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PARLIAMENTARY INQUIRY INTO THE HEALTH BENEFITS OF BREASTFEEDING

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TABLE OF CONTENTS

TERMS OF REFERENCE COVERED BY THIS SUBMISSION

EXECUTIVE SUMMARY

This submission addresses three primary terms of references of the Parliamentary Review, the extent of the health benefits of breastfeeding, initiatives to encourage breastfeeding and the effectiveness of current measures to promote breastfeeding. What is covered in these terms of reference is briefly described below.

The Extent Of The Health Benefits Of Breastfeeding

With relation to the extent of the health benefits of breastfeeding, breastfeeding has been shown to have protective effects against three significant public health problems:

- Child overweight and obesity
- Child and adolescent mental health morbidity
- Asthma and allergies

Breastfeeding for at least six months has been shown to be protective against overweight and obesity later in childhood. Breastfeeding is superior to formula feeding because it has specific and non-specific factors including the essential fatty acids, that may have long term consequences for mental health throughout life. Studies that fulfilled strict criteria for assessing causality have shown a protective effect of breastfeeding on asthma and atopy in childhood.

Given the many benefits conferred by breast milk, all mothers should be encouraged and supported to continue full breastfeeding for six months and beyond in order to promote the optimum health and well-being of their infants into childhood and adolescence.

Initiatives To Encourage Breastfeeding

The Baby Friendly Hospital Initiative (BFHI) has been adopted by over 70 countries and although Australia adopted it in 1994 there are still only 48 accredited hospitals and only two of those are in Western Australia. BFHI should be supported as the primary initiative to encourage and support breastfeeding from birth. Although more than 84% of Australian women initiate breastfeeding by 3 months only 60% are still breastfeeding and by 6 months less than 40% continue to breastfeed.

Information that will allow Effective Planning of a Contextual, Multi-Level, and Collaborative Health Promotion Strategy for Breastfeeding

Based on the benefits of breastfeeding, and the low duration of any and exclusive breastfeeding in Australia, there is a clear need for strategies and interventions aimed at improving the duration of breastfeeding practice within Australia. A multi-level Ecological Model of Factors Affecting Breastfeeding Practices is suggested as the way to commence a nationwide breastfeeding public health promotion campaign.

THE EXTENT OF THE HEALTH BENEFITS OF BREASTFEEDING

Breastfeeding is internationally recognised as the optimal method of infant feeding (1, 2). The composition of breast milk constantly changes to provide the ideal balance of nutrients for an infant during various stages of development. Breastfeeding results in a number of positive health outcomes for the infant. Benefits such as easy digestibility, improved immunological function (3), reduced risk of infectious diseases such as gastrointestinal illnesses, respiratory illness, otitis media (4-8), and reduced risk of SIDS (9, 10)have all been associated with breastfeeding. Long-term benefits such as improved cognitive functioning (11-13), lower risk of obesity (14, 15), diabetes (16, 17), asthma (18, 19) and childhood leukaemia (20, 21) later in life have also been associated with breastfeeding. Although infant formula manufacturers attempt to replicate the composition of breast milk, it is highly complex, and includes hormones, bioactive factors, active enzymes, immunoglobulins and compounds with unique structures that cannot yet be replicated in the laboratory (22).

Furthermore, the benefits of breastfeeding are not limited to the infant. A number of maternal benefits are associated with breastfeeding. These benefits include a faster return to pre-pregnancy weight (23), delayed return of menstruation and fertility (24) and reduced risk of breast cancer (25, 26). Additionally, economic and environmental benefits are reported (27). These include decreased annual health care costs (28), lower environmental burden due to fewer formula cans and bottles, and decreased energy demands due to transportation of artificial feeding products (29).

Based on these well-documented benefits of breastfeeding, the World Health Organisation (WHO) has produced breastfeeding guidelines (for both the developing and developed nations). These state that infants should be breastfed *exclusively* (i.e. breast milk as the only source of nutrition) until around 6 months, and that breastfeeding should continue (with the introduction of appropriate foods after 6 months – i.e. *any* breastfeeding) until at least 2 years of age (30). Based on these recommendations, the 1993 Australian government document *Goals and Targets for Australia's Health in the Year 2000 and Beyond* (31) provided a goal for the year 2000 of 90% of infants being breastfed on hospital discharge and 75% of infants receiving *any* breast milk at six months. Since then, the NMHRC have added that by 2008 a suitable goal would be 40% of infants being *exclusively* breastfed at six months (32).

Despite the health benefits, clear recommendations made by WHO and national aims of breastfeeding practice, duration of breastfeeding in Australia is significantly lower than desired (33-35). In Perth, a recent report (36) indicates initiation rates are high (above 90%), but 41% of infants receive regular formula feeding by four weeks and only 45.9% of infants receive *any* breast milk after six months. The proportion of mothers who are breastfeeding *exclusively* at 6 months is very low (less than 1%). These findings indicate that while the discharge goal of 90% has been met, the duration goal set for 2000 had not been met by 2005, and the current rates of exclusive breastfeeding at six months are not on track for 2008 targets.

To gain an idea of the costs associated with the low duration of breastfeeding in Australia, an economic analysis conducted using data from an ACT population examined the costs associated with hospitalisation due to five illnesses associated with infant formula feeding. The findings indicated that if the goal set by the NHMRC was met, and 40% of infants were being exclusively breastfed until six months, $1.4 million per annum would be saved on *infant hospitalisation costs alone* (37). Translated to the WA population, this would result in a saving of over $8.5 million. This figure does not include savings due to maternal and economic benefits, or longer term benefits of breastfeeding such as lower chance of obesity, or higher cognitive abilities.

The Effect Of Breastfeeding On Child Overweight And Obesity

Breastfeeding and early overweight

Breastfeeding has been shown to protect against child obesity and cardiovascular risk outcomes (38), and is "dose related"(39), the longer an infant is breastfed, the lower the risk of obesity (40). This may be because breastfeeding may attentuate subsequent programming effects. Our aim was to determine whether earlier regular formula feeding influences growth particularly overweight in children. The public health importance of this question arises from the possibility that knowledge of any specific postnatal nutritional influence on later child health may provide an opportunity for intervention during infancy.

Substantial evidence over 40 years indicates that early nutrition and growth affects long term cardiovascular health (41). The theory is that a high nutrient diet in infancy adversely programs the principal components of the metabolic syndrome by promoting growth acceleration (upward centile crossing) (41) therefore slower growth benefits later cardiovascular disease and its risk factors. Singhal showed that early growth acceleration programmed the abnormal vascular biology associated with early atherosclerosis, whereas slower growth was beneficial (42). Baird showed that infants who were at the highest end of the distribution of weight or body mass index or who grow rapidly during infancy are at increased risk of subsequent obesity (43).

The adverse long term effects of early growth acceleration emerge as fundamental in later overweight and obesity (44). Childhood growth acceleration (erroneously called catch-up growth) is associated with later insulin resistance, obesity and cardiovascular disease, dyslipidemia, raised insulin concentration and increased insulin growth factor 1 (45). Growth acceleration is highest in early infancy suggesting that this period may be critical. Furthermore, early programming of the Hypothalamic-Pituitary-Adrenal (HPA) axis could directly affect later cardiovascular disease (CVD) and non-insulin dependent diabetes (NIDDM).

Our hypothesis was that early and regular formula feeding promotes early growth acceleration, which could adversely program cardiovascular health and several researchers have reported such observations.

Breastfeeding and cardiovascular risk factors

Breastfed infants show slower growth than formula fed infants (46) especially in the early weeks when breastfeeding is not fully established and may have lower rates of CVD, hypercholesterolemia, obesity, NIDDM and high blood pressure later on in life. An increased nutrient intake in infancy was associated with higher blood pressure in adults (47) and an earlier adiposity rebound as indicator of faster growth (48) was associated with risk of later obesity. Singhal suggests these data show a causal link between breastfeeding and decreased risk of developing the metabolic syndrome (41, 49, 50).

Faster early growth of formula fed versus breastfed infants would program the metabolic syndrome. Early growth acceleration adversely programmed insulin resistance irrespective of birth size suggesting postnatal growth rather than intrauterine growth is of paramount importance (42). High ponderal index at birth was associated with shorter duration of breastfeeding (51) and both of these factors were associated with higher BMI at 12 months (51). Furthermore early dietary habits have been related to later BMI and obesity and studies suggest breastfeeding may reduce the risk (52) but sugar sweetened drinks and fast food may increase the risk (53-56).

A goal for research is to identify periods in which intervention is likely to be most beneficial. Because the greatest change in growth rate (crossing of centiles) occurs early in infancy, growth

acceleration during this period might have the greatest effect. The large effect size of nutritional manipulation during this critical period lends support to this theory. The effect of early growth and nutrition on later cardiovascular health is substantial with breastfeeding showing reduced diastolic blood pressure (50), lower cholesterol concentration (57), decreased markers of insulin resistance, and Lawlor suggests that the effect of breastfeeding on systolic blood pressure may amplify with increasing age (58). Martin showed a dose response with increased breastfeeding associated with increased reductions in blood pressure and concluded that breastfeeding may have important public health benefits with regard to reduced risk of cardiovascular disease (59).

Breastfed and formula fed infants have a different hormonal response to feeding. Formula provokes a greater insulin response and possible early fat deposition (60, 61). Singhal states that the effect of early growth and nutrition on later cardiovascular health is substantial and the effect of growth acceleration on later insulin resistance is also substantial (62).

Growth acceleration explained the adverse effects of a nutrient enriched diet on later insulin resistance and blood pressure. For insulin resistance, growth in just the first two weeks of life seemed critical with an effect of early catch-up growth on later concentration of insulin like growth factor-1 (48). Martin also showed in a longitudinal study some evidence of linear increase in the effect of breastfeeding on height (p for trend =0.034 and leg length p for trend =0.006 but not trunk length p=0.14) (47). These differences persisted into adulthood.

Breastfeeding and later overweight and obesity

Breastfeeding has been shown to protect against overweight and obesity (63-65) although many studies have not found an effect before five years of age (66-70) and most not finding an effect on obesity in children older than five years of age (71-75). Breastfeeding showed increasing body fatness in two studies (76, 77) but a protective effect in six studies (63-65, 78-80). The impact of breastfeeding on obesity has been examined in earlier studies but no effect was observed (81, 82). On the other hand, a protective effect has been reported in a Canadian cross-sectional study of 1320 adolescents born in the late 1960s (78).

