What kinds of policy and programme interventions contribute to reductions in maternal mortality?

The effectiveness of primary level referral systems for emergency maternity care in developing countries



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List of abbreviations

CBA Controlled Before After (study)

CENTRAL Cochrane Central Register of Controlled Trials

CI Confidence Interval

CINAHL Cumulative Index to Nursing and Allied Health Literature

EPOC Cochrane Effective Practice and Organisation of Care

ITS Interrupted Time Series (study)

MeSH Medical Subject Headings

OR Odds Ratio

RCT Randomised Controlled Trial WHO World Health Organization

Brief dissemination summary

Many pregnancy complications are unpredictable and many women in developing countries live far away from where life-saving care is available. Referral interventions aim to address these problems. A systematic literature review was conducted to assess studies on the transfer of women with emergency obstetric complications from their homes, or from first contact with the health service, to an emergency obstetric care facility. Nineteen studies were included that assessed the effect of referral interventions from rural settings in Bangladesh, Burkina Faso, Guatemala, India, Indonesia, Malawi, Nepal, Pakistan, Zambia and Zimbabwe. In several South Asian settings, the organisation of communities to generate funds for transport, implemented as part of other community mobilisation activities, reduced neonatal deaths. The studies from Zambia and Zimbabwe suggested that the use of maternity waiting homes may reduce stillbirths. There is some evidence that referral interventions improve the utilisation of health services.

This review has strengthened the evidence for continuing to implement interventions that overcome delays in reaching obstetric care during emergencies. There are constraints limiting the conclusiveness of the evidence. Continued inclusion of referral interventions within maternal and newborn health programmes and as part of wider health system improvements is recommended, but practices in monitoring, research and evaluation of these interventions need to be improved.

Scientific abstract

Background

Many pregnancy complications are unpredictable and many women in developing countries live far away from where life saving care is available. Referral interventions aim to address these problems. Referral systems are multi-dimensional and have many components, but this study focuses on those which enable women to reach an appropriate health facility after a decision to seek help is made.

Objective

To assess the effects of interventions for timely emergency obstetric referral to higher levels of care in developing countries and to identify explanatory factors.

Methods of the review

Search methods

MEDLINE, EMBASE, CAB, CINAHL, the Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Effective Practice and Organisation of Care (EPOC) Reviews were searched with no date or language restrictions. Reference lists in other reviews and relevant articles were also searched.

Selection criteria

Randomised or quasi-experimental studies with a control or comparison group. Participants were women in developing countries experiencing an emergency obstetric complication and requiring transfer to a comprehensive emergency obstetric care facility. Outcome measures were maternal and neonatal mortality, service utilisation and process measures such as referral rates and time.

Data collection and analysis

Appraisal of titles and abstracts followed by independent assessment of selected full-text articles by at least two independent reviewers. A meta-analysis was conducted to estimate the pooled effects of interventions.

Results

Of 19,484 hits, 19 papers met the inclusion criteria. The included studies were randomised controlled trials (RCTs) or quasi-experimental studies in rural settings in Africa, Asia or South America. Interventions were organisational or structural in nature, or contained both characteristics. The studies did not show statistically significant reductions in maternal mortality. Reductions in neonatal death were noted in four RCTs comprising multiple components, including generation of transport funds in community groups (OR 0.69 95% CI 0.53, 0.90). Sub-group analysis revealed no reduction in stillbirths in the complex RCTs (OR 0.85 95% CI 0.67, 1.08) but stillbirths decreased in studies of maternity waiting homes (OR 0.52 95% CI 0.34, 0.80). There was some evidence of increased utilisation of health facilities and health professionals. The included studies did not allow assessment of factors explaining the effects of the interventions.

Conclusions

The effects on health outcomes of referral interventions which improve women's ability to reach appropriate care during an obstetric emergency are unclear. Conclusions are limited by difficulties in isolating the effects of multiple components and factors related to the design of some studies. We recommend continued inclusion of referral interventions within maternal and newborn health programmes and as part of wider health system improvements, but urge implementers to improve practices in monitoring, research and evaluation of these interventions.

1. Background

Maternal mortality in developing countries is showing signs of a decline. New modelled data from the World Health Organization and other independent sources report reductions in maternal mortality of between 22% and 34% since 1990 (Hogan et al. 2010, WHO 2010). The maternal mortality ratio is now estimated to be 260 per 100,000 live births in 2008 (WHO 2010). Despite this good news, it is still unlikely that the millennium development goal target reduction of 75% from 1990 levels to 120 maternal deaths per 100,000 live births in 2015 will be reached.

The health of women and their children are interlinked and many factors that contribute to the high levels of mortality are common to mothers and their newborn children. These factors are wide ranging and include the low status of women, cultural and economic barriers, poor nutrition, conditions such as HIV/AIDS or malaria, lack of appropriate health care facilities and poor access to skilled and emergency obstetric care. Many obstetric emergencies such as haemorrhage and obstructed labour are unpredictable and can have catastrophic consequences within a short time. For example, a serious post partum haemorrhage can lead to the death of a woman in less than two hours and the unborn foetus may succumb much earlier (AbouZahr 1998). In the poorest countries, two thirds of women deliver at home, far from emergency services or without access to a health professional (UNICEF 2009). Maternal and neonatal deaths could therefore be prevented if functional referral systems were in place to allow pregnant women to reach the appropriate health services when complications occur.

In the period remaining up to 2015, global agencies and country governments will make concerted efforts to scale up and speed up the effective coverage of maternity services. This review assesses evidence on the effectiveness of referral interventions that will inform the implementation of policies and programmes to improve access to maternity care.

1.1 Definitional and conceptual issues

1.1.1 Description of the problem

Any intervention to improve access requires consideration of a multitude of socio-economic and cultural factors, but one aspect of access involves the establishment of referral systems. The importance of referral in maternal and newborn care, especially in the event of an obstetric emergency, is related to the unpredictability of pregnancy complications, many of which cannot be dealt with at the primary level. Furthermore, pregnancy complications can progress rapidly to become severe and life threatening, emphasising the crucial role of referral in providing quality maternity services. The three delays model (Thaddeus and Maine 1994) provides a conceptual framework of the factors influencing the timely arrival to appropriate care in obstetric emergencies.

The 'three delays' are: (i) delays in the recognition of the problem and the decision to seek care in the household; (ii) delays in reaching the appropriate facility; and (iii) delays in the care received once the woman reaches the facility. Although distance and cost of care are among the major factors in the decision to seek care (the Phase I delay), the quality of care provided by facilities and the communities' perception of the quality may also influence the decision. The second delay of the model, Phase II, is concerned with the delay in arrival at the health facility, after the decision to seek care has been made. This phase is determined by the distribution and location of health facilities and health professionals equipped to deal with emergency obstetric and neonatal care, as well as the

availability and costs of transportation and communication systems to reach facilities. These delays affect both urban and rural areas, but are possibly most common and severe in rural areas, where health professionals may not be available, transport and communication systems may be limited, and road conditions changeable, depending on the season. The third, or Phase III, delay occurs at the facility level, where delays in various aspects of care provision, such as staff shortages, staff attitudes and skills, lack of functioning equipment, unreliable drug and blood supplies, or inadequate management structures, individually or together, reduce the quality of care available.

The delays of interest in this review are the Phase II delays - those experienced after the decision to seek care is made, and before obtaining necessary care. The reasons that these delays occur have been well documented and include difficult geographical terrain, the cost of transport, the lack of phones and vehicles, suboptimal distribution and location of health facilities or poor decision making by health professionals (Thaddeus and Maine 1994, Jahn and de Brouwere 2001).

1.1.2 Description of the intervention

This study focuses on interventions which:

- refer pregnant and post-partum women suffering from an emergency (life threatening) obstetric complication
- refer women from home to basic-level health facilities (health centres) and from health centre to hospital (but not referral between hospitals).
- have been studied or tested in developing countries.

