Kangaroo Mother Care and Neonatal Outcomes: A Meta-analysis

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abstract

CONTEXT: Kangaroo mother care (KMC) is an intervention aimed at improving outcomes among preterm and low birth weight newborns.

OBJECTIVE: Conduct a systematic review and meta-analysis estimating the association between KMC and neonatal outcomes.

DATA SOURCES: PubMed, Embase, Web of Science, Scopus, African Index Medicus (AIM), Latin American and Caribbean Health Sciences Information System (LILACS), Index Medicus for the Eastern Mediterranean Region (IMEMR), Index Medicus for the South-East Asian Region (IMSEAR), and Western Pacific Region Index Medicus (WPRIM).

STUDY SELECTION: We included randomized trials and observational studies through April 2014 examining the relationship between KMC and neonatal outcomes among infants of any birth weight or gestational age. Studies with <10 participants, lack of a comparison group without KMC, and those not reporting a quantitative association were excluded.

DATA EXTRACTION: Two reviewers extracted data on study design, risk of bias, KMC intervention, neonatal outcomes, relative risk (RR) or mean difference measures.

RESULTS: 1035 studies were screened; 124 met inclusion criteria. Among LBW newborns, KMC compared to conventional care was associated with 36% lower mortality(RR 0.64; 95% [CI] 0.46, 0.89). KMC decreased risk of neonatal sepsis (RR 0.53, 95% CI 0.34, 0.83), hypothermia (RR 0.22; 95% CI 0.12, 0.41), hypoglycemia (RR 0.12; 95% CI 0.05, 0.32), and hospital readmission (RR 0.42; 95% CI 0.23, 0.76) and increased exclusive breastfeeding (RR 1.50; 95% CI 1.26, 1.78). Newborns receiving KMC had lower mean respiratory rate and pain measures, and higher oxygen saturation, temperature, and head circumference growth.

LIMITATIONS: Lack of data on KMC limited the ability to assess dose-response.

CONCLUSIONS: Interventions to scale up KMC implementation are warranted.

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Dr Boundy conceptualized and designed the study, conducted the literature review, collected the data, conducted the analyses, created the tables and figures, and drafted and revised the manuscript; Dr Dastjerdi conducted the literature review, collected and cleaned the data, assisted with table and figure creation, and critically reviewed the manuscript; Dr Spiegelman contributed to the study design, statistical analyses, and data interpretation and critically reviewed the manuscript; Drs Fawzi, Missmer, and Lieberman contributed to the study design and data interpretation and critically reviewed the manuscript; Ms Kajeepeta conducted the literature review, collected the data, assisted with figure creation, and critically reviewed the manuscript;Dr Wall contributed to the conceptualization and design of the study and data interpretation and critically reviewed the manuscript; Dr Chan conceptualized and designed the study, designed the data collection

To cite: Boundy EO, Dastjerdi R, Spiegelman D, et al. Kangaroo Mother Care and Neonatal Outcomes: A Meta-analysis. *Pediatrics.* 2016;137(1):e20152238

An estimated 4 million infants die each year during their first 4 weeks of life.[1] Although important progress has been made toward Millennium Development Goal 4 to reduce mortality in children <5 years old, less improvement has been achieved in the neonatal period.[2] Infants born before term or at low birth weight (LBW) are at elevated risk of neonatal mortality and morbidity, inhibited growth and development, and chronic disease.[1,3,4] Health technologies such as incubators can help improve outcomes in high-risk infants; however, such equipment is not widely available in low- and middle-income countries, where 99% of all neonatal deaths occur.[1] Effective and low-cost alternative methods of neonatal care are needed.

In 1978, Dr Edgar Rey Sanabria introduced kangaroo mother care (KMC) in Bogotá, Colombia as an alternative to incubators for LBW infants.[5] The World Health Organization defines KMC with 4 components: early, continuous, and prolonged skin-to-skin contact (SSC) between the newborn and mother, exclusive breastfeeding, early discharge from the health facility, and close follow-up at home.[6] KMC is postulated to improve neonatal outcomes by maintaining the infant's temperature and other vital sign parameters through SSC and by providing the benefits of breastfeeding.[5] These effects are thought to be beneficial for all newborns but may be especially advantageous for preterm infants.

In previous meta-analyses, KMC was found to reduce the risk of morbidity and mortality among LBW infants.[7,8] In randomized controlled trials (RCTs), SSC alone has also been associated with improved breastfeeding, cardiorespiratory stability, and improved responses to procedural pain.[9,10] Although these reviews have provided important evidence on the effectiveness of KMC, they are limited to specific outcome measures and newborn populations, and they have included only RCTs, with the exception of Lawn et al 2010.[7] To give a more complete understanding of the potential benefits and drawbacks of KMC, this systematic review and meta-analysis aims to provide a comprehensive summary of observational studies and RCTs on KMC and neonatal outcomes.

METHODS

Search Strategy and Selection Criteria

The literature search for this review included original reports, direct queries of authors of published articles, and program reports. We identified studies through electronic database searches of PubMed, Embase, Web of Science, Scopus, African Index Medicus (AIM), Latin American and Caribbean Health Sciences Information System (LILACS), Index Medicus for the Eastern Mediterranean Region (IMEMR), Index Medicus for the South-East Asian Region (IMSEAR), and Western Pacific Region Index Medicus (WPRIM) by using the terms "kangaroo mother care," "kangaroo care," and "skin to skin care" through April 24, 2014. We also conducted hand searches of reference lists of published systematic reviews. To search the gray literature for unpublished studies, we explored programmatic reports and requested data from programs implementing KMC.

We included studies using any definition of KMC with at least the SSC component and any neonatal outcome. We excluded studies with nonhuman subjects, <10 participants, nonprimary data collection or analysis, lack of a comparison group without KMC, and those that did not report a quantitative effect measure. We did not limit our analysis to studies of newborns with a specific gestational age or birth weight.

