

# Breastfeeding and the Prevention of Chronic Disease, With a Focus on Obesity and Vascular Disease

**EDITH KERNERMAN, IBCLC, NBCI**

## The System

Human milk is a special ***human information support system*** that protects preterm infants and newborns.

Human milk provides the infant with

1. Protection
  - Prevent infection/ infectious agents e.g. gastroenteritis, respiratory infection, otitis media, Giardiasis, Shigellosis
  - Allow infection but minimize symptoms resulting from infection
    - May be biologically equivalent to vaccination
2. Information
3. Nutrition

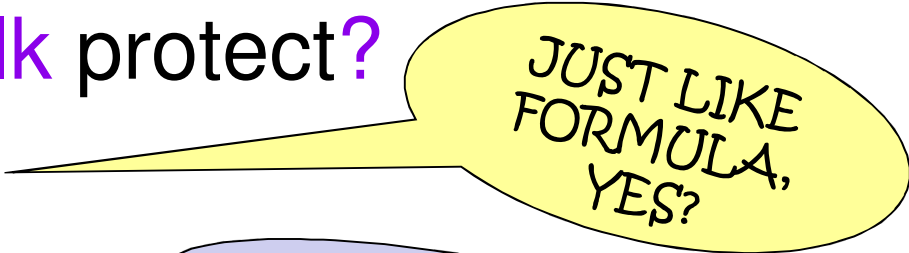
*Stephen Buescher, MD, ILCA 2006*

# Objectives

The **System of Breastfeeding**.

How does **Breastmilk** protect?

**What** is it?



JUST LIKE  
FORMULA,  
YES?

What is it **not**?




FORMULA

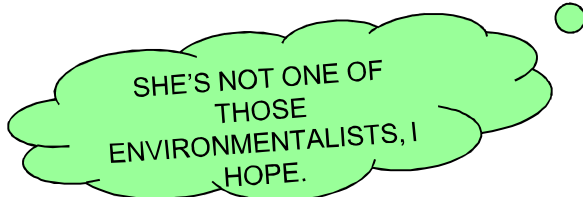
How does **Breastfeeding** protect?

**What** does it protect us **from**?

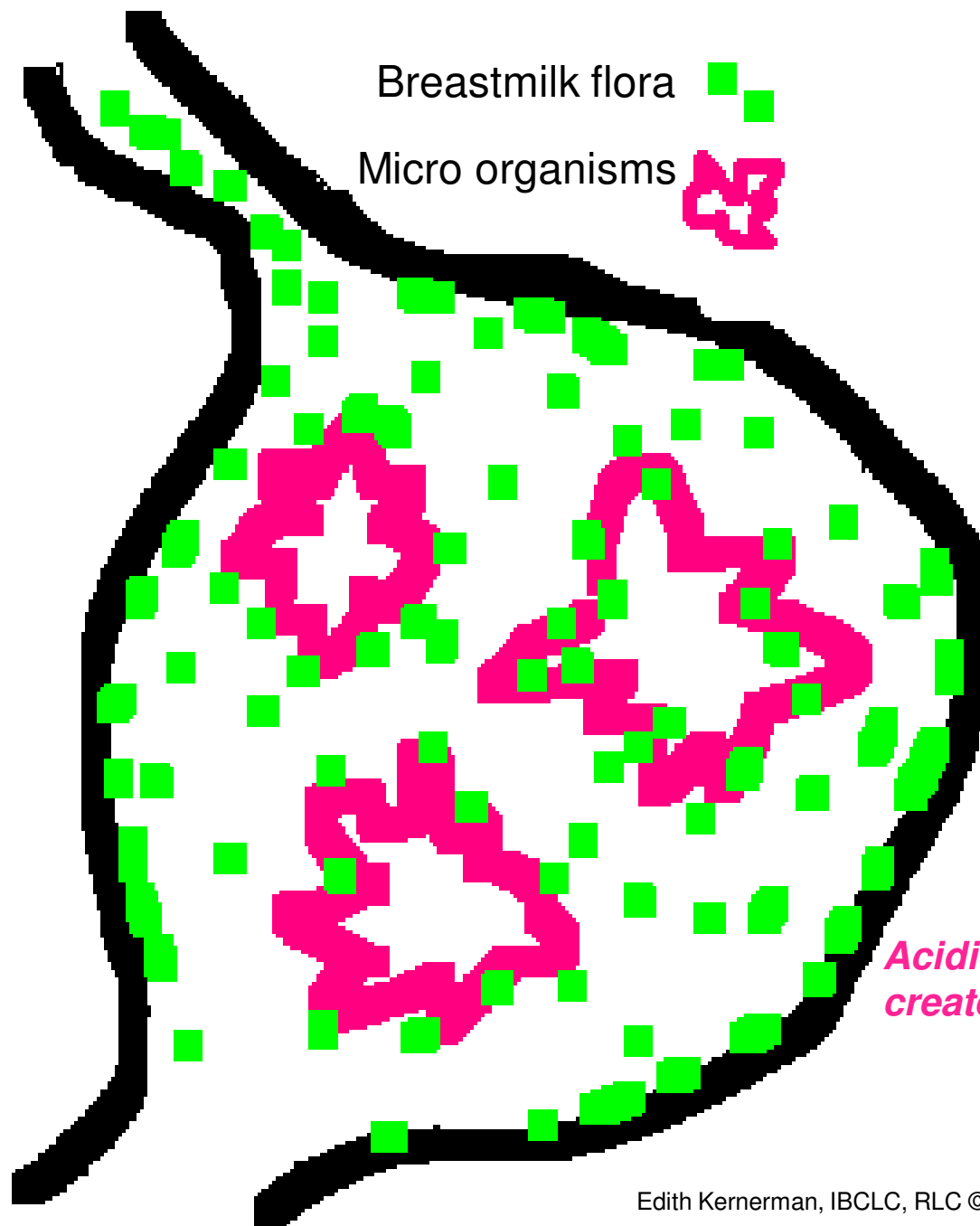
**Who** does it protect?



