



INTERNATIONAL LACTATION CONSULTANT ASSOCIATION

Risks of Not Breastfeeding

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The biological norm for infant feeding is breastfeeding. Any substitution can result in significant adverse consequences for both mother and baby. Human milk is the preferred form of nutrition for nearly all infants. Breastfeeding is the preferred mode of delivery. The body of literature on health outcomes has grown considerably since 1980. There are still some limitations in research related to inconsistent definitions of exclusivity and/or duration and some conflicting data. Overall, however, the data is clear that infants and young children who are fed formula are at increased risk for compromised nutritional status, growth and development and overall health and survival.

Since breastfeeding is the norm for infant feeding it must be considered the control group in any research study. Use of formula or a different feeding method would then be the intervention, and research results would be reported as either a risk or benefit from using this intervention. Unfortunately most breastfeeding research has been done with the reverse model.^{1,2} Bottle feeding of formula has been used as the norm or control group with breastfeeding being the intervention. This is why results are usually reported as benefits of breastfeeding rather than risks of formula. In this paper we talk about the risks of not breastfeeding; however the results from many of the studies cited are reported as benefits of breastfeeding.

UNIQUE COMPONENTS OF HUMAN MILK AND BREASTFEEDING

The components of human milk offer the newborn robust protection against infection. Even partial daily feedings of human milk reduces the risk of infection in preterm infants by fifty percent.³ Immune cells, immunoglobulins, long chain polyunsaturated fatty acids, cytokines, nucleotides, hormones, and bioactive peptides – all elements of human milk – play a vital role in aiding the immune system of the newborn.⁴ Glycans, prevalent anti-infective agents, are known to inhibit pathogenesis.

Glycans work by counteracting the ability of pathogens to bind to the newborn's host cell receptors. They are also resistant to digestion and can therefore easily bind to the host cell receptors in the newborn's gut.⁵

Oligosaccharides retard the growth of enteric pathogens by producing organic acids that cause cell wall lysis.⁶

Secretory immunoglobulin A (sIgA) antibodies are responsible for: (1) the prevention of bacteria and viruses from binding to mucosal surfaces (2) neutralizing microbial toxins and (3) increasing virus excretion in the newborn.⁴ Found in highest concentration in the maternal colostrum, sIgA is the major immune defense in the newborn's intestines and offers protection against gastrointestinal infections.⁷ Along with lactoferrin, an iron-binding whey protein, sIgA resists digestion and finds its way into the intestinal tract of the newborn.⁶

Lactoferrin promotes epithelial growth and protects the newborn against certain bacteria and fungi by damaging the outer membranes of pathogens.^{3,8} Xanthine oxidase (XO), an essential enzyme found in human milk and located on the outer surfaces of fat globules, attracts pathogens to bind to it therefore diverting bacteria away from their target (inclusive of the digestive tract).⁹ In addition, barrier protection, bacterial cell wall lysis, prevention of

inflammation, and the creation of a hostile gastrointestinal milieu, from the presence of *Lactobacilli* and *Bifidobacteria*,¹⁰ can all be attributed to the ingestion of human milk in the newborn period.^{3,11}

Human milk has been shown to be effective against such bacteria as *Escherichia coli*, *Vibrio cholerae*, *Campylobacter*, *Shigella*, and *Giardia lamblia* as well as in the viral defense of rotavirus, cytomegalovirus, influenza virus, respiratory syncytial virus (RSV), and *pneumococcus*.^{4,9} Proteins found in human milk have been shown to inhibit the attachment of these bacteria and viruses to host cell walls.⁴ Therefore, not breastfeeding an infant is associated with increased episodes of gastroenteritis, upper and lower respiratory tract infections, urinary tract infections, neonatal septicemia, necrotizing enterocolitis, and acute otitis media.¹¹ Human milk contains differentiated epithelial and putative stem cells. The presence of nestin-positive putative mammary stem cells indicates that expressed human milk may be a unique source from which mammary stem cells may be obtained.¹²

Human milk is associated with the promotion of intestinal maturation and growth in the newborn period of life.^{8,13} High concentrations of epidermal growth factors, vitamins, minerals, peptides and nucleotides facilitate optimal feeding tolerance in newborns. Present in human milk and not in infant formula, cysteine and taurine, lipase, pancreatic secretory trypsin inhibitor (PSTI), long chain polyunsaturated fatty acids, nucleotides, and gangliosides all support gastric integrity, rapid emptying time, and increased feeding tolerance in the newborn period of life.¹⁴ Decreased gastric integrity and delayed gastric emptying time are associated with gastrointestinal dysmotility, predisposing the infant to feeding intolerance and increased risk for extrauterine growth restriction.¹⁴

