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OPEN

SYSTEMATIC REVIEWS

Home-based neonatal care by community health workers for preventing mortality in neonates in low- and middle-income countries: a systematic review

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The objective of this review is to assess the effect of home-based neonatal care provided by community health workers (CHWs) for preventing neonatal, infant and perinatal mortality in resource-limited settings with poor access to health facility-based care. The authors conducted a systematic review, including meta-analysis and meta-regression of controlled trials. The data sources included electronic databases, with a hand search of reviews, abstracts and proceedings of conferences to search for randomized, or cluster randomized, controlled trials evaluating the effect of home-based neonatal care provided by CHWs for preventing neonatal, infant and perinatal mortality. Among the included trials, all from South Asian countries, information on neonatal, infant and perinatal mortality was available in five, one and three trials, respectively. The intervention package comprised three components, namely, home visits during pregnancy (four trials), home-based preventive and/or curative neonatal care (all trials) and community mobilization efforts (four trials). Intervention was associated with a reduced risk of mortality during the neonatal (random effects model relative risk (RR) 0.75; 95% confidence intervals (CIs) 0.61 to 0.92, $P=0.005$; $I^2=82.2\%$, $P<0.001$ for heterogeneity; high-quality evidence) and perinatal periods (random effects model RR 0.78; 95% CI 0.64 to 0.94, $P=0.009$; $I^2=79.6\%$, $P=0.007$ for heterogeneity; high-quality evidence). In one trial, a significant decline in infant mortality (RR 0.85; 95% CI 0.77 to 0.94) was documented. Subgroup and meta-regression analyses suggested a greater effect with a higher baseline neonatal mortality rate. The authors concluded that home-based neonatal care is associated with a reduction in neonatal and perinatal mortality in South Asian settings with high neonatal-mortality rates and poor access to health facility-based care. Adoption of a policy of home-based neonatal care provided by CHWs is justified in such settings.

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INTRODUCTION

The last three decades have witnessed a significant fall in infant mortality rates in developing countries, whereas neonatal mortality rates have decreased at a slower pace.[1,2] Estimates published in 2008 suggest that about 41% of all under-five mortality occurs in the neonatal period,[3] contributing four million deaths worldwide each year.[4] Nearly all (99%) global neonatal mortality occurs in developing countries.[3] Lowering this mortality is vital for achieving further reductions in infant and child mortality.[1,5–8]

Among neonatal deaths, three quarters occur during the first week of life whereas 25 to 45% occur within the first 24 h. The majority of neonatal deaths happen at home against a backdrop of rural poverty, unskilled neonatal care and a suboptimal or absent referral system; a strategy that promotes universal access to antenatal care, skilled birth attendance and early postnatal care has the potential to contribute to a sustained reduction in neonatal mortality.[1,5] A complementary approach is community-based delivery of key newborn health interventions. Two related modalities have been attempted in programs and research trials in the last decade. The first approach involves home visits and other community activities for the promotion of optimal newborn-care practices. The second approach, in addition to the promotion of preventive interventions, includes home-based management of perinatal and neonatal morbidities such as birth asphyxia and neonatal sepsis.

Since utilization of health facilities for neonatal health is low, the potential complementary role for home-based newborn care in accelerating the decline in neonatal deaths to achieve Millennium Development Goal 4 needs to be assessed. Recent reviews have evaluated the efficacy of community-based interventions, including home-based neonatal care, in reducing neonatal mortality.[9,10] In these reviews, the relative paucity of eligible trials necessitated the inclusion of non-randomized or quasi-randomized trials, which partially compromised the quality of synthesized evidence. Following the recent publication of randomized controlled trials, updating the available systematic reviews to guide relevant policy is necessary.

The objective of this review is to assess the effect of home-based neonatal care provided by community health workers (CHWs) for preventing neonatal mortality in resource-limited settings with poor access to health facility-based care.

METHODS

Criteria for considering trials for this review included the following:

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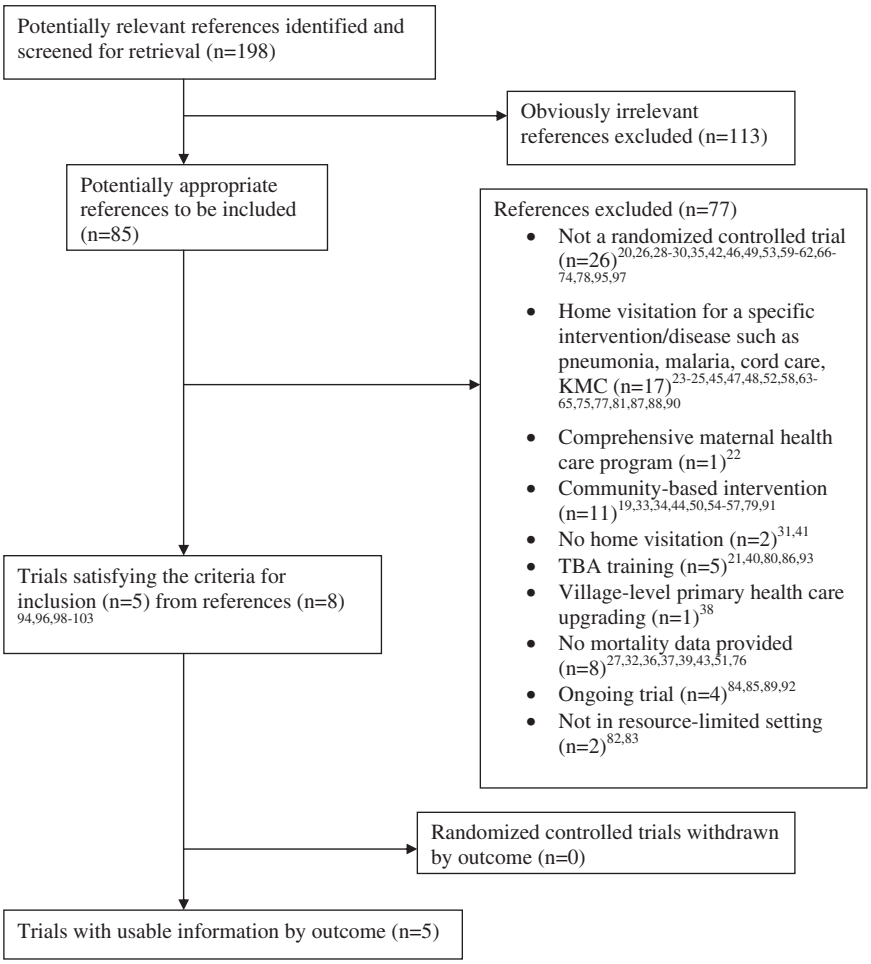

Figure 1. Trial flow for selection of randomized controlled trials. KMC, kangaroo mother care; TBA, traditional birth attendant.

Types of trials

Trials evaluating home-based neonatal care provided by CHWs with a concurrent control group and a random design, with individual or cluster allocation, were eligible for inclusion. Trials primarily evaluating home-based neonatal care following birth in a facility or hospital were excluded.

Types of participants

The trial population comprised neonates (first 28 days of life, or the first month of life where not specified in days) born in resource-limited settings with poor access to health facility-based care.

Types of interventions. Experimental interventions comprised promotion of optimal neonatal care practices at home, with or without home-based treatment of neonatal morbidities, delivered by CHWs during the neonatal period, with or without additional interventions during pregnancy and/or childbirth. The experimental intervention was compared with controls who did not receive any home-based intervention by CHWs during the neonatal period.

Interventions during pregnancy included: (i) promotion of antenatal care; (ii) health education and/or counseling of the mother regarding desirable practices during pregnancy; or (iii) promotion of delivery in a hospital or at home by a skilled birth attendant.

Interventions during childbirth included: (i) education about safe and/or clean delivery practices; or (ii) implementation of safe delivery practices in case of domiciliary deliveries.

Interventions during the neonatal period consisted of: (i) care of the newborn immediately after birth, including keeping the baby warm, neonatal resuscitation (if required) and early initiation of breastfeeding; (ii) health education and/or counseling of families regarding neonatal care practices such as exclusive breastfeeding, keeping the baby warm and hygienic cord care; (iii) education to improve caregiver recognition of life-threatening neonatal problems; (iv) education to improve health care-seeking behaviors; (v) identification of signs of severe neonatal morbidities and referral to a health facility; or (vi) home-based management of neonatal morbidities.

The term 'community health worker' included any of the following personnel: village or CHWs or volunteers (paid/unpaid), public health nurse or auxiliary nurse.

Types of outcome measures

Primary outcomes. All-cause mortality included: (i) neonatal deaths due to any cause during the period between initiation of the intervention and the last follow-up within the first month of life; and (ii) infant deaths due to any cause during the period between initiation of the intervention and the last follow-up within the first year of life.

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Secondary outcomes. These secondary outcomes included: (i) perinatal mortality rate; and (ii) cause-specific mortality including deaths due to neonatal sepsis, tetanus, asphyxia and prematurity (as defined by the authors, irrespective of single- or multiple-cause assignment).

Search methods for identification of trials

We searched computerized bibliographic medical databases, including Medline, Cochrane Controlled Trials Register in the Cochrane Library, EMBASE, Health Services Technology, Administration, and Research (HealthSTAR) and clinical trials websites through 5 May 2012. For PubMed the following search strategy was used:
(newborn or neonat* OR peri-natal) AND ('community' OR community-based OR home OR home-based OR domiciliary OR rural OR traditional OR village OR village-based) AND (mortality OR death OR survival OR outcome) AND (Clinical Trial[ptyp] OR Randomized Controlled Trial[ptyp] OR Controlled Clinical Trial [ptyp] OR Evaluation Studies[ptyp] OR Journal Article[ptyp]) AND (infant [MeSH]) AND (Humans[Mesh]).