NEXT, SHE'S  
GONNA SAY IT  
PROTECTS US  
ALL? YAWN...



SHE'S NOT ONE OF  
THOSE  
ENVIRONMENTALISTS, I  
HOPE.



*“Breastfeeding influences many potentially pathogenic microbes in the gut microflora so that they have a lower capacity to cause infections by limiting their ability to bind to and pass into tissues through the gut mucosa”*

*Lars Hanson*

*Acidic environment  
created in the gut*

<b><u>Infant Condition</u></b>	<b><u>Breastfed</u></b>	<b><u>Not Breastfed</u></b>
Otitis Media <sup>1,2,3</sup>	Confers Protection	Increased Risk
Lower Respiratory Tract Infection <sup>4,5,6</sup>	Confers Protection	Increased Risk, Dose response
Gastrointestinal Infection <sup>7,8,9</sup>		Increased Risk
Necrotising Enterocolitis <sup>10,11</sup>		Increased Risk
Obesity/Diabetes 1,2/Metabolic Disease 12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34		Increased Risk
Neuro-development <sup>34,35,36,37,38,39</sup>	Mixed Results, Confers protection	Mixed Results, Increased Risk
Cognitive Development <sup>39,96</sup>	Confers Protection, Dose response	
Maternal-infant Bonding and Empathy <sup>40</sup>		
Sudden Infant Death Syndrome (SIDS) <sup>41,42,43,44,45,46</sup>	Reduces Risk, Protective	Increased Risk
Asthma and Allergy <sup>47,48,97,101</sup>	Confers Protection, Dose response	Increased Risk, Dose response
Atopic Dermatitis <sup>49,50</sup>		Increased Risk
Childhood Cancer <sup>51,52,53,54</sup>		Increased Risk, Dose response
Osteoporosis <sup>55,56</sup>	Confers Protection	
Mortality and Morbidity <sup>57,98</sup>	Reduced Risk, Dose response	
Multiple Sclerosis <sup>58</sup>		
Cardiovascular disease <sup>59,60</sup>	Confers Protection	
Schizophrenia <sup>61</sup>		Increased Risk, Dose response
Alcoholism <sup>62</sup>		Increased Risk
Stress and Depression, Mental Health <sup>63,100</sup>	Confers Protection	Increased Risk, Dose response
Pyloric Stenosis <sup>64</sup>		

<b><u>Maternal Condition</u></b>	<b><u>Breastfed at Least One Baby</u></b>	<b><u>Did Not Breastfeed</u></b>
Breast Cancer <sup>65,66,67,68,69,70,71,72,73,102</sup>		Increased Risk, Dose response
Ovarian Cancer <sup>74,75,103</sup>		Increased Risk
Diabetes 2, Maternal Metabolism, Cardiovascular Disease <sup>76,77,78,79,80,81,82,83,84</sup>	Confers Protection, Dose response	Increased Risk
Osteoporosis <sup>85,86</sup>	Confers Protection	
Stress and Depression <sup>87,88,89,90,91,92,104</sup>	Confers Protection	Increased Risk
Rapid return to Fertility <sup>93</sup>	Confers Protection, Dose Response	Increased Risk

**Chart: Edith Kernerman & Frances Egner-Chaddah © 2012, Updated and Revised, Edith Kernerman & Tristan Kiraly © 2014**

# How might breastfeeding protect?

- ❖ A more mature (a normal) immune system compared to artificially fed children
- ❖ An immune system that protects against infection (some cancers probably caused by viruses)
  - Breastmilk contains factors which may specifically kill tumour cells (MAL or multimeric alpha-lactalbumin)
  - Breastmilk contains greater quantities of anti-oxidants (carotenoids, selenium, etc)
  - Prevents DNA damage?

*Dundaroz R, Aydin HI, Ulucan H, et al.2002*

*Håkansson A, et al 1995*

*Håkansson A, Andréasson J, Zhivotovsky B, Karpman D, Orrenius S, Svanborg C. et al 1999*

This slide courtesy of Jack Newman

# How Breastfeeding Protects

Objective: to examine the contribution of a broad range of external influences to the gut microbiotic composition in early infancy.

- Fecal samples from over 1000 infants (taken from the KOALA Birth Cohort Study in the Netherlands),
- 1 month of age,
- real-time polymerase chain reaction assays to count
  - bifidobacteria,
  - *Escherichia coli*,
  - *Clostridium difficile*,
  - *Bacteroides fragilis* group,
  - lactobacilli,
  - total bacterial counts.
- To determine: potential determinants of the gut microbiotic composition

*Penders, J, et al, Netherlands 2006*

## RESULTS

Infants born through cesarean section had lower numbers of bifidobacteria and *Bacteroides*, whereas they were more often colonized with *C difficile*, compared with vaginally born infants. Exclusively formula-fed infants were more often colonized with *E coli*, *C difficile*, *Bacteroides*, and lactobacilli, compared with breastfed infants. Hospitalization and prematurity were associated with higher prevalence and counts of *C difficile*. Antibiotic use by the infant was associated with decreased numbers of bifidobacteria and *Bacteroides*. Infants with older siblings had slightly higher numbers of bifidobacteria, compared with infants without siblings.

