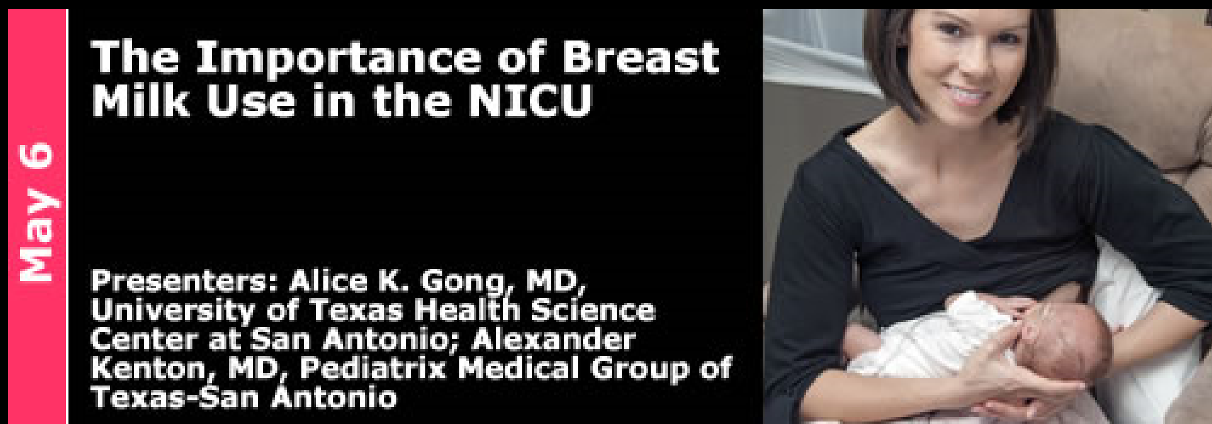
DSHS Grand Rounds



Logistics

Registration for free continuing education (CE) hours or certificate of attendance through TRAIN at:

https://tx.train.org

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1. webinar: http://www.dshs.state.tx.us/grandrounds/webinar-no-CE.shtm
2. live audience: sign in at the door

For registration questions, please contact Laura Wells, MPH at
CE.Service@dshs.state.tx.us

Logistics (cont.)

Slides and recorded webinar available at:

http://www.dshs.state.tx.us/grandrounds

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For those in the auditorium, please come to the microphone to ask your question.

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Disclosure to the Learner

Requirement of Learner

Participants requesting continuing education contact hours or a certificate of attendance must register in TRAIN, attend the entire session, and complete the online evaluation within two weeks of the presentation.

Commercial Support

This educational activity received no commercial support.

Disclosure of Financial Conflict of Interest

The speakers and planning committee have no relevant financial relationships to disclose.

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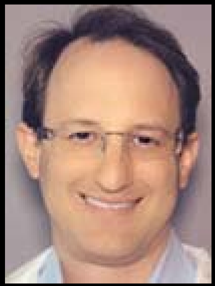
Kirk Cole
Interim DSHS Commissioner
is pleased to introduce our
DSHS Grand Rounds speakers

The Importance of Breast Milk Use in the NICU

Alice K. Gong, MD
Professor of Pediatrics, Rita and William Head
Distinguished Professor of Environmental and
Developmental Neonatology,
UT Health Science Center at San Antonio



Alexander Kenton, MD
Pediatrix Medical Group of Texas-San Antonio

The Importance of Breast Milk Use in the NICU

Alice Gong, M.D.
Professor of Pediatrics
Rita and William Head Distinguished Professor of
Environmental and Developmental Neonatology
UTHSCSA

Alex Kenton, M.D.

"A pair of mammary glands has the advantage over the 2 hemispheres of the most learned professor's brain, in the art of compounding a nutritious fluids for infant."

-Oliver Wendell Holmes

WE MAKE LIVES BETTER
UT HEALTH SCIENCE CENTER
SAN ANTONIO

Objectives

- Outline specific properties of human milk making it unique and important to the development of the GI and immune system.
- Recognize the impact of human milk feedings in promoting the health of infants.
- Describe the specific mortality and morbidity benefits, and consequential cost savings by the use of human milk as the sole nutritional source for premature infants.

Human Milk

- Best for human neonates, infants, and mothers
- Facilitate transition of *in utero* to *ex utero* life
- Diverse array of bioactive substances to developing infant during critical times of brain, immune, and intestinal tract development.

