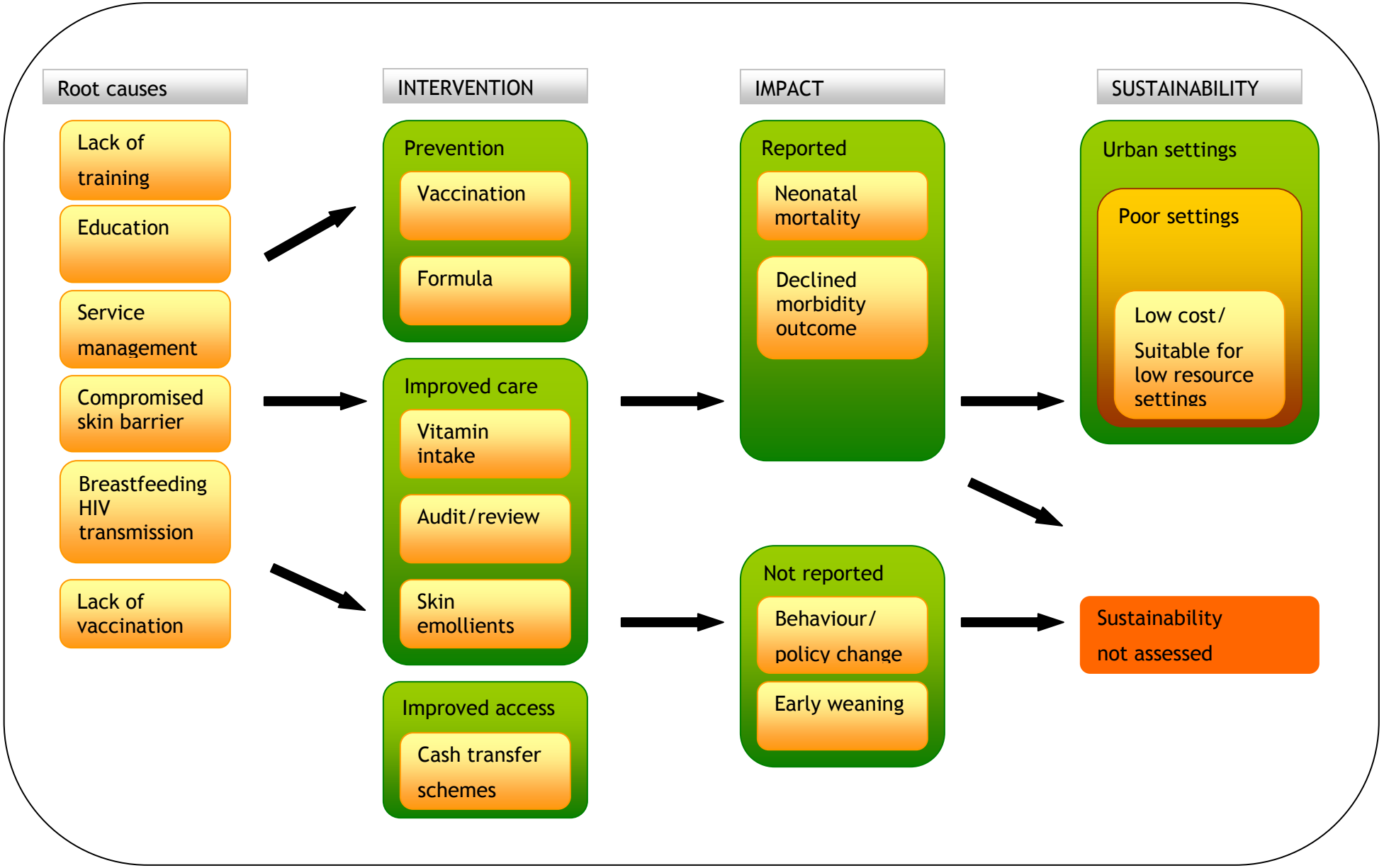


Figure 4.2: Causal chain for infant and neonatal mortality



4.3 Summary of results of causal chain analysis

We identified seven high-quality items with evidence of successful interventions in terms of maternal and infant outcomes. The heterogeneity of the successful interventions we report here reflects our deliberately inclusive search and inclusion strategy. There are four studies (Appendix 4.9) where the positive mortality outcome was clearly targeting or, with disaggregation, could be shown to have a beneficial effect for poor urban populations. In keeping with our inclusive approach to addressing this question, however, we also present a second table (Appendix 4.10) to show those high-quality studies (n=3) with positive impact(s) on maternal and infant outcomes that (based on circumstantial evidence, for example the site of intervention) we have every reason to believe addressed a poor urban population, though this was either not stated explicitly or was unclear.

Returning to the four studies, generalising from so few is inadvisable, and just one of the papers (Darmstadt *et al.*, 2008) dealt with infant mortality. Notable, however, is that two out of the four involved service (re)organisation in some form for maternal healthcare (Munjanja *et al.*, 1996; Dumont *et al.*, 2006), albeit with rather different recommendations. Munjanja *et al.*'s (1996) study in Zimbabwe tested whether reducing the number of routine antenatal visits and tests for routine pregnancies might have had a negative impact on mortality outcomes. Their study, using a RCT design, found no significant change in perinatal and maternal mortality. Dumont *et al.*'s (2006) Senegalese study using before and after study design showed that, when applied to qualified professionals (physicians, midwives, managers), the Maternal Deaths Review (MDR) helped to improve the organisation of care, leading to significant decline in overall mortality over the study's three year period.[16]

The Darmstadt *et al.* (2008) study in Bangladesh, using a prospective, randomised controlled design, showed significant reductions in neonatal mortality rates for preterm neonates (≤33 weeks) at risk of skin infections who received emollient skin-barrier therapy. A companion paper (Le Fevre *et al.*, 2010) (++)/(+) on the cost-effectiveness of this intervention is reviewed elsewhere in this report.

Whilst all of these three interventions showed significant impact on maternal or neonatal mortality, none dealt with the issues involved in accessing the services where the interventions were provided, although the economic evaluation accompanying the last study did look at issues of sustainability. The one study that did deal with issues around accessing health services is that by Lim *et al.* (2010), which considered the impact of India's JSY conditional cash-transfer scheme on maternal health outcomes through analyses of the National Family Health Service (NFHS). The claims made for the JSY programme in India by Lim *et al.* (2010) are not without critique (Das *et al.*, 2010), some of which the authors have acknowledged (Lim *et al.*, 2011), in particular that their analyses of demand-side interventions such as the JSY cannot deal with supply-side issues such as facility readiness.

Turning to the studies that did not specifically report on urban areas, the three successful high-quality interventions identified to impact on infant mortality involved four very different kinds of intervention. Studies by Cobra *et al.* (1997) and Taha *et al.* (1997) targeted infants in general. The study by Taha *et al.* (1997) on vaginal cleansing to reduce bacterial infections, which are substantial in many

[16] A linked, but separate study by Dumont *et al.* (2005) using a similar approach is listed in Appendix 4.10 for high-quality, positive interventions, but ones without explicit application to poor urban populations.

resource-poor settings, whilst not a controlled experimental study, provided convincing evidence for significant impact on early neonatal mortality rates.

The final successful intervention addressing maternal mortality involved a change to service intervention in Senegal (Dumont *et al*., 2005), and it is worth noting that it referred to the same setting as that in Dumont et al. (2006) in Table 4.1, namely, the introduction of routine audits of maternal deaths as a tool to improve service delivery, underlining the importance of facility-based quality improvement measures. MDR does appear to be another relatively low cost and high impact intervention.

5. Strengths and limitations

Summary

Limitations include:

- Bias towards English language literature
- Bias against modelling-based economic evaluations
- Restriction to maternal or infant mortality outcomes, excluding non-mortality health outcomes for mothers and infants
- Problems in identifying 'poor' populations and reliance on the use of proxies for 'poor'

5.1 Search strategy

There are a number of limitations in our review. One key issue is a bias towards English language literature. By restricting our search strategy to largely English language databases, we may have missed relevant studies in other languages, this is despite the fact that some databases do provide English language abstracts for non-English language papers. We have tried to mitigate against this by examining relevant papers in French, Spanish and Italian. Moreover, while we do not have the resources for additional translation, we have also sought to identify potentially relevant papers in other languages whose English language abstracts appear relevant.

In developing and refining our search strategy, it became clear that it would be difficult to come up with a comprehensive set of terms to cover the many different definitions of poverty and urbanicity. We sought to counter this risk by not including any specific poverty or urbanicity terms in our search strategy, and instead sought to identify studies that looked at maternal and child health in our target countries and then to determine whether these studies did focus on our target population. Our study protocol indicated that we would make our initial decisions on inclusion/exclusion on the basis of study abstracts/summaries. However it had to be acknowledged that relevant papers might not provide sufficient detail on target population to judge whether a paper focused on urban, poor populations from the abstract alone. We tried to account for this by erring on the side of retrieval of full text papers where a study appeared relevant in all respects other than having an indication of geographical location or socio-economic status of the target population.

Our primary search strategy may also not have been sensitive enough to pick up economic evaluations which were based on modelling rather than empirical studies; while we did search both Econlit and the NHS Economic Evaluation Database, a supplemental search of several key databases making use of key economic evaluation terms was conducted to see whether any additional studies could be identified, including the Office of Health Economics Health Economics Evaluation Database (HEED). Given the limited number of effectiveness studies that looked at interventions specifically for urban populations and reported maternal and/or infant mortality outcomes, this is not surprising.

Another challenge has been the limited functionality of some databases, which in some cases have made it difficult to construct complex search strategies and/or to import records electronically into EndNote. In some cases, the lack of functionality

meant that we did not do more than a cursory search of several databases identified in our initial strategy (Appendix 2.2). In saying this, the functionality of the main databases used in this review, including PubMed and POPLINE, had reasonable functionality. Some databases also did not include abstracts as part of their bibliographic records, limiting their usefulness. This potentially means that we may have missed some relevant studies, although we have searched through a broad range of databases in health, development and social sciences. We have also tried to counter any limitations through running a number of more limited search strategies on these databases, as well as through citation searching of references of included studies and handsearching of a number of key journals and websites. Despite searches of a range of governmental and international agencies, non-governmental organisations and some other websites, and searching databases that picked up on discussion papers and theses, there may also be additional grey literature sources that might have been searched in more detail had resources permitted.

5.2 Scope of review

It is also important to acknowledge that by restricting the focus of our review to studies that had maternal or infant mortality as one of the outcomes, as indicated in our revised protocol, we have certainly excluded bodies of evidence related to non-mortality maternal and infant health outcomes in poor urban populations, including those that produced a large volume of evidence. This includes work produced by, for example, Cooper *et al.* (2002) and colleagues in a poor peri-urban location (Khayelitsha) in South Africa, work by the African Population and Health Research Center (APHRC, 2002a, 2002b) in Nairobi, and a range of individual studies (e.g. Mullany *et al.*, 2007). Qualitative studies that looked at the reasons for uptake and continued participation in maternal and infant health services, but did not look at the relationship with changes in mortality outcomes were excluded from the analysis, but would also have been a valuable additional source of information. Such studies could also have helped in understanding the impacts of different contexts and cultures on the use of services. For instance Fotso *et al.* (2009a, 2009b) looked at factors that influenced women's maternal health service seeking behaviours in the slums of Nairobi.

We have already acknowledged that there were major problems in identifying 'poor' populations – we took an inclusive strategy and included measures that are frequently used as proxies for 'poor'. Indeed when we read full text articles, it became clear that many studies, while implicitly focusing on individuals in poor countries, did not specifically report socio-economic status or other measures of poverty.

The quality and heterogeneity of studies identified has also meant that we have had to undertake a narrative review rather than meta analyses.

6. Conclusions and recommendations

Summary

Interventions supported by the review are already present in existing WHO guidelines, but do not specifically address the effectiveness of different models of service delivery.

Interventions in urban areas need to specifically consider the question 'Who gains?' or 'Who loses?' as a result of an intervention.

Research should be clearer about the definitions used for common measures (e.g., urban, poor, poverty) in the reporting of interventions in the literature.

In order to understand what works to reduce maternal and infant mortality among poor urban people in LICs and LMCs, there is a need for interventions (and their robust evaluation) that specifically target this group. There will be more to learn from studies that do not explicitly mention whether they target urban populations, possibly contacting study authors to obtain more information on target populations in order to consider the potential relevance of approaches in an urban context. There are a very limited number of interventions targeting the urban poor's access to and use of MCH services, and even fewer that use mortality indicators as their outcomes. This small evidence base is out of step with the growing interest in, and scale of, urban poor people (ref major reports e.g. UNHABITAT, 2010) and there are growing calls, which this review adds to, for a move from description to evaluation (Freudenberg *et al.*, 2005; Harpham, 2009). We know that MCH interventions are complex and difficult to evaluate (Ronsmans *et al.*, 2003). Set against the backdrop of rapidly growing and highly mobile urban poor populations, their evaluation becomes even more complex. We suggest that future interventions in urban areas (even those not necessarily targeting the urban poor) need to specifically consider the question 'Who gains?' or 'Who loses?' as a result of an intervention. In addition there is a need to address the question of sustainability in low resource environments such as urban slums. Most of the studies we looked at did not consider the long-term implications and how the interventions might have had an impact on policies or on behavioural changes.

Our approach, reflecting our pre-review mapping of the possible evidence, is that the best available evidence is preferable to not using any evidence. Despite the inclusivity of our approach, both in terms of item identification, study design, data type and definitions (for example, a broad approach to defining 'poor'), we know very little about the most effective models to reduce maternal and infant (including neonate) mortality among poor, urban populations. For example, despite the volume of work that shows that geographic access to health services for the urban poor tends to be lower than that of their rural counterparts, our search did not yield one intervention considering the mortality outcomes of differential access, such as access to EmOC, for the urban poor; however, the Lim *et al.* (2010) (++)/(++) study did separately look at urbanicity and poverty and impacts on infant mortality rates. To make sure that we were not unnecessarily restricting our searches, and mindful of the relative rarity of maternal mortality events, we also included severe acute maternal morbidity (SAMM) (haemorrhage, dystocia, hypertension, sepsis, incomplete abortion, Caesarean section (CS), hysterectomy, and blood transfusion) (World Health Organization, 2011b), but this still yielded

very little. Only one paper (de Bernis *et al.*, 2000) (+)/(+) looked specifically at the link between service delivery and maternal mortality and morbidity for urban populations with contrasting health care service provision. This study, from Senegal, showed that an area where women were more likely to deliver in hospitals with trained midwives had lower levels of maternal mortality than an area where most women gave birth in district health centres, usually assisted by TBAs, implying that access to skilled health care is fundamental. Given that the distribution of women by socio-economic groups was very similar in both communities, most of the effect could be attributed to these differentials in service provision.

Our searches and analyses encountered major problems in identifying 'poor' populations. Whilst we took an inclusive strategy and included measures that are frequently used as proxies for 'poor' (e.g., material ownership indices), much of the evidence uncovered by our searches treated terms such as 'poor' and 'poverty' as unproblematic – especially that produced in the medical literature. There is a need for greater clarity about the definitions used for common measures (e.g., urban, poor, poverty) in the reporting of interventions in the literature. Without this clarity, the potential usefulness of high-quality studies for understanding what works to improve the health of the urban poor is greatly reduced.

Secondary analyses of datasets such as the DHS and MICS are widely used in the study of the urban poor (and many were identified in our initial searches but excluded from the review). Such datasets represent an important source of descriptive information, but their explanatory power is very limited, even when data are disaggregated to identify the urban poor in wealth quintiles based on material ownership. The evidence base, where it does disaggregate and identify (however loosely) the urban poor, tends to compare and contrast with rural populations. Whilst this approach is intuitive and relatively easy to operationalise, especially for secondary analyses of large-scale datasets such as the DHS, we need to remember that 'the urban health goal is not simply to be better on average than rural areas. The ambition must be to attain good health for all absolutely' (Dye, 2008, p.768).

What, then, are the methodological issues involved in studying the health of poor urban people? Our review found few studies for inclusion that acknowledged and studied the urban poor as an individual (highly heterogeneous) group. Many descriptive studies either compare urban poor with urban non-poor and/or rural populations. Poor urban settings can introduce methodological issues that make intervention delivery and evaluation difficult, above and beyond those limitations that might exist in a LIC setting. However, it is important to remember that poor urban populations do not just live in slums or informal settlements. There are many poor urbanites who do not live within slums. Non-slum dwelling urban poor are just as 'invisible' in the evidence our search produced.

There is a lag between researchers' (and funders') intervention research interests, but also, we would argue, a degree of inertia. Long-term funding for non-urban poor settings that evaluate health interventions make compelling arguments for continued funding, in part to protect time series data. Many longitudinal study sites in more rural settings have made efforts to capture population movements to and from urban areas (Collinson and Adazu, 2006). However, the continued concentration of, for example, Demographic Surveillance Sites in LICs and LMCs in largely rural settings means that data with explanatory power continue to be absent for many urban poor.

Urban upgrading programmes (also called slum upgrading or improvement programmes) are complex interventions and can include better provision of health services in general and MCH services in particular as part of a bundle of services (Field and Kremer, 2006). Given that MDG7 Target 11 'By 2020, to have achieved a significant improvement in lives of at least 100 million slum dwellers' has generated the production and consumption of much data about slum dwellers' lives, it was surprising that we found no relevant MCH evidence produced by evaluations before and after urban upgrading. Urban upgrading evaluations have tended to rely on changes in tenure and access to water and sanitation. Even when health outcomes are the focus, research has tended to evaluate the impact on infectious diseases (for example, Butala *et al.*, 2010). One forthcoming item we did identify was the proposed 3ie synthetic review *Slum Upgrading Strategies and Their Effects on Health and Social Outcomes* by Saith *et al.* (forthcoming), as yet not released.

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Appendices

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Conflicts of interest

The authors declare no conflicts of interest.