## CONCLUSIONS

The most important determinants of the gut microbiotic composition in infants were the *mode of delivery, type of infant feeding, gestational age, infant hospitalization, and antibiotic use by the infant*. *Term infants who were born vaginally at home and were breastfed exclusively seemed to have the most “beneficial” gut microbiota (highest numbers of bifidobacteria and lowest numbers ...*

*My emphasis*



Kinda like baby's own little army...

The microbes colonizing the newborn, especially those in the gut, are the major stimulus for normal growth and development of the baby's immune system. As a result, the immune system becomes capable of defending the baby against infections.

*Lars Hanson, 2004*

## Hygiene Hypothesis

An abnormal intestinal colonization of the neonate adds to an increased risk of allergic diseases

*Lars Hanson, 2004*

## Barker Hypothesis

Early life experience can contribute to the adult risk of diseases such as obesity, hypertension, ischemic heart disease and glucose intolerance.

*Barker DJP, 1992*

# What are the stakes? Where does Breastfeeding Confer Protection?

Breastfeeding and Infant and Maternal Health Outcomes In Developed Countries

Ip S, Chung M, Raman G, et al  
April 2007

<http://www.ahrq.gov/downloads/pub/evidence/pdf/brfout/brfout.pdf>

*This slide and the following 3 courtesy of Hilary deVeber*

# Infant Health Outcomes

Outcome	BRF Type	Risk Reduction	Compared with
AOM	Ever	↓23%	Never BRF
	Exclusive 3-6 mos	↓50%	All Formula
GE less than 1 yr	BF	↓64%	Not BF
Severe LRTI (hosp.)	Excl. 4 mths.	↓72%	All Formula
Atopic dermatitis w/ FHx ATOPY	Excl. 3 mths.	↓42%	BRF < 3 mths.
Asthma, □ FHx Asthma	BRF > 3 mths.	↓27%	No BRF
+ FHx Asthma		↓40% for <10 yrs age grp.	
Obesity Adol. and adult	BF	↓7-24% ↓4% per mo.	Never
Diabetes Type 1 Childhood	BF ≥ 3 mths.	↓19%	BF < 3 mths.

