

Infant formula compared to breast milk for the prevention of allergies in neonates

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SUMMARY STATEMENT

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REQUEST

Infant formula compared to breast milk for the development of allergies in neonates

REQUESTED BY

Carol Godham, Midwifery Clinical Educator- Student Midwives, Women's Health, Monash Medical Centre, Clayton.

METHODOLOGY

Search Strategy

The Centre for Clinical Effectiveness defines the 'best available evidence' as that research we can identify that is least susceptible to bias. We determine this according to pre-defined National Health and Medical Research Council (NHMRC, 2000) criteria (see Appendix 1).

First, we search for systematic reviews, evidence based clinical practice guidelines, health technology assessments and randomised controlled trials. If we identify sound, relevant material of this type, the search stops. Otherwise, our search strategy broadens to include studies that are more prone to bias, less generalisable or have other methodological difficulties. We include case-control and longitudinal cohort studies in our critical appraisal reports. While we cite observational and case series studies, and narrative reviews and consensus statements, in our reports we do not critically appraise them. Such studies can produce accurate results but they are generally too prone to bias to allow determination of their validity beyond their immediate setting.

Details of Evidence Request

Patients (Subjects): Neonates
Intervention: Breast milk
Comparison: Infant formula
Outcome: Development of allergies

Search terms

(see Appendix 2 for exact search strategy)

Intervention: breast-feed\$, breast feed\$, breast feeding, breast fed, breast-fed, breastfed, breastfeed
Comparison: formula, infant food, bottle feeding, bottle feed\$, bottle fed, S26, karicare, enfasoy
Outcome: allergy, allerg\$, hypersensitivity, atopic, atopy

Resources Searched

We searched the following databases and internet websites:

The Cochrane Library (CD-ROM) Issue 1 2001

Medline (OVID)- 1966 to February 2001

Best Evidence (OVID)- 1991 to January/February 2001

CINAHL (OVID)- 1982 to February 2001

Current Contents (OVID)- 1993 Week 26 to 2001 Week 15

PREMEDLINE (OVID)- April 2, 2001

Australasian Medical Index- April 4, 2001

National Guideline Clearinghouse- April 4, 2001

Refinements, Searching & Reporting Constraints

We included items of evidence that were available to us on 3 April 2001. We only included articles published in the last 10 years. Critical appraisal was performed on the subset of studies published in English.

Inclusion Criteria

- Primary studies comparing infant formula with breast feeding for the prevention of allergies in neonates.

Exclusion Criteria

- Animal studies
- Studies on cost effectiveness
- Studies that were not randomised
- Study published in a language other than English
- Study that presented data included in another published report

RESULTS

From our sources we identified 23 potentially relevant articles. We obtained the full text of these articles to determine their relevance.

After examination of the 23 articles, the following were excluded as follows:

Reason for exclusion	Number
Cost effectiveness studies	3
Controlled trials, cohort or case-control analytic studies	11
Study where data was already included in another report	4
Consensus/ Non evidence-based guidelines	1
Total	19

Four articles then remained for appraisal. These studies are classified as follows:

Study design of included studies	Number
Systematic reviews or meta-analyses	1
Evidence-based clinical practice guidelines	1
Randomised controlled trials	1
Pseudorandomised controlled trials	1
Total	4

Based on our refinements, searching and reporting constraints, we are reasonably confident these articles represent the most relevant findings published to date.

EVIDENCE SUMMARIES

Format

Evidence summaries are presented as spreadsheets attached to this report. Each spreadsheet contains the article citation, details of the study design, patient description, scientific validity of the article, results, and pertinent remarks from the authors and Centre for Clinical Effectiveness reviewer.

REFERENCES

ARTICLES CRITICALLY APPRAISED FOR THIS REPORT

Level I evidence- systematic review/ meta-analysis

Baumgartner M, Brown CA, Secretin MC *et al.* (1998). Controlled trials investigating the use of one partially hydrolyzed whey formula for dietary prevention of atopic manifestations until 60 months of age: an overview using meta-analytical techniques. *Nutrition Research* 18: 1425-1442.

