

INFANT FEEDING AND COGNITIVE DEVELOPMENT: EVIDENCE FOR PUBLIC HEALTH DECISION MAKING

Prepared For: Region of Peel, Public Health
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July 24, 2009

Table of Contents

INTRODUCTION	3
METHODS	3
Search Results	4
Relevance assessment results – Reasons for Exclusion	4
Quality Assessment	4
Interpretation and Applicability Review.....	5
RESULTS AND CONCLUSIONS	5
SUMMARY CONCLUSIONS.....	7
RECOMMENDATIONS.....	7
APPENDIX 1: SEARCH STRATEGY.....	8
<i>Medline:</i>	8
Embase:	8
CINAHL:	9
APPENDIX 2: SEARCH RESULTS	10
APPENDIX 3: RELEVANCE ASSESSMENT RESULTS	11
APPENDIX 4: REFERENCE LIST OF INLCUED STUDIES	17
APPENDIX 5 – QUALITY ASSESSMENT TOOL CAUSATION STUDIES	18
APPENDIX 6 – QUALITY ASSESSMENT TOOL – INTERVENTION STUDIES	19
APPENDIX 7: INCLUDED STUDIES - QUALITY ASSESSMENT RESULTS.....	23

INTRODUCTION

The purpose of this commissioned work was to understand the evidence about infant feeding and cognitive development to inform public health programs. We sought to identify, compile, quality assess, summarize and interpret the evidence more recent than 2005 in the context of the “Formula No Thanks” Peel Public Health Media Campaign.

The specific search questions were:

1. Do healthy full term infants, less than 6 months of age and living in developed countries who are exclusively breastfed or given only breastmilk and no other artificial milk substitute, compared to babies of the same description who are given both breastmilk and formula, show any differences in cognitive development, social intelligence, learning potential, short term intelligence (childhood), or long term intelligence (adult)?
2. Do healthy full term infants, less than 6 months of age and living in developed countries who are fed formula or mixed feedings of formula and breast milk, compared to babies of the same description who are exclusively formula fed, show any differences in incidence of learning problems or disabilities, cognitive development, short term intelligence (childhood), or long term intelligence (adult)?

METHODS

The literature was searched to identify relevant articles that were published between 2005 and 2009. A systematic review published by the Agency for Healthcare Research and Quality (AHRQ) in 2006 was understood to effectively capture and summarize the evidence to 2006. The new search was retrospective to 2005 to capture any articles that may have been in the publication process between 2005 and 2006. This strategy was designed to be comprehensive to identify literature published since the AHRQ review.

Searches were conducted on June 10, 2009 in Medline, Embase, and CINAHL (2005-2009). Keyword terms drawn from the research questions were used in conjunction with known synonyms and relevant indexing terms from each of the three databases searched. An initial search was run in Medline and reviewed by a health sciences librarian for completeness, then modified as required for Embase and CINAHL. In cases where a relevant keyword was not available as an indexing term, the keyword was included in the search as a text word along with the indexing terms. Search terms were combined using Boolean operators and were limited to results relating to humans, and in the English language.

The complete search strategy is outlined in Appendix 1.

Search Results

The searches yielded 1260 citations (Medline [220], CINAHL [294] and EMBASE [746]). Seven articles were forwarded for inclusion by Peel Health staff, two of which had not been identified in our database searches. One (Anderson, 1999) was outside the search date range and was found to be included in the AHRQ systematic review. The other (Caspi, 2007) was outside the search terms, but included in the results of the search based on a recommendation from Peel Health. Titles and abstracts of 1261 articles were screened for relevance, and 56 articles were retrieved in full text for a more detailed review of the full document versions.

The 56 articles were assessed applying the following relevance criteria:

1. Must include a population of healthy, full-term infants in developed country(ies) who are exclusively breastfed or given only breastmilk, or who are exclusively given artificial milk substitute (infant formula).
2. Must compare the relationship between breastfeeding or infant formula, and cognitive development.
3. Must provide data on outcomes related to cognitive development/ function/ ability
4. Must be an English language primary study or review (and may be an overview) published between 2005 and 2009

Relevance assessment results – Reasons for Exclusion (see Appendix 3).

A total of 46 papers were excluded:

Not a study or review – 31 studies.

Not a relevant population, not comparing the relationship between breastfeeding or formula and outcomes, or not providing data on outcomes – 14 studies.

Duplicate title – 1 study.

The remaining ten papers were distributed for full quality assessment and interpretation. See Appendix 4 for the Reference List of included papers.

Quality Assessment

All 10 papers were assessed for methodological quality. Seven of the ten papers were causation studies, and of those, 4 were found to be of weak quality and 3 were of moderate quality. The lone included intervention study was found to be of moderate quality. Two papers were book chapters and were not quality assessed; however, their reference lists were reviewed for papers not captured in the search, and the chapters were used as background, with other more recent journal articles providing current, first-hand data.

Quality assessment using either the Tool for Causation Studies or the Tool for Intervention Studies was therefore completed for 8 papers; the two book

chapters were not quality assessed. Quality assessment tools are included in Appendices 5 and 6.

Results of the quality assessment are in Appendix 7. Given that no papers were of strong quality, only the 4 papers of moderate quality were included in the interpretation of results.

Interpretation and Applicability Review

Health Evidence staff together with Peel Health staff met to review all quality assessments, and to discuss the relevance and applicability of the evidence in consideration of existing Peel Health programs. The following summarizes the discussion.