A lateral search using the link of related articles in PubMed was done for articles initially selected from the search strategy. We also reviewed the reference lists of identified articles and hand-searched reviews, bibliographies of books and abstracts and proceedings of international conferences and meetings. Experts in the field were contacted to identify any additional or ongoing trials. The title and abstract of the trials identified in the computerized search were scanned to exclude trials that were obviously irrelevant. Full texts of the identified trials that fulfilled the inclusion criteria were reviewed. To avoid publication bias, we attempted to include both published and unpublished trials.

Quality assessment

In order to enhance the validity of the meta-analysis, the quality of the identified trials was assessed by Cochrane Collaboration's tool for assessing the risk of bias.[11] This tool assesses the degree to which: (i) the allocation sequence was adequately generated (sequence generation); (ii) the allocation was adequately concealed (allocation concealment); (iii) knowledge of the allocated interventions was adequately prevented during the study (blinding); (iv) incomplete outcome data were adequately addressed; (v) reports of the study were free of suggestion of selective outcome reporting; and (vi) the study was apparently free of other problems that could put it at high risk of bias (for example, conflict of interest, premature trial termination). Each domain was allocated one of the three possible categories for each of the included studies: 'Yes' for low risk of bias, 'No' for high risk of bias and 'Unclear' where the risk of bias was uncertain or unknown.

Data abstraction

Data abstraction was done in duplicate using a standard questionnaire. The data included in the review were derived from the published manuscript or as provided by the authors for unpublished trials. Requests to the original investigators for additional data and information were made if required. Data entry and initial analysis were performed on SPSS (IBM, Armonk, NY, USA) (Version 14.0) software.[12]

Analysis

Meta-analysis was performed with a user-written program on STATA (version 9.2) software (StataCorp, College Station, TX, USA).[13] The presence of bias in the extracted data was evaluated quasi-statistically using a funnel plot.[14] The effect measure was plotted against the standard error of the effect size on a log scale.

Table 1. Reasons for exclusion of individual references

Reference	*Reasons for exclusion*
Alisjahbana *et al.*[22]	Comprehensive maternal health care program
Bang *et al.*[23–25]	Home visitation for a specific intervention, pneumonia; not a randomized controlled trial
Bilenko *et al.*[26]	Not a randomized controlled trial
Bolam *et al.*[27]	Mortality data not available
Daga *et al.*[28,29]	Not a randomized controlled trial
de Francisco *et al.*[30]	Not a randomized controlled trial
Edgerley *et al.*[31]	No home visitation by CHWs
Fauveau *et al.*[32]	Mortality data not available
Foord[33]	Community-based intervention
Fox-Rushby[34]	Community-based intervention
Fullerton *et al.*[35]	Not a randomized controlled trial
Greenwood *et al.*[21]	TBA training, not home visitation
Haider *et al.*[36,37]	Mortality data not available
Hill *et al.*[38]	Village-level primary health care (upgrading)
Jakobsen *et al.*[39]	Mortality data not available
Jokhio *et al.*[40]	TBA training, no planned postnatal home visitation
Kielmann *et al.*[41]	No home visitation by CHWs
Kwast *et al.*[42]	Not a randomized controlled trial
Leite *et al.*[43]	Mortality data not available
Mbonye *et al.*[45]	Home visitation for a specific intervention, malaria
McPherson *et al.*[46]	Not a randomized controlled trial
Meegan *et al.*[47]	Home visitation for a specific intervention, cord care
Mehnaz *et al.*[48]	Home visitation for a specific intervention, cord care
Mercer *et al.*[49]	Not a randomized controlled trial
Morrow *et al.*[51]	Mortality data not available
Mullany *et al.*[52]	Home visitation for a specific intervention, cord care
Nankunda *et al.*[53]	Not a randomized controlled trial
O'Rourke *et al.*[54]	Community-based intervention
Osrin *et al.*[19,44,50]	Community-based intervention
Perry *et al.*[56]	Community-based intervention
Phillips *et al.*[55,57]	Community-based intervention
Pratinidhi *et al.*[20,59]	Not a randomized controlled trial
Saleem *et al.*[58]	Home visitation for a specific intervention, cord care
Sibley *et al.*[60]	Not a randomized controlled trial
Sibley *et al.*[61]	Not a randomized controlled trial
Sibley *et al.*[62]	Not a randomized controlled trial
Sloan *et al.*[63]	Home visitation for a specific intervention, KMC
Taha *et al.*[64]	Home visitation for a specific intervention, cord care
Tielsch *et al.*[65]	Home visitation for a specific intervention, cord care
Bang *et al.*[66–74]	Not a randomized controlled trial
Ahmed *et al.*[75]	Home visitation for a specific intervention, KMC
Arifeen *et al.*[76]	Mortality data not available
Arifeen *et al.*[77]	Home visitation for a specific intervention, cord care
Awasthi *et al.*[78]	Not a randomized controlled trial
Azad *et al.*[79]	Community-based intervention
Gill *et al.*[80]	TBA training, no planned postnatal home visitation
Hodgins *et al.*[81]	Home visitation for a specific intervention, cord care
Katz *et al.*[82]	Not in resource limited setting
Lee *et al.*[83]	Not in resource limited setting
Lewyca *et al.*[84]	Ongoing trial
Mann *et al.*[85]	Ongoing trial
Matendo *et al.*[86]	TBA training, no planned postnatal home visitation
Mullany *et al.*[87]	Home visitation for a specific intervention, cord care
Odendaal *et al.*[88]	Home visitation for a specific intervention, accident prevention
Pasha *et al.*[89]	Ongoing trial
Soofi *et al.*[90]	Home visitation for a specific intervention, cord care
Tripathi *et al.*[91]	Community-based intervention
Wallin *et al.*[92]	Ongoing trial
Wu *et al.*[93]	TBA training
Bhutta *et al.*[95]	Not a randomized controlled trial
Baqui *et al.*[97]	Not a randomized controlled trial

Abbreviations: CHW, community health worker; KMC, kangaroo mother care; TBA, traditional birth attendant.

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Table 2. Characteristics of included randomized controlled trials

Study	*Type of study*	*Intervention*		*Subjects*	*Results*	*Remarks*
		Experimental group	*Control group*			
Kumar *et al.*, India[96]	Cluster-randomized trial	Preventive package of interventions for essential newborn care Birth preparedness Clean delivery and cord care Thermal care (including KMC) Breastfeeding promotion Danger sign recognition With or without use of a liquid crystal hypothermia indicator (Thermospot) Significant behavior change management targeted at multiple levels of society through personalized or group approach CHWs delivered the packages via Collective meetings and folk song group meetings Two home visits during pregnancy for birth preparedness, and Two visits in first week post delivery for routine newborn care	Control arm received the usual services of governmental and non-governmental organizations in the area	3810 total births	Neonatal mortality RR 0.51 (0.36–0.73) Stillbirths RR 0.85 (0.56–1.29) Improvements in birth preparedness, hygienic delivery, thermal care (including skin-to-skin care), umbilical cord care, skin care and breastfeeding There was little change in care-seeking	The intervention that included the use of the Thermospot did not seem to have an advantage over the package of essential newborn care Significant community mobilization and behavior-change communication
Baqui *et al.*, Bangladesh[94,99]	Cluster-randomized trial	Community meetings with pregnant women and female family members Meetings with husbands/heads of households in mosques and markets Advocacy meetings with local leaders Orientation for TBAs (2 days) on cleanliness during delivery, maternal danger signs and newborn care Twice per month community surveillance to identify pregnant women Two antenatal home visits to promote birth and newborn-care preparedness Postnatal home visits on days 1, 3 and 7 to reinforce birth and newborn-care preparedness, and provide counseling for breastfeeding Algorithm-based routine household screening of newborns on days 1, 3 and 7; referral of sick newborns to government health facilities; and treatment in the home with injectable antibiotics if disease not severe or referral failed.	Comparison arm received the usual health services provided by the government, non-governmental organizations and private providers Refresher training for government workers was provided	30 119 live births	Home-care arm: Neonatal mortality RR 0·66 (0·47–0·93) Improvement in (at least one) antenatal check-ups from a trained provider, iron and folate supplements intake, initiation of early and exclusive breastfeeding, delayed bathing, cord care	Each CHW was responsible for a population of about 4000, which was similar to the primary health care worker to population ratio in the Bangladesh government health system, thus facilitating sustainability and scalability of the home-care service delivery approach
Darmstadt *et al.*, Bangladesh[102,103]	Cluster-randomized trial	CHWs made two home visits scheduled at 12–16 weeks and 32–34 weeks to: Promote ANC (making three ANC visits from a health center or satellite clinic, receiving two doses of tetanus toxoid vaccine, iron-folic acid supplementation, eating extra food) Care-seeking for maternal danger signs Promote birth planning Distribute clean delivery kit at the second antenatal visit for use by birth attendant Promote newborn-care preparedness Feeding colostrum to the newborn; initiating breastfeeding immediately after birth; practicing exclusive breastfeeding up to 6 months; and feeding the newborn frequently in the proper position day and night Delaying bathing of the newborn for 72 h	Routine care	9857 live births	Neonatal mortality RR 0.87 (0.68–1.12)	