Examples of these interventions include:

- use of technologies such as telephones, adaptations to vehicles or telemedicine interventions (Geerts et al. 2004, Hofman et al. 2008, Lungu et al. 2001)
- various financing and incentive schemes to assist transfer during an emergency (Barbey et al. 2001, Essien et al. 1997, Hossain and Ross 2006)
- clinical guidelines, protocol and ways of monitoring women at risk of, or with complications (Kongnyuy et al. 2008, McCaw-Binns et al. 2004)
- reorganisation or ways of delivering services such as introduction of intermediatelevel maternity units (including maternity waiting homes), emergency response teams, referral centres or outreach clinics (Chandramohan et al. 1995, Fahdhy and Chongsuvivatwong 2005, Foord 1995).
- mobilisation and use of health workers and community members to act as advocates and companions during referral (Alisjahbana et al. 1995, Bailey et al. 2002, Jokhio et al. 2005, Manandhar et al. 2004)

Many of the interventions described were implemented as a complex set of activities, thus comprised multiple components. They not only aimed to reduce delays in reaching a facility but also addressed barriers in decision making, and/or improved the provision of care after reaching a facility.

1.1.3 How the intervention might work

The interventions can be hypothesised to work by directly addressing the barrier or problem identified, as depicted in Figure 1. The shaded grey area is the focus of the interventions to address Phase II delays. Although the problems identified in the diagram are presented as distinct from each other, it is likely that they are interlinked, so one intervention might affect more than one problem area or lead to several consequences.

For example, if a health facility was placed nearer to women's homes to improve the distribution of services, it is possible that access to a phone or specialised emergency vehicle might also be improved. It is also likely that travel time to that facility will be affected. This may have positive consequences (such as decreased travel time or increased utilisation of the service) but may also have negative or unintended effects (for example, if the health provider in the facility is over-worked and does not effectively carry out triage of cases, s/he may cause delays in referring the most urgent cases). Similarly, investigating Phase II delays in isolation may be an oversimplification as Phase I and III factors will have effects on decisions, for example, willingness to pay for transport costs. Referral interventions thus work through complex mechanisms and it is unlikely that a study on Phase II delays will comprehensively capture all the pathways through which the intervention could work.

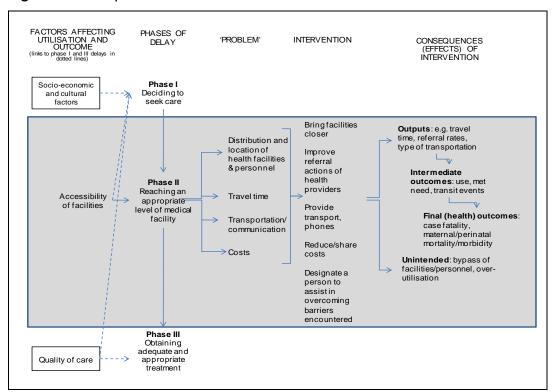


Figure 1: Conceptual framework for the review

Adapted from Thaddeus and Maine 1994

1.2 Aims and rationale for current review

1.2.1 Why it is important to do this review

A number of reviews on referral systems exist. The three delays model (Thaddeus and Maine 1994) has been described above. An assessment of maternity referral systems was conducted which provided a framework for factors likely to improve the implementation of referral interventions (Murray and Pearson 2006). Criteria important for strategic decision making in establishing referral systems was highlighted in another review, where the authors emphasised the need for referral systems to encompass both emergency and elective situations and be improved as part of a system-wide endeavour (Jahn and de Brouwere 2001). Another paper summarised existing technologies and described a range of transport options, mostly integrated with physical communication systems such as radio, maternity waiting homes and birth and emergency preparedness plans. Most of the studies

found did not assess the effect of the interventions using a comparison group (Krasovec 2004). Barriers and solutions to address Phase II delays were described most recently by Holmes and Kennedy (2010) in a wide and comprehensive review. The authors recommend working across different sectors, including transport, infrastructure, telecommunications, microfinance and industry, applying and using new technologies and investing in improving access, especially for women living in remote locations.

It is generally agreed that maternal and neonatal deaths could be prevented if functional referral systems were in place to allow pregnant women to reach the appropriate health services when complications occur. Various interventions to improve referral systems, many of them new and innovative, are currently recommended and described. Yet rigorous evidence synthesising the effects of these interventions is scarce. The diversity of interventions and settings, studies with different measures of effects and variation in the quality of studies makes a comprehensive review challenging. This situation has led to uncertainties in what needs to be done to improve referral for obstetric emergencies, what interventions to implement in which settings and how interventions can be scaled up when appropriate. This systematic review provides a contribution to knowledge in this field by focusing on study design and quality of evidence.

1.2.2 Objectives

The overall objective is to assess the effects of interventions for timely emergency obstetric referral in developing countries. Referral of the pregnant or postpartum woman is the focus of interest. This will have implications on the well-being of the mother, and of the unborn and newborn baby, so maternal and perinatal outcomes are of interest, along with process indicators of service utilisation, timeliness and delays.

The specific objectives are:

- To compare the effects of different referral interventions.
- To compare the effects of interventions disaggregated by sub-groups and settings, categorised according to:
 - o maternal and neonatal mortality
 - o rural, urban or intermediate settings
 - o geographical terrain
 - o different periods of pregnancy (antenatal, intrapartum, postpartum)
 - o wealth
 - o functionality of the health system
 - origin and initiator of intervention.
- To identify factors explaining the effects of the various interventions.

1.3 Review questions

The overall review question was:

What are the effects of primary level referral systems for emergency maternity care in developing countries and how might such interventions work?

The specific sub-questions were:

 What are the effects of different referral interventions which aim to surmount delays experienced after the decision to seek care is made, and before obtaining necessary care? (also known as Phase II delays)

- Do the effects vary in the different settings and groups listed below?
 - o maternal and neonatal mortality
 - o rural, urban or intermediate settings
 - o geographical terrain
 - o different periods of pregnancy (antenatal, intrapartum, postpartum)
 - o wealth
 - o functionality of the health system
 - o origin and initiator of intervention
- What are the factors or mechanisms through which the effects of the various interventions might work?

2. Methods used in the review

2.1 Identifying and describing studies

2.1.1 Defining relevant studies: inclusion and exclusion criteria

Types of studies

Randomised controlled trials (RCTs) or quasi-experimental studies with a control or comparison group, including: non-randomised prospective studies with a comparison group, controlled before-after (CBA) studies and interrupted time series (ITS) of referral systems for emergency maternity care from published and grey literature.

Exclusions: Studies without a comparison group.

Types of participants

Pregnant and post-partum women with an obstetric complication, referred as an emergency from the community or from a primary care centre to a higher-level comprehensive emergency obstetric care facility.

Exclusions: Referrals of the newborn baby, women with non-maternity-related conditions or non-emergency referral cases, women transferred between hospitals.

Types of interventions

Interventions which improved emergency referral during pregnancy (antenatal, during labour or during the postpartum period up to 42 days after delivery) were included. These may have been single interventions (e.g. transport, incentives), combinations of interventions (where the referral intervention affecting the Phase II delay was one of several other interventions), or changes in the way that interventions were delivered (e.g. improving linkages between different referral levels). Interventions had to have aimed to overcome delays in reaching the appropriate facility (Phase II delay). Interventions which were combined or had multiple components were included provided at least one component addressed Phase II delays.

Exclusions: Interventions that only improved Phase I and III delays, including those that changed decision making in service users, were transfers between tertiary care centres, or were non-emergency referrals.

Settings

All developing countries were potentially eligible for inclusion. Developing countries included low-income, lower-middle income and upper-middle income economies as classified by the World Bank (2011).

Exclusions: Refugees, war zones, mass casualties. Although we acknowledge that the inclusion of special settings in developed (high-income) countries such as rural Australia could provide relevant information, we did not include these as resource availability and the existing health system infrastructure might influence the feasibility and effectiveness of the interventions.

Types of outcome measures

In accordance with our conceptual framework (Figure 1) the types of measures reviewed lie on a pathway from direct effects of the intervention (outputs of intervention) to the final desired health outcomes of improved mortality and morbidity.

The primary outcomes in this study were health outcomes such as maternal and neonatal mortality and morbidity, including near misses, stillbirths, live births, complications and case fatality rates. These were included where recorded.