RESULTS AND CONCLUSIONS

Overall, the findings of the studies were inconclusive to directly answer the research questions, which ideally would have required a body of methodologically-strong causation studies directly comparing breast feeding to infant formula feeding based assessment of appropriate outcomes (and similar outcomes across studies), using valid and reliable measurement tools, and with sufficient attention to potential confounding variables. There was considerable heterogeneity among the included studies. Studies differed in design, they assessed different variables thought to be related to cognitive outcomes, used a variety of methods to collect data, various tools to assess outcomes, and studied different populations in diverse settings. The heterogeneity among the studies makes it challenging to compare across studies and develop definitive conclusions.

More specifically, variables that may influence cognitive outcomes in the studies included home environment, exclusive breastfeeding, and fatty acid metabolism. Studies assessed a variety of outcomes including cognitive development, intelligence, verbal ability, developmental delay, and IQ. Several studies assessed cognitive ability or IQ, but used different scales or tools (e.g. Peabody Individual Achievement Test, Wechsler Scales of Intelligence), and at different end points (e.g. at 4 years of age, at adolescence, at adulthood). Studies were of retrospective design (e.g. one study extracted data from the National Longitudinal Study of Adolescents) and prospective design (e.g. longitudinal birth cohort study) and used a variety of data collection methods or data sources. In addition, the studies included different populations and characteristics (e.g. low income, siblings) and settings (e.g. U.S., Belarus and Australia).

While some of the studies found an association between breast-feeding and cognitive benefits, these studies tended to be rated as having lower methodological quality using the critical appraisal tool. Furthermore, those studies reporting a positive relationship between breastfeeding and cognitive development, tended to not control for confounding variables, such as, mother's

IQ. Studies assessed as being of higher methodological and controlling for confounding factors, tended to not report a significant relationship between breastfeeding and cognitive development.

Below is a brief summary of the findings of the 8 included research studies (7 causation studies and one intervention study). The two book chapters are not summarized here.

In Kramer et al. (2008), children who were breastfed had higher intelligence scores. However, the results were insignificant for 4 of the 7 aspects of the Wechsler intelligence scale, and for the remaining 3 aspects the confidence intervals were wide meaning that it was quite possible that at the lower end of the confidence interval the effect size was not clinically meaningful. Though this randomized controlled trial set in Belarus was well done, limited information was provided about the representativeness of the study sample and the 34 clinics participating. This makes it difficult to determine the generalizability of these results to the Canadian context.

Lawlor et al. (2006) studied an Australian cohort to determine infant and maternal predictors of intelligence at 5 and 14 years. They found that of 11 characteristics associated with intelligence, parental education, family income and breastfeeding were the strongest predictors. Limitations were that the study included low birthweight infants and that follow up included only 50% of the original cohort, with low SES participants most likely to be lost to follow up.

Evenhouse et al. (2005), using retrospective data from the U.S. National Longitudinal Study of Adolescent Health, compared breastfed and non-breastfed siblings, and found a 'causal' connection between breastfeeding and intelligence. The study controlled for birth weight, birth order, parental investment, and gender. A limitation in the study is that no formula feeding information was collected, so that the definition of breast-feeding is unclear.

Sacker et al. (2006) studied a cohort in the UK to examine the association between breastfeeding and developmental delay. They found that infants never breastfed were more likely to have gross motor delay at 9 months of age even when biological, socioeconomic or psychosocial factors were controlled for. The protective effect was not found for fine motor delay.

Gibson-Davis (2006) found that maternal intelligence scores explained the association between breastfeeding and higher intelligence in 3 year olds.

Similarly, Der (2006) included sibling analysis and found that the association between breastfeeding and children's mental ability was small and insignificant when maternal IQ was controlled for in the analysis, and that maternal IQ was the most influential among relevant confounders.

Caspi et al, (2007) studied the moderating effect of the gene FADS2 on fatty acid metabolism and found that among breast fed infants, those with the FADS2 gene

had higher IQ scores indicating that the ability to metabolize fatty acids could explain the higher IQ scores.

Zhou et al, (2007) looked at duration of breast-feeding and intelligence, controlling for home environment and socioeconomic characteristics. They found that home environment explained the association between breastfeeding and intelligence. Of note, the scale used to measure intelligence was designed for use with children at high risk and so may not accurately assess the outcome for non-high risk children.

SUMMARY CONCLUSIONS

- Studies included were of moderate or weak quality.
- Some studies found a positive association between breast feeding and cognitive development.
 - Where an association was present, the confidence intervals were wide, meaning the effect size could be too small to be clinically important.
 - Breastfeeding was often inadequately defined or measured. It was unclear in several studies whether populations studied were exclusively breast fed, and breast feeding status was inconsistently/unreliably measured.
- Maternal IQ and socio-environmental factors appear to explain any effect, meaning that it is not feasible to attribute the observed improvements in cognitive outcomes to feeding method alone, since maternal IQ and socio-environmental factors appear to explain many of the differences in cognitive outcomes.
- Where there was an association between breast feeding and cognitive outcomes, it is unknown whether the association is explained by some component of breast milk, or by socio-environmental factors, meaning that it is not possible to conclusively attribute any improvements in outcomes to breast milk alone.