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Table 2. (Continued)

Study	Type of study	Intervention		Subjects	Results	Remarks
		Experimental group	*Control group*			
		Umbilical area care Monitoring baby for signs of infection; and seeking care immediately from CHW or health facility if the newborn has any danger signs Four home visits on postnatal days 0, 2, 5 and 8 to: Reinforce newborn care messages provided through prenatal visits Provide counseling for routine breastfeeding and for breastfeeding difficulties Surveillance of newborn illness: identify sick neonates based on a clinical algorithm. Referral-level evaluation or, if referral fails, continue monitoring according to the clinical algorithm.				
Bhutta *et al.*, Pakistan[101]	Cluster-randomized trial	LHWs received additional training on: Basic ANC including rest and nutrition counseling Screening for common illnesses Iron, folate and tetanus toxoid administration Liaison with TBAs (Dais) to identify births Mouth-to-mouth resuscitation Training in group counseling and communication strategies Promotion of early breastfeeding (within the first hour) and colostrum administration (avoidance of prelacteal feeds) Promotion of delayed bathing and improved home care for low birth weight infants Recognition of sick newborn babies and danger signs for referral Basic training and linkage of TBAs with LHWs LHWs encouraged to visit mothers twice during pregnancy and within 24 h of birth. In addition, visits were encouraged on days 3, 7, 14 and 28 after birth Community organization, mobilization and group education sessions	LHWs received training in: Promotion of ANC Iron and folate use in pregnancy Immediate newborn care Cord care (cleaning and avoiding the use of traditional materials, such as ash and lead powder) Promotion of exclusive breastfeeding Training in community mobilization by building support groups Recognition of neonatal illness Referral for care TBAs linked with LHWs and trained on promotion and use of clean delivery kits	23 834 total births	Neonatal mortality RR 0.85 (0.76–0.96) Stillbirths RR 0.79 (0.68–0.92) Perinatal mortality RR 0.83 (0.74–0.93) 24% increase in receiving at least one ANC 22% increase in birth attendance by skilled attendant	
Bhandari *et al.*, India[100]	Cluster-randomized trial	All CHWs, auxiliary nurses and physicians trained in improving case management skills TBAs invited for orientation on clean delivery, cord care and newborn care Supervision of CHWs and nurses strengthened Task-based incentives expanded to include IMNCI activities (postnatal home visit, treating sick newborns and children and running women's group meetings). Drug depots established in villages to ensure regular supply of IMNCI drugs to CHWs CHWs (Anganwadi workers) made postnatal home visits on days 1, 3 and 7 to promote early and exclusive breastfeeding, delaying bathing, keeping the baby warm, cord care and care-seeking for illness. They assessed newborns for signs of illness at each visit and treated or referred them.	CHWs, nurses and physicians continued to provide their routine services	60 480 total births	Infant mortality HR 0.85 (0.77–0.94) Neonatal mortality beyond the first 24 h HR 0.86 (0.79–0.95) Optimal newborn care practices were significantly more common in the intervention clusters	Neonatal mortality RR 0.91 (0.80–1.03) Neonatal mortality significantly lower in intervention clusters in subgroup born at home (adjusted HR 0.80 (0.68–0.93) but not in subgroup born in a health facility 1.06 (0.91–1.23) (*P* for interaction = 0.001)

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Table 2. (Continued)

Study	Type of study	Intervention		Subjects	Results	Remarks
		Experimental group	*Control group*			
		They additionally visited low birth weight infants on days 14, 21 and 28. CHWs (accredited social health activists), nurses and physicians treated sick newborns and older children according to IMNCI guidelines. CHWs (accredited social health activists) ran women's group meetings in every village every 3 months				

Abbreviations: ANC, antenatal care; CHW, community health worker; HR, hazarad ratio; IMNCI, integrated management of newborn and childhood illness; KMC, kangaroo mother care; LHW, lady health worker; TBA, traditional birth attendant.

Table 3. Details of CHW characteristics and interventions

CHW characteristics and interventions	*Kumar et al., India*[96]	*Baqui et al., Bangladesh*[94,99]	*Darmstadt et al., Bangladesh*[102,103]	*Bhutta et al., Pakistan*[101]	*Bhandari et al., India*[100]
Level of education	12 years	—	—	8 Years formal schooling	—
Paid/unpaid	US$ 30–40 per month	—	—	Transport cost	Incentives for postnatal home visits, treating sick newborns and children, and running women's group meetings
CHW: population ratio	1:1000	1:4000	1:4000	1:1000–1500	1:1000
Duration of training	7 Days	6 Weeks	36 Days	5 Days LHW, 3 Days TBA	8 Days
Provision of equipment and drugs	Yes	No	No	No	Yes
Duration of intervention	16 Months	30 Months	24 Months	36 Months	14 Months
Birth and newborn-care preparedness	Yes	Yes	Yes	Yes	Yes
Provision of ANC	Yes	Yes	Yes	Yes	No
TBA training	No	Yes	Yes	Yes	Yes
Postnatal visits	Yes	Yes	Yes	Yes	Yes
Promotion of breastfeeding	Yes	Yes	Yes	Yes	Yes
Neonatal case management	No	Yes	Yes	No	Yes
Newborn resuscitation	No	No	No	No	No
Cost per neonatal death averted	-	US$ 2995	-	-	-
Population	104 123	480 000	292 000	318 226	1 100 000
Control group neonatal mortality rate/ 1000 live births	84.2	48	24.8	51.3	32.4

Abbreviations: ANC, antenatal care; CHW, community health worker; TBA, traditional birth attendant; '-', no information.

Table 4. Training and supervision of CHWs

Study	*Training of the health worker*	*Supervision of the health worker*
Kumar *et al.*, India[96]	CHWs (saksham sahayak) Combination of classroom-based and apprenticeship-based field training Over 7 days On knowledge, attitudes and practices related to essential newborn care within the community, behavior change management and trust building After training, suitable candidates closely mentored and supervised by a regional program supervisor ($n=4$) responsible for 6–7 saksham sahayaks, for an additional week before final selection made	Regional program supervisors had daily meetings with their team to discuss the work plan, progress, challenges and lessons learned Monthly program meetings took place in which all four regional teams came together to discuss experiences Performance assessment of saksham sahayaks by feedback from community members, spot checks by their supervisors during home visits and community meetings to assess their level of community engagement, and monitoring by the supervisors of whether targets for home visits and community meetings were being met
Baqui *et al.*, Bangladesh[94,99]	CHWs 6 Weeks of hands-on supervised training in a tertiary-care hospital and in households Training included skills development for behavior-change communication, provision of essential newborn care, clinical assessment of neonates and management of sick neonates with an algorithm adapted from the IMCI materials	Refresher training sessions for management of maternal and newborn complications were provided for government health workers in all three study arms
Darmstadt *et al.*, Bangladesh[102,103]	CHWs: Trained for 36 days on pregnancy surveillance, counseling and negotiation skills, essential newborn care, neonatal illness surveillance and management of illness based on a clinical algorithm adapted from IMCI materials TBAs: 2-Day orientation session on the aims and activities of the project, essential newborn care practices, and indications for referral of newborns and mothers	After initial training and evaluation, routine monitoring and refresher training were provided each fortnight
Bhutta *et al.*, Pakistan[101]	Standard LHW training takes 18 months, including 3 months of lectures In the intervention group: Addition of an extra day every 3 months (six extra days). Additional curriculum (for intervention village clusters): Promotion of adequate maternal nutrition and rest Early breastfeeding (within the first hour) and colostrum administration (avoidance of prelacteal feeds) Thermoregulation Home care of low birth weight infants Treatment of neonatal pneumonia with oral trimethoprim-sulphamethoxazole Recognizing sick newborns and danger signs Training in group counseling and communication strategies TBAs: 3-Day voluntary training program in basic newborn care	Standard curriculum (all village clusters): Promotion of ANC Iron and folate use in pregnancy Immediate newborn care Cord care (cleaning and avoiding the use of traditional materials, such as ash and lead powder) Promotion of exclusive breastfeeding monthly refresher sessions of 1 day each
Bhandari *et al.*, India[100]	Anganwadi workers (village-based child development and nutrition workers) and their supervisors, accredited social health activists (village-based health workers), and auxiliary nurse-midwives were trained with the 8-day IMNCI Basic Health Worker Course Government sector physicians involved in child care were trained with the 11-day IMNCI course for physicians Medically qualified private providers practicing in the intervention areas were offered participation in a single session of 6h adapted from the IMNCI course for physicians Private practitioners who were not medically qualified were also invited for orientation sessions that took place on two consecutive days for about 3 h TBAs in the intervention areas were invited for a 4-h orientation on clean delivery, cord care and newborn care	Trainers subsequently visited trainees at their place of work to review their performance, overcome challenges to implementation, and support the use of skills learned

Abbreviations: ANC, antenatal care; CHW, community health worker; IMCI, integrated management of childhood illness; IMNCI, integrated management of newborn and childhood illness; LHW, lady health worker; TBA, traditional birth attendant.

