Community-based strategies including tetanus vaccination for preventing neonatal and/or maternal tetanus

Review of published reviews

1. Introduction

Maternal and neonatal tetanus (MNT) continues to be a serious public health problem. Despite the call by the World Health Assembly in 1988 to eliminate the disease, twenty-one countries, mainly in Africa and Asia, had not eliminated the disease by July 2015 and a few of the validated countries with interruption of services were at risk of "relapse".

MNT persists predominantly in very difficult to access areas where service delivery is generally compromised, affecting the poorest and least educated populations. Hence, MNT is a strong indicator of inequity in the provision of health services such as immunization and other related services.

Tetanus is caused by a neurotoxin produced by the gram-positive bacterium *Clostridum tetani* which forms spores. Tetanus begins when spores are introduced into damaged tissue. The disease may affect any age group, and case-fatality rates are high even where modern intensive care is available. The overall tetanus case-fatality rate varies between 10% and 70%, depending on treatment, age and general health of the patient. Without hospitalization and intensive care, fatality is almost 100% among the oldest and the youngest patients. In settings with optimal care, it may be reduced to 10–20%. The overwhelming majority of tetanus cases are birth-associated and occur in developing countries among newborn babies or in mothers following unclean deliveries and poor postnatal hygiene. [1]

Neonatal tetanus is defined as disease onset within the first 28 days of life, maternal tetanus is defined as disease during pregnancy or within 6 weeks of the end of pregnancy (independent of pregnancy ending with birth, miscarriage or abortion).

Tetanus can be prevented through immunization with tetanus-toxoid (TT) (-containing) vaccine (TTCV) which is recommended by WHO as part of routine immunization to children and women of reproductive age (WRA) in particular in high risk areas. [1] To obtain long-lasting immunity, after a primary series, booster doses are required. Neonatal tetanus (NT) can be prevented by immunizing WRA with tetanus toxoid, either during pregnancy or outside of pregnancy. This protects the mother and - through a transfer of tetanus antibodies to the fetus - also her baby. Additionally, clean (chord) practices when a mother is delivering a child are also important to prevent neonatal and maternal tetanus.

Beyond immunization, single interventions associated with a reduction in neonatal deaths tetanus include a) Hand washing of birth attendant with soap before birth; b) facility birth; c) Clean birth

surface; d) Cutting of the umbilical cord using a clean implement; e) Clean cord tying; f) postnatal cord antimicrobial applications; g) Avoidance of harmful postnatal cord applications.[2]

Impressive progress and achievements have been made to date for decreasing mortality related to neonatal and/or maternal tetanus. Successful implementation of MNT elimination activities that include among others, TT vaccination (including campaigns in high risk districts) as well as supplementary immunization activities (SIAs) targeted at WRA in high risk districts/population groups contributed to the declined from over 780,000 in 1988 to 49,000 in 2013 of the global estimated burden of neonatal tetanus. [1]. Improvement in third dose of Diphtheria-Tetanus-Pertussis (DTP3) vaccine coverage over the years has also positively impacted on reducing the incidence of MNT.

An improvement in access to skilled health professionals and use of the antenatal care (ANC) services to promote more visits, assess women and advise them on immunization and safe delivery practices and other health services opportunities have further contributed to the reduction of neonatal and maternal tetanus.

ANC is generally comprised of the following interventions: 1. Health promotion and education, 2. Disease prevention including immunization against tetanus, 3. Early detection and treatment for complications and diseases, 4. Birth preparedness and counselling of the pregnant woman on delivery, and 5. Complication readiness including an emergency plan for complicated deliveries. [3]

Community-based delivery strategies are widely recognized as important to deliver key maternal and child survival interventions [4-8]. These interventions, which often include ANC, have proven to be acceptable and feasible in the context of low resource settings. [9] Community-based interventions involve community health workers (CHWs) delivering preventive and therapeutic interventions such as immunization and antibiotics at home, community mobilisation through women's support groups, community mobilisers working through individual and group sessions, and community-based interventions delivered through non-governmental organisations or community volunteers. [5]