RECOMMENDATIONS

- The literature to date does not support a claim of superior cognitive function or ability as a result of breast-feeding. A high-quality review published in 2007, along with several more published studies were considered in drawing this conclusion. Public health programs should convey that there are benefits to breastfeeding but should not suggest cognitive benefits.
- At this time, a synthesis of the available literature does not suggest superiority of breast milk compared to formula for improved cognitive development..

APPENDIX 1: SEARCH STRATEGY

Medline:

Database: Ovid MEDLINE(R) <1996 to May Week 5 2009>

Search Strategy:

-
- 1 Child Development/ or Cognition Disorders/ or cognitive development.mp. (35028)
 - 2 exp Intelligence/ or social intelligence.mp. (5671)
 - 3 Social Behavior/ or social behaviour.mp. or Social Behavior Disorders/ (15204)
 - 4 exp Learning/ or exp Learning Disorders/ or learning potential.mp. (110539)
 - 5 short term intelligence.mp. (0)
 - 6 long term intelligence.mp. (2)
 - 7 Intelligence Tests/ (2750)
 - 8 exp Cognition Disorders/ or exp Cognition/ or cognition.mp. (76232)
 - 9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (192781)
 - 10 exp Infant Formula/ (1105)
 - 11 Bottle Feeding/ae [Adverse Effects] (274)
 - 12 breast feeding.mp. or exp Breast Feeding/ (11470)
 - 13 Milk, Human/ (4665)
 - 14 10 or 11 or 13 or 12 (15185)
 - 15 14 and 9 (718)
 - 16 limit 15 to (english language and humans and yr="2005 -Current") (267)
 - 17 from 13 keep 1-220 (220)
 - 18 from 17 keep 1-220 (220)
 - 19 from 18 keep 1-220 (220)

Embase:

Database: EMBASE <1996 to 2009 Week 23>

Search Strategy:

-
- 1 exp Cognitive Development/ (1898)
 - 2 exp Child Development/ (9185)
 - 3 cognition disorders.mp. or exp Cognitive Defect/ (36968)
 - 4 exp Wechsler Intelligence Scale/ or exp Emotional Intelligence/ or exp Intelligence Test/ or exp Intelligence Quotient/ or intelligence.mp. or exp Intelligence/ or exp Stanford-Binet Intelligence Scale/ (16230)
 - 5 short term intelligence.mp. (0)
 - 6 long term intelligence.mp. (3)
 - 7 exp Cognition/ or social intelligence.mp. (392198)
 - 8 social behaviour.mp. or Social Behavior/ (11482)

- 9 exp Learning Test/ or exp Learning/ or exp Social Learning/ or learning.mp.
or exp Learning Disorder/ (123175)
- 10 6 or 3 or 7 or 9 or 2 or 8 or 1 or 4 or 5 (446452)
- 11 infant formula.mp. or exp Artificial Milk/ (4020)
- 12 exp Infant Feeding/ (12249)
- 13 exp Bottle Feeding/ (784)
- 14 exp Breast Milk/ or exp Breast Feeding/ or breastfeeding.mp. (14685)
- 15 breast feeding.mp. (11579)
- 16 11 or 13 or 12 or 15 or 14 (18127)
- 17 16 and 10 (1848)
- 18 limit 17 to (human and english language and yr="2005 -Current") (746)
- 19 from 18 keep 1-500 (500)

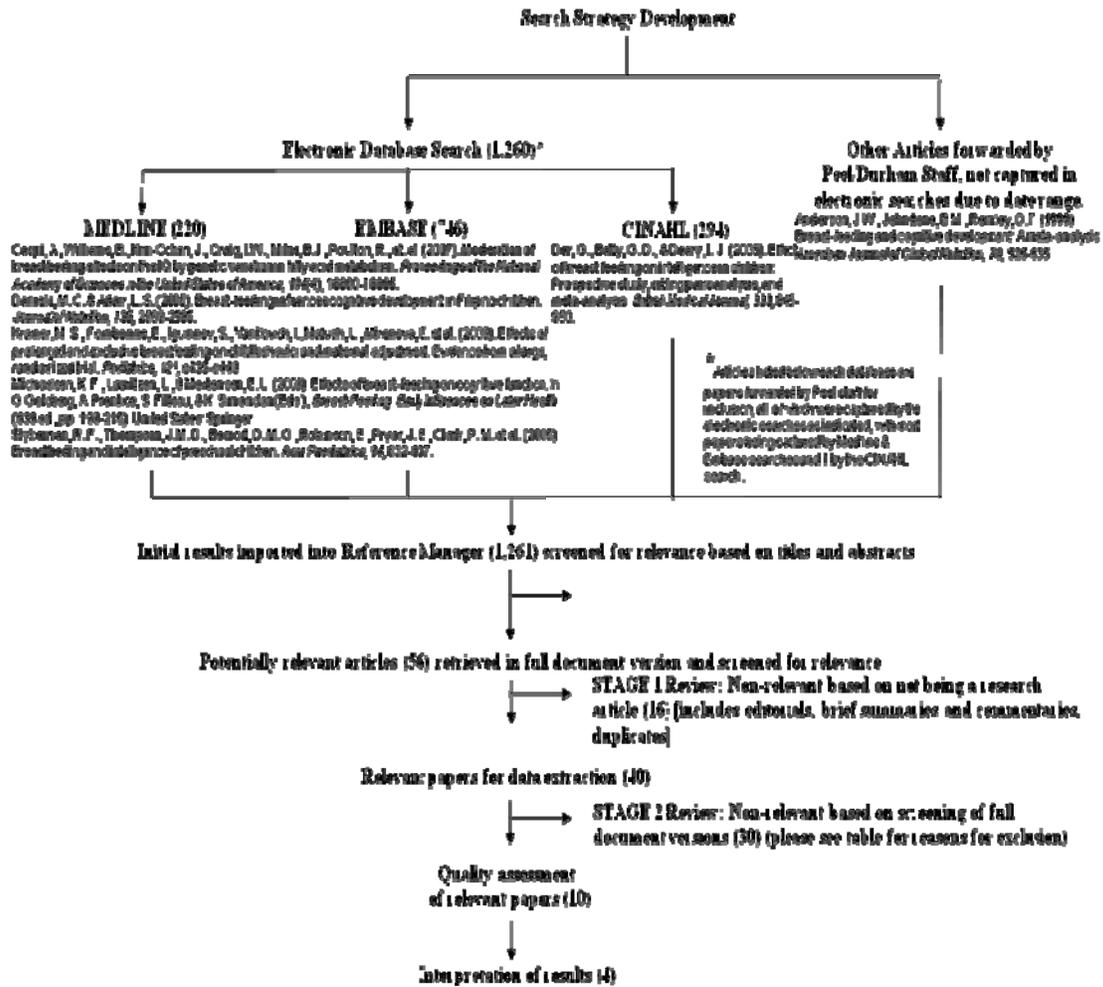
CINAHL:

SEARCH APPEARANCE IN CINAHL - EbscoHost

Limited by English; January 2005-June 2009; Taxonomy specifications not required

((MH Human Development+ or MH Cognition Disorders or MH "Mental Disorders Diagnosed in Childhood"+)) or (MH Intelligence+) or ((MH Social Behavior or MH Social Behavior Disorders+)) or ((MH Learning+ or MH Learning Disorders+)) or (MH Intelligence Tests) or ((MH Cognition+) or TX ("cognitive development" or "short term intelligence" or "long term intelligence" or "learning potential"))

APPENDIX 2: SEARCH RESULTS



APPENDIX 3: RELEVANCE ASSESSMENT RESULTS

	Author, (Year), Part of Title	Relevance Assessment Criteria Met or Unmet (Yes, No) / Reason if applicable				Decision to Include	Notes
		Must include a population of healthy full term infants in developed country(ies) who are exclusively breastfed or given only breastmilk, or artificial milk substitute.	Must compare the relationship between breastfeeding or infant formula, and cognitive development.	Must provide data on cognitive development/ function/ ability outcomes	Must be an English language primary study or review (and may be an overview) published between 2005 and 2009		
1.	Anderson, 1999 <i>Breast-feeding and cognitive development: A meta-analysis</i>						Already included in Ip (AHRQ review)
2.	Ashwell, 2005 <i>Highlights of 'early nutrition and its later consequences'</i>	NA	NA	NA	Not a study or review	No	Conference paper
3.	Bainbridge, 2008 <i>Higher IQs for breastfed babies.</i>	NA	NA	NA	Not a study or review	No	Commentary / announcement re Kramer
4.	Bond, 2008 <i>Randomized trial provide strong evidence that prolonged, exclusive breast-feeding enhances cognitive development in children.</i>	NA	NA	NA	Not a study or review	No	Commentary
5.	Buyken, 2008 <i>Effects of breastfeeding on health outcomes in childhood: beyond dose-response relations...</i>	NA	NA	NA	Not a study or review	No	Letter to the editor
6.	Caspi, 2007 <i>Moderation of breastfeeding effects on the IQ by genetic variation in fatty acid metabolism</i>	2 cohorts in New Zealand, Wales	Breast fed vs. non breast fed and fatty acid metabolism	IQ outcomes	Primary study	Yes	
7.	Clark, 2006 <i>Breast feeding and mental and motor development at 51/2 years</i>	5 year old, from low SES status families, who were full term infants in Chile	Breastfed infants – who may have been fed cow's milk	Cognitive, motor, language outcomes	Primary study	No	Dissimilar population; inability to determine feeding
8.	Daniels, 2005 <i>Breast-feeding influences cognitive development in Filipino children.</i>	Normal and low birthweight children	Compares breast fed < 6 months to breastfed for	Cognitive outcomes reported	Primary study	No	Doesn't add anything new to the Ip review; study population dissimilar