Level III-1 evidence- Pseudorandomised controlled trial

Juvonen P, Mansson M, Andersson C *et al.* (1996). Allergy development and macromolecular absorption in infants with different feeding regimens during the first three days of life. A three-year prospective follow-up. *Acta Paediatrica* 85: 1047-1052.

Lindfors A and Enocksson E (1988). Development of atopic disease after early administration of cow milk formula. *Allergy* 43: 11-16.

Evidence based guideline

Wang EEL (1994). Breast feeding. Canadian Task Force on the Periodic Health Examination. *Canadian Guide to Clinical Preventive Health Care*, Health Canada, Ottawa 232-42.

ARTICLES NOT CRITICALLY APPRAISED

Cost effectiveness studies

Drane D (1997). Breastfeeding and formula feeding: a preliminary economic analysis. *Breastfeeding Review* 5: 7-15.

Hoey C and Ware JL (1997). Economic advantages of breast-feeding in an HMO: setting a pilot study. *American Journal of Managed Care* 3: 861-865.

Montgomery DL and Splett PL (1997). Economic benefit of breast-feeding infants enrolled in WIC. *Journal of the American Dietetic Association* 97: 379-385.

Controlled trials, cohort or case-control analytic studies

Chandra RK, Puri S and Hamed A (1989). Influence of maternal diet during lactation and use of formula feeds on development of atopic eczema in high risk infants. *Bmj* 299: 228-230.

Chandra RK (1997). Five-year follow-up of high-risk infants with family history of allergy who were exclusively breast-fed or fed partial whey hydrolysate, soy, and conventional cow's milk formulas. *Journal of Pediatric Gastroenterology & Nutrition* 24: 380-388.

de Seta L, Siani P, Cirillo G *et al.* (1994). [The prevention of allergic diseases with a hypoallergenic formula: a follow-up at 24 months. The preliminary results]. *Pediatria Medica e Chirurgica* 16: 251-254.

Giovannini M, Agostoni C, Fiocchi A *et al.* (1994). Antigen-reduced infant formulas versus human milk: growth and metabolic parameters in the first 6 months of life. *Journal of the American College of Nutrition* 13: 357-363.

Halken S, Host A, Hansen LG *et al.* (1993). Preventive effect of feeding high-risk infants a casein hydrolysate formula or an ultrafiltrated whey hydrolysate formula. A prospective, randomized, comparative clinical study. *Pediatric Allergy & Immunology* 4: 173-181.

Halken S, Hansen KS, Jacobsen HP *et al.* (2000). Comparison of a partially hydrolyzed infant formula with two extensively hydrolyzed formulas for allergy prevention: A prospective, randomized study. *Pediatric Allergy & Immunology* 11: 149-161.

Isolauri E, Sutas Y, Makinen-Kiljunen S *et al.* (1995). Efficacy and safety of hydrolyzed cow milk and amino acid-derived formulas in infants with cow milk allergy. *Journal of Pediatrics* 127: 550-557.

Keller KM, Burgin-Wolff A, Lippold R *et al.* (1996). The diagnostic significance of IgG cow's milk protein antibodies re-evaluated. *European Journal of Pediatrics* 155: 331-337.

Miskelly FG, Burr ML, Vaughan-Williams E *et al.* (1988). Infant feeding and allergy. *Archives of Disease in Childhood* 63: 388-393.

Odelram H, Vanto T, Jacobsen L *et al.* (1996). Whey hydrolysate compared with cow's milk-based formula for weaning at about 6 months of age in high allergy-risk infants: effects on atopic disease and sensitization. *Allergy* 51: 192-195.

Saarinen KM, Juntunen-Backman K, Jarvenpaa AL *et al.* (1999). Supplementary feeding in maternity hospitals and the risk of cow's milk allergy: A prospective study of 6209 infants. *Journal of Allergy & Clinical Immunology* 104: 457-461.

Study where data was already included in another report

Chandra RK, Singh G and Shridhara B (1989). Effect of feeding whey hydrolysate, soy and conventional cow milk formulas on incidence of atopic disease in high risk infants. *Annals of Allergy* 63: 102-106.

Chandra RK and Hamed A (1991). Cumulative incidence of atopic disorders in high risk infants fed whey hydrolysate, soy, and conventional cow milk formulas. *Annals of Allergy* 67: 129-132.