Data Abstraction

All article abstracts were screened by 2 independent reviewers. When eligibility for inclusion was unclear from the abstract, the full text was screened. Two reviewers then abstracted data from all articles meeting the inclusion criteria. At each stage, reviewers compared results to ensure agreement, and in cases of disagreement, a third party acted as tiebreaker. Data from articles in English, Spanish, and Portuguese were abstracted by 2 fluent speakers. For articles in less common languages, a single native speaker abstracted data. If an article was missing key information, we contacted authors by e-mail to request data.

We collected information on study design, setting, participant characteristics, description of KMC and comparison groups, follow-up time, outcomes, assessment of bias, and measures of association. Relative risks (RRs) or mean difference (MD) effect estimates with 95% confidence intervals (CIs) were extracted. We collected exposure data on KMC components, clinical stabilization criteria for starting KMC, and duration of SSC promoted and practiced.

Study Quality

Two independent reviewers assessed the methodological quality of studies in 5 domains: selection bias, information bias, detection bias, attrition bias, and other bias.[11] For observational studies, an additional domain for confounding was assessed. Each domain was categorized as high, low, or unclear risk of bias. We then created an overall assessment of bias for each study. For RCTs, if both selection and information bias were low risk, the overall risk of bias was considered low. If either domain was high risk, the overall risk of bias was designated as high. For observational studies, if selection bias, information

bias, and confounding were all low risk, the overall risk of bias was considered low. If any of those 3 domains was high risk, the overall risk was considered high. Otherwise, the overall risk of bias was considered unclear.

Statistical Analysis

We used the random effects estimator to assess the effect of KMC compared with conventional care on each neonatal outcome.[12] For dichotomous outcomes, we report summary estimates as RR and 95% CI. For studies that did not report an RR, we calculated the RR and SE from the data if available. For continuous outcomes, we report summary estimates as MD and 95% CI. When different units or scales were used across studies, we calculated the standardized mean difference (SMD).[11] When available, estimates adjusted for confounding were used rather than crude. Estimates that were presented only as medians rather than means, only as odds ratios without raw data to calculate the RR, or those with 0 cells were excluded from summary measures.[13–28]

We performed sensitivity analyses by restricting the analyses to RCTs and adjusted RR estimates for dichotomous outcomes and by restricting the analyses to RCTs and randomized crossover studies for continuous outcomes. To assess between-study heterogeneity, we report the I^2 statistic and the P value for the Q statistic.[12,29,30] The I^2 statistic quantifies the amount of variation in the effect estimate attributable to between-study heterogeneity, reported as a percentage, with a higher I^2 indicating more heterogeneity. We conducted subgroup analyses and metaregression for outcomes with data from ≥10 studies. We explored these predetermined subgroups: year, study type, sample size, location, country-level economy,[31] country-level neonatal mortality rate in 2013,[32] infant gestational age and birth weight, KMC components, KMC initiation criteria, SSC duration, and study quality classification. In metaregression analyses, we report the residual I^2, indicating the amount of remaining heterogeneity in the effect estimate after adjustment for a given characteristic. The indicator method was used for missing covariate information in metaregressions.[33]

We assessed publication bias by visual inspection of funnel plots of effect size and SE for asymmetry and by Begg's rank correlation and Egger's linear regression tests.[34,35] We conducted meta-analyses by using Stata statistical software (version 13.1), and risk of bias figures were created in RevMan software (version 5.3).

RESULTS

Our search identified 2515 records (Fig 1). We then identified 29 additional records related to KMC through crosscheck of reference lists, communication with an author,[36] and programmatic reports. After 1006 duplicates were removed, 1035 records underwent abstract screening. Of those, 527 did not meet inclusion criteria. Full-text articles for the remaining 508 records were then assessed and of those, 384 did not meet inclusion criteria. This review and meta-analysis includes 124 studies that reported an association between KMC and ≥1 neonatal outcome. One hundred eleven (90%) were in English, 7 (6%) in Portuguese, 4 (3%) in Spanish, and 2 (2%) in Farsi. We e-mailed 8 authors to obtain additional information[37–44] and received a response with data from 2.[38,39]

Study Characteristics

Of the 124 included studies, 110 (89%) were published between 2000 and 2014 (Table 1). Seventy-six studies (61%) had <100 participants. Fifty-five (44%) were RCTs, 8 (6%) were randomized crossover trials, and 61 (49%) were observational or nonrandomized intervention studies. Most studies (n = 113, 94%) were in middle- or high-income countries and were conducted in health facilities (n = 118, 98%).

Among studies reporting gestational age, the majority (n = 61, 68%) were among preterm infants <37 weeks' gestation; 17 (19%) were among full-term infants, defined as ≥37 weeks, and 12 (13%) were among infants of all gestational ages. Similarly, 47 studies (58%) were among LBW infants (≤2500 g), an additional 15 (19%) were among very LBW infants (≤1500 g), 9 (11%) were among non-LBW infants, and 10 (12%) were among infants of all birth weights. Forty-three studies (35%) did not specify infants' birth weight, and 34 (27%) did not specify gestational age, but all studies reported either birth weight or gestational age, except for 1.[45]

Most studies (n = 71, 68%) defined KMC as SSC only, 14 (13%) defined KMC as SSC plus promotion of exclusive breastfeeding, 20 (19%) included an early discharge or follow-up component, and 19 (15%) did not describe the components of their KMC intervention. SSC was initiated immediately after birth in 7 studies (8%), whereas 41 (48%) had stability criteria to be met before SSC initiation, and 27 (31%) had other non–stability-related initiation criteria. Eleven studies (14%) looking at pain-related outcomes started SSC around the time of an infant procedure. Fifty-two studies (66%) promoted <4 hours of SSC per day, 20 (25%) promoted ≥22 hours per day, and few studies (n = 7, 9%) had a duration between 4 and 21 hours per day. Thirty-eight studies (31%) did not specify when SSC was initiated, and 45 studies (36%) did not report the daily duration of SSC mothers were instructed to