Other measures were collected to identify factors which could explain the effects of the various interventions. These measures lie on a hierarchy of consequences of the intervention, as depicted in Figure 1. Such measures included:

- Intermediate outcomes such as utilisation levels and met need (proportion of complications seen to expected complications) for obstetric care.
- Process measures or outputs of the intervention such as travel time, referral rates, type of transportation or communication, direct and indirect costs (payments for transport, health facility fees, loss of income), women's knowledge of pregnancy or postpartum complications and satisfaction with intervention.

2.1.2 Identification of potential studies: search strategy

Electronic searches

The search strategy was run in MEDLINE on the OVID platform. We used terms such as transfer, referral, types of transport (e.g. ambulances, bicycles), training and emergency obstetric services. Search terms are detailed in Appendix 2.1. The search strategy was adapted and run on CINAHL, EMBASE, CAB Abstracts, Effective Pregnancy and Organisation of Care (EPOC) Reviews and the Cochrane Central Register of Controlled Trials (CENTRAL) by selecting appropriate MeSH and/or keywords from their respective thesauri. No date or language restrictions were applied.

Searching other resources

Reference lists of reviews and of included studies were screened for potentially relevant primary studies and reports. Personal contacts provided additional papers.

2.2 Data collection and analysis

Citations identified from electronic searches were downloaded to a Reference Manager 12 database. Published studies and unpublished papers and reports were considered for relevance. An initial appraisal of titles and abstracts was conducted independently by two reviewers (LK, MA) based on the inclusion criteria. Abstracts of the resulting potentially eligible studies were reviewed by JH and SM. Relevant full text articles were retrieved and assessed for eligibility by at least two reviewers (JH and SM or MA or LK) (Figure 2). Disagreements about inclusion were resolved by discussion among review team members. Authors of papers were contacted where necessary and this provided additional information and unpublished data in a few instances.

Included studies were entered into Review Manager 5. Data of study characteristics and relevant outcomes were extracted. The interventions were categorised using the EPOC taxonomy of interventions for practice change (Walter, Nutley and Davies 2003). Organisational interventions included those which involved a change of role of the health worker or skill mix, creation of multidisciplinary teams or ways of working, integration of services and motivational aspects. Structural interventions included those which changed the site or setting of service delivery or physical structure. Other groups, such as financial,

professional and regulatory interventions, were described in the EPOC taxonomy, but were not applicable to the studies included in this review.

A meta-analysis of relevant outcomes was conducted to determine the pooled estimates of effects of interventions by outcome measures. Heterogeneity was explored by analysing RCTs separately from other study designs, categorising interventions by their characteristics, conducting statistical tests (chi-square and I-square index), using a random effects model and presenting data visually. Data were displayed as odds ratios, forest plots and tables, and in narrative form.

Quality assessment of each study was guided by Effective Public Health Practice Project (EPHPP 2009) tools. Quality assessment was based on selection bias, study design, confounders, blinding, data collection methods, withdrawals and dropouts. Two reviewers (JH, LK) independently assigned quality scores and compared judgements. Uncertainties were resolved through discussion between three reviewers (JH, LK and SM). Each of the aspects of quality was assessed based on the EPHPP criteria.

2.3 Deviations from the original protocol

Deviations from the original protocol were as follows:

- Types of interventions: We originally intended to include interventions used to stabilise and/or treat the woman before arrival at the facility/during referral, including obstetric first-aid techniques, use of the anti-shock garment and drugs for community/lower-level health facility use such as oxytocin and misoprostol. On further consideration, we felt that these interventions were not designed to reduce Phase II delays, but aimed to either obviate the need for referral, or to keep a woman alive while awaiting referral, so they were excluded.
- Search strategy. In addition to our search described above, we also intended to search LILACS, POPLINE, Reproductive Health Gateway, id21, Africa Journals Online, African Health Line, India Med and Institute of Tropical Medicine databases and sites. However, in the course of our review, we found that a recent comprehensive literature review describing referrals relating to Phase II delays had recently been made (Holmes and Kennedy 2010). We anticipated significant duplication if we continued searching all the databases originally planned. On conducting pilot searches we found many duplicate papers and no new hits. We therefore confined our search as described in our search methods and supplemented this from reference lists in review papers.

3. Results

3.1 Studies included from searching and screening

Our database search identified 19,484 citations. After initial screening, 618 abstracts remained. These were assessed for relevance and 381 excluded, necessitating retrieval of 237 full text articles. In addition, 133 other records, mostly unpublished reports, were obtained by contacting people and from references in review articles. Many of the unpublished reports did not have abstracts, so full texts were screened, eventually resulting in the inclusion of five papers. A total of 242 full text articles were retrieved. Five of these papers were in Spanish, French, Norwegian or Chinese. These were translated or discussed with research colleagues fluent in those languages and all eventually excluded. Nineteen papers were eventually included which met the study criteria (Figure 2).

The 19 papers included described 14 interventions, as five papers investigated the same intervention but provided supplementary information to the original paper. Three papers studied one intervention in Matlab, Bangladesh (Fauveau et al. 1991, Maine et al. 1996, Ronsmans et al. 1997), two described a study in Dinajpur, Bangladesh (Barbey 2001, Hossain and Ross 2006), two a study in Burkina Faso (FCI 2007, Brazier et al. 2009) and two of the same maternity waiting home intervention in Zimbabwe (Chandramohan et al. 1994, 1995). The remaining 10 interventions were represented by one paper each.

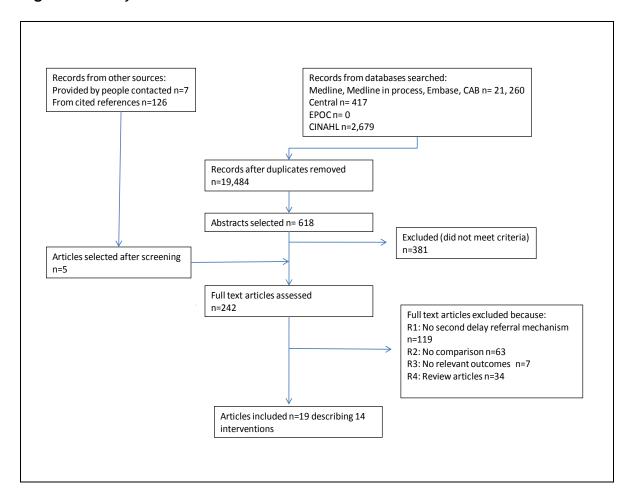


Figure 2: Study selection flow chart

3.2 Characteristics of the included studies

Characteristics of studies are summarised in Table 1. The included interventions were four cluster RCTs, five controlled before-after studies and five cohort studies. Seven studies were located in Asia, six in sub-Saharan Africa and one in Central America. In Asia, three were implemented in Bangladesh, and one each in India, Indonesia, Nepal and Pakistan. In sub-Saharan Africa, three were in Zimbabwe and one each in Burkina Faso, Malawi and Zambia. One study was implemented in Guatemala.

Several studies were of interventions that not only addressed delays in reaching a health facility, but also influenced Phase I (decision making) delays, Phase III (adequate and appropriate treatment) delays or other aspects of health services. As interventions addressing Phase II delays were the ones of interest in this study, Table 1 shows these interventions separately from the others. Some studies described combinations of interventions relevant to Phase II delays, for example, establishment of birthing homes was combined with provision of radios and ambulances in Indonesia (Alisjahbana et al. 1995). Other studies were of single interventions such as maternity waiting homes (Chandramohan et al. 1994, Lonkhuijzen et al. 2003, Millard et al. 1991, Tumwine and Dungare 1996). One study (Lungu et al. 2001) studied two interventions in separate arms. Of the two interventions, only one was relevant to Phase II delays (bicycle ambulances) while the other was a community transport plan which was primarily addressing decision making in communities. The studies were categorised as follows.

