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Scaling up interventions to eliminate neonatal tetanus: Factors associated with the coverage of tetanus toxoid and clean deliveries among women in Vientiane, Lao PDR

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ABSTRACT

The Lao People's Democratic Republic (PDR) is one of seven countries that have not eliminated maternal and neonatal tetanus in more than 50% of districts. We conducted a community-based household survey to assess the achievements of strategies towards maternal and neonatal tetanus elimination in the capital province. The coverage of tetanus toxoid (TT) was 79.7% by the protection-at-birth (PAB) method. The percentages of deliveries attended by skilled personnel and of deliveries at a health facility were 68.4% and 63.7%, respectively. The progress towards eliminating neonatal tetanus in Lao PDR is not sufficient despite the study sites being placed in the capital province. The lack of continuum of care for mothers and newborns is the major obstacle to scale up the tetanus toxoid coverage and PAB as well as clean deliveries.

1. Introduction

Neonatal tetanus is one of the major causes of neonatal deaths. It can be prevented by simple and cost-effective interventions including tetanus toxoid (TT) vaccine and clean delivery among pregnant women. Neonatal tetanus nevertheless continues to be a major public health problem in low-income countries, mostly in Asia and Africa [1]. Since 1989, a joint effort to eliminate maternal and neonatal tetanus by the year 2005 had been implemented, notably by the World Health Organization (WHO), the United Nations Children's Fund (UNICEF), and the United Nations Population Fund (UNFPA). In their strategy document, the elimination of neonatal tetanus is defined as less than one case per 1000 live births in every district in every country [2]. To achieve this goal, scaling up of TT and clean deliveries, together with timely and accurate surveillance systems, have been promoted [3].

Such a concerted effort has contributed to a substantial reduction in the burden of neonatal tetanus around the world. Although there is no consistent time-series estimate of the burden of neonatal tetanus, one study suggested that in 1988, neonatal tetanus accounted for 787,000 neonatal deaths globally [1]. The recent estimate from a systematic review of available data showed that, in 2000, the number of neonatal deaths from tetanus was around 200,000 (or 7% of all neonatal deaths) [4]. However, neonatal deaths in developing countries often take place at home and the lack of death registration with causes of death makes it difficult to assess the true magnitude of the disease burden from neonatal tetanus. One government report suggested a mortality rate from neonatal tetanus of 0.1 per 1000 live births in 2000 [5], but the subsequent retrospective verbal autopsy study in rural areas reported a much higher cause-specific mortality rate, ranging from 8.6 to 10.5 per 1000 live births [6].

Neonatal tetanus is still endemic in Lao PDR—one of the poorest countries in the world—due to the stagnation of both TT and clean delivery coverage. Although vaccine has been offered free of charge throughout the country, the nationwide coverage from the latest UNICEF's Multiple Indicators Cluster Survey (MICS3) in 2006 showed that the proportion of pregnant women who received at least two doses of TT (TT2+) was 38%, a decline from 45% in MICS1 (1995) [7,8]. Laotian government's report, which is not nationally representative, also consistently suggests the declining trend in TT2+ coverage since 2000 [8].

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Table 1
Sample characteristics.

		n	(%)
Age	Mean ± SD	30.7 ± 6.9	
	15–19	5	(2.4)
	20–29	100	(47.2)
	30–39	79	(37.3)
	40–45	28	(13.2)
Ethnicity			
	Lao Lum	210	(99.1)
	Lao Theung	2	(0.9)
Distance to hospital			
	≤3 km	67	(28.2)
	>3 km	145	(71.8)
Household monthly income (Kip)[a]			
	Median	400,000	
	Lowest quartile (<200,000)	47	(22.2)
	Middle 50% (200,000–600,000)	113	(53.3)
	Highest quartile (>600,000)	52	(24.5)
Husband's education (years)			
	Mean ± SD	7.8 ± 4.0	
	0	13	(6.1)
	1–5	65	(30.7)
	≥6	134	(63.2)
Wife's education (years)			
	Mean ± SD	6.2 ± 3.2	
	0	7	(3.3)
	1–5	111	(52.4)
	≥6	94	(44.3)
Parity			
	Mean ± SD	2.3 ± 1.4	
	Primiparous	71	(33.5)
	Multigravida	141	(66.5)
Wife's occupation			
	Housewife	78	(36.8)
	Work outside	134	(63.2)
Radio usage			
	No	52	(24.5)
	Yes	160	(75.5)
Key source of information			
	Village staff	156	(73.6)
	Others	56	(26.4)
Total number		212	

[a] 10,000 Kip = US$ 1 (September, 2005).

Likewise, the WHO–UNICEF estimate of the protected-at-birth (PAB), which takes into account the duration between last TT and delivery and is more accurate measure of the effectiveness of TT, has declined from 58% in 2000 to 47% in 2007 [9]. Studies in rural areas showed that geographical barriers and lack of knowledge were the two major obstacles in scaling up vaccine coverage [10,11].

The clean delivery coverage is also low, as shown in official report in 2001: the proportion of deliveries assisted by skilled personnel such as medical doctor, nurse, and midwife and of institutional deliver was 21% and 15%, respectively [12]. Data from MICS2 in 1999 are consistent with these findings [13]. In addition, unhygienic practices by non-skilled personnel are very common. Some report cases where the umbilical cord is cut with a kitchen knife or piece of bamboo. Traditional beliefs are influential factors tending to lower the clean delivery coverage rate [10,11].

Despite the efforts made by UNICEF, which launched the major activity to eliminate neonatal tetanus in Lao PDR in 2003, the coverage of interventions to tackle neonatal tetanus show a declining trend during the past 5 years. As no community-based representative household surveys of vaccine practices and clean delivery have been done recently, the major objective of the present study was to identify the factors associated with scaling up of the tetanus toxoid and clean delivery coverage in Lao PDR in the context of maternal and neonatal tetanus elimination.

2. Methods and materials

2.1. Study sample

This study employed multi-stage probabilistic sampling. In the first stage, five districts with a total population of 5653 were selected randomly from eight districts in Vientiane Municipality. One village from each district was selected randomly. In Lao PDR, a typical village consists of 20 subunits, which in general include 10 households. In the final stage, we selected subunits randomly and visited all households within a subunit to sample up to 30% of all registered women with children under 5 years of age.

A face-to-face interview with 212 mothers in total selected from 806 households was done from September to October 2005. These five villages were accessible by car within two hours from the center of the capital. We asked village leaders to request the mothers to stay at home on the day of the interview. The study team included two Expanded Program on Immunization officers, a gynecologist from the National Medical University of Lao PDR, three trained staff members with a medical background, and a Japanese researcher. Informed consent was obtained from the respondents before the interview.

2.2. Questionnaire

The survey questionnaire was developed by modifying and refining a field manual developed by WHO and the questionnaires used previously in Lao PDR [14]. The local expert translated the draft

Table 2
Characteristics at last delivery.

	n	(%)
Protected at birth		
Yes	169	(79.7)
No	43	(20.3)
Minimum 2 doses of TT		
Yes	109	(51.4)
No	103	(43.6)
Confirmation of TT		
Vaccination card	167	(78.8)
Recall	45	(21.2)
Number of antenatal care visits		
Mean±SD	5.7 ± 3.0	
0	14	(6.6)
≥1	198	(93.4)
Antenatal care from skilled personnel[a]		
Yes	189	(95.5)
No	9	(4.5)
Antenatal care including TT counseling		
Yes	168	(84.8)
No	30	(15.2)
Delivery assistance		
Skilled personnel[a]	145	(68.4)
Others	67	(31.6)
Delivery at health facility		
Yes	135	(63.7)
No	77	(36.3)
Previous death of child		
Yes	40	(18.9)
No	172	(81.1)
Total number	212	

[a] Skilled personnel is defined as medical doctor, nurse or midwife.

Table 3
Multivariate logistic regression model.