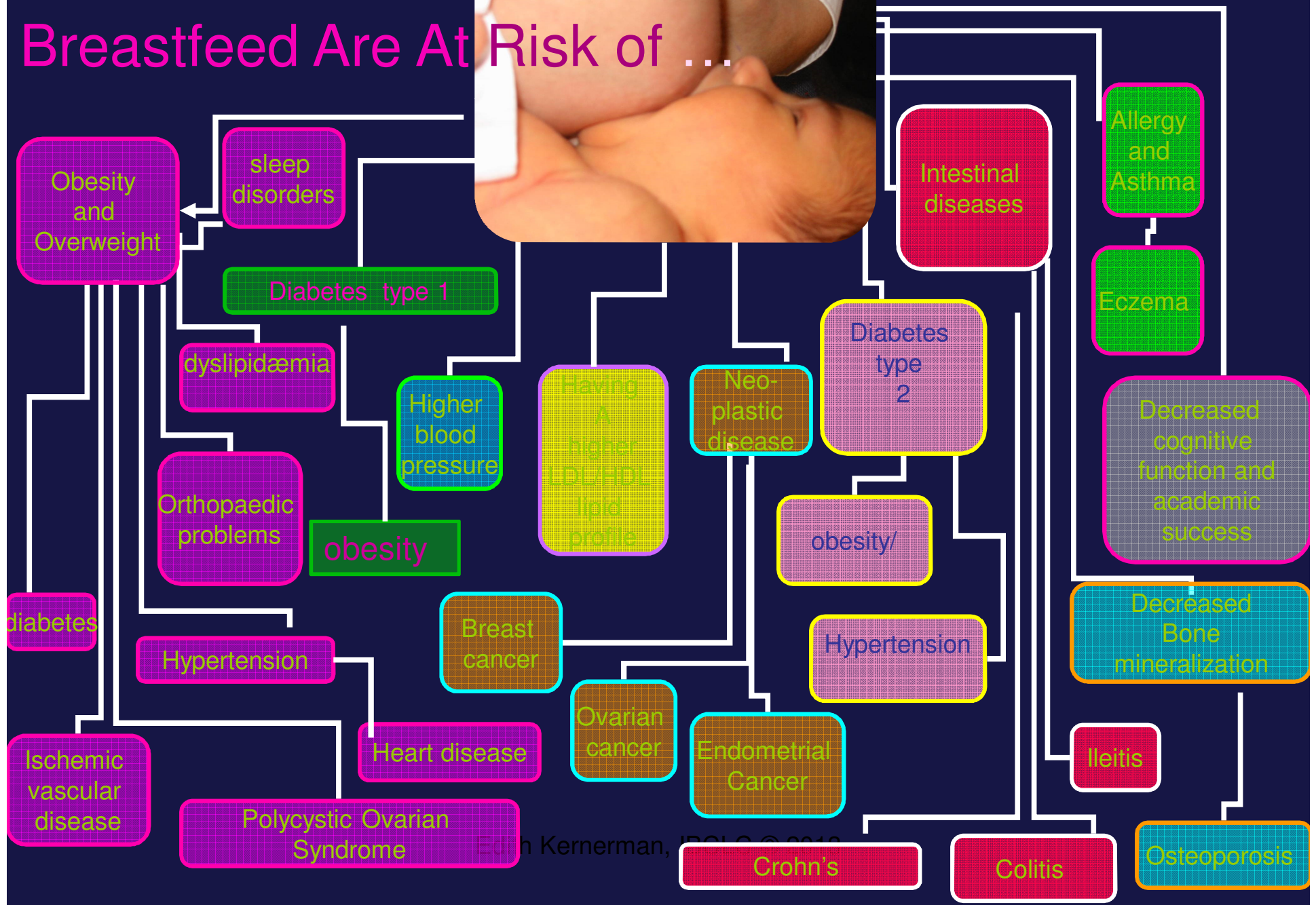
# Infant Health Outcomes - Slide 2

Outcome	BRF Type	Risk Reduction	Compared with
Diabetes Type 2 Adults	BF ever “in infancy”	↓39%	Never
Leukemia	BF > 6 mths.	ALL ↓19% AML ↓15%	Not BF for 6 mths.
NEC	Fed EBM	↓5% Studies heterogenous 4 - 80%	Formula
SIDS	Ever BRF	↓36%	Never
Cardiovascular Disease		unclear	
Infant mortality overall		unclear	
Term infant cognitive performance		unclear	( see recent studies confirming effect, increased IQ )
Preterm /LBW cognitive performance		unclear	comment as above

# Maternal Outcomes

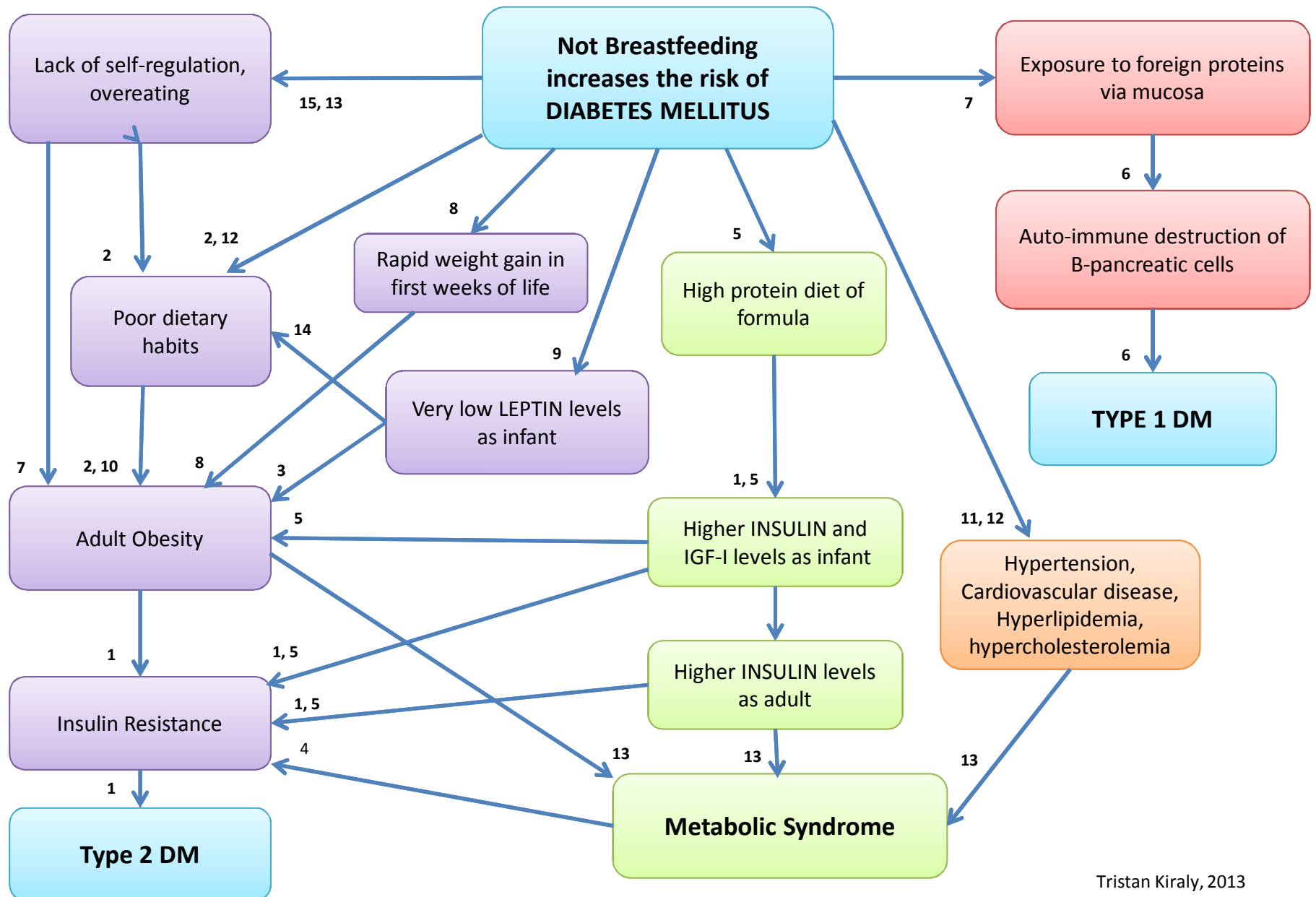
Outcome	BRF Type	Risk Reduction	Compared with
Ovarian Cancer	BRF > 12 mths.	↓21%	Never
Breast Cancer	Per 1 year of BRF	↓4%- 28% per yr of brf.	Never
Type 2 Diabetes (no GDM) (if GDM, no sign redn.)	BF > 1 year	↓4%-12% per yr of brf.	Formula
PPD	Early cessation or no BRF ever	assoc.with some redn...	
Osteoporosis		No effect	
Return to pre pregnancy wt		Unclear	

NOT  
Risk of ...