Reilly (83) found eight factors in early life associated with an increased risk of obesity in childhood but this did not include infant feeding. The apparent protective effect of exclusive breastfeeding on obesity at age 7 years observed in the univariate analysis remained (OR 0.70) but was reduced following adjustment for the 8 other factors (birth weight, parental obesity, sleep duration, television viewing, size in early life, weight gain in infancy, catch-up growth and early adiposity rebound). Catch-up growth between birth and two years and an adiposity rebound and high rates of weight gain in the first 12 months were independently associated with obesity at age 7. The authors did not state that these identified weight gain factors were all potentially associated with increased bottle feeding and are plausibly on the causal pathway for obesity later in childhood (84).

Bergmann found that maternal BMI of > or =27, bottle-feeding, maternal smoking during pregnancy, and low social status were risk factors for overweight and adiposity at 6 years of age (85). Early bottle-feeding brings forward the obesity rebound, predictive of obesity in later life. Stettler and colleagues found that after adjustment for important confounding factors, weight gain during the first week of life was significantly associated with adult overweight status as was weight gain during the first 112 days of life (86). These authors concluded that in formula-fed infants, weight gain during the first week of life may be a critical determinant for the development of obesity several decades later. Their results contribute to the understanding of chronic disease programming and suggest new approaches to obesity prevention.

Conventional wisdom was that there was a period of relative grace from becoming overweight, and chubby babies were a sign of good health in many societies. Children who were overweight at 1

and 3 years old were thought to have no increased risk of obesity as adults, but after that age the risk rises regardless of parental weight (87). However a large multicentre trial of 20,000 infants followed in detail for 7 years showed that rapid weight gain during the first 4 months of life was associated with an increased risk of overweight status at 7 years (88, 89).

Recent studies have applied more rigorous epidemiology to larger sample sizes with an increase in the quality of the evidence. Von Kries analysed 9400 German children in a cross-sectional study in Bavaria (90) to consider the impact of breastfeeding on the prevalence of being overweight or obese in 5 and 6-year-old children. Obesity was assessed as having a BMI above the 97th percentile. The prevalence of obesity in children who had never been breastfed was 4.5% compared to 2.8% in breastfed children. Breastfed children were protected against obesity (Odds ratio [OR] 0.75 95% Confidence Interval [CI] 0.57-0.98) and overweight (OR 0.79; 95%CI 0.68-0.93). These authors concluded that breastfeeding may help decrease the prevalence of obesity in childhood, which may eventually result in a reduction in the prevalence of cardiovascular disease and other associated diseases. Although genetic risk as measured by maternal BMI was not considered in this study and although breastfeeding data were collected retrospectively, the study had a large sample size and a protective effect of breastfeeding on obesity was demonstrated (63, 90).

Burke and colleagues studied 2087 children followed from before birth to 8 years of age (91). In this study, infants breastfed > 12 months were leaner at 1 year but not at 8 years. However breastfeeding for 4 months or less was associated with a greater risk of overweight at any point until 8 years of age. There has been considerable debate as to whether breast-feeding protects against childhood obesity. Dewey studied growth patterns for weight, length, head circumference and indices of body composition (92), and found that infants breastfed for ≥ 12 months were leaner than formula fed infants (93) as did Burke (91). Although the role of breastfeeding in obesity has been controversial (66) Grummer Strawn found that the rate of overweight at 4 years was highest among children never breastfed or who were breastfed for < 1 month (65a) and as Burke showed (91) overweight through childhood decreased with increasing breastfeeding duration.

Gillman and colleagues studied 15,000 children whose mothers were participants in the Nurses Health Study (65). The wealth of data available in this study allowed for adjustment for a range of potentially confounding factors. The results were summarised "....our findings indicate that infants who were predominantly fed breast milk in the first 6 months of life had a lower prevalence of overweight 9 to 14 years later. Compared with infants predominantly fed infant formula, the estimated relative reduction in risk was approximately 22%. In addition, the apparent protective effects were larger with increasing duration of breastfeeding."

The NHANES lll survey provided further evidence for an association between breastfeeding and obesity. Hediger analysed a sample of 2685 US-born children between the ages of 3 and 5 years (64). After adjusting for potential confounders, there was a reduced risk of being at risk of overweight in "ever breastfed" children, adjusted odds ratio of 0.63 (0.41-0.96). Although the retrospective nature of the breastfeeding data collection may have contributed to a weak statistical effect, the large number of mothers who never breastfed (46%) and who were overweight or obese (36%) may have introduced bias to this study. Furthermore because the children were between 3 and 5 years-of-age, those children who were fatter may have reached the period of adiposity rebound earlier than children of normal weight.

Different definitions of breastfeeding and lack of data on exclusive breastfeeding might explain some of the inconsistent results observed in studies on breastfeeding and obesity (52). Two systematic reviews and one meta-analysis have addressed the question of breastfeeding and obesity (14, 40, 94). Arenz (14) analysed nine studies with more that 69,000 participants and concluded that breastfeeding has a small but consistent protective effect against childhood obesity (OR 0.78; 95%

CI 0.71, 0.85). Owen's review (94) of 61 studies provided data from 28 studies (298,000 participants) of high quality. A pooled analysis of these studies indicated that breastfeeding was associated with a reduced risk of obesity compared to formula feeding (OR 0.87; 95% CI 0.85, 0.89). Studies reporting a quantitative estimate provided consistent evidence of a relationship between breastfeeding and a decreased risk of obesity. The systematic reviews and meta-analysis where never versus ever breastfed were studied found a similar pooled odds ratio of protection. The meta-analysis (40) examined the effect of breastfeeding duration and the results from this analysis suggests a dose dependent association between longer duration and decrease in risk of overweight (< 1 month of breastfeeding: OR 1.0 95% CI 0.65, 1.55; 1-3 months OR 0.81 95% CI 0.74, 0.88; 4-6 months OR 0.76 95% CI 0.67, 0.86; 7-9 months OR 0.67 95% CI 0.55, 0.82; > 9 months OR 0.68 95% CI 0.50, 0.91). Therefore increasing breastfeeding duration could form an important part of population strategies to prevent obesity.

Taken together these studies provide powerful support for the hypothesis that breastfeeding, and particularly predominant (or exclusive) breastfeeding is protective against the development of obesity through childhood and into adolescence. Since it is known that obese adolescents are very likely to become obese adults the importance of breastfeeding as a preventive measure is apparent.

Breastfeeding and later growth in Australia

There are few databases in Australia that allow us to explore the relationship between breastfeeding and later growth in Australia. However some information is available from a National Nutrition Survey undertaken on 14,000 persons around Australia (95). By linking several databases it was possible to identify 405 children aged 2-3 years where data on feeding history and some parental health data was also available (unpublished data). The BMI of the children was calculated and was classified as normal or overweight according to the classification proposed by Cole (96).

The significant factors associated with overweight and obesity were found to be:

- Exclusive breastfeeding to 24 weeks was protective
- Introduction of cows milk after 12 months as protective
- Parents BMI was correlated to child BMI

From the first Perth Infant Feeding study (1993) (97, 98) a total of 137 infants were followed up after a period of nine years. The children were again classified according to the Cole (7) criteria (Table 1). Breastfeeding to more than 24 weeks was protective of being overweight in boys and girls (unpublished data).

Causal Pathway

The association between breastfeeding and BMI does not establish causality. A dose response observed with the duration of breastfeeding is consistent with a causal association (66) but confounders may co-vary with breastfeeding. Furthermore, adjustment may negate the effect of breastfeeding hence, the effect of breastfeeding on obesity remains controversial.

Mechanisms of the protective effects of breastfeeding on child obesity

Genetic influence on childhood obesity

Genetic influence evidenced by parental obesity, is the strongest determinant of childhood obesity (64, 65, 99) and studies which have not controlled for the genetic influence on childhood obesity are likely to overestimate the influence of environmental factors including early diet. Early infant feeding is one of the most powerful environmental factors determining early growth and development and may influence gene expression (100). Exciting research has emerged in nutrient-gene interaction knowledge (101) and it has been shown that nutrients have influence on gene

expression and translation. Hence this is an area of cutting edge research (102) and a possible role and plausible mechanism of breastfeeding in development of obesity must be considered along with genetic and environmental influences (103).

Behavioural and hormonal mechanisms

Generally breastfed infants are leaner than formula-fed infants (81, 82, 93) and behavioural and hormonal mechanisms may explain this difference (61, 104-107).

The first mechanism is behavioural as bottle feeding may promote more parental control and less self regulation than breastfeeding. Focus groups (108) of low-income mothers participating in a nutrition program revealed that most believed a heavy infant was a healthy infant and supplemented the diets of their infants to alleviate fears that their child was not getting enough to eat. Thus while formula fed infants are governed by judgment of the feeding parent, breastfed infants have more discretion over their milk consumption than formula fed infants. Food preferences subsequent to breastfeeding may be affected by mode of feeding as breastfed infants more readily accept novel foods (61, 109, 110). It is argued that regulation of intake differs between breast and bottle fed babies and that breastfeeding enables the infant to develop the capacity to self-regulate as opposed to responding to the judgement exercised by the parent or carer in the case of formula feeding (93). Maternal feeding styles that are less controlling and more responsive to infant cues of hunger and satiety allow infants greater self regulation of energy intake (111). Furthermore, mode of infant feeding may influence acceptance of solid foods at a later age (109), with breastfed children less likely to be fussy eaters.

Socioeconomic, psychological, behavioural, ethnic and cultural influences additionally affect the emergence of childhood obesity such as food preferences, food availability, physical activity and sedentary behaviour (112). Because obesity is multifactorial, disentangling the breastfeeding effect is difficult and requires control of confounding variables for which information may not always be available or complete.

The second avenue by which breastfeeding may result in different body composition as compared to formula-feeding is through the many bioactive compounds that are found in breast milk. Plausible biological mechanisms underlying the protective effect of breastfeeding against obesity are based on the unique composition of human milk and the metabolic and physiologic responses to human milk (113, 114). Breastfed infants absorb less energy per volume than formula fed infants as well as receiving modifying growth factors that inhibit adipocyte differentiation (113, 115). A further explanation is that plasma insulin levels are higher in formula-fed infants than those who are breast-fed (61, 116, 117) which may be due to the higher protein content of formula that in turn influences levels of circulating amino acid (117, 118). While this difference could well explain higher levels of fat deposition in formula-fed infants, it would be expected to have a far greater effect on adipocyte size rather than adipocyte number at this stage of life (119) and thus the effect may be transient. Differential endocrine responses to formula and breast milk promote increased body fat deposition. Further, the hormone leptin, as a regulator of food intake and energy metabolism has been shown to be higher in breastfed and bottle fed infants (120). However Lonnerdal and Havel (116) found that serum leptin levels were not higher in breast-fed infants than those fed formula and concluded that the contribution from breast milk was unlikely to explain observed differences in body composition resulting from feeding mode.