In the absence of bias, because of the sampling variability, the graph takes the form of an inverted funnel. In the presence of bias, the corner of the funnel is distorted or missing. Formal statistical tests for funnel plot asymmetry, namely the Begg's and Egger's methods, were also conducted with the user-written 'metabias' command in STATA (version 9.2) software.[15,16] Pooled estimates (relative risk (RR) with 95% confidence intervals (CIs)) of the evaluated outcome measures were calculated by the generic inverse variance method by the user-written 'metan' command[15,17] in STATA (version 9.2) software. The natural logarithm converted values of the individual trial RRs, and their standard errors were used for computing the pooled estimates as

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Table 5. Details of risk of bias assessment for individual trials

Bias	*Author's judgment*	*Support for judgment*
Kumar et al., India[96]		
Random sequence generation (selection bias)	Low risk	The 39 cluster units were allocated randomly to the three study groups by stratified cluster randomization, yielding three allocation sequences of 13 clusters each
Allocation concealment (selection bias)	Low risk	Randomization was carried out at Johns Hopkins University using STATA 7.0
Blinding of participants and personnel (performance bias)	Low risk	Blinding not possible with this type of intervention
Blinding of outcome assessment (detection bias)	Low risk	Evaluation system was independent of program implementation, and standard procedures were established to guide evaluation team recruitment, training and supervision, and to preserve separation from the program
Incomplete outcome data (attrition bias)	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	Study registered at clinicaltrials.gov, no. NCT00198653
Other bias	Low risk	Funded by the United States Agency for International Development (USAID) (Delhi) and Save the Children Saving Newborn Lives program
Baqui et al., Bangladesh[94,99]		
Random sequence generation (selection bias)	Low risk	Twenty-four clusters were randomly assigned to one of two intervention arms (home care or community care) or to the comparison arm with computer-generated pseudo-random number sequence without stratification or matching
Allocation concealment (selection bias)	Low risk	Computer-generated randomization was implemented by a study investigator who had no role in the implementation of the study
Blinding of participants and personnel (performance bias)	Low risk	Blinding was not possible due to the type of intervention
Blinding of outcome assessment (detection bias)	Low risk	Data collectors, supervisors and researchers had no role in implementation of the intervention
Incomplete outcome data (attrition bias)	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	Study is registered with ClinicalTrials.gov, no. 00198705
Other bias	Low risk	Funding was provided by USAID and the Save the Children Saving Newborn Lives Program with a grant from the Bill & Melinda Gates Foundation
Darmstadt et al., Bangladesh[102,103]		
Random sequence generation (selection bias)	Unclear risk	Twelve rural unions, excluding a central urban union, were randomly allocated to either comparison or intervention arm using computer-generated pseudo-random number sequence without stratification or matching. Areas were assigned randomly to achieve geographic balance of villages, as well as cluster and birth cohort size and mortality rate. Omission of the central urban union appears justified because of proximity to referral hospital, however, omission of stratification and matching is a deviation from protocol
Allocation concealment (selection bias)	Low risk	Computer-generated randomization implemented by study investigator with no role in implementation
Blinding of participants and personnel (performance bias)	Low risk	Blinding not possible with this type of intervention
Blinding of outcome assessment (detection bias)	Low risk	CHWs provided record of every newborn in intervention clusters, but not comparison ones. Therefore, field workers ascertained and recorded outcome of all reported pregnancies in all communities, and records were compared with those of the CHWs.
Incomplete outcome data (attrition bias)	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	Protocol and CONSORT checklist available as supporting information
Other bias	Low risk	Funding from Wellcome Trust and USAID. Support for data analysis and manuscript preparation provided by Save the Children Saving Newborn Lives program
Bhutta et al., Pakistan[101]		
Random sequence generation (selection bias)	Low risk	Restricted, stratified sampling was used to allocate 20 clusters to intervention and control groups. Three strata were identified on the basis of size and the number of LHWs per 1000. Researchers identified 126 random allocations that resulted in similar population sizes in the two groups and, for example, similar numbers of live births and neonatal mortality. One scheme was selected from this list using a computer-generated random number
Allocation concealment (selection bias)	Low risk	As above
Blinding of participants and personnel (performance bias)	Low risk	Blinding not possible with this type of intervention
Blinding of outcome assessment (detection bias)	Low risk	Data collectors and their supervisors were masked to cluster allocation, but data analysts were not
Incomplete outcome data (attrition bias)	Low risk	Attrition of pregnancies reported as minimal, although attrition of neonates not reported
Selective reporting (reporting bias)	Low risk	Registered with International Clinical Trials Registry, no. ISRCTN16247511
Other bias	Low risk	Funded by grants from the World Health Organization and the Save the Children Saving Newborn Lives program

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Table 5. (Continued)

Bias	*Author's judgment*	*Support for judgment*
Bhandari et al., India[100]		
Random sequence generation (selection bias)	Low risk	An independent epidemiologist generated 10 stratified randomization schemes to allocate the clusters to intervention or control groups. Three of these were excluded because of large differences in important indicators. One of the seven remaining allocation schemes was selected by a computer-generated random number
Allocation concealment (selection bias)	Low risk	As above
Blinding of participants and personnel (performance bias)	Low risk	Blinding not possible with this type of intervention
Blinding of outcome assessment (detection bias)	Low risk	Study-field workers were not involved with implementation. The surveillance team was not told the intervention status of the community they visited
Incomplete outcome data (attrition bias)	Low risk	Attrition was 0.37%
Selective reporting (reporting bias)	Low risk	Clinical trials no. NCT00474981; Clinical Trials Registry India no. CTRI/2009/091/000715
Other bias	Low risk	Funded by the World Health Organization (Geneva) (through an umbrella grant from USAID), the United Nations Children's Fund (New Delhi) and the Research Council of Norway

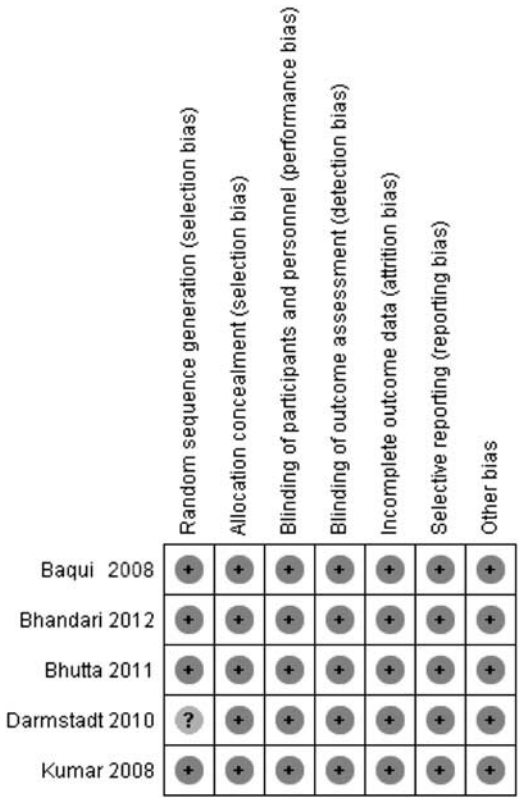

Figure 2. Graphical summary of risk of bias assessment in included trials.

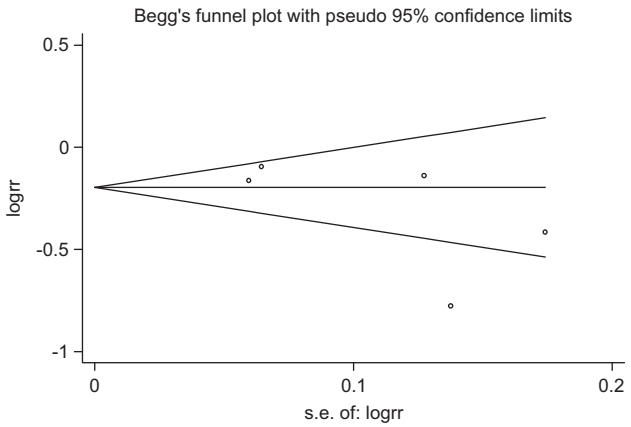

Figure 3. Funnel plot for detection of publication bias. s.e., standard error.

recommended.[17] These pooled estimates were expressed in an exponential form. This program also computes formal tests of heterogeneity, namely, the statistic Cochran Q and I^2 (variation in pooled estimate attributable to heterogeneity).

One option for analyzing the data was to calculate the change in mortality rates (from baseline to the end of the intervention or observation period) in the intervention and control groups separately, and then construct RRs and 95% CIs for the difference in the change between the two groups. The other option was to calculate the RR and 95% CIs on the basis of a comparison of mortality rates at the end of the intervention or observation period in the intervention and control groups. We utilized the second option because baseline and/or change data were not available for all included trials. For computing the summary RR, we required individual trial RR and 95% CI or standard error. In the case of cluster-randomized trials citing cluster-adjusted values, we used the reported values. For trials reporting only cluster-specific data, we used a random-effects version of the STATA procedure XTLOGIT to derive an odds ratio, allowing for the cluster design. Random effects were fitted for each village, and the odds ratio was used to give an estimate of RR in the rare outcomes we were modeling.

The outcome variables were pooled using both fixed-effects and random-effects model assumptions. No comprehensive rules exist on when to use these models; debate continues in the statistical community. The underlying assumption for the fixed-effects model is that each trial estimates the same true population value for the effect of interest, and thus the differences between observed results of trials can be accounted for fully by sampling variation. Random-effects models assume that a distribution of population effects exists and is generated by a distribution of possible trial effect situations. Thus, outcomes of trials may differ both because of sampling variation and true differences in effects.