PSTI, a 56-amino acid peptide responsible for the protection of the pancreas from auto-digestion, has additional health benefits to the animal and human gut. It is found in highest concentrations in maternal colostrum. Using an animal rat model, it has been shown that when comparing rats fed human milk via gavage to rats receiving a commercial formula feed, the gastric damage was reduced by 75% amongst rats fed human milk over the rats fed commercial formula. When applied to a human population, the authors recommend that feeding neonates human colostrum will aid in the establishment and maintenance of human gut integrity.¹⁵

INFANT HEALTH OUTCOMES

There are significant risks to an infant's health when human milk is not provided. Table 1 provides an overview of these outcomes. The U.S. Agency for Healthcare Research and Quality (AHRQ) screened over 9,000 abstracts from studies conducted in developed countries across the world. They reviewed 43 primary studies on maternal health outcomes, 43 on infant health outcomes and 29 systematic reviews or meta-analyses that covered 400 individual studies.¹⁶ A history of breastfeeding was associated with a reduction in many types of infections, sudden infant death syndrome, obesity, necrotizing enterocolitis, atopic dermatitis, childhood cancers, asthma, and type 1 and 2 diabetes.¹⁶ The relationship between breastfeeding and cardiovascular disease was unclear, as well as the relationship between breastfeeding and mortality in developed countries.¹⁶

Short-term Infant Health Outcomes

Infection

Not breastfeeding significantly increases an infant's risk of illness from infectious diseases. For every additional month of full breastfeeding, 30.1% of hospitalizations resulting from infection could have been prevented.¹⁷ An estimated 53% of diarrhea hospitalizations and 27% of lower respiratory tract infections could have been prevented monthly by exclusive breastfeeding and 31% and 27% respectively by partial breastfeeding.¹⁸

Formula feeding places infants at increased risk of acute otitis media (AOM) and respiratory tract infections. When examining ever breastfeeding with feedings that were 100% formula, the risk of AOM was decreased by 23% (9%-36%).¹⁶ Exclusive breastfeeding for 3 or 6 months increased the risk reduction to 50% (confidence interval [CI] 30%-64%).¹⁶ In addition there is good evidence from seven studies that demonstrate a 72% reduction in the risk for hospitalization from lower respiratory tract infections in infants who were exclusively breastfed for > 4 months (95% CI 46%-86%).¹⁶

A dose response relationship between duration and exclusivity of breastfeeding and protection from many types of infections has been noted in several studies.^{17,18,19} One nationally represented study noted increased risk for both respiratory tract infection and otitis media in children who were exclusively breastfed for only 4 months versus 6 months.²⁰

Similarly, a beneficial relationship between breastfeeding and infection prevention has been demonstrated for preterm infants (or very low birth weight infants [VLBW]). The use of human milk for feeding was found to be associated with a lower risk of urinary tract infection (odds ratio [OR] 0.314, 95% CI 0.0140-0.707, $P < 0.009$) when compared with preterm infants who were not breastfed.²¹ A protective dose response relationship between human milk and sepsis prevention has also been found.²² An analysis that adjusted for birth weight, sex, and ethnicity revealed that the mean number of episodes of sepsis for infants receiving at least 50 mL/kg/day of human milk was lower by a factor of 0.27 (95% CI, 0.08-0.95) compared with infants receiving formula, thus indicating an increased risk of sepsis in formula fed infants.²²

Sudden Infant Death Syndrome

Not breastfeeding increases the chance of an infant dying from sudden infant death syndrome (SIDS). In a 2009 German study, exclusive breastfeeding at one month of age halved the risk of SIDS, and partial breastfeeding at one month of age also reduced the risk.²³ Being exclusively breastfed in the last month of life further reduced the risk of SIDS, as did being partially breastfed.²³ In addition, an AHRQ 2007 meta-analysis found that breastfeeding was associated with a 36% (95% CI 19%-49%) risk reduction of SIDS compared to not breastfeeding.¹⁶

Mortality

Not breastfeeding significantly increases a child's risk of dying in infancy. In both developed and developing countries, breastfeeding and human milk protects against post-neonatal death.^{24,25,26}

In developing countries infants who are not breastfed have higher rates of diarrhea and respiratory diseases, both of which are main causes of infant death. A cohort case study in Ghana found a marked dose response of increasing risk of neonatal mortality with increasing delay in initiation of breastfeeding from 1 hour to day 7.²⁴ Overall 16% of neonatal deaths could have been saved if all infants were breastfed from day 1 and 22% if breastfeeding was started within the first hour after birth.²⁵ A similar study in Bangladesh concluded that infant mortality could be reduced by almost one-third if the prevalence of exclusive breastfeeding in the first four months could be raised to 80%.²⁶

In the United States infectious disease accounts for a smaller portion of infant mortality. Formula fed infants are at increased risk of mortality, however. Children who were ever breastfed were found to have 0.79 times reduction in post neonatal mortality when compared with children never breastfed. Longer breastfeeding was associated with lower risk.²⁴ Additionally, if 90% of families in the United States breastfed exclusively for 6 months, 911 deaths would be prevented; and 841 deaths would be prevented if exclusive breastfeeding were increased to 80%.²⁷