# h Kernerman, IDOL @ 2015

# The breastfed infant is protected against developing Diabetes Mellitus because....



### **Diabetes Chart Works Cited:**

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- 8) Singhal A, Farooqi I, O’Rahilly S, Cole T, Fewtrell MJ, and Lucas A. Early nutrition and leptin concentrations in later life. *Am J Clin Nutr* 2002; 75:993-9

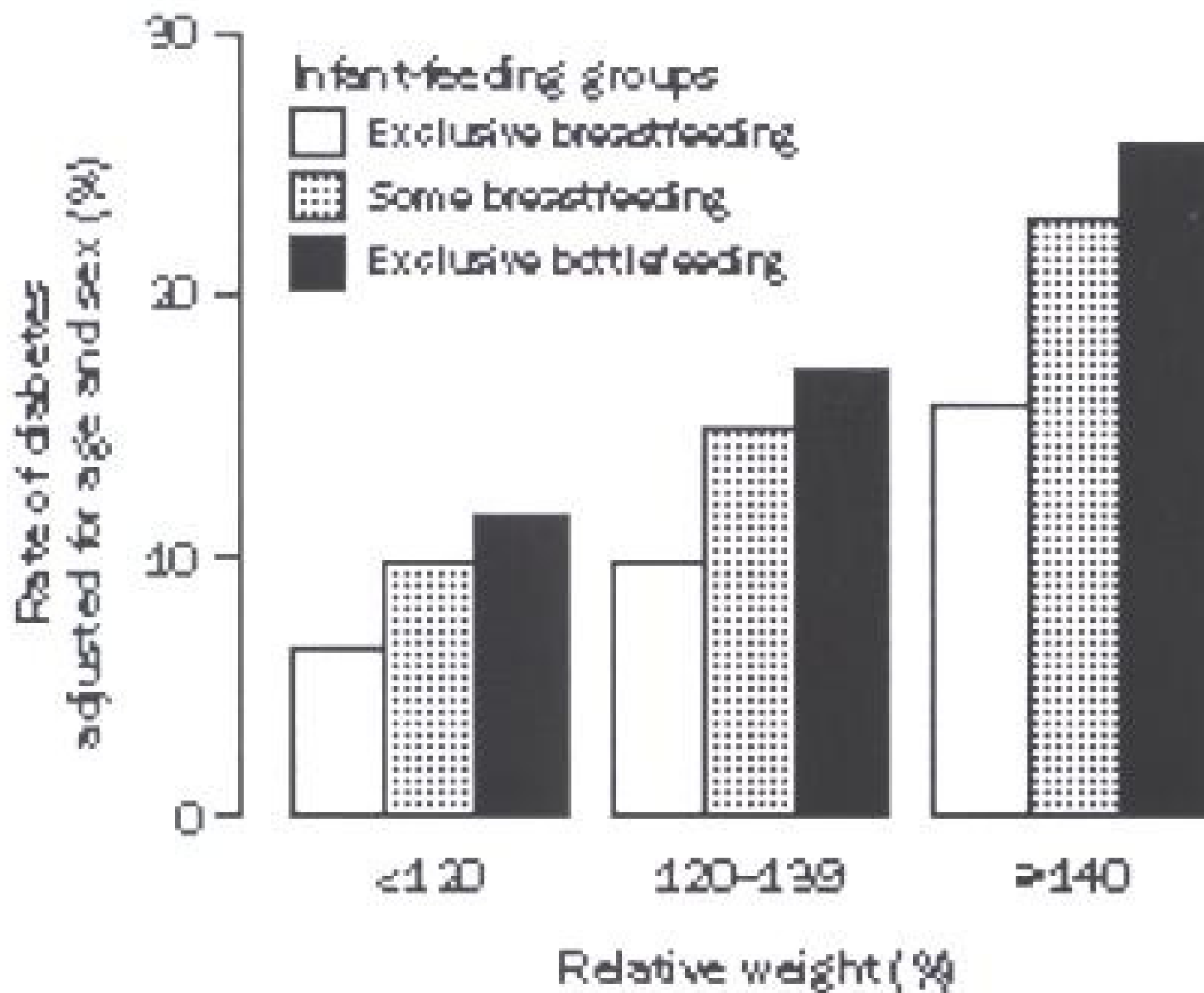


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- 14) Geddes D and Prescott S. Developmental Origins of Health and Disease: The Role of Human Milk in Preventing Disease in the 21<sup>st</sup> Century. *J Hum Lact.* 2013: February 4
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## WHY MIGHT THERE BE AN INCREASED RISK OF DIABETES?

- Formula increases insulin stimulation (compared to breastmilk)  
→ Insulin resistance (type 2)
- Increase risk of overweight /obesity (type 2)
- Amino acids in cow's milk → stimulation of antibodies against pancreatic  $\beta$  cells → type 1

How does breastfeeding protect? Mucosal immunity



Rate of NIDDM (adjusted for age and sex) by infant-feeding group and relative weight

## BRAIN: Probit Study

**Context:** The evidence that breastfeeding improves cognitive development is based almost entirely on observational studies and is thus prone to confounding by subtle behavioral differences in the breastfeeding mother's behavior or her interaction with the infant.

**Objective:** To assess whether prolonged and exclusive breastfeeding improves children's cognitive ability at age 6.5 years

**Design:** Cluster-randomized trial, with enrollment from June 17, 1996, to December 31, 1997, and follow-up from December 21, 2002, to April 27, 2005

**Setting:** Thirty-one Belarussian maternity hospitals and their affiliated polyclinics.  
**Participants:** A total of 17 046 healthy breastfeeding infants were enrolled, of whom 13 889 (81.5%) were followed up at age 6.5 years

**Intervention:** Breastfeeding promotion intervention modeled on the Baby-Friendly Hospital Initiative by the World Health Organization and UNICEF

**Main Outcome Measures:** Subtest and IQ scores on the Wechsler Abbreviated Scales of Intelligence, and teacher evaluations of academic performance in reading, writing, mathematics, and other subjects.