Given that the deadline for achieving elimination by 2015 was not met, the Strategic Advisory Group of Experts (SAGE) on immunization established a Working Group on maternal and neonatal tetanus elimination and broader tetanus control elimination in October 2015 to review the current evidence and propose next steps for MNT elimination and broader tetanus prevention for consideration by SAGE. In particular, the Working Group was tasked to discuss the role of strengthening integration of TT containing vaccines into antenatal care and other delivery platforms (e.g. school-based vaccination) and strategies to ensure clean deliveries as part of the "reset" agenda. Further the Working Group was asked to think out of the box including on how to capitalize on infant routine immunization and on the strategies that have to be adapted to the local context, like conflict affected areas, and linkages with other programmes targeting the poor and marginalized groups.

This review aims at identifying systematic reviews on community strategies targeted at the prevention of MNT morbidity and mortality and description of the impact of these interventions.

2. Methods

To identify relevant literature on community-based strategies for prevention of MNT, the following search strategy to answer the specific "Population (P), Intervention (I), Comparison (C), Outcome (O)- question" was applied:

Population/Setting	Intervention	Comparison	Outcomes
Pregnant women, neonates. Global, with focus on low- and middle income countries.	Community based strategies which either: a) Include tetanus immunization activities AND/OR b) aim at preventing tetanus related mortality	No intervention/ alternative interventions.	Primary outcome: Maternal and neonatal tetanus related mortality. Secondary outcome: Maternal immunization coverage.
PICO Question: What is the impact of community-based interventions on pregnant women and/or neonates compared to no intervention or alternative interventions in preventing maternal and neonatal deaths or increasing maternal immunization coverage?			

As the primary outcome, effect of the intervention on maternal and neonatal tetanus related mortality was defined. As immunization of pregnant women has shown to be effective in reducing [10] neonatal tetanus, this secondary outcome was chosen as a proxy for reduction of neonatal tetanus.

The specific search strategy can be found in Annex 1 Search termsDatabases searched were Pubmed and the Cochrane library. The search was conducted in July 2016 without time or language restrictions for reviews published by 10 July 2016. In addition, references of eligible reviews were screened to identify further publications. Experts of the SAGE Working Group on maternal and neonatal tetanus elimination and broader tetanus control were consulted to provide further relevant articles. Titles and abstracts of all identified publications were reviewed and screened for eligibility. Reviews were included when the following inclusion criteria were met:

Table 1: Inclusion and exclusion criteria

Inclusion Criteria	Exclusion criteria
a) were systematic or descriptive reviews or meta-analysis of community-based interventions or strategies aiming at reduction of maternal or neonatal mortality b) were published in journals, books or websites c) were written in English language d) included tetanus immunization as single intervention or integrated as one part of the delivered intervention e) reported interventions relate to: community-based intervention packages including home-based interventions f) reported outcomes related to: specific (tetanus related) neonatal and maternal mortality, tetanus immunization status, neonatal or maternal tetanus	a) Original studies b) Guidelines c) Letters d) Editorials

3. Results

The search yielded a total of 169 reviews, 13 full-text articles [2;10-22] were assessed for eligibility of which 7 were considered as relevant to address the research question. For the excluded studies screened for eligibility, see Annex 2. One systematic review meeting the inclusion criteria was retrieved manually and included in the review. [23] (see Figure 1). Table 2 presents a summary of the purpose, setting, outcomes, interventions, number of studies included as well as main outcomes of the retrieved reviews.