Weight

Not breastfeeding increases a child's risk of being both overweight and obese. The estimated percentage of 6-11 year old U.S. children considered to be obese has more than quadrupled to 19% since 1960.²⁸ Infants who have never been breastfed are at higher risk for later childhood obesity than infants who have ever been breastfed. Increased breastfeeding duration is associated with lower rates of childhood obesity. Infants who are breastfed more intensively during early infancy (≤ 6 months) will be less likely to have excess weight during late infancy (>6 months). Of 1896 infants whose weight was measured during the second half of infancy, 246 (13%) were categorized as having excess weight. Infants fed with low ($<20\%$ of milk feeds being breast milk) and medium (20%-80%) breastfeeding intensity in the first half of infancy were at least 2 times more likely to have excess weight during the second half of infancy than those breastfed at high intensity ($>80\%$).

Infants who emptied bottles in early infancy were 69% more likely than those who rarely emptied bottles to have excess weight during late infancy.²⁸ Another study found that weight gain in the first week of life in formula fed infants is a critical determinant for the development of obesity and overweight several decades later in life.²⁹

Temperature and Respiratory Regulation

Bottle feeding puts an infant at risk for physiological instability. Oxygen saturation and body temperature were found to be significantly lower in preterm infants who were bottle fed versus those who were directly breastfed. There were 2 episodes of apnea

(breath pause more than 20 seconds) and 20 episodes of oxygen desaturation ($\text{PaO}_2 < 90\%$) during bottle-feeding and none during breastfeeding.³⁰ Preterm infants who were bottle-fed with a high-flow nipple had more frequent apnea and oxygen desaturation.³⁰

Necrotizing Enterocolitis

Not breastfeeding significantly increases an infant's risk of necrotizing enterocolitis (NEC). NEC occurs in 3-10% of VLBW infants and rarely in compromised term infants. It is associated with an increased morbidity and mortality, including growth and neurodevelopmental impairment, infection and increased need for central line placement.^{31,32} Because the development of NEC is associated with increased complications, lengths of hospital stay are increased for infants who develop NEC, costing an additional average of \$216,666 per survivor.³² For every 25% increase in human milk proportion in the first 14 days, the odds of NEC decreased by 38% and those infants that received at least 50% human milk in the first 14 days of life had a six fold decrease in the development of NEC.³¹

Pain

Not breastfeeding increases the infant's response to pain. An analysis of eleven studies demonstrates that both breastfeeding and human milk are pain relieving. Neonates who were swaddled or received a pacifier exhibited more crying times (proportion and duration) and increased heart rates when compared to breastfeeding infants. Pain scores were significantly worse (more pain) for infants who were not breastfeeding.³³

Long-term Infant Health Outcomes

Atopic Dermatitis

Not breastfeeding increases an infant's risk of atopic dermatitis. In a meta-analysis of 18 prospective cohort studies on full term infants, breastfeeding was associated with a 42% reduction in the risk of atopic dermatitis (95% CI 8%-59%).¹⁶ However this research did not specify atopic dermatitis of infancy versus persistent or new atopic dermatitis of older children. Further research is warranted on atopic dermatitis before the age of 2 versus older children.

Childhood Cancers

Being fed formula in infancy increases a child's risk of cancer. Several studies have found increased risk of childhood cancers, including leukemia, lymphoma, and Hodgkin's disease when children have not been breastfed.^{34,35,36} In addition, the AHRQ 2007 meta-analysis found that breastfeeding at least 6 months was associated with a 19% (95% CI 9-29%) reduction of childhood acute lymphocytic leukemia.¹⁶ The meta-analysis also noted that a six-month breastfeeding duration was associated with a 15% (95% CI 2%-27%) risk reduction in acute myelogenous leukemia.¹⁶

Asthma

Not breastfeeding increases the risk of asthma in childhood.^{37,38,39} Breastfeeding for at least 3 months is associated with a 27% (95% CI 8%-41%) reduction in the risk of asthma in families where there is no history of asthma. For families with a history of asthma there is a more profound risk reduction. Breastfeeding for 3 months was associated with a 40% (95% CI 18%-57%) risk reduction for asthma in children less than 10 years of age.¹⁶ Further research is warranted on the relationship between breastfeeding and asthma in older children.

Cognitive and Brain Development

Not breastfeeding is associated with poorer scores on developmental and cognitive screening tools. Not being breastfed has been associated with poorer cognitive development in both term and preterm infants.^{40,41,42,43,44,45,46,47,48} The percent of expressed human milk that infants receive correlates significantly with all intelligent quotient scores and with IQ scores for boys.⁴⁹ In the same study, the percent of expressed human milk correlated with increasing total brain volume and white matter volume. The effects of early diet were particularly strong in boys where the effect of human milk was noted more strongly on white matter development than gray matter.⁴⁹

Type 1 and Type 2 Diabetes

Children who are fed formula have an increased risk of diabetes. Breastfeeding for at least 3 months reduces the risk by 19 to 27% of childhood type 1 diabetes compared to breastfeeding less than 3 months.¹⁶ In the same report, breastfeeding in infancy was associated with a 39% (95% CI 15%-56%) risk reduction compared to infants who were not breastfed. Risk factors for diabetes are multifactorial so breastfeeding is just one of many ways to reduce risk.

