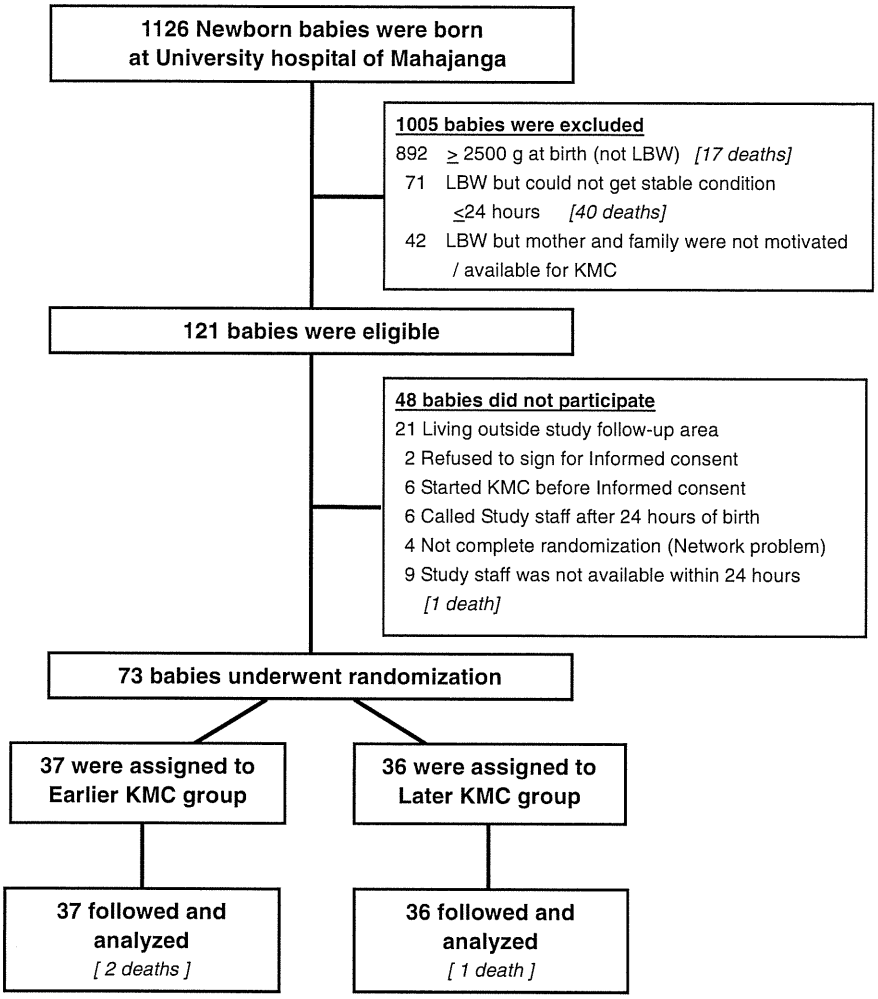

Figure 2 Enrolment, randomization and follow-up of the study participants.

The number of hypothermia cases within 48 h postbirth was 0 in the earlier KMC group and two in the later KMC group. By contrast, number of hyperthermia incidences within 48 h postbirth was seven in the earlier KMC group and three in the later KMC group. In most of these cases, hyperthermia lasted for only a few hours and infants showed no other clinical symptoms indicating infection.

The mean duration of hospitalization was shorter in the earlier than in the later KMC group (6.68 days vs. 7.58 days; MD, −0.91; 95% CIs, −3.01 to 1.19; p = 0.39). In the earlier KMC group, more cases were discharged within 7 days than in the later KMC group (27 vs. 24; MD 1.09; 95% CIs, 0.81–1.48; p = 0.62).

In subgroup analyses, infants with birth weight greater than 2000 g exhibited significantly less body weight loss from birth to 24 h and to 48 h in earlier compared with later KMC group (Table 4).

DISCUSSION

In this study, earlier (within 24 h postbirth) continuous KMC on relatively stable LBW babies in a resource-limited country, as a complement to conventional care, had higher, but not statistically significant, mortality in the first 28 days postbirth. These results are inconsistent with those of Worku et al. (9), in which earlier continuous KMC for LBW infants in a resource-limited country had reduced neonatal mortality (RR, 0.59; 95% CIs,0.34–1.04; p = 0.06). However, Worku et al. did not include stabilization as an eligibility requirement.

Beginning continuous KMC earlier appears to reduce weight loss in the early days after birth. Reduction of body weight loss may be critical for fragile LBW premature babies to survive their early days of life (25).

Although the findings regarding mortality suggest the possibility that earlier continuous KMC might increase mortality, this conclusion is difficult to justify based on there having been only two deaths versus one. Yet the finding cannot be ignored, either. In future studies, even in a resource-limited country, any deaths that do occur should be thoroughly investigated, perhaps through autopsies to rule out internal congenital anomalies. In particular, congenital cardiac abnormalities should be considered, as they may produce no visible symptoms, not even a murmur.

Table 1 Characteristics of study participants

	Earlier KMC group (N = 37)	Later KMC group (N = 36)
Birth weight – grams		
Mean (SD)	2075.2 (272.4)	2077.5 (291.6)
Birth weight* n (%)		
2000≤	15 (40.5)	15 (41.7)
2001–2500	22 (59.4)	21 (58.3)
Gestational age at birth – weeks		
Mean (SD)	36.6 (2.18)	36.0 (2.06)
Gestational age at birth – n (%)		
32–33	2 (5.4)	5 (13.9)
34–36	19 (51.4)	14 (38.9)
37≥	16 (43.2)	17 (47.2)
Classification based on Lubchenco's charts – n (%)		
Preterm AGA	16 (43.2)	18 (50.0)
Preterm SGA	5 (13.5)	1 (2.8)
Term AGA	2 (5.4)	3 (8.3)
Term SGA	14 (37.8)	14 (38.9)
Gender – n (%)		
Male	16 (43.2)	25 (69.4)
Delivery type* – n (%)		
Normal delivery	27 (73.0)	26 (72.2)
Caesarean	10 (27.0)	10 (27.8)
Apgar score at 5 min* – n (%)		
0–6	2 (5.4)	1 (2.8)
7–10	35 (94.6)	35 (97.2)
Elapsed time (hours) from birth to randomization * – n (%)		
0–12	15 (40.5)	14 (38.9)
12–24	22 (59.5)	22 (61.1)

AGA = appropriate for gestational age; SGA = small for gestational age.
*Characteristics were used in the minimization programme.