Figure 1: PRISMA flow diagram

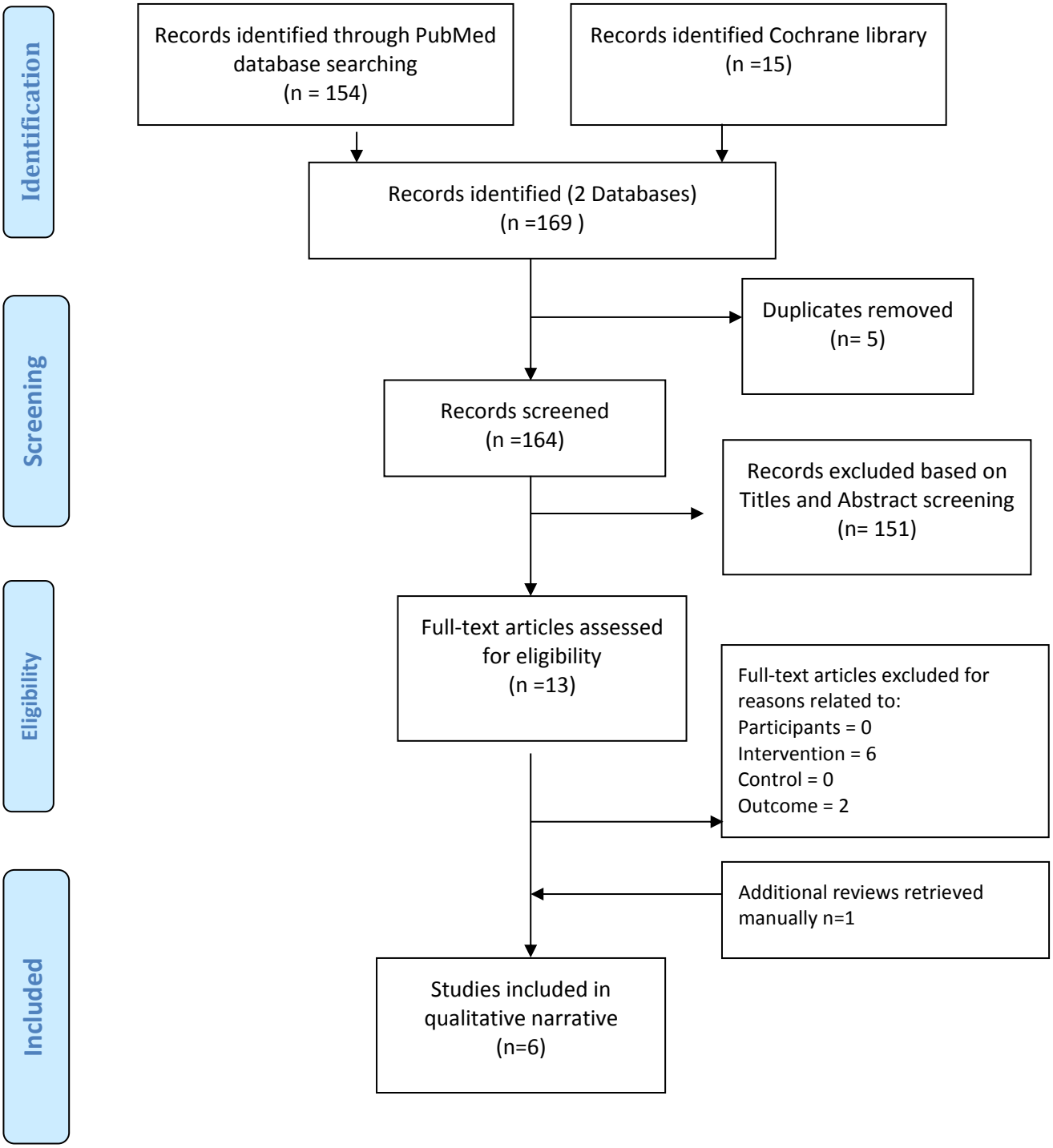

Table 2: Summary of literature reviews on community-based strategies including tetanus vaccination for preventing neonatal and/or maternal tetanus