**Results:** The experimental intervention led to a large increase in exclusive breastfeeding at age 3 months (43.3% for the experimental group vs 6.4% for the control group; *P.001*) and a significantly higher prevalence of any breastfeeding at all ages up to and including 12 months.

The experimental group had higher means on all of the Wechsler Abbreviated Scales of Intelligence measures, with cluster-adjusted mean differences (95% confidence intervals) of 7.5 (0.8 to 14.3) for verbal IQ, 2.9 (−3.3 to 9.1) for performance IQ, and 5.9 (−1.0 to 12.8) for full-scale IQ. Teachers' academic ratings were significantly higher in the experimental group for both reading and writing.

**Conclusion:** These results, based on the largest randomized trial ever conducted in the area of human lactation, provide strong evidence that prolonged and exclusive breastfeeding improves children's cognitive development.

## (Blog about Most Recent Probit)

“However, just because this study found no link does not mean there is no link between breastfeeding and lower risk of obesity. This is because the PROBIT study design only supported the detection of extremely large differences in obesity rates attributable to exclusive breastfeeding. It was not designed to be able to detect any moderate or smaller differences. Furthermore, the study did NOT compare breastfed infants to fully formula-fed infants, further diminishing the chance of finding any differences in health outcomes. Because exclusively formula-fed infants were not even included in PROBIT, one cannot draw any conclusions about the safety of formula feeding in terms of obesity risk.”

*Nathan Nickel, Melissa Bartick, 2013*

## Brain Power

Pinpointed genes that explains why breast is best for brainpower.

In a study of more than 3000 breast-fed infants, researchers found breastfeeding raised a child's IQ by an average of nearly seven points if they had a particular version of a gene known as FADS2. They said that the vast majority of the children in the study had this version of the gene.

The gene helps convert dietary fatty acids into the polyunsaturated fatty acids found naturally in human milk.

...findings support...idea that the nutritional content of breast milk affects human IQ.

..."It depends to some extent on the genetic make-up of each infant."

...study...showed a baby's intellectual development was influenced by genes and the environment. "We're finding that nature and nurture work together."

...show that most of the children — 90 per cent — had a version of the gene that resulted in higher IQ scores if they were breast-fed.

The remaining 10 per cent had a version of the gene that showed no IQ advantage or disadvantage from breastfeeding.

...intelligence was not the only benefit to babies from breastfeeding.

...breast milk was also nutrient rich, easily digestible and helped boost an infant's immune system.

## WEIGHT: Fast early gain

Significant increase in risk of overweight status in adulthood, associated with increasing weight gain in the first week of life

Stettler N, *et al.* 2005

Yadav M, *et al* 2000.

The *exclusively* breastfed, *well gaining* 5 month old is getting NO MORE milk than the exclusively breastfed, well gaining 1 month old, even though the 5 month old is twice as heavy

Newman  
Kent 2007



## WEIGHT: Review of the Evidence:

11 studies

prevalence of overweight in children older than 3 years of age

sample size of 100 per feeding group,

8 showed a lower risk of overweight in children who had been breastfed,

3 "negative" studies lacked info on the exclusivity of breastfeeding.

dose-response relationship with duration of breastfeeding was observed in some, but not all, of the "positive" studies.

Possible mechanisms:            learned self-regulation of energy intake,  
   metabolic programming in early life,  
   residual confounding by parental attributes.

If the association is causal, the effect probably small compared to other factors that influence child obesity, such as parental overweight.

Dewey, K.G.,2003,

# WEIGHT: LEPTIN

- Protein found in breastmilk
- Hormone that regulates energy, decreases food intake, increases energy expenditure
- Breastmilk is the main source of leptin in the first half of breastfeeding
- Milk leptin correlates positively with maternal plasma leptin and maternal bmi
- Produced by adipose and other tissues to signal receptor sites throughout the body of the adequacy of energy stores
- Main physiologic role of leptin: Regulation of the neuroendocrine system during starvation
- Leptin appears to provide moderate protection from excess weight gain
- Total deficiency or resistance to leptin causes severe obesity

*Gillman, M, 2007*  
*Miralles, Olga, 2006*  
*Rexford, S. et al 1996*  
*Stettler, N, 2005*  
*Taveras, EM 2006*  
*Weyermann, M 2006*

# LEPTIN

- Satiety-- early satiety and tighter energy regulation establishing a different “set point” in breastfed infants
  - prime or set the endocrine system at a different homeostatic energy regulation balance
  - positive effect on satiety and regulation of energy intake
- Leptin intake during lactation prevents obesity and affects food intake and food preferences in later life
- Infant body weight in first 2 yrs may be influenced by milk leptin concentration in the 1<sup>st</sup> stages of lactation
- Negative correlation with infant bmi at 18 and 24 mo

*Gillman, M, 2007*  
*Miralles, Olga, 2006*  
*Rexford, S. et al 1996*  
*Stettler, N, 2005*  
*Taveras, EM 2006*  
*Weyermann, M 2006*

# LEPTIN

- Leptin levels  $\uparrow$  negative feedback signal controlling energy homeostasis limiting obesity in times of nutritional abundance
  - Leptin  $\downarrow$  during starvation and totally deficient ob mice have endocrine abnormalities similar to those of starvation
- Preventing starvation with exogenous leptin (ie in breastmilk) blunts changes in gonadal, adrenal, and thyroid axes in male mice, and prevents starvation-induced delay in ovulation in female mice

*Gillman, M, 2007  
Miralles, Olga, 2006  
Rexford, S. et al 1996  
Stettler, N, 2005  
Taveras, EM 2006  
Weyermann, M 2006*