MATERNAL HEALTH OUTCOMES

There are significant risks to a mother's health when she does not breastfeed. Table 1 provides an overview of these outcomes. A mother's infant feeding decision can impact her risk of breast cancer, ovarian cancer, cardiovascular disease, diabetes, hypertension and hyperlipidemia.⁵⁰ Premature weaning or not breastfeeding at all are associated with health risks for mothers. Both short-term and long-term health outcomes have been described. The degree to which these health outcomes are realized depends on the duration, frequency and exclusivity of breastfeeding. In many studies, the associations are reported based on lifetime duration of breastfeeding rather than on the duration of breastfeeding for each pregnancy.

The AHRQ review¹⁶ concluded that there is consistent evidence to suggest an association between not having breastfed and an increased risk of breast cancer, ovarian cancer, and type 2 diabetes. A relationship was reported between a short duration of breastfeeding or not breastfeeding and postpartum depression. No association was found between breastfeeding and osteoporosis; an unclear relationship was found between breastfeeding and return to pre-pregnancy weight.¹⁶

Short-term Maternal Health Outcomes

Maternal Weight

Some, but not all, studies have found that not breastfeeding is associated with increased maternal weight. The Cochrane Review reports that exclusive breastfeeding for six months helps the mother lose weight.⁵¹ In studies where weight loss was measured and not estimated, women who had a shorter duration of breastfeeding did not lose as much weight or fat stores at 3 to 6 months postpartum as those who breastfed longer.⁵² Meta-analysis by the AHRQ found that based on the results of three prospective cohort studies, the effect of breastfeeding on return to pre-pregnancy weight was negligible. Four additional prospective cohort studies showed unclear effects.¹⁶

Low-income primiparous women who introduced complementary foods at 4 to 6 months of age were found to be heavier than mothers who were exclusively breastfeeding their infants.⁵³ Many other factors have more significant effects on postpartum weight retention or weight loss than breastfeeding, including gestational weight gain, baseline body mass index, and ethnicity and energy intake. Women who ate less food, gained less weight in pregnancy and were breastfeeding at one year retained significantly less weight than women who ate more food, gained more weight or were not breastfeeding at one year.⁵⁴ In a large cohort study of the Nurse's Health Study II, Sichieri and colleagues did not find that the duration of exclusive breastfeeding was related to the magnitude of weight change from pre-pregnancy to 1-2 years postpartum.⁵⁵ In a Brazilian study, lactation had a small effect on weight change with an associated decrease of 300 g for each month of predominant breastfeeding among primiparous women.⁵⁶ Another Brazilian study found that longer duration of breastfeeding (>180 days compared to 30 days) was associated with decreased weight retention only in women whose baseline body fat was <30% with no effect in obese women.⁵⁷ In a small study examining changes in weight and percent body fat at 12 weeks postpartum, exclusively breastfeeding mothers had lost more total body weight (4.41 kg \pm 4.10 kg versus 2.79 kg \pm 3.09 kg; $p=0.072$) than mixed feeding mothers.⁵⁸

Blood pressure

Not breastfeeding is associated with increases in short- and long-term blood pressure. Blood pressure fell significantly by 8.8 and 7.7 mm Hg (systolic and diastolic blood pressure, respectively) with breastfeeding 2 days after birth and at 1, 10, and 25 weeks, falling within the first 10 minutes and continuing for at least 60 minutes. Basal blood pressure decreased through 6 months of breastfeeding.⁵⁹

Amenorrhea

Not breastfeeding is associated with a quicker return of fertility and increased chance of closely spaced pregnancies. Exclusively breastfeeding is associated with a longer period of amenorrhea. Amenorrhea conserves nutrients such as iron and improves maternal nutritional status and decreases the risk for iron defi-

ciency.⁵³ Breastfeeding may also suppress ovulation, delaying the menstrual cycle and increasing spacing between pregnancies. The lactational amenorrhea method (LAM) plays an important role in family planning, particularly when other forms of contraceptives are not readily available or acceptable. Women who are exclusively breastfeeding and amenorrheic reportedly have a very small risk of getting pregnant.⁶⁰

Postpartum Depression

Not breastfeeding is associated with an increased risk of postpartum depression. A qualitative systematic review to examine the relationship between postpartum depression and infant feeding found seven studies demonstrating an association between bottle feeding and higher levels of depressive symptomatology.⁶¹ Breastfeeding is consistently associated with a decrease in depressive symptomatology and lower mean depression scores than bottle-feeding mothers. In addition studies suggest that mothers with depressive symptomatology were significantly more likely to discontinue breastfeeding earlier than mothers without symptoms.⁶¹ Based on prospective cohort studies there is an association between not breastfeeding or short duration of breastfeeding and postpartum depression.¹⁶