Title, first author, year of publication	Description of the review			Number of studies included in review	Main conclusions of review
	Purpose	Outcome(s)	Interventions		
Home visits by community health workers to prevent neonatal deaths in developing countries: a systematic review. Gogia S. et al. 2010.	To determine whether home visits for neonatal care by community health workers can reduce infant and neonatal deaths and stillbirths in developing countries. Retrieved evidence from South Asia.	Outcome of interest: **Cause-specific neonatal mortality due to tetanus.** **Receipt of 2 dose TT immunization in pregnant women.** The primary outcome was the all-cause neonatal mortality rate, defined as the number of deaths from any cause in infants up to the age of 28 completed days (or 1 month) divided by the number of live births in the study population. Secondary outcomes included cause-specific neonatal mortality, deaths due to stillbirth rate, and care practices during pregnancy and delivery and in the postnatal period in trials providing data on neonatal mortality.	Included trials comparing groups that received different experimental interventions, including home visits for neonatal care by community health workers, with a control group that did not receive any home-based intervention by community health workers during the neonatal period. The interventions used were surveillance to identify pregnant women, home visits during pregnancy and after birth, community group education sessions and folk song meetings, advocacy with local leaders and health facility strengthening for maternal/neonatal care.	Total number of references included (n=13), which pertained to 5 trials: Baqui 2008 [24] Bhutta 2008 [4] Kumar 2008 [25] Baqui 2008 [26] Bang 1999 [27]	**Home-based neonatal care.** Only one trial [27] from India presented cause-specific mortality data for neonates but this trial did not contain information on the impact of the intervention on tetanus specific mortality. Four trials [4;24-26]reported a positive effect on receipt of ≥2 doses tetanus toxoid during pregnancy following home-based interventions (pooled relative risk of 1.11(1.04–1.18 95% CI)). Overall, there was evidence of a reduced risk of death during the neonatal period in association with home-based neonatal care; the pooled relative risk was 0.62 (95% CI: 0.44–0.87; I2 = 86.4%; p = 0.000).
Title, first author, year of publication	Description of the review			Number of studies included in review	Main conclusions of review
	Purpose	Outcome(s)	Interventions		
Home-based care for preventing neonatal mortality Gogia S. et al. 2016.	Assessment of the effect of home-based neonatal care provided by community health workers.	Outcomes of interest: **Cause-specific mortality including deaths due to neonatal tetanus.** Further outcomes included: Primary outcomes. All-cause mortality included: (i) neonatal	Experimental interventions comprised promotion of optimal neonatal care practices at home, with or without home-based treatment of neonatal morbidities, delivered by community health workers	Total number of references included (n=8), which pertained to 5 trial: Baqui 2008 [26] Bhandari 2012[28]	**Home-based neonatal care provided by community health workers.** Only one trial provided cause-specific mortality data in neonates in the form of rates in each comparison group without cluster-adjustment HRs. Darmstadt et al 2010 [29] reported that over the trial period, a number of tetanus-related deaths didn't decrease in the comparison group: 3

	Retrieved evidence from South Asia.	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. Secondary outcomes. These secondary outcomes included: (i) perinatal mortality rate; and (ii) cause-specific mortality including deaths due to neonatal sepsis, asphyxia and prematurity.	(CHWs) during the neonatal period, with or without additional interventions during pregnancy and/or childbirth. 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 counselling 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	Darmstadt 2010 [29] Bhutta 2011 [5] Kumar 2008 [25]	deaths at baseline (4.5% of all deaths [95% CI: 0.9–12.5]; 3 deaths at endline (2.3 [0.5–6.6])); and decreased in the intervention group from 2 deaths at baseline (4.8 [95% CI: 0.6–16.2]) to 1 death at endline (1.1 [95% CI: 0.0–5.8]). Overall, the intervention was associated with a reduced risk of all-cause mortality during the neonatal period; the pooled relative risk was 0.75 (95% CI 0.61 to 0.92, P = 0.003)

			problems; (iv) education to improve health care-seeking behaviours; (v) identification of signs of severe neonatal morbidities and referral to a health facility; or (vi) home-based management of neonatal morbidities.		
Title, first author, year of publication	Description of the review			Number of studies included in review	Main conclusions of review
	Purpose	Outcome(s)	Interventions		
Interventions to reduce neonatal mortality from neonatal tetanus in low and middle income countries--a systematic review. Khan et al. 2013.	Systematic review of original studies and systematic reviews to understand the interventions that have had a substantial effect on reducing neonatal mortality in low and middle income countries. Retrieved evidence from low- and middle-income countries.	Outcome of interest: **Reduction of neonatal mortality due to neonatal tetanus.**	Interventions meant to reduce neonatal mortality.	Total number of studies included (n=5). Of these 5 studies, 2 were original studies and 3 systematic reviews or reviews: Roper 2007 [19] Blencowe 2010 [30] Lassi 2010[31] Vandelaer 2009 [32] Ghosh 2010 [33]	**Community based interventions for reducing neonatal mortality.** For the results from the updated Cochrane systematic review [34], see respective summary below (Lassi et al. 2015). No additional quantitative effect of community based interventions was reported.
Title, first author, year of publication	Description of the review			Number of studies included in review	Main conclusions of review
	Purpose	Outcome(s)	Interventions		