		Protection-at-birth		Delivery by skilled birth attendant		Delivery at health facility	
		OR	95% CI	OR	95% CI	OR	95% CI
Age	Younger than 30	1		1		1	
	30 or more	0.93	0.38–2.27	1.91	0.82–4.45	2.37	1.04–5.42
Distance to hospital	≤3 km	1		1		1	
	>3 km	0.62	0.24–1.57	1.66	0.72–3.81	1.74	0.79–3.84
Household income	≤Median	1		1		1	
	>Median	1.6	0.65–3.89	0.42	0.19–0.93	0.58	0.27–1.25
Husband's education	≤5	1		1		1	
	>6	1.08	0.41–2.84	0.88	0.41–1.91	0.71	0.33–1.51
Wife's education	≤5	1		1		1	
	>6	2.48	1.04–5.88	0.45	0.21–0.96	0.47	0.23–0.98
Wife's occupation	Housewife	1		1		1	
	Work outside	0.544	0.23–1.31	2.17	0.94–5.00	2.43	1.10–5.40
Radio usage	No	1		1		1	
	Yes	1.45	0.76–2.77	1.11	0.66–1.86	1.24	0.75–2.07
Key person of TT	Village staff	1		1		1	
	Others	0.62	0.27–1.42	1.82	0.82–4.04	3.06	1.38–6.81
Parity	Primipara	1		1		1	
	Multigravida	8.38	2.35–29.84	1.27	0.50–3.22	1.06	0.44–2.60
Previous death of child	No	1		1		1	
	Yes	0.71	0.28–1.84	0.57	0.25–1.31	0.41	0.18–0.91
Antenatal care received a minimum of four times	No	1		1		1	
	Yes	1.2	0.42–3.48	3.85	1.52–9.80	4.24	1.65–10.87
Antenatal care including TT counseling	No	1		1		1	
	Yes	3.12	1.16–8.43	1.04	0.39–2.78	0.91	0.34–2.42

questionnaire into Laotian, and a back translation was done by two trained researchers to check consistency. After a pilot test, the final set of modules was agreed upon among Laotian researchers and interviewers, including (1) socio-demographic characteristics, (2) complete history of TT vaccination, (3) knowledge about TT, (4) detailed birth and pregnancy history with information about related medical care practices, (5) child health outcomes, (6) attitudes and practices related to health-related activities. In addition to the face-to-face interviews with administration of the questionnaire, information on the participants' immunization history around the last pregnancy and delivery of their youngest child was recorded from vaccination cards where available. If respondents did not keep vaccination records, approximate dates of TT were collected from mothers' recall [15,16].

2.3. Statistical analysis

All statistical analysis was done by SPSS version 11.0J. The coverage of interventions was estimated for TT2+ during the last pregnancy, PAB, and clean deliveries. We estimated PAB by counting children whose mothers met the following criteria: (A) two or more doses of TT during the last pregnancy; (B) one TT during the last pregnancy and one or more doses prior to the last pregnancy; and (C) no TT during the latest pregnancy, but two or more doses prior to the last pregnancy and mothers still in the expected period of protection at the last delivery [17]. In case the mothers were classified as category (C), they are considered to be protected if the following conditions are met: (1) received at least two doses of TT, the last within the prior 3 years; (2) received at least three doses, the last within the prior 5 years; (3) received at least four doses, the last within 10 years; or (4) received at least five doses during lifetime [17].

The coverage of clean delivery was estimated by the percentage of deliveries which took place at a health facility and by the percentage of deliveries which were assisted by certified medical personnel (medical doctor, nurse, or midwife), regardless of the place of delivery. Multivariate logistic regression was used to assess the relationship between the intervention coverage and covariates.

3. Results

Table 1 shows the sample characteristics of 212 respondents in the present study. Respondents were women with children less than 5 years of age, and primarily of Lao Lum ethnic origin. Their mean age was 30.7 years with a standard deviation of 6.9 years. The overall response rate was 100%.

Respondents had immunization records with the type and dates of past vaccinations. Table 2 represents the coverage of interventions for neonatal tetanus. The coverage of tetanus toxoid among mothers measured by TT2+ during the last pregnancy and PAB were slightly higher than national averages in previous surveys: 51.4% and 79.7%, respectively. The proportions of delivery attended by skilled personnel and delivery at health facility were 68.4% and 63.7%, respectively.

The regression results of the multivariate logistic models are shown in Table 3. Outcome variables included PAB, delivery assisted by skilled birth attendant (doctor, nurse, or midwife), and delivery at a health facility, and their association with explanatory variables was examined.

Table 3 represents the adjusted odds ratios for the explanatory variables on outcome variables. Neonates who were born to the mothers with higher education, who had experienced delivery before, and who had received antenatal care (ANC) with counseling about TT were more likely to be protected against tetanus at birth. Mothers who had an occupation and more chances to receive antenatal care were more likely to deliver assisted by a skilled birth attendant or deliver at a health facility. Monthly household income was also associated with assisted delivery. Mother's age, deaths of a

child in the past and key person for TT (i.e., a person who encourages mothers to get vaccinated for TT such as members of Lao Women's Union) were also associated with institutional delivery. Traditional practices during pregnancy were common among respondents but were not statistically significant.

4. Discussion

This study was, as far as we know, the first community-based study to investigate simultaneously the coverage of tetanus toxoid vaccination and clean delivery in Lao PDR in the context of the maternal and neonatal tetanus elimination initiative. In this study, the coverage of tetanus immunization was 51.4% when measured as TT2+ during the last pregnancy and 79.7% when PAB was used. The coverage estimates in the present study were higher than national averages (38.1% and 55.5% for TT2+ during the last pregnancy and PAB, respectively) but consistent with the results for the urban area (47.4% and 69.6% for TT2+ and PAB, respectively) [7]. Relatively high coverage in the present study is not surprising as the study was done in the capital where many Expanded Program on Immunization activities as well as routine activities and campaigns have been in place. The discrepancy between TT2+ during the last pregnancy and PAB suggests that evaluation only by TT2+ would underestimate the protection against tetanus [18].

Facility-based records are generally poor sources of representative PAB data and thus periodic household surveys or a combination of the two measures would be necessary to obtain consistent and timely information on PAB, particularly in rural areas. Furthermore, it is important to scale up the coverage of DTP1 sufficiently so that PAB estimates can provide accurate monitoring [18]. The national coverage of DTP1 by 12 months of age was 64.1% in 2006 [7]. Thus, in Laos, TT and DPT continue to be an integral part of an Expanded Program on Immunization program not only to maximize the accuracy of PAB monitoring but also to prevent tetanus more effectively.

In the latest MICS3, 20.3% and 67.8% of deliveries in 2006 were assisted by skilled birth attendants in Lao PDR as a whole and in the urban area, respectively [7]. In the present study, 68.4% of deliveries were assisted by skilled birth attendants. According to the classification suggested by Roper et al., the study area with the coverage of clean delivery less than 70% and TT2+ less than 80% in the setting without robust surveillance system is categorized as high risk area concerning to the risk of neonatal tetanus [1]. More efforts to promote clean delivery are needed. Given the low coverage of delivery by skilled birth attendant and given the lack of emergency obstetric services, more effective use of available services and training of traditional birth attendants, although controversial in its efficacy, should be considered with operational research if needed [19–21].

There was a statistically significant positive association between antenatal care services and the coverage of tetanus toxoid and clean deliveries, which is consistent with previous studies in other countries [22–24]. However, the causal relationship between ANC, skilled birth attendants, and immunization is difficult to confirm. In the present study, the distance from health facilities, which was one of the key determinants of service coverage in previous studies, was not associated with any of the dependent variables. Possible explanations might be that the study site was located in the capital province and health facilities were accessible by road vehicles. The majority of them were classified as "Zone 0" or "Zone 1", which is located within approximately 15 km from the nearest health facility, according to the classification used by EPI programs in Lao PDR.

This study has several limitations. First, 21.2% of respondents did not have a vaccine card, and thus information on vaccination status was based on mothers' recall, which is obviously subject to recall bias. However, the recent analysis of the extent of recall bias by using the same cohorts in two consecutive Demographic and Health Surveys showed that any potential differences in rates due to recall were within the survey's sampling error [16]. Thus, we combined information both from vaccination card and mothers' recall when estimating the coverage of tetanus toxoid. Second, the present study would have missed those mothers whose children had died in the period between birth and the survey due to neonatal tetanus. Although the coverage estimate was consistent with other nationally representative survey [7,13], the exclusion of such mothers would have over-estimated the coverage of tetanus toxoid and underestimated the magnitude of the problem. Third, TT2+ in the present study was evaluated when two or more doses during last pregnancy were given within 5 years. Routine vaccine coverage in the government reports are based on the data collected for each calendar year. Therefore, figures from this study and figures from routine activity are not directly comparable. Finally, the study design does not allow an assessment of causal relationships, because it was a cross-sectional study designed to assess the current situation in Lao PDR.

Despite these limitations, however, and despite the fact that the study sites were located in the capital province, the present study shows that the progress made towards eliminating neonatal tetanus in Lao PDR is insufficient. The lack of continuum of care for mothers and newborns is the major obstacle to scaling up of tetanus toxoid coverage and PAB as well as clean deliveries. Although the Global Immunization Vision and Strategy (GIVS) launched in 2005 focuses on rural areas [25], its current status in Lao PDR is insufficient to achieve the goal of eliminating neonatal tetanus.

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1. Introduction

Neonatal tetanus is one of the major causes of neonatal deaths. It can be prevented by simple and cost-effective interventions including tetanus toxoid (TT) vaccine and clean delivery among pregnant women. Neonatal tetanus nevertheless continues to be a major public health problem in low-income countries, mostly in Asia and Africa [1]. Since 1989, a joint effort to eliminate maternal and neonatal tetanus by the year 2005 had been implemented, notably by the World Health Organization (WHO), the United Nations Children's Fund (UNICEF), and the United Nations Population Fund (UNFPA). In their strategy document, the elimination of neonatal tetanus is defined as less than one case per 1000 live births in every district in every country [2]. To achieve this goal, scaling up of TT and clean deliveries, together with timely and accurate surveillance systems, have been promoted [3].

