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Clean birth and postnatal care practices to reduce neonatal deaths from sepsis and tetanus: a systematic review and Delphi estimation of mortality effect

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Abstract

Background: Annually over 520,000 newborns die from neonatal sepsis, and 60,000 more from tetanus. Estimates of the effect of clean birth and postnatal care practices are required for evidence-based program planning.

Objective: To review the evidence for clean birth and postnatal care practices and estimate the effect on neonatal mortality from sepsis and tetanus for the Lives Saved Tool (LiST).

Methods: We conducted a systematic review of multiple databases. Data were abstracted into standard tables and assessed by GRADE criteria. Where appropriate, meta-analyses were undertaken. For interventions with low quality evidence but a strong GRADE recommendation, a Delphi process was conducted.

Results: Low quality evidence supports a reduction in all-cause neonatal mortality (19% (95% c.i. 1–34%)), cord infection (30% (95% c.i. 20–39%)) and neonatal tetanus (49% (95% c.i. 35–62%)) with birth attendant handwashing. Very low quality evidence supports a reduction in neonatal tetanus mortality with a clean birth surface (93% (95% c.i. 77-100%)) and no relationship between a clean perineum and tetanus. Low quality evidence supports a reduction of neonatal tetanus with facility birth (68% (95% c.i. 47-88%). No relationship was found between birth place and cord infections or sepsis mortality. For postnatal clean practices, all-cause mortality is reduced with chlorhexidine cord applications in the first 24 hours of life (34% (95% c.i. 5–54%, moderate quality evidence) and antimicrobial cord applications (63% (95% c.i. 41–86%, low quality evidence). One study of postnatal maternal handwashing reported reductions in all-cause mortality (44% (95% c.i. 18–62%)) and cord infection ((24% (95% c.i. 5-40%)).
Given the low quality of evidence, a Delphi expert opinion process was undertaken. Thirty experts reached consensus regarding reduction of neonatal sepsis deaths by clean birth practices at home (15% (IQR 10–20)) or in a facility (27% IQR 24–36)), and by clean postnatal care practices (40% (IQR 25–50)). The panel estimated that neonatal tetanus mortality was reduced by clean birth practices at home (30% (IQR(20–30)), or in a facility (38% (IQR 34–40)), and by clean postnatal care practices (40% (IQR 30–50)).

Conclusion: According to expert opinion, clean birth and particularly postnatal care practices are effective in reducing neonatal mortality from sepsis and tetanus. Further research is required regarding optimal implementation strategies.

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Background

More than half a million newborns are estimated to die each year from serious neonatal infections, accounting for about 15% of all neonatal deaths globally [1]. The most vulnerable time for both the mother and newborn is during birth and in the hours and days immediately after childbirth. Around 75 percent of neonatal deaths occur during the first week of life, with the majority in the first 48 hours [2], which is also the period of highest risk for mothers [3]. In populations with very high neonatal mortality, up to half of neonatal deaths may have an infectious cause [4,5].

It is estimated that 30-40% of infections resulting in neonatal sepsis deaths are transmitted at the time of childbirth and have early onset of symptoms (developing during the first 72 hours after birth) [6,7]. In low income countries, about 60% of births occur without a

approaches including behaviour change communications, commodity provision, or training of attendants, or combinations of these, and the context may involve a facility birth or a home birth. Hand-washing with soap results in a large reduction in hand contamination, even when washed with unclean water [20], and birth attendant and maternal hand washing have been associated with reductions in neonatal mortality [21]. However cul-

Intervention definitions

Interventions considered in this review include clean birth practices at home or in a health facility, including hand washing, clean cord cutting and tying, clean birth surface, clean perineum, topical antiseptic applications to the cord and skin, and clean birth kit use. In addition clean postnatal newborn care practices and applications