Evidence from community level inputs to improve quality of care for maternal and newborn health: interventions and findings. Lassi ZS et al. 2014.	Review of all available systematic reviews published before May 2013 on pre-defined community level interventions. Retrieved evidence from high-, middle- and low income countries.	Outcome of interest: **Maternal TT Immunization status.** Other outcomes: Neonatal morbidity and mortality, maternal mortality, frequency of inappropriate and potentially harmful practices.	1. Outreach services (including home visitation and referrals): these services mainly include ANC, skilled birth attendance and early postnatal care (PNC) 2. Task shifting: these services include substituting specialized personnel with healthcare workers that are lesser trained but can perform some aspects of the tasks. 3. Training: this includes training of mid-level health workers to overcome the failure of providing birthing women with skilled attendance. 4. Formation of support groups for community mobilization: these services include community support groups and women's groups to enable the community to provide support to pregnant women and families throughout pregnancy and delivery.	Total number of studies included (n=43). Of these, 17 assessed outreach services (home visitation and referrals), 6 task shifting, 18 human resource/ training and 2 community mobilization. On the outcome of maternal tetanus immunization status 1 review included: Gogia 2010 [11]	**Intervention 1: Outreach services, home visitation and referrals** Home visits by community health workers (CHW) to improve neonatal health was associated with improved maternal TT immunization coverage (RR: 1.11, 95% CI: 1.04-1.18) [11] Intervention 2, 3 and 4 did not assess the effects on maternal TT immunization rates. No impact of interventions on cause-specific mortality was reported.
Title, first author, year of publication	Description of the review			Number of studies included in review	Main conclusions of review
	Purpose	Outcome(s)	Interventions		
Community-based intervention	To assess the effectiveness of	Outcome of interest: **TT immunization in pregnant women.**	Intervention packages that included additional training of outreach	Total number of studies included (n=26).	**Community-based intervention packages**. Statistically significant impact of community-based intervention packages was observed on maternal TT

packages for reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes. Lassi ZS et al. 2015	community-based intervention packages in reducing maternal and neonatal morbidity and mortality; and improving neonatal outcomes. Retrieved evidence from developing countries.	Other outcomes: Maternal mortality, Neonatal mortality (primary outcomes) and further secondary outcomes.	workers (residents from the community who are trained and supervised to deliver maternal and newborn care interventions to her target population) namely, lady health workers/visitors, community midwives, community/village health workers, facilitators or TBAs in maternal care during pregnancy, delivery and in the postpartum period; and routine newborn care.	Seven studies reported on the outcome on tetanus toxoid immunization status: Azad 2010 [35] Baqui 2008 [26] Darmstadt 2010[29] Gill 2011[36] Kumar 2008 [25] Midhet 2011 [37] Tripathy 2010 [38]	immunization (average RR 1.05; 95% CI: 1.02 to 1.09; seven studies, n = 71.279. [25;26;29;35-38]
Title, first author, year of publication	Description of the review			Number of studies included in review	Main conclusions of review
	Purpose	Outcome(s)	Interventions		
Health system and community level interventions for improving antenatal care coverage and health outcomes (Review). Mbuagbaw L et al. 2015	To assess the effects of health system and community interventions for improving coverage of antenatal care and other perinatal health outcomes. Retrieved evidence from high-, middle- and low income countries.	Outcome of interest: **The proportion of women with tetanus protection at birth.** Further outcomes included: 1. Coverage of ANC: the proportion of pregnant women who attend at least four ANC visits during pregnancy. 2. Pregnancy-related deaths: the proportion of women who die during pregnancy or 42 days after, irrespective of cause (primary outcomes) as well as further secondary outcomes.	All interventions aiming at improving ANC aiming at the community or at the health system. These could consist of: 1. Policy changes. 2. Health worker education. 3. Re-organisation of health services. 4. Mass media campaigns. 5. Social mobilisation. 6. Information-education-communication (IEC). 7. Financial incentives. 8. Behaviour change interventions.	Total number of studies included (n=34). Seven studies reported on the comparison of one intervention versus no intervention: Proportion of women with tetanus protection at birth: Lund 2012 [39] Persson 2013 [40] Barber 2008 [41] Morris 2004 [42] Baqui 2008 effect	**Health system and community level interventions.** Single interventions did not improve the proportion of women receiving TT protection, compared to no intervention. (average OR 1.03, 95% CI 0.92 to 1.15; studies = 8).[26;29;39-44] Combined interventions improved the proportion of women who had tetanus protection (average OR 1.48, 95% CI 1.18 to 1.87; studies = 3). [25;37;42] There was no evidence of group differences for women who received tetanus protection using a combination of interventions (average OR1.07, 95%CI 0.80 to 1.43; studies = 2; p = 0.18) [35;38].