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	Others	56	(26.4)
Total number		212	

[a] 10,000 Kip = US$ 1 (September, 2005).

Likewise, the WHO–UNICEF estimate of the protected-at-birth (PAB), which takes into account the duration between last TT and delivery and is more accurate measure of the effectiveness of TT, has declined from 58% in 2000 to 47% in 2007 [9]. Studies in rural areas showed that geographical barriers and lack of knowledge were the two major obstacles in scaling up vaccine coverage [10,11].

The clean delivery coverage is also low, as shown in official report in 2001: the proportion of deliveries assisted by skilled personnel such as medical doctor, nurse, and midwife and of institutional deliver was 21% and 15%, respectively [12]. Data from MICS2 in 1999 are consistent with these findings [13]. In addition, unhygienic practices by non-skilled personnel are very common. Some report cases where the umbilical cord is cut with a kitchen knife or piece of bamboo. Traditional beliefs are influential factors tending to lower the clean delivery coverage rate [10,11].

Despite the efforts made by UNICEF, which launched the major activity to eliminate neonatal tetanus in Lao PDR in 2003, the coverage of interventions to tackle neonatal tetanus show a declining trend during the past 5 years. As no community-based representative household surveys of vaccine practices and clean delivery have been done recently, the major objective of the present study was to identify the factors associated with scaling up of the tetanus toxoid and clean delivery coverage in Lao PDR in the context of maternal and neonatal tetanus elimination.

2. Methods and materials

2.1. Study sample

This study employed multi-stage probabilistic sampling. In the first stage, five districts with a total population of 5653 were selected randomly from eight districts in Vientiane Municipality. One village from each district was selected randomly. In Lao PDR, a typical village consists of 20 subunits, which in general include 10 households. In the final stage, we selected subunits randomly and visited all households within a subunit to sample up to 30% of all registered women with children under 5 years of age.

A face-to-face interview with 212 mothers in total selected from 806 households was done from September to October 2005. These five villages were accessible by car within two hours from the center of the capital. We asked village leaders to request the mothers to stay at home on the day of the interview. The study team included two Expanded Program on Immunization officers, a gynecologist from the National Medical University of Lao PDR, three trained staff members with a medical background, and a Japanese researcher. Informed consent was obtained from the respondents before the interview.

2.2. Questionnaire

The survey questionnaire was developed by modifying and refining a field manual developed by WHO and the questionnaires used previously in Lao PDR [14]. The local expert translated the draft

Table 2
Characteristics at last delivery.

	n	(%)
Protected at birth		
Yes	169	(79.7)
No	43	(20.3)
Minimum 2 doses of TT		
Yes	109	(51.4)
No	103	(43.6)
Confirmation of TT		
Vaccination card	167	(78.8)
Recall	45	(21.2)
Number of antenatal care visits		
Mean±SD	5.7 ± 3.0	
0	14	(6.6)
≥1	198	(93.4)
Antenatal care from skilled personnel[a]		
Yes	189	(95.5)
No	9	(4.5)
Antenatal care including TT counseling		
Yes	168	(84.8)
No	30	(15.2)
Delivery assistance		
Skilled personnel[a]	145	(68.4)
Others	67	(31.6)
Delivery at health facility		
Yes	135	(63.7)
No	77	(36.3)
Previous death of child		
Yes	40	(18.9)
No	172	(81.1)
Total number	212	

[a] Skilled personnel is defined as medical doctor, nurse or midwife.

Table 3
Multivariate logistic regression model.

		Protection-at-birth		Delivery by skilled birth attendant		Delivery at health facility	
		OR	95% CI	OR	95% CI	OR	95% CI
Age	Younger than 30	1		1		1	
	30 or more	0.93	0.38–2.27	1.91	0.82–4.45	2.37	1.04–5.42
Distance to hospital	≤3 km	1		1		1	
	>3 km	0.62	0.24–1.57	1.66	0.72–3.81	1.74	0.79–3.84
Household income	≤Median	1		1		1	
	>Median	1.6	0.65–3.89	0.42	0.19–0.93	0.58	0.27–1.25
Husband's education	≤5	1		1		1	
	>6	1.08	0.41–2.84	0.88	0.41–1.91	0.71	0.33–1.51
Wife's education	≤5	1		1		1	
	>6	2.48	1.04–5.88	0.45	0.21–0.96	0.47	0.23–0.98
Wife's occupation	Housewife	1		1		1	
	Work outside	0.544	0.23–1.31	2.17	0.94–5.00	2.43	1.10–5.40
Radio usage	No	1		1		1	
	Yes	1.45	0.76–2.77	1.11	0.66–1.86	1.24	0.75–2.07
Key person of TT	Village staff	1		1		1	
	Others	0.62	0.27–1.42	1.82	0.82–4.04	3.06	1.38–6.81
Parity	Primipara	1		1		1	
	Multigravida	8.38	2.35–29.84	1.27	0.50–3.22	1.06	0.44–2.60
Previous death of child	No	1		1		1	
	Yes	0.71	0.28–1.84	0.57	0.25–1.31	0.41	0.18–0.91
Antenatal care received a minimum of four times	No	1		1		1	
	Yes	1.2	0.42–3.48	3.85	1.52–9.80	4.24	1.65–10.87
Antenatal care including TT counseling	No	1		1		1	
	Yes	3.12	1.16–8.43	1.04	0.39–2.78	0.91	0.34–2.42

questionnaire into Laotian, and a back translation was done by two trained researchers to check consistency. After a pilot test, the final set of modules was agreed upon among Laotian researchers and interviewers, including (1) socio-demographic characteristics, (2) complete history of TT vaccination, (3) knowledge about TT, (4) detailed birth and pregnancy history with information about related medical care practices, (5) child health outcomes, (6) attitudes and practices related to health-related activities. In addition to the face-to-face interviews with administration of the questionnaire, information on the participants' immunization history around the last pregnancy and delivery of their youngest child was recorded from vaccination cards where available. If respondents did not keep vaccination records, approximate dates of TT were collected from mothers' recall [15,16].

2.3. Statistical analysis

All statistical analysis was done by SPSS version 11.0J. The coverage of interventions was estimated for TT2+ during the last pregnancy, PAB, and clean deliveries. We estimated PAB by counting children whose mothers met the following criteria: (A) two or more doses of TT during the last pregnancy; (B) one TT during the last pregnancy and one or more doses prior to the last pregnancy; and (C) no TT during the latest pregnancy, but two or more doses prior to the last pregnancy and mothers still in the expected period of protection at the last delivery [17]. In case the mothers were classified as category (C), they are considered to be protected if the following conditions are met: (1) received at least two doses of TT, the last within the prior 3 years; (2) received at least three doses, the last within the prior 5 years; (3) received at least four doses, the last within 10 years; or (4) received at least five doses during lifetime [17].

The coverage of clean delivery was estimated by the percentage of deliveries which took place at a health facility and by the percentage of deliveries which were assisted by certified medical personnel (medical doctor, nurse, or midwife), regardless of the place of delivery. Multivariate logistic regression was used to assess the relationship between the intervention coverage and covariates.

3. Results

Table 1 shows the sample characteristics of 212 respondents in the present study. Respondents were women with children less than 5 years of age, and primarily of Lao Lum ethnic origin. Their mean age was 30.7 years with a standard deviation of 6.9 years. The overall response rate was 100%.

Respondents had immunization records with the type and dates of past vaccinations. Table 2 represents the coverage of interventions for neonatal tetanus. The coverage of tetanus toxoid among mothers measured by TT2+ during the last pregnancy and PAB were slightly higher than national averages in previous surveys: 51.4% and 79.7%, respectively. The proportions of delivery attended by skilled personnel and delivery at health facility were 68.4% and 63.7%, respectively.

The regression results of the multivariate logistic models are shown in Table 3. Outcome variables included PAB, delivery assisted by skilled birth attendant (doctor, nurse, or midwife), and delivery at a health facility, and their association with explanatory variables was examined.

Table 3 represents the adjusted odds ratios for the explanatory variables on outcome variables. Neonates who were born to the mothers with higher education, who had experienced delivery before, and who had received antenatal care (ANC) with counseling about TT were more likely to be protected against tetanus at birth. Mothers who had an occupation and more chances to receive antenatal care were more likely to deliver assisted by a skilled birth attendant or deliver at a health facility. Monthly household income was also associated with assisted delivery. Mother's age, deaths of a

child in the past and key person for TT (i.e., a person who encourages mothers to get vaccinated for TT such as members of Lao Women's Union) were also associated with institutional delivery. Traditional practices during pregnancy were common among respondents but were not statistically significant.

