Topical emollients to prevent infection in preterm infants: Cochrane review

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Introduction
Breakdown of the developmentally immature epidermal barrier may permit entry for micro-organisms leading to invasive infection in preterm infants. Topical emollients (ointments, creams, or oils) may improve skin integrity and barrier function and thereby prevent invasive infection, a major cause of mortality and morbidity in preterm infants. We conducted a Cochrane systematic review to assess the effect of topical application of emollients on the incidence of invasive infection, other morbidity, and mortality in preterm infants.

Methods
We searched the Cochrane Central Register of Controlled Trials (2014, Issue 7), MEDLINE, EMBASE, and CINAHL (to August 2014), conference proceedings and previous reviews. We included randomised controlled trials (RCTs) that assessed the effect of prophylactic application of topical emollient on the incidence of invasive infection, mortality, other morbidity, and growth and development in preterm infants. Two review authors assessed trial eligibility and risk of bias and undertook data extraction independently. We used a fixed-effect model in meta-analyses and explored the potential causes of heterogeneity in sensitivity analyses.

Results
We identified 16 RCTs (figure 1). Methodological quality varied with lack of clarity on methods to conceal allocation in half of the trials and lack of blinding of carers or investigators in all of the trials being the main potential sources of bias.

Comparison 1: Topical ointment or cream vs. routine skin care
Eight trials (2086 infants) examined the effect of topical ointments or creams. Most participants were very preterm infants cared for in health-care facilities in high-income countries. Overall, meta-analyses did not find a statistically significant difference in the incidence of invasive infection (risk ratio [RR] 1.13, 95% confidence interval [CI] 0.97, 1.31) or mortality before hospital discharge (RR 0.87, 95% CI 0.75, 1.03). In the pre-specified subgroup analysis, meta-analysis found a borderline statistically significant higher incidence of invasive infection in high income countries: typical RR 1.20 [95% CI 1.01, 1.42], 6 trials, 386 infants (figure 2). In pre-specified subgroup analysis, meta-analysis revealed a borderline statistically significant lower incidence of mortality in low- and middle-income countries: typical RR 0.82 [95% CI 0.69, 0.98], 2 trials, 535 infants (figure 3).

Comparison 2 Topical Oil vs. Routine Skin Care
Nine trials (904 infants) assessed the effect of sunflower, sunflower seed, and other vegetable oils. Eight of these trials were undertaken in low- or middle-income countries and all were based in health-care facilities rather than home or community settings. Meta-analyses did not find a statistically significant difference in the incidence of invasive infection (RR 0.98, 95% CI 0.65, 1.46) or neonatal mortality (RR 0.94, 95% CI 0.82, 1.09).

Infants massaged with vegetable oil had a statistically significantly higher rate of weight gain (about 2.5 g/kg/day), linear growth (about 1.2 mm/week), and head growth (about 0.5 mm/week) (figure 4). These meta-analyses contained substantial heterogeneity. There are not yet any data at all on long-term growth and developmental outcomes.

Conclusions
The available data do not provide clear evidence that the use of emollient therapy prevents invasive infection or neonatal death in preterm infants in either high-income or middle- or low-income settings. Some evidence of an effect of topical vegetable oils on neonatal growth exists but this should be interpreted with caution because lack of blinding may have introduced caregiver or assessment biases. Since these interventions are low-cost, readily accessible and generally acceptable, further randomised controlled trials, particularly in both community- and health care facility-based settings in low-income countries, may be justified.