				[26] Darmstadt 2010 [29] Villar 2001 [43] Basinga 2011[44] Three studies reported on the combination of interventions versus no intervention: Proportion of women with tetanus protection at birth: Kumar 2008 [25] Midhet 2010 [37] Morris 2004 [42] Two studies reported on the combination of interventions versus one intervention: Proportion of women with tetanus protection at birth: Azad 2010[35] Tripathy 2010 [38]	

The majority of the reviews were published in the last 3 years (n=5/6). The numbers of studies included in the retrieved reviews ranged from 5 to 43 (median: 19.5 studies).

Of the 6 reviews, 3 focused on low- and middle income countries, 1 on low-, middle- and high income countries and 2 on South Asia.

Only 1 review [13]focused specifically on the topic of reducing neonatal tetanus mortality. The remaining 5 studies focused on reduction of overall neonatal mortality, improvement of the quality of care for maternal and newborn health and improvement of antenatal care coverage and health outcomes.

In total, 3 reviews assessed the cause-specific neonatal mortality due to tetanus as an outcome [11;13;23]. Of the retrieved reviews, 4 [11;16;18;34] assessed the proportion of women with tetanus protection at birth as an outcome.

Out of the 6 reviews, although 3 reviews assessed neonatal tetanus mortality rates, only 1 review retrieved primary evidence, including raw case counts, on this outcome: Gogia et al 2016 [23] reported on one cluster-randomized controlled trial [29], which was assessed to be of low risk of bias. Darmstadt et al 2010 [29],from January 2004 to December 2006, compared the impact of community-level interventions which had been developed based on findings from formative research on newborn care practices in the study population. The trial was conducted in a sub-district of Bangladesh. The intervention arm included a total of 9.987 women of reproductive age with 5.031 pregnancy outcomes, the comparison arm included 11.153 women of reproductive age with a total of 5.669 pregnancy outcomes. The intervention used was a preventive service delivery strategy to promote birth and newborn care practices, through home visits by CHWs. CHWs were trained to promote antenatal care, including receiving two doses of tetanus toxoid vaccine, promote birth planning, distribute clean delivery kits and promote newborn-care preparedness. Neonatal tetanus-specific mortality estimates did not vary significantly by time or study arm. The intervention did further not significantly decrease the all-cause neonatal mortality which is in contrast to the conclusions of the review by Gogia et al 2016 [23], as well as the earlier review by Gogia et al conducted in 2010[11] which reported a positive effect on decreasing neonatal mortality in various settings in South Asia. [25-27]

This review of reviews further assessed the impact of community based interventions aiming at increasing the number of women with tetanus protection at birth. From the review conducted by Gogia et al 2010 [11], the interventions described in the retrieved publications were integrated packages of health education and services, delivered by community-based auxiliary nurses/midwife workers in rural districts of northern India [24] ; in rural Pakistan, a package of community based interventions for improving perinatal care were delivered by lady health workers and traditional birth attendants [4]; also in rural India a preventive package of interventions for essential newborn care (birth preparedness, clean delivery and cord care, thermal care (including skin-to-skin care), breastfeeding promotion, and danger sign recognition) along with provision of a hypothermia indicator delivered by community health workers via collective meetings and two antenatal and two postnatal household visitations [25]; and in Bangladesh (the study described in the previous paragraph), female CHWs identified pregnant women, made two antenatal home visits to promote birth and newborn-care preparedness, made postnatal home visits to assess newborns on the first, third, and seventh days of birth, and referred or treated sick neonates[26]. The pooled RR of these 4

studies was 1.11(95% CI 1.04 – 1.18) of receipt of ⩾2 TT doses following home-based interventions. The studies identified by Lassi et al 2014[16] also referred to this review.