Junoven P, Mansson M and Jakobsson I (1994). Does early diet have an effect on subsequent macromolecular absorption and serum IgE? *Journal of Pediatric Gastroenterology & Nutrition* 18: 344-349.

Porch MC, Shahane AD, Leiva LE *et al.* (1998). Influence of breast milk, soy or two hydrolyzed formulas on the development of allergic manifestations in infants at risk. *Nutrition Research* 18: 1413-1424.

Consensus/ Non evidence-based guidelines

Anonymous (1997). Breastfeeding and the use of human milk. American Academy of Pediatrics. Work Group on Breastfeeding. *Pediatrics* 100: 1035-1039.

APPENDIX 1

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Levels Of Evidence

Based on "How to use the evidence: assessment and application of scientific evidence" (National Health & Medical Research Council, Canberra, 2000):

Level I		Evidence obtained from a systematic review (or meta-analysis) of all relevant randomised controlled trials.
Level II		Evidence obtained from at least one randomised controlled trial.
Level III	-1	Evidence obtained from pseudorandomised controlled trials (alternate allocation or some other method).
	-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies or interrupted time series with a control group.
	-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies or interrupted time series without a parallel control group.
Level IV		Evidence obtained from case series, either post-test or pretest/post-test.

APPENDIX 2

Search strategy

	Search terms for MEDLINE, CINAHL, EBM- Best Evidence, PREMEDLINE, Current Contents
1	breast-feed\$.tw
2	exp Breast Feeding/
3	breast feed\$.tw
4	breast fed\$.tw
5	breast-fed.tw
6	breastfed.tw
7	breastfeed\$.tw
8	or/1-7
9	formula.tw
10	infant food/
11	exp Bottle Feeding/
12	bottle feed\$.tw
13	bottle fed.tw
14	S26.tw
15	karicare.tw
16	enfasoy.tw
17	or/9-16
18	allerg\$.tw
19	hypersensitivity/
20	atopic.tw
21	atopy.tw
22	or/18-21
23	8 and 17 and 22

<p>Evidence Summary Systematic Review</p> <p>Infant formula compared to breast milk for allergy</p>	<p style="text-align: center;">Study 1</p> <p style="text-align: center;">Baumgartner M, brown RN, Secretin M-C et al (1998) Controlled trials investigating the use of one partially hydrolysed whey formula for dietary prevention of atopic manifestations until 60 months of age: An overview using meta-analytical techniques. Nutrition Research 18 (8): 1425-42</p>
<p>STUDY DESIGN & NHMRC LEVELS OF EVIDENCE</p>	<p>Systematic review with meta-analysis Level I evidence</p>
<p>DESCRIPTION: Subjects, Interventions, Comparisons, Outcomes, Inclusion & Exclusion Criteria</p>	<p>Patients: Infants at high risk for the development of allergy (judged according to parental allergy history) Intervention: Nestle HA moderately hydrolysed whey formula Comparison: Breast milk (BF), breast milk with maternal diet restrictions (BF/diet) and/or cows milk adapted formula (CMF) Outcomes: Development of atopic symptoms Exclusion criteria: Only included randomised studies addressing dietary attempts at prevention of atopic symptoms in infancy and childhood. Studies were only included if they evaluated the effect of feeding in the first few months of life, and exclusivity of feeding for a minimum of three months. All studies were required to incorporate the Nestle HA moderately hydrolyzed whey formula as a study group.</p>
<p>VALIDITY: Methodology, rigour, selection, opportunity for bias</p>	<p>Focused question: Yes Search strategy: Literature search (1985 to 1997) using Medline. No search terms were specified Assessed validity: Assessed whether studies were randomised controlled trials, and excluded them if they were not. No other assessment of the quality of included studies was performed Consistent results: No tests of heterogeneity are reported Appropriate analysis of results: Analysis seems appropriate Potential for bias: There is a potential conflict of interest with Nestle conducting the systematic review of their own product.</p>
<p>RESULTS: Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate</p>	<p>15 studies were identified and met the inclusion criteria for the review. Nine of these studies were excluded from the meta-analysis due to insufficient or inappropriate data. Thirteen of the 15 studies directly compared breast feeding with infant formula. Data is presented for 10 of these 13 studies. Nine out of these 10 studies showed no statistically significant difference in incidence of atopic symptoms.</p>
<p>AUTHORS COMMENTS: Risk/benefit, limitations</p>	<p>"Breastfeeding or exclusive feeding of a moderately hydrolysed formula (Nestle HA formula) for at least three months in infants at high risk for the development of allergic disease, decreases the incidence of atopic manifestations until 60 months of age."</p>
<p>REVIEWER'S COMMENTS: Risk/benefit, methodology, conclusions</p>	<p><u>Strengths</u></p> <ul style="list-style-type: none"> • Clear inclusion and exclusion criteria <p><u>Weaknesses</u></p> <ul style="list-style-type: none"> • There is a conflict of interest • Results may not be generalisable to other types of formula, or to infants who are not at a high risk for allergy development • The search strategy was narrow and relevant studies may have been missed. • There was no appraisal of the quality of the included studies other than to state study design • There were no tests of heterogeneity reported so results may not have been consistent between studies • Data was not available for all included studies