In the present trial, the family support frequency and feeding methods were not significantly different between the two groups. These results were partly consistent with previous publications (27). Additional evaluations are needed to examine the possible role of these factors.

Study design

The results pertaining to the primary outcome were inconclusive because of the very low proportion of event (infant deaths), which may cause overestimation of the effect size. The proportion of event in the previous retrospective data we used for our estimation, which included all infants born at our facility (22), may have been higher than that for the infants eligible for this study, which only included infants that had reached stabilization. Future studies using the same eligibility criteria should include many more participants in order have enough mortality events to reach a definitive conclusion. We could not extend our study period to obtain more participants because of lack of funds.

Before this study, continuous KMC had conventionally been initiated approximately 48–72 h postbirth. As a result of the necessity of early intervention in the trial, KMC was initiated earlier than conventionally (mean hours postbirth: earlier KMC group 19.76 h, later KMC group 33.00 h). There was only a half day difference in the onset of continuous KMC between the two groups.

Several factors prevented this study from leading to a definitive conclusion. Particularly important factors included selection of the primary outcome, expected effect size and contents of the intervention. In addition, patient characteristics at the study site may have changed after a pilot study was completed. These changes may have affected the proportion of the event. This study would have benefited from more careful designing prior to its ethical approval and implementation. Future studies of KMC should be designed more carefully based on our study and on reports of other studies.

One of the strengths of our study was higher proportion of follow-up compared with other studies (13–15,28). One research coordinator was responsible for follow-up visits on days 14 and 28 exclusively. The research coordinator managed home visit appointments and data collections by himself. Most families welcomed the follow-up home visit and often requested more frequent visits.

Excluded populations

In our study, 48.3% (113/234) of LBW infants were excluded. Furthermore, 90.9% (40/44) of mortalities occurred in the excluded LBW newborns, because their condition did not become stable within 24 h postbirth (Fig. 2). To reduce the number of excluded babies, Worku et al. included infants prior to stabilization and those born outside the study facilities. Despite this expanded eligibility, half of the LBW infants were not eligible. These

Table 2 Kangaroo Mother Care (KMC) practice characteristics

	Earlier KMC group N = 37 Incidence (%) Mean (SD) or Median (quintile)	Later KMC group N = 36 Incidence (%) Mean (SD) or Median (quintile)	Risk ratio or mean differences (95% CI)	p-value
KMC onset (hours postbirth)				
Mean	19.76 (14.33)	33.00 (13.18)	−13.24 (−6.813–−19.673)	<0.01
Median	19.00 (13.00–23.00)	28.50 (25.00–40.25)		<0.01
Others help to perform KMC from 24 to 48 h postbirth	22 (59.5)	21 (58.3)	1.02 (0.65–1.62)	1.00
Own mother's milk feeding*				
From birth to 24 h postbirth	20 (54.1)	19 (52.8)	1.02 (0.65–1.62)	1.00
From 24 to 48 h postbirth	17 (48.6)	18 (50.0)	0.92 (0.56–1.45)	0.82

*Exclusive breastfeeding and tube/spoon/cup feeding of own mother's milk (not including mixed feeding or formula feeding).

Table 3 Primary and secondary outcomes

	Earlier KMC group N = 37 Incidence (%) or mean (SD)	Later KMC group N = 36 Incidence (%) or mean (SD)	Risk ratio or mean differences (95% CI)	p-value/adjusted p-value**
Primary outcome				
Mortality during the first 28 days postbirth	2 (5.4)	1 (2.8)	1.95 (0.18–20.53)	1.00
Secondary outcomes				
Morbidities during the first 28 days postbirth	5 (13.5)	10 (27.8)	0.58 (0.24–1.44)	0.23/0.24
Severe infection	3 (8.1)	7 (19.4)		
High fever diagnosed Malaria	0 (0.0)	2 (5.6)		
Re-hospitalization	2 (5.4)	1 (2.8)		
Body weight change (g)				
From birth to 24 h*	−34.81 (71.54)	−73.97 (48.91)	39.16 (10.30–68.03)	0.01/0.02
From birth to 48 h*	−77.89 (100.06)	−121.19 (60.45)	43.30 (4.59–82.01)	0.03/0.053
From birth to Day14*	207.78 (226.01)	195.64 (188.28)	12.14 (−85.23–109.52)	0.79/0.98
From birth to Day 28*	713.24 (371.24)	654.39 (394.31)	58.85 (−119.83–237.53)	0.50/0.60
Adverse events				
Body temperature <35.5°C during hospitalization	2 (5.4)	3 (8.3)	0.65 (0.12–3.66)	0.67
Body temperature <35.5°C during Out Patient Visit	1 (2.7)	2 (5.6)	0.49 (0.05–5.13)	0.61
Body temperature >37.5°C during hospitalization	13 (35.1)	12 (33.3)	1.05 (0.56–1.99)	1.00
Heart rate (>180 or <100) during hospitalization	1 (2.7)	1 (2.8)	0.97 (0.06–15.0)	1.00
Apnea (>20 sec) during hospitalization	0 (0.0)	1 (2.8)	–	–
Duration of hospitalization (day)	6.68 (0.74)	7.58 (0.75)	−0.91 (−3.01–1.19)	0.39
Discharge within 7 days postbirth	27 (72.97)	24 (66.67)	1.09 (0.81–1.48)	0.62

*p-values adjusted with birth weight.
**p-values adjusted with birth weight, Apgar score and gender.

exclusions were mainly attributable to high risk deliveries or delayed referral to the study facility (9). In our study, excluded LBW newborns were in such severe conditions that the mother, family members and staff could not perform KMC. Thus, it was difficult to reduce the number of babies excluded from our study. In referral hospitals in resource-limited countries, like those in Worku et al. and in this study, these excluded babies may benefit most from earlier KMC, especially in reducing mortality. In reality, however, many obstacles exist for KMC performance for unstable babies including adequate technique, reliable relationship between family and staff, and cultural acceptance. Moreover, earlier KMC is not a substitute for neonatal intensive care. An additional, adequate way of implementing earlier KMC would be needed to benefit these infants.