4. Discussion

This study was, as far as we know, the first community-based study to investigate simultaneously the coverage of tetanus toxoid vaccination and clean delivery in Lao PDR in the context of the maternal and neonatal tetanus elimination initiative. In this study, the coverage of tetanus immunization was 51.4% when measured as TT2+ during the last pregnancy and 79.7% when PAB was used. The coverage estimates in the present study were higher than national averages (38.1% and 55.5% for TT2+ during the last pregnancy and PAB, respectively) but consistent with the results for the urban area (47.4% and 69.6% for TT2+ and PAB, respectively) [7]. Relatively high coverage in the present study is not surprising as the study was done in the capital where many Expanded Program on Immunization activities as well as routine activities and campaigns have been in place. The discrepancy between TT2+ during the last pregnancy and PAB suggests that evaluation only by TT2+ would underestimate the protection against tetanus [18].

Facility-based records are generally poor sources of representative PAB data and thus periodic household surveys or a combination of the two measures would be necessary to obtain consistent and timely information on PAB, particularly in rural areas. Furthermore, it is important to scale up the coverage of DTP1 sufficiently so that PAB estimates can provide accurate monitoring [18]. The national coverage of DTP1 by 12 months of age was 64.1% in 2006 [7]. Thus, in Laos, TT and DPT continue to be an integral part of an Expanded Program on Immunization program not only to maximize the accuracy of PAB monitoring but also to prevent tetanus more effectively.

In the latest MICS3, 20.3% and 67.8% of deliveries in 2006 were assisted by skilled birth attendants in Lao PDR as a whole and in the urban area, respectively [7]. In the present study, 68.4% of deliveries were assisted by skilled birth attendants. According to the classification suggested by Roper et al., the study area with the coverage of clean delivery less than 70% and TT2+ less than 80% in the setting without robust surveillance system is categorized as high risk area concerning to the risk of neonatal tetanus [1]. More efforts to promote clean delivery are needed. Given the low coverage of delivery by skilled birth attendant and given the lack of emergency obstetric services, more effective use of available services and training of traditional birth attendants, although controversial in its efficacy, should be considered with operational research if needed [19–21].

There was a statistically significant positive association between antenatal care services and the coverage of tetanus toxoid and clean deliveries, which is consistent with previous studies in other countries [22–24]. However, the causal relationship between ANC, skilled birth attendants, and immunization is difficult to confirm. In the present study, the distance from health facilities, which was one of the key determinants of service coverage in previous studies, was not associated with any of the dependent variables. Possible explanations might be that the study site was located in the capital province and health facilities were accessible by road vehicles. The majority of them were classified as "Zone 0" or "Zone 1", which is located within approximately 15 km from the nearest health facility, according to the classification used by EPI programs in Lao PDR.

This study has several limitations. First, 21.2% of respondents did not have a vaccine card, and thus information on vaccination status was based on mothers' recall, which is obviously subject to recall bias. However, the recent analysis of the extent of recall bias by using the same cohorts in two consecutive Demographic and Health Surveys showed that any potential differences in rates due to recall were within the survey's sampling error [16]. Thus, we combined information both from vaccination card and mothers' recall when estimating the coverage of tetanus toxoid. Second, the present study would have missed those mothers whose children had died in the period between birth and the survey due to neonatal tetanus. Although the coverage estimate was consistent with other nationally representative survey [7,13], the exclusion of such mothers would have over-estimated the coverage of tetanus toxoid and underestimated the magnitude of the problem. Third, TT2+ in the present study was evaluated when two or more doses during last pregnancy were given within 5 years. Routine vaccine coverage in the government reports are based on the data collected for each calendar year. Therefore, figures from this study and figures from routine activity are not directly comparable. Finally, the study design does not allow an assessment of causal relationships, because it was a cross-sectional study designed to assess the current situation in Lao PDR.

Despite these limitations, however, and despite the fact that the study sites were located in the capital province, the present study shows that the progress made towards eliminating neonatal tetanus in Lao PDR is insufficient. The lack of continuum of care for mothers and newborns is the major obstacle to scaling up of tetanus toxoid coverage and PAB as well as clean deliveries. Although the Global Immunization Vision and Strategy (GIVS) launched in 2005 focuses on rural areas [25], its current status in Lao PDR is insufficient to achieve the goal of eliminating neonatal tetanus.

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Original Article

Meta-analysis of physiological effects of skin-to-skin contact for newborns and mothers

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Abstract ***Background***: Skin-to-skin care has been adopted all over the world, although physiological changes during or after it have not been evaluated very well. The purpose of the present study was therefore to investigate whether skin-to-skin contact for newborn babies and their mothers affects body temperature, heart rate and oxygen saturation of the babies.
Methods: Studies investigating body temperature, heart rate and oxygen saturation of babies during and/or after skin-to-skin contact were systematically searched and reviewed. Meta-analyses to examine the effects and meta-regression analyses to investigate correlations between the effects and birthweight, duration of the care, environmental temperature, and resources of the setting, were conducted.
Results: A total of 23 studies were included. Meta-analyses showed evidence of an increase in body temperature (weighted mean difference [WMD] 0.22°C, $P < 0.001$) and a decrease in saturation of babies (WMD –0.60%; $P = 0.01$) during skin-to-skin care, compared with those before skin-to-skin care. Increase in body temperature was more evident in middle–low-income settings (WMD, 0.61°C, $P < 0.001$) than high-income settings (WMD 0.20°C, $P < 0.001$). Both the positive effect on body temperature and the negative effect on saturation were more marked in cold environments than where the environmental temperature was higher (WMD 0.18°C, $P < 0.001$; WMD –0.82%, $P = 0.02$).
Conclusion: Skin-to-skin care is effective in increasing the body temperature of babies, especially where resources are limited and the environment is cold. Decreased oxygen saturation of the babies, however, warrants further prospective studies to confirm the findings.

Key words meta-analysis, infant, patient safety, skin-to-skin, systematic review.

Kangaroo Mother Care is originally a package of care including continuous skin-to-skin contact and exclusive breast-feeding for low-birthweight infants and their mothers.[1] The package was invented in Colombia as an alternative to an incubator, and has spread around the world, mainly where resources are relatively limited.[2] A systematic review as well as randomized controlled trials on this care found significantly better cost and clinical effectiveness including reduction in neonatal morbidity, increase in breast-feeding rates, and improved psychological and behavioral change in both mothers and babies, compared with standard incubator care in such settings.[1]

This care has also been adopted in relatively affluent areas to facilitate mother–infant bonding as well as to promote breast-feeding. The adaptations include (i) skin-to-skin care immediately after birth for term infants and their mothers,[3] and (ii) intermittent skin-to-skin care for stable low-birthweight infants.[4]

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Previous studies have found greater benefit for these adaptations of skin-to-skin care of newborn infants and their mothers in relatively affluent settings, compared with standard care. These include increase in breast-feeding rates, and positive psychological and behavioral impact on both mothers and babies.[1] Inclusion criteria for this care, however, particularly in areas of relative affluence have not been well established. There have been reports of further exploration of skin-to-skin care for sick low-birthweight infants even on mechanical ventilators,[5–9] and continuous skin-to-skin care for all low-birthweight infants in modern neonatal intensive care.[10]

Previous studies have attempted to address the potential adverse effects of skin-to-skin care, particularly hypothermia, apnea of prematurity and respiratory state.[11] The vast majority of such studies conducted in relatively resource-affluent settings were before–after studies with a relatively small sample size; hence the question remains unanswered.[12] Recently there have been several reports of 'apparently life-threatening events' in both term and preterm newborns who were having skin-to-skin care.[13,14] Therefore there is need for greater understanding of the physiological status of babies during skin-to-skin care.

The aim of the present study was therefore to investigate whether skin-to-skin contact for both low- and

normal-birthweight infants and their mothers alters physiological parameters including temperature, heart rate and saturation.

Methods

The criteria for inclusion into the present systematic review were as follows.

Types of studies

Comparison of physiological parameters of infants before starting skin-to-skin contact with parameters during and/or after skin-to-skin contact was the main criterion. The most likely study designs were before-and-after studies, although data from randomized controlled trials and cohort studies were also considered.

Types of participants

Newborn infants aged up to 28 days old were considered. Subgroup analysis of low- and normal-birthweight infants was planned. Infants with chronic lung disease, congenital heart disease, and those on mechanical ventilators were excluded, because their usual physiological values were considered significantly different from infants without these conditions. Gestational age and birthweight were included in a meta-regression analysis.

Types of intervention

Skin-to-skin contact between mother and newborn infants regardless of duration was considered. Duration of contact was included in a meta-regression analysis.

Types of outcomes measures

For all three parameters, mean differences and their standard deviations before and during, as well as for before and after, were extracted from included studies. Details of measurement of body temperature, heart rate and saturation are as follows.