Arenz (14) and Owen (94) both concluded that breastfeeding has a small but consistent protective effect against obesity in children. Accelerated postnatal weight gain is intrinsically damaging possibly because fetal growth restriction leads to reduced cell numbers, and subsequent catch-up growth is achieved by overgrowth of a limited cell mass (121). The increased risks for diseases in adulthood such as Type 2 diabetes and hypertension, associated with small size at birth are

exacerbated in those children who become obese (39, 121, 122) and the importance of nutrition in early childhood growth is emphasised by the marked difference in growth rates between breast- and bottle-fed babies (46, 123).

Breastfeeding may protect against overfeeding, calorie excess and hence future obesity (63). Formula fed infants have higher total energy (124), protein (104) and micronutrient intakes (125) than do breastfed infants and this stimulates increased secretion of insulin (61), higher output of hepatic glucose (105) and Insulin Growth Factor (IGF binding protein-1) (106). The phenomenon of early nutrition having long-term effects on growth, metabolism and health (39) has been termed "nutritional programming" and has been defined as a long term change in the structure and function of an organism resulting from a stimulus acting at a critical period of development in early life (104, 126, 127). Infants receiving formula consume 66 - 70% more protein compared with breastfed infants (107, 128), a fact that may explain why breastfed infants are leaner than formula fed infants at one year (93). It cannot be excluded that differences in energy intake or other confounding factors play a role in the development of infant adiposity (93, 107, 129). However one longitudinal study of children did not indicate that total energy intake at 12 weeks was a major determinant of body fatness at 2 - 3.5 years (130).

Growth velocity may be a relevant influence in the causal pathway of obesity as suggested for fetal programming of metabolic disease (131, 132) and associations between protein intake and growth velocity and weight gain have been reported (105, 128). Infants one week of age who were fed formula with a higher protein: energy ratio showed a tendency for higher body weight gains than those fed formula with a lower ratio (128) and infants fed formula with a higher protein: energy compared with the breastfed group had a higher BMI (133). The biological mechanism that potentiates an association between early life dietary protein intake and obesity may be linked to glucose metabolism (104). Formula fed infants with higher protein intakes, insulin secretion and hepatic glucose output (60, 105) because IGF-1 is regulated by dietary protein intake (106) and both insulin and IGF-1 are required for pre-adipocyte differentiation and adipogenesis induction. Alternatively, reduced amino acid concentrations induce IGF-1 expression participating in down-regulation of growth (134). These changes in circulating amino acids in formula fed compared to breastfed infants have effects on circulating amino acid concentrations such as protein related alterations of energy expenditure, influences on hormones and growth factors and adipose tissue metabolism in response to perturbations of amino acid homeostasis brought about by gene expression regulation (104).

How important is the relationship between overweight in infancy and later overweight and obesity and does the method of infant feeding make a difference? There has been interest in feeding methods and the growth of infants and child and adult obesity for many years. However in early studies the difficulty of isolating confounding factors led to inconclusive results. For example in a paper in 1980 Kramer recognised the difficulty of studying obesity and breastfeeding and in particular the difficult of isolating the effects of social class and associated factors (78). To overcome these difficulties Kramer undertook a further study and found that being overweight at 12 months was related to feeding method – breastfed babies were lighter (79) (we now know that breastfed infants are likely to be about 0.5 Z scores less at 12 months than formula fed infants, about 4-500 grams).

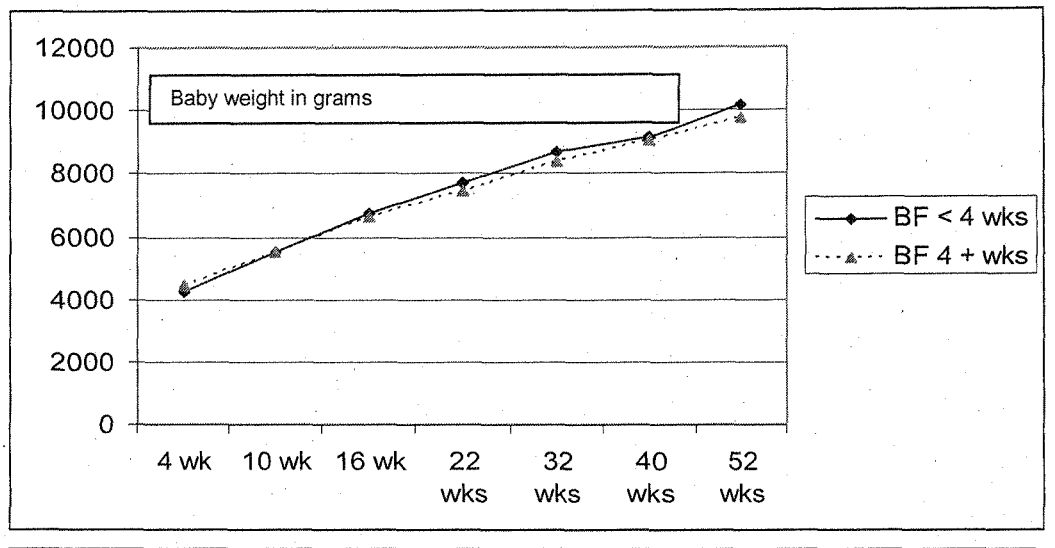
Regardless of the explanations for differences in body composition between breast-fed and formula-fed infants, it is not clear whether these would account for protective influences on the risk of overweight or obesity later in life. Indeed Butte and colleagues (135) suggest that changes due to mode of infant feeding do not persist into the second year of life.

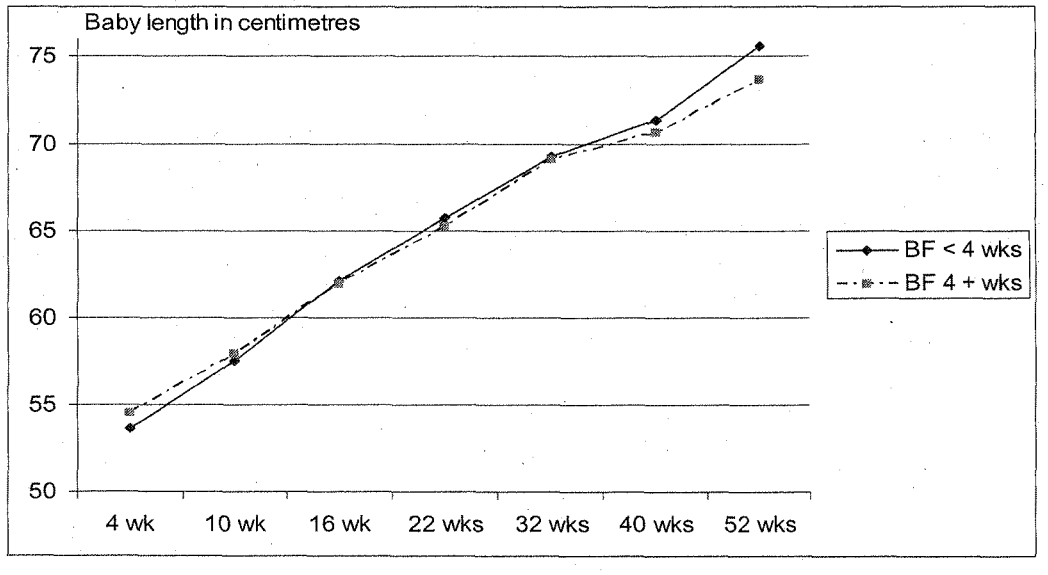
Adiposity rebound

The BMI curve rises during the first year of life so that one year old children appear chubby, but the curve decreases following the first year to about six years of age when fatness increases again (119). This increase is termed the adiposity rebound.

Baby weight in grams fatness decrease after one year of age varies between children so that the adiposity rebound can occur between four and eight years with the earlier the rebound, the higher the adiposity at the end of growth. In fact among children who become obese the adiposity rebound occurs as early as three years of age, as compared to about six years for children of normal BMI (119).

Figures 1a and 1b Baby weight in grams and baby length in centimeters by breastfeeding duration (<4 weeks; 4+ weeks) (136)





Adipocyte cell size increases during the first year of life and then decreases, increasing again from approximately 6 years of age. The duration of fatness decrease after one year of age is a better predictor of adult fatness than fatness in early childhood (119). Transient obesity in early childhood could involve the increase in cell size but persistent obesity commencing with an early adiposity rebound could be associated with early cell multiplication. One aspect which requires clarification is the impact of breastfeeding on the timing of the adiposity rebound (137). For this reason an understanding of the role of infant feeding mode on the adiposity rebound in future research is of utmost importance.

Perth Infant Feeding Study Mark II

Data from a prospective cohort study to 52 weeks are given in Table 1 (data provided from the Perth Infant Feeding Study II – PIFS II). (108, 109). In PIFS II 578 mothers were followed-up with regular telephone interviews for 52 weeks (at weeks 4, 10, 16, 22, 32, 40 and 52 after birth). At each time point mothers were asked to report the weight (in grams) and length (in centimetres) of their baby as recorded by the child health nurse in their infant health booklet at the time of the most recent clinic visit.

An infant was considered *fully breastfed* if he/she had received only breast milk but with occasional other liquids (usually water) and no formula or solids. Breastfeeding was the *predominant* feeding method of the infant if fully breastfed. This definition was selected because we found that the exclusive breastfeeding definition (138) was too restrictive, as most mothers had given some water to their infant since birth. The age that regular formula feeds were introduced was used as the primary infant feeding variable signifying the end of predominant breastfeeding and the age that regular formula milk feeds commenced. *Regular formula feeding* was described as the age that the infant started to receive a bottle on a regular basis i.e. daily but did not preclude breastfeeding. Formula milks were defined as artificial food in powdered form that were reconstituted by dilution with water to prepare a formula feed for infants. In some countries such as the UK and the USA ready made formula (already reconstituted) is currently available but was not yet available in Australia at the time of this survey.