Secondary outcomes

Results of secondary outcomes were partly consistent with the previous publications. The effect of earlier KMC on reduced infection and re-admission were similar to those reported by Charpak et al. However, continuous KMC

Table 4 Subgroup analysis comparing body weight loss from birth to 24 h and 48 h by birth weight (>2000 g or ≤2000 g)

	Earlier KMC group	Later KMC group	Mean differences (95% CI)	p-value*/adjusted p-value**
Body weight loss from birth to 24 h				
Birth weight >2000 g				
n	22	21	49.33 (12.95–85.72)	0.01/0.01
Mean (g) (SD)	−45.00 (67.87)	−94.33 (48.10)		
Birth weight ≤2000 g				
n	15	15	25.60 (−19.53–70.73)	0.26/0.63
Mean (g) (SD)	−19.87 (76.48)	−45.47 (37.8)		
Body weight loss from birth to 48 h				
Birth weight >2000 g				
n	22	21	60.69 (3.47–117.91)	0.04/0.06
Mean (g) (SD)	−83.55 (116.56)	−144.24 (58.47)		
Birth weight ≤2000 g				
n	15	15	19.33 (−26.72–65.39)	0.40/0.73
Mean (g) (SD)	−69.60 (72.40)	−88.93 (48.38)		

*p-values adjusted with birth weight.
**p-values adjusted with birth weight, Apgar score and gender.

intervention was begun only when infants became completely stable, median age eligibility was day 4 (14). The body weight changes from birth to 48 h, and day 14 and 28 postbirth were not consistent with the study by Chwo et al., (7) in which KMC was initiated early but was intermittent and not continuous. The earlier discharge rate in this study during the first week is similar to that reported by Worku et al. (9). One third of the infants in this study experienced hyperthermia during hospitalization, but the frequency was not significantly different between earlier and later KMC groups. A recent RCT from India also reported a high proportion of hyperthermia in both groups (KMC group 13/103 (12.6%), conventional care group 18/103 (17.5%), p = 0.33) (28). Generally, skin-to-skin care can protect infants from hypothermia, especially where resources are limited and where the climate is relatively cold (29). In a hot and humid area such as our study site, one should be wary of the possibility of hyperthermia while practicing KMC at high room temperatures, as reported by Ludington et al. (30).

Earlier and later KMC groups differed in mean body weight change. However, there was no difference in feeding method from birth to 24 and 48 h postbirth, suggesting that feeding method is not associated with body weight increase.

CONCLUSION

Earlier (initiation within 24 h postbirth) continuous KMC for relatively stable LBW babies in a resource-limited country, as a complement to conventional care, had higher, but not statistically significant, mortality in the first 28 days postbirth.

Although earlier continuous KMC resulted in significantly less weight loss from birth to 24 and 48 h postbirth without serious adverse events, the mortality data calls for caution in recommending this method for institutional settings. Additional, adequately designed studies of earlier continuous KMC are needed to examine its effectiveness.

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CONFLICTS OF INTEREST

We have no conflicts of interest to declare.

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添付資料　12

Diagnostic performance of urine dipstick testing in children with suspected UTI: a systematic review of relationship with age and comparison with microscopy

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REGULAR ARTICLE

Diagnostic performance of urine dipstick testing in children with suspected UTI: a systematic review of relationship with age and comparison with microscopy

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Abstract

Background: Prompt diagnosis of urinary tract infection (UTI) in children is needed to initiate treatment but is difficult to establish without urine testing, and reliance on culture leads to delay. Urine dipsticks are often used as an alternative to microscopy, although the diagnostic performance of dipsticks at different ages has not been established systematically.

Method: Studies comparing urine dipstick testing in infants versus older children and urine dipstick versus microscopy were systematically searched and reviewed. Meta-analysis of available studies was conducted.

Results: Six studies addressed these questions. The results of meta-analysis showed that the performance of urine dipstick testing was significantly less in the younger children when compared with older children ($p < 0.01$). Positive likelihood ratio (LR) of both nitrite and leucocyte positive 38.54 [95% confidence interval (CI) 22.49–65.31], negative LR for both negative 0.13 (95% CI 0.07–0.25) are reasonably good, and those for young infants are less reliable [positive LR 7.62 (95% CI 0.95–51.85) and negative LR 0.34 (95% CI 0.66–0.15)]. Comparing microscopy and urine dipstick testing, using bacterial colony count on urine culture showed no significant difference between the two methods.

Conclusion: Urine dipstick testing is more effective for diagnosis of UTI in children over 2 years than for younger children.

INTRODUCTION

Prompt diagnosis of all cases of urinary tract infection (UTI) in children through a simple, sensitive test is desirable to initiate timely treatment for relief of symptoms and minimize risk of renal scarring (1). In addition, where imaging and other interventions are considered necessary after recovery from UTI, accurate diagnosis, avoiding false-positive cases, is necessary to minimize the risk of inappropriate investigation. Although UTI is more common at a young age and the risk of acquiring a new renal scar is greater, the prevalence of positive samples among infants with fever, the primary symptom, is relatively low at 5–10% (1). In addition, the diagnosis is much more challenging because of the lack of localizing signs and symptoms, difficulty in urine collection and higher risks of contaminated samples.

The standard test for diagnosis of UTI has been evidence from urine culture yielding a colony count of greater than 10^5 cfu/mL of a pure growth of bacteria (2–4). However, this method requires an incubation period of 24 h or more, reducing the performance of this test in managing acutely sick children. Urine microscopy of the same sample, looking for leucocytes and bacteria, can provide immediate diagnostic information to enable the initiation of treatment. However, this requires examination by trained staff and specialist equipment and, unless equipment and expertise are available on site, it involves transfer of the sample to a laboratory. Dipstick testing of freshly voided urine for leucocytes and nitrites, indicating the presence of white cells and bacteria respectively, is particularly convenient, suitable for use at home, surgery or bedside and requires less skill than microscopy.