3.2.1 Organisational interventions

Six interventions were organisational in nature. They targeted women and community members including traditional birth attendants (TBAs). In the five studies set in South Asian countries, community groups were organised to generate emergency funds for transport. Some studies indicated that the idea of emergency funds was generated through community mobilisation activities and was not pre-decided (Azad et al. 2010, Manandhar et al. 2004), although the origin of the intervention was not so clearly described in other studies. The interventions included other components, such as improving integration between different health providers (Bhutta et al. 2008), education and awareness raising of complications (Azad et al. 2010, Kumar et al. 2008) and upgrading of facilities (Hossain and Ross 2006). The sixth study, conducted in the rural highlands of Guatemala, comprised slightly different organisational mechanisms. In this study, TBAs were described as actively taking part in referral by accompanying women to health facilities and helping women surmount cost and institutional barriers during transportation. Health facilities were encouraged to change practices by welcoming TBAs as birth companions (Bailey et al. 2002).

3.2.2 Structural interventions

This group comprised seven interventions, one from Indonesia, while the others were in sub-Saharan African settings. Five of the interventions were described in separate studies which assessed the establishment or use of what is commonly known as a maternity waiting home. This is a structure where women can live away from their own homes, so that they can be physically close to a health facility where care can be provided when labour starts or if complications occur. Various names were used to describe these interventions, including maternity waiting shelters, birthing homes and antenatal villages. The interventions were all slightly different. In Indonesia, the birthing home intervention was combined with several other health service improvements and located near a rural health centre (Alisjahbana et al. 1995). In contrast, the four sub-Saharan African studies described maternity waiting homes which were located next to, or a short distance from a hospital maternity ward. The criteria for which women used these maternity waiting homes varied within and across these four studies. Some women were advised to stay in the waiting home because of risk factors or complications while others stayed by choice, even if they had no medical reason to do so. One study specifically investigated a transport intervention. Bicycles were located in the community in Malawi (Lungu et al. 2001). Two others included transport and communication interventions with other activities. An ambulance was located at a district hospital in Burkina Faso and radio communications systems improved (Brazier et al. 2009), while in Indonesia, a similar improvement was implemented by providing a vehicle for a sub-district area and connecting health facilities with radios (Alisjahbana et al. 1995).

3.2.3 Mixed interventions

The Matlab-based studies from Bangladesh possessed a mix of organisational and structural interventions (Fauveau et al. 1991, Maine et al. 1996, Ronsmans et al. 1997). Matlab is a rural, flood-prone sub-district in Bangladesh where a demographic surveillance is sited. The set of interventions targeted health providers and health services. The Phase II intervention involved the provision of boats and ambulances, but in addition to these structural elements, also included organisational interventions such as assigning boatmen and helpers to accompany women during emergency referral as well as linking up these activities with ambulances for onward referral to a district hospital. The intervention contained other components, including posting of nurse midwives in health outposts to work with community health workers and TBAs.

Table 1: Summary of characteristics of included studies

Author/ Country	Study design	Setting	Level of care at referral centre	Participants	Intervention relevant to Phase II delay	Other interventions	Initiator of intervention
ORGANISATIONA	L (communit	y-based)					
Azad (2010) Bangladesh	RCT	Rural	NR	I: 20,943 births C: 22,774 births	Women accompanied to facilities Community emergency funds	Participatory women's groups Training TBAs	Academic and NGO
Bailey (2002) Guatemala	СВА	Rural (high- lands)	NR	I: 1,819 women C: 1,699 women	TBAs enabled to surmount obstacles to transport including cost, institutional barriers Health facilities encouraged to welcome TBA as birth companion	TBA training in detection, management and timely referral of complicated obstetric and neonatal cases	Academic and NGO
Bhutta (2008) Pakistan	RCT	Rural	NR	I: 2,932 live births C: 2,610 live births	Community groups establish emergency transport fund	Lady health worker training and TBA partnership, TBA newborn care training, community health education	Academic and government

Author/ Country	Study design	Setting	Level of care at referral centre	Participants	Intervention relevant to Phase II delay	Other interventions	Initiator of intervention
Hossain (2006) and Barbey (2001) Bangladesh	СВА	NR	Health centre	I: 713 births C: 796 births Comparison: 792 births	Community groups establish fund for emergency transport hospital fees Volunteers to accompany women or provide financial support	Upgraded facilities, birth planning, community support system, volunteers to donate blood	NGO, United Nations and government
Kumar (2008) India	RCT	Rural	NR	I: 1,522 live births C: 1,079 live births	Community groups establish emergency transport fund	Community members provide newborn care, birth preparedness, clean delivery	NR
Manandhar (2004) Nepal	RCT	Rural	Health centre	I: 3,036 pregnancies C: 3,344 pregnancies	Community groups establish emergency transport fund	Participatory women's groups led by trained facilitators. Form and content of discussions varied	NR
STRUCTURAL							
Alisjahbana (1995) Indonesia	Cohort	Rural	Health centre and hospital	I: 2,275 women C: 1,000 women	Birthing homes established Radio communication and ambulance transportation	Physicians, midwives trained on case management, homebased action records, TBA training, improving women's knowledge	NR

Author/ Country	Study design	Setting	Level of care at referral centre	Participants	Intervention relevant to Phase II delay	Other interventions	Initiator of intervention
Brazier (2009) and FCI (2007) Burkina Faso	СВА	Rural	Health centre and hospital	I: 2,554 women C: 2,859 women	Ambulance purchase Radio call system	Obstetric care training, equipment and supplies, quality assurance, management systems	NR
Chandramohan (1994, 1995) Zimbabwe	Cohort	Rural	Hospital	6,438 women	Building a maternity waiting home	None	Hospital advisory board
Lonkhuijzen (2003) Zambia	Cohort	Rural	Hospital	510 women	Maternity waiting home	None	NR
Lungu (2001) Malawi	СВА	Rural	Health centre	I: 41 women C: 53 women	Bicycle ambulance placed in community	Community transport plan in other arm of study	Bilateral donor and government
Millard (1991) Zimbabwe	Cohort	Rural	Hospital	854 births	Antenatal village	None	NR
Tumwine (1996) Zimbabwe	Cohort	Rural	Hospital	1,053 births	Maternity waiting shelter	None	NR
MIXED	•	- 1	•		-		-
Fauveau (1991), Maine (1996)and Ronsmans (1997) Bangladesh	СВА	Rural (flood plain)	Health centre and hospital	l: 4,424 C: 5,206	Boats, boatmen, helpers to accompany women Referral chain with ambulances for onward referral	Nurse-midwives posted in outposts to work alongside community health workers and TBAs	Academic

NR=Not reported, I=Intervention group, C=Control group, TBA=traditional birth attendant

3.3 Quality assessment

The quality assessment ratings are summarised in Table 2. Four studies randomly allocated participants to intervention or control areas. Most of the included studies were somewhat likely to be representative of the target population although some of the studies on maternity waiting homes (Lonkhuijzen et al. 2003, Tumwine and Dungare 1996) referred high-risk women from an antenatal clinic, increasing the likelihood of selection bias. Differences between intervention and control groups were not reported in many of the non-randomised studies, raising concerns about potential confounding factors. The difficulty of blinding the investigators to visible, community-based interventions was identified as a specific limitation in a few studies (Azad et al. 2010, Kumar et al. 2008, Manandhar et al. 2004). It was not mentioned in other studies, but the feasibility of using this particular criterion in visible community interventions is limited.

Several studies described the use of standard validated tools for data collection such as verbal autopsy (Azad et al. 2010, Ronsmans et al. 1997) and demographic and health survey questionnaires (Brazier et al. 2009). Other studies did not describe data collection tools in detail nor efforts to ascertain the reliability or validity of the tools. Withdrawal and dropout rates were reported in about half the studies.