In total, 870 of the 1068 women eligible to participate were contacted and 578 completed baseline questionnaires, representing 68% of women contacted and 55% of eligible women. By 4 weeks 46% of infants were receiving regular formula feeds and 48% had ceased to fully breastfeed. By 6 months almost all babies (99%) were not predominantly breastfed and 80% were either receiving only formula feeds or receiving regular formula feeds.

Means from Students t-tests showed that infants fully breastfed for 4 or more weeks were heavier at 4 weeks than babies not fully breastfed (P=0.022) (Table 1), but this relationship was reversed between 10 and 16 weeks. We showed a mean difference of 407 grams less in infants breastfed for one month or longer but by 52 weeks fully breastfed infants were lighter than formula fed infants (P=0.041) (Figure 1a). The same relationship was apparent for baby length at 4 weeks (P=0.005) with breastfed babies being slightly shorter at 52 weeks (P=0.001) (Figure 1b). If regular formula was given at an earlier age a significant difference was apparent between babies defined as normal weight or overweight (> 85th centile of weight/length at 52 weeks). From a survival analysis overweight infants were significantly more likely to have been given regular formula (cessation of full breastfeeding) at an earlier age (Kaplan Meier log rank test =6.70; P=0.0097) (Figure 2).

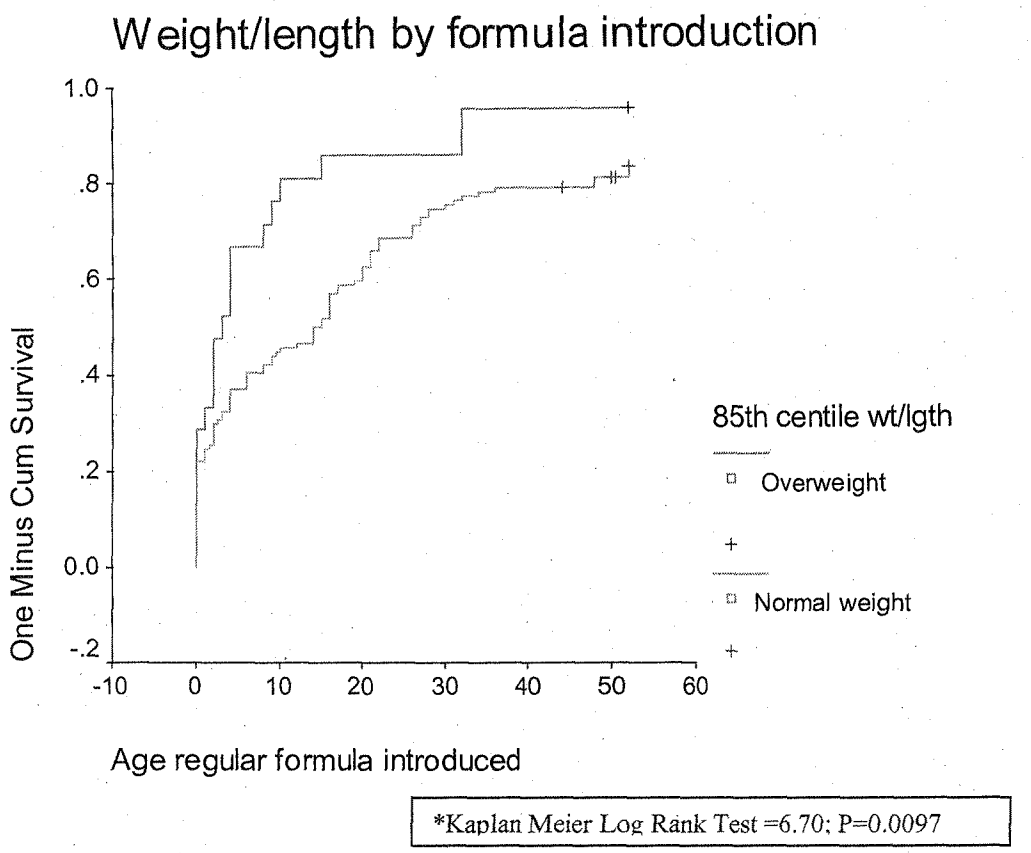
In PIFS II we showed a positive association between an increase in weight and length gain at 52 weeks of age with early and regular formula consumption in infancy. Our findings are consistent with the hypothesis that early weight and length gain are influenced by early postnatal nutrition. The findings from our study agree with those of others, that formula feeding is associated with increased postnatal weight and length gain, and is biologically plausible.

These data support recommendations of extended and full breastfeeding (138). Although breastfeeding initiation rates have increased (139), in the PIFS study 31% received formula in the first week of life and full breastfeeding rates were low at 4 weeks (48%). The possibility of postnatal nutritional influences on later child and adult health suggest that interventions to promote full breastfeeding may have long-term benefits.

Table 1: Mean difference in baby weight and length by feeding method (136)

	Method of feeding					
Baby weight	0= Formula < 4 wks 1= Fully breastfed 4+ wks	N	Mean grams	Std. Deviation SD	Sig 2 tailed P-value	Mean difference
4 wk	0	180	4257	750		
	1	278	4418	709	.022	-161
10 wk	0	138	5508	881		
	1	217	5540	789	.724	-33
16 wk	0	112	6725	1092		
	1	191	6614	1048	.389	111
22 wks	0	100	7706	1175		
	1	173	7449	1082	.074	258
32 wks	0	97	8660	1204		
	1	169	8369	1029	.047	291
40 wks	0	100	9115	1331		
	1	152	9031	1120	.600	85
52 wks	0	77	10138	1388		
	1	135	9731	1377	.041	407
Baby length			Mean centimetres			
4 wk	0	148	53.6	2.9		
	1	235	54.5	2.8	.005	-.849
10 wk	0	95	57.5	3.8		
	1	158	57.9	3.3	.374	-.414
16 wk	0	72	62.1	3.3		
	1	151	61.9	3.7	.801	.124
22 wks	0	71	65.7	3.5		
	1	110	65.2	4.4	.444	.451
32 wks	0	57	69.2	3.2		
	1	123	69.1	3.0	.825	.111
40 wks	0	65	71.3	4.0		
	1	99	70.6	3.1	.230	.704
52 wks	0	53	75.6	3.2		
	1	86	73.7	3.5	.001	1.90
			*equal variances not assumed			

Figure 2: Proportion of infants receiving regular formula by age and baby overweight (> 85th centile weight/length) in a survival (one minus cumulative survival) analysis (Kaplan Meier log rank test)*(136)



West Australian Pregnancy Cohort Study

The West Australian Pregnancy Cohort Study (WAPCS) is a prospective birth cohort study followed up from before birth to eight years of age (140) that provided infant feeding data collected at 1, 2 and 3 years. These data were confirmed by the child health research nurse and weight and length data were collected by research nurses at 1, 3, 6 and 8 years .

Our findings from the WAPCS (91) suggest that infants fed breast milk for a shorter duration had a higher height and weight and calculated body mass index (BMI) at one year, and experienced more overweight and obesity when compared with infants fed other sources of milk at less than four months of age and following adjustment for maternal factors and parity throughout childhood (OR 1.87; 95% CI 1.21, 2.89; p=0.005) (Table 2).

Several factors strengthen confidence in the validity of these findings. Duration of full breastfeeding as an independent factor demonstrated a weak association with child BMI at ages 3, 6 and 8 years. Adjustment was made for a number of associated factors including parity, maternal education, smoking behaviour, and maternal BMI (before pregnancy). However, rapid growth during the first year of life was associated with increased BMI at the age of 6 & 8 years in both boys and girls (141) providing the link between early feeding method and later obesity.

Table 2: Odds ratio estimates from Generalized Estimating Equations with exceeding the 95th percentile for weight-for length at 1 year and BMI at 3, 6 and 8 years as the dependent variable (91).

	Odds ratio	95% confidence limits		P
Model 1[1]				
Reference category breastfed >12 m				
≤ 4 months	1.83	1.20	2.78	0.005
5-≤8 months	1.49	0.94	2.37	0.089
9-≤12 months	1.36	0.84	2.19	0.209
>12 months	1.00			
Model 2[2]				
Reference category breastfed >12 m				
≤ 4 months	1.87	1.21	2.89	0.005
5-≤8 months	1.53	0.95	2.45	0.080
9-≤12 months	1.36	0.83	2.22	0.218
>12 months	1.00			

1 Adjusted for birthweight, gestational age, ethnicity and sex

2 Additional adjustment for maternal BMI before pregnancy, maternal smoking during pregnancy, first child, and maternal education

Summary

As with other programming effects, the effect of early diet and growth on later cardiovascular health may amplify with age therefore the early postnatal period is particularly important for targeting interventions. Our findings suggest the promotion of breastfeeding which decreases the risk of early over-nutrition and over-growth particularly in the early weeks of life. Because postnatal factors may be amenable to intervention the contribution of postnatal programming to cardiovascular health is of particular importance to science and public health. Further research is of high priority in the interests of population health – the magnitude of the effect size suggests that early nutrition and growth will make a major contribution to long term cardiovascular risk.

In 1985 Dietz summarised the assessment of programs for childhood obesity: "only reducing the number of hours children watched television qualified as a potentially effective preventive and therapeutic strategy for childhood obesity"(142). In 2001 Dietz stated that "breastfeeding may be added as a preventive intervention." (87).

How much could be gained by increasing the prevalence of exclusive breastfeeding to six months? It is possible to extrapolate the Gillman results (65) to Australia for example, where currently around 50% of infants are breastfed to six months. Assuming this could be increased to 80% or 90%, this would represent a reduction of 7% or 9% in the prevalence of adolescent obesity. For younger children a risk reduction of about 30% in obesity at 39-42 months of age in breastfed children is suggested. A possible adverse effect of formula milk on postnatal weight gain and infant health remains of contemporary public health relevance.

To summarise our current knowledge:

- Overweight infants are more likely to become overweight children, adolescents and adults.
- Breastfeeding to six months of age reduces the rate of overweight and obesity.
- Given the other known benefits of breastfeeding, increasing the risk of exclusive breastfeeding to six months would be a very worthwhile public health measure.
- A possible adverse effect of formula milk on postnatal weight gain and infant health remains of contemporary public health relevance.