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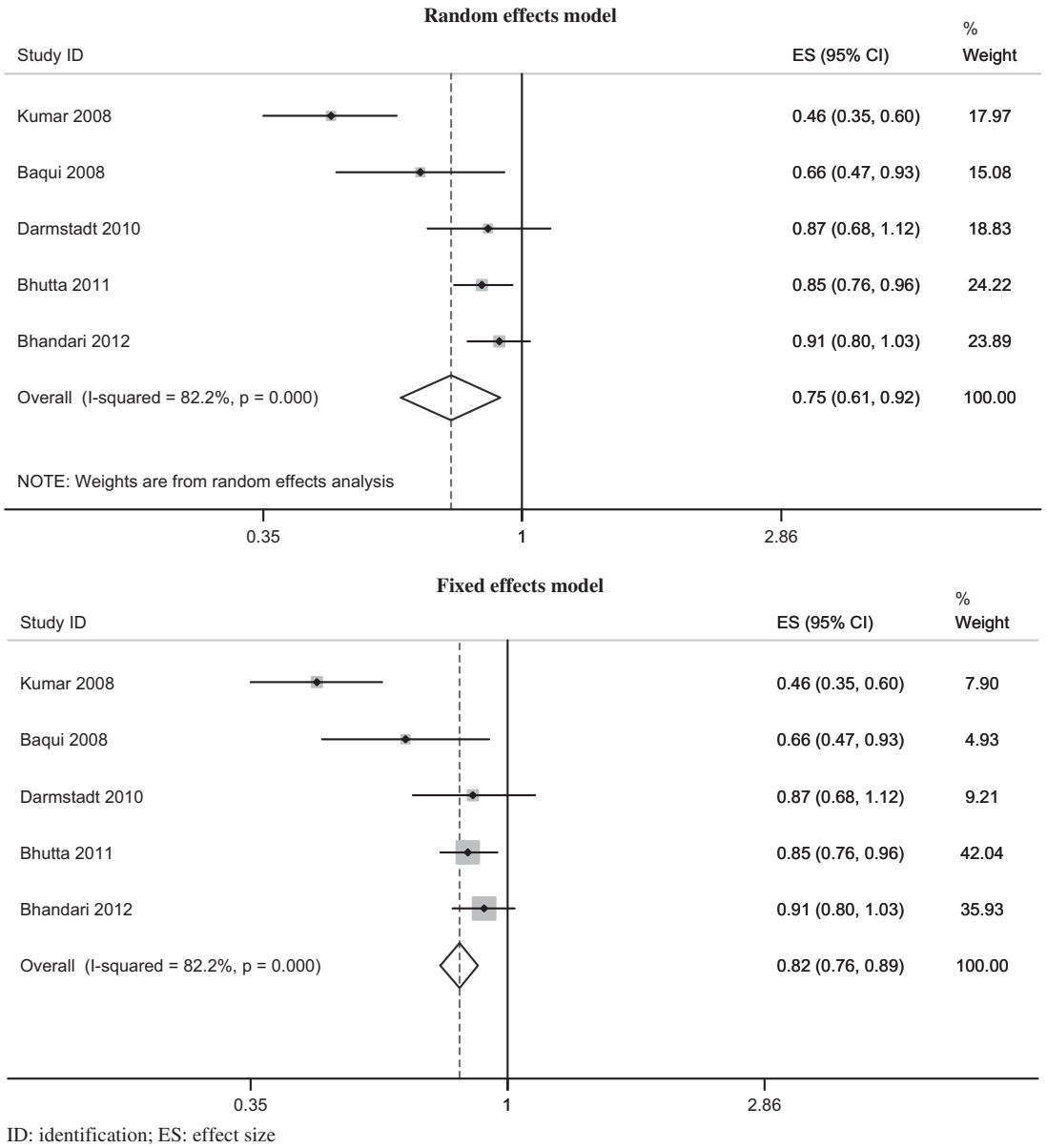

ID: identification; ES: effect size

Figure 4. Forest plot for relative risk of neonatal mortality.

Both random- and fixed-effects models can be appropriately applied to pooling of data and also for evaluating the sensitivity of results to differing model assumptions. The random-effects model is generally preferred in the presence of significant heterogeneity.

Sensitivity and subgroup analyses

Sensitivity and sub-group analyses were performed only for the primary outcome, all-cause neonatal mortality, to explore heterogeneity and also as a hypothesis-generating exercise. The following pre-specified sensitivity and subgroup analyses were performed: (i) preventive interventions versus preventive and curative interventions (antibiotics for neonatal sepsis) to examine the potential effect of adding curative treatment; (ii) high (>50 neonatal deaths per 1000 live births) versus low ($\leqslant 50$ neonatal deaths per 1000 live births) baseline neonatal mortality (derived from the control group) to examine the possibility of a greater benefit in populations with higher baseline mortality; (iii) proportion of neonates receiving a postnatal visit ($<50\%$ versus $\geqslant 50\%$) to examine the effect of the extent of coverage on mortality; and (iv) various elements of risk of bias assessment (low risk versus unclear and high risk). The contribution of these variables to heterogeneity was also explored by meta-regression using the 'metareg' command in STATA (version 9.2) software with the restricted maximum likelihood option.[18]

RESULTS

Trial flow

A total of 85 potentially eligible references were identified.[19–103] Among these, 77 references were excluded[19–93,95,97] (Figure 1). The reasons for excluding these references are detailed in Table 1. The remaining eight references, which pertained to five trials, were included in the review.[94,96,98–103]

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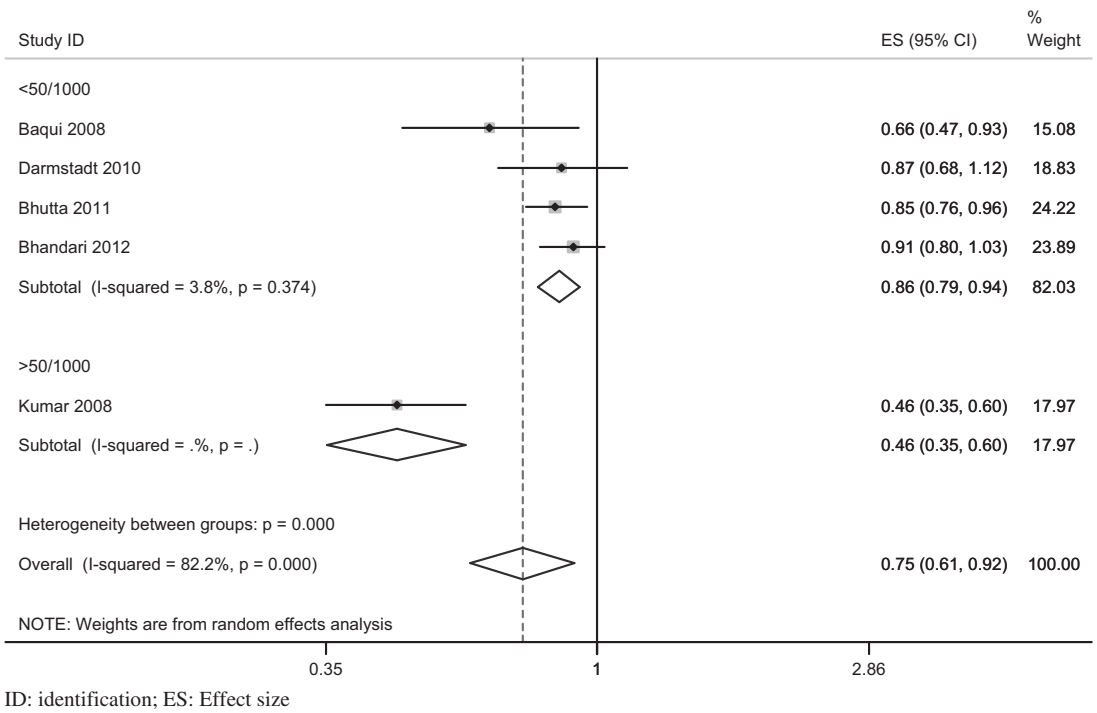
Table 6. Sensitivity and subgroup analyses for the RR of neonatal mortality[a]

Stratification variable	*No. of trials*	*Random-effects model RR (95% CI);* P-*value*	*Fixed-effects model RR (95% CI);* P-*value*	*Tests for heterogeneity* I^2*(%);* Q (P-*value)*	P-*value for heterogeneity in subgroups*
Overall	5	0.75 (0.61, 0.92); 0.005	0.82 (0.76, 0.89); < 0.001	82.2; 22.42 (0.000)	NA
Baseline neonatal mortality rate (per 1000 live births):					
< 50/1000	4	0.86 (0.79, 0.94); < 0.001	0.86 (0.80, 0.93); < 0.001	3.8; 19.3 (0.374)	< 0.001
> 50/1000	1	0.46 (0.35, 0.60)	0.46 (0.35, 0.60)		
Type of care					
Preventive	3	0.71 (0.49, 1.01); 0.056	0.79 (0.71, 0.87); < 0.001	88.60; 17.54 (< 0.001)	0.17
Preventive and curative (antibiotics)	2	0.81 (0.60, 1.09); 0.168	0.88 (0.78, 0.99); 0.028	66.6; 2.99 (0.084)	
Coverage (%) of home visits					
< 50%	1	0.85 (0.76, 0.96)	0.85 (0.76, 0.96); 0.006	NA	0.45
⩾ 50%	4	0.71 (0.52, 0.97); 0.032	0.80 (0.73, 0.88); 0.000	86.3; 21.85 (0.000)	

Abbreviations: NA, not applicable; RR, relative risk. [a]The pre-specified sensitivity analyses for the various elements of risk of bias could not be performed because, except for an unclear risk of selection bias in one trial, all studies were assessed to be at low risk of bias for all elements.