Sleep

Not breastfeeding is associated with increased sleep disturbances and overall less sleep. Exclusive breastfeeding, including nighttime feedings, has been reported to improve sleep. Mothers who supplement with formula at night, even when the father takes over the nighttime feedings to allow the mother to get more sleep, have been found to sleep 40-45 minutes less and to have more sleep disturbances than mothers who exclusively breastfeed their infants including overnight feedings.⁶² Bedding in, in order to facilitate breastfeeding initiation in the initial postpartum period has also shown to have no adverse effect on the amount of sleep that both baby and mother receive.⁶³

Long-term Maternal Health Outcomes

Breast Cancer

Not breastfeeding increases a woman's risk for breast cancer.^{16,64,65,66} Lactogenesis leads to terminal differentiation of the breast tissue, which may reduce malignant transformation.⁵⁰ A lifetime history of breastfeeding for less than 12 months is associated with an increased risk for breast cancer. Women with breast cancer have been found to have been less likely to have breastfed, and if they did breastfeed their average lifetime duration was shorter (9.8 versus 15.6 months) compared to women without breast cancer. In addition, for each year a woman breastfeeds in her lifetime there is a 4.3% reduction in the risk of breast cancer.⁶⁴ Compared to women who never breastfed, parous women who reported ever lactating had a reduced risk of breast cancer (OR=0.83, 95% CI 0.63-1.09).⁶⁵ A reduced risk was observed in women who breastfed >3 children (OR =0.53,95% CI 0.27-1.04) and in women who breastfed the first child >13 months (OR =0.47,95% CI 0.23-0.94).⁶⁵

Table 1 — Health Outcomes Associated with Not Breastfeeding

Infant Health Outcomes	Maternal Health Outcomes
Increased incidence and severity of infection: otitis media, lower respiratory tract infection, urinary tract infection, diarrhea, bacterial meningitis, sepsis	Higher prevalence of hypertension, diabetes, hyperlipidemia, cardiovascular disease, metabolic syndrome
Increased rate of sudden infant death syndrome (SIDS), necrotizing enterocolitis (NEC), post neonatal deaths	Increased risk of breast cancer, ovarian cancer, rheumatoid arthritis, postpartum depression
Increased risk of atopic dermatitis, leukemia, lymphoma, Hodgkin's disease, asthma, diabetes	Reduction in bone health
Impaired temperature and respiratory regulation	Increased sleep disturbances
Lack of pain relief	Decreased postpartum weight loss
Decreased cognitive development	Lack of amenorrhea
Increased obesity	

Ovarian cancer

Not breastfeeding increases a woman's risk of ovarian cancer. Breastfeeding significantly and positively decreases lifetime ovulation thus reducing the risk of ovarian cancer.^{67,68} Women who do not breastfeed also have poorer outcomes if they do develop ovarian cancer.⁶⁹ The protective effect of breastfeeding on ovarian cancer may be attributed to the partial inhibition of ovulation from elevated follicle-stimulating hormone and prolactin levels and lower luteinizing hormone levels in lactating women. A large, prospective study found that breastfeeding for 18 or more months was associated with a significant decrease in ovarian cancer risk compared to never breastfeeding (relative risk [RR]= 0.66, 95% CI 0.46-0.96).⁷⁰ For each month of breastfeeding the relative risk is decreased by 2%.⁷⁰ The strong inverse relationship between total lifetime months of breastfeeding and ovarian cancer occurrence does not appear to be related to parity.⁶⁸

Cardiovascular Disease

Not breastfeeding is associated with an increased risk of cardiovascular disease. Women who breastfed for a shorter duration experienced higher rates of hypertension, diabetes, hyperlipidemia and cardiovascular disease.⁷¹ A dose-response relationship shows that women who report a lifetime history of breastfeeding >12 months were less likely to have hypertension (OR 0.88, P<.001), diabetes (OR 0.80, P<.001), hyperlipidemia (OR 0.81, P<.001), or cardiovascular disease (OR 0.91, P=.008) than women who never breastfed.⁷¹ It is estimated that among parous women who did not breastfeed compared to women who breastfed > 12 months,

42.1% versus 38.6% would have hypertension, 5.3% versus 4.3% would have diabetes, 14.8% versus 12.3% would have hyperlipidemia, and 9.9% versus 9.1% would have developed cardiovascular disease when postmenopausal.⁷¹ Furthermore, a cross-sectional study of parous women aged 45-58 free of cardiovascular disease found that compared to women who breastfed all of their children at least three months, women who never breastfed were more likely to have aortic calcifications (OR 5.26, 95% CI 1.47-20.00) increasing their risk of future cardiovascular disease.⁷²