The Effects Of Breastfeeding On Child And Adolescent Mental Health

Neuro-behavioural development is an essential aspect of childhood development and one in five children now have some mental health problem in Australia (143, 144). Between 10 and 20 percent of children worldwide have one or more mental or behavioural problems and these have been listed as one of the six priority areas for future strategic directions for improving the health and development of children and adolescents (145). While evidence shows that social, economic and psychological disadvantages associated with poverty, low parental income and education, single-parenthood and living in deprived areas are key risk factors for child mental health disorders (146-149), little is understood about the potential impact of early infant feeding on subsequent mental health.

Breastfeeding plays an essential but often underestimated role in childhood development (150-154) and has long term consequences for overall development (8, 155). Compelling evidence now exists for a relationship between breastfeeding, early developmental milestones (156, 157) and cognitive development from longitudinal (158-163), experimental (164) and neurodevelopmental studies (165-169) although these findings are controversial, with one study suggesting that following adjustment for maternal intelligence positive breastfeeding effects were weakened (170). We have previously shown that babies breastfed for longer than six months (171) had higher IQ scores than babies breastfed for less time, and our findings agree with a systematic review (172).

Further reliable information on the association between breastfeeding and the development of mental health through childhood is required before it is possible to state its true effect. Previous research has established that the social, economic and psychological characteristics of parents are some of the key determinants of child mental health (146-149, 173), and these factors are also significantly associated with breastfeeding initiation and duration (98), it is essential to adequately adjust for these potential confounders before we can firmly establish an independent impact of breastfeeding on child mental health.

The research to date has been limited in empirically examining the relationship between breastfeeding and child and adolescent mental health (174). We have shown that breastfeeding for six months or longer is associated with a reduction in mental health problems throughout childhood and adolescence (175). At the domain level this association was stronger for the externalizing than the internalizing domain, and was stronger within the domains with advancing age, indicating that the effect of adequate breastfeeding on mental health may magnify with age although we did not show any interaction between breastfeeding and age. We have demonstrated a significant association between breastfeeding and child mental health that persists after adjustment for social, economic and psychological factors previously found to be associated with both breastfeeding and child mental health in the literature (146-149, 173).

Although limited, previous research on child mental health outcomes associated with breastfeeding suggests that infants who are breastfed have a distinct developmental advantage over non breast-fed infants, particularly for babies born preterm (155, 169, 173, 176-182). Specifically, low birth-weight infants who were fed breast milk had significantly higher scores for engagement, emotional regulation and total behaviour on the Bayley Developmental Scale (182). However in that study it was not possible to differentiate the effects of feeding at the breast versus the feeding of breast milk through a tube or bottle, in contrast to our study that collected information on the feeding method (182). Jones et al. (2004) found that depressed mothers who had stable breastfeeding patterns were less likely to have infants with highly reactive temperaments(173). Hart et al. (2003) found that breastfed infants were also more able to face aversive stimuli with greater degrees of control, show more appropriate amounts of change in levels of arousal, and more able to return moderate states of

arousal(169). However, both studies were based on a small sample of mother-infant dyads (N < 90). Montgomery et al.(2006) show that children who had been breastfed exhibited greater resilience against stress and anxiety associated with parental separation and divorce at age 10 (181). But the information on breastfeeding duration was collected at age 5 and thus prone to recall bias. Hart et al. (2003) found that breastfed infants were also more able to face aversive stimuli with greater degrees of control, show more appropriate amounts of change in levels of arousal, and more able to return moderate states of arousal (169).

The effect of feeding type on infant health and development was first discussed more than half a century ago when breastfed babies were reported to have better cognitive outcomes in childhood than artificially fed babies (174, 183-187).

In terms of intelligence, the breastfed infant has been found to have an advantage over the non breastfed infant (188-191), although results in some studies have been criticised for neglecting the possible genetic influence of maternal IQ (192), and maternal intelligence 'per se' (170). At 5 years of age, children who had been breastfed achieved higher scores than non breastfed children on the Peabody Picture Vocabulary Test Revised (PPTV-R), a standardised measure of verbal intelligence, and there was a positive linear relationship between test score and duration of breastfeeding (158). These results persisted even after adjusting for a number of sociodemographic variables. Similar results were found when measuring PPTV-R scores and breastfeeding duration in 6 year olds, where children who were exclusively breastfed for 6 months or longer had superior scores than those children never breastfed, even after adjusting for maternal sociodemographic and psychological characteristics (171).

There is growing scientific interest in the possibility that early nutrition is an environmental factor associated with the increase in mental health and behavioural problems (193) which has occurred in most developed countries in the past 30 years (194). Given the persistence over time of the health benefits associated with breastfeeding, it would be pertinent for any study of the relationship between breastfeeding and child mental health to be conducted within a developmental trajectory framework (155, 158, 171, 180, 189, 195-199). The relatively few studies which have considered nutritional factors in the development of child and adolescent mental health (and ill health) have been limited by retrospective data collection, a failure to adjust for major covariates such as maternal stress in pregnancy and/or a failure to collect confirmatory information of mechanisms.

There are several possible mechanisms that may explain the association between breastfeeding and child mental health. First, stimulation associated with maternal contact during breastfeeding may have a positive effect on development of neuroendocrine aspects of the stress response as indicated by animal models (200). This hypothesis is informed by research based on animal models that show: rats that experienced a greater frequency of maternal contact during nursing in the first 10 days after birth (licking and grooming) showed a more controlled response to acute stress as adults (eg, a lower magnitude of hypothalamic-pituitary-adrenal (HPA) response) (201, 202). Research has shown that the pattern of mother-infant interaction differed between breastfeeding and bottle feeding: the percentage of mutual touch, tactile stimulation and mother's gaze to infant and the duration of these interactions were significantly elevated during breastfeeding than bottle-feeding (203)

Second, it has been proposed that breast feeding is a marker of other unmeasured maternal characteristics. For example, mothers who breast feed their infants may have personal and family characteristics that directly influence the child's stress-response or anxiety following divorce (181). Similarly breastfeeding mothers may have exposure to superior prenatal conditions as women who breastfeed are also more likely to engage in health-enhancing behaviour in general. Our analysis has adjusted or tested for a number of these maternal characteristics, such as emotional upset during

pregnancy and smoking in pregnancy, experience of emotional disturbance after birth (baby blues), postnatal depression as diagnosed by a doctor, and maternal happiness at various developmental stages of the child. Yet breastfeeding for 6 months or longer remained a significant predictor for better child mental health through out early and mid childhood and into adolescence.

Another possible pathway is that breast milk itself may contain elements relevant to the stress response. For example, the hormone leptin in breast milk may reduce stress in infants through its action on the hippocampus, hypothalamus, pituitary, and adrenal glands as suggested by Montgomery et al (181), whereas formula may have a depressant effect on newborn behavior (204). Further, the specific fatty acid content of breast milk is essential for central nervous system development, including the brain in the neonate (205-207). Because maternal milk is a rich source of fatty acids essential for development (208-214), breastfeeding may have long-term consequences for child mental health outcomes.

There is reluctance in previous studies to suggest an association between breastfeeding and child mental health partly due to the possibility of alternative explanations such as parenting behaviours (215) and parental cognitive ability (11) and partly due to the concern for creating guilt in women who do not breastfeed (216). It would appear that, in developed nations at least, breastfeeding is generally more likely to be practiced in communities with greater economic and social resources (182, 190) and the associated confounding effects complicate the interpretation of this association (98, 182, 190, 217, 218). Hence, many researchers have been hesitant to eliminate alternative causal pathways for the relationship between breastfeeding and mental health outcomes (188, 190, 219). However breastfeeding may ameliorate some of the complex health issues faced by low-income families.

An increase in mental health and behavioural problems has occurred in most developed countries in the past 30 years (220, 221). Knowledge as to the prevention of child mental health problems is thus essential. Recent research findings in brain biochemistry and neural development are contributing to a clearer understanding of the links between nutritional intake, central nervous system and immune function, and psychological health status (222) and dietary behavior has been shown to be strongly associated with self-perceived general and mental health status in childhood (223, 224). The World Health Organisation goal is to enable the breastfeeding of all infants to six months and beyond up to two years (138) and in order to achieve this goal more education about the benefits of breastfeeding is required but support of breastfeeding mothers is essential. The aim is to increase breastfeeding rates globally and to ensure that all mothers are at their optimum level of nutrition while breastfeeding. Mothers and fathers must be educated about the importance of the mother-infant dyad interactions and the positive benefits of breastfeeding not only on the physical health but also the mental wellbeing of the child.

Key Issues

Breastfeeding is superior to formula feeding because it has specific and non-specific factors including the essential fatty acids, that may have long term consequences for child mental health throughout life.

All mothers should be encouraged and supported to continue full breastfeeding for six months and beyond in order to promote the optimum health and well-being of their infants into childhood and adolescence.

The Effect Of Breastfeeding On Childhood Asthma

Epidemiological evidence

The primary objective is to assess the evidence of whether breastfeeding protects against asthma and atopic disease for the long-term (long-term is defined here as > five years of age). Two main types of observational epidemiological studies have been used to test this hypothesis. These are cohort studies of random samples of children and cohort studies of children with a family history of asthma or atopy. In each study type, exposure and outcome data are collected either prospectively or retrospectively.

The criteria for assessing the adequate measurement of exposure, outcome and statistics of cohort studies are given in Table 3(225).

In retrospective studies breastfeeding data are collected backwards in time. Asthma and atopy may be measured currently. Retrospective studies of breastfeeding and asthma have either shown no association (226-228), a reduced risk (78, 226, 229-231) or an increased risk (232). According to the criteria in Table 3, late maternal recall of breastfeeding is not acceptable. Only prospective studies, which collect exposure data forward in time, are included in this review.

Table 3: Criteria for assessing the adequacy of cohort studies for the effect of breastfeeding on the development of asthma and allergy (225).

Measurement	*Criteria*	
Exposure	1.	Non-reliance on late maternal recall of breastfeeding
	2.	Blind ascertainment of infant feeding history
	3.	Sufficient duration of breastfeeding
	4.	Sufficient exclusivity of breastfeeding
Outcome	5.	Strict diagnostic criteria
	6.	Blind ascertainment of outcomes
	7.	Consideration of severity of outcome
	8.	Consideration of age of onset of outcome
Statistics	9.	Control for confounding factors
	10.	Assessment of dose-response effects
	11.	Assessment of effects in children at high risk of outcome
	12.	Adequate statistical power

Prospective cohort studies classify subjects in the study on the basis of presence or absence of exposure. The relevant events, both exposures and the outcomes of interest have not yet occurred when the study is initiated. In some prospective studies, the exposure may have occurred but the outcomes have not yet occurred. The studies that met the criteria in Table 3 with children followed to more than five years, are reviewed after a brief discussion of the excluded population studies.