Human Milk

- prevent microorganisms from penetrating body
  - bind to microbes to block them from attaching to and crossing through the mucosa.
  - Lessen supply nutrients that harmful bacteria need to survive in the digestive tract.
  - immune cells phagocytes microbes directly.
  - produces chemicals that stimulates infant's own immune response.

Lactogenesis

- Stage 1 (15-20 weeks of pregnancy)
  - Mammary gland becomes competent – alveolar cells differentiated from secretory cells. High progesterone and estrogen keep milk secretion in check (Endocrine control).
  - Lactose, total protein, immunoglobulins increase within glandular fluid
  - Na, Cl decrease

Lactogenesis

- Stage 2 (day 2 or 3 to day 8 after birth)
  - Onset of copious milk secretion; tight junctions in alveolar cell closes
  - Blood flow, oxygen, glucose uptake, and citrate increase
  - Removal of placenta (Progesterone) necessary.
    - Progesterone receptors lost in lactating mammary tissue, decreasing inhibitory effect
  - Maternal secretion of insulin, GH, cortisol, and PTH facilitate mobilization of nutrients and minerals for lactation
  - Endocrine control to **Lactogenesis Stage 3, autocrine (supply-demand)**

Involution – Loss of Supply

- Regular extraction of milk ceases (supplementation added)
- Prolactin decreases; buildup of inhibiting peptides leads to decrease milk supply
- Cessation of milk secretion leads to apoptosis of mammary epithelium, remodeling of gland to prepregnant state

Lactation

- Process of milk secretion – continue as long as milk is removed from gland on regular basis
- 2 essential homones in combination
  - Prolactin to maintain secretion
  - Oxytocin to produce let-down to allow extraction of milk
- Volume of milk secreted is adjusted to requirements of infant by local factors
  - Feedback inhibitor of lactation (FIL)
  - Stretching and flattening of mammary epithelial cells

Review of Milk Production

- Synthesis continuously and secreted into alveolar lumen, stored until ejected.
- **Prolactin** mediates CNS regulation of **milk secretion.**
- **Oxytocin** participates in neuroendocrine reflex that stimulates myoepithelial cells that leads to **milk ejection**.
- Letdown inhibited, milk cannot be removed, local mechanisms bring about inhibition of milk secretion.
- With consistent partial removal of milk, local factors (FIL) adjust milk secretion to new steady state.
- Milk removal ceases, involution sets in and gland loses competency to secrete milk in days to weeks.

- With proper support, 97% of women can successfully breastfeed their infants!
  - Essential for species survival
  - Why?

- Primates give birth to babies that remain vulnerable for a long period of time
  - Human babies cannot be independent for many years
  - Capability of developing tremendous abilities given time and encouragement.
- Normal neurobiological development requires prolonged access to the mother.
- Breastfeeding provides access to high quality food and proximity and frequent interaction with a primary caregiver for optimal outcomes.

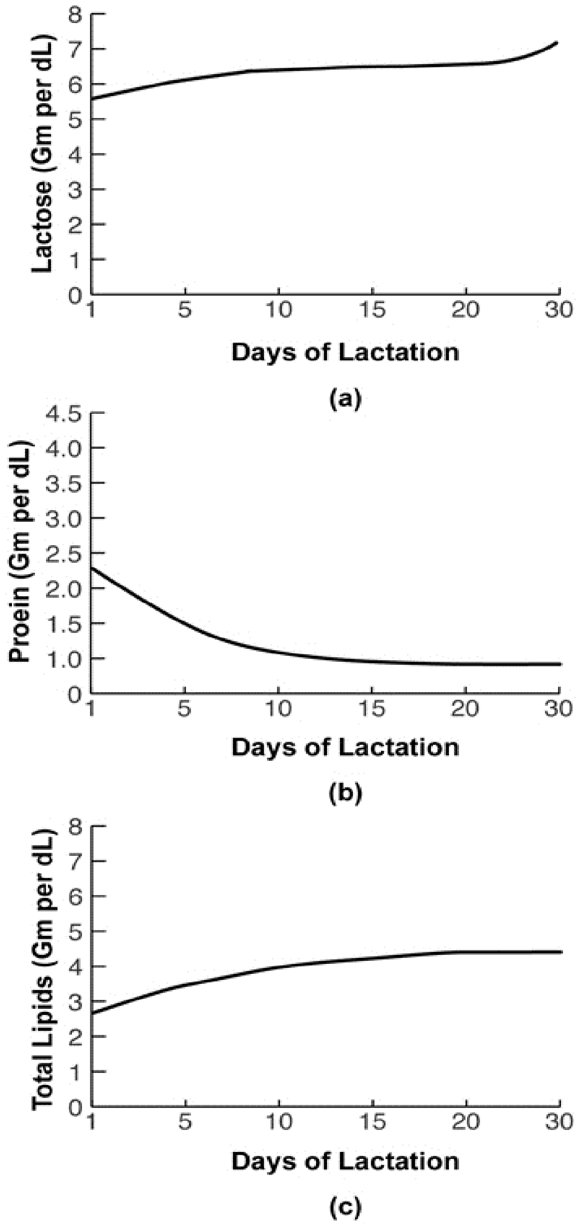
Human Milk - What's in it?