EXPLANATION OF TERMINOLOGY USED IN SPREADSHEET

Level of evidence: A hierarchy of study evidence that indicates the degree to which bias has been eliminated in the study design.

Focussed question: The review should address a clearly focused issue, in terms of the population studies, the intervention given and the outcomes considered.

Search strategy: A description of methods used to identify relevant studies from various computer databases and other sources.

Systematic review: The process of systematically locating, appraising and synthesising evidence from scientific studies in order to obtain a reliable overview.

Validity: The degree to which reviewers assessed the quality of the studies they included

Of measurement: an expression of the degree to which a measurement measures what it purports to measure; it includes construct and content validity.

Of study: the degree to which the inferences drawn from the study are warranted when account is taken of the study methods, the representativeness of the study sample, and the nature of the population from which it is drawn (internal and external validity, applicability, generalisability).

Consistent results: The similarity of results from the included studies. Often called heterogeneity which refers to the differences in treatment effect between studies contributing to a meta analysis (systematic review). If there is significant heterogeneity, this suggests that the trials are not estimating a single common treatment effect.

Appropriate analysis of results: When study results are pooled in a meta-analysis it is important that the results are combined in appropriate manner. The studies should be sufficiently similar in study design, the results of included studies should be clearly displayed and reasons for any variation in results should be discussed.

Potential for bias: Bias is a systematic deviation of a measurement from the 'true' value leading to either an over or underestimation of the treatment effect. Bias can originate from many different sources, such as allocation of patients, measurement, interpretation, publication and review of data.

<p style="text-align: center;">Evidence Summary Therapy/Intervention</p> <div style="border: 1px solid black; padding: 5px; margin: 10px auto; width: fit-content;"> <p>Infant formula compared to breast milk for allergy</p> </div>	<p style="text-align: center;">Study 1</p> <p>Junoven P, Mansson M, Anderson C et al (1996) Allergy development and macromolecular absorption in infants with different feeding regimens during the first three days of life. A three year prospective follow-up.</p>	<p style="text-align: center;">Study 2</p> <p>Lindfors A, Enocksson E (1988) Development of atopic disease after early administration of cow milk formula. Allergy 43:11-16</p>
<p>STUDY DESIGN & NHMRC LEVELS OF EVIDENCE</p>	<p>Pseudorandomised Controlled Trial Level III-1 evidence</p>	<p>Pseudorandomised Controlled Trial Level III-1 evidence</p>
<p>DESCRIPTION: Patients (subjects), Intervention, Comparisons, Outcomes, Inclusion & Exclusion Criteria</p>	<p>Patients (subjects): Healthy term infants Intervention: Human milk (HM) Comparisons: Cows milk formula (CMF), or casein hydrolysate formula (CHF) Outcomes: Macromolecular absorption, development of allergies (according to skin prick tests) Incl & Excl Criteria: None stated</p>	<p>Patients (subjects): Infants of normal birth weight, gestational age and without major neonatal problems Intervention: Breastfeeding Comparisons: Cow milk formula Outcomes: Symptoms of atopic disease, serum IgE concentrations Incl & Excl Criteria: Infants were included if they had a brithweight within -1SD and -2SD, and a gestational age of 37-42 weeks.</p>
<p>VALIDITY: Methodology, rigour, selection</p>	<p>Randomisation: Yes, by day of month that the mother was born. The difference in the number of infants allocated to each group may indicate that groups were not truly randomised (HM-53, CMF-39, CHF-37). Blinding: Not possible to blind staff and mothers to type of feeding allocation All patients accounted for: Yes Patients treated equally: The infants were treated equally during the three days that they were fed according to the study regime. There may have been large differences in how infants were treated during the next three years and this may have affected outcomes. Similar groups: Baseline characteristics are presented although tests of statistical significance were not performed. There were more subjects in the HM group. There were roughly equal numbers of females/males. Infants in the CMF group had a higher mean birth weight. Infants in the HM group had more family history of allergy and more mothers who smoked. The CHF group had less double family history of allergy and less mothers who smoked.</p>	<p>Randomisation: Yes, using alternate allocation. The wards changed their feeing routine the first day of every other month. Blinding: The paediatricians were unaware of the feeding regimen. All patients accounted for: Yes, one infant with a cow milk allergy was transferred to the breastfeeding group. Patients treated equally: Infants in the formula group received fixed doses at regular intervals whereas there was no attempt to adjust the amount of feeding for the breastfeeding group. Similar groups: More infants in the breastfeeding group had a family history of allergy. The groups were similar for duration of breastfeeding.</p>