Not breastfeeding results in an increased risk of hypertension, compared to women who breastfed for a month or longer. In particular, no lactation combined with obesity increased the risk for hypertension ($P=0.028$ for interaction).⁷³ Women who have never breastfed were found to have an increased future risk of cardiovascular and metabolic disease in a 3-year prospective study of lactating and non-lactating women from preconception to post-weaning.⁷⁴ Low-density lipoprotein cholesterol (+6.7 mg/dl, $P<.05$) and fasting insulin (+2.6 microunits, $P=.06$) increased more for parous women who did not lactate than for parous women who lactated.⁷⁴ High-density lipoprotein decreased less (-1.3 mg/dl versus -7.3 mg/dl; $P<01$) in women who lactated >3 months compared to women who breastfed <3 months.⁷⁴ Lactation may attenuate metabolic risk factors and affect the future risk of cardiovascular and metabolic disease.⁷⁴

Long duration of breastfeeding is associated with a reduced risk of coronary heart disease.⁵⁰ Compared with parous women who never breastfed, women who breastfed for a lifetime total of 2 years or longer had a 23% reduced risk of coronary heart disease (95% CI 6%-38%, P for trend = .02) after adjusting for age, parity, stillbirth history, early-adult adiposity, parental history, and lifestyle factors. This effect may be due to the influences of lactation on carbohydrate and lipid metabolism. Furthermore, oxytocin released during the milk ejection reflex has been linked to regulation of blood pressure and cardiovascular function and may reduce the response to stress in lactating mothers.

Type 2 Diabetes

Not breastfeeding is associated with an increased risk of type 2 diabetes. A shorter duration of lactation was associated with an increased incidence of type 2 diabetes among parous women. For each additional year of lactation, for women who gave birth in the previous 15 years, the risk was decreased by 15% (95% CI 1%-27%) in the Nurses' Health Study (NHS) study and by 14% (95% CI 7%-21%) in NHS II controlling for other relevant risk factors for type 2 diabetes including current body mass index.⁷⁵

A large prospective study found that the total duration of breastfeeding and duration of breastfeeding per child were associated with a reduced risk of type 2 diabetes compared to women who never breastfed. The adjusted RR for years of breastfeeding and risk of type 2 diabetes were 1.0, 0.88, 0.89, 0.88, 0.75 and 0.68 for 0, >0 to 0.99, >0.99 to 1.99, >1.99 to 2.99, >2.99 to 3.99 and ≥ 4 years of breastfeeding. The adjusted RR for years of breastfeeding per child and risk of type 2 diabetes were 1.00, 0.91, 0.87, and 0.87 ($p=0.11$ for trend) for 0, >0 to 0.49, >0.49 to 0.99, and ≥ 1 years of breastfeeding per number of births.⁷⁶

Metabolic Syndrome

Not breastfeeding increases a woman's risk of metabolic syndrome. The duration of lactation was found to impact the prevalence of metabolic syndrome (insulin resistance, dyslipidemia, hypertension and obesity) in midlife parous women. Women who had breastfed for shorter periods experienced increased incidence of metabolic syndrome. Parous women who had ever breastfed had a significantly lower prevalence of metabolic syndrome with an OR 0.77 (95% CI 0.62-0.96) after adjusting for confounding factors. Women who had ever breastfed were significantly less likely to have impaired fasting glucose ($P<.01$), elevated blood pressure ($P=0.48$) or abdominal obesity ($P<.01$).⁷⁷ There was a statistically significant correlation between the duration of lactation and high density lipoprotein (HDL) cholesterol levels and an inverse correlation with low density lipoprotein (LDL) cholesterol, and fasting levels of both glucose and insulin. The rate of metabolic syndrome is significantly higher with a decreased duration, suggesting a dose-response relationship.⁷⁷

Bone Health

Not breastfeeding may increase a woman's risk of osteoporosis. While some evidence shows no difference in bone mineral density,⁷⁸ research has shown that breastfeeding during adolescence may be associated with higher bone mineral density in young adulthood when compared to adolescent mothers who did not breastfeed and may be protective to bone health.⁷⁹ Although not all studies have shown a difference,⁸⁰ a longer duration of breastfeeding may be associated with a reduced risk of hip fracture after adjusting for confounding factors. Among parous women, there was a 13% reduced risk associated with every 6 month increase in breastfeeding per child.⁸¹ Therefore, there is a reduction in risk for hip fractures observed in women with extended duration of breastfeeding.