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Appendix 2.1: Inclusion and exclusion criteria

Criterion	Inclusion	Exclusion
Types of studies	Randomised controlled trials Non-randomised controlled trials Observational studies with control groups Longitudinal time series studies Systematic reviews of these interventions Economic evaluations and modelling studies of relevant interventions Qualitative evaluations looking at implementation of relevant interventions	Editorial, commentaries or book reviews Policy analyses Qualitative secondary analyses
Types of participants	Studies including: Mothers and/or infants up to age of 24 months AND poor populations; AND urban, or semi-urban, or peri-urban settings AND low income and lower middle income countries[18]	Studies that include only: Children aged more than 24 months OR non-poor urban populations OR rural settings OR upper middle-income countries countries in Europe
Types of intervention	Studies on interventions broadly defined as actions concerned with improving the access, utilisation or effectiveness of maternal and infant health services in areas serving urban poor populations	Studies that did not clearly distinguish effects from other non-targeted health interventions, such as the provision of potable water
Types of outcomes	Studies which have one or more of the following indicators as outcomes: maternal, infant, neonatal, perinatal, post-neonatal mortality, and still-birth; severe acute maternal morbidity (SAMM) (haemorrhage, dystocia, hypertension, sepsis, incomplete abortion, Caesarean section (CS), hysterectomy, and blood transfusion)	Studies which have one or more of the following indicators as outcomes: Children mortality where the age is not specified Maternal morbidity other than SAMM

[18] http://data.worldbank.org/about/country-classifications/country-and-lending-groups

Language	Studies published in English, French, Spanish and Italian	Studies published in languages other than English, French, Spanish or Italian.
Time	Studies published from 1987 onwards	Studies published before 1987

Appendix 2.2: Search strategy for electronic databases

Medline/PubMed and PsychINFO

Maternal Health Services /

Pregnancy /

Infant /

Abortion, Induced /

Obstetric Surgical Procedures /

Pregnancy Complications /

Vaginal Fistula /

OR / 1-7

Infant Mortality /

Maternal Mortality /

Perinatal Mortality /

OR / 9-11

Africa /

Central America /

China /

India /

Melanesia /

(Afghanistan OR Guinea OR Nepal OR Bangladesh OR Guinea-Bissau OR Niger OR Benin OR Haiti OR Rwanda OR Burkina Faso OR Kenya OR Sierra Leone OR Burundi OR Korea (NOT South Korea OR Republic of Korea) OR Solomon Islands OR Cambodia OR Kyrgyz OR Somalia OR Central African Republic OR Lao OR Tajikistan OR Chad OR Liberia OR Tanzania OR Comoros OR Madagascar OR Togo OR Congo OR Malawi OR Uganda OR Eritrea OR Mali OR Zambia OR Ethiopia OR Mauritania OR Zimbabwe OR Gambia OR Mozambique OR Ghana OR Myanmar OR Burma OR Angola OR India OR São Tomé OR Armenia OR Iraq OR Senegal OR Belize OR Jordan OR Sri Lanka OR Bhutan OR Kiribati OR Sudan OR Bolivia OR Kosovo OR Swaziland OR Cameroon OR Lesotho OR Syria OR Cape Verde OR Maldives OR Thailand OR China OR Marshall Islands OR Timor OR Micronesia OR Tonga OR Côte d'Ivoire OR Ivory Coast OR Moldova OR Tunisia OR Djibouti OR Mongolia OR Turkmenistan OR Ecuador OR Morocco OR Tuvalu OR Egypt OR Nicaragua OR Ukraine OR El Salvador OR Nigeria OR Uzbekistan OR Georgia OR Pakistan OR Vanuatu OR Guatemala OR Papua New Guinea OR Vietnam OR Guyana OR Paraguay OR West Bank OR Gaza OR Honduras OR Philippines OR Yemen OR Indonesia OR Samoa).ti, ab

OR / 13-18

8 AND 12 AND 19

Limit 20 to year 1987-

Embase

Maternal-Care /

Pregnancy /

Infant /

Induced-Abortion /

Obstetric-Care /

Pregnancy-Complication /

OR / 1-6

Infant-Mortality /

Prenatal-Mortality /

Perinatal-Mortality /

Maternal-Mortality /

OR / 8-11

Africa /

Central America /

Developing-Country /

Melanesia /

China /

India /

(Afghanistan OR Guinea OR Nepal OR Bangladesh OR Guinea-Bissau OR Niger OR Benin OR Haiti OR Rwanda OR Burkina Faso OR Kenya OR Sierra Leone OR Burundi OR Korea (NOT South Korea OR Republic of Korea) OR Solomon Islands OR Cambodia OR Kyrgyz OR Somalia OR Central African Republic OR Lao OR Tajikistan OR Chad OR Liberia OR Tanzania OR Comoros OR Madagascar OR Togo OR Congo OR Malawi OR Uganda OR Eritrea OR Mali OR Zambia OR Ethiopia OR Mauritania OR Zimbabwe OR Gambia OR Mozambique OR Ghana OR Myanmar OR Burma OR Angola OR India OR São Tomé OR Armenia OR Iraq OR Senegal OR Belize OR Jordan OR Sri Lanka OR Bhutan OR Kiribati OR Sudan OR Bolivia OR Kosovo OR Swaziland OR Cameroon OR Lesotho OR Syria OR Cape Verde OR Maldives OR Thailand OR China OR Marshall Islands OR Timor OR Micronesia OR Tonga OR Côte d'Ivoire OR Ivory Coast OR Moldova OR Tunisia OR Djibouti OR Mongolia OR Turkmenistan OR Ecuador OR Morocco OR Tuvalu OR Egypt OR Nicaragua OR Ukraine OR El Salvador OR Nigeria OR Uzbekistan OR Georgia OR Pakistan OR Vanuatu OR Guatemala OR Papua New Guinea OR Vietnam OR Guyana OR Paraguay OR West Bank OR Gaza OR Honduras OR Philippines OR Yemen OR Indonesia OR Samoa).ti, ab

OR / 13-19

7 AND 12 AND 20

Limit 21 to publications after 1986

ASSIA

DE="infant mortality"

DE="maternal mortality"

DE="perinatal morbidity mortality"

1 OR 2 OR 3

Infant* OR Matern* OR Baby OR Babies OR newborn OR mother* OR pregnan* OR gravida OR gestat* OR primipar* OR fetal OR foet* OR birth* OR C-section* OR Caesarean OR Caesarean OR peripart* OR prepart* OR intrapart* OR postpart* OR sepsis OR eclampsia* OR dystocia OR hysterectomy OR pelvic fistula OR pelvic fistulae OR episiotomy OR perineum OR uterine rupture OR abruptio placentae OR placental abruption OR still-birth OR abortion OR natal* OR perinatal OR prenatal OR antenatal OR postnatal OR breastfeed*)

(multipart* NOT multiparty)

5 OR 6

(mortality OR death* OR fatal*)

7 AND 8

4 OR 9

DE=("obstetrics" or "childbirth" or "birth centres" or "Caesarean section" or "home birth" or "labour" or "dystocia" or "shoulder dystocia" or "premature labour" or "natural childbirth" or "placenta" or "vacuum extraction" or "vaginal birth" or "waterbirth" or "infancy" or "pregnancy" or "abortion" or "illegal abortion" or "partial birth abortion" or "selective abortion" or "wrongful birth" or "ectopic pregnancy" or "false pregnancy" or "gestational trophoblastic disease" or "in vitro fertilization" or "intracytoplasmic sperm injection" or "miscarriages" or "multiple pregnancy" or "planned pregnancy" or "unwanted pregnancy" or "maternal health care" or "antenatal care" or "antenatal education" or "perinatal care" or "postnatal care")

(Afghanistan OR Guinea OR Nepal OR Bangladesh OR Guinea-Bissau OR Niger OR Benin OR Haiti OR Rwanda OR Burkina Faso OR Kenya OR Sierra Leone OR Burundi OR Korea (NOT South Korea OR Republic of Korea) OR Solomon Islands OR Cambodia OR Kyrgyz OR Somalia OR Central African Republic OR Lao OR Tajikistan OR Chad OR Liberia OR Tanzania OR Comoros OR Madagascar OR Togo OR Congo OR Malawi OR Uganda OR Eritrea OR Mali OR Zambia OR Ethiopia OR Mauritania OR Zimbabwe OR Gambia OR Mozambique OR Ghana OR Myanmar OR Burma OR Angola OR India OR São Tomé OR Armenia OR Iraq OR Senegal OR Belize OR Jordan OR Sri Lanka OR Bhutan OR Kiribati OR Sudan OR Bolivia OR Kosovo OR Swaziland OR Cameroon OR Lesotho OR Syria OR Cape Verde OR Maldives OR Thailand OR China OR Marshall Islands OR Timor OR Micronesia OR Tonga OR Côte d'Ivoire OR Ivory Coast OR Moldova OR Tunisia OR Djibouti OR Mongolia OR Turkmenistan OR Ecuador OR Morocco OR Tuvalu OR Egypt OR Nicaragua OR Ukraine OR El Salvador OR Nigeria OR Uzbekistan OR Georgia OR Pakistan OR Vanuatu OR Guatemala OR Papua New Guinea OR Vietnam OR Guyana OR Paraguay OR West Bank OR Gaza OR Honduras OR Philippines OR Yemen OR Indonesia OR Samoa).ti, ab

10 AND 11 AND 12

Limit 13 to publications after 1986

PAIS, IBSS

(Infant* OR Matern* OR Baby OR Babies OR newborn OR mother* OR pregnan* OR gravida OR gestat* OR primipar* OR fetal OR foet* OR birth* OR C-section* OR Caesarean OR Caesarean OR peripart* OR prepart* OR intrapart* OR postpart* OR sepsis OR eclampsia* OR dystocia OR hysterectomy OR pelvic fistula OR pelvic fistulae OR episiotomy OR perineum OR uterine rupture OR abruptio placentae OR placental abruption OR still-birth OR abortion OR natal* OR perinatal OR prenatal OR antenatal OR postnatal OR breastfeed*).ti, ab, kw

(Mortality OR death* OR fatal*)

1 AND 2

DE="mortality"

DE=("maternal and infant welfare" OR "clinics maternity services" OR “pregnancy" OR "abortion" OR "mothers" OR "infants")

4 AND 5

3 OR 6

Limit 7 to publications after 1986

Western Pacific Region Index Medicus

Maternal Health Services /

Pregnancy /

Infant /

Abortion /

Induced OR Obstetric Surgical Procedures /

Pregnancy Complications /

Vaginal Fistula /

OR/ 1-7

Infant Mortality, ti, ab, kw

Maternal Mortality, ti, ab, kw

Perinatal Mortality, ti, ab, kw

OR/ 9-11

8 AND 12

13 NOT (Singapore OR South Korea OR Japan OR Malaysia)

Limit 14 to publications after 1986

POPLINE

Maternal Health, ti, kw

Infant, ti, kw

Infant health, ti, kw

Abortion, ti, kw

Obstetrics, ti.kw

Pregnancy, ti, kw

Infant Mortality, ti, kw

Maternal Mortality, ti, kw

Perinatal Mortality, ti, kw

Neonatal Mortality, ti, kw

OR / 1-10

Urban areas, ti, kw

Urban population, ti, kw

OR/ 12-13

11 AND 14

Limit 15 to publications after 1996

ECONLIT

Infant mortality, ti, ab, kw

Maternal mortality, ti, ab, kw

Perinatal mortality, ti, ab, kw

Neonatal mortality, ti, ab, kw,

Birth, ti, ab. kw

Abortion, ti, ab, kw

Obstetric*

Appendix 2.3: Search strategy for websites

To facilitate website searches, Google Advanced was used to search individual domains. The search strings were

Infant mortality

Maternal mortality

Only items in English were sought, and the first 20 items were reviewed for relevance. All of the websites that were searched have been tagged as *LSEDFID_SysRev2011* in Diigo (http://www.diigo.com/user/LSE_DFID) to facilitate sharing.

Appendix 2.4: Journals handsearched

All issues of the following journals published online between 1 January 2008 and 1 October 2010 were handsearched electronically:

Bulletin of the World Health Organization

BMC Pregnancy and Childbirth

BMC Health Services Research

BMC Public Health

BMC Women's Health

British Medical Journal

Health Policy and Planning

Journal of Tropical Pediatrics

Social Science and Medicine

PLoS ONE

PLoS Medicine

Appendix 2.5: Coding tool

GENERAL

ID
Unique study ID

AUTHORS
Authors Surname, Initial
(e.g. Coast E; Leone T)

PUB DATE
Publication date (Year)
(e.g. 1978)

PUB TYPE
Type of publication.
Select as many responses as required.

peer-reviewed journal article

non-peer-reviewed journal article/evaluation

book/book chapter

none of the above (please enter details)

FUNDING
What is the source of funding for the intervention?
Select as many responses as required.

public
(e.g. government, including government-funded research councils)

private
(e.g. company)

third sector
(e.g. NGOs, INGOs, charities, civil societies)

unclear/not stated

N/A

CONTEXT

COUNTRY
In which country(ies) or region(s) was the study conducted? Give the list of countries. Detail regions if individual countries are not listed.

(e.g. Nepal, Bangladesh OR Sub-Saharan Africa, South-East Asia)

URBANITY
In which settings is the study conducted?
Select as many responses as required

urban

peri-urban

rural

POOR PROFILE
Is the study population identified as "poor"?

yes

no

unclear/not stated

N/A

POOR CLASSIFICATION
On what bases is the study population identified as "poor"?
Select as many responses as required

absolute income

relative income (self-defined/researcher-defined/wealth index)

place of residence

education

SES/"class"

none of the above (please enter details)

unclear/not stated

N/A

INTERVENTION

INTERVENTION FOCUS (CATEGORIES)
What categories the intervention belongs to? Select as many response as required.

prevention
(e.g. education, immunization, nutrition)

improving the quality of care
(e.g. training, curricula, devices, drugs)

improving the access to care
(e.g. physical access, financial access)

INTERVENTION SUPPLY-DEMAND
Is the intervention focused on supply- or demand-side factors?
Select as many responses as required

supply-side
(e.g. training of service provider, changes in type of staffing, use of lay or community workers, reduction in distance to available facilities)

demand-side
(e.g. education of women, reduction in fees, vouchers, incentives, cash transfers, peer encouragement for service use)

unclear/not stated

INTERVENTION FOCUS (HEALTH)
What is the focus of the intervention?
Select as many responses as required

maternal health

neonatal health
(1-28 days)

infant health
(<1 year)

none of the above (please enter details)

MORBIDITY TARGET (MATERNAL HEALTH)
Which morbidity is the intervention set out to prevent maternal death from? Select as many response as required.

complication of unsafe abortion

hypertensive disorders
(e.g. pre-eclampsia, eclampsia)

postpartum haemorrhage

antepartum haemorrhage

dystocia
(e.g. abnormal foetal lie or presentation, rupture of uterus)

puerperal sepsis

direct obstetric causes not specified

malaria

HIV/AIDS

none of the above (please enter details)

MORBIDITY TARGET (NEONATAL/INFANT HEALTH)
Which morbidity is the intervention set out to prevent newborn death from? Select as many responses as required.

intra-partum related
(e.g. 'birth asphyxia')

preterm
(e.g. immaturity, low birth weight, and complications of pre-term birth)

sepsis/pneumonia

tetanus

congenital abnormalities

diarrhoea

neonatal morbidity (not specified)

infant morbidity (not specified)

none of the above (please enter details)

INTERVENTION TARGET POPULATION
Who is the intervention targeting?
Select as many responses as required.

women in general

specific sub-group of women (please enter details)
(e.g. HIV-positive pregnant women)

neonates in general

specific sub-group of neonates (please enter details)
(e.g. high risk babies such as low-birth babies)

infants
(<1 year)

specific sub-group of infants (please enter details)
(e.g. high risk infants such as HIV-exposed)

none of the above (please enter details)

AGENT
Who delivered the MCH intervention?
Select as many responses as required.
(please enter details on each agent role)

obstetrician

non-specialised doctor

midwife

nurse-midwife

nurse

auxiliary midwife

community health worker

lady health worker

traditional birth attendant

shopkeeper

pharmacist

family member/mother

women's group

none of the above (please enter details)

unclear/not stated

N/A

SETTING TYPE
What sort of setting was the MCH intervention delivered in?

government

not-for-profit
(e.g. FBO, charity, PNFP)

for profit

none of the above (please enter details)

unclear/not stated

SETTING SPECIFY
Where the MCH intervention was delivered? Select as many responses as required.

central hospital

district hospital

primary health centre

community health post

community

home

shops

pharmacy

none of the above (please enter details)

unclear/not stated

N/A

INTERVENTION
What is delivered as MCH intervention? Select as many responses as required.

education

surgical procedure

drug treatment

vaccination

nutrition

other types of care (not included above)
(e.g. Kangaroo Mother Care)

commodities
(e.g. bed net, birth kit)

financing

regulating

service organization

none of the above (please enter details)

unclear/not stated

N/A

Intervention (education)
What type of education is delivered as MCH intervention? Select as many as required.

hygiene-cord

breast feeding

newborn care seeking

newborn emergency (danger sign)

newborn warmth

birth planning (maternal emergency)

post natal home self-care

post natal maternal emergencies

counselling and testing for HIV

none of the above (please enter details)

unclear/not stated

Intervention (surgical procedure)
What type of surgical procedure is delivered as MCH intervention? Select as many responses as required.

destructive operation

episiotomy

hysterectomy

c-section

none of the above (please enter details)

unclear/not stated

Intervention (drug treatment)
What type of drug treatment is delivered as MCH intervention? Select as many as required.

antibiotics
(please specify if known – e.g., penicillin)

antihypertensive
(please specify if known)

ARV

vermicidal
(e.g. alvendazole)

intermittent presumptive treatment

uterotonics
(e.g. misoprostol)

none of the above (please enter details)

unclear/not stated

Intervention (vaccination)
What type of vaccination is delivered as MCH intervention? Select as many responses as required.

BCG
(Tuberculosis)

Polio

DTP
(Diphtheria, Tetanus, Pertussis)

HBV
(Hepatitis B Virus)

none of the above (please enter details)

unclear/not stated

Intervention (nutrition)
What type of nutrition is delivered as MCH intervention? Select as many responses as required.

macronutrients
(e.g. protein, carbohydrates, fat)

single micronutrient
(e.g. vitamin A, zinc, iron, folic acid, magnesium, calcium)

multiple micronutrient
(please enter details of types of micronutrients)

none of the above (please enter details)

unclear/not stated

Intervention (other type of care not specified above)
What type of care was delivered as MCH intervention? Select as many responses as required.

care during the antenatal period (please enter details)

care during labour and delivery (please enter details)
(e.g. clean delivery technique, uterine massage)

postpartum care (please enter details)
(e.g. include newborn warmth, hygiene cord care.)

none of the above (please enter details)

unclear/not stated

Intervention (commodities)
What type of commodity was delivered as MCH intervention? Select as many responses as required.