<p style="text-align: center;">Evidence Summary Therapy/Intervention</p> <div style="border: 1px solid black; padding: 5px; margin: 10px auto; width: 80%;"> <p style="text-align: center;">Infant formula compared to breast milk for allergy</p> </div>	<p style="text-align: center;">Study 1 (cont...)</p> <p style="text-align: center;">Junoven P, Mansson M, Anderson C et al (1996) Allergy development and macromolecular absorption in infants with different feeding regimens during the first three days of life. A three year prospective follow-up.</p>	<p style="text-align: center;">Study 2 (cont...)</p> <p style="text-align: center;">Lindfors A, Enocksson E (1988) Development of atopic disease after early administration of cow milk formula. Allergy 43:11-16</p>
<p>RESULTS: Generally favourable or unfavourable, specific outcomes of interest, estimate of experimental effect and precision if appropriate</p>	<p>During the three year follow up period, 11 infants developed obvious manifestations of allergic disease (four in the HM group, three in the CMF group, and four in the CHF group). All four infants that developed allergic symptoms in the HM group had a family history of allergy, three out of the four had positive skin prick tests, and total S-IgE values were normal. In the CMF group no infants had positive skin prick test, two out of the three infants had family histories of allergy and all had normal S-IgE values. In the CHF group three out of four infants had family histories of allergy, two had positive skin prick tests, two had high S-IgE values, one had low S-IgE values and the other had normal values.</p>	<p>At the end of follow up significantly more infants in the breastfeeding group had allergy symptoms. A total of 20/109 in the formula group compared to 32/98 in the breastfeeding group developed one or more allergy symptoms ($p < 0.05$). Among infants with a negative family history for allergy there were more infants in the breastfeeding group than in the formula group who developed allergy symptoms (11/41 versus 10/59). In the groups with single hereditary the symptoms of allergy were similar in the formula and breastfeeding groups (8/31 versus 10/39). Among infants with double hereditary, 2/19 in the formula group compared to 11/18 in the breastfeeding group developed allergy symptoms ($p < 0.01$). Twelve out of 154 infants had high IgE levels.</p>
<p>AUTHOR(S) CONCLUSIONS: Limitations, implications for practice and research</p>	<p>“No differences were found in allergic symptoms between the three groups. The difference between infants of the CHF group and those of the HM and CMF groups concerning total IgE is noteworthy. In an attempt to clarify these differences we are carrying out immunological studies of specific IgE and IgG antibodies”.</p>	<p>“Our study implies that early feeding during the first days of life with a cow milk formula, before the introduction of breastmilk, may reduce the incidence of allergy symptoms before 18 months of age in infants with a family history of allergy.”</p>
<p>OUR COMMENTS: Opportunity for bias, weakness and strength</p>	<p>Strength/s:</p> <ul style="list-style-type: none"> • All patients were accounted for <p>Weakness/es:</p> <ul style="list-style-type: none"> • The three groups were different at baseline for family history of allergy and mothers smoking • The groups may not have been truly randomised • Infants may have been treated differently during the 3 years follow up period. This makes it difficult to attribute differences in allergies to the first three days of life. 	<p>Strength/s:</p> <ul style="list-style-type: none"> • All patients were accounted for • Paediatricians were blinded to group allocation when making assessment of allergy symptoms <p>Weakness/es:</p> <ul style="list-style-type: none"> • The groups were not truly randomised • The groups differed in terms of family history of allergy at the start of the study • The two groups did not receive the same amount of feeding