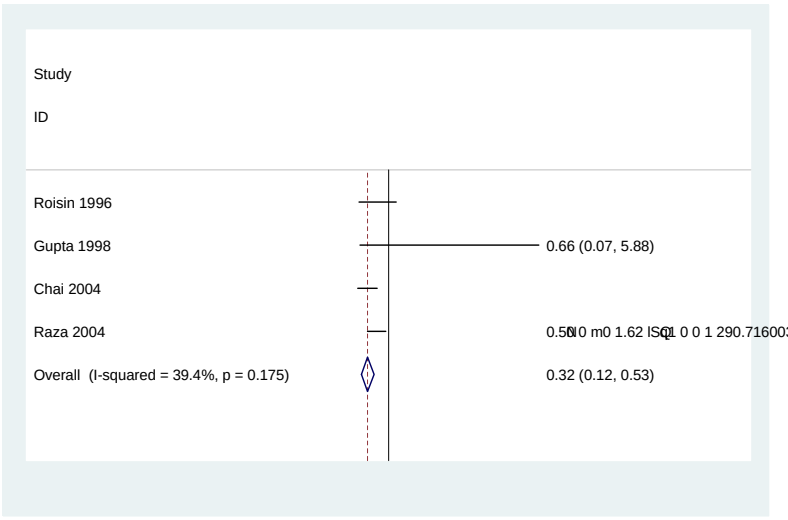
containing at least the minimum commodities required to facilitate clean cutting and tying of the umbilical cord e.g. a clean blade, clean cord tie or clamp.

From a programmatic viewpoint, how to change complex behaviours and cultural norms that govern practices around the time of birth is of great importance, but is not the focus of this paper (Figure 1).

Neonatal outcomes definitions

We used cause of death definitions consistent with the Child Health Epidemiology Reference Group (CHERG) based on ICD 10 rules [1,43]. Our outcomes of interest

effect of the clean practices is likely to be larger, and the evidence more applicable to decision makers in the countries using the LiST tool. The order of the results section follows the list in table 1



reductions in the incidence of cord infection associated with birth attendant hand-washing: aRR=0.73 (95% CI 0.64 – 0.84) [11] and aRR=0.58 (95% CI 0.40 – 0.84) [58], respectively. (Figure 4b)

c. Clean perineum (washed prior to birth)

Two case-control studies reported no association after adjustment between cleaning the perineum, with soap and water, and reduction in the incidence of neonatal tetanus [51,65]. No evidence on the effect of cleaning of the perineum on sepsis or infection was identified.

d. Clean birth surface (new or clean sheet or mat)

Two case-control studies controlling for potential confounders examined the association between using a clean plastic sheet as a birth surface and incidence of neonatal tetanus and reported aOR=0.31 (95% CI 0.10 – 0.91)[66] and aOR=0.03 (95% CI 0.002 – 0.34) [55]. One cohort study from Tanzania, with nearly universal kit use in the study population, did not find evidence of a protective effect of using a clean plastic sheet on incidence of cord infection after adjusting for potential confounding factors. However, the adjusted relative risk is not presented [56].

e. Cutting of the umbilical cord using a clean implement

Seven observational studies (4 case-control, 2 cohort, 1 adopter vs. non-adopter) were identified which examined the association of using a clean implement (a new/ boiled/ sterile blade or scissors) to cut the cord with neonatal sepsis or tetanus.

Five of these studies from Asia and one from Senegal examined the effect on neonatal tetanus incidence or mortality. Two case-control studies and one cohort study which sought to adjust for confounders reported strong evidence of lower neonatal tetanus mortality associated with use of clean cord cutting tools [aOR=0.3 (95% CI 0.13 – 0.62)[60], aOR=0.4 (95% CI 0.24 – 0.66) [61], and aOR0.25 (95% CI 0.08 – 0.75)][63].Three studies did not find strong statistical evidence of an association between tetanus and the use of an old razor blade or scissors versus a new blade after controlling for potential confounders but no parameter estimates were reported [51,64,66].

One study of clean birth kits from Tanzania examined the effect of the use of a new blade on cord infection. There was no reduction in cord infection associated with the use of new blades [aOR=1.1 (0.43 – 3.05)]. However, the level of new blade use was >95%, and those not using new blades may have used boiled blades [59].

f. Clean cord tying

Four case-control studies examined the association between use of a 'new clean thread' to tie the umbilical cord at birth and neonatal tetanus incidence or mortality. A study from Uganda using hospital-based cases reported an aOR of 0.1 (95% CI 0.01 – 1.1) for clean cord tie use [55]. The three other studies reported no difference after adjusting for potential confounders, but do not present adjusted odds ratios [52,64,66].