- Water – 88%
- Carbohydrate (5.6-6.9%)
  - Lactose synthesized within alveolar cell
  - α-glucosides
- Lipids (3.4-4.4%)
  - Triglycerides contained in fat globules surrounded by membranes produced by alveolar acini
    - Membranes complex of phospholipids, glycolipids, triglycerides, cholesterol, proteins (emulsifier)
  - short-chain FA and long-chain polyunsaturated FA
    - Large amounts omega 6 and omega 3 LCPFA
- Protein (whey:casein – 60-65:35-40)
  - Mixture of casein, albumin, lactalbumin, immunoglobulins, and lysozyme
  - Nonprotein nitrogen – free amino acids, urea
  - Colostrum higher than mature milk due to increase IG

Characteristics

- Nonuniform – changes over time, over course of feeding with diurnal variation, and as infant matures.
  - Colostrum lower fat but higher protein and minerals.
  - Fore milk lower fat, as session progresses fat increases with hind milk thought to facilitate satiety
  - Diurnal varies reflecting maternal diet and daily hormonal fluctuations.
- pH – 7.08 (6.35-7.65)
  - Colostrum – 7.45, 7.0 in transition milk, slow rise to average of 7.4 by age 10 months.
  - Foremilk more acidic than hindmilk

Changes in Milk Appearance and Composition Over Time



Lactose, Protein, and total lipid concentrations in human milk.

TABLE 1-1

Comparison of Colostrum (day 1) and Mature Human Milk*

Constituent (per liter)	Colostrum	Mature Milk
Energy (k cal)	670	750
Lactose (g)	20.0	35.0
Protein (g)	32.0	9.0
Fat (g)	12.0	38.0

*Data adapted from Lawrence and Lawrence (2005), pp 110 and tables 4-5 and 4-7, pp113

Colostrum – The First Vaccine, Liquid Gold

- First fluid after delivery, distinct in volume, appearance, composition
- Primary function – immunologic and trophic
  - Rich in sIgA, lactoferrin, leukocytes, EGF
  - Low lactose
  - High Na, Cl, Mg
  - Low K, Ca
- As mammary epithelium tight junction closes, Na:K declines, lactose increases – signaling secretory function of transitional milk production

Human Milk

- Enzymes to assist digestion and absorption
  - Biosynthesis of milk
    - Lactose synthetase, fatty acid synthetase, thioesterase
  - Digestion of proteins, fats, carbohydrates
  - Transport moieties for minerals

Immunologic Properties

- Human milk IG
  - All different ABs (M, A, S, G, E)
  - sIgA – source of passively acquired immunity before endogenous production

Immunoglobulins in Human Milk

	Output - mg/24 hours		
Day Postpartum	**IgG**	**IgM**	**IgA**
1	80	120	11,000
3	50	40	2,000
7	25	10	1,000
8 – 50	10	10	1,000