For some studies it was unclear as to whether they met the criteria (233, 234). A cohort of 1661 infants recruited between 1972 and 1973 was assessed from ages 9 to 26 years using respiratory questionnaires, pulmonary function tests and allergy skin tests. Following multifactor adjustment breastfeeding showed odds ratios of 1.94 (95%CI: 1.42-2.65 $p<0.0001$) for current asthma at 9 years and 1.83 (1.35-2.47 $p<0.0001$) for current asthma at 9-26 years by repeated measures

analysis. This result shows that breastfeeding is a risk for asthma and is contrary to the findings of numberous other studies (235). This study has a number of limitations. Children were enrolled at the age of 3 years when data on breastfeeding recall were collected from mothers. As with most historical studies, the results of this study cannot be easily generalised to present times when health and lifestyle practices have changed. The cohort was enrolled at a time (early 1970s) when breastfeeding rates were low. In the hospital, suckling times and number of feeds were restricted and built up over several days. In addition, long periods of separation of mother and baby and nightly formula feeds could have limited establishment of breastfeeding (236-238). In the cohort, 47% of babies were never breastfed and the modal time of cessation of breastfeeding was just 5-11 weeks. This study does not meet criteria 1, 3 and 4 given in Table 3; that is non-reliance on late maternal recall of breastfeeding, sufficient duration of breastfeeding and sufficient exclusivity of breastfeeding. Neither does the study meet criteria 9, 10 and 11; that is controlling for major confounders such as rates of infections, evidence of a dose-response effect, and assessment of children at high risk of allergic outcome.

In relation to scientific rigour, to study the effect of breast milk on the development of asthma and allergy, all of the 12 standards of biologic and methodological criteria1 should be met.

One long-term study of 256 healthy babies followed from before birth to 17 years met all criteria in Table 3 and showed significant protection by breastfeeding at least for the first 17 years of life (239). The value of this study lies in the duration of the follow-up and in the comprehensive collection of exposure and outcome data. In this study a clear prophylactic relationship between breastfeeding and atopic disease was found that was not modified by family history of atopic illness.

The Tucson Children's Respiratory Study of 1246 healthy infants was designed to investigate risk factors for lower respiratory tract illness. Established between 1980 and 1984 detailed pediatric assessments were followed at defined intervals. When the cohort was six-years-of-age, recurrent wheeze was less common in non-atopic children who were breastfed as infants, compared to non-atopic children who were not breastfed (154) signaling a difference in atopic status between breastfed or non-breastfed infants. At 11 years(240) an association between breastfeeding and asthma differed with maternal asthma status. Among children with a maternal history of asthma, the percent of children who developed asthma was 9% for the never breastfed, 36% for those breastfed for three months or less and 57% for those breastfed for four months or longer. However, breastfed children were significantly less likely to wheeze at age six, nine or 11 years if they had not been diagnosed with asthma at any age. A limitation of this study was that formula feeding was prevalent in the United States at the time of study recruitment (241) (more than 50%) and data on formula introduction were not collected, therefore a measure of exclusive breastfeeding was not possible.

In the Dundee Infant Feeding Study, 674 children were followed from birth to seven years (242). The prevalence of wheeze, breathlessness or cough at age 7 was significantly reduced if a child had been exclusively breastfed for at least 15 weeks ($P<0.05$).

The Western Australian Pregnancy Cohort Study (19) included 2187 children followed to 6 years. This study showed a significant reduction in the risk of childhood asthma at age 6 years if other milk was introduced before 4 months in either atopic or non-atopic children (140, 243). The strengths of this study include its representativeness of the general population, its sample size and high response rate. Collection of outcome data (including respiratory history) was prospective, by diary card, at frequent intervals and based on validated questionnaires.

Summary
Studies that met the criteria for inclusion in this review of the long term effects of breastfeeding on asthma and atopic disease demonstrate a pattern of protection with breastfeeding and a risk of formula. In studies that met all recommended standards the odds ratios consistently exhibited an expected direction of effect that suggest biological plausibility and specific protective effects of breast milk. Although the range of magnitude of effect is not large (1.2-1.5), in population terms this is large enough to be of public health significance.

Inconsistency in the literature is due to researchers measuring different aspects of atopy and asthma in children of different ages and using different ways of measuring those outcomes. The use of multivariate statistical models does not allow for entire control of confounding variables as there are many factors that may influence both the mother's likelihood of breastfeeding and the risk of children developing asthma or atopy.

Meta-analyses
A meta-analysis of nine studies examined the association between breastfeeding and the development of asthma (244). The meta analysis showed that children breastfed for at least three months of age were significantly protected from the development of asthma by an estimated odds of 0.80. Other meta-analyses(245) conclude a similar protective effect of between 26% - 30% from exclusive breastfeeding during the first 3 months of life against developing asthma, allergic rhinitis and atopic eczema later in childhood.

Studies of children with a family history
The prospective family cohort study classifies subjects on the basis of presence or absence of the disease in the mother or father or both. As in the population cohort study, the relevant exposure and outcome events, both have not yet occurred when the study is initiated.

In Canada, researchers assessed the effect of different formulas on atopic disease in a double-blind study of high-risk infants (246, 247). A protective effect of exclusive breastfeeding for four months or longer against atopic disease until at least five years (OR: 0.42 95% CI: 0.20, 0.89) compared to infants fed cow's milk based or soy formula was apparent. Whey hydolysate reduced the incidence of atopic symptoms in high-risk infants (OR: 0.32 95% CI: 0.16, 0.65) and this approach appeared beneficial compared to breastfeeding without maternal dietary restriction, or soy-based formula feeding.

Making sense of the epidemiological evidence
A number of key issues complicate the interpretation of the available evidence and are often not taken into full and proper consideration. These issues include: low statistical power; misclassification of information; causal pathway modeling; and effect modification (statistical interaction).

Asthma and atopy are complex multifactorial diseases and therefore it is inevitable that most single causes (i.e. breastfeeding) will have relatively small effects on overall disease prevalence. On the basis of published meta-analyses, the true relative risk linking breastfeeding to childhood asthma may be 1.2 to 1.3 (248). In terms of breastfeeding where a large proportion of infants are exposed to early formula feeding, small odds ratios such as this have public health importance. Consequently, studies that appear large by conventional standards may be under-powered and the interpretation of individual non-significant results may be misleading (249, 250).

Both the primary exposure (breastfeeding) and the primary outcomes (asthma, atopic disease, and eczema) are subject to serious potential misclassification, particularly when assessed

retrospectively. Study results may be confounded by the early introduction of infant formula as small amounts of early formula milk may be damaging to the developing infant immune system.

A complex disease such as asthma is likely to arise from the action of a series of etiological determinants extended along several complex causal pathways. A given secondary exposure may either be a confounder and therefore we need to adjust for it or may be part of the causal pathway linking the exposure to the outcome of interest and therefore we must not adjust for it. In other words, inappropriate adjustment for determinants lying on a causal pathway of interest may lead to shrunken estimates and inflated standard errors and will reduce an already limited statistical power.

There is the possibility that the association between breastfeeding and asthma and atopy varies at different levels of a key third variable such as the underlying genetic risk of atopy. In fact, evidence would suggest that this may be the case (240, 251). Such interactions not only complicate interpretation, but also reduce statistical power.

Given these considerations for the effect of breastfeeding, we would expect relatively small relative risks with large standard errors. This means that, even if a real association between breastfeeding and asthma/atopy exists many studies will generate non-significant estimates, and a non-trivial proportion will produce estimates that apparently go in the wrong direction. Two complementary solutions to this problem are to 1) carry out meta-analyses (245); and 2) undertake large population-based studies with careful assessment of exposures, outcomes and relevant confounders.

When the exposure is both common and modifiable and the outcome is costly in terms of mortality, morbidity and economics, a small relative risk is of major public health relevance. The putative association between childhood asthma/atopy and breastfeeding unquestionably meets these criteria.

Previous studies that have shown a protective effect of breastfeeding on asthma and atopy have fulfilled strict criteria for assessing causality from observational studies (252), that is biological plausibility, consistency of findings, strength of association, temporality (exposure to breastfeeding before atopy develops) and a dose-response relationship.

Biological plausibility

A large body of literature on the biochemistry of human milk provides biological plausibility for the hypothesis that breastfeeding protects against the development of asthmatic and allergic symptoms. Breastmilk contains a vast array of beneficial and multifunctional compounds including antimicrobial, immunomodulating and bioactive molecules that may have imprinting and subsequent long-term effects (151, 253-258). These molecules exhibit pleiotropic functionality (259), are well adapted to infants' mucosal sites and are not well represented in infant formula. Breastmilk is also a rich source of omega-3 fatty acids, which have anti-inflammatory effects. It is not currently known which of the many components in milk may account for the protective effect but several mechanisms are likely (115, 259-261).

Mechanisms whereby breastfeeding could impact on asthma and atopic disease

There are five mechanisms whereby breastfed children may show a reduced occurrence of asthma and atopic disease. These are listed in Table 4 and described below.

1. Breastfed infants are less exposed to foreign dietary antigen

A breastfed infant is less exposed to foreign dietary antigen in cow's milk although there are antigens in mothers milk. Some exclusively breastfed infants develop allergic reactions to cow's milk protein (β-lactoglobulin) (262) but the incidence of this is very low (0.5-1.7%) in comparison to the incidence in unselected populations of infants (2%-3%)(263).

The young infant's gut is immature, and may poorly exclude multiple allergens or large quantities of allergens that can react with the system of sensitisation. The benefits of exclusive breastfeeding derive not only from elimination of cow's milk protein but from local protection of human milk in the bowel. For example secretory IgA coats the mucosa and blocks entrance of antigens (264).

Many children do receive proteins from cow's milk formula in the first days of life(265, 266) that may initiate sensitisation in susceptible individuals. Subsequent exposure even to minute quantities of β-lactoglobulin in breast milk may elicit an allergic manifestation that may be associated with IgE mediated adverse reactions.

Table 4: Mechanisms whereby breastfeeding could impact on asthma and atopic disease

1.	Breastfed infants are less exposed to foreign dietary antigen.
2.	Human milk contains factors that promote gastrointestinal mucosa maturation, allowing early 'closure' of macromolecular absorption.
3.	By decreasing the incidence of infection and possible altering the gut microflora that can act as an adjuvant for ingested food proteins, the possibility of sensitisation may be reduced.
4.	Human milk has functional immunomodulatory and anti-inflammatory factors that curtail macromolecular uptake.
5.	Cytokines and growth factors in human milk may play an important role in modulating the development of asthma.