**Table 1:** Breast milk hormones.

Hormone	Year of discovery	Receptor	Detection of receptor in intestine	Main functions	Year of discovery in breast milk	Method of detection in breast milk	Detection in umbilical cord blood
Leptin	1994	Ob-receptor	In humans [17]	Anorexigenic effect	1997	RIA [1, 18], ELISA [16]	[12, 19, 20]
Adiponectin	1995	Adipo-R1 Adipo-R2	In humans [21]	Improvement of insulin sensitivity, increase in fatty acid metabolism, anti-inflammatory and anti-atherogenic properties	2006	RIA [2], ELISA [22]	[20]
Ghrelin	1999	Growth hormone secretagogue receptor -1a	In humans [23]	Orexigenic action; stimulation of GH secretion; stimulation of acid gastric secretion and motility	2006	RIA [4, 24]	[25]
IGF-I	1950	IR IGF-IR IGF-IIR Insulin receptor-related receptor IR-IGF-IR hybrid receptor	In humans [26]	Primary mediator of growth hormone effects; role in the regulation of postnatal human growth from late infancy onward	1984	RIA [3]	Ibáñez L et al., 2008; Lagiou P et al., 2009
Resistin	2001	Unknown	Unknown	Regulation of insulin sensitivity	2008	ELISA [6]	[27]
Obestatin	2005	GPR39	In mice [28]	Anorexigenic effect?	2008	RIA [5]	Unknown?

# Why would breastfeeding protect?



# THE MOTHER WHO DOES NOT BREASTFEED HER BABY IS AT RISK OF...



## METABOLIC DISORDERS

Women who exclusively breastfeed for a longer duration may have a slight improvement in their postpartum weight loss.

*Kramer & Kakuma 2002*

Breastfeeding has been linked to a small reduction in risk of the mother developing type 2 diabetes, as long as she did not develop gestational diabetes.

*Ip et al. 2007*

Subsequent research suggests that breastfeeding for as little as one month may be protective against maternal type 2 diabetes.

*Schwarz et al 2010*

*With thanks to H. deVeber*



## Weight loss

- Maternal wt loss was greater in BF than Formula feeding mothers, especially between 3-6 months
- Frequency and total breastfeeding times were related to wt loss in the bf group at 6-12 months

*Dewey KG, 1993*

- Association between BF and postpartum weight retention and that prolonged BF might contribute to decreased wt retention

*Kag, 2004*

## CANCER

### Lactation and Incidence of Premenopausal Breast Cancer, *A Longitudinal Study*

60 075 parous women participating in the prospective cohort study of the Nurses' Health Study II from 1997 to 2005. Our primary outcome was incident premenopausal breast cancer.

**Conclusion:** In this large, prospective cohort study of parous premenopausal women, having ever breastfed was inversely associated with incidence of breast cancer among women with a family history of breast cancer.

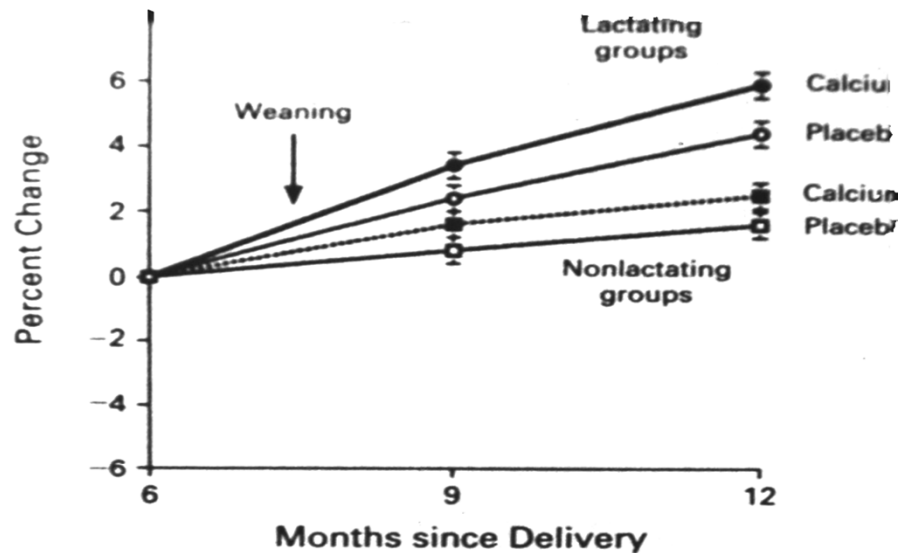
*Stuebe, A. et al, 2009*

## Duration of Lactation and Risk Factors for Maternal Cardiovascular Disease

139,681 post-menopausal women, average age 63,  
1-6 months → had less diabetes, less high blood pressure and less high cholesterol  
7 months → significantly less likely to have developed cardiovascular disease compared to women who had never breastfed.  
12 months → 10 per cent less likely to have had a heart attack or stroke or developed heart disease when they were older

*Bimla Schwarz, E. et al. 2009*

## Osteoporosis The Effect of Calcium Supplementation on Bone Density during Lactation and after Weaning



**Figure 2.** Effects of Calcium Supplementation and Lactation on the Mean ( $\pm$ SE) Percent Change in the Bone Mineral Density of the Lumbar Spine during the Second Six Months Post-Partum.

Values are adjusted for base-line bone mineral density, height, weight, change in weight, dietary intake of calcium, and level of physical activity.  $P < 0.001$  for the effect of calcium;  $P < 0.001$  for the effect of weaning; and  $P = 0.36$  for the interaction between calcium supplementation and weaning. The lactating women were fully breast-feeding at base line, and the arrow indicates the average time at which breast-feeding was completely ended.

