A systematic review and narrative synthesis of antenatal interventions to improve maternal and neonatal health in Nepal

Miriam Toolan, MBBS; Katie Barnard, MA; Mary Lynch, BSc; Nashna Maharjan, MHPE; Meena Thapa, MD; Nisha Rai, MD; Tina Lavender, PhD; Michael Larkin, PhD; Deborah M. Caldwell, PhD; Christy Burden, MD; Dharma S. Manandhar, Hon FRCPCH; Abi Merriel, PhD

BACKGROUND: Maternal and neonatal mortality rates remain high in many economically underdeveloped countries, including Nepal, and good quality antenatal care can reduce adverse pregnancy outcomes. However, identifying how to best improve antenatal care can be challenging.

OBJECTIVE: To identify the interventions that have been investigated in the antenatal period in Nepal for maternal or neonatal benefit. We wanted to understand their scale, location, cost, and effectiveness.

STUDY DESIGN: Online bibliographic databases (Cochrane Central, MEDLINE, Embase, CINAHL Plus, British Nursing Index, PsycInfo, Allied and Complementary Medicine) and trial registries (ClinicalTrials.gov and the World Health Organization Clinical Trials Registry Platform) were searched from their inception till May 24, 2020. We included all studies reporting any maternal or neonatal outcome after an intervention in the antenatal period. We screened the studies and extracted the data in duplicate. A meta-analysis was not possible because of the heterogeneity of the interventions and outcomes, so we performed a narrative synthesis of the included studies.

RESULTS: A total of 25 studies met our inclusion criteria. These studies showed a variety of approaches toward improving antenatal care (eg, educational programs, incentive schemes, micronutrient supplementation) in different settings (home, community, or hospital-based) and with a wide variety of outcomes. Less than a quarter of the studies were randomized controlled trials, and many were single-site or reported only short-term outcomes. All studies reported having made a positive impact on antenatal care in some way, but only 3 provided a cost-benefit analysis to support implementation. None of these studies focused on the most remote communities in Nepal.

CONCLUSION: Our systematic review found good quality evidence that micronutrient supplementation and educational interventions can bring important clinical benefits. Iron and folic acid supplementation significantly reduces neonatal mortality and maternal anemia, whereas birth preparedness classes increase the uptake of antenatal and postnatal care, compliance with micronutrient supplementation, and awareness of the danger signs in pregnancy.

Key words: antenatal care, antenatal education, birth preparedness, cash incentive, female community health volunteers, global health, maternity incentive, maternal mortality, micronutrients, neonatal mortality, participatory learning, systematic review

Introduction
The United Nations’ Sustainable Development Goals (SDG) demand significant reductions in global maternal and neonatal mortality by 2030, with targets of no more than 70 maternal deaths per 100,000 deliveries and no more than 12 neonatal deaths per 1000 live births. Effective antenatal care can improve both maternal and neonatal outcomes, but its design and provision is complex.
South Asia reduced its maternal mortality ratio (MMR) by nearly 60% between 2000 and 2017, and Nepal’s efforts contributed to that success with a reduction by 79% (from 901 to 186 per 100,000) between 1990 and 2017. This is despite widespread poverty after the civil war (1996–2006), geographic challenges of mountainous regions, and extensive earthquake damage in 2015. However, if the SDG targets are to be met, the progress must be accelerated.

The improvements in maternal, neonatal, and child health (MNCH) in Nepal have often been attributed to the government’s commitment to make maternity care accessible to all. Their safe motherhood program includes the provision of free maternity services in government hospitals and involves the “Aama” maternity incentive scheme, which provides a small monetary incentive for giving birth in a facility with a skilled birth attendant (SBA) and giving attendance at 4 antenatal appointments. However, several community-based trials in the antenatal period have been conducted in South Asia since 1990, showing that antenatal interventions in this region can significantly improve MNCH outcomes, and these may have contributed to the advancements seen in Nepal. For example, in Uttar Pradesh, India, a community-based behavior-change intervention led to a 54% reduction in the neonatal mortality (NMR). In Pakistan, an intervention to provide outreach antenatal care through extra training for traditional birth attendants showed a 30% reduction in neonatal morbidity, although the effect on maternal mortality was less conclusive. In Makwanpur, Nepal, a participatory intervention with women’s groups led to a 29% reduction in the NMR and an 80% reduction in the MMR. Pharmacologic treatments in the antenatal period have also been shown to improve outcomes—the provision of low-dose aspirin in pregnancy has been shown to reduce the rates of preeclampsia, preterm birth, and fetal and neonatal death. Calcium supplementation has been shown to reduce the rates of preeclampsia and maternal mortality or serious morbidity. To date, there has been no comprehensive overview of antenatal interventions that have already been trialed in Nepal (and to what effect).

Our aim was to identify the antenatal interventions already trialed in Nepal and understand their scale, location, cost, and effectiveness. In doing so, we aimed to establish the interventions that have the greatest potential to improve maternal and neonatal outcomes within Nepal and in other comparable settings worldwide.

**Materials and Methods**

**Search strategy**

Online bibliographic databases (Cochrane Central, MEDLINE, Embase, CINAHL Plus, British Nursing Index, PsycInfo, Allied and Complementary Medicine) and trial registries (ClinicalTrials.gov and the World Health Organization Clinical Trials Registry Platform) were searched from inception till May 24, 2020. There were no language restrictions, and both free-text and subject headings were used. The free-text search terms used included “Nepal* and Antenatal*,” “Antepartum,” “Prenatal,” “Perinatal,” and “birth preparedness.” The full search strategy is available in Appendix A. The reference lists of all included articles were screened.

**Study selection**

We included all the studies reporting outcomes following an antenatal intervention in Nepal. The study participants were pregnant women and their partners and families. We considered studies of all designs but excluded those where only abstracts, protocols, or trial registrations were available or where the results were not published.

The protocols for included studies were covered as they provided a methodological background. We included the articles describing interventions in all settings, and no restrictions were placed on the year of study or the length of follow-up. Multicountry studies were included as long as it was possible to extract the Nepali data. The eligibility of the studies was assessed by at least 2 of the authors (K.B., M.T., M.L., N.M., A.M.), with conflicts resolved by discussion.

**Data extraction**

We used a data extraction form to collect the data in duplicate from the included studies. The data extracted included the intervention, outcomes, aims, study design, information about participants, location and duration of study, and any cost-effectiveness analysis. Any discrepancies were resolved by discussion.

**Quality assessment**

We assessed the risk of bias and the quality of studies using standardized tools. To assess the quality of included studies, we used the Consolidated Standards of Reporting Trials
(CONSORT) checklist for randomized trials. Strengthening the Reporting of Observational studies in Epidemiology (STROBE) for observational studies, Consolidated Criteria for Reporting Qualitative Research (COREQ) for qualitative studies, and Standards of Quality Improvement Reporting Excellence (SQUIRE) for quality improvement. To assess the risk of bias, we used the Newcastle-Ottawa scale for nonrandomized studies and the Cochrane risk of bias tool for randomized controlled trials (RCTs). We used the Weight of Evidence tool for assessing the relevance of the study and to summarize the findings of our quality and the risk of bias assessments (Table 1). We developed a scoring system to enable the classification of the studies into high, medium, and low quality using the CONSORT, STROBE, and SQUIRE tools, respectively (Table 2). We developed a further scoring system to enable the classification of studies into low, medium, and high risk of bias using the Newcastle-Ottawa scale (Table 3). The numerical thresholds for each category were determined through discussion, with all the authors performing quality assessment. The studies assessed using COREQ and the Cochrane risk of bias tool were discussed and categorized on a case-by-case basis. We did not exclude any study based on the risk of bias or quality assessment results but followed the Cochrane guidance for reporting the effects of interventions and the certainty of the evidence provided. Owing to the large number of different outcomes in this review, we did not specify the smallest important difference for each outcome before analysis. We assessed the importance of the effects seen based on how likely it seemed that our conclusions would hold if the true effect lay near either end of the 95% confidence interval.

Analysis
Owing to the heterogeneity in the study design and the outcomes reported, it was not possible to perform a meta-analysis. Instead, we performed a narrative synthesis using Popay methodology. We tabulated the findings of the included studies and grouped the studies by the reported outcome.

Registration
The review protocol was registered with the International Prospective Register of Systematic Reviews (registration number, CRD42019128545). The review conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Appendix B, PRISMA reporting checklist).

Funding
The funding for this project was provided by the University of Bristol Global Challenges Research Fund, and 2 members of the research team were funded by the National Institute for Health Research. Neither funder played any role in the study design.