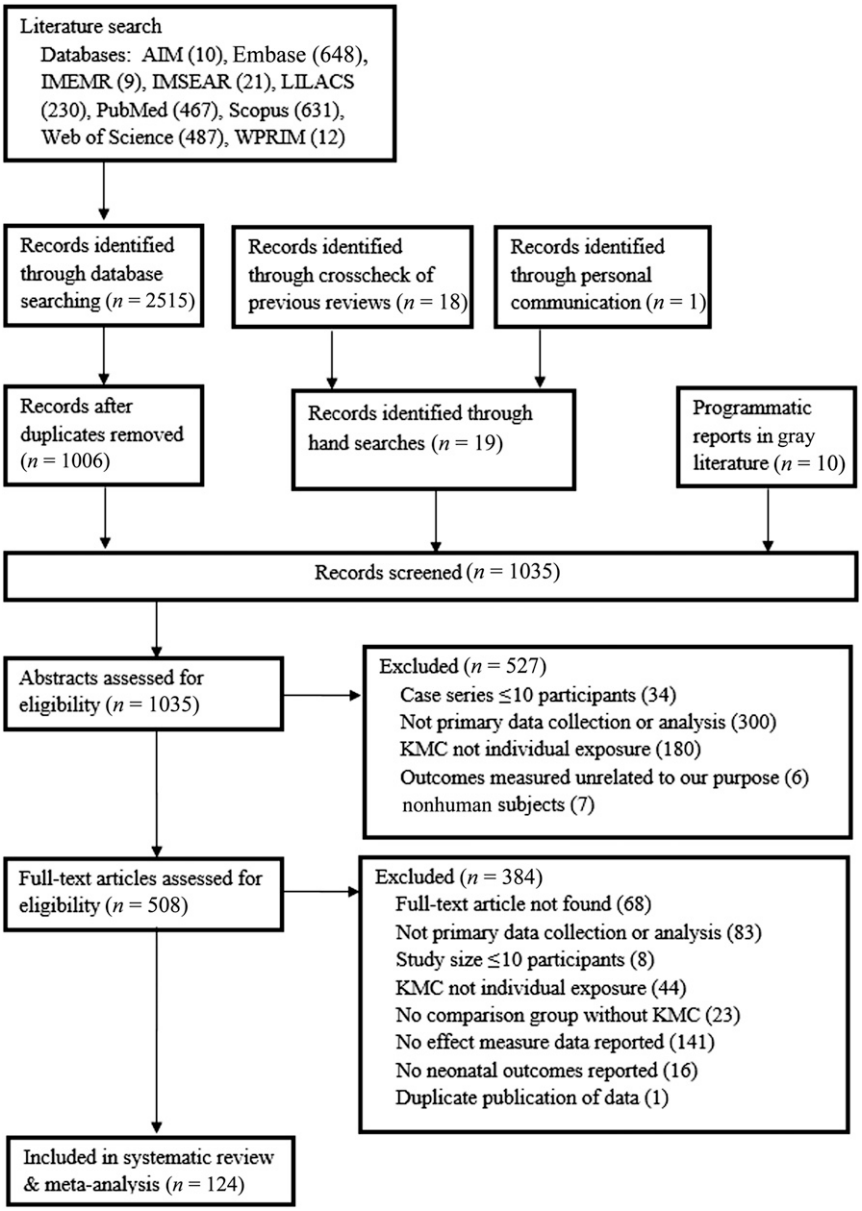

FIGURE 1
Flow diagram for identification of included studies.

practice. Information on duration of SSC actually practiced rather than promoted was only available in 16 studies (13%). Details of each included study are presented in Supplemental Table 16.

Meta-analysis

Summary RR estimates for dichotomous outcomes are reported in Table 2, and MD estimates for continuous outcomes are reported in Table 3.

Mortality

Compared with conventional care, KMC was associated with a 23% lower risk of mortality at each study's latest follow-up time (n = 16; 95% CI, 0.60, 0.99; I^2 = 67%) (Fig 2). Among 11 studies reporting mortality during the first 45 days of life, there was nonsignificant 21% decrease in mortality with KMC (95% CI, 0.57 to 1.10; I^2 = 77%), whereas the 7 studies reporting mortality at 3, 6, or 12 months of age showed 41% lower mortality in the KMC groups compared with controls (95% CI, 0.43 to 0.82; I^2 = 0%) (Table 2).

Among LBW newborns <2000 g, KMC decreased mortality at latest follow-up time by 36% (n = 15; 95% CI, 0.46 to 0.89; I^2 = 72%). In the 2 studies of infants of all birth weights, KMC did not significantly affect mortality (RR 1.04; 95% CI, 0.82 to 1.33; I^2 = 0%). Additional subgroup analyses of study characteristics and KMC components for mortality

at latest follow-up are presented in Supplemental Table 4. We did not find important differences in the effect of KMC on mortality by location, country-level economy, or neonatal mortality rate. Two studies whose KMC intervention included SSC, exclusive breastfeeding, early discharge, and close follow-up showed a stronger protective effect of KMC against mortality (RR 0.43; 95% CI, 0.19 to 0.98) than studies using other KMC definitions. Similarly, when mothers were encouraged to provide SSC plus ≥1 other component, KMC was protective against mortality (n = 9; RR 0.65; 95% CI, 0.48 to 0.89), whereas studies where KMC was defined as SSC alone did not (n = 5; RR 0.71; 95% CI, 0.33 to 1.52). There was no difference in mortality between studies including promotion of exclusive breastfeeding in their KMC definition compared with those that did not.