2. Human milk contains factors that promote gastro-intestinal mucosa maturation thereby allowing early 'closure' of macromolecular absorption

The most striking interaction between diet and intestinal development occurs immediately following the first feed of mother's milk that may be due to an expression of genes triggered by milk constituents.

3. By decreasing the incidence of infection and possible altering the gut microflora that can act as an adjuvant for ingested food proteins, the possibility of sensitisation may be reduced

Control of colonisation of mucosal surfaces by organisms is the most important task of the mucosal immune system. In addition to respiratory microbial agents, the commensal (normal, healthy) microbial flora of the gastrointestinal tract stimulate the functional maturation of the immune system (267). This is accomplished through humoral and cellular mechanisms which control the growth of bacterial, viral and parasitic organisms and non-cellular elements. Microbial products of the gastrointestinal flora may activate the antigen presenting mechanism of dendritic cells, polarising towards a Th1 memory (268, 269). In early life Th1 and Th2 cell populations possess the potential of reversibility towards the alternate cytokine type but the reversibility is lost after long term stimulation by microbes (270).

Oligosaccharides in human milk may promote the development of bifidus flora by the provision of substrate for lactobacillus bifidus, the healthy bacteria, while limiting the growth of potentially pathogenic bacteria (271).

Nucleotides in human milk have multiple functions (272, 273) which include effects on gut microflora (274), intestinal growth and development (275) and the response to immunization (276).

Milk leukocytes survive in the gastrointestinal tract tolerating pH, temperature, osmolarity and resist proteolytic degradation by trypsin. They adhere to the gut epithelium and persist in the intestine for up to 60 hours. It is thought that the ability of milk immunocompetent cells to survive in the gastrointestinal tract, to secrete cytokines and to migrate across the neonatal intestinal mucosa

to the systemic circulation allows them to potentate not only the local response of the gastrointestinal tract but also their systemic immune responses (258).

Human milk lipids contain preformed long chain polyunsaturated fatty acids (omega-3) in large amounts, which serve as precursors of biologically potent mediators (e.g. the eicosanoids; prostaglandins, thromboxanes and leukotrienes) as well as vital structural components of membrane systems in all tissues (164). It is thought that fatty acids are important cell signalling molecules (277) acting rapidly and directly to alter the transcription of specific genes (278) involved in inflammation such as IL-1β. The very long chain fatty acids (EPA and DHA) suppress IL-1β mRNA, a finding that may be important in asthma prevention (279).

The fatty acid composition of breast milk from the mothers of children with newly developed atopic dermatitis was observed to be lower than normal demonstrating an abnormal fatty acid status in atopic subjects (280). This may account for some of the inconsistent results from studies of the effect of breastfeeding on the subsequent development of atopic dermatitis (281) and more recently asthma (282). Infants need the correct amount and balance of fatty acids for normal immune system development and an imbalance may lead to hypersensitisation. One study investigated the supplementation of pregnant mothers with fatty acids and subsequent fatty acid in cord blood, and found that fatty acid levels were higher in the cord blood of infants of supplemented mothers (283).

4. Human milk has functional immunomodulatory and anti-inflammatory factors that curtail macromolecular uptake

Breastfed infants appear to have more effective immune function, reflected by an ability to mount a targeted response to a potential pathogen (284).

Human milk may have systemic immunomodulating properties (285) which are long lasting and which may protect against a number of diseases (286-290) including allergy (291). Such clinical and experimental observations suggest that human milk has the ability to modulate the development of the infant's own mucosal and systemic immune systems which may be associated with immunoregulatory agents present in colostrum and mature milk.

Immunomodulating factors in human milk include α-tocopherol, β-casomorphins, prolactin and anti-inflammatory agents. These direct-acting factors protect by non-inflammatory mechanisms, including enzymes that degrade inflammatory mediators. The anti-inflammatory agents in human colostrum and mature milk include lactoferrin, lysozyme, antioxidants, cytokines, secretory IgA and hormonal factors that down-regulate inflammation (253). Specifically, lactoferrin and sIgA inhibit endotoxin induced inflammatory cytokine release (292, 293).

Mammalian cells have developed an elaborate antioxidant defence system that includes both non-enzymatic antioxidants (e.g. glutathione, vitamins C and E [α-tocopherol] and β-carotene) and lactoferrin as well as enzymatic activities (e.g. glutathione peroxidase, catalase, and other hemoprotein peroxidases) both of which play a significant part in the anti-inflammatory system of human milk.

5. Cytokines and growth factors in human milk may play an important role in modulating the development of asthma

The presence of cytokines, hormones and growth factors in human milk play an important role in modulating the development of atopic disease. Cytokines are soluble glycoproteins with established actions on the immune system (294). They are pluripotent polypeptides that act in autocrine/paracrine fashions binding to specific cellular receptors, operating in networks and orchestrating immune system development and functions(295). Early milk has an abundance of

these components at a time when neonatal organ system immaturity exists, suggesting that the bioactive compounds of milk may be important in neonatal development (296).

Human milk contains several known growth factors including Epidermal Growth Factor (EGF) and Transforming Growth Factor (TGF)(297). Both promote the maturation of gastrointestinal and respiratory mucosa restricting the penetration of harmful antigenic material and contributing to the anti-inflammatory effect of human milk.

Conclusion

Human milk feeding appears to be of considerable relevance to the development of the immune system in infancy and may therefore impact upon the incidence and severity of subsequent asthma and atopy later in life. As evidenced by the studies that met the strict criteria for the study of breastfeeding and atopic disease, all demonstrated a protective effect of breast milk feeding or conversely, a risk of formula feeding. However, the continuing protective effect of breastfeeding on asthma and atopy later in adolescence and adulthood has yet to be confirmed in larger longitudinal studies. Because achievements in promoting breastfeeding have been based on consistent scientific evidence, they should not be eroded on the basis of a few studies that show a negative relation to asthma. It is essential that scientists strive to collect better evidence to support or refute causal associations between breastfeeding and childhood illnesses.

Until more rigorous and more direct evidence is collected, links between breastfeeding and the development of allergic illness in adulthood based on studies in which bias and confounding cannot be controlled and mechanisms have not been investigated, should not be incorporated in public health messages. Given the many benefits conferred by breast milk, breastfeeding should continue to be promoted as the preferred infant feeding method for the first 6 months and up to two years(138).

INITIATIVES TO ENCOURAGE BREASTFEEDING

The Baby Friendly Hospital Initiative (BFHI) has been adopted by over 70 countries and although Australia adopted it in 1994 there are still only 48 accredited hospitals and only two of those are in Western Australia. Although more than 84% of Australian women initiate breastfeeding (298) by 3 months only 60% are breastfeeding and by 6 months less than 40%

Table 5: Ten steps to successful breastfeeding (299)

1. Have a written breastfeeding policy that is routinely communicated to all health care staff.
2. Train all health care staff in skills necessary to implement this policy.
3. Inform all pregnant women about the benefits and management of breastfeeding.
4. Help mother's initiate breastfeeding within a half-hour of birth.
5. Show mothers how to breastfeed and maintain lactation even if they are separated from their infants.
6. Give newborn infants no food or drink other than breast milk, unless medically indicated.
7. Practice rooming-in - allow mothers and infants to remain together 24 hours a day.
8. Encourage breastfeeding on demand.
9. Give no artificial teats or pacifiers (also called dummies or soothers) to breastfeeding infants.
10. Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from hospital or clinic.

There is enough evidence to support a breastfeeding health promotion campaign in Australia to ensure that all hospitals become baby-friendly and that all mothers are encouraged and supported to breastfeed for at least the first six months of an infant's life. The BFHI is a joint initiative of the World Health Organisation and UNICEF, aimed at promoting implementation of the Innocenti Declaration (1990)(300). This Declaration stated that it was the right of every woman to breastfeed her baby and the right of every baby to receive nothing but breast milk until 4-6 months of age (In April 2002 this was changed to until 6 months of age). Nutrition is essential to the health and development of infants and children. Breastfeeding is superior to infant formula feeding because in addition to breast milk's nutritional advantages, it protects against infections and has long term consequences for metabolism and disease later in life (301).

The Baby Friendly Hospital Initiative addresses the major factors of modern childbirth practices in the developed world which have contributed to the erosion of breastfeeding world wide.
The "Ten Steps to Successful Breastfeeding" summarise the practices necessary to support the initiation of Breastfeeding (299). Breastfeeding is a key public health issue and increasing the initiation and duration rates of breastfeeding represents an important health promotion challenge and is an area in which health professional can make a real difference.

The Baby Friendly Hospital Initiative in Australia has been slow to become accepted by Health Professionals. There has been a complacency about breastfeeding which needs to be addressed. There is a wealth of evidence which has been generated over the last 10 years to support the benefits of breastfeeding a child exclusively until 6 months of age. Roughly 2000 papers on breastfeeding and human milk are listed on Medline since the year 2000 (302).

Over worked staff, lack of skills in assisting with attachment difficulties, inconsistent advice, noise, embarrassment have been identified by women as concerns during their initial hospital stay. Most mothers do not anticipate problems with breastfeeding and health professionals may inadvertently contribute to this veil of secrecy by focusing on the benefits of breastfeeding rather than the practicalities and problems that can be encountered in the early weeks. (303)

BFHI Australia
The aim of the BFHI in Australia is to encourage a global standard for maternity services and give every baby the best start in life by creating a health care environment where breastfeeding is the norm and where maternity facilities follow practices known to promote the health and well-being of babies and their mothers.

The five key objectives of BFHI in Australia have been identified as:

1. Increase the number of hospitals accredited 'Baby-Friendly' according to the "Ten Steps to Successful Breastfeeding"
2. Maintain the BFHI accreditation process of hospitals in all states, rural and remote areas of Australia according to established criteria.
3. Train accredited assessors and educators within hospitals and community to provide consistent information on which assessors and educators base their accreditation benchmark.
4. Keep up-to-date with the latest breastfeeding research so it can be used to assist the BFHI process.
5. Improve initiation and continuation of breastfeeding rates in all communities in WA.