Bed net

birth kit

none of the above (please enter details)

Intervention (financing)
what type of financing was delivered as MCH intervention? Select as many responses as required.

tax credit

subsidy

user fee reduction

user fee abolition

cash transfer

cash voucher

none of the above (please enter details)

unclear/not stated

Intervention (regulating)
What type of regulating was introduced as MCH intervention? Select as many responses as required.

law

professional regulation

curricula

none of the above (please enter details)

unclear/not stated

Intervention (service organization)
What type of service organization was introduced as MCH intervention? Select as many responses as required.

introduction of specialised services

reduction in distance to facilities

training

new staff

staff role reduction

none of the above (please enter details)

unclear/not stated

Intervention (details)

INTERVENTION START
Start date (Month/Year)
(##/#### OR 00/####)
(e.g. 12/2010, 00/2010)

month/year
##/#### OR 00/#### (if only year stated)
(e.g. 12/2008, 00/2008 if only year stated)

unclear/not stated

N/A

INTERVENTION END
End date (Month/Year)
(##/### OR 00/####)
(e.g. 12/2010, 00/2010)

month/year
##/#### OR 00/#### (if only year stated)
(e.g. 12/2008, 00/2008 if only year stated)

unclear/not stated

N/A

INTERVENTION DURATION
What is the length of the intervention? (Number of months)

number of months
##
(e.g. 4, 12)

unclear/not stated

N/A

INTERVENTION DETAILS
Give details (not reported elsewhere) about the intervention (e.g., intensity)

Intervention (comparison group)
(applied to controlled experimental study, experimental study without concurrent control, observational studies with comparison group)

INTERVENTION COMPARISON SPECIFIC
What is delivered to the comparison group (specific to the comparison group)?

normal/existing service/financing mechanism/regulation (please enter details)

alternative interventions/service/financing mechanism/regulation (please enter details)

no intervention

INTERVENTION COMPARISION COMMON
Were common MCH services/financial mechanism/regulation delivered to both the exposure and comparison groups?

yes (please enter details)

no

unclear/not stated

STUDY DESIGN

STUDY TYPE
What is the design of the study?
Select as many responses as required

controlled experimental study
(e.g. randomised controlled trial, cluster randomised trials, non-randomised controlled trials)

experimental study without concurrent control
(e.g. interrupted time series, pre/post-test)

observational studies with comparison group
(e.g. cohort studies, case-control studies, cross-sectional studies)

observational studies without comparison group
(e.g. descriptive)

economic evaluation/modelling studies

qualitative studies
(e.g. focus groups)

review
(e.g. systematic review, rapid evidence appraisal, systematic mapping etc.)

none of the above (please enter details)
(e.g. ecological studies)

DATA TYPE

DATA TYPE
What sorts of data are presented in this study?
Select as many responses as required

quantitative

qualitative

DATA LONGITUDINAL
Are the data longitudinal?

yes

no

unclear/not stated

OUTCOMES

MORTALITY OUTCOME TYPES
Which mortality outcomes are measured in this study?
Select as many responses as required

VARIABLES
Prioritise binary variables *(e.g. death and survivors)*.
If not then enter continuous variable *(e.g. ratio=number of death/number of live births)*.

DENOMINATORS
For 'maternal mortality rate' the denominator will be 100,000 live births.
For the other mortalities 1,000 live births.

COMMENTS
When data are available for number of 'survivors', then transform it and enter the number of 'death'.

maternal mortality
(during pregnancy and within 42 days of termination of pregnancy)

perinatal mortality
(stillbirth and <7 days)

early neonatal mortality
(<7 days)

late neonatal mortality
(7-28 days)

neonatal mortality
(1-28 days)

post-neonatal mortality
(28 days – 1st birthday)

infant mortality
(<1 year)

late maternal mortality
(more than 42 days but less than one year after termination of pregnancy)

SAMM
please specify which maternal morbidity was measured (e.g., haemorrhage, dystocia, hypertension, sepsis, incomplete abortion) or which signs were used (e.g., C-section, hysterectomy, blood transfusion)

stillbirth

none of the above (please enter details)

BASELINE OUTCOME
Are data presented on outcome(s) prior to intervention?

yes

no

Outcomes (experimental study without concurrent control)

M&E WAVES
Please enter details

At how many points in time was outcome measured (baseline included)?
(e.g. 3)

M&E WAVE FIRST
Date of the first wave (Month/Year)
(##/### OR 00/####)
(e.g. 12/2010, 00/2010)

M&E WAVE LAST
Date of the last wave (Month/Year)
(##/### OR 00/####)
(e.g. 12/2010, 00/2010)

M&E DURATION SPACE
Were waves equally spaced?

yes

no

unclear/not stated

N/A

M&E DURATION PERIODICITY
what was the periodicity of waves? (number of months)
(e.g. 6)

OUTCOMES (observational studies with comparison group)

DATASET AGE: OLDEST
Date of the oldest dataset used in the analyses (Year)
(e.g. 1990)

DATASET AGE: RECENT
Date of the most recent dataset used in the analyses (Year)
(e.g. 2010)

OUTCOMES (observational studies without comparison group)

DATASET AGE: OLDEST
Date of the oldest dataset used in the analyses (Year)
(e.g. 1990)

DATASET AGE: RECENT
Date of the most recent dataset used in the analyses (Year)
(e.g. 2010)

OUTCOMES (review)

ITEM AGE: OLDEST
Date of the oldest item included in the review (Year)
(e.g. 1990)

ITEM AGE: RECENT
Date of the most recent item included in the review (Year)
(e.g. 2010)

FINDINGS

INTERVENTION CLAIMS
What claims are made for the effects of the intervention?
Select as many responses as required

positive

neutral

negative

unclear/not stated

N/A

MORTALITY OUTCOME FINDINGS: SUMMARY
What are the findings with relation to impact on mortality outcomes? (please enter details)

COMMENTS
Any general comments on study not coded elsewhere

QUALITY ASSESSMENT

THEORY

THEORY
Does the study use a particular theoretical perspective?
(e.g. community-based approach, peer involvement, psychological support, network)

yes (please enter details)

no

unclear/not stated

AIMS

AIMS
Is there a clear statement of the aims of the research?

yes

no

AIMS DETAILS
Describe the aims of the research

STUDY DESIGN

Study design (controlled experimental study)

RANDOMISATION TYPE
At what level are the randomised assignments done?
Select as many responses as required

individual

household

community/administrative grouping

facility

allocation not randomised

none of the above (please enter details)

unclear/not stated

N/A

T&C SELECTION
Give details about the selection criteria for T&C groups
(e.g. population, facility – dependent on unit of study)

T&C MATCHING
Are T&C groups matched on explicit criteria?

yes

no

unclear/not stated

N/A

T&C MATCHING LIST
On what variables are T&C groups matched?
Select as many responses as required

socio-demographic variables
(e.g. SES, ethnicity etc.)

access to service/intervention

geographic location

none of the above (please enter details)

T&C GEOGRAPHY
Is the control group geographically separate from the treatment group?

yes

no

unclear/not stated

N/A

T&C CONTAMINATION
Is control contamination addressed in the item being reviewed (e.g. article)?
Control contamination here refers to interaction between the T&C groups (e.g. the intervention group passes on information to the control group in a health education intervention)

yes (please enter details)
(e.g. intention to treat)

no

unclear/not stated

N/A

PARTICIPANT BLINDING
Were the participants blinded?

yes

no

unclear/not stated

N/A

OBSERVER BLINDING
Were the observers blinded?

yes

no

unclear/not stated

N/A

Study design (experimental study without concurrent control)

GROUPS SELECTION
Was the group selection specified?
(e.g. inclusion/exclusion criteria)

yes (please enter details)
Give selection criteria for groups (e.g. population, facility – dependent on unit of study)

no

unclear/not stated

N/A

M&E INFO
Is the outcome measured before and after the intervention?

yes

no

unclear/not stated

N/A

M&E METHOD
Is the measurement method the same pre- and post?

yes

no

unclear/not stated

N/A

M&E METHOD CHANGE
If the measurement method is not the same pre- and post, then is any reason given for changing the measurement pre- and post?

yes (please enter details)

no

unclear/not stated

BIASES/LIMITATIONS
Is there discussion of possible biases or limitations?

yes

no

unclear/not stated

Study design (observational studies with comparison group)

GROUPS SELECTION
Was the group selection specified?
(e.g. inclusion/exclusion criteria)

yes (please enter details)
Give selection criteria for groups (e.g. population, facility – dependent on unit of study)

no

unclear/not stated

N/A

DATASET TYPE
What kind of dataset was used?
Select as many responses as required

nationally representative survey

ad hoc survey

in depth qualitative interviews

civil registration

census

hospital records

surveillance system

none of the above (please enter details)

DATASET LIMITATIONS
Does the study discuss the limitations of the datasets used?

yes

no

unclear/not stated

DATASET BIAS DISCUSSION
Does the study discuss possible biases or caveats or limitations?

yes

no

unclear/not stated

Study design (observational studies without comparison group)

DATASET TYPE
What kind of dataset was used?
Select as many responses as required

nationally representative survey

ad hoc survey

in depth qualitative interviews

civil registration

census

hospital records

surveillance system

none of the above (please enter details)

DATASET LIMITATIONS
Does the study discuss the limitations of the datasets used?

yes

no

unclear/not stated

DATASET BIAS DISCUSSION
Does the study discuss possible biases or caveats or limitations?

yes

no

unclear/not stated

Study design (economic evaluation/modelling studies)

ECONOMIC EVALUATION/MODELLING
Separate validated criteria for economic evaluations used by Evers et al (2005) will be used; supplemented by Philips et al (2004) guidance for modelling

Study design (qualitative studies)

QUALITATIVE DATA
What method(s) is(are) used to produce the qualitative data?
Select as many responses as required

in-depth interviews

focus groups

observation

none of the above (please enter details)

N/A

Study design (review)

PEER REVIEW
Has the review study been subject to peer review?

yes

no

unclear/not stated

REVIEW TYPE
What kind of review?

systematic review

synthetic review

systematic mapping

none of the above (please enter details)

unclear/not stated

PEER REVIEW
Has the review study been subject to peer review?

yes

no

unclear/not stated

SELECTION

SELECTION METHODS
What selection method was used?

sampling

overall population

SELECTION AIMS
Was the selection strategy relevant for the aims of the study?

yes

no

unclear/not stated

SELECTION SIZE
What was the sample size?
(e.g. 80)

SELECTION SIZE JUSTIFICATION
Is the sample size justified in the item?
(e.g. statement justifying the sample size choice)

yes

no

SELECTION ORIGIN
Is it explicit where the study participants were selected from?

yes

no

SELECTION ORIGIN JUSTIFICATION
Is it explicit why this setting was chosen?

yes

no

SELECTION SELECTION
Is it explicit who was selected?

yes

no

SELECTION SELECTION JUSTIFICATION
Is it explicit why the study participants were selected?

yes

no

SELECTION SELECTION DETAILS
Is it explicit how the study participants were selected?

yes

no

SELECTION CHARACTERISTICS
Is information given on the characteristics of the study participants?
(e.g. possible sources of confounders)

yes (please enter details)

no

SELECTION (SAMPLING)
(applied if selection=sampling)

SAMPLING METHOD
What sampling method was used? Please describe the method of sampling.

stratified

random

systematic

convenience

judgement

quota

snowball

RDS

none of the above (please enter details)

unclear/not stated

Selection (overall population)

SELECTION DETAIL
Please describe the method of selection.

DATA

DATA COLLECTION
Is it explicit how the data were collected?

yes

no

DATA COLLECTION JUSTIFICATION
Is explicit justification given for collecting the data in this way?
(e.g. sentence)

yes

no

DATA RECORDS
Is it explicit how the data were recorded?

yes

no

DATA MODIFIED
Were the data collection methods modified during the process?

yes

no

DATA MODIFIED JUSTIFICATION
If data collection methods were modified during the process, then is justification provided?

yes

no

N/A

DATA COLLECTOR
Is it explicit who collected the data?

yes

no

ANALYSES

DATA ANALYSES
Is it explicit how the analysis was done?

yes

no

ANALYTIC APPROACH
Is there an explicit justification for the analytic approach?

yes

no

unclear/not stated

DATA TRIANGULATION
Have different sources of data about the same issue been compared (triangulation)?

yes

no

unclear/not stated

ANALYSIS REPEAT
Was analysis repeated by more than one researcher to ensure reliability?

yes

no

unclear/not stated

ANALYSES (controlled experimental study, experimental study without concurrent control, observational studies with comparison group)

QUANTITATIVE DATA BASELINE
Were exposure and comparison groups similar at baseline?

yes

no

unclear/not stated

QUANTITATIVE DATA ADJUSTED
If exposure and comparison groups were not similar at baseline, then were data adjusted for confounders?

yes

no

N/A

QUANTITATIVE DATA CONFOUNDERS
If data were adjusted for confounders, then what groups of confounder were included? Select as many responses as required

residence

wealth

ethnic group

age

education

parity

none of the above (please enter details)

N/A

ETHICS

ETHICS
Does the study provide evidence that it has been granted ethical clearance by an appropriate authority?

yes

no

ETHICS EXPLAINED
Is it explicit how the purpose of the research was explained and presented to participants?

yes

no

FEEDBACK
Have/will attempts be made to feedback results to participants?

yes

no

unclear/not stated

REFUSAL

REFUSAL RATE
Is participation refusal rate explicit?

yes

no

REFUSAL JUSTIFICATION
Is it explicit why some participants chose not to take part?

yes

no

FINDINGS

FINDINGS SUPPORT
Do the data presented support the authors' interpretations/findings?

yes

no

FINDINGS CONTRADICT
Are negative, unusual or contradictory cases presented?

yes

no

FINDINGS INTERPRETATIONS
Is there discussion of the evidence both for and against the researchers' interpretations?

yes

no

FINDINGS CONGRUENCE
Does the item demonstrate conceptual and/or theoretical congruence between this and other research?
Select as many responses as required

yes

no

unclear/not stated

FINDINGS GENERALIZABILITY
Are the findings of the study transferable to the source population?

yes

no

unclear/not stated

BIAS/LIMITATIONS
Is there discussion of possible biases or limitations?

yes

no

unclear/not stated

RESEARCHER REFLEXIVITY
(applied to all studies reporting on primary sources)

REFLEXIVITY
Is it clear whether researchers critically examined their own role, potential bias and influence?

yes

no

RESEARCHER RELATIONSHIP
Has the relationship between researchers and participants been considered?

yes

no

CONFLICT

CONFLICT
Do the authors identify a potential conflict of interest?

yes

no

unclear/not stated

OVERALL

OVERALL
As far as can be ascertained from the paper, what was the overall quality of the study?

high

medium

low

META ANALYSIS

META ANALYSIS INCLUSION
Are the results appropriate for meta analysis?

yes

no

unclear/not stated

META ANALYSIS DATA
Which findings are appropriate for meta analysis? (please enter details)

Appendix 2.6: Quality appraisal checklist: quantitative studies

Quantitative studies checklist for NICE (2009)

Study identification (Include full citation details)		
Study design:		
Guidance topic:		
Assessed by:		
Section 1: Population		
1.1 Is the source population or source area well described? Was the country (e.g. developed or non- developed, type of healthcare system), setting (primary schools, community centres etc.), location (urban, rural), population demographics etc. adequately described?	☐ ++ ☐ + ☐ – ☐ NR ☐ NA	Comments:
1.2 Is the eligible population or area representative of the source population or area? Was the recruitment of individuals/clusters/areas well defined (e.g. advertisement, birth register)? Was the eligible population representative of the source? Were important groups underrepresented?	☐ ++ ☐ + ☐ – ☐ NR ☐ NA	Comments:
1.3 Do the selected participants or areas represent the eligible population or area? Was the method of selection of participants from the eligible population well described? What % of selected individuals/clusters agreed to participate? Were there any sources of bias?	☐ ++ ☐ + ☐ – ☐ NR ☐ NA	Comments:

Were the inclusion/exclusion criteria explicit and appropriate?		
Section 2: Method of selection of exposure (or comparison) group		
2.1 Selection of exposure (and comparison) group. How was selection bias minimised?	☐ ++ ☐ + ☐ – ☐ NR ☐ NA	Comments:
2.2 Was the selection of explanatory variables based on a sound theoretical basis? How sound was the theoretical basis for selecting the explanatory variables?	☐ ++ ☐ + ☐ – ☐ NR ☐ NA	Comments:
2.3 Was the contamination acceptably low? Did any in the comparison group receive the exposure? If so, was it sufficient to cause important bias?	☐ ++ ☐ + ☐ – ☐ NR ☐ NA	Comments:
2.4 How well were likely confounding factors identified and controlled? Were there likely to be other confounding factors not considered or appropriately adjusted for? Was this sufficient to cause important bias?	☐ ++ ☐ + ☐ – ☐ NR ☐ NA	Comments:
2.5 Is the setting applicable to the UK? Did the setting differ significantly from the UK?	☐ ++ ☐ + ☐ – ☐ NR ☐ NA	Comments:

Section 3: Outcomes		
3.1 Were the outcome measures and procedures reliable? Were outcome measures subjective or objective (e.g. biochemically validated nicotine levels [++] vs self-reported smoking [−]). How reliable were outcome measures (e.g. inter- or intra-rater reliability scores)? Was there any indication that measures had been validated (e.g. against a gold standard measure or assessed for content validity)?	☐ ++ ☐ + ☐ − ☐ NR ☐ NA	Comments:
3.2 Were the outcome measurements complete? Were all or most of the study participants who met the defined study outcome definitions likely to have been identified?	☐ ++ ☐ + ☐ − ☐ NR ☐ NA	Comments:
3.3 Were all the important outcomes assessed? Were all the important benefits and harms assessed? Was it possible to determine the overall balance of benefits and harms of the intervention versus comparison?	☐ ++ ☐ + ☐ − ☐ NR ☐ NA	Comments:
3.4 Was there a similar follow-up time in exposure and comparison groups? If groups are followed for different lengths of time, then more events are likely to occur in the group followed-up for longer distorting the comparison. Analyses can be adjusted to allow for differences in length of follow-up (e.g. using	☐ ++ ☐ + ☐ − ☐ NR ☐ NA	Comments:

person-years).		
3.5 Was follow-up time meaningful? Was follow-up long enough to assess long-term benefits and harms? Was it too long, e.g. participants lost to follow-up?	☐ ++ ☐ + ☐ – ☐ NR ☐ NA	Comments:
Section 4: Analyses		
4.1 Was the study sufficiently powered to detect an intervention effect (if one exists)? A power of 0.8 (i.e. it is likely to see an effect of a given size if one exists, 80% of the time) is the conventionally accepted standard. Is a power calculation presented? If not, what is the expected effect size? Is the sample size adequate?	☐ ++ ☐ + ☐ – ☐ NR ☐ NA	Comments:
4.2 Were multiple explanatory variables considered in the analyses? Were there sufficient explanatory variables considered in the analysis?	☐ ++ ☐ + ☐ – ☐ NR ☐ NA	Comments:
4.3 Were the analytical methods appropriate? Were important differences in follow-up time and likely confounders adjusted for?	☐ ++ ☐ + ☐ – ☐ NR ☐ NA	Comments:
4.4 Was the precision of association given or calculable? Is association meaningful? Were confidence intervals (CIs) and/or p- values for effect estimates given or	☐ ++ ☐ + ☐ – ☐ NR	Comments:

possible to calculate? Were CIs wide or were they sufficiently precise to aid decision-making? If precision is lacking, is this because the study is under-powered?	☐ NA	
Section 5: Summary		
5.1 Are the study results internally valid (i.e. unbiased)? How well did the study minimise sources of bias (i.e. adjusting for potential confounders)? Were there significant flaws in the study design?	☐ ++ ☐ + ☐ –	Comments:
5.2 Are the findings generalisable to the source population (i.e. externally valid)? Are there sufficient details given about the study to determine if the findings are generalisable to the source population? Consider: participants, interventions and comparisons, outcomes, resource and policy implications.	☐ ++ ☐ + ☐ –	Comments:

Appendix 2.7: Quality appraisal checklist: qualitative studies

Qualitative studies checklist for NICE (2009)

Study identification Include author, title, reference, year of publication		
Guidance topic:	Key research question/aim:	
Checklist completed by:		
Theoretical approach		
1. Is a qualitative approach appropriate? For example: Does the research question seek to understand processes or structures, or illuminate subjective experiences or meanings? Could a quantitative approach better have addressed the research question?	☐ Appropriate ☐ Inappropriate ☐ Not sure	Comments:
2. Is the study clear in what it seeks to do? For example: Is the purpose of the study discussed – aims/objectives/research question/s? Is there adequate/appropriate reference to the literature? Are underpinning values/assumptions/theory discussed?	☐ Clear ☐ Unclear ☐ Mixed	Comments:
Study design		
3. How defensible/rigorous is the research design/methodology? For example: Is the design appropriate to the research question? Is a rationale given for using a qualitative approach?	☐ Defensible ☐ Indefensible ☐ Not sure	Comments:

Are there clear accounts of the rationale/justification for the sampling, data collection and data analysis techniques used? Is the selection of cases/sampling strategy theoretically justified?		
Data collection		
4. How well was the data collection carried out? For example: Are the data collection methods clearly described? Were the appropriate data collected to address the research question? Was the data collection and record keeping systematic?	☐ Appropriately ☐ Inappropriately ☐ Not sure/ inadequately reported	Comments:
Trustworthiness		
5. Is the role of the researcher clearly described? For example: Has the relationship between the researcher and the participants been adequately considered? Does the paper describe how the research was explained and presented to the participants?	☐ Clearly described ☐ Unclear ☐ Not described	Comments:
6. Is the context clearly described? For example: Are the characteristics of the participants and settings clearly defined? Were observations made in a sufficient variety of circumstances? Was context bias considered?	☐ Clear ☐ Unclear ☐ Not sure	Comments:
7. Were the methods reliable? For example: Was data collected by more than one method? Is there justification for	☐ Reliable ☐ Unreliable ☐ Not sure	Comments:

triangulation, or for not triangulating? Do the methods investigate what they claim to?		
Analysis		
8. Is the data analysis sufficiently rigorous? For example: Is the procedure explicit – i.e. is it clear how the data was analysed to arrive at the results? How systematic is the analysis, is the procedure reliable/dependable? Is it clear how the themes and concepts were derived from the data?	☐ Rigorous ☐ Not rigorous ☐ Not sure/not reported	Comments:
9. Are the data 'rich'? For example: How well are the contexts of the data described? Has the diversity of perspective and content been explored? How well has the detail and depth been demonstrated? Are responses compared and contrasted across groups/sites?	☐ Rich ☐ Poor ☐ Not sure/not reported	Comments:
10. Is the analysis reliable? For example: Did more than one researcher theme and code transcripts/data? If so, how were differences resolved? Did participants feed back on the transcripts/data if possible and relevant? Were negative/discrepant results addressed or ignored?	☐ Reliable ☐ Unreliable ☐ Not sure/not reported	Comments:
11. Are the findings convincing? For example:	☐ Convincing ☐ Not convincing	Comments:

Are the findings clearly presented? Are the findings internally coherent? Are extracts from the original data included? Are the data appropriately referenced? Is the reporting clear and coherent?	☐ Not sure	
12. Are the findings relevant to the aims of the study?	☐ Relevant ☐ Irrelevant ☐ Partially relevant	Comments:
13. Conclusions For example: How clear are the links between data, interpretation and conclusions? Are the conclusions plausible and coherent? Have alternative explanations been explored and discounted? Does this enhance understanding of the research topic? Are the implications of the research clearly defined? Is there adequate discussion of any limitations encountered?	☐ Adequate ☐ Inadequate ☐ Not sure	Comments:
Ethics		
14. How clear and coherent is the reporting of ethics? For example: Have ethical issues been taken into consideration? Are they adequately discussed e.g. do they address consent and anonymity? Have the consequences of the research been considered i.e. raising expectations, changing behaviour?	☐ Appropriate ☐ Inappropriate ☐ Not sure/not reported	Comments:

Was the study approved by an ethics committee?		
Overall assessment		
As far as can be ascertained from the paper, how well was the study conducted (see guidance notes)?	☐ ++ ☐ + ☐ –	Comments:

Appendix 2.8: Quality appraisal checklist: cost-effectiveness studies

	Question	Yes	No
1.	Is the study population clearly described?		
2.	Are competing alternatives clearly described?		
3.	Is a well-defined research question posed in answerable form?		
4.	Is the economic study design appropriate to the stated objective?		
5.	Is the chosen time horizon appropriate to include relevant costs and consequences?		
6.	Is the actual perspective chosen appropriate?		
7.	Are all important and relevant costs for each alternative identified?		
8.	Are all costs measured appropriately in physical units?		
9.	Are costs valued appropriately?		
10.	Are all important and relevant outcomes for each alternative identified?		
11.	Are all outcomes measured appropriately?		
12.	Are outcomes valued appropriately?		
13.	Is an incremental analysis of costs and outcomes of alternatives performed?		
14.	Are all future costs and outcomes discounted appropriately?		
15.	Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?		
16.	Do the conclusions follow from the data reported?		
17.	Does the study discuss the generalizability of the results to other settings and patient/client groups?		
18.	Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?		
19.	Are ethical and distributional issues discussed appropriately?		

Item		Yes	No	Not clear	Not appropriate
Study design					
1.	The research question is stated.				
2.	The economic importance of the research question is stated.				

Item		Yes	No	Not clear	Not appropriate
3.	The viewpoint(s) of the analysis are clearly stated and justified.				
4.	The rationale for choosing alternative programmes or interventions compared is stated.				
5.	The alternatives being compared are clearly described.				
6.	The form of economic evaluation used is stated.				
7.	The choice of form of economic evaluation is justified in relation to the questions addressed.				
Data collection					
8.	The source(s) of effectiveness estimates used are stated.				
9.	Details of the design and results of effectiveness study are given (if based on a single study).				
10.	Details of the methods of synthesis or meta-analysis of estimates are given (if based on a synthesis of a number of effectiveness studies).				
11.	The primary outcome measure(s) for the economic evaluation are clearly stated.				
12.	Methods to value benefits are stated.				
13.	Details of the subjects from whom valuations were obtained were given.				
14.	Productivity changes (if included) are reported separately.				
15.	The relevance of productivity changes to the study question is discussed.				
16.	Quantities of resource use are reported separately from their unit costs.				
17.	Methods for the estimation of quantities and unit costs are described.				
18.	Currency and price data are recorded.				
19.	Details of currency of price adjustments for inflation or currency conversion are given.				
20.	Details of any model used are given.				
21.	The choice of model used and the key parameters on which it is based are				

Item		Yes	No	Not clear	Not appropriate
	justified.				
Analysis and interpretation of results					
22.	Time horizon of costs and benefits is stated.				
23.	The discount rate(s) is stated.				
24.	The choice of discount rate(s) is justified.				
25.	An explanation is given if costs and benefits are not discounted.				
26.	Details of statistical tests and confidence intervals are given for stochastic data.				
27.	The approach to sensitivity analysis is given.				
28.	The choice of variables for sensitivity analysis is justified.				
29.	The ranges over which the variables are varied are justified.				
30.	Relevant alternatives are compared.				
31.	Incremental analysis is reported.				
32.	Major outcomes are presented in a disaggregated as well as aggregated form.				
33.	The answer to the study question is given.				
34.	Conclusions follow from the data reported.				
35.	Conclusions are accompanied by the appropriate caveats.				

Appendix 2.9: Electronic databases excluded

In addition to databases included in our search protocol, 22 further databases were examined and were excluded on the basis of lack of functionality (in particular the lack of MeSH terms or key words, and the lack of a reference manager tool to export references), country or topic coverage, or lack of access.

Database	**MeSH terms/ key words**	**Reference manager export**	**Comments**	**Address**
AfricaBib	No	No	No abstract	http://www.africabib.org/
African Studies Centre, Leiden	Not clear	No	-	http://opc4-ascl.pica.nl/LNG=EN/
CAB Direct (was Rural Development Abstract)	Yes	Yes	-	http://www.cabdirect.org/
Cross searcher	Not clear	Yes	-	http://zw4gk5cr3l.cs.serialssolutions.com/?SS_LibHash=ZW4GK5CR3L&authRedirect=1
Database of African Theses and Dissertations (DATAD)	Not accessible	Not accessible	Not accessible	http://www.aau.org/datad/database/qufind.php
EthOS	No	No	-	http://ethos.bl.uk/Home.do;jsessionid=311101362E2EAE41F73A605EB834BBBE
Google Scholar	No	No	No abstract	http://scholar.google.co.uk/
Google Search (Advanced)	No	No	-	http://www.google.co.uk/advanced_search?hl=en

Index Medicus for South East Asia Region (IMSEAR)	Yes	No	No abstract	http://imsear.hellis.org/
Index Medicus for the Eastern Mediterranean Region (IMEMR)	Yes	No	No abstract	http://www.emro.who.int/Library/Databases/wxis.exe/Library/Databases/iah/?IsisScript=iah/iah.xic&base=imemr&lang=i
Index to Theses	No	No	-	http://www.theses.com/
IndMed	No	No	-	http://indmed.nic.in/
MedCarib	Yes	No	-	http://bases.bireme.br/cgi-bin/wxislind.exe/iah/online/
OPENSIGLE	No	Unclear	-	http://www.greynet.org/opensiglerepository.html
Proquest Dissertations and Theses	No	Yes	-	http://proquest.umi.com.gate2.library.lse.ac.uk/login
Quarterly Index of African Periodical Literature	No	No	No abstract	http://memory.loc.gov/misc/qsihtml/
REPIDISCA (Pan American Information Network on Environmental Health)	No	Yes	No abstract	http://regional.bvsalud.org/php/index.php?lang=en
Scopus	Not accessible	Not accessible	Not accessible	http://www.info.sciverse.com/scopus/
Social Care Online (former Care Data)	No	Yes	-	http://www.scie-socialcareonline.org.uk/
SocIndex	Not accessible	Not accessible	Not accessible	
South Africa Medical Database (SAMED)	Yes	Unclear	-	http://www.mrc.ac.za/SamedSearch/

Web of Knowledge (including ISI Citation Indices and Conference Proceedings Citation Index)	No	Yes	-	http://apps.isiknowledge.com/UA_GeneralSearch_input.do?product=UA&search_mode=GeneralSearch&SID=P25idBcjMbaljDe18d1&preferencesSaved= http://apps.webofknowledge.com/UA_GeneralSearch_input.do?product=UA&search_mode=GeneralSearch&SID=4A59eIB69CO7oGoDIAa&preferencesSaved=

Appendix 3.1: Details of studies included in the review

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Aaby (2002)	Guinea-Bissau peri-urban	Clinical Vaccinations	No intervention	Observational studies with comparison group	Children up to 20 months in a war situation	313	N/ A	neutral	+	+
Aaby (2005)	Guinea-Bissau urban/ peri-urban/ rural	Clinical Vaccinations	No intervention	Observational studies with comparison group	Infants in general	6,159	N/ A	neutral	++	+
Abdel (2010)	Egypt, South Africa; urban	Clinical Other clinical management: uterine massage	Normal/ existing service/ financing mechanism/ regulation	Controlled experimental study	Women in general	951 (Egypt)	30	negative	+	-
Abdul (2007)	Nigeria peri-urban	Clinical Drug treatment (including micronutrient supplementation) : induction of labour	Normal/ existing service/ financing mechanism/ regulation	Controlled experimental study	Women needing induction	62	12	neutral	-	+

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Aboud (2009)	Malawi, Tanzania, Zambia urban	Clinical Drug treatment (including micronutrient supplementation) : antibiotics	No intervention	Controlled experimental study	HIV-infected pregnant women	1,829	20	neutral	++	+
Adewole (2000)	Nigeria urban	Clinical Drug treatment (including micronutrient supplementation) : anti-convulsant	N/ A	Observational studies without comparison group	Women with eclampsia	21	17	positive	-	-
Afolabi (2010)	Nigeria urban	Clinical Drug treatment (including micronutrient supplementation) : active management of third stage of labour	Alternative interventions/ service/ financing mechanism/ regulation	Controlled experimental study	Women in labour with term pregnancies and having vaginal delivery	200	unclear/ not stated	positive	+	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Agarwal (2007a)	India urban	Clinical Surgical/ instrumental procedures	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women with post-Caesarean pregnancy	424	12	positive	+	++
Agarwal (2007b)	India urban	Non-clinical Service organization: discharge and admission procedure in neonatal units	N/ A	Experimental study without concurrent control	Women in general	7,938	8	positive	-	+
Ahmed (2004)	Nigeria urban	Non-clinical Service organization: financing	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Poor women with uterine rupture	1,360	11	positive	-	-
Alemen (1998)	Nicaragua urban	Non-clinical Service organization: training and audit	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Neonates in general	N/ A	unclear/ not stated	positive	-	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Alwen (2005)	Egypt urban	Complex	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general	unclear/ not stated	N/ A	positive	-	+
Amin (1992)	Sierra Leone urban	Clinical Vaccination	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Infants in general	2,276	N/ A	positive	-	-
Awan (1989)	Pakistan urban	Non-clinical Service organization: training and audit	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general Infants in general	unclear/ not stated	unclear/ not stated	positive	+	-
Bakr (2005)	Egypt urban	Clinical Other clinical management	No intervention	Observational studies with comparison group	Women in general Neonates in general	4,415	3	positive	+	-
Bashir (1991)	Pakistan urban	Non-clinical Service organization: financing	N/ A	Observational studies without comparison group	Women in general	55,560	unclear/ not stated	positive	-	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Bashir (1995)	Pakistan urban	Complex	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general	unclear/ not stated	unclear/ not stated	positive	-	-
Becquet (2007)	Cote d'Ivoire urban	Non-clinical Nutrition (including breastfeeding)	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	HIV-infected mothers	557	25	neutral	++	++
Begum (2000)	Bangla-desh urban	Clinical Drug treatment (including micronutrient supplementation) : anti-convulsant	N/ A	Observational studies without comparison group	Women with eclampsia	879	18	positive	-	-
Benn (2008a)	Guinea-Bissau peri-urban	Clinical Vaccinations	No intervention	Controlled experimental study	Neonates in general	4,345	24	neutral	+	++

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Benn (2008b)	Guinea-Bissau peri-urban	Clinical Vaccinations	Alternative interventions/ service/ financing mechanism/ regulation	Observational studies with comparison group	Neonates in general	4,345	24	neutral	++	++
Benn (2010)	Guinea-Bissau urban	Clinical Vaccinations	No intervention	Controlled experimental study	Low birthweight neonates	1,717	N/ A	negative	++	++
Bergman (1994)	Zimbabwe urban	Non-clinical Service organization: Kangaroo Mother Care	No intervention	Observational studies with comparison group	Low birthweight neonates	126	63	positive	-	-
Bergsjo (1989)	China urban	Clinical Drug treatment (including micronutrient supplementation): induction of labour	No intervention	Controlled experimental study	Women with uncomplic-ated pregnancies going beyond 42 weeks gestation	188	unclear/ not stated	positive	-	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Bergstrom (1991)	Mozam-bique urban	Clinical Drug treatment (including micronutrient supplementation) : antibiotics	No intervention	Controlled experimental study	Women with preterm rupture of membranes	92	N/ A	positive	+	+
Bhakoo (1989)	India urban	Non-clinical Service organization: discharge and admission procedure in neonatal units	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	High-risk neonates	5,283	unclear/ not stated	positive	+	+
Bhatt (1989)	India urban/ peri-urban	Non-clinical Service organization: training and audit	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general	6,093	unclear/ not stated	positive	-	-
Bhutta (2004)	Pakistan urban	Non-clinical Service organization: discharge and admission procedure in neonatal units	No intervention	Observational studies with comparison group	Neonates with LBW (<1,500g)	509	unclear/ not stated	positive	+	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Blencowe (2009)	Malawi urban	Non-clinical Service organization: discharge and admission procedure in neonatal units	No intervention	Observational studies with comparison group	Neonates with LBW (<2000g)	256	6	unclear/ not stated	+	+
Borulkar (1998)	India urban	Complex	N/ A	Observational studies without comparison group	Neonates requiring special care	2,266	unclear/ not stated	unclear/ not stated	-	-
Brown (1996)	Papua New Guinea urban	Complex	N/ A	Observational studies without comparison group	Neonates with LBW (<1,500g)	98	unclear/ not stated	N/ A	-	-
Bugalho (1993)	Mozam-bique urban	Non-clinical Service organization	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general Neonates in general	134,408	120	unclear/ not stated	-	-
Campbell (2005)	Egypt urban/ peri-urban/ rural	Complex	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general	unclear/ not stated	unclear/ not stated	positive	+	+

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Cattaneo (1998)	Ethiopia, Indonesia, Mexico urban	Non-clinical Service organization: Kangaroo Mother Care	Normal/ existing service/ financing mechanism/ regulation	Controlled experimental study economic evaluation/ modelling studies	Infants with LBW (1,000-1,999g)	100	12	neutral	++	++
Chaudhuri (1994)	India urban	Clinical Drug treatment (including micronutrient supplementation): anti-convulsant	Alternative interventions/ service/ financing mechanism/ regulation	Controlled experimental study	Women with history of eclampsia	59	12	positive negative	+	+
Chinayon (1998)	Thailand urban	Clinical Drug treatment (including micronutrient supplementation): anti-convulsant	N/ A	Observational studies without comparison group	Women with eclampsia	90	unclear/ not stated	positive	+	+
Chomba (2008)	Zambia urban	Non-clinical Service organization: increasing investment and scaling up	alternative interventions/ service/ financing mechanism/ regulation	Observational studies with comparison group	Neonates in general	41,282	unclear/ not stated	positive	+	++