Results
The searches retrieved 4909 records, with a further 20 records identified through other sources. After deduplication, 1419 records remained, of which 1093 were included studies and grouped the studies by the reported outcome.

Effect of interventions
Owing to the diversity of interventions, we have presented the findings according to the outcome measures.

Maternal clinical outcomes. Iron supplementation reduces iron deficiency anemia. Notably, 6 studies involved iron supplementation, and all showed reductions in the rates of iron deficiency anemia. The mean hemoglobin (Hb) increased following treatment with iron sucrose therapy and with iron supplementation alongside vitamin A and riboflavin. Greater improvements in the Hb levels were seen when an educational package was delivered alongside the supplementation, compared with supplementation alone or supplementation with pill counting, although the differences in the mean change to hemoglobin were small. Another study showed that nutritional counseling accompanied by dietary assessment and menu planning leads to slightly greater increases in Hb levels than nutritional education alone. The final study found that women who were not compliant with iron supplementation antenatally were 24 times more likely to be anemic (Hb<110) 1 month postpartum compared with those who were compliant.

Vitamin A supplementation reduces night blindness. Both studies involving vitamin A supplementation showed a reduction in night blindness. One showed that the symptoms of night blindness improved after 6 weeks of supplementation regardless of the source of the vitamin A; however, the biggest improvements in the plasma retinol concentrations were found in the groups receiving vitamin A from goat liver or capsule supplements. The other study showed that in women reporting night blindness preintervention, bigger improvements to pupillary thresholds were seen when vitamin A supplements were accompanied by iron and riboflavin, compared with the supplements being taken alone.

Influenza vaccination slightly reduces laboratory-confirmed influenza among infants but not mothers. One RCT showed that the influenza
vaccination may have slightly reduced maternal influenza-like illnesses, but it made little or no difference to infant influenza-like illnesses. Meanwhile, the same vaccination slightly reduced the rate of laboratory-confirmed influenza among infants but had no important effect on the rate of laboratory-confirmed influenza among mothers. 36, 47, 48

Antenatal pelvic floor muscle training is acceptable to pregnant women. One feasibility study concluded that pelvic floor muscle training (PFMT) is feasible and acceptable alongside antenatal care (ANC). Women who attended 4 PFMT sessions reported between 50% and 100% daily compliance with pelvic floor exercises. This feasibility study was not powered to identify a reduction in the symptoms of urinary incontinence or pelvic organ prolapse. 33

**Neonatal clinical outcomes.** Iron–folic acid supplementation reduces neonatal mortality. Taking any iron–folic acid (IFA) supplementation during pregnancy was shown to reduce the risk of neonatal mortality by 42% in one study, but the effect was bigger (55%) when the mothers took 150 to 240 supplements of any dosage during pregnancy or when mothers took >90 supplements and started these before 5 months gestation (57% reduction). 39

Education, supplements, and food incentives all reduce rates of low birthweight babies. One study found a 25% reduction in the proportion of low birthweight babies when women took a multiple micronutrient tablet instead of a standard IFA. 25, 49 Another study showed that extra training for female community health volunteers (FCHVs) and health-promoting text messages for pregnant women reduced the rates of low birthweight babies. 27, 50 A final study showed that education alongside food incentives probably led to a small increase in the average birthweight, but education alone and education with cash incentives made little or no difference to the average birthweight. 29, 51, 52

**Pregnancy and birth knowledge.** Birth preparedness classes and group antenatal care improve awareness of danger signs in pregnancy and knowledge of essential newborn practices. Attendance of birth preparedness classes (BPCs) was shown to increase the use of essential newborn practices such as breastfeeding within an hour of birth in one study, 36 whereas another showed an increase in the awareness of pregnancy-related danger signs following BPCs. 36, 53, 54 A further study found moderate evidence that women who attended BPCs with their husbands increased their knowledge scores slightly more than women attending alone. 24, 55 This may be because of increased communication between spouses regarding health practices during or after the classes, leading to a better understanding and retention of new information. A similar finding was reported by a study looking at the impact of group ANC in comparison with individual ANC. They found that women in group ANC were better at identifying the danger signs in pregnancy and reported enjoying their ANC more. 24, 55, 56 There were no important differences between the 2 groups for any of the other maternal or neonatal outcomes assessed.

**Education about medication increases compliance and reduces self-medicating.** Two hospital-based interventions showed that knowledge regarding medication use improved following counseling sessions. 11, 35 One of these studies showed that medication education reduced self-medication by the patients, whereas the other showed a slightly improved compliance with iron supplementation when compared with pill counting only. 21 In a final,
community-based study, it was found that training FCHVs to give enhanced counseling may have increased iron and folic acid supplementation compliance rates, but the certainty in the evidence is very low because of large differences in the baseline compliance rates for the participants in the intervention and control sites.40

Healthcare utilization. Community birth preparedness classes may increase attendance of antenatal care. All 3 large studies looking at BPCs (with 6285 participants collectively) showed an increase in the ANC attendance after intervention.31,36,53,54,58–60 One reported a 24% increase in the number of women attending ≥2 ANC visits31 after BPCs, whereas the other 2 showed increases in the proportion of women receiving care at least once in their pregnancy.36,39,61 How-ever, in one of these studies, the rate change in women attending 4 ANC visits was lower in the intervention group compared with the control group, which highlights the possibility of confounding factors increasing the ANC visit numbers around the time the study was taking place. This reduces the certainty with which these increases in care-seeking can be associated with the BPCs alone.28 The uptake and awareness of the government’s “Aama Programme,” for example, was increasing over the period of this study (2011–2014), and it provided women throughout Nepal with a monetary incentive for attending 4 ANC appointments.42 Women’s literacy in Nepal, which has been linked with improved health awareness and outcomes in general, also increased over this period.42

Maternity incentive schemes increase attendance of antenatal care. In a study assessing the impact of the government-funded maternity cash incentive program, women were 6 times more likely to have attended 4 ANC visits after the implementation of the policy than before it.42 However, rising education levels in the intervening period are also strongly associated with increasing ANC visits. Therefore, in the absence of a control group, it is again difficult to rule out the confounding factors contributing to this observed trend. The final study in this group used qualitative methods to further explore the link between incentives and ANC attendance. It found that caregivers and stakeholders saw cash incentives as a motivating factor in pregnant women’s attendance of ANC visits, although the women themselves had mixed ideas about the influence of this incentive.44

The relationship between birth preparedness classes and uptake of skilled birth attendants is uncertain. Two studies found that BPCs led to an increase in the use of SBAs by pregnant women,36,53 but a third study found that the use of SBAs remained low and unchanged after the introduction of BPCs.31 A fourth study showed that women who were attending BPCs and knew any antepartum, intrapartum, or postpartum danger signs were more likely to deliver at a health facility.37,28–40 However, this study did not test the effect of the birth preparedness intervention directly but rather tested the effect of pregnant women’s levels of birth preparedness knowledge. Therefore, firm conclusions about causation cannot be made.

Birth preparedness classes increase uptake of postnatal services. The same study which found no increase in SBA use found an increase in the use of postnatal services with a birth preparedness package.31 Another BPC study found that increases in the uptake of postnatal services were slightly

### TABLE 2

| Scoring criteria for quality assessment | Low | Medium | High |
|----------------------------------------|-----|--------|------|
| CONSORT                                | 0–11| 12–20  | 21–25|
| STROBE                                 | 0–8 | 9–15   | 16–22|
| SQUIRE                                 | 0–25| 26–40  | 41–50|
| COREQ                                  | Determined through case-by-case discussion |

CONSORT: Scores were awarded out of maximum of 25. Points were awarded if specific, relevant details were present in the background, methodology, analysis, and results. Points were also awarded if the trial was registered before commencing recruitment, if a protocol was publicly available, and if any sources of funding were disclosed.

STROBE: Scores were awarded out of a maximum of 22. Points were awarded if specific, relevant details were present in the background, methods, analysis, and results, and if limitations and generalisability were addressed. Points were also awarded for disclosure of sources of funding.

SQUIRE: Scores were awarded out of 50. Points were awarded for a clear title, abstract and background; for discussion of strengths, limitations, and generalisability; and for providing clear conclusions including the practical usefulness of the intervention going forward.

COREQ: Determined through case-by-case discussion.

Toolan. A systematic review of antenatal interventions in Nepal. Am J Obstet Gynecol Glob Rep 2022.