		born in the Philippines	12 – 18 months				
9.	Dee, 2007 <i>Associations between breast feeding practice and young children's language and motor skill development.</i>	Children in the U.S.	Breastfeeding vs. no breastfeeding	Language and motor skill development	Primary study	No	Limited outcomes reported; measure of outcomes was mother's level of concern
10.	Der, 2006 <i>Effect of breast-feeding on intelligence.</i>	Healthy full term, breast fed children, siblings in the U.S.	Breastfed vs. breastfed	Cognitive outcomes reported	Primary study	Yes	Controls for confounders by comparing siblings; controls for maternal IQ
11.	Der, 2008 <i>Results from the PROBIT breast feeding trial may have been over interpreted.</i>	NA	NA	NA	Not a study or review	No	Letter to the editor
12.	Deshpande, 2008 <i>Exclusive breast feeding for the first 6 months.</i>	NA	NA	NA	Not a study or review	No	Clinical update
13.	Elwood, 2005 <i>Long term effect of breast feeding : cognitive function in the Caerphilly cohort.</i>	Men who were healthy full term and LBW babies in Wales	Breast fed vs. not breastfed	Cognitive outcomes reported	Primary study	No	Study population was grown men in Wales
14.	Evenhouse, 2005 <i>Improved estimates of the benefits of breast-feeding...</i>	Adolescents in the U.S.	Breastfed vs. not breastfed	Cognitive outcomes reported	Primary study	Yes	Important for sibling comparison data; no data on formula/ supplementation - unable to determine breastfeeding exclusivity
15.	Fewtrell, 2007 <i>Optimal duration of exclusive breastfeeding: what is the evidence to support current recommendations?</i>	NA	NA	NA	Not a study or review	No	WHO recommendations
16.	Gibson-Davis, 2005 <i>Breast feeding and verbal ability...</i>	3 year olds in the U.S.	Breastfed vs. not breastfed	Vocabulary outcomes	Primary study	Yes	Good control for extensive set of demographic, home environment factors
17.	Gordon, 2008 <i>Breast feeding, breast milk feeding, breastfeeding and IQ: unknown and known knows.</i>	NA	NA	NA	Not a study or review	No	Letter to the editor
18.	Gubala, 2007 <i>Merits of breastfeeding through the toddler years.</i>	NA	NA	NA	Not a study or review	No	Letter to the editor

19.	Hadders-Algra, 2005 <i>The role of long chain poly-unsaturated fatty acids...</i>	Children	Formula vs. LCPUFA supplemented formula	Many	Overview	No	Looks at the role of LCPUFA; no methods reported for the overview
20.	Heinig, 2007 <i>Assessment of children's growth and development ...</i>	NA	NA	NA	Not a study or review	No	Editor's note
21.	Jacobson, 2006 <i>Breast-feeding and intelligence in children.</i>	NA	NA	NA	Not a study or review	No	Editorial
22.	Kramer, 2008 <i>An intervention promoting exclusive and prolonged breastfeeding improved verbal intelligence scores in children at 6.5 years.</i>	NA	NA	NA	Not a study or review	No	Commentary by Simmer, K
23.	Kramer, 2008 <i>Effects of prolonged and exclusive breastfeeding on child behavior and maternal adjustment: evidence from a large, randomized trial.</i>	Maternity hospitals in Belarus	Breastfed; exclusive breastfed at 3 months; exclusive breastfed at 6 months	Non-cognitive outcomes	Primary study	No	Looks at maternal adjustment outcomes
24.	Kramer, 2008 <i>Breastfeeding and child cognitive development.</i>	Maternity hospitals in Belarus	Breastfed; exclusive breastfed at 3 months; exclusive breastfed at 6 months	Cognitive outcomes	Primary study	Yes	
25.	Lawlor, 2002 <i>Early life predictors of child intelligence: findings from the Mater University study of pregnancy and its outcomes</i>	5 year olds in Australia	Breastfeeding	Intelligence	Primary study	Yes	Effects of early life determinants on childhood intelligence
26.	Leung, 2005 <i>Breast is best for babies...</i>	NA	NA	NA	Not a study or review	No	Original article
27.	Lundberg, 2008 <i>Does breast feeding improve child cognitive development.</i>	NA	NA	NA	Not a study or review	No	Medical Minute
28.	McCartney, 2007 <i>Mixed messages over breast milk..</i>	NA	NA	NA	Not a study or review	No	Observation
29.	Mendoza-Salonga, 2007 <i>Nutrition and brain development.</i>	NA	NA	NA	Not a study or review	No	Editorial
30.	Michaelsen,	Children, adults	Breast fed vs. non breast fed	Intelligence	Book chapter	Yes	Includes a very comprehensive

	2009 <i>Effects of breastfeeding on cognitive function.</i>						literature review
31.	Mortnesen, 2007 <i>Neurodevelopment effects of breast feeding.</i>	NA	NA	NA	Not a study or review	No	Commentary
32.	Petryk, 2007 <i>Breast Feeding and Neurodevelopment. A literature review.</i>	Children and adults	breastfeeding	Neurodevelopment outcomes including neuromotor, visual and cognitive development; educational achievement and social adaptation	Book chapter	Yes	Well done literature review/ book chapter.
33.	Pivik, 2007 <i>The influence of infant diet on early development changes in processing of human voice speech stimuli...ERP variations in breast and milk formula-fed infants t 3 and 6 months after birth</i>	Healthy infants	Breast fed vs. not breast fed	Processing language stimuli outcomes	Primary study	No	
34.	Poulton, 2008 <i>Effects of prolonged and exclusive breastfeeding on childhood behavior and maternal adjustment: evidence from a large randomized trial..</i>	NA	NA	NA	Not a study or review	No	Commentary
35.	Reading, 2007 <i>[Commentary on] Effect of breast feeding on intelligence in children: prospective study, sibling pairs analysis, and meta-analysis</i>	NA	NA	NA	Not a study or review	No	Commentary
36.	Reilly, 2005 <i>Duration of exclusive breast feeding introduction of complementary feeding may be necessary before 6 months.</i>	NA	NA	NA	Not a study or review	No	
37.	Ribas-Fito, 2007 <i>Beneficial Effects of breast feeding on cognition regardless of DDT concentrations at birth</i>	Healthy children, Spain	Compares breastfed babies with high vs. low concentrations of DDT	Cognitive outcome data provided	Primary study	No	
38.	Sacker, 2006	Healthy full	Breast fed vs.	Developmental	Primary	Yes	