A systematic review was published by Whiting et al. (5) who described the performance of both dipstick and microscopy against urine culture as a gold standard. However, they did not consider the effect of age or urine collection method on test performance, nor did they compare the performance of dipstick and microscopy directly. The aim of this study is to evaluate the effect of age on performance

of dipstick testing for UTI and to compare dipsticks with microscopy.

METHOD

Searching the literature

Systematic searches to answer the clinical questions were executed using the following core databases via the OVID platform: Medline (1966 onwards), Cochrane Central Register of Controlled Trials (2nd Quarter 2006), Cochrane Database of Systematic Review (2nd Quarter 2006), Database of Abstracts of Reviews of Effects (2nd Quarter 2006), Embase (1980 onwards) and Cumulative Index to Nursing and Allied Health Literature (1982 onwards), all up to May 3, 2009.

Search strategies combined relevant controlled vocabulary and natural language in an effort to balance sensitivity and specificity. Both generic and specially developed methodological search filters were used appropriately. The list of Search Strategy is in Appendix S1.

Searches were not restricted by language, but non-English language studies were only translated where they were identified as highly significant to the clinical question, or a paucity of equivalent quality English language research meant the clinical question could not be addressed any other way.

There was no systematic attempt to search grey literature (conferences, letters, abstracts, theses and unpublished trials). Hand searching of journals not indexed on the databases was not undertaken.

Selection of studies

Two independent reviewers (RM and AF) selected full text articles by screening title and abstract yielded from the search mentioned above. Only studies including both leucocyte esterase and nitrite and comparing microscopy and urine dipstick testing to diagnose UTI in children, using urine culture as gold standard, were considered.

Studies in population of children already known to have significant pre-existing uropathy or underlying renal disease, urinary catheters *in situ*, neurogenic bladder, immunosuppressed children and children or neonates in intensive care units were excluded.

In the absence of a validated tool to rank quality of studies for this type of test, this review used a hierarchy for evidence of performance of diagnostic tests developed by NICE following the QUADUS tool that takes into account the various factors likely to affect the validity of the included studies (6).

Data analysis

The bivariate random-effects model estimated summary measures in meta-analysis and also their 95% confidence intervals (CI) with SAS version 9.1 (7,8). Positive and negative likelihood ratios were calculated for different cut-off values (9). Test for interaction by age was conducted in full models. Further sub-group analyses were conducted to obtain the diagnostic performance for older children and younger children.

RESULTS

Diagnostic performance of urine dipstick testing by age

Only six studies assessed diagnostic performance of both leucocyte esterase and nitrite and leucocyte esterase or nitrite compared with laboratory outcome of urine culture, so the data could include both symptomatic and asymptomatic patients (10–15).

Diagnostic performance for all of the six studies is presented in the Table 1. The results showed that the ability of dipsticks to rule bacteriuria either in or out was reasonably good, as positive likelihood ratio when both nitrite and leucocyte are positive is 34.61 [95% CI 17.81–63.33], and negative likelihood ratio when both nitrite and leucocyte are negative is 0.15 [95% CI 0.08–0.29].

Two studies compared infants and young children under 1 and 2 years with older children (10,11). In the younger age groups, the performance of dipsticks for both ruling in and out bacteriuria was less reliable than in older children. In particular, testing for interaction showed significant difference in ability to rule in bacteriuria between the two age groups.

Microscopy versus urine dipstick

Diagnostic performance of both microscopy and dipstick urine testing in the included studies are presented in Table 2. Only the study by Sharief assessed the performance of both microscopy and dipstick urine testing against culture results as a reference standard and stratified the results by the age groups (10). Two values were considered as criteria for a positive microscopy, one used cut-off value of 10 white blood cell (WBC) counts per high power field for pyuria and moderate bacteriuria and the other used cut-off value of 5 WBC counts per high power field for pyuria and occasional bacteriuria.

Ruling in UTI in younger children: The LR+ was higher for the dipstick than microscopy, 6.24 vs. 1.63 (95% CI 1.14–34.22 vs. 1.24–2.13), in children younger than 1 year when a cut-off value of 5 WBC per high power field was used. Thus, neither test performed very well. When a cut-off value of 10 was used, microscopy had a higher LR+ than dipstick testing at 15.6 vs. 6.24 (95% CI 4.16–58.44 vs. 1.14–34.22).

Ruling out UTI in younger children: Microscopy had a lower LR– than the dipstick, 0.27 vs. 0.31 (95% CI 0.07–0.99 vs. 0.13–0.71), in children younger than 1 year when a cut-off value of 5 WBC per high power field was used. When a cut-off value of 10 was used, dipstick testing had a lower LR– than microscopy, 0.31 vs. 0.66 [95% CI 0.13–0.71 vs. 0.44–0.97].

Ruling in UTI in older children: In the older age group, dipstick testing was better than microscopy for making a positive diagnosis of bacteriuria with a higher LR+ than microscopy at 27.10 vs. 1.69 [95% CI 11.44–64.21 vs. 1.52–1.87] when a cut-off value of 5 WBC per high power field was used. Where a cut-off value of 10 was used, dipstick testing again had a higher LR+ than microscopy at 27.10 vs. 10.84 [95% CI 11.44–64.21 vs. 5.95–19.75].