ID: identification; ES: Effect size

Figure 5. Forest plot for relative risk of neonatal mortality stratified by baseline neonatal mortality rate (random effects model).

Trial characteristics

Table 2 summarizes the characteristics of included trials. All five trials were conducted in South Asia, and all were cluster-randomized trials, which provided cluster-adjusted mortality data.

Intervention package

Table 3 summarizes the CHW characteristics and intervention package used in the included trials. Substantial heterogeneity was evident for these aspects.

Training and supervision of health workers

Table 4 summarizes the duration and content of training provided to the CHWs delivering the intervention in the respective trials. Substantial heterogeneity was evident for these aspects.

Risk of bias assessment

The risk of bias assessment for these trials is detailed in Table 5 and depicted graphically in Figure 2. Except for an unclear risk of selection bias in one trial, all studies were assessed to be at low risk of bias for all elements.

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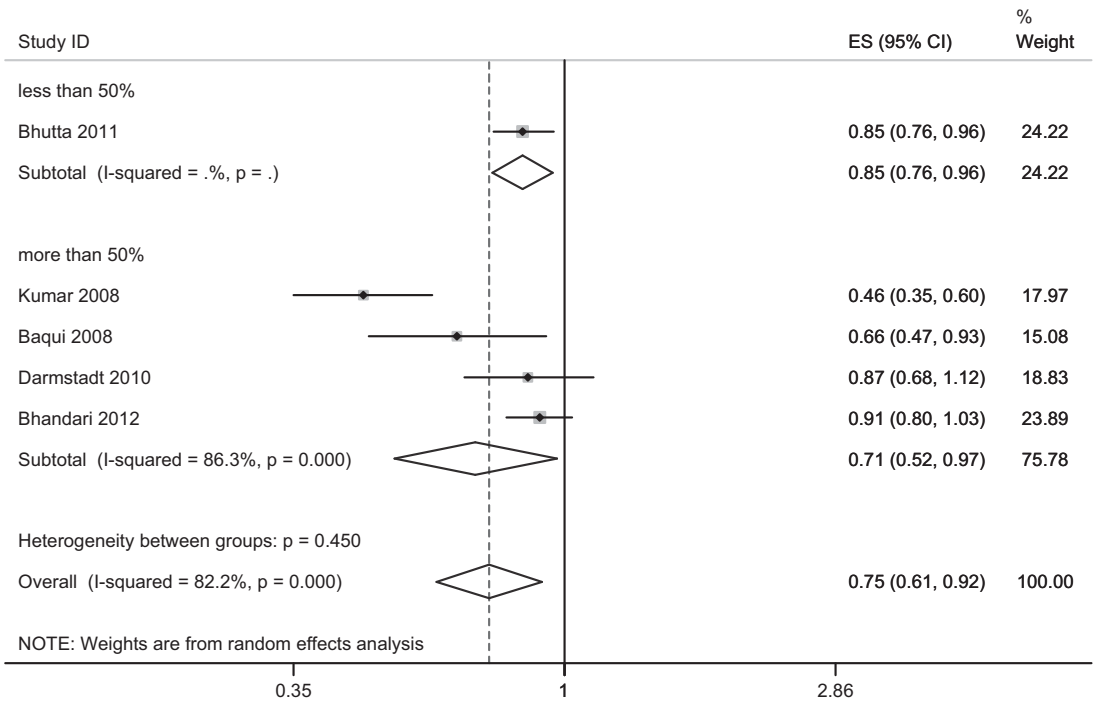
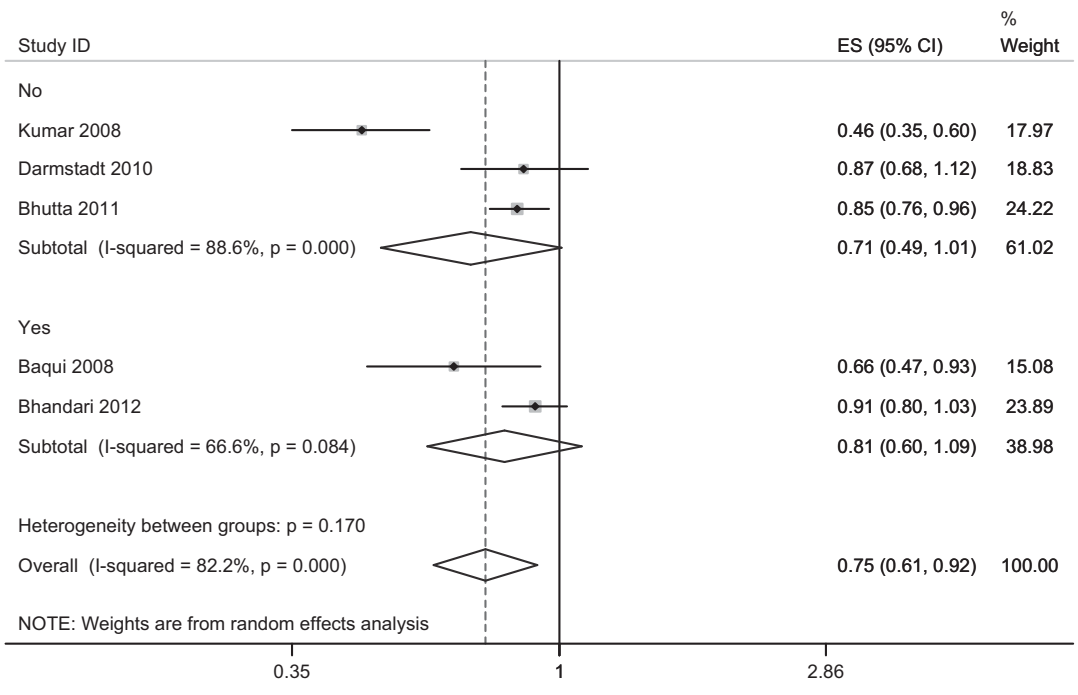


ID: identification; ES: effect size

Figure 6. Forest plot for relative risk of neonatal mortality stratified by coverage of home visits (random effects model).



ID: identification; ES: effect size

Figure 7. Forest plot for relative risk of neonatal mortality stratified by presence of curative intervention (antibiotics) for sepsis (random effects model).

Quantitative data synthesis

All five trials provided neonatal mortality data,[94,96,98–103] and three trials provided perinatal mortality data.[96,100,101] One trial provided infant mortality data,[100] and one trial provided cause-specific mortality data.[102]

The Shivgarh (India) trial[96] had two very similar intervention groups, with home-based essential newborn care as the core intervention. One intervention group additionally used a technology called 'Thermospot' to help caregivers decide if

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Table 7. Program coverage and RR of neonatal mortality in individual trials

Study	*Program coverage (%)*	*Parameter*	*RR of neonatal mortality*
Kumar *et al.*, India[96]	67.9	Postnatal visit (day 0)	0.50 (0.36–0.69)
Baqui *et al.*, Bangladesh[94,99]	62.0	Postnatal visit (days 0 and 1)	0.66 (0.47–0.93)
Darmstadt *et al.*, Bangladesh[102,103]	69.0	Postnatal visit (days 0 and 1)	0.86 (0.68–1.09)
Bhutta *et al.*, Pakistan[101]	63.0	Group session attendance	0.85 (0.76–0.96)
	34.0	Postnatal visit within 72 h	
Bhandari *et al.*, India[100]	45.6	Women's group meeting in last 3 months	0.91 (0.80–1.03)
	56.6	Postnatal visit (days 0 and 1)	

Abbreviation: RR, relative risk.

Table 8. Sepsis treatment in relation to RR of neonatal mortality in individual trials[a]

Study	*Antibiotics*		*RR of neonatal mortality*
	Oral	*Intravenous*	
Kumar *et al.*, India[96]	–	–	0.50 (0.36–0.69)
Baqui *et al.*, Bangladesh[94,99]	–	+	0.66 (0.47–0.93)
Darmstadt *et al.*, Bangladesh[102,103]	–	–	0.86 (0.68–1.09)
Bhutta *et al.*, Pakistan[101]	–	–	0.85 (0.76–0.96)
Bhandari *et al.*, India[100]	+	–	0.91 (0.80–1.03)

Abbreviations: RR, relative risk; '–', not included; '+', included. [a]No trials provided asphyxia treatment.

Table 9. Meta-regression analysis for neonatal mortality (univariate)[a]

Trial characteristic	*Univariate analysis Ratio of RRs (95% CI); I^2*	P
Baseline neonatal mortality rate $< 50/1000$ or $\geqslant 50/1000$ live births	0.99 (0.97, 1.00); 0.551	0.065
Type of neonatal care Preventive versus preventive and curative (antibiotics)	1.12 (0.44, 2.83); 0.854	0.726
Coverage of neonatal home visits $\geqslant 50\%$ versus $< 50\%$	0.99 (0.97, 1.02); 0.854	0.507

Abbreviation: RR, relative risk; [a]The pre-specified meta-regression analyses for the various elements of risk of bias could not be performed because, except for an unclear risk of selection bias in one trial, all studies were assessed to be at low risk of bias for all elements.

their newborn's temperature was low. We therefore excluded the intervention arm with 'Thermospot' and used the data provided by the authors comparing only the home-based neonatal care group with the control group.