### TABLE 3

| Scoring criteria for risk of bias assessment | High | Medium | Low |
|---------------------------------------------|------|--------|-----|
| Newcastle-Ottawa scale                      | 1–4  | 5–6    | 7–9 |
| Cochrane risk of bias                       | Determined through case-by-case discussion |

Newcastle-Ottawa scale: Scores awarded out of 9 based on how well the study meets the criteria related to participant selection (up to 4 points); how well the study controls for confounding factors (up to 2 points); and for the reporting of study outcomes (up to 3 points). A low score suggests the study carries a high risk of bias, and a high score suggests a low risk of bias.

Toolan. A systematic review of antenatal interventions in Nepal. Am J Obstet Gynecol Glob Rep 2022.
### TABLE 4
Included studies

| Study | Intervention details | Study details | Outcomes |
|-------|----------------------|---------------|----------|
| Acharya et al., 2018 | 1. Capacity building of FHWs (reinforcement training on maternal and newborn health followed by regular supervision) for the promotion of health-seeking behavior among pregnant women, including birth preparedness. 2. Periodic health promotion tests to pregnant women about maternal and child health components. | Design: Cluster RCT  Setting: Community  Duration: Unclear  District: Dhanusha  No. received intervention: 426 | Low birthweight (LBW): Mothers in the intervention area were less likely (aOR, 0.37; 95% CI, 0.16–0.83) to have an LBW baby than mothers not in the intervention area.  Cost: Not documented. |
| Singh et al., 2018 | The intervention involved questionnaires about the symptoms of urinary incontinence (UI) and pelvic organ prolapse (POP) before and after 4 sessions of pelvic floor muscle training (PFMT). The training sessions involved a video and teaching sessions with a specialized women’s health physiotherapist. These 4 PFMT sessions were held alongside regular antenatal care (ANC) appointments. | Design: Cohort  Setting: Hospital  Duration: 11 mo  District: Karpalanchok  No. received intervention: 164 | Acceptability of intervention: Notably, 57% of the pregnant women attended ≥4 PFMT visits and approximately 50% of these women reported 50% –100% adherence to daily PFMT. Even though most of them did not suffer from UI or POP, the women met for PFMT visits and performed PFMT at home. They reported they were motivated to prevent these conditions.  Symptoms of POP or UI: There was no difference in the symptoms of POP or UI between the women who attended all 4 sessions of PFMT and those who attended 0–3 sessions.  Cost: Not documented. |
| Adhikari et al., 2009 | Iron supplementation: Daily dose of 60 mg of elemental iron, alone or with pill counting (unused pills counted monthly) and/or education programme concerning iron and anemia (an initial direct counseling session and an educational brochure). | Design: RCT  Setting: Hospital  Duration: 3 mo  District: Kathmandu  No. received intervention: 320 | Hemoglobin (Hb) levels: Education alone significantly increased Hb (difference in mean change, 0.23 g/dL; 95% CI, 0.07–0.39), as did education with pill count (difference in mean change, 0.26 g/dL; 95% CI, 0.10–0.42). Compared with the control group, pill count did not significantly increase Hb.  Anemia prevalence: Education alone reduced anemia prevalence (OR, 0.41; 95% CI, 0.18–0.91), as did education with pill count (OR, 0.35; 95% CI, 0.16–0.78; P < 0.01). Compared with the control group, pill count did not significantly reduce anemia.  (Education groups only) knowledge about anemia and iron intake during pregnancy: The mean knowledge scores among women in the education alone and education with pill count groups at the baseline evaluation were 9.4 and 10.7 and at the end of the study were 24.7 and 25.2, respectively. No significant difference in knowledge about anemia and iron intake during pregnancy (P = 0.65).  (Pill count groups only) pill compliance: Iron supplementation compliance was higher in the education with pill count group than the pill count only group (88% vs 73%, P < 0.001).  Cost: Not reported. |
| Bhatt et al., 2017 | Government Free Delivery Care policies, notably the “Aama Programme,” which provided cash incentives for women completing ≥4 ANC visits. | Design: Cross-sectional  Setting: Hospital  Duration: Unclear (>15 y)  District: Nationwide  No. received intervention: 16,837 | Attendance of 4 ANC visits: Between 1994 and 2011, women visiting 4 ANC has increased from 9.2% to 54.3%. After adjusting for FDC policy, individual, and community level factors, women were 3 times more likely to attend 4 ANC visits than women who were pregnant when there was no incentive scheme (aOR, 3.020; P < 0.001). Similarly, women were 6 times (aOR, 6.006; P < 0.001) more likely to have attended 4 ANC visits after the implementation of “Aama.”  Cost: Not documented. |
| Choulagai et al., 2017 | Intervention to increase skilled birth attendant (SBA) service utilization. The intervention elements included the following: promotion of family support to pregnant women for childbirth in a health facility and training for health facility staff in communication skills to encourage a women-friendly environment. | Design: Cluster RCT  Setting: Community  Duration: 19 mo  District: Bajhang, Dailekh, Kanchanpur  No. received intervention: 2096 control | SBA attendance: Skilled birth care increased from 30.4% (baseline) to 56.5% (after intervention) in the intervention group. This change is 5.0% (P = 0.06) greater than the rate change in the control group.  ANC visits: Notably, 92.4% of participants in the intervention group attended at least 1 ANC visit after intervention, compared with 83.4% at baseline. This change is 4.0% (P = 0.03) greater than the rate change in the control group. In addition, 60.9% of participants in the intervention group attended ≥4 ANC visits after intervention, compared with 46.4% at baseline. However, this change is 3.1% lower than the rate change in the control group. The mean number of ANC visits in the intervention group increased from 2.8 to 3.3, which is 0.2 greater than the change in the control group.  Cost: Not documented. |
| Bhandari et al., 2014 | Women were grouped into low- or high-risk categories using a simple scoring system based on obstetrical history. Changes to risk categorization were made as pregnancy progressed to take into account new information, for example, breech, APH. | Design: Cohort  Setting: Community  Duration: 12 mo  District: Dulegauda, Tanahu  No. received intervention: 187 | Neonatal complications: The frequency of complications, for example, feeding problems, jaundice, and oral thrush was higher (27.79%) in the high-risk groups as compared with 3.6% in the low-risk groups.  LBW: Of 46 high-risk pregnancies, 6 (13.04%) resulted in LBW newborns. The corresponding number in the low-risk group was 5 (3.55%).  Neonatal death: Neonatal deaths were 1 (0.7%) in the low-risk and 3 (6.52%) in the high-risk group.  Cost: Not documented. |