Table 1 Diagnostic performance of leucocyte esterase and/or nitrite on urine dipstick testing for urinary tract infection in children

Study	Country	Age	Manufacturer	Reference test	Nitrite or LE		Nitrite and LE	
					Positive LR (95% CI)	Negative LR (95% CI)	Positive LR (95% CI)	Negative LR (95% CI)
Sharief (10)	UK	<1 year (N = 124)	Multistix (Bayer)	10^5 cfu/mL	2.7	0.38	13.0	0.84
		1–16 years (N = 209)			3.8	0.25	35.6	0.45
Shaw (11)	US	<2 years (N = 145)	Multistix (Bayer)	Cath x 10^3 cfu/mL	9.4	0.31	6.24	0.88
		2–19 years (N = 346)		CVU x 10^5 cfu/mL	3.9	0.17	27.1	0.49
Dayan (12)	US	<2 months (N = 193)	Super UA	SPA x 10^3 cfu/mL CVU x 10^5 cfu/mL	10.5	0.16	107.7	0.69
Wiggelinkhuizen (13)	South Africa	<12 years (N = 962)	Combur9 (BM) Multistix (Ames)	Not clear	3.0	0.07	58.5	0.39
					3.1	0.08	47.8	0.38
Marsik (14)	US	-21 years (N = 601)	Chemstrip (Biodynamics)	SPA any bacteria Cath x 10^3 cfu/mL CVU x 10^5 cfu/mL	3.1	0.16	27.2	0.39
Woodward (15)	UK	-15 years (N = 134)	Multisticx (Bayer)	10^5 cfu/mL and WBC 20/mL	8.6	0.04	197.1	0.19
Pooled likelihood ratios		Total	All age		5.11 (3.00–8.70)	0.15 (0.08–0.29)	34.61 (17.81–63.33)	0.47 (0.35–0.64)
		Sub-group (only studies by Sharief and Shaw included)	Mainly infants		3.79 (2.03–6.07)	0.34 (0.15–0.66)	7.62 (0.95–51.85)	0.88 (0.66–1.00)
			Mainly older children		4.49 (2.86–7.12)	0.13 (0.07–0.25)	38.54 (22.49–65.31)	0.40 (0.34–0.47)
			Test for interaction by age		p = 0.12		p = 0.01	

Cfu = colony forming unit; Cath = urine taken by catheter; CVU = clean void urine; SPA = supra-pubic aspiration; WBC = white blood cell.

Ruling out UTI in older children: When microscopy was compared with dipstick testing for ruling out a diagnosis of UTI in children 2 years or older, microscopy had a lower LR– than dipstick testing, 0.04 vs. 0.17 [95% CI 0.00–0.59 vs. 0.07–0.41] when a cut-off value of 5 WBC per high power field was used, whereas the opposite was found when a cut-off value of 10 WBC was used; LR– for dipstick and microscopy respectively of 0.17 vs. 0.51 [95% CI 0.07–0.41 vs. 0.35–0.73].

Overall, the evidence shows that to make a rapid diagnosis of UTI, the dipstick test has the highest LR+ in children of 2 years and older with microscopy using a cut-off value of >10 WBC per high power field having the highest LR+ for the children under 2 years of age. To exclude a diagnosis of UTI in children younger than 2 years, microscopy with a cut-off value of 5 WBC per high power field has a marginally better LR– than dipstick testing, 0.27 vs. 0.31.

DISCUSSION

A systematic search was carried out to look for studies comparing urine dipstick testing in children by age and between dipstick testing and microscopy. The quantity and quality of the studies were reasonable, but only two of the six studies identified provided data for comparison of age groups and one study for urine testing methods (10–15). Overall, dipstick testing performed well against urine culture for ruling in UTI when positive for both Nitrite and LE and for ruling out UTI when negative for both tests. While ability of dipsticks to rule bacteriuria both in and out in older children was good, performance was significantly less reliable in younger age groups when compared with older children. The data did not address the performance of tests when only one parameter was positive, although this is a common scenario. For infants less than 1 year, microscopy using a cut-off value of moderate bacteria and 10 WBC per high power field showed the best diagnostic accuracy, and dipsticks did not perform as well.

As the number of suitable studies was small, the results must be interpreted with caution. The studies were laboratory based studies using colony count as the gold standard, but did not provide evidence of acute symptomatic UTI in every case and were likely to have included children tested during follow up who may have had asymptomatic bacteriuria. Variation in performance of tests at different ages is not clear, but is likely to be because of combinations of anatomical, physiological and pathological factors that mature with age. This includes changes in bacterial colonization, susceptibility and host response to infection, clinical presentation, use of diapers and difficulty in urine collection in children who are not yet toilet trained.

The comparison was carried out between microscopy and dipstick, and these two methods each have advantages and problems. Urine microscopy can provide information on the presence of white cells and bacteria, which is indicative of UTI. However, when samples are transferred to the laboratory, there is a time delay because of transporting and storing the sample. Microscopy can be carried out very

Table 2 Likelihood ratios of diagnosing UTI using microscopy or dipstick by age group

Children	Microscopy (>5 wbc/hpf for pyuria and few bacteria for bacteriuria)		Microscopy (>10 wbc/hpf for pyuria and moderate bacteria for bacteriuria)		Dipstick urine testing (both leucocyte esterase and nitrite)	
	Younger than 1 years	1 year or older	Younger than 1 year	1 year or older	Younger than 1 year	1 year or older
LR+ (95% CI)	1.63 (1.24–2.13)	1.69 (1.52–1.87)	15.6 (4.16–58.44)	10.84 (5.95–19.75)	6.24 (1.14–34.22)	27.1 (11.44–64.21)
LR– (95% CI)	0.27 (0.07–0.99)	0.04 (0.00–0.59)	0.66 (0.44–0.97)	0.51 (0.35–0.73)	0.31 (0.13–0.71)	0.17 (0.07–0.41)

quickly by a clinician at the bedside or in a clinic, but requires a microscope, counting chamber, training, skill and quality control. Although technically possible and effective for diagnosis of UTI, it is not widely used and difficult to sustain in the community without a dedicated service.

Dipstick testing for UTI with nitrite and leucocyte esterase can provide information on the presence of bacteria and white cells, which is safe, simple and quick. It has the potential to provide an immediate answer to the question of whether a sick infant or child with non-specific symptoms such as fever is likely to have a UTI or not and it is appropriate to start antibiotics. The nitrite test detects the presence of bacteria producing nitrite reductase in the urine. This is an enzyme that reduces nitrites to nitrites; however, it is not present in all uropathogens and, even when the pathogens produce the enzyme, the test is more likely to be positive if the urine has been incubated in the bladder for several hours. As infants have small bladders and micturate frequently, the test may be less effective in this age group. This test is thus highly specific for UTI but not sensitive in all cases.

Leucocyte esterase is an enzyme present in white cells that are almost invariably present when urine is infected. However, this test is non-specific as pyuria may be present as a result of other causes of fever or in response to non-steroidal anti-inflammatory agents, such as ibuprofen often given to febrile infants. The LE test may be positive even if the leucocytes have been lysed and are not visible on microscopy. This test is therefore sensitive but non-specific.