Studies instructing mothers to start SSC after stability criteria was met showed a similarly protective effect against mortality (n = 9, RR 0.57; 95% CI, 0.34 to 0.97) as those that started SSC immediately (n = 3, RR 0.51; 95% CI, 0.33 to 0.78) (Supplemental Fig 3). Eleven studies promoting ≥22 hours of SSC per day showed a protective effect of KMC (RR 0.64; 95% CI, 0.44 to 0.92) on mortality, whereas there was no association in the 1 study promoting 4 to 8 hours per day or the 4 studies that did not define SSC duration (Supplemental Fig 4).

Breastfeeding

KMC increased the likelihood of exclusive breastfeeding at hospital discharge or 40 to 41 weeks postmenstrual age by 50% (n = 13; 95% CI, 1.26 to 1.78; I^2 = 93%) (Supplemental Fig 5). KMC increased the likelihood of exclusive breastfeeding across nearly all subgroups of study, infant, and KMC characteristics (Supplemental Table

TABLE 1 Characteristics of Included Studies (n = 124)

Characteristic	Number of Studies, n (%)
Year of publication	
1988–1999	14 (11)
2000–2009	58 (47)
2010–2014	52 (42)
Sample size	
<50	43 (35)
50–<100	33 (27)
100–<200	21 (17)
≥200	27 (22)
Study type	
RCT	55 (44)
Cohort	17 (14)
Pre–post	23 (19)
Intervention trial (nonrandomized)	8 (6)
Randomized crossover	8 (6)
Crossover (nonrandomized)	3 (2)
Case–control	2 (2)
Chart review	5 (4)
Facility evaluation	2 (2)
Interview or survey	1 (1)
Region (World Health Organization)	
Africa	11 (9)
Americas	50 (41)
Eastern Mediterranean	11 (9)
Europe	19 (16)
Southeast Asia	20 (17)
Western Pacific	9 (7)
Multiple	1 (1)
Country-level economy (World Bank)	
Low income	7 (6)
Middle income	65 (54)
High income	48 (40)
Multiple	1 (1)
Country-level neonatal mortality ratio, deaths/1000 live births	
<5	52 (43)
5–<15	36 (30)
15–<30	29 (24)
≥30	4 (3)
Setting	
Urban	92 (90)
Rural	4 (4)
Mixed	6 (6)
Facility type	
NICU or step-down unit	51 (42)
Health facility	67 (55)
Community or population based	3 (2)
Gestational age at birth	
Preterm, <37 wk	34 (38)
Very preterm, <34 wk	27 (30)
Full-term, ≥35–37 wk	17 (19)
All gestational ages	11 (12)
Comparison: preterm vs full term	1 (1)
Birth wt	
LBW, ≤2500 g	47 (58)
Very LBW, ≤1500 g	15 (19)
Normal birth wt, ≥2500 g	9 (11)
All birth weights	10 (12)
KMC components	
SSC only	71 (68)
SSC + EBF	14 (13)
SSC + EBF + DC	1 (1)
SSC + EBF + DC + FU	4 (4)

TABLE 1 Continued

Characteristic	Number of Studies, *n* (%)
SSC + DC	1 (1)
SSC + DC + FU	7 (7)
SSC + EBF + FU	7 (7)
SSC initiation time	
Immediately after birth	7 (8)
After stability criteria met	41 (48)
After other criteria met	27 (31)
For a painful procedure	11 (13)
SSC duration promoted, h/d	
<2	38 (48)
2–<4	14 (18)
4–<9	6 (8)
9–<12	0
12–<22	1 (1)
≥22	20 (25)
Number of days of SSC promoted	
1–5	47 (75)
6–<30	9 (14)
≥30	2 (3)
Dependent on hospital stay	5 (8)

DC, early discharge; EBF, exclusive breastfeeding; FU, follow-up after discharge.

5). At 1- to 4-month follow-up, KMC increased the likelihood of exclusive breastfeeding by 39% (*n* = 8; 95% CI, 1.11 to 1.74; I^2 = 60%) (Table 2). KMC did not have a significant impact on the MD in time to breastfeeding initiation (*n* = 4; SMD −1.07; 95% CI, −2.30 to 0.17; I^2 = 97%) (Table 3). Several studies looked at other feeding outcomes that were too heterogeneous to combine into a summary estimate.[62–64,72,77,96,118,119]

Infection

Risk of infection during study follow-up was not statistically different between KMC and control groups (*n* = 12; RR 0.67; 95% CI, 0.43 to 1.05; I^2 = 60%) (Table 2). When data were stratified by infection type, however, KMC was associated with 47% lower risk of sepsis (*n* = 8; 95% CI, 0.34 to 0.83; I^2 = 25%) but did not have an effect on methicillin-resistant *Staphylococcus aureus* or other severe infections (*n* = 4; RR 1.00; 95% CI, 0.40 to 2.46; I^2 = 77%) (Supplemental Fig 6). KMC did not have a significant effect on risk of necrotizing enterocolitis (*n* = 3; RR 0.96; 95% CI, 0.45 to 2.04) (Table 2). All studies that examined sepsis and necrotizing enterocolitis were among infants <2250 g at birth.

Among RCTs, KMC decreased risk of infection by 49% (*n* = 9; 95% CI, 0.32 to 0.81) (Supplemental Table 6). Nine studies that had stability criteria before initiating SSC showed a protective effect of KMC against infection (RR 0.50; 95% CI, 0.33 to 0.77), whereas the 2 studies that had other non–stability-related criteria before initiation did not (RR 1.00; 95% CI, 0.69 to 1.45).

Heart Rate

KMC did not have a significant effect on mean heart rate (*n* = 15; MD 0.41 beats per minute; 95% CI, −2.25 to 1.42; I^2 = 46%) (Supplemental Fig 7). No statistical or clinically significant differences were noted in subgroup analysis of study, infant, or KMC characteristics (Supplemental Table 7).