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Cobra (1997)	Indonesia peri-urban	Clinical Drug treatment (including micronutrient supplementation)	Alternative interventions/ service/ financing mechanism/ regulation	Controlled experimental study	Infants in general	617	4	positive	++	++
Colonna (1990)	Mozam-bique urban	Non-clinical Service organization: discharge and admission procedure in neonatal units	N/ A	Observational studies without comparison group	Low birth-weight neonates	100	9	neutral	-	-
Darmstadt (2004)	Egypt urban	Clinical Other clinical management	Normal/ existing service/ financing mechanism/ regulation	Controlled experimental study	Preterm infants	10,403	unclear/ not stated	positive	+	+
Darmstadt (2008)	Bangla-desh urban	Clinical Other clinical management	No intervention	Controlled experimental study	Preterm infants	497	55	positive	++	++

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
De Bernis (2000)	Senegal urban/ peri-urban	Non-clinical Service organization: provider model	Alternative interventions/ service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general	3,476	19	positive	+	+
De Long (1997)	China peri-urban	Clinical Drug treatment (including micronutrient supplementation): potassium iodate	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general Neonates in general Infants in general	1,995 (in 1988); 1,595 (in 1995)	unclear/ not stated	positive	+	+
De Muylder (1989)	Zimbabwe urban	Non-clinical Service organization: training and audit	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general	unclear/ not stated	unclear/ not stated	positive	-	-
De Silva (1999)	Sri Lanka urban/ rural	Clinical Drug treatment (including micronutrient supplementation): anthelmintics	No intervention	Observational studies with comparison group	Women in general	7,012	4	positive	+	++

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Des-champs (2009)	Haiti urban	Non-clinical Nutrition (including breastfeeding)	N/ A	Observational studies without comparison group	Pregnant, HIV-positive women Neonates born to HIV-positive mothers	348	unclear/ not stated	positive	+	-
Dumont (2005)	Senegal urban	Non-clinical Service organization: training and audit	alternative interventions/ service/ financing mechanism/ regulation	Observational studies with comparison group	Pregnant women with haemorrhagic and hypertensive complications	1,678	12	positive	++	++
Dumont (2006)	Senegal urban	Non-clinical Service organization: training and audit	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Pregnant women admitted to hospital for childbirth	25,954	36	positive	++	++
Ekouevi (2008)	Cote d'Ivoire urban	Clinical Drug treatment (including micronutrient supplementation): antiretrovirals	Alternative interventions/ service/ financing mechanism/ regulation	Observational studies with comparison group	Women with advanced HIV disease	1,288	48	positive	+	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Enakpene (2010)	Nigeria urban	Clinical Other clinical management	No intervention	Observational studies with comparison group	Women with umbilical cord prolapse (UCP)	72	120	positive	+	-
Enweronu (2008)	Ghana urban	Non-clinical Service organization: increasing investment and scaling up	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Neonates requiring intensive care	3,893	N/ A	positive neutral	+	-
Etuk (2000a)	Nigeria urban	Clinical Other clinical management	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general	672	unclear/ not stated	positive	-	-
Etuk (2000b)	Nigeria urban	Clinical Other clinical management	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general	672	unclear/ not stated	positive.	-	-
Fabamwo (2010)	Nigeria urban	Clinical Other clinical management	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general	1,133	6	positive	-	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Fawzi (2007)	Tanzania urban	Clinical Drug treatment (including micronutrient supplementation) : Micronutrient supplementation	No intervention	Controlled experimental study	HIV-negative pregnant women	8,137	36	neutral	++	++
Fekih (2002)	Tunisia urban	Clinical Drug treatment (including micronutrient supplementation) : steroids	No intervention	Controlled experimental study	Women 26-34 weeks gestation at high-risk of premature delivery	118	18	positive	+	-
Fenton (1999)	Malawi urban	Clinical Other clinical management	No intervention	Observational studies with comparison group	Women needing Caesarean section	3,665	18	neutral	+	-
Fetuga (2010)	Nigeria urban	Clinical Vaccinations	alternative interventions/ service/ financing mechanism/ regulation	Observational studies with comparison group	Neonates in general	175	N/ A	neutral	+	+

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Garly (2003)	Guinea-Bissau peri-urban	Clinical Vaccinations	alternative interventions/ service/ financing mechanism/ regulation	Controlled experimental study	Neonates in general Infants in general	1,813	unclear/ not stated	positive	+	-
Garly (2004)	Guinea-Bissau urban	Clinical Vaccinations	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Infants in general	5,441		negative	+	++
Gray (1991)	Thailand urban	Clinical Drug treatment (including micronutrient supplementation) : oral contraceptive	No intervention	Observational studies with comparison group	Women in general	4,303	unclear/ not stated	negative	+	+
Iqbal (2004)	India urban	Clinical Other clinical management	No intervention	Observational studies with comparison group	Women with prolonged pregnancy (> or = 294 days)	100	12	positive	+	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Jakobsen (2008)	Guinea-Bissau urban/ peri-urban	Non-clinical Nutrition (including breastfeeding)	No intervention	Controlled experimental study	Infants in general	1,721	unclear/ not stated	negative	++	++
Joshi (2007)	India urban	Clinical Drug treatment (including micronutrient supplementation)	N/ A	Observational studies without comparison group	Neonates with primary pulmonary hypertension	18	unclear/ not stated	positive	-	-
Kaestel (2005)	Guinea Bissau urban	Clinical Drug treatment (including micronutrient supplementation) : micronutrient supplementation	Normal/ existing service/ financing mechanism/ regulation	Controlled experimental study	Pregnant women	1,670	22	neutral	++	++
Kamilya (2005)	India urban	Clinical Drug treatment (including micronutrient supplementation) : anti-convulsant	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women with eclampsia	1,646	26	positive	-	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Kietinun (1993)	Thailand urban	Clinical Drug treatment (including micronutrient supplementation) : antimalarial	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Pregnant women with malaria	678	unclear/ not stated	positive	-	-
Kongnyuy (2008)	Malawi urban/ peri-urban	Non-clinical Service organization: training and audit	Normal/ existing service/ financing mechanism/ regulation	Experimental study without concurrent control	Women receiving EmOC	unclear/ not stated	unclear/ not stated	positive	+	+
Kuhn (2008)	Zambia urban	Non-clinical Nutrition (including breastfeeding)	Normal/ existing service/ financing mechanism/ regulation	Controlled experimental study	HIV-infected women HIV-infected infants	958	40	negative	++	++
Kum-wenda (2008)	Malawi urban	Clinical Drug treatment (including micronutrient supplementation)	Normal/ existing service/ financing mechanism/ regulation	Controlled experimental study	Infants born to HIV-infected mothers	3,276	3	neutral	++	++

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Kupka (2008)	Tanzania urban	Clinical Drug treatment (including micronutrient supplementation) : micronutrient supplementation	Alternative interventions/ service/ financing mechanism/ regulation	Controlled experimental study	HIV-infected pregnant women	915	unclear/ not stated	negative	++	-
Le Fevre (2010)	Bangla-desh urban/ peri-urban/ rural	Clinical Other clinical management	Alternative interventions/ service/ financing mechanism/ regulation	Economic evaluation/ modelling studies	Preterm neonates	497	1	positive	++	+
Lim (2010)	India urban/ peri-urban/ rural	Non-clinical Service organization: financing	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	In some Indian states, all women were eligible for the intervention. In others, only women with a below the poverty line card were eligible.	unclear/ not stated	unclear/ not stated	positive	++	++

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Lincetto (2000)	Mozam-bique urban	Non-clinical Service organization: Kangaroo Mother Care	N/ A	Observational studies without comparison group	Neonates with LBW (<1800g)	32	unclear/ not stated	neutral	-	-
Malaba (2005)	Zimbabwe urban	Clinical Drug treatment (including micronutrient supplementation)	No intervention	Controlled experimental study	Neonates born to HIV negative mothers	14,110	26	negative	++	++
Malhotra (1994)	India urban	Clinical Surgical/ instrumental procedures	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women with preterm breech delivery	224	48	neutral	+	-
Mandel-brot (2002)	Cote d'Ivoire Burkina Faso; urban	Clinical Other clinical management	No intervention	Controlled experimental study	Infants born to HIV infected mothers	111	9	neutral	++	+

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Martins Cesario (2008)	Guinea Bissau urban	Clinical Vaccinations	alternative interventions/ service/ financing mechanism/ regulation	Controlled experimental study	Neonates in general	1333	10	neutral	++	++
Mbaruku (1995)	Tanzania urban	Non-clinical Service organization	No intervention	Observational studies with comparison group	Women in general	132 maternal deaths	unclear/ not stated	positive	-	-
Mbori-Ngacha (2001)	Kenya urban	Non-clinical Nutrition (including breastfeeding)	Normal/ existing service/ financing mechanism/ regulation	Controlled experimental study	HIV-1 infected women	425	78	neutral	++	++
Miller (1994)	Egypt urban	Clinical Drug treatment (including micronutrient supplementation)	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Infants in general	1,038	unclear/ not stated	positive	+	++

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Miller (2009)	China urban/ peri-urban/ rural	Clinical Other clinical management: non-pneumatic anti-shock garment	Alternative interventions/ service/ financing mechanism/ regulation	Controlled experimental study	Women with obstetric haemorrhage	960	20	positive	+	++
Mirghani (2000)	Sudan urban	Complex	N/ A	Observational studies without comparison group	Pregnant women with diabetes in Sudan	74	24	positive	-	-
Mswia (2003)	Tanzania urban/ rural	Complex	No intervention	Observational studies with comparison group	Women in general Neonates in general	unclear/ not stated	unclear/ not stated	positive	+	++
Munjanja (1996)	Zimbabwe urban/ peri-urban	Clinical Other clinical management: antenatal care programme	Normal/ existing service/ financing mechanism/ regulation	Controlled experimental study	Women in general	15,532	24	neutral	++	++
Nagai (2010)	Mada-gascar urban	Non-clinical Service organization: Kangaroo Mother Care	Normal/ existing service/ financing mechanism/ regulation	Controlled experimental study	Neonates with LBW (<2500g)	73	12	neutral	++	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Nahar (2004)	Bangla-desh urban	Clinical Drug treatment (including micronutrient supplementation: induction of labour	N/ A	Observational studies without comparison group	Women with eclampsia or pre-eclampsia	135	22	unclear/ not stated	-	-
Naz (2005)	Pakistan urban	Clinical Drug treatment (including micronutrient supplementation) : anti-convulsant	N/ A	Observational studies without comparison group	Women with eclampsia	52	16	N/ A	++	++
Ndibazza (2010)	Uganda peri-urban/ rural	Clinical Drug treatment (including micronutrient supplementation) : anthelmintics	Alternative interventions/ service/ financing mechanism/ regulation	Controlled experimental study	Pregnant women in second or third trimester	2,507	31	negative	++	+

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Nduati (2001)	Kenya urban	Non-clinical Nutrition (including breastfeeding)	Alternative interventions/ service/ financing mechanism/ regulation	Controlled experimental study	HIV-1 infected women	425	59	negative	++	-
O' Hare (2006)	Uganda urban	Non-clinical Service organization: training and audit	Normal/ existing service/ financing mechanism/ regulation	experimental study without concurrent control	Neonates in general	420	1	positive	-	-
Okaro (2001)	Nigeria urban	Complex	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general	60,310	unclear/ not stated	negative	-	-
Orji (2003)	Nigeria urban	Clinical Surgical/ instrumental procedures	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Singleton mothers with breech delivery	244	unclear/ not stated	positive	-	-
O'Rourke (1995)	Guatemala urban	Non-clinical Service organization: training and audit	No intervention	Observational studies with comparison group	Women in general	733	12	neutral	+	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Padman-aban (2009)	India urban/ peri-urban/ rural	Complex	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women in general	unclear/ not stated	N/ A	unclear/ not stated	-	+
Pereira (1996)	Mozam-bique urban	Clinical Surgical/ instrumental procedures	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women with Caesarean section	2,071	unclear/ not stated	positive	-	-
Richard (2008)	Burkina Faso urban	Non-clinical Service organization: training and audit	Normal/ existing service/ financing mechanism/ regulation	Experimental study without concurrent control	Women needing CS	1,371	unclear/ not stated	positive	++	++
Ronsmans (2001)	Indonesia peri-urban/ rural	Non-clinical Service organization: financing	No intervention	Experimental study without concurrent control	Women in general	unclear/ not stated	unclear/ not stated	positive negative	+	+
Roth (2004)	Guinea-Bissau urban	Clinical Vaccinations	No intervention	Observational studies with comparison group	Neonates in general Infants in general	7,138	unclear/ not stated	positive	+	+

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Saleem (2007)	Pakistan urban	Clinical Other clinical management	No intervention	Controlled experimental study	Women in general	197	unclear/ not stated	neutral	+	+
Sasidharan (2005)	India urban	Non-clinical Service organization: discharge and admission procedure in neonatal units	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	High risk neonates	unclear/ not stated	unclear/ not stated	positive	-	-
Shantharam Baliga (2007)	India urban	Non-clinical Service organization: increasing investment and scaling up	Normal/ existing service/ financing mechanism/ regulation	Experimental study without concurrent control	Neonates requiring special care	8,051	36	positive	+	++
Sharieff (2008)	Pakistan urban	Non-clinical Nutrition (including breastfeeding)	No intervention	Economic evaluation/ modelling studies	Infants in general	N/ A	4	positive	+	-
Shihadeh (2001)	Jordan urban	Clinical Surgical/ instrumental procedures	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Mothers with instrumental deliveries	570	unclear/ not stated	positive	-	+

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Strand (2009)	Angola urban	Non-clinical Service organization: training and audit	Normal/ existing service/ financing mechanism/ regulation	Experimental study without concurrent control	Women referred for obstetric emergencies	249	7	positive	-	+
Taha (1997)	Malawi urban	Clinical Other clinical management	Normal/ existing service/ financing mechanism/ regulation	Controlled experimental study	Women in general	6,968	6	positive	++	++
Tukur (2007)	Nigeria urban	Clinical Drug treatment (including micronutrient supplementation) : induction of labour	Alternative interventions/ service/ financing mechanism/ regulation	Controlled experimental study	Women with antepartum eclampsia	50	unclear/ not stated	positive	+	-
Tukur (2010)	Nigeria urban	Clinical Drug treatment (including micronutrient supplementation) : anti-convulsant	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women with eclampsia	131	36	positive	-	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Walter (2006)	Zambia urban	Clinical Drug treatment (including micronutrient supplementation) : antiretrovirals	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	HIV-infected women	255	11	positive	+	+
Worku (2005)	Ethiopia urban	Non-clinical Service organization: Kangaroo Mother Care	Normal/ existing service/ financing mechanism/ regulation	Controlled experimental study	Neonates with LBW	123	12	positive	-	+
Yan (1989)	China urban	Complex	No intervention	Observational studies with comparison group	Women in general	unclear/ not stated	unclear/ not stated	positive	-	-
Zhu (1997)	China urban	Non-clinical Service organization: training and audit	Alternative interventions/ service/ financing mechanism/ regulation	Observational studies with comparison group	Neonates in general	4,751	24	positive	-	-

Study	Setting	Intervention type	Comparison	Study design	Target population	Sample size	Length (months)	Intervention claims	Internal validity	External validity
Ziadeh (1997)	Jordan urban	Clinical Surgical/ instrumental procedures	Normal/ existing service/ financing mechanism/ regulation	Observational studies with comparison group	Women with preterm breech presentation	98	12	neutral	-	-
Ziadeh (2000)	Jordan urban	Clinical Surgical/ instrumental procedures	N/ A	Observational studies without comparison group	Triplets	41	66	negative	-	-

Appendix 3.2: Studies excluded after full-text screening

Anonymous works

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Appendix 3.3: Unobtainable studies

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Appendix 3.4: Studies identified as interesting and relevant, but not included in review

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Maternal health and safe motherhood: findings from concluded research studies (1995) World Health Statistical Quarterly, *48(1), 2-3.Authored works*

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Appendix 3.5: Studies screened by title/abstract, but not by full-text (in an excluded foreign language)

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Zhang X S, Wang L H, Guo S F (2003) [An analysis of related factors for maternal mortality rate at county level]. *Zhonghua Yu Fang Yi Xue Za Zhi,* 37(5), 342-345.

Appendix 4.1: Included items dealing with clinical interventions and maternal mortality

Author (year) (IV)/(EV)	Target population	Brief intervention description	Targeted outcome(s)	Findings summary
Surgical/instrumental procedures				
Agarwal (2007a) (+)/(++)	Women with post-Caesarean pregnancy	Comparison of CS and vaginal birth after Caesarean (VBAC).	Neonatal mortality Perinatal mortality Stillbirth	VBAC is associated with higher perinatal mortality and maternal morbidity.
Malhotra (1994) (+)/(-)	Women with preterm breech delivery	CS: The general policy of this hospital does not favour routine use of CS for a preterm breech foetus. Before 33 completed weeks of gestation, CS is occasionally performed for foetal indication unless associated with adverse obstetric factors. The indications for CS for a preterm breech after 33 weeks are the same as for a singleton term breech foetus. All the CS and a majority of the vaginal deliveries were attended by a paediatrician who assessed the newborn for gestational age, congenital abnormality and birth injury, and assigned the Apgar score.	Combined intrapartum and neonatal deaths	Although the combined intrapartum and neonatal mortality was significantly higher for vaginal delivery (35.9% vs 17.7%), there was no significant difference when the data was correlated with birthweight or gestational age.

Orji (2003) (-)/(-)	Singleton mothers with breech delivery	Planned vaginal delivery vs planned CS delivery for breech delivery.	Perinatal mortality	Claims that the outcomes for planned vaginal deliveries may be no worse than planned Caesarean sections, given appropriate selection criteria and management. There was no difference in perinatal mortality. Low Apgar scores were more common on vaginal delivery group but traumatic morbidity was not. Maternal morbidity was higher in Caesarean section group.
Shihadeh (2001) (-)/(+)	Mothers with instrumental deliveries	Retrospective comparison of forceps and vacuum extraction delivery.	Perinatal mortality	Maternal birth canal and genital tract lacerations were significantly more common in forceps delivery. There was increased infant morbidity and mortality from vacuum extraction deliveries but overall vacuum extraction was recommended.
Ziadeh (1997) (-)/(-)	Women with preterm breech presentation	Abdominal vs vaginal delivery for singleton preterm breech.	Early neonatal mortality Stillbirth	There was no significant difference in intrapartum death and early neonatal mortality between those who delivered vaginally and those who delivered by Caesarean section (16.6 vs 15.6%). So even with optimum neonatal care facilities, Caesarean section does not offer any advantage over vaginal delivery in a developing country.