EXPLANATION OF TERMINOLOGY USED IN SPREADSHEET

Level of evidence: A hierarchy of study evidence that indicates the degree to which bias has been eliminated in the study design.

Intervention: A therapeutic procedure such as treatment with a pharmaceutical agent, surgery, a dietary supplement, a dietary change or psychotherapy.

Randomisation: A process of allocating participants to treatment or control group within a controlled trial by using a random mechanism, such as coin toss, random number table or computer-generated random numbers. Study subjects have an equal chance of being allocated to an intervention or control group; thus, the two groups are comparable. Randomisation ensures that the results are not biased by the selection of particular types of patients to receive a specific therapy.

Blinding: Blinding or masking is a process used in epidemiological studies and clinical trials in which the observers and the subjects have no knowledge as to which treatment groups subjects are assigned. It is undertaken in order to minimise bias occurring in patient response and outcome measurement.

All patients accounted for: Once patients are randomly allocated to a specific group and withdraw before study conclusion, they have to be accounted for in order to ensure that patients withdrawing from the study are not significantly different from those continuing in the study. The final analysis should be conducted on an intention-to-treat basis, which includes the results of withdrawn patients in the analysis.

Patients treated equally: To be able to attribute any difference in the observed outcome to the intervention, study patients need to be treated equally in every way except for the intervention being evaluated.

Similar groups: Baseline characteristics of patients that are also likely to affect results should be evenly distributed between the intervention and control groups. Following proper randomisation, patients' attributes would be expected to be equally distributed between groups.

Validity:

Of measurement: an expression of the degree to which a measurement measures what it purports to measure; it includes construct and content validity.

Of study: the degree to which the inferences drawn from the study are warranted when account is taken of the study methods, the representativeness of the study sample, and the nature of the population from which it is drawn (internal and external validity, applicability, generalisability).

Potential for bias: Bias is a systematic deviation of a measurement from the 'true' value leading to either an over (or under) estimation of the treatment effect. Bias can originate from many different sources (including allocation of patients, measurement, interpretation, publication and review of data).

<p>Evidence Summary Clinical Guideline</p> <p>Infant formula compared to breast milk for allergy</p>	<p style="text-align: center;">Guideline 1</p> <p style="text-align: center;">Wang EL (1994). Breast feeding. Canadian Task Force on the Periodic Health Examination. Canadian Guide to Clinical Preventive Health Care, Health Canada, Ottawa 232-42</p>
<p>GUIDELINE DEVELOPMENT SOCIETY/ GROUP</p>	<p>Canadian task force on preventive health care</p>
<p>CLINICAL APPLICABILITY</p>	<p>Objectives: To assess the effectiveness of breast feeding in prevention of adverse outcomes, and the efficacy of interventions to encourage breast feeding. Guideline topic: Breast feeding Patient population: Mothers of infants Health provider population: It is not stated who the guideline is intended for</p>
<p>VALIDITY</p>	<p>How consensus was reached: Not stated, although there is only one author listed for the guideline Identification of evidence: A Medline search to December 1993 using subjects headings. References were also searched Evaluation of evidence: Several recommendations were assigned a level of evidence. Mostly the study design is mentioned. Links made between recommendations and evidence: The recommendations link to the appropriate reference, but not always to a level of evidence Costs and benefits: There was a discussion of benefits, but not costs</p>
<p>MULTIDISCIPLINARY PROCESS</p>	<p>Conflicts of interest: None stated or identified Funding: Canadian government Guideline development group: There is no description of the development group. We are unable to assess whether it was multidisciplinary and included consumers</p>
<p>CLINICAL FLEXIBILITY</p>	<p>Exceptions/ flexibility: There was no discussion of exceptions Patient preferences considered: No consideration of patient preferences is discussed. Ethical issues: No ethical issues are raised or discussed</p>
<p>CLARITY</p>	<p>Clearly worded: Yes Presentation: Clearly presented Ease of use: Yes and recommendations are summarised in their own section</p>
<p>RELIABILITY/ REPRODUCABILITY</p>	<p>Independent review: The guideline was reviewed externally Pilot/ pre-testing: Not stated Process of development documented: The search details were included. No other details on development were outlined</p>
<p>SCHEDULED REVIEW</p>	<p>Date of issue: 1994 Expiry date/ scheduled review: Not stated</p>
<p>APPLICATION</p>	<p>Guidelines for dissemination and implementation: No implementation strategies were discussed Guidelines for evaluation: No evaluation strategy is proposed</p>
<p>RELEVANT RECOMMENDATIONS & CORRESPONDING LEVELS OF EVIDENCE:</p>	<p>Exclusion of various foods from the diet of breast feeding mothers may be useful in a subpopulation at increased risk of atopy (positive family history or markers such as increased cord IgE). Evidence from randomised controlled trials. No level of evidence stated.</p>