Respiration and Oxygenation

Compared with conventional care, KMC was associated with a non–statistically significant reduction in risk of apnea among 6 studies of LBW infants <2000 g (RR 0.39; 95% CI, 0.13 to 1.14; I^2 = 42%) (Table 2). On average, newborns receiving KMC had a respiratory rate 3 breaths per minute slower (*n* = 12; 95% CI, −5.15 to −1.19; I^2 = 75%) and oxygen saturation 0.9% higher than controls (*n* = 14; 95% CI, 0.35 to 1.45; I^2 = 92%) (Supplemental Figs 8 and 9). Across subgroup analyses, KMC was associated with lower respiratory rate and higher oxygen saturation (Supplemental Tables 8 and 9).

Temperature

Compared with conventional care, KMC was associated with 78% lower risk of hypothermia (*n* = 9; 95% CI, 0.12 to 0.41; I^2 = 71%) and 23% lower risk of hyperthermia (*n* = 3; 95% CI, 0.59 to 1.01; I^2 = 0%) (Table 2). Mean body temperature of infants receiving KMC was 0.24°C higher than in controls (*n* = 14; 95% CI, 0.15 to 0.33; I^2 = 82%) (Supplemental Fig 10). This effect was similar across subgroups of study, infant, and KMC characteristics (Supplemental Table 10).

Hypoglycemia and Cortisol

KMC was strongly protective against hypoglycemia in 2 studies of LBW infants (RR 0.12; 95% CI, 0.05 to 0.32; I^2 = 0%) (Table 2). Standardized mean cortisol levels were not significantly different between KMC and control groups (*n* = 3; SMD −0.44; 95% CI, −0.94 to 0.06; I^2 = 54%) (Table 3).

Hospital Stay

KMC decreased the likelihood of hospital readmission by 58% in 2 studies (95% CI, 0.23 to 0.76; I^2 = 0%) (Table 2). Length of hospital stay did not differ significantly between KMC and control groups (*n* = 12; MD −0.68 days; 95% CI, −2.11 to 0.75; I^2 = 95%) (Supplemental Fig 11, Supplemental Table 11). One study reported length of hospital and NICU stays stratified by birth weight and found shorter hospital stays in the KMC group compared with controls among infants <1500 g and in length of NICU stay among infants 1201 to 1500 g.[120]

Growth

Various infant growth outcomes were examined across studies. We looked at the effect of KMC on

TABLE 2 RR and 95% CI for the Effect of KMC Compared With Conventional Care on Dichotomous Neonatal Outcomes

Outcome	All Studies					RCT and Adjusted Observational Studies				
	n	RR (95% CI)[a]	*P*	Test for Heterogeneity (*P*)	I^2, %[b]	*n*	RR (95% CI)[a]	*p*	Test for Heterogeneity (*P*)	I^2, %[b]
Mortality										
Latest follow-up[46–61]	16	0.77 (0.60 to 0.99)	.05	<.01	67	12	0.95 (0.73 to 1.23)	.69	.13	32
≤45 d[46–55,58]	11[c]	0.79 (0.57 to 1.10)	.17	<.01	77	7	1.16 (0.91 to 1.47)	.23	.29	18
3–12 mo[46,47,56,57,59–61]	7[c]	0.59 (0.43 to 0.82)	<.01	.63	0	6	0.67 (0.47 to 0.96)	.03	.88	0
LBW <2000 g[46–54,56–61]	15	0.64 (0.46 to 0.89)	.01	<.01	72	11	0.86 (0.59 to 1.24)	.41	.10	38
All birth weights[50,55]	2	1.04 (0.82 to 1.33)	.73	.83	0	1	1.06 (0.80 to 1.41)	.70	—	—
Exclusive breastfeeding										
Discharge or 40–41 wk PMA[28,50,59,62–71]	13	1.50 (1.26 to 1.78)	<.01	<.01	93	8	1.25 (1.10 to 1.42)	<.01	<.01	59
1–4 mo old[45,62,63,65,69,72–74]	8	1.39 (1.11 to 1.74)	.01	.02	60	6	1.53 (1.08 to 2.18)	.02	<.01	71
Other										
Infection[15,27,28,48,52,53,58,60,65,67,75,76]	12	0.67 (0.43 to 1.05)	.08	<.01	60	10	0.60 (0.36 to 1.01)	0.05	<.01	65
Sepsis[15,27,28,48,52,53,58,65]	8	0.53 (0.34 to 0.83)	.01	.23	25	7	0.44 (0.29 to 0.66)	<.01	.49	0
NEC[49,58,65]	3	0.96 (0.45 to 2.04)	.92	.45	0	3	0.96 (0.45 to 2.04)	.92	.45	0
Hypothermia[15,18,36,48,52,58,65,77,78]	9	0.22 (0.12 to 0.41)	<.01	<.01	71	7	0.28 (0.15 to 0.53)	<.01	.01	65
Hyperthermia[15,48,52]	3	0.77 (0.59 to 1.01)	.06	.88	0	3	0.77 (0.59 to 1.01)	.06	.88	0
Apnea[27,46,48,52,58,65]	6	0.39 (0.13 to 1.14)	.09	.12	42	6	0.39 (0.13 to 1.14)	.09	.12	42
Hypoglycemia[27,48]	2	0.12 (0.05 to 0.32)	<.01	.53	0	2	0.12 (0.05 to 0.32)	<.01	.53	0
Readmission[60,74]	2	0.42 (0.23 to 0.76)	<.01	1.00	0	1	0.42 (0.14 to 1.29)	.13	—	—

NEC, necrotizing enterocolitis; PMA, postmenstrual age.

[a] Random effects estimates.

[b] I^2 variation in RR or MD attributable to heterogeneity.