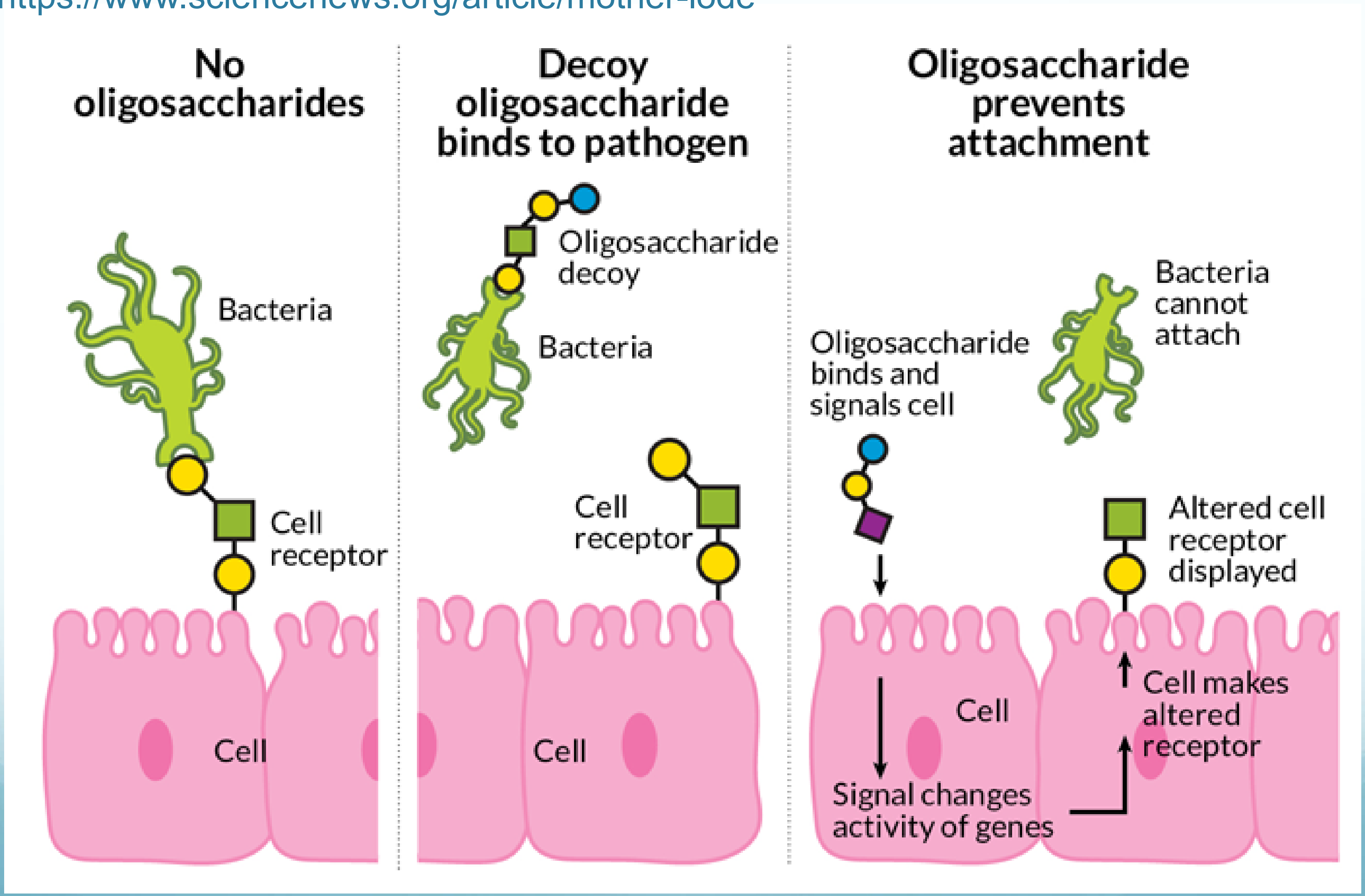
Adapted from: Remington JS and Klein JO (2001) *Infectious Diseases of the Fetus and Newborn, Fifth Edition.*

Immunologic Properties

- Lactoferrin (binds Fe)
  - Multiple anti-inflammatory and antimicrobial properties
  - Involved in phagocytic killing and immune response
  - Acts synergistically with anti-staphylococcal and anti-*Candida* agents (rHL)
- Lysozyme
  - Enhances sIgA bactericidal activity against g – organisms.
- Oligosaccharides
  - Intercept bacteria and form harmless compounds to be excreted

Superhero sugars in breast milk make the newborn gut safe for beneficial bacteria

by Jessica Shugart 2:05pm, December 27, 2013
https://www.sciencenews.org/article/mother-lode



Immunologic Properties

- Milk Lipids
  - Damage membranes of enveloped viruses
- Mucins
  - Adhere to bacteria and viruses and help them be eliminated
- Interferon and fibronectin
  - Antiviral activities
  - Enhance lytic properties of milk leukocytes