Lassi et al 2015 [34] also reported significant impact of community-based intervention packages on maternal TT immunization (average RR 1.05; 95% CI 1.02-1.09). Seven studies were included which reported on the outcome on tetanus toxoid immunization status. Concerning the interventions used, Azad et al 2010 [35] investigated the impact of facilitators which convened groups every month to support participatory action and learning for women, and to develop and implement strategies to address maternal and neonatal health problem in Bangladesh; Gill 2011[36] used traditional birth attendants trained in neonatal resuscitation , and providing a single dose amoxicillin coupled with facilitated referral of infants to a health centre. Midhet et al 2011[37] provided women (and in parts their husbands) in rural Pakistan with information on safe motherhood through pictorial booklets and audiocassettes; traditional birth attendants were trained in clean delivery and recognition of obstetric and newborn complications; and emergency transportation systems were set up. Tripathy 2010 [38], in rural settings in India, used facilitators to convened community groups every month to support participatory action and learning for women, and facilitated the development and implementation of strategies to address maternal and newborn health problems. Darmstadt 2010 [29], Kumar 2008 [25] and Baqui 2008[26] used the interventions as outlined above.

In contrast to the other reviews which assessed the impact of a specific type of intervention on a predefined outcome, Mbuagbaw L et al. 2015 [18] assessed the impact of single versus combined interventions aiming at improving ANC aiming at the community or at the health system level. This included policy changes, the education of health workers, a re-organisation of health services, mass media campaigns and social mobilisation, interventions using the concept of IEC, financial incentives and behaviour change interventions. Although there were no estimates on the effect of the intervention(s) on neonatal or maternal tetanus mortality, the review concluded that a single intervention compared to no intervention and a combination of interventions versus one intervention had no significant impact on receipt of TT during pregnancy. Combined interventions did improve the proportion of women who had tetanus protection at birth with an OR of 1.48, (95% CI 1.18- 1.87), compared to no intervention. Two studies which reported the positive effect of the combined intervention were Midhet et al 2011[37] and Kumar 2008 [25] (see above for more information). Morris 2004 [42] assessed the effect of monetary incentive to the uptake of preventive care, comparing: money to households; resources to local health teams combined with a community-based nutrition intervention; both packages; and neither. Tetanus toxoid immunisation were not affected, with an OR of 1.03 (95% CI 0.63, 1.68) for combined intervention vs. no intervention.

Concerning the ratings of the quality of evidence, Gogia et al. 2010 [11] reported that the quality was assessed on the basis of the methods used for sampling and allocation. [45] Gogia et al 2016 [23]reported that the quality of the retrieved trials was assed using the Cochrane Collaboration risk of bias tool. [46] Khan et al 2013 [13] did not report on any risk of bias assessment of the retrieved evidence. Lassi et al 2014 [16] rated the overall quality of the retrieve reviews based on the AMSTAR criteria. Lassi et al 2015 [34] and Mbuagbaw et al 2015 [18]used the Cochrane Collaboration risk of bias tool for assessment of the quality of the reviewed studies.[46] Mbuagbaw graded the body of evidence using the GRADE approach.

4. Discussion

In terms of the findings of this review of pre-existing systematic reviews, the beneficial effect of community-based interventions on reduction of overall neonatal mortality was demonstrated. This review of reviews confirms that community-based interventions in particular, but not exclusively, in low- and middle-income settings remain a valid strategy for decreasing maternal and neonatal mortality and improving health outcomes in mothers and infants. [11;16;23] Nevertheless, little information could be retrieved on the effect of these interventions on cause-specific mortality, i.e. reducing maternal and neonatal tetanus. Although immunizing pregnant women has contributed greatly to the overall reduction of neonatal tetanus mortality, we could not retrieve a large number of reviews [11;16;18;34] reporting on the impact of community based interventions on the outcome of immunization status in pregnant women. It needs to be assessed whether tetanus immunization is not routinely included in community based interventions, or whether this outcome was perceived to be captured by measuring all-cause neonatal mortality.