Body temperature of infants

Temperature was measured either axially or rectally, before, during and after skin-to-skin contact. When studies used both axial and rectal measurements, rectal measurement was used: this was regarded to reflect the core temperature of infants, and is hence clinically more important.

Heart rate of infants

Heart rate was measured using monitoring devices, before, during and after skin-to-skin contact. Heart rate measurement was taken as an average of certain observation periods. Details of measurement in each of the included studies are described in Table 1.

Oxygen saturation of infants

Saturation was measured through the skin using monitoring devices, before, during and after skin-to-skin contact. Saturation measurement was taken as an average of certain observation periods. Details of measurement in each of the included studies are described in Table 1.

Search strategy for identification of studies

An information specialist conducted a systematic search of the following online databases: MEDLINE (1966–August 2006); EMBASE (1980–August 2006); CINAHL (1982–August 2006); Cochrane Central Register of Controlled Trials (3rd quarter 2006); POPLINE; LILACS; and African Index Medicus.

The main subject headings and free text terms used were: 'kangaroo'; 'kmc'; 'skin to skin'; 'infant'; 'baby'; 'newborn'; 'neonate'. The search was not limited by language; the search was limited to humans. No attempt was made to search gray literature (i.e. literature that is not published in academic peer reviewed journals and available through indexed databases for review).

Review procedure

Two reviewers (RM and RK) independently assessed the methodological quality of each identified study, and any discrepancy in quality assignment was planned to be solved in discussion with the third reviewer (TN), although no discrepancies occurred.

Weighted mean difference (WMD) and confidence intervals were calculated for each comparison. A meta-regression analysis was conducted to investigate correlations between the effects and other potential effect modifiers including low/normal birthweight, duration of skin-to-skin contact, annual average temperature of the city where the study was conducted (as a proxy for the environmental temperature), and resource of the setting (high or middle–low income). When evidence of correlation was found in the meta-regression analysis, subgroup analysis by the parameter(s) was conducted. Birthweight and duration of skin-to-skin care were extracted as either means or medians from the included studies. The income status (high, middle or low), defined by the World Bank,[15] was also extracted from included studies. Annual average temperature of the city where each study was conducted was obtained from the Global Historical Climatology Network.[16] Duration of skin-to-skin care and temperature of the city was examined as a continuous variable in the meta-regression analysis, but when they were found to be related to the effects, 10°C for the city temperature and 90 min for the duration of skin-to-skin contact were used as the cut-offs for the subgroup analyses. These cut-offs were used for the sake of convenience only.

Ethics approval

This study was conducted using original articles that have been published in the public domain, therefore the obtaining of ethics approval was considered unnecessary.

Results

Description of studies

The search yielded 1087 citations. A total of 47 potentially relevant articles were obtained for further assessment. Of these 47 articles, 24 articles (23 studies) were included in the review (Table 1);[11,17–39] the remaining 23 articles were excluded.[7,40–61]

The reasons for exclusion included (i) not giving SD in eight articles;[40,45,52,54,55,57,59,60] (ii) point estimates were provided by median and/or range in five articles;[42–44,49,56] (iii) data shown only

Table 1 Description of included studies

Study	Place of study	Temperature of the city†	N	Income setting	Preterm/ Term	Birthweight (g)	Gestational age (weeks)	Duration of SSC (min)s	Outcome measurements	
Author, published year	City, country	(°C)							Timing	Parameters
Acolet *et al.* 1989[28]	London, UK	10.4	9	High	Preterm	1060	28	10	Before/during/after	Heart rate/saturation
Bauer *et al.* 1997[23]	Berlin, Germany	8.9	22	High	Preterm	1200	29	60	Before/during/after	Temperature/heart rate
Bosque *et al.* 1995[24]	San Francisco, USA	14.1	8	High	Preterm	1061	28	240	Before/during/after	Temperature/heart rate
Bystrova *et al.* 2003[32]	St Petersburg, Russia	5.3	44	Middle	Term	3574	39	90	Before/during	Temperature
Chiu *et al.* 2005[30]	Cleveland, USA	10	39	High	Term	3396	39	30	Before/during/after	Temperature
Christensson *et al.* 1992[31]	Madrid, Spain	14.2	25	High	Term	3385	N/R	90	Before/during	Temperature
Christensson *et al.* 1995[33]	Madrid, Spain	14.2	14	High	Term	3155	40	80	Before/during	Temperature
Clifford & Barnsteiner 2001[34]	Philadelphia, USA	12.2	7	High	Preterm	779	26	71.5	Before/during/after	Temperature/heart rate/ saturation
Durand *et al.* 1997[36]	El Paso, USA	17.5	25	High	Term	N/R	N/R	120	Before/during	Temperature
Fohe *et al.* 2000[25]	Magdeburg, Germany	8.6	53	High	Preterm	1247	30	90	Before/during/after	Temperature/heart rate/ saturation
Gardner 1979[38]	Chicago, USA	11	10	High	Term	N/R	N/R	15	Before/during	Temperature
Huang *et al.* 2002[39]	Taipei, Taiwan	21.9	24	Middle	Term	N/R	N/R	60	Before/during	Temperature/heart rate/ saturation
Ibe *et al.* 2004[27]	Lagos, Nigeria	26.5	13	Low	Preterm	N/R	33	240	Before/during/after	Temperature
Karlsson 1996[29]	Goteborg, Sweden	6.7	9	High	Term	3100	39	60	Before/during	Temperature
Legault & Goulet 1995[26]	Montreal, Canada	6.3	61	High	Preterm	1225	30	30	Before/during/after	Temperature/heart rate/ saturation
Ludington *et al.* 1991[18]	Los Angeles, USA	16.5	12	High	Preterm	2130	35	180	Before/during	Temperature/heart rate/ saturation
Ludington *et al.* 1993[37]	Cali, Colombia	23.7	11	Middle	Preterm	2237	36	120	Before/during	Temperature
Ludington *et al.* 1999[20]	Cali, Colombia	23.7	6	Middle	Preterm	2300	36	360	Before/during/after	Temperature
Ludington *et al.* 2000[11]	Richland, USA	12.1	16	High	Preterm	1411	31	150	Before/during/after	Temperature
Ludington *et al.* 2004[12]	Richland, USA	12.1	11	High	Preterm	1876	34	180	Before/during/after	Temperature/heart rate/ saturation
Messmer *et al.* 1997[22]	Miami Beach, USA	23.5	20	High	Preterm	1315	28	60	Before/during/after	Heart rate/saturation
Closa *et al.* 1998[35]	Tarragona, Spain	16.2	38	High	Preterm	1452	32	60	After/during/after	Temperature/heart rate/ saturation
Wieland *et al.* 1995[19]	Berlin, Germany	8.9	39	High	Preterm	1110	28	60	After/during/after	Temperature/heart rate/saturation

†Annual average temperature obtained from the Global Historical Climatology Network.[16]
N/R, not reported.

in a graphical manner in two articles;[41,53] (iv) only single measurement provided in two articles;[47,51] (v) only proportion of babies with hypothermia presented in one article;[46] (vi) only heart rate variability presented in one article;[48] (vii) heart rate measured but not presented in one article;[50] (viii) outcome reported as stability of cardiorespiratory system in preterm infants (SCRIP) score in one article;[58] (ix) case report format of one baby and skin-to-skin care provided with mechanical ventilation;[7] and (x) case report format of five babies with congenital heart diseases requiring open heart surgery.[61]

Among the included 23 studies, 13 studies used case-series (before–after studies),[19–25,28–30,34,35,38] five studies were randomized controlled trials and only data from the arm in which babies had skin-to-skin care were extracted,[11,17,18,32,33] one study was a cross-over trial,[27] and the remaining four were cohort studies.[26,31,36,37,56]

Eighteen studies were conducted in high-income countries (nine in the USA,[11,17,18,21,22,24,30,34,36,38] three in Germany,[19,23,25] three in Spain,[31,33,35] one in Canada,[26] one in the UK[28] and one in Sweden[29]), while one was in an upper–middle-income country (Russia),[32] three were in lower–middle-income countries (two in Colombia[20,37] and one in Taiwan[39]) and one in a low-income country (Nigeria).[27]

Fifteen studies measured body temperature, heart rate and/or saturation of low-birthweight infants,[11,17–28,34,35,37] and the remaining eight studies measured these in term and normal-birthweight infants.[29–33,36,38,39]

The UK study reported results for both preterm infants with normal lungs and with chronic lung disease.[28] Only the data for those with normal lungs were extracted for the present review.

Methodology

The included studies were reasonably homogenous. Heterogeneity in reporting and measuring the physiological parameters was found. Studies used different criteria for stable babies, and some studies did not provide detailed criteria.