Table 2: Quality assessment summary table

Author, year	Selection bias	Study design	Confounder	Blinding	Data collection methods	Withdrawal/ dropouts
Alisjahbana (1995)	Moderate	Moderate	Weak	Weak	Moderate	Strong
Azad (2010)	Moderate	Strong	Strong	Weak	Strong	Strong
Bailey (2002)	Strong	Weak	Weak	Weak	Weak	Strong
Bhutta (2008)	Moderate	Strong	Weak	Moderate	Strong	Weak
Brazier (2009), FCI (2007)	Moderate	Moderate	Weak	Weak	Moderate	Weak
Chandramohan (1994)	Moderate	Moderate	Weak	Weak	Weak	Strong
Chandramohan (1995)	Moderate	Moderate	Moderate	Weak	Weak	Weak
Fauveau (1991)	Moderate	Weak	Strong	Weak	Moderate	Weak
Hossain 2006), Barbey (2001)	Moderate	Moderate	Weak	Weak	Moderate	Weak
Kumar (2008)	Moderate	Strong	Moderate	Weak	Strong	Strong
Lonkhuijzen (2003)	Weak	Moderate	Weak	Weak	Weak	Strong
Lungu (2001)	Moderate	Moderate	Strong	Weak	Weak	Strong
Maine (1996)	Moderate	Weak	Weak	Weak	Weak	Weak
Manandhar (2004)	Moderate	Strong	Strong	Weak	Strong	Strong
Millard (1991)	Moderate	Moderate	Weak	Weak	Weak	Weak

Author, year	Selection bias	Study design	Confounder	Blinding	Data collection methods	Withdrawal/ dropouts
Ronsmans (1997)	Not applicable	Moderate	Moderate	Weak	Strong	Weak
Tumwine (1996)	Weak	Moderate	Weak	Weak	Weak	Weak

3.4 Effects of interventions

Effects of the interventions on maternal mortality were variable. An overall reduction in maternal mortality (OR 0.67 95% CI 0.19, 2.31) was seen in the three RCTs of community-targeted organisational interventions, but did not achieve statistical significance (Azad et al. 2010, Bhutta et al. 2008, Manandhar et al. 2004). Substantial statistical heterogeneity was present ($I^2 = 79\%$), with some studies showing a benefit but not others. None of the trials aimed to study the effect of interventions on maternal mortality so the sample sizes were not of adequate magnitude to measure this outcome with statistical confidence.

Of the non-randomised studies reporting maternal mortality, the mixed organisational-structural intervention (Fauveau et al. 1991), which enumerated deaths and births within a surveillance site, showed a reduction in maternal mortality (OR 0.35 95% CI 0.14, 0.88). A subsequent study. which used some of the same data but looked at mortality trends over a longer period, did not (Ronsmans et al. 1997). The two other studies of maternity waiting homes (Chandramohan et al. 1994, Tumwine and Dungare 1996) had small numbers of maternal deaths and did not show reductions in maternal mortality. Figure 3 summarises the findings of the studies which reported data on maternal mortality.

Maternal case fatality was only available from one study and showed no difference between intervention and control groups (OR 0.68 95% CI 0.06, 7.69), data not given (Maine et al. 1996).

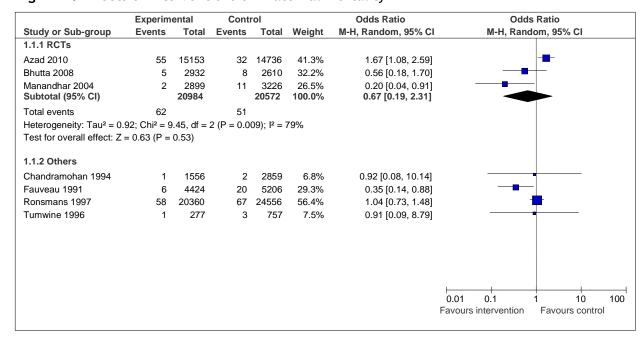


Figure 3: Effects of interventions on maternal mortality

Figures 4 and 5 illustrate findings on neonatal and perinatal deaths. Neonatal mortality was the primary outcome investigated in the four RCTs (Azad et al. 2010, Bhutta et al. 2008, Kumar et al. 2008, Manandhar et al. 2004). These studies showed significant reductions in neonatal deaths (OR 0.69 95% CI 0.53, 0.90) and perinatal deaths (OR 0.78 95% CI 0.61, 1.00) in the intervention groups. Neonatal deaths were not significantly reduced in non-randomised studies, but one study showed a reduction in perinatal deaths (OR 0.58 95% CI 0.39, 0.88) (Chandramohan et al. 1995).

Figure 4: Effects of interventions on neonatal mortality

	Interven	ntion	Cont	rol		Odds Ratio	Odds Ratio
Study or Sub-group	Events Total		Events Total		Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
2.3.1 RCTs							
Azad 2010	515	15153	557	14736	30.2%	0.90 [0.79, 1.01]	•
Bhutta 2008	121	2932	156	2610	25.3%	0.68 [0.53, 0.86]	-
Kumar 2008	64	1522	91	1079	21.4%	0.48 [0.34, 0.66]	-
Manandhar 2004 Subtotal (95% CI)	76	2899 22506	119	3226 21651	23.1% 100.0 %	0.70 [0.52, 0.94] 0.69 [0.53, 0.90]	•
Total events	776		923				
2.3.2 Others							
2.3.2 Others Chandramohan 1995	13	1556	38	2859	68.8%	0.63 [0.33, 1.18]	-
	13 8	1556 477	38 10	2859 322	68.8% 31.2%	0.63 [0.33, 1.18] 0.53 [0.21, 1.36]	-
Chandramohan 1995							-

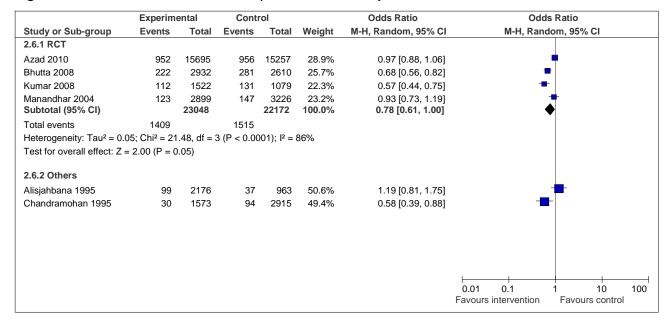


Figure 5: Effects of interventions on perinatal mortality

Figures 6 and 7 shows the effects of interventions on utilisation of health facilities in studies where sufficient data was available to ascertain odds ratios. Two studies (Alisjahbana et al. 1995, Manandhar et al. 2004,) show an improvement in utilisation of health facilities and in deliveries with health professionals (doctor, nurse or midwife). Two other studies (Bhutta et al. 2008, Kumar et al. 2008) demonstrated improvements in one of these two indicators of utilisation.

Figure 6: Effects of interventions on utilisation of health facilities

	Interven	tion	Contr	ol		Odds Ratio (Non-event)	Odds Ratio	(Non-event)
Study or Sub-group	Events	Total	Events Total		Weight	M-H, Random, 95% CI	M-H, Rand	lom, 95% CI
3.2.1 RCTs								
Bhutta 2008	121	395	48	375	36.7%	0.33 [0.23, 0.48]	-	
Manandhar 2004	201	2945	66	3270	63.3%	0.28 [0.21, 0.37]	•	
3.2.2 Others								
Alisjahbana 1995	114	2275	16	1000	100.0%	0.31 [0.18, 0.52]	-	
							0.01 0.1	1 10 10
							Favours intervention	Favours control

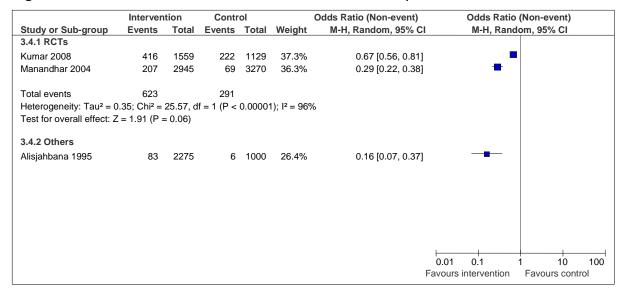


Figure 7: Effects of interventions on deliveries with health professionals

3.4.1 Effects of interventions by sub-groups

Neonatal deaths may be divided into early and late deaths. Early neonatal deaths occur in the first seven days of life and late neonatal deaths occur after the seventh day but before the first 28 days of completed life. Total neonatal mortality was shown in Figure 4. In Figures 8 and 9, the data is disaggregated by early and late neonatal deaths. In the RCTs, both early and late neonatal deaths were reduced in intervention groups. One non-randomised study (Tumwine and Dungare 1996) provided data on small numbers of early neonatal deaths but no difference in effect was seen between intervention and control groups.