Toolan. A systematic review of antenatal interventions in Nepal. Am J Obstet Gynecol Glob Rep 2022. (continued)
| Study                                      | Intervention details                                                                 | Study details       | Outcomes                                                                 |
|--------------------------------------------|--------------------------------------------------------------------------------------|---------------------|--------------------------------------------------------------------------|
| Devkota et al.,35 2017                    | Antenatal counseling regarding medication use.                                        |                     | Knowledge: The mean knowledge scores increased from 8.8±3.6 to 12.8±1.27 of 20. This encompassed knowledge about their complications, their medicine name and uses, and medicine safety. Attitude: The mean attitude scores increased from 15.2±1.9 to 17.8±1.55 of 20. Medicine practice: The mean practice scores increased from 11.8±2.6 to 15.96±2.05 of 20. The percentage of respondents taking medicines without consultation reduced from 64.2% to 2.2%. Cost: Not documented. |
| Flueckiger et al.,36 2018                  | Monetary incentives for attending 4 ANC visits and delivering in a healthcare facility. |                     | Motivation for attending 4 ANC visits: All mothers and caregivers expressed that the primary motivation for ANC attendance and institutional delivery is concern for the health of the mother and baby. Mothers were divided on whether the monetary incentive was motivating for them to attend ANC visits. All caregivers noted the monetary incentive as a motivating factor. The majority of the stakeholders expressed that the monetary incentive plays a motivating role in ANC attendance and that attendance has increased. Cost: Not documented. |
| Graham et al.,22 2007                     | Vitamin A (and iron and riboflavin) supplementations: Nightblind pregnant women were randomly assigned to receive (6 wk per week) vitamin A and iron (from 6 wk to 12 wk) a vitamin A–fortified rice curry dish providing 850 μg retinal activity equivalents of either 0.3 mg Fe and 6 mg riboflavin (FeR+VA) capsule or a placebo control (RA only) capsule. |                     | Women who were iron deficient at baseline (n=38) had significantly greater improvement in PT score with iron and riboflavin supplementation than without (P<.05). Iron and riboflavin supplements significantly reduced the prevalences of riboflavin deficiency (from 60% to 6%, P<.001), iron deficiency anemia (from 35% to 15%, P<.007), and abnormal PT (from 87% to 30%, P<.05) from baseline. Mean increases in erythrocyte riboflavin (P<.0001) and plasma ferritin (P=.01) were greater in the FeR+VA group than in the VA only group. Cost: Not reported. |
| Haskell et al.,2005                        | Vitamin A and iron (and riboflavin) supplementations: women received (6 d/wk for 6 wk) a meal supplemented with 850 μg vitamin A equivalents as retinyl palmitate, vitamin A–fortified rice, goat liver, amaranth leaves, carrots, or 2000 μg vitamin A as retinyl palmitate. |                     | Symptoms of night blindness: Dark adaptation improved on average in all groups of night blind women who received small daily doses of vitamin A for 6 wk, regardless of the source of vitamin A. At the end of the study, only 2 women (0.6%) reported that they still had symptoms of night blindness. Pupillary threshold: Among women who initially reported night blindness, the initial and final mean P Ts were −0.71±0.44 and −1.42±0.02 log cd/m² (P<.001), respectively, which indicates improvement in dark adaptation after 6 wk of supplementation. Mean P Ts decreased significantly (P<.001) in all treatment groups during the 6-wk intervention. Change in plasma retinol concentrations: Among the women who initially reported night blindness, the initial and final mean plasma retinol concentrations were 0.96±0.05 μmol/L and 1.07±0.05 μmol/L, respectively (P<.001). The final mean plasma retinol concentration in the goal liver group was significantly (P<.05) higher than that in the group that received the same prescribed amount of vitamin A but significantly different from the final mean concentration in the high-dose capsule group. Change in plasma carotenoids, ferritin, zinc, and Hb concentrations: The final mean plasma concentrations of carotenoids and α-tocopherol differed significantly by treatment group in response to supplementation. Cost: Not reported. |
| Hodgins et al.,23 2010 VRG 2007             | A community level birth preparedness package, incorporating home-based antenatal counseling, postnatal home visits, and prescriptions of iron/folate in pregnancy and iron and vitamin A postnatally. |                     | From Valley Research Group (VRG) report: Knowledge: Awareness among recently delivered women of at least 3 pregnancy-related danger signs also increased significantly (26%-54% in Jhapa, 46%-87% in Banke, and 17%-67% in Kanchanpur). Service utilization: The percentage of recently delivered women (RDW) who received prenatal care at least once from appropriate ANC providers increased (from 74% at baseline to 88% at follow-up in Jhapa, 77%-91% in Banke and 81%-88% in Kanchanpur). Use of skilled birth attendants increased. Overall, at follow-up 45% of the RDW in Jhapa (vs 36% at baseline), 17% in Banke (vs 11% at baseline) and 24% in Kanchanpur (vs 17% at baseline) reported delivering their last child with the assistance of skilled providers (doctor, staff nurse, or auxiliary nurse midwife [ANN]). Care-seeking during emergencies: The percentage of RDW who sought care from a health facility for danger signs during labor increased in Banke (25%-31%) and in Kanchanpur (30%-46%) but remained essentially unchanged in Jhapa (54% at baseline; 55% at follow-up). Cost: The booklet cost $0.60 to produce. Other cost details not reported. |
| Karkee et al.,26 2013b                     | The Birth Preparedness and Complication Readiness (BP/CR) program, initiated in 2002 by the government. |                     | Association between obstetrical knowledge and place of delivery: Women who acknowledged that unexpected problems could occur during pregnancy and childbirth were more likely (OR, 5.83; 95% CI, 2.95–11.52) to deliver at a health facility than others unaware of the possible consequences. Women who knew any antepartum danger sign (OR, 2.16; 95% CI, 1.17–3.98), any intrapartum danger sign (OR, 3.47; 95% CI, 1.93–6.25), tended to deliver at a health facility. Cost: Not documented. |
| Kozuki et al.,27 2016a                     | Training of ANMs to perform ultrasound. ANMs were then sent on home visits to screen pregnant women for the 3 risk factors—fetal |                     | Accuracy of noncephalic presentations: The positive predictive value ranged from 92.6% to 100%, and the negative predictive values were all nearly 100%. Accuracy of placenta praevia: There was 100% agreement between ANMs and reviewers about 2 partial or complete placenta previa cases. |
### TABLE 4
**Included studies (continued)**

| Study | Intervention details | Study details | Outcomes |
|-------|----------------------|---------------|----------|
| **Presentation, multiple gestation, and placental position.** | District: Sariha No. received intervention: 815 women | Accuracy of multiple gestations: For multiple gestation, the ANM and the reviewer readings agreed 100% of the time, but sensitivity had wide confidence intervals as a result of the small number of cases. Facility delivery rate (Kozuki et al., 2015): We saw no statistically significant difference in the facility delivery rate between the ultrasound and comparison group. Cost: The estimated cost of the ultrasound machine, gel, personnel and training over 5 y was $10,335 for 15,000 births. Estimated that 160 perinatal deaths may be averted with early diagnosis; a cost of $65 per life saved. |
| McPherson et al., 2006 | The birth preparedness package (BPP) implemented through the government health system in Siraha, Nepal, during 2003–2004. The package includes interpersonal communications with clients, a flip-chart for use by community health workers, and key chains with key messages for pregnant women. Design: Before and after study Setting: Community Duration: 2 y District: Sariha No. received intervention: 182 | Changes in essential newborn care: The endpoint estimates for essential newborn practices promoted through the BPP increased by 20%–30% compared with the baseline. The birth preparedness index (BPI): The BPI increased from 33% at baseline to 54% at endpoint. Use of antenatal and postnatal care: Attendance at ≥2 ANC visits increased from 49% to 73% (P=.001). The use of postnatal care services within 1 wk of delivery increased from 11% to 25% (P<.01), whereas the use within 6 wk of delivery doubled from 17% to 34% (P=.02). Skilled birth attendance: The use of SBAs at endpoint remained unchanged from baseline at 17%. Care-seeking during emergencies: Of women who reported emergencies, the percentage who received treatment at a health facility remained constant at baseline and endpoint. Cost: Not reported. |
| Mullany et al., 2007 Mullany et al., 2009 | Two 35-min health education sessions, received by pregnant woman with or without her partner. First session received at enrollment; second session received 4–6 wk later. In addition, women received a health education flipper. Design: RCT Setting: Hospital Duration: 5 mo District: Kathmandu No. received intervention: 145—with husbands 148—woman alone 149—control | Mullany et al., 2007 Birth preparedness: Women in the couples group were nearly twice as likely as control group women to report making ≥3 birth preparations (21.8% vs 10.9%). None of the birth preparedness outcomes was different between women in the couples group vs women in the woman-alone group. Healthcare utilization: Women assigned to the couples group were more likely to attend the postpartum visit than participants assigned either to the control group (81% vs 47%, RR: 1.29; 95% CI, 1.04–1.56) or to the woman-alone group (81% vs 49%, RR: 1.25; 95% CI, 1.01–1.54). Mullany et al., 2009 Maternal and reproductive health knowledge levels of pregnant women: Women educated with husbands increased their knowledge scores by an average of 67.7% from baseline to follow-up, compared with 61.6% and 54.7% in the women-alone and control groups respectively. Cost: Not reported. |
| Nisar and Dibley, 2014 Nisar et al., 2015 | Any antenatal iron—folic acid supplements taken for at least a day during pregnancy. Design: Retrospective cohort Setting: Community Duration: 15 y District: Nationwide No. received intervention: 2001–4700 2006—4140 2011–4051 Total: 12,891 | Nisar et al., 2015 Early neonatal mortality (deaths <3 d of age): With any use of IFA supplements, the risk of early neonatal mortality was reduced by 45% (aHR, 0.55; 95% CI, 0.38–0.79; P<.002) Neonatal mortality (deaths <31 d of age): With any use of IFA supplements, the risk of neonatal mortality was reduced by 42% (aHR, 0.58; 95% CI, 0.39–0.85; P<.001) for neonatal mortality. Approximately 55% reduction in the risk of neonatal mortality in infants whose mothers consumed 150–240 supplements in their pregnancy. Protective effect of an early start of IFA supplements (first 2 mo) in pregnancy on the risk of neonatal mortality (53%; P=.023) Nisar et al., 2014 Early neonatal mortality: The risk of early neonatal death was significantly reduced by 51% (aHR, 0.49; 95% CI, 0.32–0.75) in with any use of IFA compared with none. Early initiation of IFA: When supplementation started at or before 20 wk, the adjusted risk of early neonatal mortality was reduced by 53% in Nepal compared with no IFA. Greater use: When >90 IFA supplements were used and started at or before 20 wk, the adjusted risk of early neonatal deaths was reduced by 57%. A total of 4600 early neonatal deaths could be prevented annually if all pregnant women used >90 IFA supplements and started at or before the fifth month of pregnancy. Cost: Not reported. |
| Osrin et al., 2005 Hindle et al., 2008 | Dietary supplement, UNIMMAP, taken daily from the 12th wk of gestation—all minimum—until delivery, compared with a daily supplement of iron (60 mg) and folic acid (400 μg) recommended by the government. The UNIMMAP contains vitamin A 800 μg, vitamin E 19 mg, vitamin D5 μg, vitamin B1 1.4 mg, vitamin B2 1.4 mg, niacin 18 mg, vitamin B6 1.9 mg, vitamin B12 2.6 μg, folic acid 400 μg, vitamin C 70 mg, iron 30 mg, zinc 15 mg, copper 2 mg, selenium 65 μg and iodine 150 μg. Design: RCT Setting: Hospital Duration: 2 y District: Janakpur, Dhanusha No. received intervention: 1200 | Osrin et al., 2005 Birthweight: Mean birthweight was 2733 g (SD, 422) in the control group and 2810 g (SD, 453) in the intervention group, representing a mean difference of 77 g (95% CI, 24–130; P=.004) and a relative fall in the proportion of LBW by 25%. Gestational duration: No difference was recorded in the duration of gestation (0.2 wk [−0.1 to 0.4]; P=.12), infant length (0.3 cm [−0.1 to 0.6]; P=.18), or head circumference (0.2 cm [−0.1 to 0.4]; P=.18). Hindle et al., 2006 Inflammatory markers: Blood eosinophils, plasma concentrations of the acute phase reactants C-reactive protein, alpha-1-acid glycoprotein (AGP), neopterin, and ferritin, milk KcK, and the production of interleukin (IL) 10, IL-4, interferon gamma, and tumor necrosis factor alpha in whole blood did not differ significantly between the supplemented and control groups. Cost: Not reported. |