The Sylhet (Bangladesh) trial[99] also had two intervention arms, one called 'home care' and the other 'community care'. We excluded the 'community care' arm from the analysis because the interventions in this arm did not meet the inclusion criteria for this review.

Neonatal mortality

All five trials provided neonatal mortality data.[94,96,98–103] The funnel plot (Figure 3) appeared symmetrical, and there was no evidence of significant ($P = 0.204$) bias with the Egger's (weighted regression) method. The intervention was associated with a reduced risk of mortality during the neonatal period; the pooled relative risk was 0.75 (95% CI 0.61 to 0.92, $P = 0.003$; $I^2 = 82.2\%$, $P < 0.001$) by random effects model (Figure 4) and 0.82 (95% CI 0.76 to 0.89, $P < 0.001$) by fixed-effects model.

On performing pre-specified sensitivity and subgroup analyses (Table 6) significant heterogeneity was suggested only with higher baseline neonatal mortality. Trials with a baseline rate of more than 50/1000 live births had a significantly greater reduction in neonatal mortality (RR 0.46; 95% CI 0.35 to 0.60; $P < 0.001$), compared with trials with a baseline rate $< 50/1000$ live births (RR 0.86; 95% CI 0.79 to 0.94, $P < 0.001$; heterogeneity $P < 0.001$) (Figure 5). There was no evidence of significant heterogeneity in the other two pre-specified subgroups, namely, the coverage of home visits (Figure 6) and the type of care (Figure 7). The details of program coverage and curative treatment offered in various trials are depicted in Tables 7 and 8, respectively. The pre-specified sensitivity analyses for bias could not be performed because, except for an unclear risk of selection bias in one trial, all studies were assessed to be at low risk of bias for all elements.

On performing univariate meta-regression (Table 9) analyses, none of the variables emerged as significant predictors of heterogeneity. However, baseline neonatal mortality approached conventional statistical significance ($P = 0.065$).

We conducted a *post hoc* sensitivity analysis by combining evidence from three[23–25,95,97] non-randomized or quasi-randomized trials with concurrent control groups (Figure 8). There was no evidence of significant heterogeneity ($P = 0.192$) for the comparison between randomized and non-randomized trials. With the random effects model, the RR for randomized trials was 0.75 (95% CI 0.61 to 0.92; $I^2 = 82.2\%$) and for non-randomized trials was 0.67 (95% CI 0.40 to 1.13; $I^2 = 89.5\%$). The overall effect size with inclusion of all eight trials was 0.72 (95% CI 0.60 to 0.87; $I^2 = 83.8\%$).

Infant mortality

Data were available from one trial that showed a significant decline in infant mortality with RR of 0.85 (95% CI 0.77 to 0.94).[100]

Perinatal mortality rate. Data were pooled from three trials.[96,100,101] There was evidence of a reduced risk of perinatal mortality; the pooled RR was 0.78 (95% CI 0.64 to 0.94, $P = 0.009$; $I^2 = 79.6\%$, $P = 0.007$) by random-effects model (Figure 9). A similar result was obtained with the fixed-effects model.

Cause-specific mortality. Only one trial provided cause-specific mortality data in neonates in the form of rates in each comparison group without cluster-adjustment RRs.[102]

Summary of findings

The GRADE summary of findings is shown in Table 10. The quality of evidence was graded as high for neonatal and perinatal mortality, and moderate for infant mortality.

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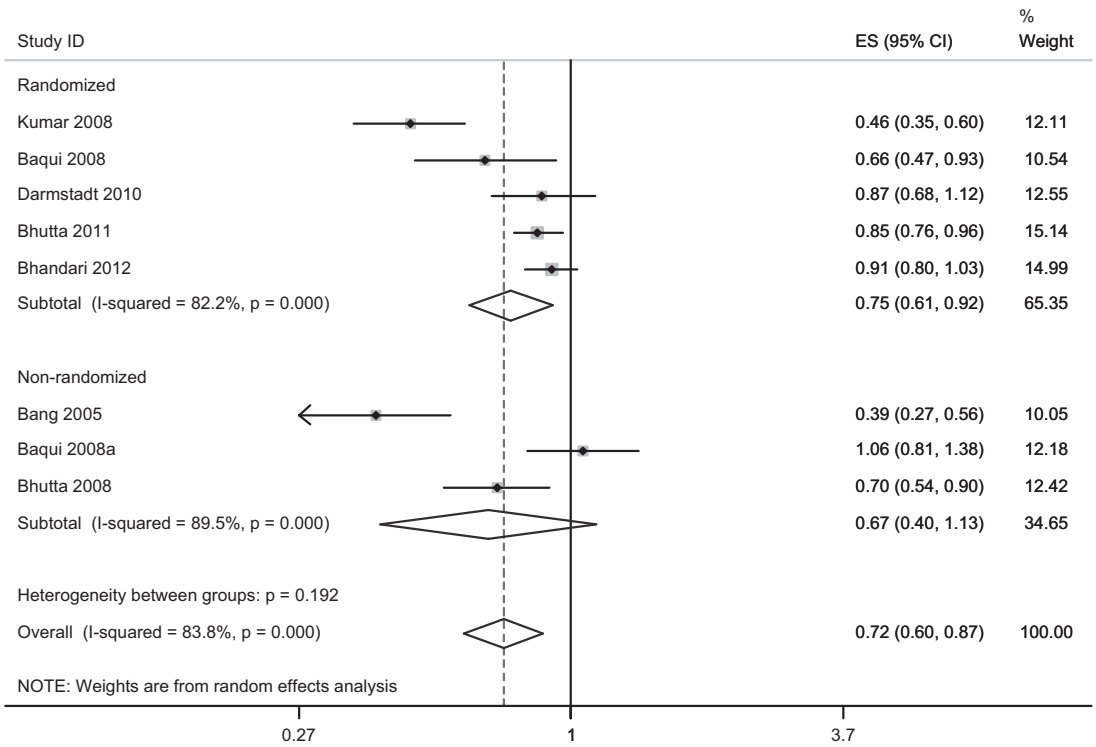

ID: identification; ES: effect size
Note: The relevant references for randomized trials are depicted in **Table 2**. The references for non-randomized trials are: Bang 2005;[67] Baqui 2008a;[97] and Bhutta 2008.[95]

Figure 8. Forest plot for relative risk of neonatal mortality stratified by randomized and three additional non-randomized trials (random effects model).

DISCUSSION

This systematic review of five cluster-randomized trials indicates that home-based neonatal care provided by CHWs is associated with significant neonatal mortality reduction in resource-limited settings with poor access to health facility-based care (high-quality evidence). Data from three trials indicated a reduction in the perinatal mortality rate (high-quality evidence). There was evidence of a reduction in infant mortality in the only trial providing this information. The baseline neonatal mortality rate emerged as a potential predictor of the neonatal mortality effect.

Strengths and limitations of analyses

This updated systematic review incorporated relevant subgroup and meta-regression analyses, and there was no evidence of publication bias. All cluster-randomized trials were appropriately combined by design effect correction for mortality outcomes. This review represents the synthesis of the most contemporary evidence for translating into public health policy as all the included trials were published within the past 5 years.

Some limitations merit consideration. First, data on perinatal mortality was limited to three trials, whereas only one trial reported infant mortality and cause-specific mortality. Second, all trials were conducted in South Asia, which limits generalizing to similar settings in other continents, particularly sub-Saharan Africa. Trials evaluating community-based interventions without a specific element of home-based neonatal care delivered by a CHW were excluded because such data had different programmatic implications from the policy under consideration.

The findings of this systematic review are in conformity with two earlier reviews on this subject, which were not restricted to randomized trials. We included only randomized controlled trials to aim for the highest quality of evidence. However, the main findings remained stable in a *post hoc* sensitivity analysis combining the evidence from three additional non-randomized or quasi-randomized trials with concurrent controls (Figure 8).

As noted earlier, no comprehensive rules exist for when to use random effects or fixed effects models for meta-analysis. Fixed-effects analysis is appropriate if there is a reasonable assumption that the trials are estimating the same underlying treatment effect (that is, they are similar enough in their populations, interventions and methods to make this plausible). Random-effects analysis assumes a distribution of effect sizes, and it estimates the center of that distribution and the uncertainty around it. It is more appropriate for situations where there are differences in design, population or intervention between included trials that may be sufficient to affect their treatment effects. We preferred the random-effects model because of significant contextual differences in included trials and documentation of statistical heterogeneity ($I^2 > 50\%$) for neonatal mortality. However, the estimates from the random- and fixed-effects models were in broad conformity (Table 6).