When comparing single interventions versus no intervention, this did not improve the proportion of women receiving TT protection. Combined interventions compared to no interventions demonstrated to be more efficient in increasing the number of women who received tetanus protection. The beneficial effects of using multicomponent interventions rather than single-component interventions has been demonstrated also in the context of increasing immunization coverage in settings with vaccine hesitancy [47] and may be effective in reaching targeted individuals and communities in obtaining and supporting tetanus immunization coverage.

It needs to be encouraged that further research on community-based interventions assesses the cause-specific mortality, in particular on tetanus-related mortality and the impact on maternal TT immunization coverage. Further, it needs to be stressed that whenever the setting allows, TT immunization of pregnant women should be included as fundamental part of community based intervention packages as well as in ANC. [2]

5. Annexes

Annex 1 Search terms

Search terms used for pubmed search:

PubMed
("neonatal tetanus"[Title/Abstract] OR "maternal and neonatal tetanus"[Title/Abstract] OR "tetanus"[Title/Abstract]) AND ("communit*"[Title/Abstract] OR "strateg*" [Title/Abstract] OR "intervention" [Title/Abstract] OR pract*[Title/Abstract]) and filtered by reviews

Cochrane Database of Systematic Reviews (CDSR)

#Tetanus

Annex 2: Excluded studies

Title	Reason for exclusion
Lambo JA et al. 2012. Neonatal tetanus elimination in Pakistan: progress and challenges.	No data on community based interventions
Demicheli V et al. 2015 Vaccines for women for preventing neonatal tetanus. Cochrane Database Syst Rev. 2015	No data on community based interventions
Lassi et al. 2015 Interventions to Improve Neonatal Health and Later Survival: An Overview of Systematic	No assessment of the impact of community based interventions.
Gyorkos TW et al. 1994 Evaluation of the effectiveness of immunization delivery methods.	No assessment of the outcomes of interest.
Roper M et al. 2007 Maternal and neonatal tetanus.	No data on the impact of community based interventions.
Thayaparan B et al. 1998 Prevention and control of tetanus in childhood	No data on the impact of community based interventions
Vandelaer J et al. 2003 Tetanus in developing countries: an update on the Maternal and Neonatal Tetanus Elimination Initiative.	No data on the impact of community based interventions.
Seaterdal I, et al. 2014 Interventions aimed at communities to inform and/or educate about early childhood vaccination.	No assessment of the outcomes of interest.

Reference List

[1] Weekly epidemiological record No2288. Tetanus vaccine, WHO position paper. 21-7-2016. Ref Type: Online Source

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[3] Kinzie B, Gomez P, Chase R. Basic Maternal and Newborn Care: A Guide for Skilled Provider. JHPIEGO Corporation, 2004, 2004.

[4] Bhutta ZA, Memon ZA, Soofi S, Salat MS, Cousens S, Martines J. Implementing community-based perinatal care: results from a pilot study in rural Pakistan. Bull World Health Organ 2008 Jun;86(6):452-9.

[5] Bhutta ZA, Soofi S, Cousens S, et al. Improvement of perinatal and newborn care in rural Pakistan through community-based strategies: a cluster-randomised effectiveness trial. Lancet 2011 Jan 29;377(9763):403-12.

[6] Bhutta ZA, Das JK, Rizvi A, et al. Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? Lancet 2013 Aug 3;382(9890):452-77.

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[8] Bhutta ZA, Salam RA, Lassi ZS, Austin A, Langer A. Approaches to improve quality of care (QoC) for women and newborns: conclusions, evidence gaps and research priorities. Reprod Health 2014 Sep 4;11 Suppl 2:S5.

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[14] Lambo JA, Nagulesapillai T. Neonatal tetanus elimination in Pakistan: progress and challenges. Int J Infect Dis 2012 Dec;16(12):e833-e842.

[15] Lassi ZS, Haider BA, Bhutta ZA. Community-based intervention packages for reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes. Cochrane Database Syst Rev 2010;(11):CD007754.

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