*Toolan, A systematic review of antenatal interventions in Nepal. Am J Obstet Gynecol Glob Rep 2022.* (continued)
### TABLE 4
Included studies (continued)

| Study | Intervention details | Study details | Outcomes |
|-------|----------------------|---------------|----------|
| **Pokharel et al.**, 2011 | Training FCHVs to give enhanced counseling to pregnant women regarding the importance of iron supplementation. FCHVs also trained to encourage women to attend antenatal appointments. | Design: Cohort study  Setting: Community  Duration: 6 y  Districts: 70 districts throughout Nepal  No. received intervention: not known | Of note, in 2009 the DHS data were used to give outcomes for women in 3 sets of districts; those where the intervention had been in place for at least 12 mo, those where the intervention had not yet been implemented, and those with no plans of implementing the intervention.  **Attendance at ANC:** Approximately 92% of respondents in intervention districts attended ANC clinics, significantly higher than in preintervention districts (66%) or nonintervention districts (86%).  **Coverage among pregnant women with any IFA:** Approximately 90% in intervention districts, significantly higher than districts that were preintervention (65%), but not significantly higher than in districts in which no intervention was planned (86%).  **Compliance with IFA supplementation:** Higher among pregnant women in intervention districts and nonintervention districts (68% and 66%) than among those from districts before intervention implementation (44%).  **Coverage of deworming tablets:** Higher in intervention districts and nonintervention districts than in districts before intervention (69% and 73%, respectively, vs 52%).  Cost: Not documented. |
| **Saville et al.**, 2018 | Participatory Learning and Action (PLA) comprises women’s groups that discuss and form strategies about nutrition in pregnancy, LBW, and hygiene. One of the 4 groups received standard care (the control group), one group received PLA only, one group received PLA plus cash transfer, and the final group received PLA plus food transfer. | Design: Cluster RCT  Setting: Community  Duration: 12.5 mo  District: Dhanusha, Mahottari  No. received intervention: Control: 5310  PLA only: 5626  PLA+cash: 7272  PLA+food: 6884  Total: 25,062 | Primary outcomes:  **Birthweight measured within 72 h:** Birthweight measured within 72 h appeared to be incrementally higher in PLA (28.9 g; 95% CI, 37.7−95.4; n=488), PLA+cash (50.5 g; 95% CI, 15.0−116.1; n=509), and PLA+food (78.0 g; 95% CI, 13.9−142.0; n=629) arms, but the only significant difference was between control and PLA plus food.  **Secondary outcomes:** No significant differences in most secondary outcomes measured.  **Institutional deliveries:** Significantly more institutional deliveries (OR, 1.46; 95% CI, 1.03−2.06; n=2651) and lower rates of colostrum discarding (OR, 0.71; 95% CI, 0.54−0.93; n=2548) were observed in the PLA+food arm compared with control (institutional delivery, n=2251; colostrum, n=2587).  Cost: Cash transfer amount and some staff costs documented, but overall costs of intervention/implementation not documented |
| **Sharma and Tiwari**, 2015 | Iron sucrose infusion: Iron sucrose was administered as 200 mg elemental iron in 100 mL of 9% normal saline infusion over 1 h everyday up to total calculated dose. | Design: Before and after study  Setting: Hospital  Duration: 12 mo  District: Kathmandu  No. received intervention: 37 (but only 7 of these antenatal women) | Hb level: Before iron sucrose therapy, the mean Hb level was 7.5 g/dL. After therapy, the mean Hb level was 10.3 g/dL.  Ferritin level: Before iron sucrose therapy, the serum ferritin was 12.8 mg/mL. After therapy, the mean serum ferritin level was 300 mg/dL.  Total iron: Before therapy, total iron was 40 mg/dL. After, it was 85 mg/dL.  Cost: Not reported. |
| **Steinhoff et al.**, 2017 | Flu vaccination: Seasonally recommended trivalent inactivated influenza vaccine | Design: RCT  Setting: Community  Duration: 2 y (12 mo × 2)  District: Sariahi  No. received intervention: 3693 | Maternal influenza-like illness: A reduction of 19% (95% CI, 1−34) in all influenza-like illnesses combining cohort 1 and 2 (RR, 0.81 [0.66−0.99]) P=0.041. Cohort 1 was not significantly different; cohort 2 was statistically different.  **Laboratory-confirmed influenza in infants:** A reduction of 30% in laboratory-confirmed influenza in infants combining cohort 1 and 2, but not statistically significant (RR, 0.70 (0.52−0.95) P=0.20).  Maternal laboratory-confirmed influenza, influenza-like illness in infants, preterm birth (RR, 0.91 [0.77−1.08]), small for gestational age births: No difference.  Birthweight: Maternal immunization reduced the rates of LBW by 15% (95% CI, 3−25) in both cohorts combined.  Adverse effects: Similar between both the groups.  Cost: Not reported. |
| **Sanuwar et al.**, 2019 | The intervention group received nutritional counseling and individualized dietary assessment and menu planning, the control group received the counseling only. | Design: Nonrandomized controlled study  Setting: Hospital  Duration: 5 mo  District: Kathmandu  No. received intervention: 53 | Maternal nutritional knowledge: Maternal nutritional knowledge scores increased by more in the intervention group (score change 8.26 of 1.05; P<.001).  Anemia: A bigger increase in Hb level was seen in the intervention group compared with the control group (change in Hb +0.56 cf +0.16; P=.002).  Anthropometric data: There was no difference between the 2 groups with respect to changes in weight or BMI and no significant difference in heights between the 2 groups.  Dietary changes: Women in the intervention group increased their intake of red meat, liver, and fish (P=.001), vitamin C rich fruits (P=.006), dairy products (P=.013), eggs (P=.016), and dark green leafy vegetables (P=.006) more than women in the control group.  Cost: Not documented. |
| **Thapa et al.**, 2016a | Calcium supplementation: Provided calcium supplementation (daily dose of 1 g of elemental calcium beginning at 4 mo gestation) through government ANC services to pregnant women. ANC providers distributed and counseled women regarding calcium use and FCHVs reinforced calcium-related messages. | Design: Cohort  Setting: Hospital and community  Duration: 14 mo  District: Dallakeh  No. received intervention: 9246 | Coverage of ANC and delivery services: Approximately 94.6% of women interviewed attended at least 1 ANC visit and received calcium.  Calcium coverage: The full course of calcium (1 gm daily for 150 d) was provided to 82.3%.  Compliance with calcium intake instructions: Full compliance was 67.3% of calcium recipients.  Discontinuation: Significant predictors of completing a full course were gestational age at first ANC visit and number of ANC visits during their most recent pregnancy (P<0.01).  Knowledge about calcium and acceptability: Notably, 99.2% reported that they took it as instructed with respect to dose, timing, and frequency.  Feasibility of the intervention: Over 97% would recommend calcium to others and would use it during a subsequent pregnancy.  Cost: Not documented. |