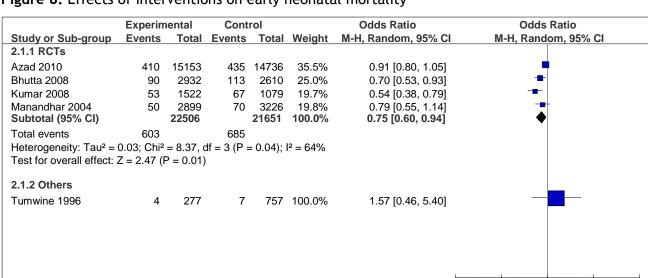


Figure 8: Effects of interventions on early neonatal mortality

0.1

Favours intervention Favours control

Odds Ratio Experimental Control Odds Ratio M-H, Random, 95% CI Study or Sub-group **Events** Total Events Total Weight M-H, Random, 95% CI 2.2.1 RCTs Azad 2010 105 15153 122 14736 35.9% 0.84 [0.64, 1.09] 0.64 [0.40, 1.02] Bhutta 2008 2932 2610 24.8% 31 43 Kumar 2008 15.2% 0.32 [0.16, 0.66] 11 1522 1079 Manandhar 2004 2899 3226 0.59 [0.36, 0.95] 26 49 24.1% Subtotal (95% CI) 22506 21651 100.0% 0.62 [0.44, 0.87] Total events 173 238 Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 7.00$, df = 3 (P = 0.07); $I^2 = 57\%$ Test for overall effect: Z = 2.73 (P = 0.006) 0.01 10 100 Favours intervention Favours control

Figure 9: Effects of interventions on late neonatal mortality

Perinatal mortality includes stillbirths and early neonatal deaths. The RCTs show an overall non-significant effect of interventions on stillbirth (OR 0.85 95% CI 0.67, 1.08). The three studies on maternity waiting homes provided data on stillbirths and showed a significant reduction in stillbirth rate when combined (OR 0.52 95% CI 0.34, 0.80) (Figure 10).

Figure 10: Effects of interventions on stillbirths

	Experim	ental	Cont	rol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
2.5.1 RCTs							
Azad 2010	542	15695	521	15257	32.5%	1.01 [0.90, 1.14]	•
Bhutta 2008	132	3064	168	2778	26.5%	0.70 [0.55, 0.88]	-
Kumar 2008	59	1581	64	1143	19.6%	0.65 [0.45, 0.94]	
Manandhar 2004 Subtotal (95% CI)	73	2972 23312	77	3303 22481	21.5% 100.0%	1.05 [0.76, 1.46] 0.85 [0.67 , 1.08]	†
Total events	806		830				
2.5.2 Others							
2.5.2 Others							
Chandramohan 1995	17	1573	56	2915	62.2%	0.56 [0.32, 0.96]	-
Millard 1991	9	486	14	336	25.7%	0.43 [0.19, 1.01]	
Tumwine 1996	3	280 2339	16	773 4024	12.1% 100.0%	0.51 [0.15, 1.77] 0.52 [0.34, 0.80]	•
Subtotal (95% CI)							
Total events	29		86				
` ,		= 0.24, df		0.89); l ²	= 0%		
Total events	0.00; Chi² =	-	= 2 (P =	0.89); l²	= 0%		

Data disaggregating the effect of interventions on wealth was available from the structural intervention in Burkina Faso involving ambulance purchase and radio call systems (Brazier et al. 2009). In the intervention district, baseline studies showed that 44% of the wealthiest women and 14% of the poorest used health facilities for childbirth. After the intervention, utilisation rates increased (Table 3) and the gap between poorest and richest groups narrowed to five percentage points. The organisational intervention in Guatemala which provided various forms of support to women during referral (Bailey et al. 2002), investigated referrals by sub-groups at different times of pregnancy (antepartum, intrapartum, postpartum). The study showed no change in referral rates after intervention for antenatal and intrapartum complications. Increases in postpartum referral were noted, but the analysis was based on fewer than 25 cases.

3.4.2 Factors explaining the effects of interventions

To identify factors explaining the effects of the various interventions, we examined indicators which measured the processes by which interventions achieved their effects, as illustrated in our conceptual pathway of problem, intervention and effect (Figure 1). None of the studies included were designed to explain the effects of interventions. Table 3 summarises these outputs and intermediate effects of the various referral interventions. The table is arranged in order of a postulated sequence of effect. For the referral intervention to have an effect, women would have to know about an intervention and/or be referred in the first instance. They would then have to comply with or use the referral intervention and subsequently overcome barriers they encountered, in order to reach appropriate care (measured using proxies such as delivery at health facility, with a health professional or met need).

Data on the explanatory mechanisms through which the referral intervention works is patchy. Some studies (Figures 6 and 7) show statistically significant improvements in utilisation of health facilities and health professionals. Most of the studies with data available only on percentage change (Table 3), show improvement in utilisation of health facilities and with health professionals in the intervention arm, although two studies did not (Azad et al. 2010, Bailey et al. 2002). The discrepancy between proportions of deliveries in health facilities and deliveries with health professionals within the same study are not always clearly explained in the papers, but are probably due to use of different denominators.

Two studies provide data on referral rate, compliance and utilisation. It is unclear whether the data presented in the Guatemalan study share the same denominators (Bailey et al. 2002). The findings from the Indonesian study have shown that 13% of women in the intervention group were referred and of these 73% complied, resulting in a 12% institutional delivery rate (Alisjahbana et al. 1995).

Four studies of maternity waiting homes provided information on travel time or distance (and health outcomes), but no other factors were described which could explain the effects of the intervention. The study on bicycle ambulances (Lungu et al. 2001) traced use rates of bicycle ambulances in villages and subsequent utilisation of health facilities. The bicycles were designed to pull a trailer-stretcher mounted on wheels the same size as those of the bicycles. Of 20 instances of use of the bicycles, only four were for obstetric referrals. The others were for other medical conditions. During the study period, more women from villages without bicycle ambulances delivered in health facilities - 70% in control villages compared to 49% of women in villages with bicycles. Furthermore, 22% of institutional deliveries during the study period came from villages provided with the bicycles and 42% from control villages (data not shown). The negative effect of the intervention on health facility utilisation was postulated to be due to a perception that bicycles brought unwanted attention to women during labour, so they preferred to walk to health facilities or deliver at home.

Table 3: Summary table of intermediate outcomes and process measures, after intervention

Study	Azad (2010)	Bailey (2002)	Bhutta (2008)	Hossain (2006), Barbey (2001)	Kumar (2008)	Manandhar (2004)	Alisjahbana (1995)	Brazier (2009), FCI (2007)	Chandramohan (1994, 1995)	Lonkhuijzen (2003)	Tumwine (1996)	Millard (1991)	Lungu (2001)	Fauveau (1991), Maine (1996), Ronsmans (1997)
Referral mechanism	Organisational interventions including community emergency transport funds and/or support to surmount institutional, cost barriers Structural interventions, including maternity wa ambulances							aiting homes, and/	or radios and/	or car or bic	ycle	Mixed, organisational and structural		
Knowledge of intervention	NR	NR	Unclear	Unclear	Unclear	Unclear	NR	NR	Yes	Yes	NR	Unclear	Yes	Unclear
Referral rate of women with complication	NR	I=49% C=38%	NR	NR	NR	NR	I=13% C=6%	Unclear	31%	I=43% C=57%	NR	I=59% C=41%	NR	NR
Compliance with/use of intervention	NR	I=78% C=69%	Unclear	NR	NR	NR	I=73% C=60%	NR	Yes ^b	Yes ^b	Yes⁵	Yes ^b	20%	NR
Travel time/ distance	NR	NR	NR	NR	NR	NR	NR	'Modal walking time >1h'	150 metres	'next to' ward	NR	2 min. walk	5km 90min.	2–4h
Costs to user	NR	NR	NR	US\$ 0.03- 0.06 ^a	NR	NR	Pay 'small' amount	'Low'	Free	US\$9	Free	NR	US\$0.1 per use	NR
Satisfaction with referral intervention	NR	NR	NR	NR	Unclear	Unclear	TBA reported loss of credibility	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Delivery in health facility	I=15% C=16%	I=49% C=52%	I=30.6% C=13%	I=21% C=5%	I=20% C=14%	I=7% C=2%	I=12% C=4%	I=57% C=36%	NR	NR	NR	NR	I=49% C=70%	NR
Delivery en route	NR	NR	NR	NR	I=1.5% C=1.7%	NR	NR	NR	NR	NR	NR	NR	NR	NR
Delivery with health professional	I=2% C=4%	NR		NR	I=27% C=20%	I=7% C=2%	I=13% C=5%	I=56% C=36%	NR	NR	NR	NR	NR	I=13%
Met need	NR	NR	NR	I=40% C=12%	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