Cells

- Macrophages
  - 40-60% cells in colostrum
  - 80-90% in mature milk
- Lymphocytes
- Polymorphonucleocytes
- Mammary epithelial cells
- Stem Cells
- HAMLET (Human a-lactalbumin Made Lethal to tumor cells) – multimeric α-lactalbumin

Cells in Human Milk: State of the Science

Journal of Human Lactation
29(2) 171–182

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DOI: 10.1177/0890334413477242
jhl.sagepub.com
SAGE

Foteini Hassiotou, PhD[1], Donna T. Geddes, PhD[1], and Peter E. Hartmann, PhD[1]

-Leukocytes, stem cells, progenitor cells, lactocytes, and myoepithelial cells present in breastmilk that infants ingest.

-Animal models demonstrated that milk leukocytes diapedese through the intestinal mucosa to enter system circulation and then are transferred to various organs and contribute to protection and immune development of the young.

-Stem cells are also transported and result in microchimerism, engrafted to infant organs, contributing to tissue homeostasis, repair, regeneration.

Bioactive Components

- Elements that affect biological processes/substrates, have impact on body function and health
  - Epidermal growth factor
  - Vascular endothelial growth factor
  - Nerve growth factor
  - Insulin-like growth factor
  - Interleukins
  - Transforming growth factor – alpha and beta
  - Erythropoietin
  - Granulocyte colony-stimulating factor

Bioactive Components

- Produced either by mammary gland epithelial cells or milk cells or transported from maternal serum.
- EGF and TGF-α higher in premature milk
- EGF, TGF-α, and human milk stimulate fetal small intestinal cell proliferation in vitro
- Maheshwari et al, 2011 - Intestinal macrophages progressively acquire a noninflammatory profile during gestational development.
  - TGF-β, particularly TGF-β_2 isoform, suppresses macrophage inflammatory responses in the developing intestine and protects against inflammatory mucosal injury.
  - Enterally administered TGF-2 protected mice from experimental NEC-like injury.

Summary of Major Differences between Human Milk and Commercial Substitutes Marketed for Normal Term Infants

	Human milk	Commercial Substitutes
Protein	Appropriate (species specific) quality/quantity, easier to digest	Corrected in quantity but not in quality (not species specific)
Fat	Appropriate quality/quantity of essential fatty acids, lipase present	Lipase absent
Vitamins	Adequate except for vitamins D and K in some situations (see text)	Vitamins added
Minerals	Correct amount	Partly corrected
Anti-infective properties	Present	Absent
Growth factors	Present	Absent
Digestive enzymes	Present	Absent
Hormones	Present	Absent

Adapted from WHO/CDR/93.6. and further modified, 2009

Breastfed infants do not share same illness or mortality rates as artificially fed children

Eglash et al, Breastfeeding. Dis Mon. 54:343-411, 2008.

Introducing Formula Increases Risk of:

- Gastroenteritis
- Asthma
- Obesity
- Type I diabetes
- Type 2 diabetes
- Leukemia
- Necrotizing enterocolitis
- Lower respiratory tract infections
- Urinary tract infections
- Otitis media
- Atopic dermatitis
- Hypertension
- High cholesterol
- SIDS

Long Term Protection Lost in Artificial Fed Infants Resulting in Increases:

- Obesity
- Type 1 and 2
- Lymphoma
- Leukemia
- Asthma
- hypercholesterolemia

Maternal Outcomes – Lack of Breastfeeding/Early Cessation

- Type 2 diabetes
- Breast cancer
- Ovarian cancer
- Postpartum depression
- Obesity
- Cardiovascular diseases

Mothers who Breastfeed

- Lower BP
- Enhance immune activity
- Increase efficiency in nutrient metabolism
- Modify calcium metabolism
- Delay fertility return

Societal Benefits

- Low cost, high quality food for babies
- Improves health and increase infant survival
- Improves maternity recovery and reduce CA
- Lowers family expenditures
- Contributes to fertility reduction
- Safe in emergency and disaster situations
- Supports environment
- Decrease workplace absence