	<i>Breastfeeding and developmental delay: findings from the millennium cohort study.</i>	term breastfed infants in the United Kingdom	non breast fed	delay outcomes	study		
39.	Schack-Nielsen, 2005 <i>Long term effects of breast feeding...</i>	Infant and mother in developed and developing countries	Various durations of breastfeeding	Growth, development, morbidity, mortality	Book chapter	No	Authors include Michaelsen, conclusions repeat Michaelsen book chapter above
40.	Schack-Nielsen, 2006 <i>Breast feeding and future health</i>	Infant and mother in developed and developing countries	Various durations of breastfeeding	Growth, development, morbidity, mortality	Book chapter	No	Authors include Michaelsen, conclusions repeat Michaelsen book chapter above
41.	Selvakumar, 2007 <i>Infant feeding practice and its effect on the growth and development of babies.</i>	Healthy babies, India	Exclusively breast fed vs. non exclusive breast feeding	Motor, language skills, social milestones	Primary study	No	Dissimilar population; no cognitive outcomes
42.	Zhou, 2007 <i>Home environment, not duration of breastfeeding, predicts intelligence quotient of children at four years.</i>	Healthy full term infants in Australia	Breast fed vs. non or short-term breast fed	IQ	Cohort study	Yes	One author (Maria Makrides) is known to have formula industry contacts – no conflict of interest was declared in the publication
43.	Slykerman, 2005 <i>Breastfeeding and intelligence of preschool children.</i>	European preschool children in Auckland who were full term and either appropriate size or small for gestational age (SGA)	Any breastfeeding vs. exclusive breastfeeding	Intelligence	Primary study	No	Dissimilar population; included SGA children
44.	Sullivan, 2008 <i>Cognitive development: breast milk benefit vs. infant formula hazard.</i>	NA	NA	NA	Not a study or review	No	Letter to the editor
45.	Summary document 2008 <i>Effects of breast feeding new results from a large randomized trail</i>	NA	NA	NA	Not a study or review	No	Summary of Kramer
46.	Weaver, 2006	NA	NA	NA	Not a	No	Guideline

	(Barclay, Weaver) <i>Feeding the normal infant, child and adolescent</i>				study or review		
47.	Wright, 2006 <i>Formula supplemented with Docosahexaenoic acid (DHA) and Arachidonic acid (ARA): a critical review of the research.</i>	Healthy full term infants	Formula including DHA (with or without ARA) vs. standard formula	Neurodevelopment outcomes included	Literature review (search to 2003)	No	Review
48.	<i>No link between breastfeeding and cognitive development researchers say.</i>	NA	NA	NA	Not a study or review	No	Not available – but likely a commentary based on 1 page length
49.	<i>Breastfeeding raises IQ</i>				Not a study or review	No	Not available – but likely a commentary
50.	<i>Assessing the evidence on LCPUFA in infant formulas</i>	NA	NA	NA	Not a study or review	No	
51.	<i>Breastfeeding and child intelligence link refuted</i>	NA	NA	NA	Not a study or review	No	Commentary
52.	<i>Breastfeeding and child intelligence link refuted</i>	NA	NA	NA	Not a study or review	No	Commentary
53.	<i>Breastfeeding and intelligence</i>	NA	NA	NA	Not a study or review	No	Commentary
54.	<i>Study hints at link between breastfeeding and intelligence</i>	NA	NA	NA	Not a study or review	No	Commentary
55.	Research Summaries #237				Not a study or review	No	
56.	Duplicate title.	NA	NA	NA	NA	No	NA

APPENDIX 4: REFERENCE LIST OF INLCUED STUDIES

- Caspi, A., Williams, B., Kim-Cohen, J., Craig, I.W., Milne, B.J., Poulton, R., et. al. (2007). Moderation of breastfeeding effects on the IQ by genetic variation in fatty acid metabolism. *Proceedings of the National Academy of Sciences in the United States of America*, 104(4), 18860-18865.
- Der G, Batty GD, Deary IJ. Effect of breast feeding on intelligence in children: prospective study, sibling pairs analysis, and meta-analysis. *BMJ: British Medical Journal* 2006 November 4;333(7575):945.
- Evenhouse E, Reilly S. Improved estimates of the benefits of breastfeeding using sibling comparisons to reduce selection bias. *Health Services Research* 2005;40(6 I).
- Gibson-Davis CM, Brooks-Gunn J. Breastfeeding and verbal ability of 3-year-olds in a multicity sample. *Pediatrics* 2006 November;118(5):e1444-e1451.
- Kramer MS, Aboud F, Mironova E, Vanilovich I, Platt RW, Matush L et al. Breastfeeding and child cognitive development: New evidence from a large randomized trial. *Archives of General Psychiatry* 2008;65(5).
- Lawlor DA, Najman JM, Batty GD, O'Callaghan MJ, Williams GM, Bor W. Early life predictors of childhood intelligence: Findings from the Mater-University study of pregnancy and its outcomes. *Paediatric and Perinatal Epidemiology* 2002;#2006(2).
- Michaelsen KF, Lauritzen L, Mortensen EL. Effects of breast-feeding on cognitive function. *Breast-Feeding: Early Influences on Later Health* *Advances in Experimental Medicine and Biology* 2009;639(pp9-215).
- Petryk A, Harris SR, Jongbloed L. Breastfeeding and neurodevelopment: a literature review. *Infants & Young Children: An Interdisciplinary Journal of Special Care Practices* 2007 April;20(2):120-34.
- Sacker A, Quigley MA, Kelly YJ. Breastfeeding and developmental delay: findings from the Millennium Cohort Study. *Pediatrics* 2006 September;118(3):e682-e689.
- Zhou SJ, Baghurst P, Gibson RA, Makrides M. Home environment, not duration of breast-feeding, predicts intelligence quotient of children at four years. *Nutrition* 2007 March;23(3):236-41.