Drug treatment (including micronutrient supplementation)				
Anti-convulsant				
Adewole (2000) (-)/(-)	Women with eclampsia	Magnesium sulphate was administered following the Zuspan regimen).	Maternal mortality (related to anaesthesia) Perinatal mortality	The results suggest there is no significant difference in the maternal and perinatal morbidity and mortality, compared to pre-magnesium sulphate era.
Begum (2000) (-)/(-)	Women with eclampsia	Low dose magnesium sulphate for eclamptic patients.	Maternal mortality	Mortality fell from 16% to 8% in one hospital following introduction of low dose magnesium sulphate.
Chaudhuri (1994) (+)/(+)	Women with history of eclampsia	All the mothers with history of eclampsia were included in the study. The cases were thoroughly examined at the time of admission and babies were followed up regularly during the hospital stay. The cases were divided into three treatment groups: • group I (diazepam) • group II (diazepam, chlorpromazine, phenargan) • group III (chlorpromazine, phenargan, pethidine).	Stillbirths Perinatal mortality	Combination of diazepam, chlorpromazine, phenargan (group II) was best for treatment of eclampsia. Combination of chlorpromazine, phenargan, pethidine (group III) led to high perinatal mortality, particularly stillbirths.

Chinayon (1998) (+)/(+)	Women with eclampsia	Revised administration of magnesium sulphate	Neonatal mortality Perinatal mortality Maternal mortality Stillbirth	A retrospective review of 90 eclamptic patients between 1987 and 1996 found three maternal deaths (3.3%). Perinatal deaths and neonatal deaths were 9 and 5 out of 75 (cases of eclampsia before pregnancy) respectively. The authors conclude that magnesium sulphate should be used routinely for eclampsia patients, ideally with intravenous loading dose followed by intramuscular injections.
Kamilya (2005) (-)/(-)	Women with eclampsia	Liberalisation of Caesarean section New guidelines to promote routine use of magnesium sulphate	Perinatal mortality Maternal mortality	From 1995 – 1997, the case fatality rate of eclampsia fell from 11.3% to 5.3%. The perinatal mortality also fell from 54.8% to 24.3%. The Caesarean section rate for eclampsia increased from near 10% to 49.7%.
Naz (2005) (++)/(++)	Women with eclampsia	Use of magnesium sulphate as anticonvulsant in management of eclampsia cases.	Maternal mortality	There was no comparison group to assess the effectiveness of magnesium sulphate. From observational data, the authors believed it to be an effective anticonvulsant in control and prophylaxis of seizures. There were 4 maternal deaths from eclampsia from 52 patients admitted.

Tukur (2010) (-)/(-)	Women with eclampsia	Magnesium sulphate was administered following the Zuspan regimen (in which the maintenance doses are given intravenously).	Maternal mortality Perinatal mortality	This study is in support of the findings that magnesium sulphate is superior to diazepam in the reduction of maternal morbidity and mortality. However, the benefit to the infant was not statistically significant.
Labour (including induction)				
Abdul (2007) (-)/(+)	Women needing induction	Induction of labour by misoprostol (intravaginal 50 microg. 6-hourly to a maximum of four doses) or oxytocin (maximum of 48 iu/min).	Maternal mortality Stillbirth	No case of maternal mortality was recorded. The efficacy of misoprostol in the induction of third trimester labour is comparable to oxytocin.
Bergsjo (1989) (-)/(-)	Women with uncomplicated pregnancies going beyond 42 weeks gestation	Induction of labour by stripping of membranes and intravenous. oxytocin infusion, with artificial rupture of membranes when the cervical opening was 3 cm or more in diameter. The control group was followed with clinical, biochemical and electronic tests, intervention being applied according to needs.	Neonatal mortality	Maternal complications and perinatal morbidity rates were equally distributed between the groups. There was one perinatal death in the induction group and two deaths among the controls. No advantage of induction shown.

Nahar (2004) (-)/(-)	Women with eclampsia or pre-eclampsia	Misoprostol in severe pre-eclampsia (group 1) and eclampsia patients(group 2) with unripe cervix. 50mg of misoprostol was used every 4 hours in cases of unripe cervix (Bishop score < or = 6). Magnesium sulphate was used routinely for patients with eclampsia.	Maternal mortality Perinatal mortality	The groups were compared to each other but no control so impact on mortality not clear. No maternal deaths recorded. Neonatal deaths were 11% in severe pre-eclampsia group and 12% in eclampsia group. Study concludes that intravaginal misoprostol is well tolerated and very effective for the induction of labour in severe pre-eclampsia and eclampsia patients with unripe cervix.
Tukur (2007) (+)/(-)	Women with antepartum eclampsia	Misoprostol. If the patient did not go into labour within four hours of inserting misoprostol, the induction was considered to have failed and emergency CS offered. CS was also offered if any other complication that warranted a CS such as foetal distress arose.	Maternal mortality Perinatal mortality	There were more maternal complications and admissions of babies into the neonatal special care unit (NSCU) in the CS group compared to misoprostol group. Maternal mortality in the two groups was similar (2% each).
Micronutrient supplementation				
Fawzi (2007) (++)/(++)	HIV-negative pregnant women	Daily multivitamins vs placebo (all women received iron and folic acid supplements).	Perinatal mortality Neonatal mortality	HIV-negative Tanzanian women who received prenatal supplementation with vitamin B complex and vitamins C and E did not have significantly reduced risks of prematurity and foetal death, but they did have significantly reduced risk of LBW.

Kaestel (2005) (++)/(++)	Pregnant women	Daily micronutrient supplementation in Guinea-Bissau. Identical capsules – group 1 with one RDA of 15 micronutrients, group 2 with two RDA of 15 micronutrients, group 3 conventional prenatal iron-folic acid supplement.	Perinatal mortality Neonatal mortality	There were no overall differences in either peri- or neonatal mortality between supplementation groups and the control group. There was no effect modification by anaemia, malaria parasitaemia, infant sex, or season of birth.
Kupka (2008) (++)/(-)	HIV-infected pregnant women	Selenium supplementation – daily tablet of 200ug elemental selenium (as selenomethionine).	Maternal mortality Perinatal mortality Neonatal mortality Infant mortality Stillbirth	Selenium had no significant effect on maternal mortality, neonatal or infant mortality. Marginal association with reduced risk of low birthweight (LBW) and increased risk of foetal death.
Anthelmintics				
de Silva (1999) (+)/(++)	Women in general	Mebendazole during pregnancy vs no anthelmintic (controls).	Perinatal mortality	The proportions of stillbirths and perinatal deaths were significantly lower in the mebendazole group, as was the proportion of LBW babies.

Ndibazza (2010) (++)/(+)	Pregnant women in second or third trimester	Randomised, double-blind, placebo controlled trial investigating albendazole and praziquantel. Hematinics and sulphadoxine-pyrimethamine for presumptive treatment of malaria were provided routinely.	Perinatal mortality	In the study area, where helminth prevalence was high but infection intensity was low, there was no overall effect of anthelminthic use during pregnancy on maternal anaemia, birthweight, perinatal mortality or congenital anomalies.
Antiretrovirals				
Ekouevi (2008) (+)/(-)	Women with advanced HIV disease	HAART	Stillbirth	Among 326 singleton infants, the overall stillbirth rate was 3.1%. There was no significant difference between the HAART and the prevention of mother-to-child transmission (PMTCT) groups.
Walter (2006) (+)/(+)	HIV-infected women	Antiretrovirals. All women with CD4 cell counts <200 cells/mL who were at 14 weeks of gestation began receiving 2 single-strength tablets (400 mg of sulfamethoxazole and 80 mg of trimethoprim) daily. Treatment was delayed until 14 weeks of gestation for those who enrolled during the first trimester.	Neonatal mortality	There was a significant decrease in neonatal mortality. Antenatal provision of cotrimoxazole for HIV-infected pregnant women with low CD4 cell counts may have indirect benefits for neonatal health.

Steroids				
Fekih (2002) (+)/(-)	Women 26-34 weeks gestation at high risk of premature delivery	Antenatal maternal corticosteroid treatment. Group 1 received intramuscularly 24 mg of betamethasone. Group 2 received no antenatal corticosteroids.	Neonatal mortality	Neonatal mortality due to respiratory distress syndrome was statistically less in group 1 than in group 2 (22.9% vs 57%). Maternal administration of corticosteroids before preterm delivery resulted in a decrease in the incidence and severity of respiratory distress syndrome and a decrease in neonatal mortality rate among premature neonates born to mothers treated versus untreated at 26-34 weeks' gestation.
Antibiotics				
Aboud (2009) (++)/(+)	Pregnant women	Pregnant women (between 20 and 24 weeks of pregnancy) were randomized to receive either antibiotics (250 mg of metronidazole 3 times a day and 250 mg of erythromycin orally 3 times a day for 7 days) or placebo.	Maternal mortality	Administration of study antibiotics (metronidazole, erythromycin) during pregnancy had no effect on maternal morbidity and mortality among HIV-infected pregnant women.

Bergstrom (1991) (+)/(+)	Women with preterm rupture of membranes	The intervention group received amoxicillin (100mg) and metronidazole (500mg), both drugs given three times daily. All patients were also routinely treated with an antimalarial dose of chloroquine. The control group was not given any pharmaceutical treatment, and labour was induced 3-24h after membrane rupture.	Maternal mortality Neonatal mortality Perinatal mortality Stillbirth	While intrauterine mortality was approximately the same in both groups, neonatal mortality differed significantly (2.6 vs 19.2%). It is concluded that an expectant attitude, rather than an active and induction-oriented one, is most favourable in cases with preterm rupture of membranes, also in settings in which prevalence figures of sexually transmitted diseases and other genital infections are high.
Active management of third stage of labour				
Afolabi (2010) (+)/(-)	Women in labour with term pregnancies and having vaginal delivery	Use of misoprostol in active management of third stage of labour to prevent primary postpartum haemorrhage. Group 1 received oral misoprostol. Group 2 received intramuscular oxytocin.	Primary postpartum haemorrhage	No occurrence of postpartum haemorrhage and no difference in secondary outcomes. Misoprostol judged as safe and effective as oxytocin.
Antimalarial				
Kietinun (1993) (-)/(-)	Pregnant women with malaria	Malaria cases were treated with a loading dose of quinine hydrochloride given intravenously at 20mg/Kg diluted in 250 ml 5% dextrose in four hours, and then doses of 10 mg/Kg given at intervals of eight hours with the same dilution and rate until the patients were able to take the drug orally; 600 mg quinine sulphate was then given orally at eight-hourly intervals for seven days.	Maternal mortality	The overall maternal mortality rate in the obstetric department fell from 341 per 100,000 live births to 54 per 100,000 within five years, partly because of the improved care of pregnant women with malaria. Whereas in 1981 there were eight deaths among 379 pregnant women with the disease, in 1986 there were no deaths among 299 such cases.

Oral contraceptive				
Gray (1991) (+)/(+)	Women in general	Injectable contraceptive Depo-Provera was used during pregnancy.	Neonatal mortality Infant mortality	Higher neonatal and infant mortality rates, but not significant after adjustment for low birthweight.
Other clinical management				
Abdel (2010) (+)/(-)	Women in general	Uterine massage was used as a means of preventing postpartum haemorrhage. It was done shortly after delivery by the research midwives. Injections of oxytocin were delayed until after the 30-minute period of massage and blood collection, unless blood loss of 500 mL was measured before that time.	Maternal mortality	Uterine massage alone was associated with more blood loss within 30 minutes after delivery compared with treatment with oxytocin with or without massage.
Bakr (2005) (+)/(-)	Women in general Neonates in general	Antisepsis intervention consisted of manually wiping the maternal birth canal with a 0.25% chlorhexidine solution in sterile water. The cleansing procedure was done at admission and at every vaginal examination before delivery. Babies born during the intervention phase were wiped all over the body with pads soaked in 0.25% chlorhexidine immediately after delivery.	Maternal mortality Neonatal mortality	Cleansing the birth canal with chlorhexidine reduced neonatal and maternal postpartum infections.

Enakpene (2010) (+)/(-)	Women with umbilical cord prolapse (UCP)	ANC. Adequate prenatal care was defined as consisting of at least four prenatal visits in the index pregnancy and/or at least one prenatal visit within the 2–4 weeks preceding the occurrence of UCP. Inadequate prenatal, or no prenatal care, is defined as poor compliance with prenatal clinic visits or non-attendance at the prenatal clinic in the four weeks preceding occurrence of UCP.	Perinatal mortality	The perinatal mortality rate (MR) was higher among women without prenatal care, 463 per 1,000 total births, as compared with 222 per 1,000 total births in women who received prenatal care.
Etuk (2000a) (-)/(-)	Women in general	Pregnancies were booked for antenatal care but delivered outside the health facilities.	Perinatal mortality	The risk of perinatal death was three times higher in pregnancies booked for antenatal care but delivered outside health facilities in Nigeria.
Etuk (2000b) (-)/(-)	Women in general	Pregnancies were booked for antenatal care but delivered outside the health facilities.	Maternal mortality	There was a significant increase in maternal mortality in pregnancies booked for antenatal care but delivered outside health facilities in Nigeria.
Fabamwo (2010) (-)/(-)	Women in general	Antenatal care in the Lagos State University Teaching Hospital (LASUTH), Nigeria.	Maternal mortality Perinatal mortality	Significant reduction in maternal mortality.
Fenton (1999) (+)/(-)	Women needing Caesarean section	Blood transfusion during CS.	Maternal mortality	No significant difference in mortality between mothers transfused and not transfused.

Iqbal (2004) (+)/(-)	Women with prolonged pregnancy (> or = 294 days)	Group A, Induction of labour was done at 42 weeks of gestation. Intervention was done if any of the factors became abnormal. Group B, pregnancies allowed to run course up to 43 weeks.	Perinatal mortality Stillbirth	Active early intervention at 42 weeks is warranted to reduce perinatal morbidity and mortality.
Miller (2009) (+)/(++)	Women with obstetric haemorrhage	To determine whether the non-pneumatic anti-shock garment (NASG) can improve maternal outcome.	Maternal mortality	The NASG showed potential for reducing blood loss and maternal mortality caused by obstetric haemorrhage-related shock.
Munjanja (1996) (++)/(++)	Women in general	Reduced antepartum care visits. In the new programme, routine maternal weight-change measurements were not done and routine urinalysis was done only at the first visit. Urinalysis was done only at follow-up visits in the new programme if the blood pressure was raised, or if there was a suspected urinary-tract infection.	Perinatal mortality	An ANC programme with fewer more objective-oriented visits can be introduced without adverse effects on the main intermediate outcome pregnancy variables. No significant difference in perinatal or maternal mortality.

Pereira (1996) (-)/(-)	Women with Caesarean section	Assistant medical officers were employed to support EmOC and the study compares outcomes of Caesareans by medical officers with those performed by obstetricians.	Maternal mortality Early neonatal mortality Stillbirth	No significant differences in the number of maternal deaths, in the duration of post-operative hospital stay, in the indications for Caesarean delivery, or the surgical interventions associated with Caesarean delivery between the two groups. The only significant difference was in superficial wound separation due to haematoma, which was slightly more common (0.35% vs 0.05%) in the group operated on by assistant medical officers (odds ratio 2.2; 95% confidence interval 1.3-3.9).
Saleem (2007) (+)/(+)	Women in general	Antisepsis intervention administered by TBAs in home deliveries to improve perinatal outcomes consisting of 0.6% chlorhexidine vaginal and neonatal wipes.	Maternal mortality Early neonatal mortality Neonatal mortality	Use of 0.6% chlorhexidine vaginal and neonatal wipes for the prevention of neonatal infection is well tolerated and seems safe. Not powered to show differences in mortality.
Taha (1997) (++)/(++)	Women in general	Cleansing birth canal with antiseptic.	Neonatal mortality Perinatal mortality Stillbirth	Perinatal mortality showed a significant but transient change during the observation period 1982-1991.

Appendix 4.2: Included items dealing with clinical interventions and infant mortality

Author (year) **(IV)/(EV)**	**Target Population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
Surgical/instrumental procedures				
Ziadeh (2000) (-)/(-)	Triplets	Caesarean section.	Perinatal mortality	Caesarean section not advantageous. Perinatal mortality was greater among C-section group but very small sample size.
Drug treatment (including micronutrient supplementation)				
Cobra (1997) (++)/(++)	Infants in general	Oral iodized oil (100 mg) administered at around 6 weeks of age and infants followed to 6 months of age.	Infant mortality	Reduction in mortality in the iodized oil group during the first 2 months of follow-up and a delay in the mean time to death among infants who died in the iodized oil group compared with infants who died in the placebo group.
de Long (1997) (+)/(+)	Women in general Neonates in general Infants in general	Potassium iodate added to irrigation water over a 2 to 4 week period.	Neonatal mortality Infant mortality	Infant mortality rates decreased in the treated areas. Similar results were seen for neonatal mortality.

Author (year) (IV)/(EV)	**Target Population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
Joshi (2007) (-)/(-)	Neonates with primary pulmonary hypertension	Introduction of nitric oxide (iNO) therapy.	Neonatal mortality	Out of 18 babies treated with iNO, 2 babies, both transported from another hospital in a critical condition, died within an hour of initiation of iNO therapy. Three babies did not show any improvement in oxygenation following initial 2 hours of iNO therapy. Therefore iNO was discontinued and all 3 of them died. Of the remaining 13 babies who had shown a significant improvement in oxygenation after initial 2 hours of iNO therapy, 6 (46 %) survived and 7 died (54 %).
Kumwenda (2008) (++)/(++)	Infants born to HIV infected mothers	Antiretroviral prophylaxis to reduce breast-milk HIV transmission. Drugs for infants in the two extended-prophylaxis groups were dispensed to the mothers starting at the 1-week study visit and at subsequent visits until the infant completed the 14-week regimen. In the extended-prophylaxis groups, the oral dose of nevirapine was 2 mg per kilogram once daily during week 2, then 4 mg per kilogram once daily during weeks 3 through 14. The oral dose of zidovudine was 4 mg per kilogram twice daily during weeks 2 through 5, 4 mg per kilogram three times daily during weeks 6 through 8, and 6 mg per kilogram three times daily during weeks 9 through 14.	Infant mortality	At 9 months, although mortality in the control group exceeded that in the intervention groups, the differences were not significant.

Author (year) (IV)/(EV)	**Target Population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
Malaba 2005 (++)/(++)	Neonates born to HIV negative mothers	A single large dose of vitamin A during the immediate postpartum period. Infants were randomly assigned to 1 of 4 treatment groups: mothers and infants received vitamin A (Aa), mothers received vitamin A and infants received placebo (Ap), mothers received placebo and infants received vitamin A (Pa), and both mothers and infants received placebo (Pp). The vitamin A dose in the mothers was 400,000 IU and in the infants was 50,000 IU. The mother-infant pairs were followed to 12 months.	Infant mortality	No significant effect in any of the intervention groups compared with the control group receiving a placebo.
Miller (1994) (+)/(++)	Infants in general	Widened availability of ORS	Infant mortality	Improvement in case management and mortality decline following increased ORS availability.
Vaccinations				
Aaby (2002) (+)/(+)	Children up to 20 months in a war situation	Diphtheria, tetanus, pertussis (DTP); polio vaccines; and measles vaccines.	Infant mortality	Measles-vaccinated children had lower mortality than measles non-vaccinated children, but the difference was more marked for girls. The reduction was unrelated to prevention against measles infection. DTP and polio-vaccinated children did not have lower mortality than non-vaccinated children.