[c] Two studies contributed data to estimates at both follow-up times of ≤45 d and 3–12 mo.[15,50]

measures of weight gain individually and by combining them using the SMD (Table 3, Supplemental Fig 12). We did not find a significant association between KMC and the SMD in weight gain or body length growth. Infants receiving KMC had head circumference growth 0.19 cm per week higher than controls in 3 studies of infants <2000 g at birth (95% CI, 0.01 to 0.37; I^2 = 89%). Among studies reporting weight gain outcomes, there were no important differences in the effect of KMC by subgroups of study, infant, or KMC characteristics (Supplemental Table 12). One additional study examined the risk of being malnourished, overweight, or obese at 5 to 6 years old and found no difference between the KMC and control groups.[121]

Pain

Several studies examined pain-related outcomes, including crying, heart rate, and pain scores during and after painful procedures (Table 3). According the Premature Infant Pain Profile scale, with a range from 0 to 21, infants receiving SSC during a painful procedure had a mean pain score 0.83 points lower than controls (n = 7; 95% CI, −1.53 to −0.13; I^2 = 88%).[122] Studies using the Neonatal Infant Pain Scale[123] (n = 3) and the Neonatal Facial Coding System[121,124] (n = 2) showed nonsignificant decreases in pain among infants receiving SSC during painful procedures compared with controls. When combined across scales using the SMD, a decrease in pain score was again noted in infants receiving SSC compared with conventional care (SMD −0.63; 95% CI, −1.09 to −0.16; I^2 = 89%) (Supplemental Fig 13). This effect was similar across subgroups (Supplemental Table 13).

TABLE 3 MD and 95% CI for the Effect of KMC Compared With Conventional Care on Continuous Neonatal Outcomes

Outcome	All Studies					RCT and Randomized Crossover Studies				
	n	MD (95% CI)[a]	*P*	Test for Heterogeneity (*P*)	I^2, %[b]	*n*	MD (95% CI)[a]	*P*	Test for Heterogeneity (*P*)	I^2, %[b]
Vital signs										
Heart rate, beats/min[38,65,79–91]	15	−0.41 (−2.25 to 1.42)	.66	.03	46	2	0.04 (−1.60 to 1.68)	.96	.60	0
Respiratory rate, breaths/min[52,65,79,81,83–90]	12	−3.17 (−5.15 to −1.19)	<0.01	<.01	75	3	−5.49 (-8.80 to −2.18)	<.01	<.01	88
Oxygen saturation, %[52,65,79–81,83–90,92]	14	0.90 (0.35 to 1.45)	<.01	<.01	92	4	1.28 (0.39 to 2.17)	.01	<.01	86
Temperature, °C[65,78–83,85–87,89,93–95]	14	0.24 (0.15 to 0.33)	<.01	<.01	82	3	0.24 (0.04 to 0.44)	.02	<.01	91
Breastfeeding initiation time, SMD[48,52,96,97]	4	−1.07 (−2.30 to 0.17)	.09	<.01	97	4	−1.07 (−2.30 to 0.17)	.09	<.01	97
Growth										
Wt change, g[14,18,53,59,98]	5	3.29 (−4.95 to 11.52)	.43	.02	67	2	8.30 (1.16 to 15.43)	.02	.31	3
Wt change, g/day[28,48,58,99,100]	5	2.58 (−0.51 to 5.67)	.10	<.01	81	4	3.04 (−1.35 to 7.43)	.18	<.01	84
Wt change, g/kg/day[49,99]	2	−0.84 (−3.39 to 1.70)	.52	.02	81	0	—	—	—	—
Wt change, SMD[14,18,28,48,49,53,58,59,98–100]	11	0.16 (−0.08 to 0.40)	.21	<.01	81	6	0.33 (−0.05 to 0.70)	.09	<.01	83
Length change, cm/wk[18,96]	2	0.15 (−0.09 to 0.39)	0.21	.03	79	2	0.15 (−0.09 to 0.39)	.21	.03	79
Length change, SMD[18,48,58]	3	0.24 (−0.02 to 0.49)	.07	.26	25	3	0.24 (−0.02 to 0.49)	.07	.26	25
Head circumference change, cm/wk[18,28,48]	3	0.19 (0.01 to 0.37)	.04	<.01	89	3	0.19 (0.01 to 0.37)	.04	<.01	89
Head circumference change, SMD[18,28,48,58]	4	0.61 (0.20 to 1.02)	<.01	<.01	77	4	0.61 (0.20 to 1.02)	<.01	<.01	77
Pain										
Pain score, SMD[38,101–109]	10	−0.63 (−1.09 to −0.16)	.01	<.01	89	8	−0.75 (−1.28 to −0.22)	.01	<.01	89
Premature Infant Pain Profile score, 0–21[38,103–105,107–109]	7	−0.83 (−1.53 to −0.13)	.02	<.01	88	5	−0.98 (−1.83 to −0.13)	.02	<.01	91
Neonatal Infant Pain Scale score, 0–7[38,102,106]	3	−1.14 (−2.34 to 0.05)	.06	<.01	85	2	−1.21 (−2.88 to 0.45)	.15	<.01	91
Neonatal Facial Coding System score, 0–10[101,102]	2	−1.40 −3.08 to 0.28)	.10	<.01	91	2	−1.40 (−3.08 to 0.28)	.10	<.01	91
Crying duration after painful stimulus, s[110–112]	3	−11.30(-19.79 to-2.80)	.01	.80	0	3	−11.30(−19.79 to −2.80)	.01	.80	0
Heart rate during painful stimulus, beats/min[111–113]	3	−7.46 (−12.98 to −1.93)	.01	.25	29	3	−7.46 (−12.98 to −1.93)	.01	.25	29
Heart rate after painful stimulus, beats/min[101,103,114,115]	4	−4.00 (−8.93 to 0.93)	.11	<.01	87	3	−7.52 (−8.47 to −6.58)	<.01	.54	0
Other										
Length of hospital stay, days[14,18,48,49,52,53,68,71,99,100,116,117]	12	−0.68 (−2.11 to 0.75)	.35	<.01	95	5	−0.38 (−2.99 to 2.23)	.78	<.01	91
Cortisol, SMD[38,95,107]	3	−0.44 (−0.94 to 0.06)	.08	.12	54	2	−0.58 (−0.88 to −0.29)	<.01	.33	0

SMD, standardized mean difference.