APPENDIX 5 – QUALITY ASSESSMENT TOOL CAUSATION STUDIES

Quality Assessment Tool - Causation

CRITERION		Points
1. What research design was used?	a) randomized controlled trial – 3 points b) cohort study – 2 points c) case-control – 1 point d) other – 0 points e) can't tell – 0 points	
2. Were there clearly identified comparison groups?	yes – 1 point no – 0 points not indicated – 0 points	
3. Were the comparison groups compared for similarity on important confounders at baseline?	yes – 1 point no – 0 points not indicated – 0 points	
4. Were the outcomes and exposures measured in the same way in the groups being compared?	yes – 1 point no – 0 points not indicated – 0 points	
5. Were the data collection tools shown to be valid?	yes, completely – 2 points somewhat – 1 point no – 0 points	
6. Were the data collection tools shown to be reliable?	yes, completely – 2 points somewhat – 1 point no – 0 points	
7. Was the follow-up sufficiently long for the outcome of interest?	yes – 1 point no – 0 points not indicated – 0 points	
8. Was the follow-up sufficiently complete?	a) 80% or above - 2 points b) 60% to <80% - 1 point c) <60% - 0 points d) not indicated – 0 points	
9. Does exposure to the agent precede the outcome?	yes – 1 point no – 0 points not indicated – 0 points	
10. Was there a dose-response gradient (as exposure increases risk of outcome increases/decreases)	yes – 1 point no – 0 points not indicated – 0 points	
11. If there were significant differences between groups at baseline were they controlled for in the analysis?	yes – 1 point no – 0 points not indicated – 0 points	
12. Were appropriate statistical tests done for the research design?	yes – 1 point RCT and cohort – relative risk (RR) no – 0 points Case-control – odds ratio (OR) not indicated – 0 points	
13. Were the 95% confidence intervals for the outcome(s) of interest precise?	yes – 1 point no – 0 points CI not indicated – 0 points	
14. Was the description of study participants detailed enough to apply the results in clinical practice?	yes completely – 2 points somewhat – 1 point no – 0 points	

TOTAL SCORE: _____

RATING (circle one) (total score 16-20) (total score 12-15) (total score 0-11)
STRONG MODERATE WEAK

APPENDIX 6 – QUALITY ASSESSMENT TOOL – INTERVENTION STUDIES



EFFECTIVE PUBLIC HEALTH PRACTICE PROJECT (EPHPP)



Ref ID: _____
Author: _____
Year: _____
Reviewer: _____

QUALITY ASSESSMENT TOOL FOR QUANTITATIVE STUDIES

COMPONENT RATINGS

A) SELECTION BIAS

(Q1) Are the individuals selected to participate in the study likely to be representative of the target population?

- 1 Very likely
- 2 Somewhat likely
- 3 Not likely
- 4 Can't tell

(Q2) What percentage of selected individuals agreed to participate?

- 1 80 - 100% agreement
- 2 60 - 79% agreement
- 3 less than 60% agreement
- 4 Not applicable
- 5 Can't tell

RATE THIS SECTION See dictionary	STRONG 1	MODERATE 2	WEAK 3
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B) STUDY DESIGN

Indicate the study design

- 1 Randomized controlled trial
- 2 Controlled clinical trial
- 3 Cohort analytic (two group pre + post)
- 4 Case-control
- 5 Cohort (one group pre + post (before and after))
- 6 Interrupted time series
- 7 Other specify _____
- 8 Can't tell

Was the study described as randomized? If NO, go to Component C.

No Yes

If Yes, was the method of randomization described? (See dictionary)

No Yes

If Yes, was the method appropriate? (See dictionary)

No Yes

RATE THIS SECTION See dictionary	STRONG 1	MODERATE 2	WEAK 3
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C) CONFOUNDERS

(Q1) Were there important differences between groups prior to the intervention?

- 1 Yes
- 2 No
- 3 Can't tell

The following are examples of confounders:

- 1 Race
- 2 Sex
- 3 Marital status/family
- 4 Age
- 5 SES (income or class)
- 6 Education
- 7 Health status
- 8 Pre-intervention score on outcome measure

(Q2) If yes, indicate the percentage of relevant confounders that were controlled (either in the design (e.g. stratification, matching) or analysis)?

- 1 80 – 100%
- 2 60 – 79%
- 3 Less than 60%
- 4 Can't Tell

RATE THIS SECTION See dictionary	STRONG 1	MODERATE 2	WEAK 3
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D) BLINDING

(Q1) Was (were) the outcome assessor(s) aware of the intervention or exposure status of participants?

- 1 Yes
- 2 No
- 3 Can't tell

(Q2) Were the study participants aware of the research question?

- 1 Yes
- 2 No
- 3 Can't tell

RATE THIS SECTION See dictionary	STRONG 1	MODERATE 2	WEAK 3
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E) DATA COLLECTION METHODS

(Q1) Were data collection tools shown to be valid?

- 1 Yes
- 2 No
- 3 Can't tell

(Q2) Were data collection tools shown to be reliable?