Author (year) (IV)/(EV)	**Target Population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
Aaby (2005) (++)/(+)	Infants in general	National immunisation days for oral polio vaccine (OPV) administered alone.	Infant mortality	OPV was associated with a beneficial effect for children under 6 months of age at the time of the campaign, but the difference was not significant for all children under 5 years of age. The effect of OPV among children less than 6 months of age could be due to selection bias but might also represent a non-specific beneficial immune stimulation.
Amin (1992) (-)/(-)	Infants in general	Expanded Programme on Immunization (EPI).	Infant mortality	There was a decline in infant mortality in 1988-89 compared to earlier periods. The decline seemed to have been the result of immunisation coverage, which had considerably increased by 1989-90, reaching above 70% of children under age 5.
Benn (2008a) (+)/(++)	Neonates in general	Infant vitamin A supplementation (VAS). Normal birthweight infants were administered 50,000 IU VAS or placebo with BCG.	Infant mortality	VAS administered with BCG vaccine at birth had no significant effect on infant mortality in this African setting.
Benn (2008b) (++)/(++)	Neonates in general	Infant VAS. Normal birthweight infants were administered 50,000 IU VAS or placebo with BCG.	Infant mortality	VAS administered with BCG vaccine at birth had no significant effect on infant mortality in this African setting.

Author (year) (IV)/(EV)	**Target Population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
Benn (2010) (++)/(++)	Low birthweight neonates	Infant VAS. Infants were administered 50,000 IU vitamin A or placebo and followed to 12 months.	Infant mortality	VAS at birth was not significantly associated with infant mortality among low birthweight neonates. A significant association was revealed between VAS and gender,: mortality decreased in boys but increased in girls.
Garly (2003) (+)/(-)	Neonates in general Infants in general	BCG vaccine.	Infant mortality	BCG-vaccinated children with a BCG scar had significantly lower mortality compared with BCG scar-negative children in the first 12 months of follow-up. The effect of BCG vaccination could be due to non-specific immune stimulation protecting against other infections.
Garly (2004) (+)/(++)	Infants in general	Hepatitis B vaccine (HBV) alongside measles vaccine.	Infant mortality	Among children enrolled in a measles vaccination trial, HBV-vaccinated children 7½-12 months of age had higher mortality than cohorts that had not received HBV, the difference being particularly strong for girls.
Fetuga (2010) (+)/(+)	Neonates in general	Expanded Programme on Immunization (EPI) and the National Programme on Immunization (NPI).	Neonatal tetanus (NNT) case fatality	Although the percentage prevalence of neonatal tetanus was lower in the later NPI period, the case fatality rate for the NPI period was higher than for the EPI period. The prevalence and mortality of NNT remains high in Nigeria despite a change in immunisation programme.

Author (year) (IV)/(EV)	**Target Population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
Martins (2008) (++)/(++)	Neonates in general	Standard Edmonston-Zagreb measles. Vaccination was administered to infants aged 4.5 months.	Post-neonatal mortality	The reduction in post-neonatal mortality was not significant.
Roth (2004) (+)/(+)	Neonates in general Infants in general	Early BCG vaccination.	Infant mortality	Mortality was lower for BCG-vaccinated than for unvaccinated LBW children controlling for available background factors. The beneficial effect on survival may not be explained by protection against tuberculosis.
Other clinical management				
Darmstadt (2004) (+)/(+)	Preterm infants	Topical application of sunflower seed oil 3 times daily during neonatal period.	Neonatal mortality	A significant reduction in mortality due to sepsis was not demonstrated in preterm infants treated by topical therapy with SSO in Egypt.
Darmstadt (2008) (++)/(++)	Preterm infants	Topical application of skin emollients as skin barrier during neonatal period.	Neonatal mortality	Both sesame seed oil (SSO) and Aquaphor significantly reduced mortality rates among preterm hospitalised infants with gestational age of 33 weeks in Bangladesh.
Le Fevre (2010) (++)/(+)	Preterm neonates	Topical application of skin emollients as skin barrier during neonatal period.	Neonatal mortality	Topical therapy with SSO or Aquaphor was highly cost-effective in reducing deaths from infection among the preterm neonates in Bangladesh.
Mandelbrot (2002) (++)/(+)	Infants born to HIV infected mothers	Vaginal cleansing with benzalkonium chloride during late pregnancy and delivery.	Infant mortality	No benefit of cleansing on mother-to-child transmission (MTCT) of HIV, perinatal mortality or infant mortality.

Appendix 4.3: Included items dealing with non-clinical interventions and maternal mortality

Author (year) **(IV)/(EV)**	**Target population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
Service organisation				
Training and audit				
Awan (1989) (+)/(-)	Women in general Infants in general	Comprehensive MCH programme in Lahore, Pakistan, with the provision of one MCH centre in each of 8 urban and 2 rural settings, with targeted staff supervision and peer review.	Maternal mortality Infant mortality	Declines in both MMR and IMR in the intervention areas, with end-point rates for IMR lower in the intervention area than the national average.
Bhatt (1989) (-)/(-)	Women in general	Establishment of routine medical audit throughout obstetrics department and confidential review of maternal deaths.	Maternal mortality	Medical audit introduced in 1965. Maternal mortality was found to have decreased by 1984.
Bugalho (1993) (-)/(-)	Women in general Neonates in general	Routine daily and weekly perinatal audit. Information was documented visibly on a board on the wall in the delivery room in which staff associated with a perinatal death were indicated by name.	Neonatal mortality Perinatal mortality Stillbirth	Perinatal mortality showed a significant but transient improvement during the observation period 1982-1991.

Author (year) (IV)/(EV)	**Target population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
de Muylder (1989) (-)/(-)	Women in general	Introduction of guidelines for management of dystocia, foetal distress, breech birth and Caesarean history at a maternity ward in Gweru, Zimbabwe.	Maternal mortality Perinatal mortality	Comparison of the two-year periods before and after the intervention showed that the maternal mortality rate declined from 2.0 to 0.5%, and the perinatal mortality rate from 71.9 to 56.2%, alongside a decline in the C-section rate.
Dumont (2005) (++)/(++)	Pregnant women with haemorrhagic and hypertensive complications	Implementation of obstetric guidelines using volunteer professionals at an obstetric unit in Senegal.	Case fatality for haemorrhage Case fatality for hypertension Case fatality for haemorrhage and hypertension	Patients characteristic-adjusted case fatality decreased during the intervention period compared with the baseline periods. Outcome improvements were more marked for hypertension than haemorrhage.
Dumont (2006) (++)/(++)	Pregnant women admitted to hospital for childbirth	Facility-based maternal death reviews (MDRs) of a district maternity hospital in Senegal.	Maternal mortality	MDR helped to improve the organisation of care, with a marked effect on the availability of life-saving interventions. Data on clinical outcomes showed a significant decrease in maternal mortality within a 3-year intervention period, in particular for deaths related to haemorrhage and hypertensive disorders.

Author (year) (IV)/(EV)	**Target population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
Kongnyuy 2008 (+)/(+)	Women receiving EmOC	Facility based MDRs and criterion-based clinical audit.	Maternal mortality	Maternal mortality decreased significantly from 250 per 100,000 women in 2005 to 222 in 2006 and 182 in 2007 ($p<0.001$).
O'Rourke (1995) (+)/(-)	Women in general	Training programme in Guatemala.	Perinatal mortality	There was no statistically significant reduction in mortality.
Strand (2009) (-)/(+)	Women referred for obstetric emergencies	Audit of records of women referred for obstetric emergencies to central hospitals in Luanda, Angola. Courses for midwives and doctors were implemented.	Maternal mortality	Following audit, maternal mortality decreased from 17.8% to nil.

Author (year) (IV)/(EV)	**Target population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
Provider models				
de Bernis (2000) (+)/(+)	Women in general	2 areas with contrasting availability of health care in Senegal: (1) where women giving birth in health centres went principally to the regional hospital and were usually assisted by trained midwives and (2) where most women gave birth in district health centres, usually assisted by TBAs.	Maternal mortality	Maternal mortality was higher in area 2 than in area 1 (874 and 151 maternal deaths per 100,000 live births, respectively).
Financing				
Ahmed (2004) (-)/(-)	Poor women with uterine rupture	Loan scheme from a hospital in Nigeria for women to purchase emergency surgical pack (loan to be paid back before discharge).	Maternal mortality	Case fatality of 38% found in a previous study from the hospital declined to 11% during the intervention. The difference was statistically significant.
Bashir (1991) (-)/(-)	Women in general	Introduction of specialised 'obstetric flying squad' which deals with emergencies at home.	Maternal mortality	In Faisalabad (Pakistan), the maternal mortality rate of 0.86/1,000 in 1989 was below the maternal mortality rate of 10.1/1,000 in 1977.

Author (year) **(IV)/(EV)**	**Target population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
Lim (2010) (++)/(++)	In some Indian states, all women were eligible for the intervention. In others, only women with a below the poverty line card were eligible.	Janani Suraksha Yojana (translated as safe motherhood scheme), a national conditional cash transfer scheme to incentivise women of low socioeconomic status to give birth in a health facility.	Maternal mortality Neonatal mortality Perinatal mortality	Findings suggest that the programme is reducing perinatal and neonatal mortality but its effect on maternal mortality remains unknown. (Note: the study may not have been powered to detect differences in maternal mortality).
Ronsmans (2001) (+)/(+)	Women in general	Safe Motherhood programme implemented by Mother Care and Ministry of Health in Indonesia. Interventions included training, deployment and supervision of a large number of professional midwives in villages; an information, education and communication (IEC) strategy to increase use of village midwives for birth; and a district-based maternal and perinatal audit (MPA).	Births admitted to hospital requiring CS or other life-saving intervention	The programme did not increase the use of specialised obstetric care for those in need. The proportion admitted to hospital for a Caesarean section declined from 1.7 to 1.4% and the proportion admitted to hospital with a complication requiring a life-saving intervention declined from 1.1% to 0.7%.

Appendix 4.4: Included items dealing with non-clinical interventions and infant mortality

Author (year) (IV)/(EV)	Target Population	Brief intervention description	Targeted Outcome(s)	Findings summary
Service organisation				
Bugalho (1993) (-)/(-)	Women in general Neonates in general	Routine daily and weekly perinatal audit. Information was documented visibly on a board on the wall in the delivery room in which staff associated with a perinatal death were indicated by name.	Neonatal mortality Perinatal mortality Stillbirth	Perinatal mortality showed a significant but transient change during the observation period 1982-1991.
Training and audit				
Aleman (1998) (-)/(-)	Neonates in general	Introduction of a registration system for births and deaths, including causes of death.	Neonatal mortality	Neonatal mortality decreased from 56/1,000 live births in 1985 to 11/1,000 in 1993.
O' Hare (2006) (-)/(-)	Neonates in general	Establishment of dedicated trained nurse team for neonatal resuscitation in a hospital in Kampala, Uganda. Five day training programme for nurses.	Neonatal mortality Stillbirth	Positive decrease in newborn deaths in babies weighing >2kg attributed to the nurse training.
Zhu (1997) (-)/(-)	Neonates in general	Training in the Neonatal Resuscitation Program Guidelines in a hospital in China.	Perinatal and neonatal mortality	Reduction in perinatal and neonatal mortality from 9.9 per 1,000 live births to 3.4 per 1,000 live births.

Author (year) (IV)/(EV)	**Target Population**	**Brief intervention description**	**Targeted Outcome(s)**	**Findings summary**
Increasing investment and scaling up				
Chomba (2008) (+)/(++)	Neonates in general	Protocol- and ENC-certified research nurses trained college-educated midwives from 18 low-risk, first-level urban community health centres, Zambia, in data collection and ENC.	Early neonatal mortality	ENC training is associated with significant decreases in early neonatal mortality: rates decreased from 11.2 per 1,000 live births to 6.2 per 1,000 following ENC implementation. Mortality for infants of mothers with 7 years of education decreased from 12.4 to 6.0 per 1,000 (P <0 .0001) but did not change significantly for those with 8 or more years of education (8.7 to 6.3 per 1,000, p = 0.14).
Enweronu (2008) (+)/(-)	Neonates requiring intensive care	Refurbishment of NSCU in Ghana.	Neonatal mortality	Improved facilities significantly improved survival of newborns <2,500 g, but was of no benefit for newborns ≥2,500 g.
Shantharam Baliga (2007) (+)/(++)	Neonates requiring special care	Scaling up of facility-based neonatal care in a district in southern India.	Neonatal mortality Perinatal mortality	Hospital perinatal and early neonatal mortality declined, as well as district-level perinatal mortality.

Author (year) (IV)/(EV)	**Target Population**	**Brief intervention description**	**Targeted Outcome(s)**	**Findings summary**
Discharge and admission procedure in neonatal units				
Agarwal (2007b) (-)/(+)	Women in general	A package of simple interventions: rational admissions and early discharge, entrusting mothers in care-giving, enforcing asepsis routines, aggressive enteral feeding, abandoning unnecessary interventions, protocol-based management, rational antibiotics and training and empowerment of nurses.	Neonatal mortality	Neonatal mortality rate declined significantly.
Bhakoo (1989) (+)/(+)	High risk neonates	In a hospital in India, reduction in admissions to NSCU of babies with birthweight more than 1,500g. Early discharge of babies to home from NSCU. Involvement of mothers in the care of high risk babies. Care of babies with specific complications outside NSCU.	Neonatal mortality	A significant fall in neonatal mortality in babies weighing less than 2 kg during 1986 as compared to 1973 (7.94% vs 12.88%; p less than 0.005), and in preterm babies the mortality fell from 26.88 to 11.5% (p less than 0.001) during 1986 due to the intervention.
Bhutta (2004) (+)/(-)	Neonates with LBW (<1,500g)	Intervention to reduce hospital stay in Pakistan. Mothers providing all basic nursing care for their infants before being discharged under supervision by a midwife or nurse following guidelines. Weekly outpatient visits after discharge was usually instituted for the first four to six weeks, with follow-up visits at longer intervals thereafter.	Infant mortality	Of 509 consecutive, very LBW infants, 494 (97%) preterm and 140 (28%) weighing < 1,000g at birth), 391 (76%) survived to discharge from the hospital. Readmission rates or adverse outcomes did not increase with early discharge.

Author (year) (IV)/(EV)	**Target Population**	**Brief intervention description**	**Targeted Outcome(s)**	**Findings summary**
Blencowe (2009) (+)/(+)	Neonates with LBW (<2,000g)	Revised discharge policy for babies with LBW in Malawi, which differed from existing WHO international guidelines.	Infant mortality	Mortality was higher amongst those discharged home at a weight <1,500g compared to those weighing more.
Sasidharan (2005) (-)/(-)	High-risk neonates	Training of mother to increase maternal involvement in care of high-risk neonates in India.	Neonatal mortality	In spite of an increase in the number of admissions during this period, significant and sustainable reduction in neonatal deaths.
Kangaroo Mother Care				
Bergman (1994) (-)/(-)	Neonates with LBW	KMC in Zimbabwe. Feeding is started from the first day, using small volumes. The mother is taught to feed weak and very LBW babies with a nanogastric tube. VLWB babies are also given a 10-day course of prophylactic antibiotics. Education to the mother was continuous. Mothers were encouraged to keep the infant in KMC until it reached 2,000g.	Infant mortality	The survival of babies born under 1,500g improved from 10% to 50%, whereas that of babies 1,500-1,999g improved from 70% to 90%.
Cattaneo (1998) (++)/(++)	Infants with LBW (1,000-1,999g)	KMC in several country contexts. Delivered for an average of about 20 hours per day, including in hospital. Mothers were encouraged to continue with KMC at home after discharge. After discharge, infants were followed up as outpatients at least four times, at 3, 10, 20 and 30 days.	Infant mortality	Deaths were recorded but the study design did not allow identification of differences in mortality.

Author (year) (IV)/(EV)	**Target Population**	**Brief intervention description**	**Targeted Outcome(s)**	**Findings summary**
Colonna (1990) (-)/(-)	Infants with LBW	Kangaroo Mother Care – nursing babies by continuously keeping them wrapped at the mothers' breasts.	Neonatal mortality	5 of the 100 newborn infants died before discharge. Almost all the remaining 95 were being breastfed at discharge and had gained on average 200g weight.
Lincetto (2000) (-)/(-)	Neonates with LBW (<1,800g)	Introduction of KMC for LBW infants in Mozambique. Staff training and ward reorganisation.	Neonatal mortality	27% death rate in babies receiving KMC versus 80% death rate for babies not receiving KMC. Survival rates increased.
Nagai (2010) (++)/(-)	Neonates with LBW (<2,500g)	Early KMC in Madagascar beginning as soon as possible in 24 hours after birth.	Neonatal mortality	Earlier continuous KMC had higher but no statistically different mortality in the first 28 days after birth.
Worku (2005) (-)/(+)	Neonates with LBW	KMC in Ethiopia.	Neonatal mortality	Survival was remarkably better for the early KMC group than babies in the conventional method of care in the first 12 hours and thereafter.

Author (year) (IV)/(EV)	**Target Population**	**Brief intervention description**	**Targeted Outcome(s)**	**Findings summary**
Nutrition (including breastfeeding practice and guidelines)				
Becquet (2007) (++)/(++)	HIV-infected mothers	HIV-infected pregnant women in Abidjan, Côte d'Ivoire, who received peripartum antiretroviral prophylaxis were presented antenatally with infant feeding interventions: either artificial feeding, or exclusive breastfeeding and then early cessation from 4 months of age. Nutritional counselling and clinical management were provided for 2 years. Breastmilk substitutes were provided free.	Infant mortality	Mortality rates did not differ significantly between the short-term breastfed and formula-fed groups. After adjustment for paediatric HIV status, they were similar to those observed among long-term breast-fed children.
Deschamps (2009) (+)/(-)	Pregnant, HIV-positive women Neonates born to HIV-positive mothers	All participants in Port-au-Prince, Haiti, received cotrimoxazole prophylaxis and infant formula for their children.	Infant mortality	The PMTCT programme described proved to be feasible and effective in reducing vertical HIV transmission in Haiti.
Jakobsen (2008) (++)/(++)	Infants in general	Promotion of exclusive breastfeeding for the first 4–6 months of life according to WHO recommendations at the time of the study. All children were followed from birth to 6 months of age.	Infant mortality	No significant reduction in mortality in the intervention group compared with the control group.