Subgroup analyses and meta-regression suggested a greater survival benefit in settings with higher baseline neonatal mortality rates. Home-based neonatal care interventions are primarily effective in reducing neonatal sepsis and mild asphyxia. As the neonatal mortality rate decreases in an area, the cause-specific mortality due to sepsis decreases and asphyxia probably remains unchanged, whereas the proportion of mortality due to preterm births (as well as the absolute number) increases. In the Mirzapur trial[102] (baseline neonatal mortality rate 27.9/1000 live births), nearly 60% of deaths were due to birth asphyxia or prematurity; the program had limitations in reaching households at critical times (that is, during labor, childbirth and immediately after

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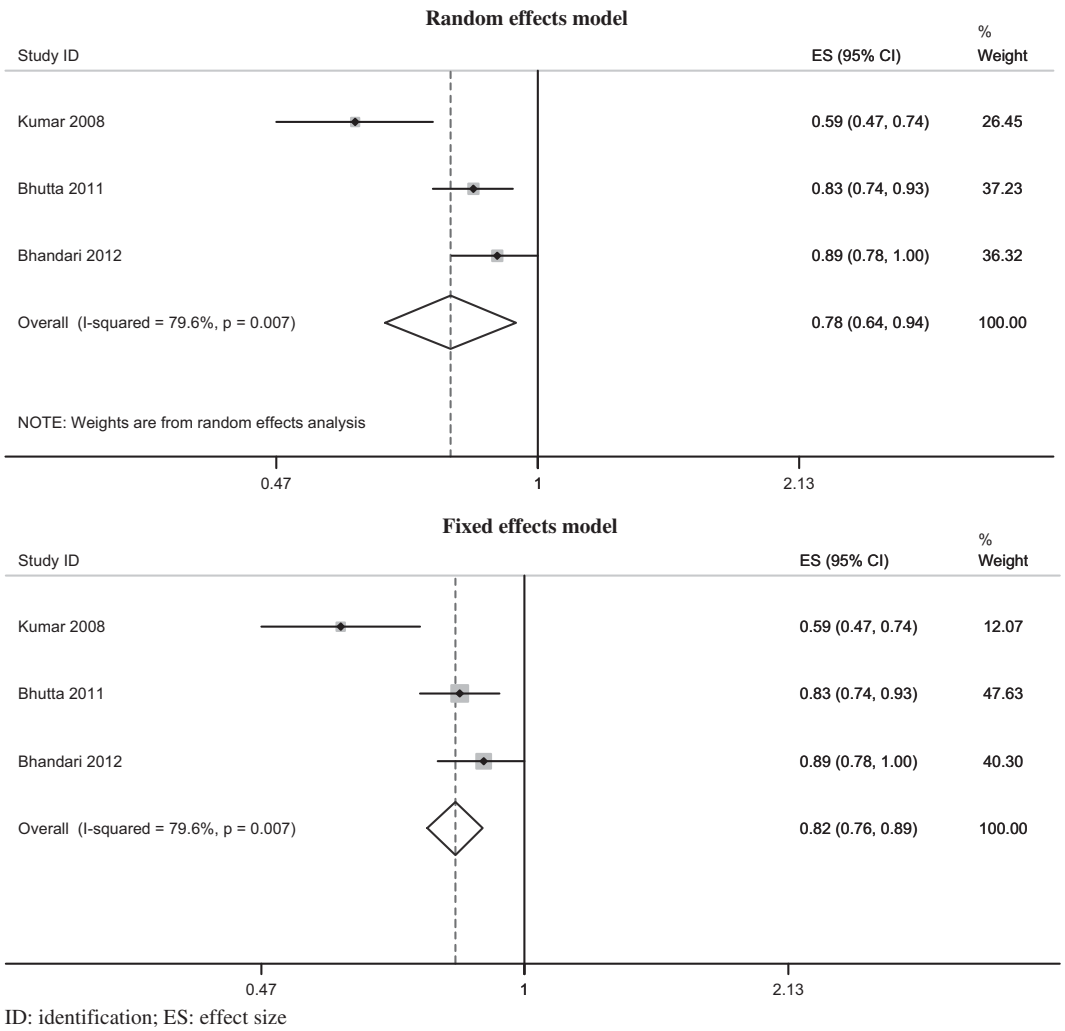

ID: identification; ES: effect size

Figure 9. Forest plot for relative risk of perinatal mortality.

delivery) to address these conditions, whereas the CHWs lacked the necessary tools and skills to effectively attend to them. Unfortunately, the other trials did not provide cause-specific mortality to explore this possibility. In settings with lower baseline neonatal mortality rates, there may be a greater role of community mobilization and effective referral to facility-based care to address these causes of death.

Program coverage did not emerge as a significant predictor of the decrease in the neonatal mortality effect. However, program coverage was defined by the number of live births receiving a postnatal home visit in the first 48 to 72 h. Hence, it does not encapsulate the whole construct of the intervention that the trials had employed; many trials had excellent community mobilization programs in spite of low coverage of postnatal visits.[101] Furthermore, with a sample size of five trials, the analysis had limited power to detect a positive predictor.

The addition of a curative component (antibiotics for neonatal sepsis) to the intervention did not emerge as a significant predictor of neonatal mortality. No included trial provided for treatment of birth asphyxia by CHWs as part of the home-based package of neonatal care, and it is unclear whether providing training and equipment to CHWs reduces mortality due to asphyxia.[68,104] As CHWs are likely to encounter asphyxia only sporadically, continued training for maintenance of skills to manage it may be challenging.

In all the trials under review, the intervention was delivered as a package comprising three components, namely, home visits during pregnancy (four trials), home-based neonatal care (all trials) and community mobilization efforts (four trials). The reduction in neonatal and perinatal mortality cannot therefore be solely ascribed to the home-based neonatal care component. However, from a programmatic perspective this is not crucial; in practice antenatal visits would be required to establish contact with pregnant women for postnatal visits, and health workers can also perform some community mobilization services.

Implications for policy

Home-based neonatal care is associated with reductions in neonatal and perinatal mortality in settings with high neonatal mortality rates and poor access to health facility-based care. The high-quality evidence in this review thus provides support for adopting a policy of home-based neonatal care provided by CHWs in such settings. Concrete recommendations cannot be made regarding the optimal timing of home visits and specific responsibilities of CHWs. However, data suggest that antenatal visits and home-based neonatal care within the first week of life should be an integral part of this intervention. Incorporating a component of community mobilization in addition to home-based neonatal care would be desirable. All the evidence pertains to

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Table 10. GRADE summary of findings

Home-based care by CHWs compared with no home-based care for neonates

Patient or population: neonates
Settings: resource-limited settings with poor access to health facility-based care
Intervention: home-based care by CHWs
Comparison: no home-based care

Outcomes	*Illustrative comparative risks[a] (95% CI)*		*Relative effect (95% CI)*	*No of participants (studies)*	*Quality of the evidence (GRADE)*	*Comments*
	Assumed risk No home-based care	Corresponding risk Home-based care by CHWs				
Neonatal mortality All-cause neonatal deaths	Low 25 per 1000[c]	19 per 1000 (15–23)[c]	RR 0.75 (0.61–0.92)	101 655 (five studies)	⊕⊕⊕⊕ High[b]	Data analyzed as cluster-adjusted risk ratios on intention-to-treat basis. The risk ratios were pooled by generic inverse variance by random-effects model.
	Moderate 45 per 1000[c]	34 per 1000 (27–41)[c]				
	High 85 per 1000[c]	64 per 1000 (52–78)[c]				
Infant mortality All-cause infant deaths	Low 40 per 1000[c]	34 per 1000 (31–38)[c]	RR 0.85 (0.77–0.94)	60 480 (one study)	⊕⊕⊕⊖ Moderate[d]	Data analyzed as cluster-adjusted risk ratios on intention-to-treat basis.
	Moderate 70 per 1000[c]	60 per 1000 (54–66)[c]				
	High 100 per 1000[c]	85 per 1000 (77–94)[c]				
Perinatal mortality All-cause perinatal deaths	Low 60 per 1000	47 per 1000 (38–56)	RR 0.78 (0.64–0.94)	87 788 (three studies)	⊕⊕⊕⊕ High[e]	Data analyzed as cluster-adjusted risk ratios on intention-to-treat basis. The risk ratios were pooled by generic inverse variance by random effects model.
	Moderate 85 per 1000	66 per 1000 (54–80)				
	High 115 per 1000	90 per 1000 (74–108)				

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: we are very uncertain about the estimate.

Abbreviations: CHW, community health worker; RR, relative risk. [a]The basis for the assumed risk (for example, the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). [b]The evidence was not downgraded for inconsistency despite significant heterogeneity (I^2 82.2% and $P < 0.001$) because baseline neonatal mortality rate emerged as a significant predictor of heterogeneity and the observed heterogeneity was between a large and small effect (benefit) in the same direction. [c]The numbers represent the actual participants, whereas the risk ratios are cluster-adjusted estimates. [d]Estimates based on a single large trial; also the trial by Bhutta *et al.*[101] presents numbers of postnatal deaths but does not provide risk ratios for post-neonatal or infant deaths. [e]The evidence was not downgraded for inconsistency despite significant heterogeneity (I^2 79.6% and $P = 0.007$) because the observed heterogeneity was between a large and small effect (benefit) in the same direction.

South Asia; however, there are no obvious reasons to suspect different results in other regions with similar neonatal mortality rates and access to health care.

Implications for future research

The following gaps in evidence should be addressed as a priority to provide further directions for policy: (i) efficacy of the intervention package in similar settings in other regions, particularly sub-Saharan Africa; (ii) evaluating the benefit of adding treatment of sepsis and birth asphyxia; (iii) the effect of the intervention package on infant and cause-specific mortality; and (vi) operational research in pilot programs to evaluate coverage levels and quality, reasons for poor performance and possible interventions for improvement.

Concluding comments

Home-based neonatal care is associated with reductions in neonatal and perinatal mortality (high-quality evidence) in South Asian settings with high neonatal-mortality rates and poor access to health facility-based care. Adopting a policy of home-based neonatal care provided by CHWs is justified in such settings.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

SG prepared the protocol, applied the search strategy and retrieved articles. HPSS finalized the protocol and search strategy. Both authors extracted data, performed the statistical analysis and contributed to the drafting of the final version of the paper, and will act as joint guarantors.

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