The classical method for diagnosis of UTI has been culture of urine showing a pure growth of >100 000 cfu/mL in a child with symptoms compatible with UTI based on the work on colony count by Kass (2–4). Colony count, which is not available until bacteria have been incubated for 24 h or more, is still used as the gold standard for diagnosis of UTI in spite of the limitations of this method for the management of sick children.

This review indicates that urine dipstick urine testing on a fresh sample can be recommended for diagnosing UTI in children over 2 years, but not for younger children. A new, good quality study, stratified by age and including a comparison between microscopy and urine dipstick testing against clinical diagnosis of symptomatic UTI is needed.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

Appendix S1 Search strategy.

Please note: Wiley-Blackwell are not responsible for the content or functionality of any supporting materials supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author for the article.

添付資料　13

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

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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† (°C)	N	Income setting	Preterm/ Term	Birthweight (g)	Gestational age (weeks)	Duration of SSC (min)s	Outcome measurements	
Author, published year	City, country								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

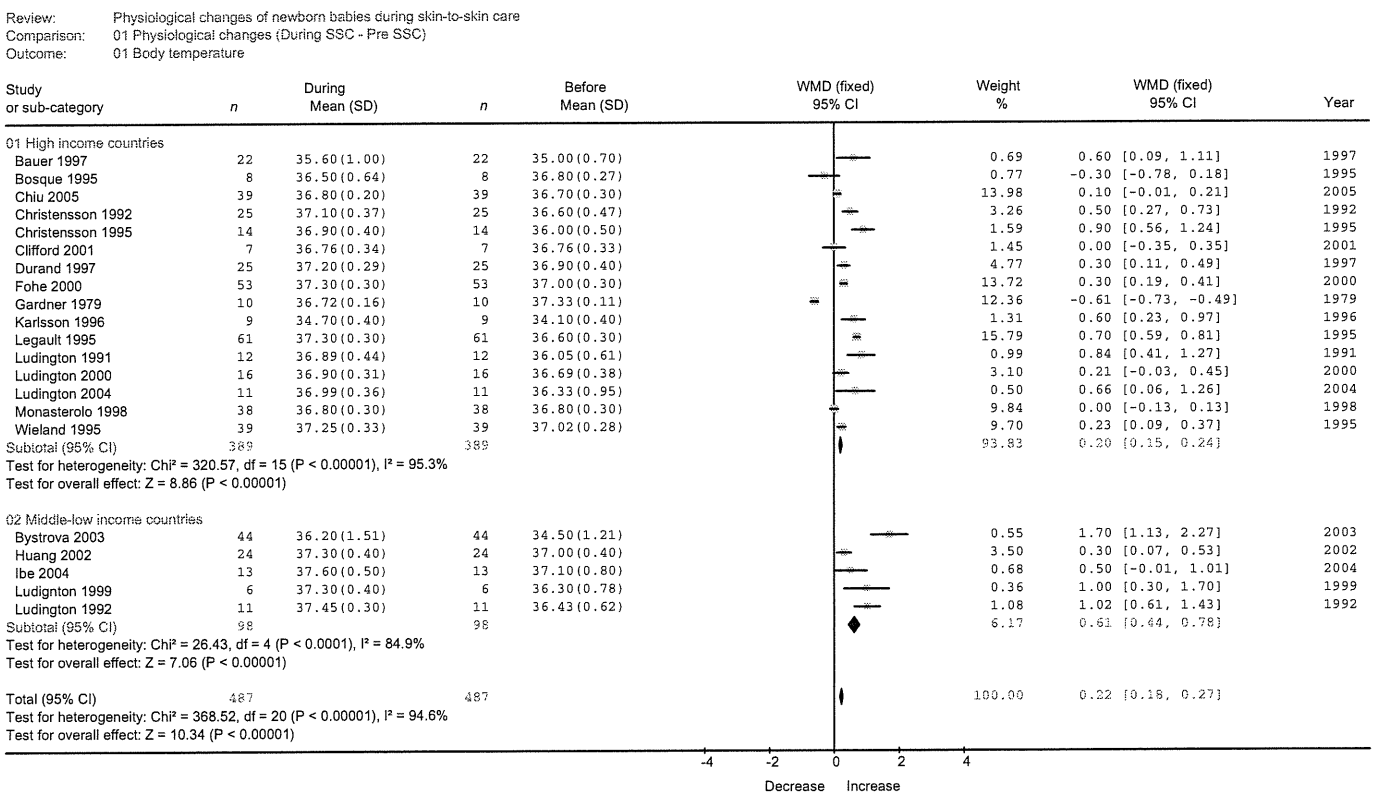

Fig. 1 Forest plot: effect on body temperature during skin-to-skin care, compared with that before skin-to-skin care, stratified by resource of settings. CI, confidence interval; SSC, skin-to-skin care; WMD, weighted mean difference.