NR=Not reported; I=intervention group, C=control group; a: reported in some community groups only; b: participants were selected based on use or non-use of maternity waiting home

Discussion

4. Discussion

Fourteen interventions from 19 papers were included in this review. We focused our review on the interventions or components of interventions which aimed to overcome Phase II delays. Of the fourteen interventions, six were organisational in nature and involved surmounting obstacles to emergency transport especially those of cost. Seven were structural in nature and involved the use of maternity waiting homes, radios and ambulances. One study used structural and organisational mechanisms to enhance various types and levels of transport and the linkages between them.

The findings of this systematic review need to be interpreted with caution. Interventions in a number of the included studies comprised several components, some of which were not related to referral. This did not allow the effects of the referral interventions to be isolated. Studies were also subject to constraints of design, methods and related factors.

4.1 Summary of main results

The success of complex, community-based interventions in reducing neonatal mortality is well documented and the subject of other systematic reviews (Kidney et al. 2009, Bhutta and Lassi 2010). In our efforts to examine these community-based interventions from the perspective of their referral components, we found evidence of a reduction in neonatal deaths from RCTs of community-based studies. The limitation in interpretation of this finding is that it is not possible to disentangle the effects of the referral from the other components. The changes observed may have been a result of the other components, or may only have occurred if the various elements were combined. We also observed an increase in utilisation of health facilities in some studies, but again, from studies of multicomponent interventions. Conclusive evidence that referral interventions reduce maternal mortality was not found. None of the included studies were of a sufficient size to investigate this relatively rare event.

Our sub-group analysis was limited by lack of data. All studies were confined to rural settings. There is weak evidence from sub-Saharan Africa suggesting that maternity waiting homes may reduce stillbirth rates. It is plausible that being in a maternity waiting home will allow women to be seen more rapidly in the case of any untoward event. Assuming that rapid and effective action (such as monitoring of foetal well-being and/or expediting delivery) is taken, an intrauterine death could be averted. The mechanisms through which this intervention might work and the factors which might be prerequisites for success (e.g. availability of surgery, or regular assessment of women staying in the maternity waiting home), could not be elicited from the studies included.

Two studies described special geographical terrain - a mountainous area in Guatemala (Bailey et al. 2002) and a flood plain in Bangladesh (Fauveau et al. 1991). None of the studies report variation of terrain within the study sites. One study improving transport and communication reported a narrowing of discrepancy in use of health facility between rich and poor women (Brazier at al 2009). Another study encouraging the use of advocates and companions during referral noted higher referral rates only for postpartum complications, although numbers of cases included in the study were small (Bailey et al. 2002). Both studies were multi-component in nature so conclusions regarding the effect of the Phase II intervention cannot be drawn.

It is postulated that the functionality of a health system may influence the effectiveness of a referral intervention, but none of the included studies provided information to assess the health system. We also attempted to identify whether the origin or initiator of an intervention was of importance (Table 1). Some studies described how the intervention What kinds of policy and programme interventions contribute to reductions in maternal mortality?

Discussion

was conceived, for example, the interventions implemented in Nepal (Manandhar et al. 2004) were informed by Bolivia's Warmi project (Howard-Grabman et al. 2002). The Indian study (Kumar et al. 2008) was influenced by the field-based Gadchiroli experience (Bang et al. 2005) and previous randomised controlled trials (Manandhar et al. 2004, Baqui et al. 2008). Maternal mortality estimates for the countries during the time of the intervention were looked up to see if there were variations in the types of interventions implemented. No discernable patterns were found in these crude attempts at sub-group analysis.

The studies included do not allow assessment of factors explaining the effects of the various interventions. None of them were designed to do so. Our attempt to use the studies to develop a causal pathway was limited by lack of data and. in some studies, the inability to isolate the effect of the referral intervention from other component interventions. There was also insufficient data to conduct regression analyses to explain effects of interventions.

4.2 Lessons learned and recommendations for policy and practice

Interventions to reduce delays in reaching an appropriate health care facility during an obstetric emergency are often implemented as one of several components simultaneously addressing other issues of access and quality such as decision making, adequacy of care and improvement of treatment modalities. This is hardly surprising, as to have the best chance of achieving reductions in maternal and neonatal mortality, interventions such as referral need to be complex in nature and work as part of the health system. We have found that such multi-component interventions with referral elements have an effect on improving health outcomes. Initiatives to improve maternal and newborn mortality should therefore continue to include interventions to improve referral. This is not at all a new recommendation; referral systems have, after all, been recognised as crucial since the Alma Ata declaration in 1978. Other studies using modelling techniques have predicted that maternal mortality decline will reach a threshold of less than 35% decline if access to emergency obstetric care is not provided, and that referral and transport strategies, alongside other interventions, could contribute to as much as an 80% reduction in maternal mortality (Goldie et al. 2010). This systematic review has strengthened the evidence for continuing to address delays in reaching obstetric care during emergencies.

As for the effect of specific interventions, common sense tells us that interventions that reduce travel time and link up the referral system are likely to be necessary. Do we need to have strong evidence of effectiveness for such decisions to be made? Perhaps not, yet this review shows that what are apparently 'good ideas' do need to be carefully assessed. The use of bicycle ambulances is one example. Examples of studies describing its utility have been reviewed (Holmes and Kennedy 2010), but this should not be assumed for all situations, as the study from Malawi demonstrates (Lungu et al. 2001). Good quality implementation research is necessary and will tell us more about factors that affect referral. Some progress has been made as regards implementation know-how. Factors that affect referral such as transport and cost barriers are thought to be substantial in rural African settings (Macintyre and Hotchkiss 1999). Requisites for implementing successful referral systems include: interventions based on need and capability, resources, linkages between referral levels, communication and transport arrangements, protocols for referral, provider performance, affordability, capacity for monitoring effectiveness and policy support (Murray and Pearson 2006). These studies go some way toward telling us about barriers and what needs to be in place for effective referral.

Many more unknowns remain. Do existing levels of maternal mortality, functioning of the health system, terrain or time of pregnancy matter when selecting which interventions to implement? Our study reveals that studies which met inclusion criteria were primarily set in rural areas - we can make no conclusions on Phase II delays in urban settings, or for that matter, any other contextual factors. Related to this is the deficit in understanding of What kinds of policy and programme interventions contribute to reductions in maternal mortality?

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mechanisms through which referral mechanisms work. Ten years ago, the tracking of individuals who have been referred was recommended (Macintyre and Hotchkiss 1999). Subsequently, the use of technologies related to transport and communication was reviewed (Krasovec 2004). The lack of high-quality studies to inform action was highlighted in that paper and the situation is unchanged today. The work by Murray and Pearson (2006) began to throw light on factors necessary to successfully implement referral interventions. The authors wrote of the need for 'theoretically informed social and organisational research' which remains unmet. Today, the literature describes a range of ideas relating to new and reinstated technologies, techniques and interventions to improve referral (Holmes and Kennedy 2010) but we are still no better informed because our knowledge is limited by studies not amenable to providing conclusive evidence. The few studies - 19 out of over 600 potentially relevant studies - which met the criteria for inclusion are testimony to the low priority given to careful design of implementation and use of best practices in monitoring and evaluation.