An urban community case-control study compared use of a cord clamp versus 'thread' to tie the cord, and found no evidence of a difference in tetanus incidence between the two groups in multivariate analysis, where home birth and cord applications were the most important risk factors [51]. A cohort study in Tanzania did not observe any association between use of the clean birth kit thread and incidence of cord infection [56], but use was near-universal.

2. Hygienic cord and skin care

a. Combined chlorhexidine cleansing of the birth canal prior to birth and/or full body newborn cleansing immediately after birth

Vaginal washing with chlorhexidine has been shown to reduce colonization rates with Group B streptococcus in high income countries [49]. The most recent Cochrane review found no strong evidence of an effect on neonatal infections [50]. Five low and middle income country-based studies were examined which all used both vaginal and neonatal wipes. Two before-and-after hospital-based studies in Egypt and Malawi reported reductions in infection-related neonatal mortality with chlorhexidine compared to routine care [RR=0.26 (95% CI0.1 – 0.7) [67] and RR=0.33 (95% CI 0.15 – 0.70)[68]. A community-based pilot randomized controlled trial (RCT) from Pakistan of chlorhexidine versus saline vaginal and neonatal wipes did not report infection-specific outcomes and was too small to conclude anything with respect to neonatal mortality [RR=0.20 (95% CI 0.01 – 4.03)] [69]. A large randomised controlled trial (RCT) from South Africa based in a hospital with low infection rates did not find evidence of a difference in rates of sepsis with chlorhexidine vaginal and neonatal wipes compared to external genitalia water wipes and neonatal chlorhexidine foot wipes RR=0.95 (95% CI 0.76 – 1.19) [70]. Consistent with this finding, a recent large RCT based in three hospitals in Pakistan, which compared chlorhexidine vaginal and neonatal wipes to saline placebo wipes, found no difference in the primary study

outcome (7 day neonatal mortality or neonatal sepsis) between the groups RR=0.91 (95%CI 0.67 – 1.24) or overall neonatal mortality at 28 days RR=0.98 (95% CI 0.68 – 1.41) [71].

neonatal mortality (sunflower oil [aRR 0.74(95% CI: 0.55–0.99) and using Aquaphor [aRR 0.67 (95% CI: 0.51–0.92)] [79]) in these preterm infants.

However, evidence of benefit is currently limited to

Hand-washing with soap prior to birth

Published data from four low or very low quality studies [60-63] are consistent in suggesting a reduction in tetanus mortality of 49% (95% CI 35 – 62%). A single study suggested benefit on all-cause neonatal mortality of 19% (95% CI 1 – 34%) [21]. Two low quality studies are consistent in suggesting a reduction in cord infection of 30% (95% CI. 20 – 39%) [11,58] (Table 3).

Other clean birth practices

All studies are consistent with a beneficial effect of clean

Table 3

Quality Assessment		Summary of Findings	
	Generalisability	Intervention	Control

Table 4

Quality Assessment								Summary of Findings				
					Generalisability			Intervention		Control		
No of studies (ref)	Intervention	Design	Limitations	Consistency	To population of interest	To intervention of interest	GRADE of evidence	No. events	No. births	No. events	No. births	Effect size (95% CI)
Neonatal Mortality (Tetanus Deaths):												
No studies identified												
Neonatal Mortality (Sepsis Deaths):												
3 (67, 68, 70)	Chlorhexidine vaginal and baby wipes	1 RCT, 2 Before and after	Hospital based studies	Heterogeneity	S.Africa, Malawi, Egypt	Yes	Moderate	21	10108	55	9612	
1 (73)	Chlorhexidine to cord (day 1)	cRCT ˇ	Single study		Nepal	Yes	Moderate		3134		3179	RR = 0.69 (0.40 - 1.18)
Neonatal Mortality (All Cause):												
1 (73)	Chlorhexidine to cord	cRCT	Single study		Nepal	Yes	Moderate	72	4924	98	5082	RR = 0.78 (0.57 - 1.07)*
1 (73)	Chlorhexidine to cord (day 1)	cRCT ˇ	Single study		Nepal	Yes	Moderate	45	3134	69	3179	RR = 0.66 (0.46 - 0.95)
1 (72)	Chlorhexidine wipes to baby	cRCT	Single study		Nepal	Yes	Moderate	264	860	263	8880	RR = 1.04 (0.87 - 1.24)
1 (72)	Chlorhexidine wipes to baby	cRCTˇ	Single study		Nepal	Low birth weight babies only	Moderate	831.1b:				