*Toolan. A systematic review of antenatal interventions in Nepal. Am J Obstet Gynecol Glob Rep 2022.* (continued)
| Study | Intervention details | Study details | Outcomes |
|-------|----------------------|---------------|----------|
| Thapa et al., 45 2019 | A trial of ANC in groups of 12 instead of individual antenatal appointments. | Design: Cluster-controlled and qualitative Setting: Community Duration: 21 mo Districts: Achham No. received intervention: 457 | Institutional birth rate or attendance of 4 ANC visits: No significant difference between intervention and control groups in institutional birth rate, attendance of 4 ANC visits, postpartum contraceptive use, stillbirth rate, perinatal mortality rate, or infant mortality rate. Women in the intervention group were better at identifying key danger signs in pregnancy \( P = 0.01 \) and were more likely to report that their antenatal appointments were "very enjoyable" (84% vs 60%). |

Costs: The costs to start-up calcium introduction in addition to MgSO4 were as follows: total fixed program cost (not including variable costs per individual), $117,656.29 (start-up costs, $44,804.09; ongoing program implementation costs, $72,852.19); $0.44 total program costs per individual. Initially $0.01/tablet (Nepali Rupees, 0.65/tablet), then US$ 0.016/tablet (Nepali Rupees (NR), 1.35/tablet). |

Maru et al., 57 2018 |  |
| Harsha Bangura et al., 56 2020 |  |

Yadav et al., 43 2019 | The study was evaluating the efficacy of the daily iron–folic acid supplementation program, available for all pregnant women in Nepal from the second trimester onward, as advised by the WHO and funded by the Government of Nepal. | Design: Cross-sectional Setting: Hospital Duration: 7 mo District: Mechi, Koshi, Sagarmatha, Sunsari and Siraha districts. No. received intervention: 328 | IFA compliance: Women who were not compliant with taking their IFA as recommended were 24 times as likely (aOR, 24.16 [10.05–58.3]) to be anemic at 1 mo postpartum. Heme iron intake: Women who reported not having heme iron in their diet were 3.3 times as likely to be anemic (aOR, 3.35 [1.4–8.1]). Ethnicity: Women from Terai castes were 2.7 times as likely to be anemic as those from mountain and hill castes (aOR, 2.725 [1.294–5.736]). |

Cost: Annual per capita cost $0.5, or per woman cost of NR 4000 ($37). |

Please note: Some studies were reported across several journal articles, for example where protocol and results were published separately. Where this was the case, we grouped all articles associated with a given study under the first author of the article reporting the majority of the results. All articles associated with each study are listed in Table 1 Column 1, with the study name highlighted in bold. 

aOR, adjusted odds ratio; aHR, adjusted hazard ratio; APH, antepartum haemorrhage; BMI, body mass index; cf, compare; CI, confidence interval; DHS, Demographic Health Survey; FCHV, female community health volunteer; FDC, free delivery care; No., number; PT, pupillary threshold; RCT, randomized control trial; WHO, World Health Organization.

Toolan. A systematic review of antenatal interventions in Nepal. Am J Obstet Gynecol Glob Rep 2022.
more marked when women were educated alongside their husbands, compared with when they received no education or were educated alone, which may be because of a male dominance in the household decision-making.

Clinical audit. Two of the studies with “capacity-building” interventions audited the results of their interventions. One found a high diagnostic accuracy for a home-based ultrasound performed by auxiliary nurse midwives (ANMs) and done for identifying non cephalic presentations, placenta previa, and multiple gestations. Another study triaged women into different risk categories and compared neonatal outcomes between the high-risk and low-risk groups, finding a higher rate of neonatal complications in the high-risk group than in the low-risk group. The data for both these studies are of limited value in demonstrating the effectiveness of the interventions because of the lack of a control group.

Cost-effectiveness. Only 3 studies reported any cost-effectiveness analysis. In one, the authors carried out an in-depth cost-effectiveness analysis of a calcium supplementation program and found a total fixed program cost of $0.44 per individual. This represents a cost per disability-adjusted life year averted of $25.33 when compared with standard magnesium treatment and is therefore favored above a willingness-to-pay threshold of around $30. The second carried out a cost-effectiveness analysis of an ultrasound program for diagnosing pregnancy complications and found a cost of $65 per life saved. In the third study, the authors found that the introduction of ANC cost approximately $0.5 per capita extra, compared with routine care, but that women enjoyed their ANC more and were better at identifying the danger signs in pregnancy. This study did not look at whether this improved the maternal or neonatal outcomes locally.

Discussion
Principal findings
We found 25 studies with diverse approaches to improving ANC in Nepal, and we identified the following 2 intervention types that accounted for a large proportion of studies conducted: interventions involving micronutrients and educational interventions. Other interventions involved cash and food incentives, staff training, and service development.

Nearly all interventions reported an improvement in the outcomes for mothers, neonates, or health system utilization. However, not all of the studies were of high quality. Some were not comparative, making it hard to ascertain their true impact; several of the observational studies did not adequately consider confounding factors. Some studies used short-term, surrogate outcome measures rather than longer-term assessments. Finally, only a few studies involve multiple sites, and all the studies conducted in hospitals were single-center studies.

Implications for future research
We found little research assessing the impact of the Government of Nepal’s “Aama Programme.” This scheme is 10 years old and yet we identified only 2 articles investigating the effectiveness of cash incentives for women attending 4 ANC visits. Several other papers not included in this review explore the effectiveness of the incentives for transportation and health facility delivery, suggesting that the ANC element has been less well-evaluated. A further gap is seen in interventions involving mobile technology. Only 1 article in our review involves an mHealth intervention component, despite the proliferation of mHealth interventions for maternal health in other low- and middle-income countries over the recent years. It is unclear whether this omission is owing
to a lack of interventions or a lack of research into this area.

There was a lack of reporting about the cost-effectiveness of interventions, with only 3 studies performing comprehensive cost-effectiveness analysis.41,45,56,57,65,66 Cost-effectiveness information is important for ensuring effective resource allocation by the government and donors.71 In future research, it is vital that this is considered.

There were clear regional concentrations of study sites, with most studies being conducted in the lowland Terai region and none in the most mountainous, difficult-to-access areas. The limited infrastructure within the Himalayas understandably makes research more difficult, but without including these communities in the trials of antenatal interventions, it will be very difficult to improve outcomes for the hardest-to-
reach groups. Finally, there were a few multisite, high-quality RCTs.

**Strengths and limitations**

A key strength of this review is its broad inclusion criteria and exclusive focus on Nepal; we are aware of only one other systematic review in maternity care that focuses on Nepal. The broad inclusion criteria may also contribute to one of the study’s weaknesses: the heterogeneity in its results. The huge breadth in interventions and outcomes we identified makes meta-analysis impossible and limits meaningful judgement about the relative effect of one intervention compared with another.

We only included studies with interventions specifically targeting pregnant women or ANC services and therefore excluded the interventions targeting all women of reproductive age or the wider community. This meant excluding some high-quality studies with interventions that report maternal and neonatal outcomes. However, broadening the focus beyond ANC was outside the scope of this review.

**Conclusion**

Our systematic review found good quality evidence that micronutrient supplementation and educational interventions can bring important clinical benefits. IFA supplementation significantly reduces neonatal mortality and maternal anemia, whereas BPCs increase the uptake of antenatal and postnatal care, compliance with micronutrient supplementation, and awareness of danger signs in pregnancy. Where there is strong evidence that an intervention may bring clinical benefit implementation studies, including participants from the hardest-to-reach communities and incorporating cost-effectiveness analyses would be beneficial in highlighting the potential barriers to uptake.

**Supplementary materials**

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.xagrr.2021.100019.