<p>Evidence Summary Clinical Guideline</p> <p>Infant formula compared to breast milk for allergy</p>	<p>Guideline 1 (cont...)</p> <p>Wang EL (1994). Breast feeding. Canadian Task Force on the Periodic Health Examination. Canadian Guide to Clinical Preventive Health Care, Health Canada, Ottawa 232-42</p>
<p>OUR COMMENTS:</p>	<p>Potential for bias: The search strategy is narrow and some relevant studies could have been missed. We have little indication of the quality of the studies the recommendations are based on.</p> <p>Strengths:</p> <ul style="list-style-type: none"> • There was a clear objective • The review was presented in a clear, easy to use way <p>Weaknesses:</p> <ul style="list-style-type: none"> • Narrow search strategy • No assessment of the quality of the included studies • Not all recommendations are linked to a level of evidence • No assessment of potential costs • The guideline development process was not clearly documented

EXPLANATION OF TERMINOLOGY USED IN SPREADSHEET

Objectives: Whether the guideline authors provided a clear reason for having developed the guideline. What the authors hoped to achieve.

Patient population: The group of patients that are the focus of the guideline.

Provider population: The group of clinicians for which the guideline has been developed.

How consensus was reached: In the event of little evidence, no evidence or conflicting evidence how was a conclusion drawn?

Identification of evidence: How did the guideline developers the appropriate research to inform their guideline?

Evaluation of evidence: How did the guideline developers evaluate the quality of the studies that they identified?

Links made between recommendations and evidence: Are there explicit links between the recommendations, citations and the associated level of evidence?

Costs and benefits: Have the guideline developers assessed the likely costs and benefits resulting from their guideline?

Multidisciplinary process: Have all of those likely to use the guideline been involved in its development. Are all relevant disciplines represented?

Conflicts of interest: Have potential conflicts in interest been discussed and stated?

Funding: Does the guideline state its funding source? Who funded the guideline?

Guideline development group: Have we been provided with a list of those involved in developing the guideline? Does the guideline list the disciplines of the guideline developers?

Exceptions/ flexibility: Does the guideline provide information about possible exceptions and variations to the guideline?

Patient preferences considered: Does the guideline outline the potential impact of patient preferences on the recommended care?

Ethical issues: Does the guideline discuss any potential ethical issues arising?

Presentation: How clearly are the guideline and recommendations presented?

Ease of use: How easy would the guideline be to actually use?

Independent review: Has the guideline been assessed by a separate party who were not involved in its development?

Pilot/ pre testing: Was the guideline trialed before final publication?

Process of development documented: Does the guideline document the process used in its formulation?

Scheduled review: Do the guideline state the need for review and set a date for such a review?

Guidelines for dissemination and implementation: Does the guideline provide recommendations for dissemination and implementation of its recommendations?

Guidelines for evaluation: Does the guideline suggest methods of evaluating the impact of implementing its recommendations?

Recommendations: What are the recommendations the guideline contains?