Author (year) (IV)/(EV)	**Target Population**	**Brief intervention description**	**Targeted Outcome(s)**	**Findings summary**
Kuhn (2008) (++)/(++)	HIV-infected women HIV-infected infants	Abrupt weaning at 4 months compared with the standard practice.	HIV-free survival	Early, abrupt cessation of breastfeeding by HIV-infected women in a low-resource setting, such as Lusaka, Zambia, did not improve the rate of HIV-free survival among children born to HIV-infected mothers and was harmful to HIV-infected infants.
Mbori-Ngacha (2001) (++)/(++)	HIV-1 infected women	Formula feeding of infants of HIV-infected women compared with breastfeeding.	Infant mortality	Similar mortality rates during the first 2 years of life. However, HIV-1-free survival at 2 years was significantly higher in the formula arm.
Nduati (2001) (++)/(-)	HIV-1 infected women	Breastfeeding and formula.	Maternal mortality Infant mortality	Mortality among mothers was higher in the breastfeeding group than in the formula group. There was an association between maternal death and subsequent infant death.

Appendix 4.5: Included items dealing with complex interventions and maternal mortality

Author (year) (IV)/(EV)	Target population	Brief intervention description	Targeted outcome(s)	Findings summary
Alwen (2005) (-)/(+)	Women in general	Safe Motherhood programmes in Upper Egypt: training; revised curricula; publication of medical protocols and services standards; upgrading of facilities; community outreach programmes; media campaigns.	Maternal mortality	Maternal mortality ratio (MMR) dropped by 52% between 1992-2000 (from 174 to 84/100,000 live births).
Bashir (1995) (-)/(-)	Women in general	Free access to obstetric care for 'deserving cases'; subsidies; training and refresher courses for TBAs; community education; introduction of specialised services; obstetric flying squad.	Maternal mortality	Trends in city-level (Faisalabad, Pakistan) maternal mortality, from 0.86/1,000 live births in 1989 to 0.64/1,000 live births in 1993.
Campbell (2005) (+)/(+)	Women in general	Safe Motherhood programmes.	Maternal mortality	The maternal mortality ratio (MMR) declined from 174 to 84/100,000 live births between 1992-93 and 2000. Improvements in parts of Egypt were due in part to extensive training, revised curricula, the publication of medical protocols and services standards, the upgrading of facilities, and successful community outreach programmes and media campaigns.
Mbaruku (1995) (-)/(-)	Women in general	There were 22 parts to the intervention: 1. Obstetrician nominated leader for intervention, change of traditional hierarchy, greater delegation to nurses and midwives.	Maternal mortality	Average maternal mortality ratio for two years before intervention was 849/100,000 live births and 275/100,000 in the period following implementation of intervention.

Author (year) (IV)/(EV)	Target population	Brief intervention description	Targeted outcome(s)	Findings summary
		2. Regular monthly meetings were arranged to enable staff to be informed and receive feedback 3. Efforts made to utilise available resources and refer to outside donors only when local resources exhausted, e.g. using local carpenters 4. Schedules for regular maintenance were started in order to prevent breakdown. 5. Maintenance of working skills was guaranteed by a number of activities. 6. Improvement of patient management by early diagnosis and treatment of diseases known to be common causes of death. 7. Efforts made to improve resuscitation of patients – training auxiliaries 8. Use of broad-spectrum antibiotics preoperatives was emphasised 9. Peripheral antenatal clinics were instructed to refer all cases of clinical anaemia early for correction 10. Better management routines in cases of severe anaemia introduced		

Author (year) (IV)/(EV)	Target population	Brief intervention description	Targeted outcome(s)	Findings summary
		11. Regular staff evaluation 12. Public complaints taken into consideration 13. Resolved to accommodate all essential staff in houses within hospital compound 14. Detailed plan for supply of essential drugs made in order to prioritise. Sub-store of drugs initiated in maternity ward 15. Small infusion production unit started 16. Vigorous campaign to encourage blood donation 17. Early provision of blood for transfusion from bank guaranteed 18. Strict norms were elaborated regarding minimum requirements to receive blood 19. Blood bottles prepared locally and donor sets made from the resterilised needles of used sets 20. Culture facilities restored 21. Local fundraising allowed the operating theatre to be repaired 22. Attention paid to proper sterilisation and		

Author (year) (IV)/(EV)	**Target population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
		disinfection of equipment		
Mswia (2003) (+)/(++)	Women in general Neonates in general	Raising the status of women; increasing the amount of health education; improving access to FP and EmOC.	Maternal mortality	In Tanzania, the maternal mortality rates in 1999 were substantially lower than at the start of surveillance (1992 for rural districts, 1993 for the urban area), although trends during the period were statistically significant at the 90% level only in the urban site.
Okaro (2001) (-)/(-)	Women in general	Safe Motherhood Initiative launched in Nigeria in 1990. Interventions included workshops for doctors and midwives referring pregnant women to the University of Nigeria Teaching Hospital, Enugu; radio and television campaigns on the need for pregnant women to seek help early; and discussion of maternal or foetal deaths within the obstetrics and gynaecology departments at the hospital.	Maternal mortality	Maternal mortality increased in the teaching hospital in Enugum Nigeria, following implementation of the Safe Motherhood Initiative.
Padmanaban (2009) (-)/(+)	Women in general	Promotion of institutional delivery; improved antenatal and postpartum care; surveillance of deaths; reviews of maternal deaths; near-miss audit; enhanced skilled care in rural areas; birth-companion programmes; and increasing the availability of blood. The state developed and added innovations to national-level programmes.	Maternal mortality	In Tamil Nadu, India, the MMR reduced from 380 per 100,000 births in 1993 to 90 in 2007.

Author (year) **(IV)/(EV)**	**Target population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
Yan (1989) (-)/(-)	Women in general	National programme in China starting in the 1950s. Interventions included: training and equipping TBAs; increasing the number of trained midwives and obstetricians; increasing the number of maternity beds; setting up a network for the care and referral of abnormal obstetric cases; introduction of ambulances.	Maternal mortality	The MMR declined sharply in China in the 1950s and 1960s. Direct obstetric deaths dropped from the average value of 82.1% of all maternal deaths in the period 1949-54 to 39.1% in the period 1979-83.

Appendix 4.6: Included items dealing with complex interventions and infant mortality

Author (year) (IV)/(EV)	**Target population**	**Brief intervention description**	**Targeted outcome(s)**	**Findings summary**
Borulkar et al (1998) (-)/(-)	Neonates requiring special care	Special care for newborns including optimum warmth, feeding, oxygen administration, resuscitation of asphyxiated babies and training.	Neonatal mortality	Neonatal survival was 61.5% in the 1,000-1,500g category and 92.5% in the 1,520-2,000g category over a five-year period. Intervention was judged to be replicable and affordable.
Brown (1996) (-)/(-)	Neonates with LBW (<1,500g)	Special care nursery. The infants were managed with warming, 'blind' antibiotic prophylaxis, intravenous fluids, nasopharyngeal oxygen for respiratory distress, and phototherapy and/or exchange transfusion for jaundice.	Infant mortality	Overall mortality was 54% and markedly inversely associated with birthweight.
Mirghani (2000) (-)/(-)	Pregnant women with diabetes	Simplified management of diabetes in pregnancy. Patients were controlled by insulin and monitored; labour was induced or C-section was performed at 38 weeks; basic resuscitation was carried out for all; hypoglycaemia was addressed in neonates; and early breastfeeding was made the norm. Babies who developed complications were managed at the special care unit.	Perinatal mortality	Perinatal mortality was higher among women with poor blood glucose control.

Appendix 4.7: Included items dealing with complex interventions and both maternal and infant mortality

Author (year) (IV)/(EV)	Target population	Brief intervention description	Targeted outcome(s)	Findings summary
Richard (2008) (++)/(++)	Women with Caesarean section	Comprehensive intervention in a district hospital in Burkina Faso to improve Caesarean delivery access and quality, including staff training, equipment, internal clinical audits, cost-sharing system, patient-provider meetings.	Maternal mortality Perinatal mortality	In this hospital, the number of C-sections increased. Hospital maternal deaths remained stable.

Appendix 4.8: Economic analyses of interventions targeted at urban dwelling poor populations to reduce maternal and infant mortality

Author (year) **(IV)/(EV) and settings**	**Intervention (I) and comparator (C)**	**Target population and duration of economic analysis**	**Study design**	**Cost results**	**Mortality-related effectiveness results**	**Perspective/price year**	**Synthesis of costs and effectiveness data**
Cattaneo (1998) (++)/(++) Ethiopia (and, Indonesia and Mexico – both excluded on income grounds)	I: Kangaroo Mother Care (KMC) C: Warm room or incubator care	100 low-birthweight babies – 1,000g-1,999g with no other major complicating factors and mother willing to collaborate. Mothers from all social groups. 30 days	RCT CEA	Cost data not reported separately for Ethiopia, but no differences in findings across countries noted. Overall across the three study areas salary costs were $11,788 in KMC group and $29,888 in comparator. Other hospital costs also lower $7,501 versus $9,876. P values not reported.	There were two deaths in the KMC group and three in the comparator group. This difference was not significant.	Health sector costs US $ price year not stated	No synthesis of costs and benefits as costs for intervention group were lower and outcomes similar.

Author (year) **(IV)/(EV) and settings**	**Intervention (I) and comparator (C)**	**Target population and duration of economic analysis**	**Study design**	**Cost results**	**Mortality-related effectiveness results**	**Perspective/price year**	**Synthesis of costs and effectiveness data**
Fekih (2002) (+)/(-) Tunisia	I: Antenatal maternal corticosteroid treatment to prevent respiratory distress syndrome in premature neonates C: No treatment	118 women (26-34 weeks gestation) at high risk of premature delivery	RCT CEA	Cost of intervention $ Tunisian 2,000 Cost savings in study group of $ Tunisian 21,000	Significantly lower neonatal mortality rates due to respiratory stress syndrome in intervention compared to control group (22.9% versus 57%).	Health sector costs Tunisian $	No synthesis of costs and benefits as costs for intervention group were lower and outcomes similar.

Author (year) **(IV)/(EV) and settings**	**Intervention (I) and comparator (C)**	**Target population and duration of economic analysis**	**Study design**	**Cost results**	**Mortality-related effectiveness results**	**Perspective/price year**	**Synthesis of costs and effectiveness data**
Le Fevre (2010) (++)/(+) Bangladesh	I: Topical emollients – synthetic Aquaphor or sunflower seed oil C: No treatment	497 low birthweight babies < 1,500 g. Pre-term infants only receiving hospital care within 72 hours of birth. 28 days	RCT CEA	Annualised total intervention costs for programme, including start-up costs US$1,834. Average cost per patient in Aquaphor, SSO and No treatment groups were $125.35, $99.47 and $93.39 respectively. P values not reported.	26% reduction in mortality with SSO compared to no treatment; or 523 years of life lost (YLL) averted. 32% reduction in mortality with Aquaphor compared to no treatment; or 649 YLL averted.	Health sector costs, including start-up costs US$ 2006 prices	For SSO, incremental cost compared to no treatment of US$ 61 per death averted or $2.15 per YLL averted. For Aquaphor incremental cost compared to no treatment of US$ 162 per death averted or $5.74 per YLL averted.

Author (year) **(IV)/(EV) and settings**	**Intervention (I) and comparator (C)**	**Target population and duration of economic analysis**	**Study design**	**Cost results**	**Mortality-related effectiveness results**	**Perspective/price year**	**Synthesis of costs and effectiveness data**
Sharieff (2008) (+)/(-) Pakistan	I: Nutritional supplement containing iron and zinc in form of sprinkles C: Placebo product	Hypothetical cohort of 5,000 6-12 month infants Effectiveness data from two RCTs Resource use data from Pakistan Sprinkles Diarrhoea study	Modelling study CBA Modelled outcomes until age 55	Net cost per child was $10 – $473 in the Sprinkles group and $1.31–$512 in the placebo group.	Based on data in effectiveness studies, estimated risk ratio in mortality for intervention group at 1 year was 0.82. Present value of net benefits including earnings from productivity in adulthood almost $800.	Health sector costs; impact on future productivity in adulthood International $ 2003 prices	Overall the present value of lifetime benefits was greater than the present value of costs of intervention.

Key: RCT – Randomised Controlled Trial; CEA – Cost-effectiveness Analysis; CBA – Cost-Benefit Analysis.

Appendix 4.9: Included items identified as high quality, with positive outcome(s) for maternal and/or infant mortality

Author (year) (IV)/(EV)	Poor urban identification	Brief intervention description	Target population	Intervention type	Setting	Targeted outcome(s)	Effect(s)
Infant							
Darmstadt (2008) (++)/(++)	Relative income: mean ±SD, 1,000 taka Maternal education Paternal education	Preterm infants (gestational age: ≤33 weeks) received daily topical applications of sunflower seed oil (SSO) or Aquaphor ointment.	Preterm infants	Clinical Other clinical management *skin therapy*	Special care nursery	Neonatal mortality	Both SSO and Aquaphor significantly reduced mortality rates among preterm hospitalised infants with gestational ages of 33 weeks in Bangladesh, by 25% to 30%.
Maternal							
Dumont (2006) (++)/(++)	Resource-poor setting	Midwives were responsible for identifying maternal deaths in the facility and they reported each case via a specific maternal deaths register. A senior gynaecologist-	Pregnant women admitted to hospital for childbirth	Non-clinical Service organisation Maternal deaths review (MDR)	District hospital	Maternal mortality	Significant decrease in maternal mortality within a 3-year intervention period, in

Author (year) (IV)/(EV)	Poor urban identification	Brief intervention description	Target population	Intervention type	Setting	Targeted outcome(s)	Effect(s)
		obstetrician reviewed all patients' charts and partographs on a daily basis, including the maternal death cases, to ensure quality of care, to provide continuous staff education and to assist with data collection. In the case of maternal death, the same gynaecologist-obstetrician interviewed the staff and the patient's family to collect information about the circumstances surrounding the death and completed a chart to capture this information. Next steps included: (1) Once a year, review of the charts by two senior obstetricians to classify the causes of death, and to identify any factors that contributed to the death that could have					particular for deaths related to haemorrhage and hypertensive disorders.

Author (year) (IV)/(EV)	Poor urban identification	Brief intervention description	Target population	Intervention type	Setting	Targeted outcome(s)	Effect(s)
		been avoided; (2) The obstetricians prepared a detailed report with their main findings and recommendations; (3) These findings were presented to the audit committee (composed of staff, local and national health authorities, and community representatives) and to representatives of international agencies and donors; (4) Agreed recommendations were implemented by the executive coordination team (composed of doctors, midwives and nurses), under the supervision of the district health manager; and (5) The following year,					

Author (year) (IV)/(EV)	Poor urban identification	Brief intervention description	Target population	Intervention type	Setting	Targeted outcome(s)	Effect(s)
		the manager of the district health service evaluated how well each recommendation had been implemented.					
Lim (2010) (++)/(++)	Place of residence Type of house Education SES/'class' Caste/tribe Wealth index based on material goods ownership	Janani Suraksha Yojana (JSY; translated as safe motherhood scheme) – a national conditional cash transfer scheme – to incentivise women of low socio-economic status to give birth in a health facility.	In some Indian states the conditional cash transfer system was available to all women whereas in other states it was only available to women who had a government card, issued to those below the poverty line	Non-clinical Service organisation Financing: Janani Suraksha Yojana	Community	Maternal mortality Neonatal mortality Perinatal mortality	Findings suggest that the programme is reducing perinatal and neonatal mortality; however, its effect on maternal mortality remains unknown. (Noted that study may not have been powered to detect differences in maternal mortality)
Munjanja (1996) (++)/(++)	Relative income	Service organisation: reduced visits for antepartum care. Routine maternal weight-change measurements were not	Women in general	Clinical Other clinical management	District hospital	Perinatal mortality	An antenatal care programme with fewer more objectively oriented visits can

Author (year) (IV)/(EV)	Poor urban identification	Brief intervention description	Target population	Intervention type	Setting	Targeted outcome(s)	Effect(s)
		done and routine urinalysis was done only at the first visit. Urinalysis was done only at follow-up visits in the new programme if the blood pressure was raised, or if there was a suspected urinary-tract infection. Blood pressure was measured at all visits except the second one, and symphyseal-fundal height (SFH) measurements were introduced into the new programme. At the second visit, the results of laboratory investigations were reviewed with the woman, but no clinical procedures were done. Based on the results of these investigations, any action needed was		*antepartum care*			be introduced without adverse effects on the main intermediate outcome pregnancy variables. No significant difference in perinatal or maternal mortality.

Author (year) (IV)/(EV)	Poor urban identification	Brief intervention description	Target population	Intervention type	Setting	Targeted outcome(s)	Effect(s)
		recommended at this visit. Patients in whom risk factors were detected later than the first visit remained in the study even if they were referred to Harare Central Hospital. The criteria for referral to hospital remained the same as in the standard programme, except for women with unknown dates and SFH measurements. In addition to palpation, the diagnosis of a large-for-dates or small-for-dates foetus was made if two consecutive readings at least 4 weeks apart were above the 95th or below the 5th centiles for gestation on the SFH nomogram for Central Africa.					

Appendix 4.10: High-quality included items with successful mortality outcomes, but not explicitly targeting urban poor populations

Author (year) (IV)/(EV)	Brief intervention description	Target population	Intervention type	Setting	Targeted Outcome(s)	Effect(s)
Infant						
Cobra (1997) (++)/(++)	Infants were allocated to receive placebo or oral iodised oil (100 mg) at about 6 weeks of age and were followed to 6 months of age.	Infants in general	Clinical Drug treatment (including micronutrient supplementation) *single micronutrient*	Home	Infant mortality	Oral iodised oil supplementation of infants may reduce infant mortality in populations at risk for iodine deficiency.
Maternal						
Dumont (2005) (++)/(++)	Emergency obstetric guidelines introduction in the Centre de Santé Roi Baudouin, Guédiawaye, Dakar, Senegal.	Women in general	Non-clinical Service organisation *obstetric guidelines*	District hospital	Case fatality for haemorrhage Case fatality for hypertension Case fatality for haemorrhage and hypertension	While staff daily supervision may have improved maternal outcome before the intervention period, audit and feedback produced marked effects on emergency obstetric care, especially for complications requiring highly trained management (e.g. pre-eclampsia).

Taha (1997) (++)/(++)	Manual cleansing of the birth canal with a 0.25% chlorhexidine gluconate solution in sterile water. Babies born during the intervention phase were wiped with pads soaked in 0.25% chlorhexidine immediately after delivery.	Women in general	Clinical Other clinical management *cleansing of the birth canal*	Central hospital	Neonatal mortality Perinatal mortality Stillbirth	Perinatal mortality showed a significant but transient change during the observation period 1982-1991.

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