**REFERENCES**

1. Neal S, Channon AA, Carter S, Falkingham J. Universal health care and equity: evidence of maternal health based on an analysis of demographic and household survey data. Int J Equity Health 2015;14:56.
2. Pandit RD. Role of antenatal care in reducing maternal mortality. Asia Oceania J Obstet Gynaecol 1992;13:1–6.
3. Oyenieke K. Can antenatal care result in significant maternal mortality reduction in developing countries? J Community Med Health Educ 2013;03:e116.
4. World Health Organization. Trends in maternal mortality: estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division. 2019. Available at: http://documents.worldbank.org/curated/en/79397156908763231/pdf/Trends-in-maternal-mortality-2000-to-2017-Estimates-by-WHO-UNICEF-UNFPA-World-Bank-Group-and-the-United-Nations-Population-Division.pdf. Accessed October 20, 2020.
5. Bhusal CL, Singh SP, Be Bc RK, et al. Effectiveness and efficiency of Aama Surakshya Kar yakram in terms of barriers in accessing maternal health services in Nepal. J Nepal Health Res Coun; 2011;9:29–37.
6. Aryal K. Maternal health care in Nepal: trends and determinants. In: Singh S, ed. Demographic health survey further analysis report 118. Published online Government of Nepal; 2019.
7. Kumar V, Mohanty S, Kumar A, et al. Effect of community-based behaviour change management on neonatal mortality in Shivgarh, Uttar Pradesh, India: a cluster-randomised controlled trial. Lancet 2008;372:1151–62.
8. Jokhio AH, Winter HR, Cheng KK. An intervention involving traditional birth attendants and perinatal and maternal mortality in Pakistan. N Engl J Med 2005;352:2091–9.
9. Manandhar DS, Osrin D, Shrestha BP, et al. Effect of a participatory intervention with women’s groups on birth outcomes in Nepal: cluster-randomised controlled trial. Lancet 2004;364:970–9.
10. Duley L, Meher S, Hunter KE, Seidler AL, Aiskie LM. Antenatal care agents for preventing preeclampsia and its complications. Cochrane Database Syst Rev 2019;2019:CD0004659.
11. Holmeyr GJ, Manyame S, Medley N, Williams MJ. Calcium supplementation commencing before or early in pregnancy, for preventing hypertensive disorders of pregnancy. Cochrane Database Syst Rev 2019;CD011192. 09.9.
12. Schulz KF, Altman DG, Moher D, Ferguson D. CONSORT. CONSORT 2010 changes to reporting randomised trials. Lancet 2010;375:1144–6.
13. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg 2014;12:1495–9.
14. Booth A. COREQ (consolidated criteria for reporting qualitative studies). In: Hannes K, ed. Guidelines for reporting health research: a user’s manual. Wiley Online Library; 2014:214–26.
15. Gwirca G, Davies L, Goodman D, et al. 2.0 (Standards for Quality Improvement Reporting Excellence): revised publication guidelines from a detailed consensus process. BMJ Qual Saf 2016;25:986–92.
16. Welts GA, Shea B, O’Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses. 2012. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed October 20, 2020.
17. Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration’s tool for assessing risk of bias in randomised trials. 2011;343:d5928.
18. Gough D. Weight of Evidence: a framework for the appraisal of the quality and relevance of evidence. Res Pap Pub Educ 2007;22:213–28.
19. Cochrane. Cochrane effective practice and Organisation of Care (EPOC). Reporting the effects of an intervention in EPOC reviews. 2017. Available at: http://epoc.cochrane.org/resources/epoc-resources-review-authors. Accessed October 20, 2020.
20. Popay J, Roberts H, Sowden A, et al. Guidance on the conduct of narrative synthesis in systematic reviews: a product from the ESRC Methods Programme. 2006. Available at: https://www.lancaster.ac.uk/media/lancaster-university/content-assets/documents/fm/dthr/hr/NSynthesisguidanceVersion1April2006.pdf. Accessed October 20, 2020.
21. Adhikari K, Liabsuatrakul T, Pradhan N. Effect of education and pill count on hemoglobin status during prenatal care in Nepali women: a randomized controlled trial. J Obstet Gynaecol Res 2009;35:459–66.
22. Graham JM, Haskell MJ, Pandey P, Shrestha RK, Brown KH, Allen LH. Supplementation with iron and riboflavin enhances dark adaptation response to vitamin A-fortified rice in iron-deficient, pregnant, nightblind Nepali women. Am J Clin Nutr 2007;85:1375–84.
23. Haskell MJ, Pandey P, Graham JM, Peerson JM, Shrestha RK, Brown KH. Recovery from impaired dark adaptation in nightblind pregnant Nepal women who receive small daily doses of vitamin A as amaranth leaves, carrots, goat liver, vitamin A-fortified rice, or retinyl palmitate. Am J Clin Nutr 2005;81:461–71.
24. Mullany BC, Becker S, Hindin MJ. The impact of including husbands in antenatal health education services on maternal health practices in urban Nepal: results from a randomised controlled trial. Health Educ Res 2007;22:166–76.
25. Osrin D, Vaidya A, Shrestha Y, et al. Effects of antenatal multiple micronutrient supplementation on birthweight and gestational duration in Nepal: double-blind, randomised controlled trial. Lancet 2005;365:955–62.
26. Steinhoff MC, Katz J, Englund JA, et al. Year-round influenza immunization during pregnancy in Nepal: a phase 4, randomised, placebo-controlled trial. Lancet Infect Dis 2017;17:981–9.

27. Acharya D, Singh JK, Kadel R, Yoo SJ, Park JH, Lee K. Maternal factors and utilization of the antenatal care services during pregnancy associated with low birth weight in Rural Nepal: analyses of the antenatal care and birth weight records of the MATRI-SUMAN trial. Int J Environ Res Public Health 2018;15:2450.

28. Choungal BP, Onta S, Subedi N, et al. A cluster-randomized evaluation of an intervention to increase skilled birth attendant utilization in mid- and far-western Nepal. Health Policy Plan 2017;32:1002–10.

29. Saville NM, Shrestha BP, Style S, et al. Impact on birth weight and child growth of Participatory Learning and Action women’s groups with and without transfers of food or cash during pregnancy: findings of the low birth weight South Asia cluster-randomized controlled trial (LBWSAT) in Nepal. PLoS One 2018;13: e0194064.

30. Sunuwar DR, Sangroula RK, Shakya NS, Yadav R, Chaudhary NK, Pradhan PMS. Effect of nutrition education on hemoglobin level in pregnant women: a quasi-experimental study. PLoS One 2019;14:e0213982.

31. McPherson RA, Khadka N, Moore JM, Sharma M. Are birth-preparedness programs effective? Results from a field trial in Siraha district, Nepal. J Health Popul Nutr 2016;34:1673/536.pdf. Accessed October 20, 2020.

32. Sharma J, Tiwari S. Intravenous iron sucrose therapy in iron deficiency anemia in antenatal and postnatal patients. JNMJ Nepal Med Assoc 2015;53:104–7.

33. Shijagurumayum Acharya R, Tvetter AT, Grotle M, Khadgi B, Braekken IH, Stuge B. Pelvic floor muscle training programme in pregnant Nepalese women-a feasibility study, Int Urogynecol J 2020;31:1609–19.

34. De A, De A, Wijesekera NA, et al. Neonatal outcome of expectant mothers at risk: a community level study in Nepal. Am J Public Health Res 2015;3:35–40.

35. Devkota R, Khan GM, Alam K, Sapkota B, Devkota D. Impacts of counseling on knowledge, attitude and practice of medication use during pregnancy. BMC Preg Childbirth 2017;17:131.

36. Hodgins S, McPherson R, Suvedi BK, et al. Testing a scalable community-based approach to improve maternal and neonatal health in rural Nepal. J Perinatol 2010;30:388–95.

37. Karkee R, Binns CW, Lee AH. Determinants of facility delivery after implementation of safer mother programme in Nepal: a prospective cohort study. BMC Preg Childbirth 2013;13:193.

38. Kozuki N, Mullany LC, Khatry SK, et al. Accuracy of home-based ultrasonographic diagnosis of obstetric risk factors by primary-level health care workers in rural Nepal. Obstet Gynecol 2016;128:604–12.

39. Nisar YB, Dibley MJ, Mebrahtu S, Paudyal N, Devkota M. Antenatal iron-folic acid supplementation reduces neonatal and under-5 mortality in Nepal. J Nutr 2015;145:1873–83.