Findings

Body temperature

Compared with the body temperature prior to skin-to-skin care, there was strong evidence of an increase in body temperature during skin-to-skin care by 0.22°C (22 studies, WMD 0.22°C; 95% confidence interval [CI]: 0.18–0.27, $P < 0.001$), and after skin-to-skin care by 0.14°C (12 studies, WMD 0.14; 95%CI: 0.09–0.18, $P < 0.001$; Figs 1,2).

When meta-regression was conducted, there was strong evidence that the effect on body temperature during skin-to-skin care compared with that before skin-to-skin care was correlated with income status of the country ($P = 0.007$) and borderline evidence that it was correlated with the temperature of the city ($P = 0.06$). No evidence was found for correlation with birthweight and duration of skin-to-skin care (Table 2). Therefore, the results of meta-analysis of the effect on body temperature during

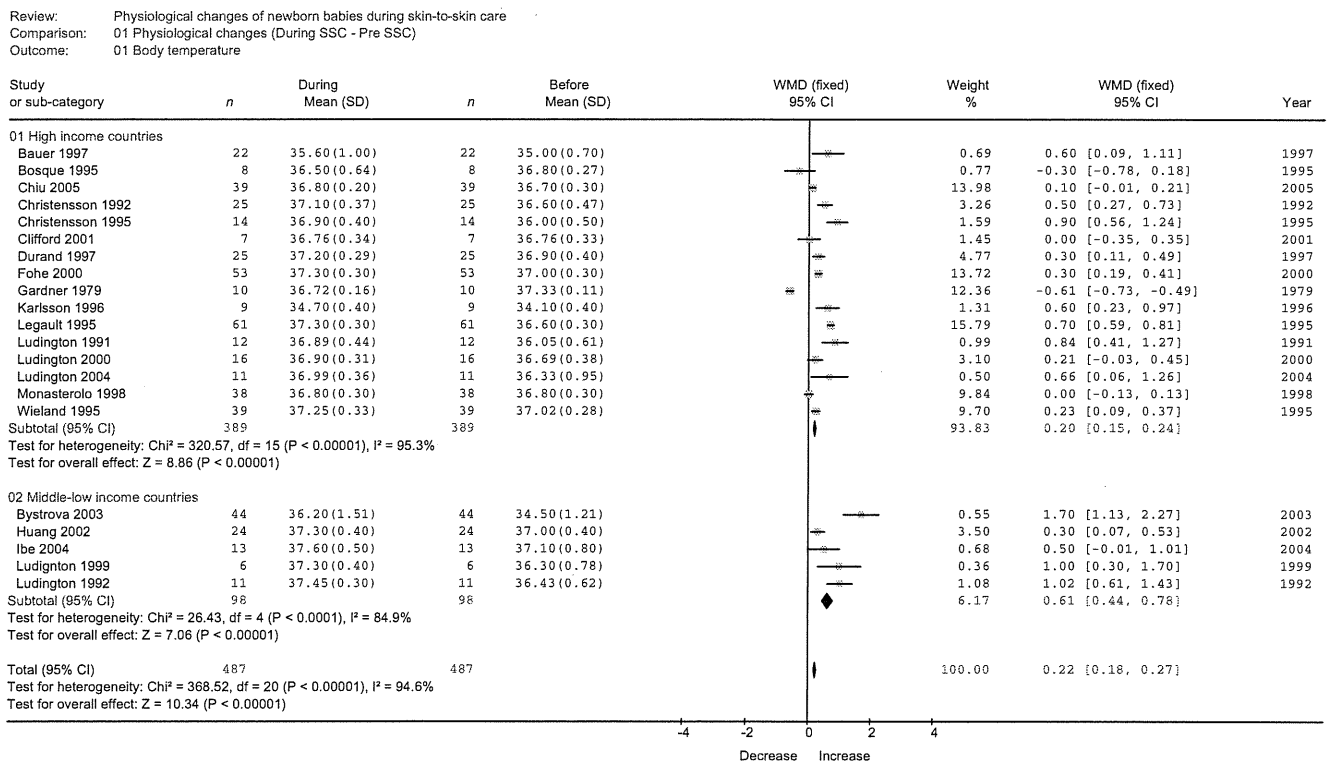

Fig. 1 Forest plot: effect on body temperature during skin-to-skin care, compared with that before skin-to-skin care, stratified by resource of settings. CI, confidence interval; SSC, skin-to-skin care; WMD, weighted mean difference.

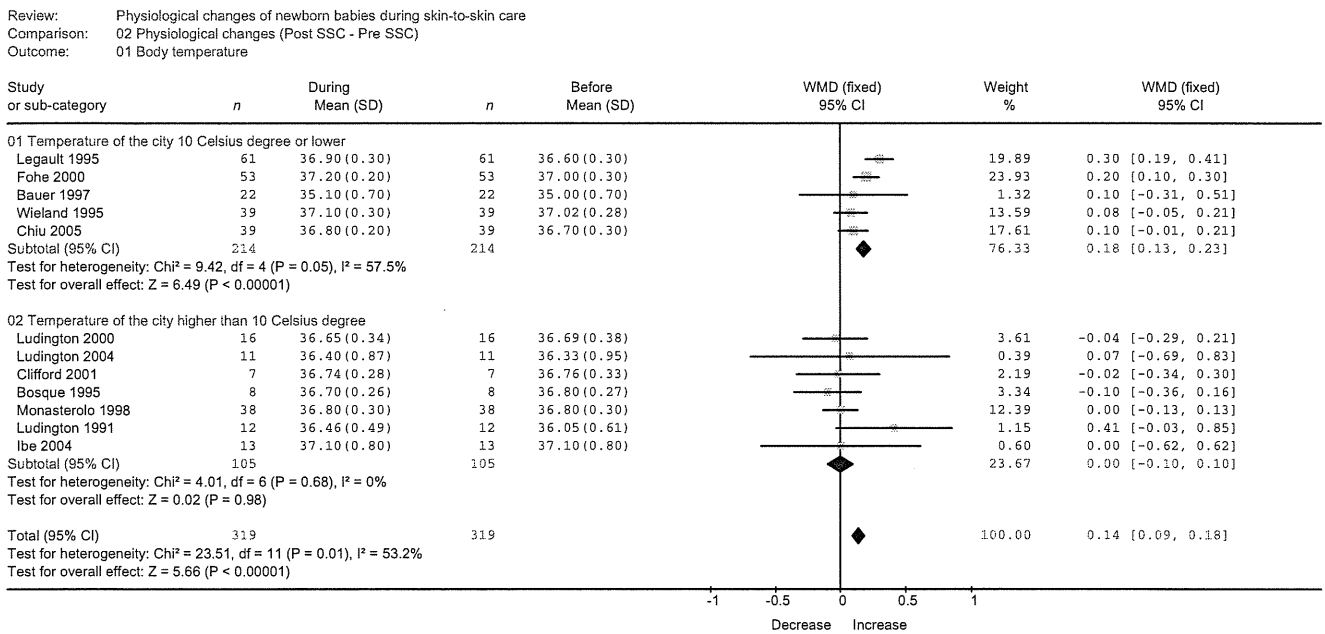

Fig. 2 Forest plot: effect on body temperature during skin-to-skin care, compared with that before skin-to-skin care, stratified by temperature of the cities. CI, confidence interval; SSC, skin-to-skin care; WMD, weighted mean difference.

skin-to-skin care were stratified by the income status of the countries (Fig. 1). Subgroup analysis showed strong evidence of a higher increase in body temperature in middle–low-income countries (five studies, WMD 0.61°C; 95%CI: 0.44–0.78) compared to high-income countries (16 studies, WMD 0.20°C; 95%CI: 0.15–0.24). When the body temperature of the babies after skin-to-skin care was compared with that before skin-to-skin care, however, there was a strong evidence of a correlation between the effect and the temperature of the city ($P = 0.004$). There was no evidence of correlation with the other parameters. The results of meta-analysis of the effect on body temperature after skin-to-skin care was stratified by temperature of the city and divided into two categories: studies conducted in cities where the annual average temperature is ≤10°C, and those in cities where the temperature is higher (Fig. 2). The subgroup analysis showed strong evidence of an increase in body temperature after skin-to-skin care in cities where the average temperature was ≤10°C (five studies, WMD 0.18°C; 95%CI: 0.13–0.23), but the effect was not sustained after skin-to-skin care in cities where the average temperature was >10°C (seven studies, WMD 0.00°C; 95%CI: −0.10 to 0.10).

Heart rate

Overall there was no evidence of a difference in heart rate between before and during skin-to-skin care (12 studies, WMD 2.04 beats/min; 95%CI: −0.04 to 4.12), and no evidence between before and after skin-to-skin care (10 studies, WMD −0.07 beats/min; 95%CI: −2.27 to 2.13; Figs 3,4). When a meta-regression analysis was conducted, however, to examine the relationship between the effect on heart rate during skin-to-skin care and other parameters, there was evidence of a correlation between the effect and income of the country ($P = 0.04$) only (Table 2). On stratifying the effect on heart rate by income status of the countries, there was evidence of an increase in heart rate by 2.82 beats/min during skin-to-skin care in high-income countries, but no evidence of such effect in middle–low-income countries (Fig. 3).