Increase in bone density after weaning, no permanent loss of bone mineral content, and full recovery after weaning

Kalkwarf, H.J., et al. 1997

## Other Sequelae

- No iron deficiency—delayed, menses, etc
- Type 2 diabetes—longer duration associated with less incidence
- Neoplastic disease—longer duration and most recent breastfeeding protective
- Breast cancer—prolactin mitigating the effects in cases of metastatic
- Ovarian cancer—breastfed vs not breastfed, unrelated to duration
  - Other studies found duration was related to risk—longer =less risk

Martin, R, 2003  
Stuebe AM, 2005  
Rosenblatt KA, 1995  
Ali, S, 2011  
Titus-Erstoff L, 2001  
Tung K-H, 2003

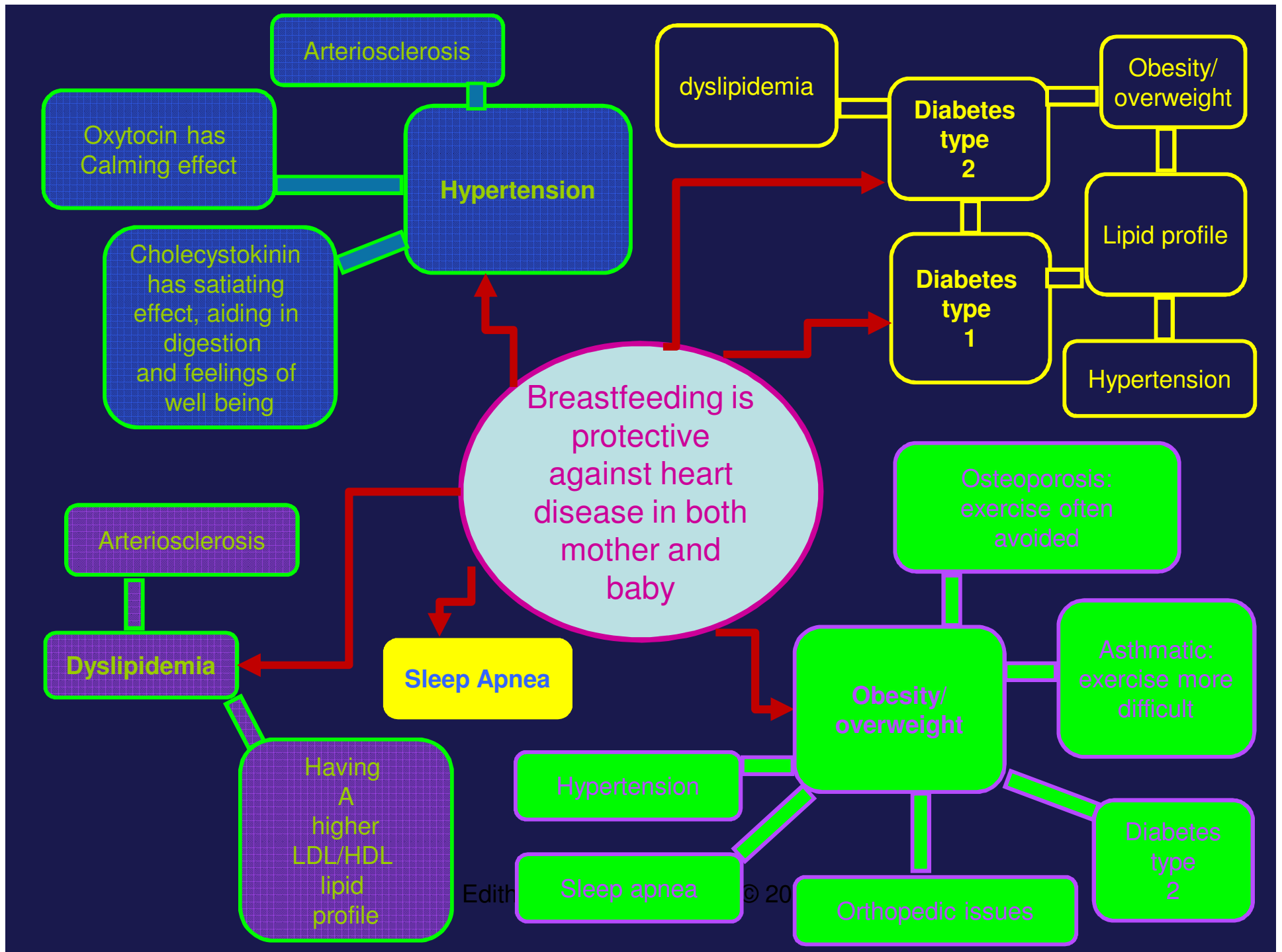
## Duration of Lactation and Risk Factors for Maternal Cardiovascular Disease

One theory is that breastfeeding lowers that risk by mobilizing fat stores. Breastfeeding has an important role in the way women's bodies recover from pregnancy," Schwarz says.

When milk isn't expressed, she said, women don't unload all the body fat stored up during pregnancy.

Prolactin and oxytocin, hormones involved in producing milk and releasing it from the body, may also have effects on a woman's heart.

*Bimla Schwarz, E. et al. 2009*



## ASSIGNMENT

- Choose between Breast Cancer, Cancer in General, Allergy in the baby, Mental Disease
- Create a chart similar to the ones I have done for heart disease and obesity
  - How does breastfeeding protect?
  - Use references
- I'LL INCLUDE THE VERY-WELL RESEARCHED, ORGANIZED, DESIGNED ONES IN MY TALK NEXT YEAR AND FUTURE YEARS AND GIVE YOU CREDIT!!
- HAVE FUN!!!!



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