40. Pokharel R, Maharjan M, Mathema P, Harvey P. Success in delivering interventions to reduce maternal anemia in Nepal: a case study of the intensification of maternal and neonatal micronutrient program. 2011. Available at: http://www.a2zproject.org/pdf/ReducingAnaemiaNepal.pdf. Accessed October 20, 2020.

41. Thapa K, Sanghvi H, Rawlins B, et al. Coverage, compliance, acceptability and feasibility of a program to prevent pre-eclampsia and eclampsia through calcium supplementation for pregnant women: an operations research study in one district of Nepal. BMC Preg Childbirth 2016;16:241.

42. Bhatt H, Tiwari S, Ensor T, Ghimire DR, Gavidia T. Contribution of Nepal’s free delivery care policies in improving utilisation of maternal health services. Int J Health Policy Manag 2018;7:645–55.

43. Yadav KD, Yadav UN, Wagle RR, Thakur DN, Dhakal S. Compliance of iron and folic acid supplementation and status of anaemia during pregnancy in the Eastern terai of Nepal: findings from hospital based cross sectional study. BMC Res Notes 2019;12:127.

44. Flueckiger RM, Colaco R, Adhikari B, et al. A community led innovation benefiting women and children: health facilities and credit cooperative work together to promote maternal health care in Sahare VDC, Nepal. Health Care Women Int 2018;39:1008–19.

45. Thapa P, Banagura AH, Nirola I, et al. The power of peers: an effectiveness evaluation of a cluster-controlled trial of group antenatal care in rural Nepal. Reprod Health 2019;16:150.

46. Nisar YB, Dibley MJ. Earlier initiation and use of a greater number of iron-folic acid supplements during pregnancy prevents early neonatal deaths in Nepal and Pakistan. PLoS One 2014;9:e112446.

47. Katz J, Englund JA, Steinhoff MC, et al. Impact of timing of influenza vaccination in pregnancy on transplacental antibody transfer, influenza incidence, and birth outcomes: A randomized trial in Rural Nepal. Clin Infect Dis 07 2018;67:334–40.

48. Tielesch JM, Steinhoff M, Katz J, et al. Designs of two randomized, community-based trials to assess the impact of influenza immunization during pregnancy on respiratory illness among pregnant women and their infants and reproductive outcomes in rural Nepal. BMC Preg Childbirth 2015;15:40.

49. Hindle LJ, Gitau R, Filteau SM, et al. Effect of multiple micronutrient supplementation during pregnancy on inflammatory markers in Nepalese women. Am J Clin Nutr 2006;84:1086–92.

50. Singh JK, Kadel R, Acharya D, Lombard D, Khanal S, Singh SP. MATRI-SUMAN: a capacity building and text messaging intervention to enhance maternal and child health service utili- zation among pregnant women from rural Nepal: study protocol for a cluster randomized controlled trial. BMC Health Serv Res 2018;18:447.

51. Harris-Fry HA, Paudel P, Harrisson T, et al. Participatory women’s groups with cash transfers can increase dietary diversity and micronutrient adequacy during pregnancy, whereas women’s groups with food transfers can increase equity in intrahousehold energy allocation. J Nutr 2018;148:1472–83.

52. Saville NM, Shrestha BP, Style S, et al. Protocol of the Low Birth Weight South Asia Trial (LBWSAT), a cluster-randomised controlled trial testing impact on birth weight and infant nutrition of Participatory Learning and Action through women’s groups, with and without unconditional transfers of fortified food or cash during pregnancy in Nepal. BMC Preg Childbirth 2016;16:320.

53. Group VR. Baseline and follow-up surveys of community-based maternal neonatal care work in Jhapa, Banke and Kanchanpur districts. Nepal Family and Health Program. 2017. Available at: http://library.nhrn.gov. nps:8080/nhrn/bitsream/handle/123456789/173/536.pdf?sequence=1. Accessed October 20, 2020.

54. McPherson RA, Tamang J, Hodgens S, et al. Process evaluation of a community-based intervention promoting multiple maternal and neonatal care practices in rural Nepal. BMC Preg Childbirth 2010;10:31.

55. Mullany BC, Lakhey B, Shrestha D, Hindin MJ, Becker S. Impact of husbands’ participation in antenatal health education services on maternal health knowledge. JNMJ Nepal Med Assoc 2009;48:28–34.

56. Harsha Bangura A, Nirola I, Thapa P, et al. Measuring fidelity, feasibility, costs: an implementation evaluation of a cluster-controlled trial of group antenatal care in rural Nepal. Reprod Health 2020;1:7:5.

57. Maru S, Nirola I, Thapa A, et al. An integrated community health worker intervention in rural Nepal: a type 2 hybrid effectiveness-implementa- tion study protocol. Implement Sci 2018;13:53.

58. Karkee R, Lee AH, Binns CW. Birth preparedness and skilled attendance at birth in Nepal: implications for achieving millennium development goal 5. Midwifery 2015;29:1206–10.

59. Karkee R, Binns C, Lee A. Does birth preparedness package increase facility delivery? Results from a prospective cohort study in Nepal. Ann Glob Health 2014;80.

60. Karkee R, Baral OB, Khanal V, Lee AH. The role of obstetric knowledge in utilization of delivery service in Nepal. Health Educ Res 2014;29:1041–8.
61. Bhandari GP, Subedi N, Thapa J, Chouлагai B, Maskey MK, Onta SR. A cluster randomized implementation trial to measure the effectiveness of an intervention package aiming to increase the utilization of skilled birth attendants by women for childbirth: study protocol. BMC Pregnancy Childbirth 2014;14:109.

62. Acharya S, Robinson-Pant A. Women, literacy and health: comparing health and education sectoral approaches in Nepal. Compare: A Journal of Comparative and International Education 2019;49:211–29.

63. Kozuki N, Mullany LC, Khatry SK, et al. Validity of home-based sonographic diagnosis of obstetric risk factors by auxiliary nurse midwives in rural Nepal. Lancet Glob Health 2016;4:S23.

64. De A, Pandey MR, Shrestha A et al. Risk screening of expectant mothers at community level in western development region of Nepal. Nepal Journal of Epidemiology 2014; 4(2). Published online. Available at: http://www.nepjol.info/index.php/NJE. Accessed October 20, 2020.

65. Thapa K, Sanghvi H, Rawlins B, et al. Coverage, compliance, acceptability and feasibility of a program to prevent pre-eclampsia and eclampsia through calcium supplementation for pregnant women: an operations research study in one district of Nepal. BMC Pregnancy Childbirth 2016;16:241.

66. Feldhaus I, LeFevre AE, Rai C, et al. Optimizing treatment for the prevention of pre-eclampsia/eclampsia in Nepal: is calcium supplementation during pregnancy cost-effective? Cost Eff Resour Alloc 2016;14:13.

67. Witter S, Khadka S, Nath H, Tiwari S. The national free delivery policy in Nepal: early evidence of its effects on health facilities. Health Policy Plan 2011;26(Suppl2):i84–91.

68. Powell-Jackson T, Hanson K. Financial incentives for maternal health: impact of a national programme in Nepal. J Health Econ 2012;31:271–84.

69. Feroz A, Perveen S, Attab W. Role of mHealth applications for improving antenatal and postnatal care in low and middle income countries: a systematic review. BMC Health Serv Res 2017;17:704.

70. Colaci D, Chaudhri S, Vasan A. MHealth interventions in low-income countries to address maternal health: a systematic review. Ann Glob Health 2016;82:922–35.

71. Zeng W, Li G, Ahn H, Nguyen HTH, Shepard DS, Nair D. Cost-effectiveness of health systems strengthening interventions in improving maternal and child health in low- and middle-income countries: a systematic review. Health Policy Plan 2018;33:283–97.

72. Bhandari A, Gordon M, Shaka G. Reducing maternal mortality in Nepal. BJOG 2011;118(Suppl2):26–30.

73. Osrin D, Mesko N, Shrestha BP, et al. Implementing a community-based participatory intervention to improve essential newborn care in rural Nepal. Trans R Soc Trop Med Hyg 2003;97:18–21.

74. Sharma S, Ev Teijlingen, Belizán JM, Hundley V, Simkhada P, Sicuri E. Measuring what works: an impact evaluation of women’s groups on maternal health uptake in Rural Nepal. PLoS One 2016;11:e0155144.

75. Sharma BB, Loxton DJ, Murray H, et al. A first step to improving maternal mortality in a low-literacy setting; the successful use of singing to improve knowledge regarding antenatal care. Am J Obstet Gynecol 2018;219:615.e1–615.e11.