CRD summary
This review aimed to assess the efficacy of human milk in preventing infection in very low birth weight, pre-term infants. The poor quality of many of the primary studies and clinical differences between them support the authors' conclusion that the evidence was inconclusive and that further well-conducted research is necessary.

Authors' objectives
To assess the efficacy of human milk (HM) feeding in reducing infection rates in very and extremely low birth weight (LBW) pre-term infants.

Searching
MEDLINE, EMBASE, CINAHL and the Cochrane Controlled Trials Register were searched, without any language restrictions, for publications from 1970 to 2003; the search terms were not fully reported. The authors also searched the reference lists of all relevant articles and reviews.

Study selection
Study designs of evaluations included in the review
It was unclear which study designs were eligible for inclusion in the review. RCTs and cohort studies were included in the review.

Specific interventions included in the review
Studies that compared HM (fortified or unfortified) with artificial formula feeding in pre-term infants were eligible for inclusion. The definitions of HM intake (exclusively HM or HM plus formula) and method of intake (oral or enteral) varied between the studies.

Participants included in the review
Pre-term infants described as having a very or extremely LBW were eligible for inclusion. The authors defined a very LBW as an infant weighing less than 1,500 g, and an extremely LBW as an infant weighing less than 1,000 g. The majority of infants included in the randomised controlled trials (RCTs) weighed more than 1,500g, and no extremely LBW infants were included. The majority of infants in the observational studies weighed less than 1,500 g.

Outcomes assessed in the review
Studies that reported infection as an independent outcome were eligible for inclusion. The studies reported on a range of infections, including: sepsis, urinary tract infections, diarrhoea, coryza, otitis media, conjunctivitis, thrush, pyoderma and bronchiolitis. Most of the studies identified infection using positive blood cultures and clinical signs. Necrotising enterocolitis was excluded from the review. Six studies looked at length of hospital stay as a secondary outcome.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors stated that each study was evaluated for definitions of HM feeding, assessment of the outcomes, potential confounding factors, and statistical analysis and power. Major methodological problems were tabulated for each study included in the review. The authors did not state how the papers were assessed for validity, or how many reviewers performed the validity assessment.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The results of the individual studies were combined in a narrative and grouped by study design in the tables.

How were differences between studies investigated?
Differences between the studies, in terms of outcome measures, definition of HM feeding, statistical analyses and confounding variables, were discussed in the body of the text.

Results of the review
Nine studies were included in the review: 3 RCTs (n=362) and 6 prospective cohort studies (n=769).

RCTs.
All 3 RCTs demonstrated a lower incidence of infections in the HM feeding group than the control group (formula or formula plus HM). None of the 3 RCTs looking at the length of hospital stay found any difference between the intervention and the control groups.

Cohort studies.
All 3 cohort studies examining sepsis demonstrated a lower incidence of sepsis in the HM feeding group (exclusively HM or HM plus formula), compared with the formula alone control group. In one additional study each, a lower incidence of diarrhoea and urinary tract infection, fewer days of urinary tract infection symptoms at 1 and 7 months, and reduced odds of infection in general, were found in the HM feeding group (exclusively HM or HM plus formula) in comparison with the formula alone control group.

One of the 3 cohort studies looking at length of hospital stay found a significant difference between the intervention and the control groups; the authors did not report in which direction.

Authors’ conclusions
The value of HM feeding for the prevention of infection in very LBW pre-term infants is still uncertain.

CRD commentary
The review addressed a clear question, although the inclusion and exclusion criteria could have been more clearly reported. While a number of electronic databases were searched without language restrictions, unpublished material was not actively sought and this might have introduced publication bias (i.e. some relevant studies might have been missed). The authors did not report the methods used to select the studies or extract the data, thus the potential for reviewer error or bias could not be assessed. The authors did not attempt to quantitatively synthesise the data; this may have been appropriate given the substantial clinical heterogeneity between the primary studies.

The authors also described a number of serious study limitations of the primary studies. The small number of studies included in the review, and their clinical heterogeneity and questionable quality, appear to support the authors’ statement that further studies are necessary. The authors only reported limited outcome data from the included studies, making it difficult for the reader to judge the validity of their interpretations.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.
Research: The authors suggested that further well-conducted trials testing the effects of HM feeding on infection rates in pre-term infants were needed. In addition, the authors made a number of suggestions for researchers to consider when designing a trial.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.