Rheumatoid Arthritis

Not breastfeeding increases a woman's risk of rheumatoid arthritis. Long-term breastfeeding is associated with a reduced risk of rheumatoid arthritis. Despite some conflicting evidence,⁸² it has been shown that a longer history of breastfeeding, ≥ 13 months, was associated with a reduced risk of rheumatoid arthritis OR 0.46 (95% CI 0.24-0.91) and breastfeeding for 1-12 months OR 0.74 (95% CI 0.45-1.20) compared to those who never breastfed.⁸³

HAZARDS OF FORMULA AND BOTTLE-FEEDING

Infant feeding methods other than direct feeding at the breast are associated with risks to the infant. This includes risks related to intrinsic components of formula, contamination of formula, and adverse health effects from the use of plastic bottles and nipples for feeding either formula or expressed human milk to the infant. Babies are also at increased risk when formula is reconstituted incorrectly,^{84,85} when powdered formula contains foreign bodies,⁸⁶ or when manufacturing errors result in excess or lack of specific nutrients.

Aluminum toxicity from contamination of infant formula is implicated in accumulation in bone and brain tissue.⁸⁷ Lack of thiamine in infant formula resulted in 15 infant hospitalizations and 2 deaths due to neurologic and cardiac effects of beriberi, a severe vitamin deficiency.⁸⁸ Excessive levels of mercury,⁸⁹ iron-to-copper ratios exceeding recommendations⁹⁰ and insufficient sodium chloride in infant formula have been described.^{91,92} See Table 2.

Pathogen Contamination

The pathogen *Enterobacter sakazakii* has been detected in commercially produced powdered infant formula. *E. sakazakii* is regarded as an emerging opportunistic human pathogen that has been linked to 76 cases of infection and 19 deaths of infants and children due to neonatal septicemia, meningitis and necrotizing enterocolitis.⁹³ Milk-based powdered infant formula serves as an ideal substrate for bacterial growth and is a source of pathogens as most formula products are intrinsically contaminated.⁹⁴ In addition to *E. sakazakii* other pathogens have been isolated from powdered infant formula including *Citrobacter diversus*, *Salmonella*, *Enterobacter*, *Klebsiella*, *Staphylococcus*, *Streptococcus*, *Clostridium botulinum* and *Yersinia* species.^{95,96,97,98} Analysis of powdered infant formula found that 6.6% of samples tested contained *E. sakazakii* and 24% of samples tested contained *Enterobacteriaceae*.⁹⁹ Opportunistic pathogens pose serious risk for food-borne infections to infants and young children.

Adulteration of Formula

Thousands of children in China, Taiwan, Vietnam and Singapore were affected by melamine added to 22 brands of infant formula; 50,000 were hospitalized and at least 6 died from acute renal failure.¹⁰⁰ Melamine had been added to disguise the low protein content resulting from diluting formula to increase profits. Adding melamine boosted the nitrogen content, increased the apparent protein content and gave the formula a more milky appearance. The adulteration was associated with the development of urinary tract stones and impaired glomerular function.¹⁰¹ Exposed children were 7.0 times more likely to have kidney stones; preterm infants were 4.5 times more likely to have kidney stones than term

infants. Although the U.S. Food and Drug Administration and the World Health Organization have established guidelines for tolerable upper limits for melamine ingestion, it is unclear how much is considered safe in young children.

Phytoestrogens in Soy Formula

Soy infant formula contains high levels of phytoestrogens including isoflavones, genistein and daidzein. These non-steroidal chemicals can have potent effects on reproductive, immune, and thyroid function. Concerns have been raised regarding the development of uterine and mammary cancer from high level exposure to phytoestrogens in early life.¹⁰² Traces of phytoestrogens have also been detected in infant and follow-up formulas other than soy-based infant formulas.¹⁰³

The amount of isoflavones ingested by infants fed soy formula as a percentage of body weight exceeds amounts reported as resulting in an increase in the length of the menstrual cycle in adult women.¹⁰⁴ Young female adults aged 20-34 years who had been fed soy formula as infants were found to have a longer duration of menstrual bleeding and greater discomfort, although no increase in menstrual blood flow was reported.¹⁰⁵ Infants with congenital hypothyroidism who consume soy formula may have difficulties managing their hormone levels due to a prolonged increase in thyroid-stimulating hormone and may require closer monitoring and increased hormone repletion.¹⁰⁶

Additional Risks of Soy Infant Formula

Soy protein formulas are not recommended for preterm infants as increased osteopenia has been reported in infants with low birth weight who receive soy protein formula, even with supplemental calcium and vitamin D.¹⁰⁶ Soy formula is often marketed and promoted to relieve perceived feeding intolerance. There is no evidence that soy formula reduces spitting up, vomiting, fussiness or colic. It does not reduce the rate of recovery from rotavirus or non-rotavirus diarrhea when compared to human milk and cow milk-based formulas. Furthermore, in infants with enterocolitis caused by cow milk protein, 30%-64% will also have soy-induced enterocolitis with bloody diarrhea, ulcerations and symptoms of inflammatory bowel disease. Severe gastrointestinal reactions to both cow milk-based formula and soy formula have been reported resulting in small bowel injury, malabsorption, hypoalbuminemia and failure to thrive.¹⁰⁶