[a] Random effects MD.

[b] I^2: variation in RR or MD attributable to heterogeneity.

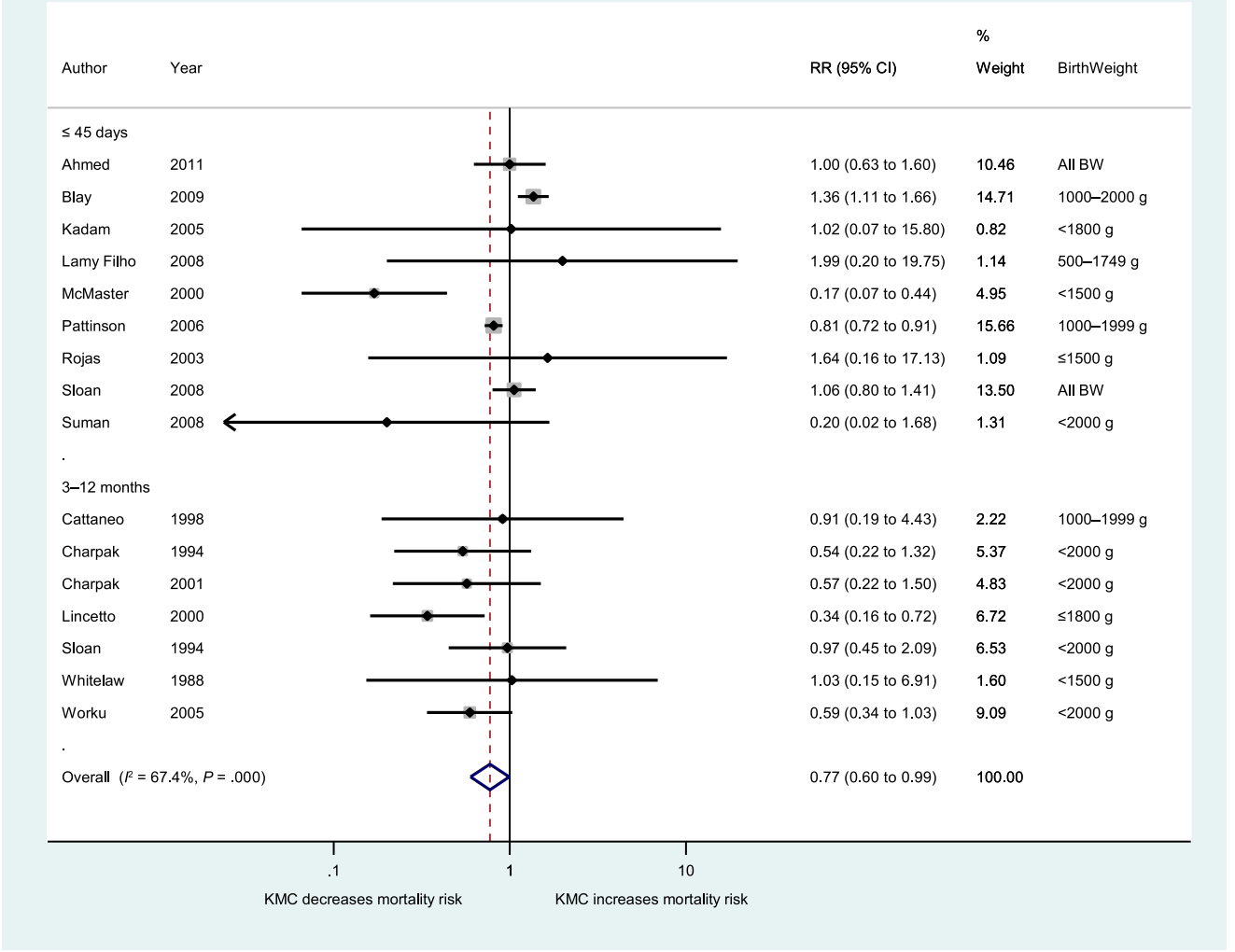

FIGURE 2
Forest plot for effect of KMC compared with conventional care on mortality at latest follow-up time, grouped by follow-up time. BW, birth weight.

After a painful stimulus, infants receiving SSC cried on average 11 seconds less than control group infants (n = 3; 95% CI, −19.79 to −2.80; I^2 = 0%) (Table 3). Among studies using infant heart rate during painful stimulus as a proxy pain measure, mean heart rate was 7 beats per minute slower in the SSC groups than controls (n = 3; 95% CI, −12.98 to −1.93; I^2 = 29%).

Other Outcomes

A variety of other neonatal outcomes were reported in a single study or in different ways across studies that could not be combined into a summary measure. Those outcomes related to illness included retinopathy, bronchopulmonary dysplasia, regurgitation, respiratory tract disease, diarrhea, and intraventricular hemorrhage.[48,49,58,60,125] Other outcomes included hyperbilirubinemia, blood pressure, stratum corneum hydration, oxygen requirement, carbon dioxide production, low-frequency/high-frequency ratio, thyroid measures, water loss, home observation of the environment, stabilization of cardiopulmonary system, and cost of care.[13,44,71,79,80,89,125–139]

Several studies also examined the effect of KMC on neurocognitive outcomes. These data were reported across different scales with endpoints at different ages and thus could not be combined into summary measures. They included assessments of behavior, mental and psychomotor development, reflexes, temperament, brain maturation, and sleep.[16,61,77,90,91,95,110,113,115,140–151]

Risk of Bias

After evaluating 5 domains of bias among the 55 RCTs, we classified 25 (45%) as overall low risk of bias,

14 (25%) as high, and 16 (29%) unclear (Supplemental Table 14; Supplemental Fig 14). When the same 5 bias domains were used plus a domain for confounding for the 69 observational studies, overall risk of bias was considered low in 29 (42%), high in 24 (35%), and unclear in 16 (23%) (Supplemental Table 15; Supplemental Fig 15). When restricted to studies with low overall risk of bias, the protective effects of KMC on mortality, exclusive breastfeeding, and infection were stronger than results obtained with all studies (Supplemental Tables 4–6). Effect estimates for continuous outcomes did not materially change when restricted to studies with low risk of bias (Supplemental Tables 7–13).