Our recommendations are as follows. Firstly, while continuing to invest in implementing referral interventions within maternal and newborn health programmes, we urge health planners to ensure that the interventions are rigorously monitored and evaluated, or operations research studies designed with controls and comparisons. Secondly, we believe that our finding of the reduction in stillbirth rates in maternity waiting home interventions needs further exploration through well-conducted studies, as the finding was based on studies with suboptimal study designs subject to biases. Finally, we believe that the type of research most relevant to referral interventions for policy and practice is not based on questions of 'what works', but should aim to understand how the interventions work and why. To this end, we recommend that the next step to build on this systematic review is to develop explanatory mechanisms for referral through the use of causal and theoretically informed models (Murray and Pearson 2006, Pawson and Tilley 2003), allowing utilisation of data from a broader range of studies than could be included in this review. Such work will limit the need for primary research and make maximum use of existing literature. We expect such work to generate knowledge on how referral interventions work, provide transferable and cumulative lessons from research which take into account contexts and result in improved learning across research, policy and practice.

5. References

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Appendix 1.1: Authorship of this report

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Conflicts of interest

SM and JH were authors on some of the studies considered for inclusion in this systematic review and were involved in the implementation of the interventions. They were not involved in the decision to include or exclude these studies in the review. The study was funded by the Department for International Development (DFID).

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Appendix 2.1: Search strategy for electronic databases

(MEDLINE search; adapted for other searches)

- 1. exp transportation of patients/
- 2. time factors/
- 3. exp transportation/
- 4. health services accessibility/
- 5. telemedicine/
- 6. remote consultation/
- 7. patient transfer/
- 8. exp transfer/
- 9. communication/
- 10. information dissemination/
- 11. interdisciplinary communication/
- 12. bicycling/
- 13. motorcycles/
- 14. (bicycle or bicycles or bicycling or bike\$ or cycle\$).ti,ab.
- 15. transport\$.ti,ab.
- 16. (car or cars or motor\$ or vehicle\$ or ambulance\$ or donkey\$).ti,ab.
- 17. (phone\$ or telephone\$ or cellphone\$ or radio\$).ti,ab.
- 18. telecommunications/
- 19. electronic mail/
- 20. radio/
- 21. Satellite Communications/
- 22. telefacsimile/
- 23. exp telephone/
- 24. exp Emergency Medical Service Communication Systems/
- 25. exp "referral and consultation"/
- 26. exp emergency service, hospital/
- 27. emergency medical services/
- 28. health services, indigenous/
- 29. emergency treatment/
- 30. triage/
- 31. first aid/
- 32. emergencies/
- 33. exp hospitalization/
- 34. delivery of health care/
- 35. after-hours care/
- 36. delivery of health care, integrated/
- 37. "medical record"/ or "medical records"/
- 38. "health education"/
- 39. (pre-hospital or prehospital).ti,ab.
- 40. (responsive\$ or referr\$).ti,ab.
- 41. ((emergency or emergencies) adj10 (health or care or service\$ or respons\$)).ti,ab.
- 42. (emergency or emergencies).ti,ab.
- 43. delay\$.ti,ab.
- 44. (timel\$ or timing).ti,ab.
- 45. "antishock garment".ti.ab.
- 46. "anti-shock garment".ti,ab.
- 47. ((matern\$ or deliver\$) adj3 (wait\$ or intermediate or outreach or out-reach or home\$)).ti,ab.
- 48. ((birth\$ or deliver\$ or emergenc\$) adj10 (plan\$ or protocol\$)).ti,ab.
- 49. ((first adj1 aid) or first-aid or (life adj1 saving)).ti,ab.
- 50. (emergenc\$ adj2 obstetri\$).ti,ab.
- 51. (obstetric adj5 care\$).ti,ab.

- 52. (TBA or traditional birth attendant).ti,ab.
- 53. ((train\$ or educat\$) adj10 (matern\$ or health\$ or professional or midwive\$ or midwife or nurs\$)).ti,ab.
- 54. ((health or basic or comprehensive) adj10 (care or service\$ or system\$ or polic\$)).ti,ab.
- 55. (BEmOC or EmOC or CEmOC).ti,ab.
- 56. (fund\$ or financ\$ or incentive\$).ti,ab.
- 57. ((guideline\$ or monitor\$ or record\$ or protocol\$) adj10 (system\$ or service\$)).ti,ab.
- 58. ((health or communit\$) adj5 (work\$ or participant\$ or profession\$ or educat\$ or fund\$ or service\$)).ti,ab.
- 59. (doctor\$ or nurse\$ or obstetr\$ or midwife\$ or midwive\$ or attendant\$).ti,ab.
- 60. or/1-59
- 61. maternal health services/ or maternal behavior/ or maternal-child nursing/ or maternal mortality/
- 62. pregnancy complications/ or pregnancy, high-risk/ or pregnancy complications, infectious/
- 63. delivery, obstetric/ or extraction, obstetrical/ or labor, obstetric/
- 64. obstetric care/
- 65. postpartum hemorrhage/
- 66. pre-eclampsia/
- 67. eclampsia/
- 68. labor complication/
- 69. pregnant women/
- 70. pregnancy/
- 71. (pregnancy or pregnant).ti,ab.
- 72. (antenatal or prenatal or antepartum or peripartum or postpartum).ti,ab.
- 73. (perinatal or postnatal).ti,ab.
- 74. (matern\$ adj5 (mortality or morbidity)).ti,ab.
- 75. ((labour or labor) adj10 (deliver\$ or birth\$ or childbirth\$)).ti,ab.
- 76. ((labour or labor) adj10 (infant\$ or baby or babies or child\$ or neonat\$ or mother\$ or matern\$)).ti,ab.
- 77. (obstructed adj5 (labour or labor)).ti,ab.
- 78. (eclampsia or pre-eclampsia).ti,ab.
- 79. ((genital or urin\$) adj5 infect\$).ti,ab.
- 80. ((obstetric or postpartum or post-partum) adj5 (haemorrhag\$ or hemorrhag\$)).ti,ab.
- 81. (ruptur\$ adj5 (uterine or uterus)).ti,ab.
- 82. or/61-81
- 83. 60 and 82
- 84. exp developing countries/
- 85. medically underserved area/
- 86. (developing adj5 countr\$).ti,ab.
- 87. ((low income or low-income or middle income) adj5 (countr\$ or area\$ or population\$ or city or cities or town\$)).ti,ab.
- 88. exp africa/
- 89. exp central america/
- 90. exp latin america/
- 91. exp south america/
- 92. exp asia/
- 93. exp caribbean region/
- 94. exp caribbean community/
- 95. or/84-94
- 96. 60 and 82 and 95
- 97. exp randomized controlled trials/
- 98. randomized controlled trial.pt.
- 99. controlled clinical trial.pt.
- 100. exp random allocation/
- 101. (random\$ or allocat\$ or assign\$).ti,ab.
- 102. exp clinical trials/
- 103. (clin\$ adj25 trial\$).ti,ab.
- 104. random\$.ti,ab.
- 105. program evaluation/
- 106. program development/
- 107. exp epidemiologic studies/

- 108. exp epidemiologic research design/
- 109. "Case-Control Studies"/
- 110. "cohort studies"/
- 111. epidemiologic methods/
- 112. Cross-Sectional Studies/
- 113. exp empirical research/
- 114. feasibility studies/
- 115. pilot projects/
- 116. comparative study/
- 117. review.pt.
- 118. review.ti,ab.
- 119. (meta-analysis or meta-analyses).ti,ab.
- 120. meta-analysis.pt.
- 121. "Costs and Cost Analysis"/
- 122. health care financing/
- 123. cost\$.ti,ab.
- 124. or/97-123
- 125. 96 and 124
- 126. human/
- 127. 125 and 126
- 128. (editorial or comment or letter or historical article).pt.
- 129. 127 not 128
- 130. case reports.pt.
- 131. 129 not 130
- 132. limit 131 to yr="1985 -Current"

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