Oxygen saturation

Overall, there was evidence that saturation of babies during skin-to-skin care was decreased by 0.60% (10 studies, WMD −0.60%; 95%CI: −1.05 to −0.15), but only borderline evidence that such an effect remained after skin-to-skin care (eight studies, WMD −0.48%; 95%CI: −0.97 to 0.02; Figs 5,6).

When meta-regression was conducted, there was no evidence of a correlation between the effect on saturation during skin-to-skin care and the parameters; therefore no subgroup analysis was conducted. There was borderline evidence, however, of a correlation between the effect after skin-to-skin care and the temperature of the cities ($P = 0.05$). The effect on saturation after skin-to-skin care was stratified by the temperature of the cities. Subgroup analysis showed that there was evidence that a decrease in saturation remained after skin-to-skin care in cities where the annual average temperature was ≤10°C (three studies, WMD −0.82%; 95%CI: −1.48 to −0.15), but there was no such effect observed in the warmer cities (five studies, WMD −0.03; 95%CI: −0.79 to 0.72; Fig. 6).

Funnel plots of all the results of the meta-analyses were examined to assess possibility of publication bias. No evidence of publication bias was observed. Duration of skin-to-skin care did not alter the association in any of the three physiological parameters.

Table 2 Results of meta-analysis and meta-regression

Meta-analysis		Effects during skin-to-skin care, compared with before skin-to-skin care					
		Body temperature (°C)		Heart rate (beats/min)		Saturation (%)	
No. studies		21		12		10	
Overall results		0.22 [0.18–0.27)	$P < 0.001$	2.04 (–0.04 to 4.12)	$P = 0.05$	–0.60 (–1.05 to –0.15)	$P = 0.01$
Test for heterogeneity		I2 = 94.6%	$P < 0.001$	I2 = 27.8%	$P = 0.17$	I2 = 12.7%	$P = 0.33$
Meta-regression analysis		Correlation coefficient	P	Correlation coefficient	P	Correlation coefficient	P
No. studies		21		12		10	
Temperature of the city	°C	–0.05	0.06	0.64	0.17	0.07	0.51
Income of the country	high/mid-low	0.82	0.007	–14.47	0.04	–0.59	0.70
Birthweight	low/normal	0.04	0.85	N/A		N/A	
Duration of skin-to-skin care	duration(min)	0.002	0.25	0.14	0.55	–0.001	0.88
Meta-analysis		Effects after skin-to-skin care, compared with before skin-to-skin care					
		Body temperature (°C)		Heart rate (beats/min)		Saturation (%)	
No. studies		12		10		8	
Overall results		0.14 (0.09–0.18)	$P < 0.001$	–0.07 (–2.27 to 2.13)	$P = 0.95$	–0.48 (–0.97 to 0.02)	$P = 0.06$
Test for heterogeneity		I2 = 53.2%	$P = 0.01$	I2 = 0%	$P = 0.86$	I2 = 0%	$P = 0.81$
Meta-regression analysis		Correlation coefficient	P	Correlation coefficient	P	Correlation coefficient	P
No. studies		12		10		8	
Temperature of the city	Celsius degree	–0.03	0.004	0.37	0.20	0.11	0.05
Income of the country	high/mid-low	0.34	0.25	N/A		N/A	
Birthweight	low/normal	–0.64	0.38	N/A		N/A	
Duration of skin-to-skin care	duration(min)	–0.0004	0.61	0.008	0.56	–0.001	0.82

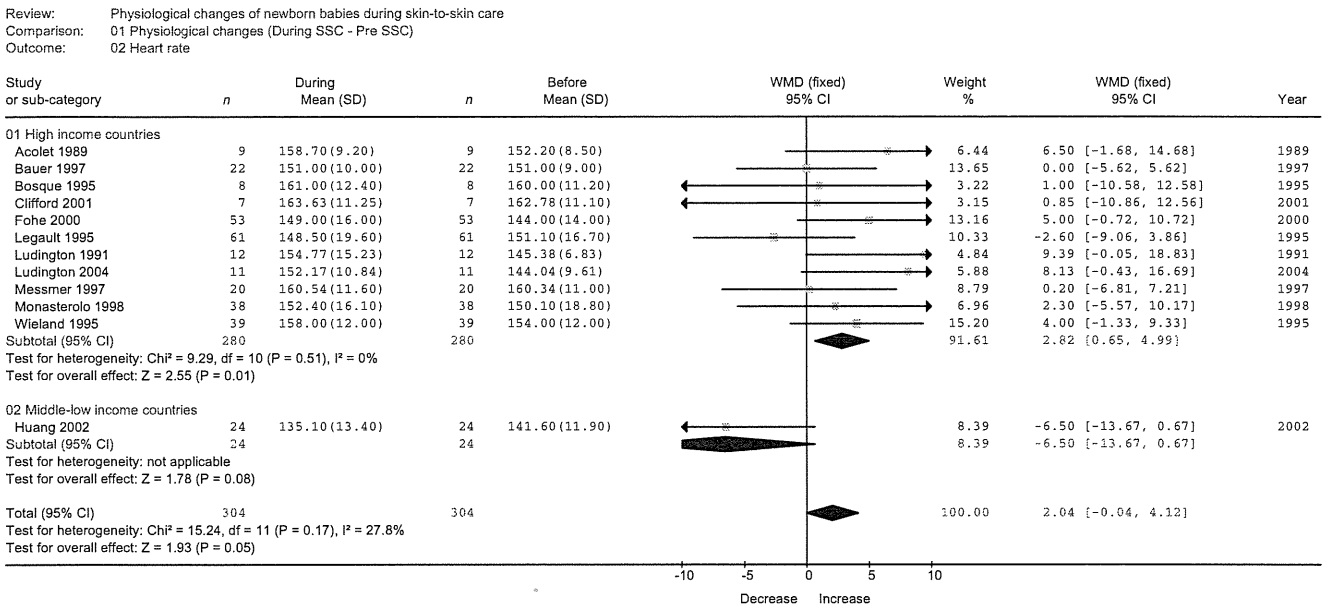

Fig. 3 Forest plot: effect on heart rate during skin-to-skin care, compared with that before skin-to-skin care, stratified by resource of the settings. CI, confidence interval; SSC, skin-to-skin care; WMD, weighted mean difference.

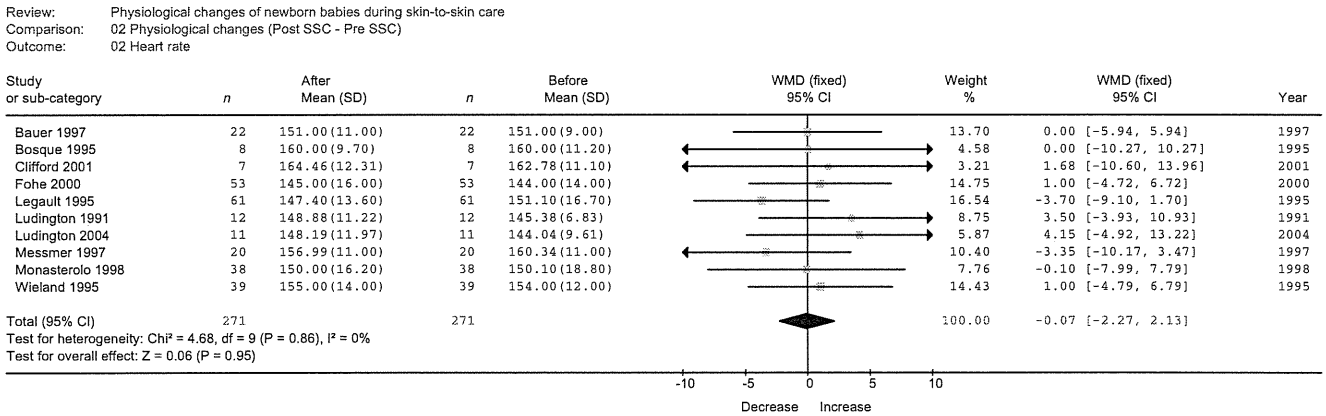

Fig. 4 Forest plot: effect on heart rate after skin-to-skin care, compared with that before skin-to-skin care. CI, confidence interval; SSC, skin-to-skin care; WMD, weighted mean difference.