Table 5

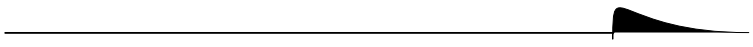
Quality Assessment					Summary of Findings						
					Generalisability		Intervention		Control		
No of studies (ref)	Intervention	Design	Limitations	Consistency	To population of interest	To intervention of interest	No. Events	No. births	No. events	No. births	Effect size (95% CI)
Neonatal Mortality (Tetanus Deaths):											
1 (18)	CBK and education	Before and after	Low quality		Masai population*	Yes	0	1984	415	5716	RR = 0.01 (0.001 - 0.09)
1 (80)	CBK, TT plus multiple interventions	Before and after	Multiple interventions		India. Lady health worker delivered	Multiple interventions	0	1951	2	1958	OR = 0.20 (0.01 - 4.18)
Neonatal Mortality (Sepsis Deaths):											
No studies identified											
Neonatal Mortality (All Cause):											
1 (81)	CBK plus multiple interventions	cRCT	Multiple interventions		Pakistan TBA delivered	Multiple interventions	340	10092	439	19432	aOR 0.71 (0.62 - 0.83)
1 (18)	CBK and education	Before and after	Low quality		Masai population*	Yes	99	1984	1984	5716	RR = 0.17 (0.13 - 0.23)
1 (80)	CBK, TT plus multiple interventions	Before and after	Multiple interventions		India lady health worker delivered	Multiple interventions	35	1951	45	1958	OR 0.78 (0.50 - 1.21)
Neonatal Sepsis incidence:											
1 (84)	CBK and demonstration	Before and after	Observational		Papua New Guinea**	Yes	1	67	8	64	OR = 0.11 (0.01 - 0.84)
Cord infection/oomphalitis:											
3 (56, 58, 59)	CBK use	Adopters vs non-adopters	Observational	Heterogeneous	Egypt, Tanzania, Nepal	Yes					aOR 0.08-0.45
1 (11)	Use of individual items in CBK	Adopters vs non-adopters	Observational		Nepal	Yes					soap aRR = 0.49 (0.43-0.56)^

*Specific cultural practices and defined neonatal death as death occuring in first 6 weeks of life **Specific cultural practices.

^ no effect of other components on multivariable analysis TT = tetanus toxoid vaccination.

Table 6 Results from the Delphi expert consensus process

		Median (%)	Range (%)	Inter-quartile Range (%)
Effect on sepsis specific neonatal mortality	1. Effect of **clean birth practices at home without a skilled attendant** on sepsis specific neonatal mortality	15	5 – 30	10 – 20
	2. Effect of **clean birth practices at home with a skilled attendant** on sepsis specific neonatal mortality	23	10 – 50	19 – 30
	3. Effect of **clean birth practices in a facility** on sepsis specific neonatal mortality	27	5 – 60	23.75 – 36.25
	4. Effect of **clean newborn care practices at home during the postnatal period** on sepsis specific neonatal mortality	95T(mor7)-3e9(mortality)]TJ9(atnj.1Tf000140h-329(ofa-24		



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Authors' contributions
JL planned the review with HB who undertook the searches and abstraction. HB and JL drafted the manuscript. ACL contributed to the design of the Delphi process. HB produced the meta-analysis. SC provided statistical support. All authors contributed to the data review and to the manuscript.

Competing interests
The authors all declare no conflict of interest.

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