In Australia, the BFHI was the responsibility of UNICEF Australia until August 1995 when UNICEF appointed the Australian College of Midwives (ACMI) to co-ordinate the Initiative. The Commonwealth Department of Health and Ageing and ACMI supported funding for the continued expansion of BFHI in Australia. Funding for BFHI at a national level has not been renewed (October 2005). BFHI on a state level is run solely by volunteers. The state branch provides information packages and resources to hospitals outlining the BFHI aims and objectives and the details of how to apply for accreditation.

BFHI WA
In Western Australia the state BFHI committee (a collaborative group of volunteers representing organisations and individuals with expertise in breastfeeding) re-convened in 2003 with a renewed commitment to BFHI WA. The state committee is responsible for protecting, promoting and supporting the objectives of BFHI, training, educating and providing assessors and educators to support accreditation processes, ensuring consistency and quality commensurate with National and International standards and benchmarks, representing WA on the BFHI national committee and providing advice and feedback in regard to the overall management of BFHI within Australia.

Why BFHI?
In spite of the recognition of the benefits of breastfeeding for infant, mother, family and community, little improvement in the long-term duration rates have been seen in Australia. The Australian National Health Survey (304) estimated 82% breastfeeding rates on hospital discharge, 57% at 3 months and just 19% fully breastfed at six months.

While rates of breastfeeding initiation are high (<90%) (139), the number of infants successfully breastfed to 6 months continues to be low (20% exclusively breastfed at 6 months)(305). A number of reasons influence the decision and ability of a mother to breastfeed her infant, factors such as socioeconomic status, education, occupation, birth method and admission to the special care nursery. Many of these factors are modifiable, hospital practices have been shown to positively influence the success of breastfeeding significantly. For example, the provision of coordinated antenatal breastfeeding education and during the postnatal period, early and unrestricted breastfeeding following the birth and thereafter, rooming in of baby with mother, feeding on demand and limited use of dummies and teats has been shown to improve early initiation rates and limit clinical problems in the early postnatal period by the provision of ongoing support for the breastfeeding dyad. Although many staff within hospitals and maternity facilities support BFHI,

and the benefits of breastfeeding are recognised, the number of hospitals accredited as 'Baby Friendly' continues to be low in WA.

The positive impact of the BFHI policy has been demonstrated by the Boston Medical Centre (USA) where the breastfeeding initiation rates rose from 58% in 1995 to 86.5% in 2000 (306) after implementation of Baby Friendly policies and achieving 'Baby Friendly' status in 1999. In the PROBIT study in the Republic of Belarus a total of 17,046 mother infant pairs were included in a randomised controlled trial to assess the impact of an experimental intervention based on the BFHI (216). Intervention sites were randomly allocated to implementation of the intervention or continuation with usual practices. The results demonstrated that infants from the intervention sites were significantly more likely than infants from the control sites to be fully breastfed for longer at any time period, with more babies breastfed to 12 months overall. An unexpected benefit of the intervention was significantly less eczema and gastrointestinal infections in the intervention cohort (307).

Social and cultural structure to support breastfeeding can have a major impact on rates and a positive outcome from implementation of BFHI policies, however a number of barriers to change and reluctance of senior management to commit to the Baby Friendly accreditation process in Western Australia remain.

Table 6: Steps to hospital implementation of the Baby Friendly Hospital Initiative

1. Form a hospital committee to disseminate knowledge.
2. Implement a breastfeeding policy which is displayed throughout the hospital.
3. Train staff in the 'breastfeeding' policy.
4. Educate mothers about the Baby Friendly Hospital Initiative.
5. Accreditation procedure.

INFORMATION THAT WILL ALLOW EFFECTIVE PLANNING OF A CONTEXTUAL, MULTI-LEVEL, AND COLLABORATIVE HEALTH PROMOTION STRATEGY FOR BREASTFEEDING.

The aim of this section is to gather and present information that will allow effective planning of a contextual, multi-level, and collaborative health promotion strategy for breastfeeding.

Based on the benefits of breastfeeding, and the low duration of *any* and *exclusive* breastfeeding observed in Perth (308), there is a clear need for strategies and interventions aimed at improving the duration of breastfeeding practice within Western Australia.

In order to develop effective strategies and interventions, the factors underlying breastfeeding practices must be understood (309). A number of studies have looked at the factors that influence breastfeeding practice. A review conducted by Scott and Binns (98) identified a number of factors associated with initiation and duration of breastfeeding. They found that mothers who were from higher socio-economic groups, who were better educated, who were older and who had previously breast fed had a higher prevalence of breastfeeding and a longer duration. Other factors influencing breast feeding practice were the perceptions of partners and family members and the mother's decision to breastfed prior to pregnancy.

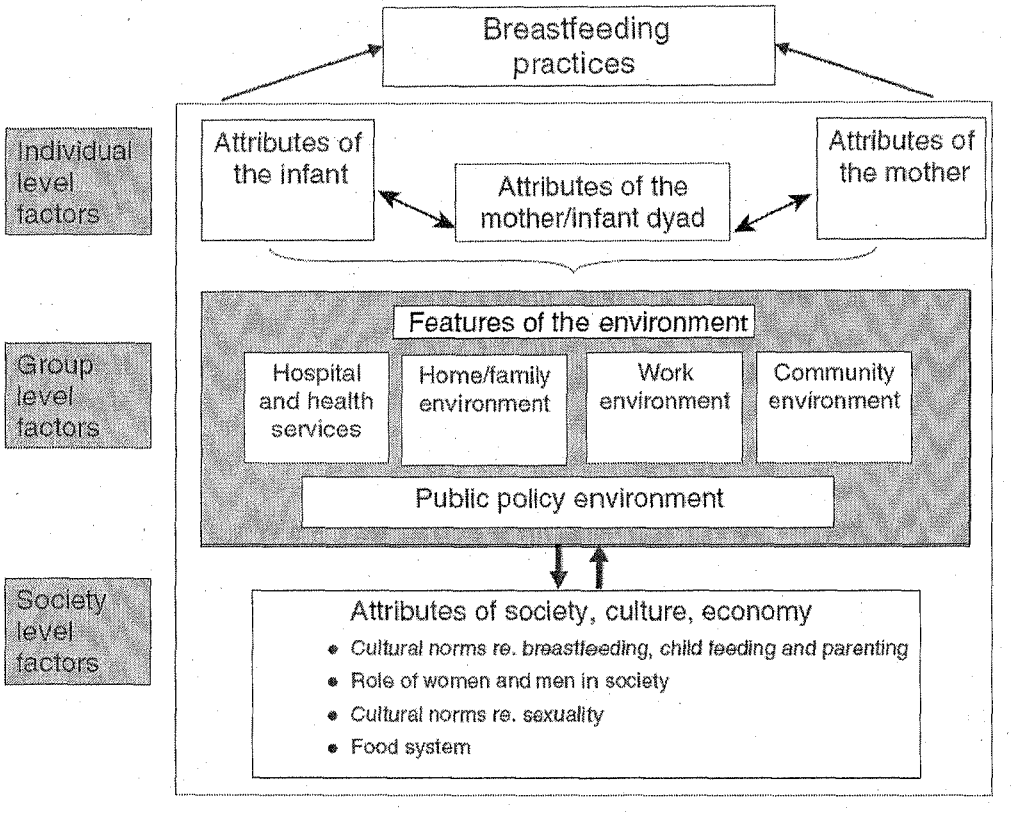
Although a number of good-quality studies have examined factors that influence breastfeeding practice specific to Australian communities, these often focus solely on individual-level factors (98, 310), look only at one factor in relation to breastfeeding practice (311-313), or take a multi-level approach with only a limited examination of some group- and society-level environments (298, 314, 315). For instance, when examining factors that influence breastfeeding practice, researchers have focused on socio-demographic variables such as household income and mother's education (316, 317). While these indicators provide valuable information on which populations may require interventions, these factors do not necessarily have a *direct influence* on breastfeeding practice (318). To better design interventions/strategies to improve breastfeeding practices, an understanding of factors that make *a direct contribution* to breastfeeding practices must be gained that will allow modifiable factors to be identified and acted upon (319).

A promising approach to examining the inter-relationship between factors influencing breastfeeding practice can be found in a cohesive model reflecting the layered relationship between these factors (320). This model developed by Tiedje and others and based on Bronfenbrenner's ecological model of human development (321) recognises the importance of interactions between families and their external environments in relation to health outcomes. Hector and others (319) further developed this model to incorporate the Ottawa Charter for Health Promotion (322) and created a conceptual framework of factors affecting breastfeeding (this framework will be referred to as the multi-level ecological model). The multi-level ecological model, adopted by NSW Health (319), proposes three levels of factors that influence breastfeeding: the individual, group, and society (Figure 3).

Individual-level factors relate specifically to the mother and child, such as a mother's attitude, resolve, and skills with regard to breastfeeding. Group-level factors refer to the environments that may have a direct influence on mothers and infants breastfeeding practices. These environments consist of hospitals/health facilities, home/peer environment, work environment, community support environment, and the public policy environment. The third level is the society-level, which creates the context in which a mother and infant will breastfeed. Society-level factors affect public opinion and expectations regarding breastfeeding (319).

Each of the three levels are interdependent, thus factors that occur at one level may influence what happens at another. For example, lack of breastfeeding acceptability within the community may influence a mother's resolve to continue breastfeeding (319), or a public campaign to encourage breastfeeding in the workplace may have little effect if workplaces are not set up to support breastfeeding mothers (323). As various factors have the ability to negate each other, a broad view is necessary when designing interventions. The lack of a contextual and multi-level approach to breastfeeding promotion has been noted as a major factor in the lack of success seen in some interventions (324, 325). Taking this multi-level approach will allow the identification of factors that need to be addressed in conjunction with each other, and will inform the development of tailored interventions that should have a more pronounced effect on breastfeeding practice (34, 309).

Figure 3. Multi-level Ecological Model of Factors Affecting Breastfeeding Practices (34)



Globally, a number of breastfeeding interventions have been trialled, ranging from education of mothers on the benefits of breastfeeding to the development of hospital-based interventions (326-328). However, while some interventions are effective in improving breastfeeding practices in some communities, the same strategy applied in another setting may not provide the same benefits (326). For example, the provision of an educational intervention in the US can be effective in improving breastfeeding practice in disadvantaged communities (327), although similar interventions with a disadvantaged Australian community may prove ineffective (329). Whilst this may be attributable in part to a lack of a multi-level approach (34), it is also likely that Australian communities (which compared to the US, have high initiation rates and longer duration) have different needs to other international communities.

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