- 1 Yes
- 2 No
- 3 Can't tell

RATE THIS SECTION See dictionary	STRONG 1	MODERATE 2	WEAK 3
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F) WITHDRAWALS AND DROP-OUTS

(Q1) Were withdrawals and drop-outs reported in terms of numbers and/or reasons per group?

- 1 Yes
- 2 No
- 3 Can't tell

(Q2) Indicate the percentage of participants completing the study. (If the percentage differs by groups, record the lowest).

- 1 80 -100%
- 2 60 - 79%
- 3 less than 60%
- 4 Can't tell

RATE THIS SECTION See dictionary	STRONG 1	MODERATE 2	WEAK 3
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G) INTERVENTION INTEGRITY

(Q1) What percentage of participants received the allocated intervention or exposure of interest?

- 1 80 -100%
- 2 60 - 79%
- 3 less than 60%
- 4 Can't tell

(Q2) Was the consistency of the intervention measured?

- 1 Yes
- 2 No
- 3 Can't tell

(Q3) Is it likely that subjects received an unintended intervention (contamination or co-intervention) that may influence the results?

- 4 Yes
- 5 No
- 6 Can't tell

H) ANALYSES

(Q1) Indicate the unit of allocation (circle one)

community organization/institution practice/office individual

(Q2) Indicate the unit of analysis (circle one)

community organization/institution practice/office individual

(Q3) Are the statistical methods appropriate for the study design?

- 1 Yes
- 2 No
- 3 Can't tell

(Q4) Is the analysis performed by intervention allocation status (i.e. intention to treat) rather than the actual intervention received?

- 1 Yes
- 2 No
- 3 Can't tell

GLOBAL RATING

COMPONENT RATINGS

Please transcribe the information from the gray boxes on pages 1-4 onto this page.

A	SELECTION BIAS	RATE THIS SECTION See dictionary	STRONG 1	MODERATE 2	WEAK 3
B	STUDY DESIGN	RATE THIS SECTION See dictionary	STRONG 1	MODERATE 2	WEAK 3
C	CONFOUNDERS	RATE THIS SECTION See dictionary	STRONG 1	MODERATE 2	WEAK 3
D	BLINDING	RATE THIS SECTION See dictionary	STRONG 1	MODERATE 2	WEAK 3
E	DATA COLLECTION METHODS	RATE THIS SECTION See dictionary	STRONG 1	MODERATE 2	WEAK 3
F	WITHDRAWALS AND DROPOUTS	RATE THIS SECTION See dictionary	STRONG 1	MODERATE 2	WEAK 3

GLOBAL RATING FOR THIS PAPER (circle one):

- 1 STRONG (four STRONG ratings with no WEAK ratings)
- 2 MODERATE (less than four STRONG ratings and one WEAK rating)
- 3 WEAK (two or more WEAK ratings)

With both reviewers discussing the ratings:

Is there a discrepancy between the two reviewers with respect to the component (A-F) ratings?

- No Yes

If yes, indicate the reason for the discrepancy

- 1 Oversight
- 2 Differences in interpretation of criteria
- 3 Differences in interpretation of study

Final decision of both reviewers (circle one):

- 1 STRONG
- 2 MODERATE
- 3 WEAK

APPENDIX 7: INCLUDED STUDIES - QUALITY ASSESSMENT RESULTS

Causation Studies									
Quality Criteria	Author/ Score								
	Caspi	Der	Evenhouse	Gibson-Davis	Lawlor	Michaelsen	Petryk	Sacker	Zhou
1. What Research Design Was Used?	2	2	1	2	2	Book chapter (no QA)	Book Chapter (no QA)	2	2
2. Were there clearly identified comparison groups?	1	1	1	1	0			1	1
3. Were the comparison groups compared for similarity on important confounders at baseline?	1	1	0	1	1			1	1
4. Were the outcomes and exposures measured in the same way in the groups being compared?	1	1	1	1	1			1	1
5. Were the data collection tools shown to be valid?	0	0	1	1	1			1	2
6. Were the data collection tools shown to be reliable?	0	0	0	1	1			0	2
7. Was the follow-up sufficiently long for the outcome of interest?	0	1	1	1	1			0	1
8. Was the follow-up sufficiently complete?	NA	0	0	0	0			1	0
9. Does exposure to the agent precede the outcome?	1	1	1	1	1			1	1
10. Was there a dose-response gradient (as exposure increases risk of outcome increases/decreases)?	NA	1	0	0	1			1	1
11. If there were significant differences between groups at baseline were they controlled for in the analysis?	1	1	1	1	1			1	NA
12. Were appropriate statistical tests done for the research design?	1	1	1	1	1			1	1
13. Were the 95% confidence intervals for the outcome(s) of interest precise?	0	0	0	0	1			0	0
14. Was the description of	0	1	2	1	1			0	0

study participants detailed enough to apply the results in clinical practice?									
TOTAL	8 (weak)	11 (weak)	10 (weak)	12 (moderate)	13 (moderate)			11 (weak)	13 (moderate)
Intervention Studies									
Quality Criteria	Kramer								
Selection Bias	Strong/Moderate								
Study Design	Strong								
Confounders	Weak								
Blinding	Moderate								
Data Collection Methods	Strong								
Withdrawals and Dropouts	Strong								
Intervention Integrity	Good								
Analyses	Done appropriately								
OVERALL	Moderate								