Publication Bias

We assessed publication bias for mortality at latest follow-up time, exclusive breastfeeding at discharge, and infection outcomes. No evidence of publication bias was noted for mortality by Begg's (P = .89) or Egger's (P = .36) tests or by visual inspection of the funnel plot (Supplemental Fig 16). Similarly, no evidence of publication bias was found for exclusive breastfeeding (Begg's P = .25; Egger's P = .12) or infection (Begg's P = .45; Egger's P = .75).

DISCUSSION

When compared with conventional care, KMC is associated with decreased mortality among newborns who survive to receive it, particularly among LBW infants. KMC also increases likelihood of exclusive breastfeeding up to 4 months of age and decreases risk of newborn sepsis, hypothermia, hypoglycemia, and hospital readmission. Additionally, infants receiving KMC have improved vital signs, greater head circumference growth, and lower pain scores. We did not find evidence of harm related to KMC.

We found a similar magnitude in reduction of mortality risk among LBW infants exposed to KMC as in previous reviews.[7,8] We did not find a significant difference in mortality in the 2 studies including all birth weights, which had not been examined in previous reviews. We noted a similar protective effect of KMC against sepsis and hypothermia, increased likelihood of exclusive breastfeeding, and lower Premature Infant Pain Profile score as described in previous work.[8–10] We did not find a significant difference in length of hospital stay, which could reflect differences in study inclusion criteria and infant characteristics compared with a previous review.[8] We found greater head circumference growth, but no difference in length or weight gain, with most measurements taken across the hospital stay period. Conde-Agudelo and Díaz-Rossello[8] reported an increase in growth parameters for KMC-exposed infants compared with controls at latest follow-up, but as in our results, no important differences in growth measured at discharge or 40 to 41 weeks' postmenstrual age.[8]

Although the improvements in respiratory rate, oxygenation, and temperature that we found associated with KMC exposure may each be of modest clinical significance, when taken together they support the hypothesis that KMC improves overall physiologic regulation in the neonate, which could have important effects on other longer-term outcomes. Lower pain measures among infants receiving KMC may also provide additional benefits for LBW infants who experience numerous injections during hospitalization.

This meta-analysis provides a comprehensive picture of the effects of KMC on neonatal health by its inclusion of all study types, outcomes, and infant populations. Therefore, we were able to look at as many studies as available for each outcome and perform sensitivity analyses. We were able to assess the effect of KMC on normal weight and term infants, albeit with limited data, and to examine several outcomes related to vital signs and procedural pain parameters that were not included in the most recent review of KMC among LBW infants.[8] We also collected detailed information on study design, newborn characteristics, and KMC components to look for differences in the effect of KMC in subgroup and metaregression analyses.

How much of KMC's effect is through SSC alone compared with KMC that includes additional components remains unclear because of the sparsity of details available on the KMC intervention practiced in many studies. When they were described, we noted heterogeneity in the definition and components of KMC and conventional care across studies. We attempted to address this limitation by performing subgroup analyses by KMC components, duration, and initiation time. The effects of KMC may be confounded with breastfeeding as a component of KMC. We explored this possibility by comparing subgroups of studies that encouraged exclusive breastfeeding as part of their intervention compared with those that did not; we did not see a consistent difference in effect.

We were limited in our ability to adequately examine the dose–response relationship between duration of SSC and neonatal outcomes because there were few studies with duration of 4 to 21 hours per day, and for any given outcome there was little variation in the SSC duration promoted across studies. We still attempted to look at the data available on SSC duration as a covariate in metaregression

analyses, and we found that variation in duration did not appear to have an important impact on the effect of KMC in these data. We could not adequately assess the impact of number of days of SSC because the majority of studies promoted a similar duration of 1 to 5 days.

CONCLUSIONS

KMC is protective against a wide variety of adverse neonatal outcomes and has not shown evidence of harm. This safe, low-cost intervention has the potential to prevent many complications associated with preterm birth and may also provide benefits to full-term newborns. The consistency of these findings across study settings and infant populations provides support for widespread implementation of KMC as standard of care for newborns. Additional research is needed to determine the ideal duration and components of KMC. Successful strategies for KMC implementation in various contexts should be disseminated among clinicians and policymakers.

ACKNOWLEDGMENTS

The authors would like to acknowledge the contributions to data abstraction and referencing by Stacie Constantian, Tobi Skotnes, Ilana Bergelson, Rodrigo Kuromoto and Eduardo Toledo. We acknowledge Kate Lobner for developing the search strategy.

ABBREVIATIONS

AIM: African Index Medicus
CI: confidence interval
IMEMR: Index Medicus for the Eastern Mediterranean Region
IMSEAR: Index Medicus for the South-East Asian Region
KMC: kangaroo mother care
LBW: low birth weight
LILACS: Latin American and Caribbean Health Sciences Information System
MD: mean difference
RCT: randomized controlled trial
RR: relative risk
SMD: standardized mean difference
SSC: skin-to-skin contact
WPRIM: Western Pacific Region Index Medicus

instruments, conducted the literature review, coordinated and supervised data collection and analyses, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

DOI: 10.1542/peds.2015-2238

Accepted for publication Oct 20, 2015

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: This study was supported by the Saving Newborn Lives initiative (SNL) of Save the Children. Dr Boundy received support from training grant T32HD060454 in reproductive, perinatal, and pediatric epidemiology from the National Institute of Child Health and Human Development, National Institutes of Health, and training grant T76MC00001 from the Maternal and Child Health Bureau. Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

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Pediatrics 2016;137;; originally published online December 23, 2015;
DOI: 10.1542/peds.2015-2238

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