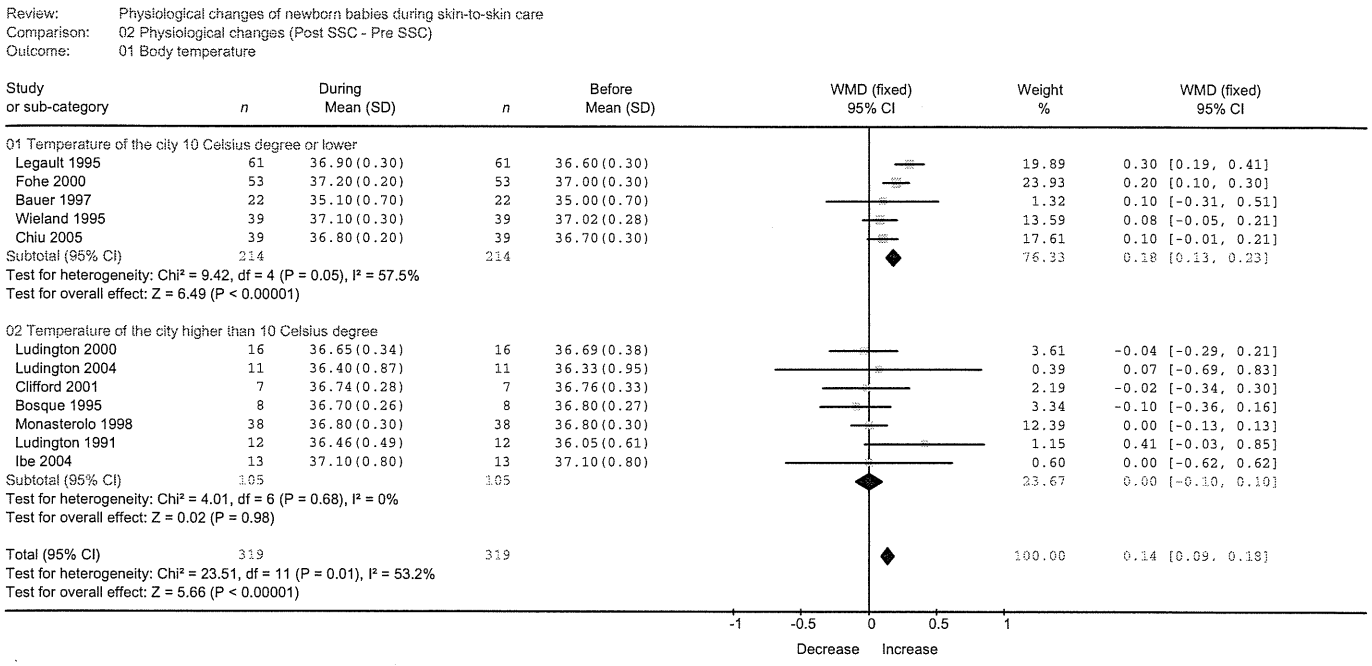

Fig. 2 Forest plot: effect on body temperature during skin-to-skin care, compared with that before skin-to-skin care, stratified by temperature of the cities. CI, confidence interval; SSC, skin-to-skin care; WMD, weighted mean difference.

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

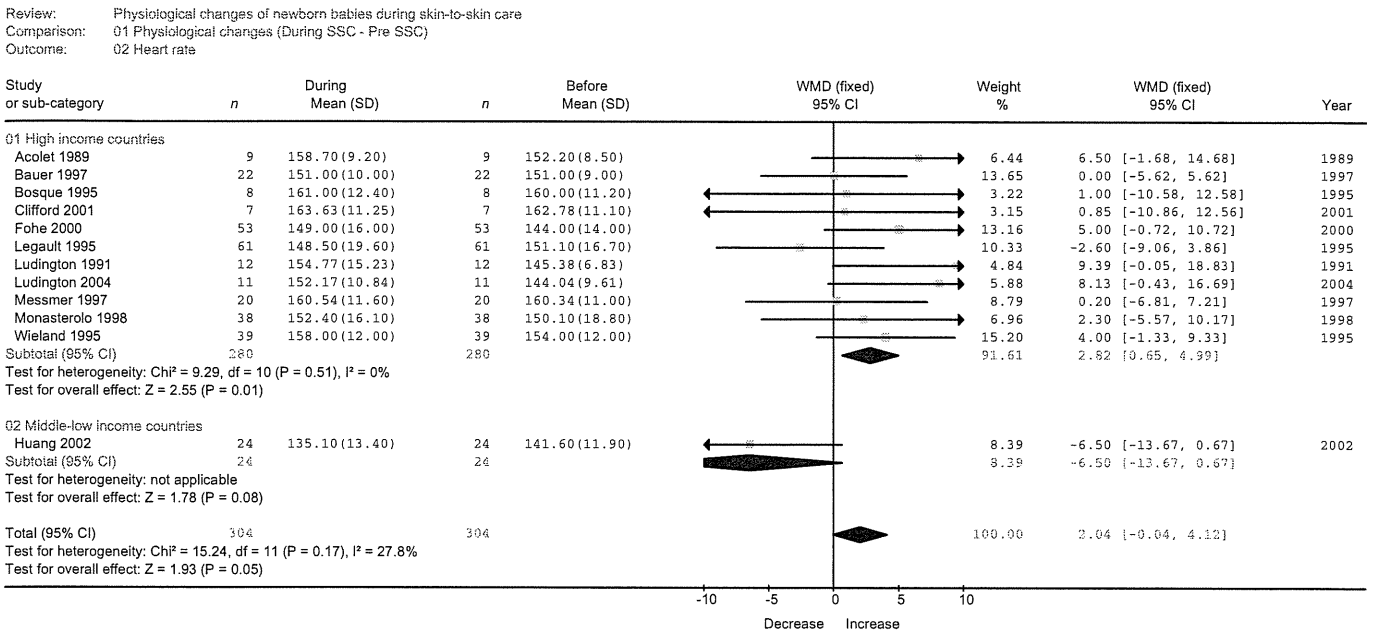

Fig. 3 Forest plot: effect on heart rate during skin-to-skin care, compared with that before skin-to-skin care, stratified by resource of the settings. CI, confidence interval; SSC, skin-to-skin care; WMD, weighted mean difference.