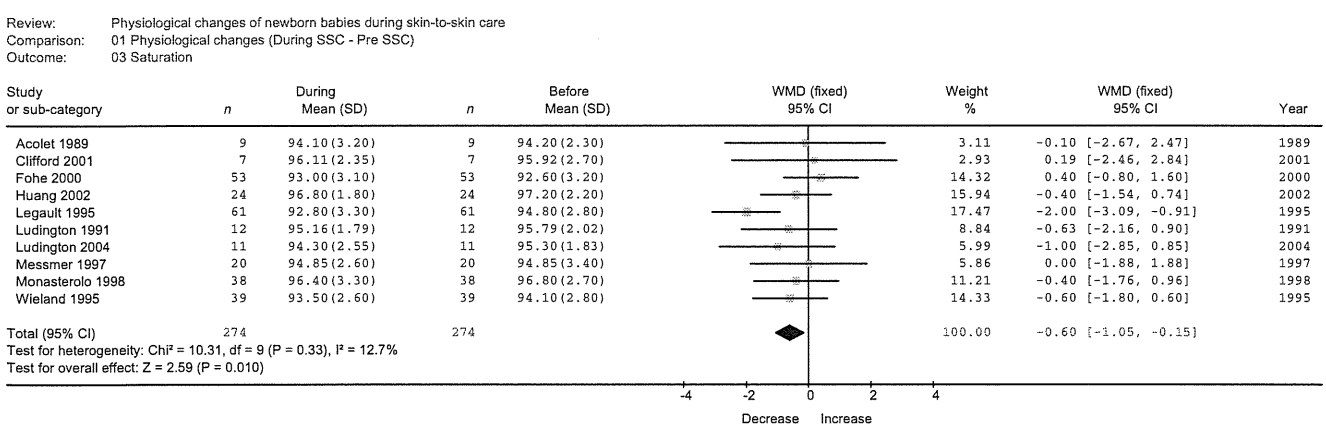

Fig. 5 Forest plot: effect on saturation during skin-to-skin care, compared with that before skin-to-skin care. CI, confidence interval; SSC, skin-to-skin care; WMD, weighted mean difference.

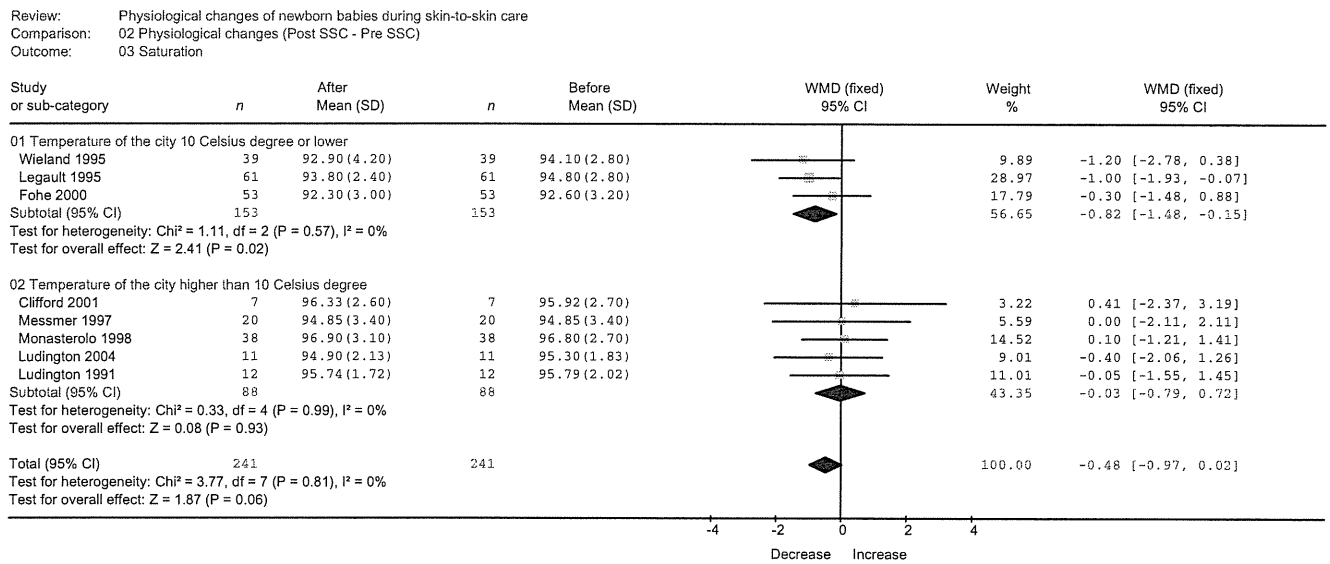

Fig. 6 Forest plot: effect on saturation after skin-to-skin care, compared with that before skin-to-skin care, stratified by temperature of the cities. CI, confidence interval; SSC, skin-to-skin care; WMD, weighted mean difference.

Discussion

Principal results

The series of meta-analyses showed that during skin-to-skin care, there was evidence of an increase in body temperature and a decrease in oxygen saturation of babies, compared with the parameters observed before starting skin-to-skin care. Increased body temperature was more evident in middle–low-income settings than high-income settings. An increase in heart rate was also observed in high-income settings during skin-to-skin care. Both the positive effect on body temperature and the negative effect on saturation seemed to be sustained in colder environments after skin-to-skin care, but there was no evidence of such a sustained effect in a warmer environment.

The present study has a number of potential limitations in the interpretation of these results.

Bias

There was no evidence of publication bias in the funnel plots (data not shown). All studies included only relatively stable infants, and the results should not be applied to those with unstable conditions. All the measurements and recording of them were conducted simultaneously; hence recall bias is unlikely. Many studies reported only the parameters for during and before skin-to-skin care, with no parameters for after skin-to-skin care. This can introduce selection bias, although analysis of only studies reporting all parameters showed a similar tendency in the results (data not shown)

Confounding

There was a possibility of confounding by factors that have not been considered in the present study. Meta-regression analysis considered temperature of the cities where the study was conducted, birthweight, duration of the skin-to-skin care and the resources of the settings. But infant age, bodyweight, and prematurity (term/preterm) were not reported in many of the studies and it was therefore not possible to consider them in the present study. But these parameters should have been captured by inclusion of birthweight in the analyses.

Measurement errors

Differences in the methods used for measuring these physiological parameters was also important. Some studies measured body temperature axially and other studies rectally. There could be a difference in effect, particularly the timing of warming effects. Saturation is also known to show slight variation with devices used, as well as where in the body it was measured. But the same measurement method was used within the studies, and overall results are likely to reflect the real differences. The means of birthweight, duration of the skin-to-skin care and resources of the settings included in the meta-regression analyses were obtained from the studies. Means may not necessarily reflect the study population, although no detailed information was given. Meta-regression analyses should be interpreted with caution.

Generalizability

Studies had certain tendencies. For example, studies examining normal-weight infants were more likely to be conducted in high-income settings, and more likely to report only parameters before and during skin-to-skin care. Studies investigating babies with congenital heart diseases and with chronic lung diseases were not considered in the present study. The results of the present meta-analysis should not be applied to babies other than stable normal and low-birthweight infants with no such particular conditions.

Plausibility of the effects

Human skin has a constant temperature with natural homeostasis. Therefore it is not surprising to see an increase in the body

temperature of babies during close contact with skin. Decrease in saturation is a new finding, and reduction of saturation does not necessarily mean apnea of prematurity, although there are often increases in apnea of prematurity observed during skin-to-skin care,[56] and the previous findings are compatible with the present one. The effect is more evident in middle–low-income settings, rather than high-income settings, although there is no clear explanation for this. Differing levels of standard care (incubator care) to maintain temperature (e.g. faulty or old incubators, lack of appropriate knowledge/skills etc.) may have contributed, but further studies to explore the findings are needed. After skin-to-skin care the effects on body temperature and saturation persisted in the colder environments. This could be due to lower baseline temperature of babies before skin-to-skin care and effects on peripheral circulation due to the temperature of the environment, although these are speculative suggestions. One interesting finding is that there might be an inverse relationship between oxygen saturation and body temperature, although this should be tested in further studies. Overall, the results are biologically plausible, although further studies to clarify the biological causation are warranted.

Implication for clinical practice

Considering the overall effects of Kangaroo Mother Care and/or skin-to-skin care in low–middle-income countries, this type of care can be promoted in these settings for stable low- and normal-birthweight infants. This does not imply any changes for current configurations. In particular, babies at risk of apnea of prematurity should not given skin-to-skin care without adequate monitoring of saturation and respiratory status. The environment seems also to play an important role in this care. Attention should be paid to ensure appropriate and adequate environment through the care.

Implication for research

Studies of skin-to-skin care on saturation and respiratory status of babies are urgently needed. Studies investigating the effect of the environment on the physiological status of the babies are also needed. The cost-effectiveness of monitoring babies during and after skin-to-skin care should also be thoroughly investigated in various settings.

Conclusion

Skin-to-skin care is an effective way to warm babies, especially where resources are limited and where the environment is relatively cold. Monitoring, however, of the saturation and respiratory status of the babies throughout the care, where resources are relatively affluent, should be considered, taking the costs of monitoring into account.

Acknowledgments

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