Bisphenol A in Bottles and Formula

Bisphenol A (BPA) is a compound in hard, clear polycarbonate plastics that mimics the effects of estrogen. It has raised concern because it interferes with hormone levels and cell signaling systems with a potentially elevated risk of uterine fibroids, endometriosis, breast cancer, decreased sperm counts, and prostate cancer. BPA acts as an endocrine disruptor with estrogenic properties. Exposure to toxic chemicals in the first few years of life when cells are undergoing programming can disrupt this delicate process making infants most vulnerable. Early life exposure to BPA may predispose or induce cancerous lesions in the mammary gland and prostate gland later in life.¹⁰⁷

Table 2 — Hazards of Infant Formula and Bottle Feeding

Hazards Associated with Use of Infant Formula and Bottle Feeding

Pathogen contamination

Manufacturing errors and warehouse contamination

Adulteration of formula

Phytoestrogens in soy formula

Bisphenol A in feeding bottles

Not breastfeeding in emergencies

Infant feeding bottles from polycarbonate containing BPA are a critical source of exposure. Boiling bottles made with BPA in the microwave or cleaning in the dishwasher is problematic as repeated exposure to high heat causes BPA to leach out.¹⁰⁸ Boiling water in the bottle in a microwave for >5 minutes for sterilization purposes and then using the sterilized water to reconstitute formula increases BPA exposure.¹⁰⁹

BPA has also been detected in samples of powdered infant milk and soy based formulas at varying concentrations indicating that BPA finds its way into food via miscellaneous pathways and at different stages of powdered milk production.¹⁰³

Feeding in Emergencies

In the event of an emergency widespread distribution of infant formula and/or powdered milks exposes infants and young children, who would otherwise be breastfeeding, to increased risk of disease and death especially from diarrhea when clean water is scarce. Use of feeding bottles increases this risk of infection due to inability to properly clean the bottles.¹¹⁰ Black and colleagues report that sub-optimal breastfeeding is responsible for 1.4 million child deaths.¹¹¹ Mothers should be reassured that human milk can contribute significant nutrition in the absence of complementary foods or safe conditions as during a disaster.¹¹²

COST

The lack of breastfeeding worldwide results in significant increased financial burden on health-care systems, insurers, governments, and families. Private and government insurers pay \$3.6 billion annually to treat conditions that are preventable by breastfeeding.¹¹³ If 90% of families in the U.S. exclusively breastfed for 6 months, the U.S. would save \$13 billion per year or \$10.5 billion with 80% compliance.²⁷

Families in 1996 averaged \$1,200 to \$1,500 per year to purchase infant formula¹¹⁴ and annual estimates of formula feeding in the U.S. are over \$2 billion.¹¹⁵ The Women, Infants, and Children (WIC) program, a supplemental food program for low-income families, spends \$578 million per year of federal funds to purchase infant formula. For every 10% increase in breastfeeding in the WIC population, a \$750,000 savings annually would be realized.¹¹⁵

Typical health-care costs of infants who are not breastfed are \$331-\$475 more per infant during the first year of life related to higher rates of respiratory illness, otitis media and gastrointestinal illness.¹¹⁶ In addition, the cost of hospitalization for respiratory illness in infants who are not breastfed is significant with a range of \$26,585-\$30,750 per 1000 infants.¹¹⁶ Breastfeeding is associated with fewer hospital admissions. In Italy, fully breastfed infants had lower costs of health-care (€34.69 [\$49.59 USD] versus €54.59 [\$78.47 USD] per infant per year for ambulatory care, and €133.53 [\$190.867 USD] versus €254.03 [\$363.11 USD] per infant per year for hospital care).¹¹⁷ Another study reports that \$200,000 is spent on each case of necrotizing enterocolitis, which occurs in 10.1% of formula fed preterm infants in the neonatal

intensive care unit (NICU) and only 1.2% of human milk fed infants in the NICU.³²

Absenteeism and healthcare costs are lower among employed breastfeeding mothers. One study found that one-day absences were more than twice as likely in mothers of formula-fed babies as compared to exclusively breastfed babies.¹¹⁸ In another study, CIGNA, a global health service company with a workplace breastfeeding program, found no negative impact on the productivity of breastfeeding employees and reported annual savings of \$240,000 in healthcare expenses for breastfeeding mothers and their children.^{119,120}

CONCLUSION

Exclusive breastfeeding is the normative standard for infant feeding. Not breastfeeding increases infant and maternal acute and chronic illnesses, and significantly increases health-care costs. There is ample evidence to support the value of human milk and breastfeeding in improving the health of infants and mothers. While breastfeeding initiation rates continue to rise, there is much work to do to improve breastfeeding exclusivity and duration. The research demonstrates that there is a dose response to breastfeeding and human milk exposure for mothers and infants. Health-care professionals must be aware of the research and find ways to share this information with families so they can make responsible, informed feeding decisions for their children.

REVIEW COMMITTEE

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