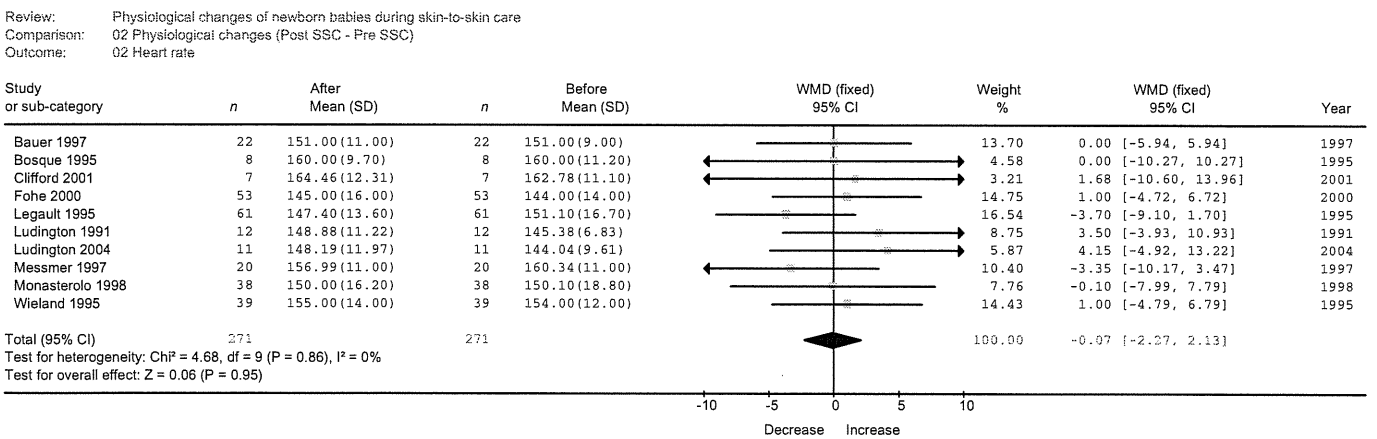

Fig. 4 Forest plot: effect on heart rate after skin-to-skin care, compared with that before skin-to-skin care. CI, confidence interval; SSC, skin-to-skin care; WMD, weighted mean difference.

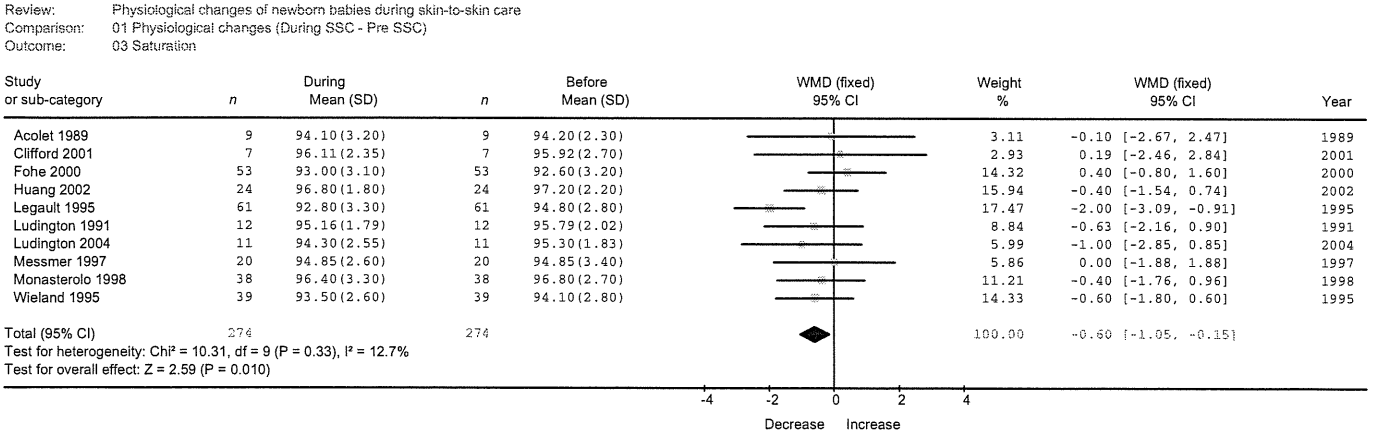

Fig. 5 Forest plot: effect on saturation during skin-to-skin care, compared with that before skin-to-skin care. CI, confidence interval; SSC, skin-to-skin care; WMD, weighted mean difference.

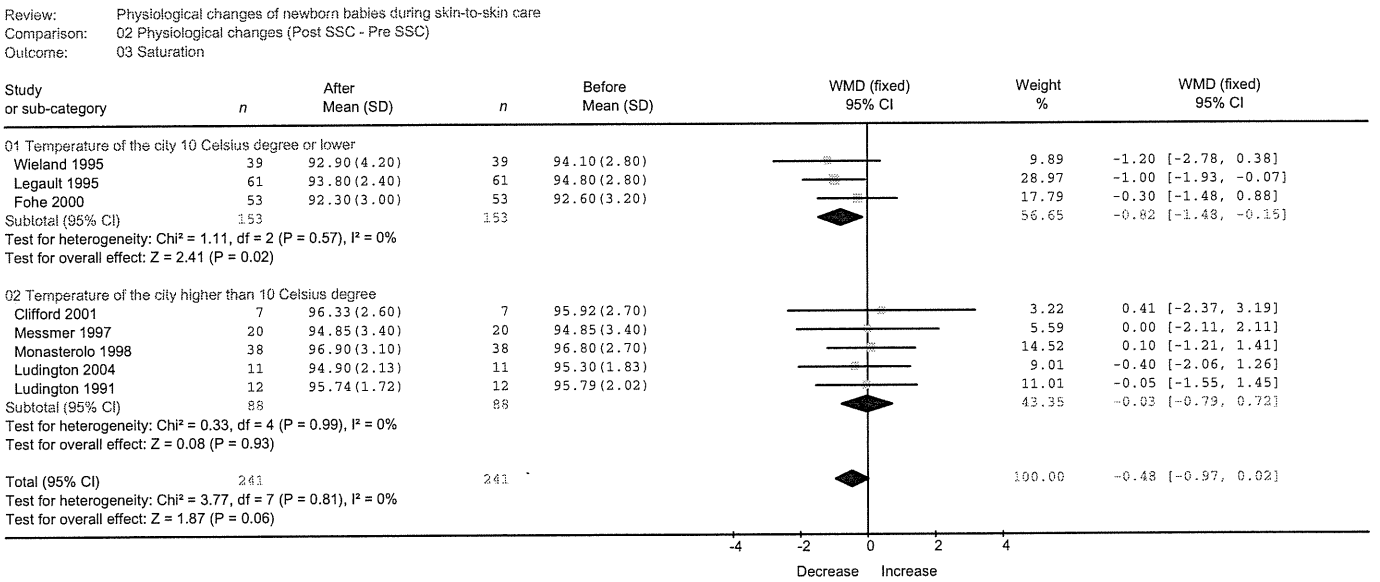

Fig. 6 Forest plot: effect on saturation after skin-to-skin care, compared with that before skin-to-skin care, stratified by temperature of the cities. CI, confidence interval; SSC, skin-to-skin care; WMD, weighted mean difference.

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.

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