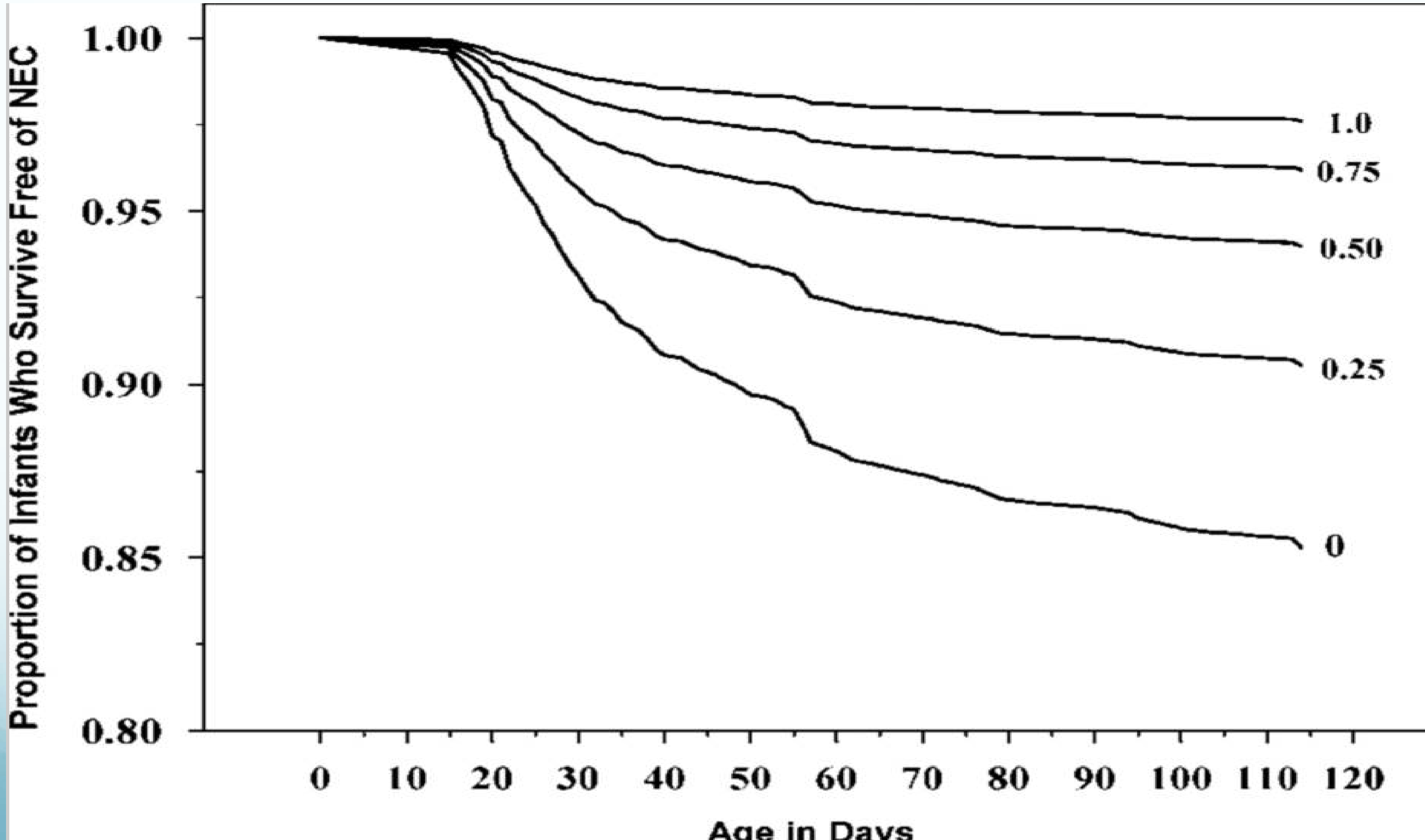
POLICY STATEMENT
Breastfeeding and the Use of Human Milk

- All Preterm Infants should receive human milk
    - Human milk should be fortified with protein, minerals, and vitamins to ensure optimal nutrient intake for infants < 1500 grams at birth
    - Pasteurized donor human milk, appropriately fortified should be used if mother's own milk is unavailable or its use is contraindicated

Why?

- Evidence that it reduces costly and handicapping morbidities such as sepsis, NEC for VLBW infants.
- BM empties stomach faster resulting in less residuals and faster realization of enteral feeding
  - Fewer IV days
  - Less side effects from TPB
  - Less infections
  - Less costly and fewer hospital days
- Human milk stimulates GI growth, motility and maturation
- Enzymes in BM help immature infants absorb and utilize nutrients more efficiently
- Reduce incidence of Necrotizing Enterocolitis.
- Higher IQ scores

Adjusted Survival Curves by Milk Proportion



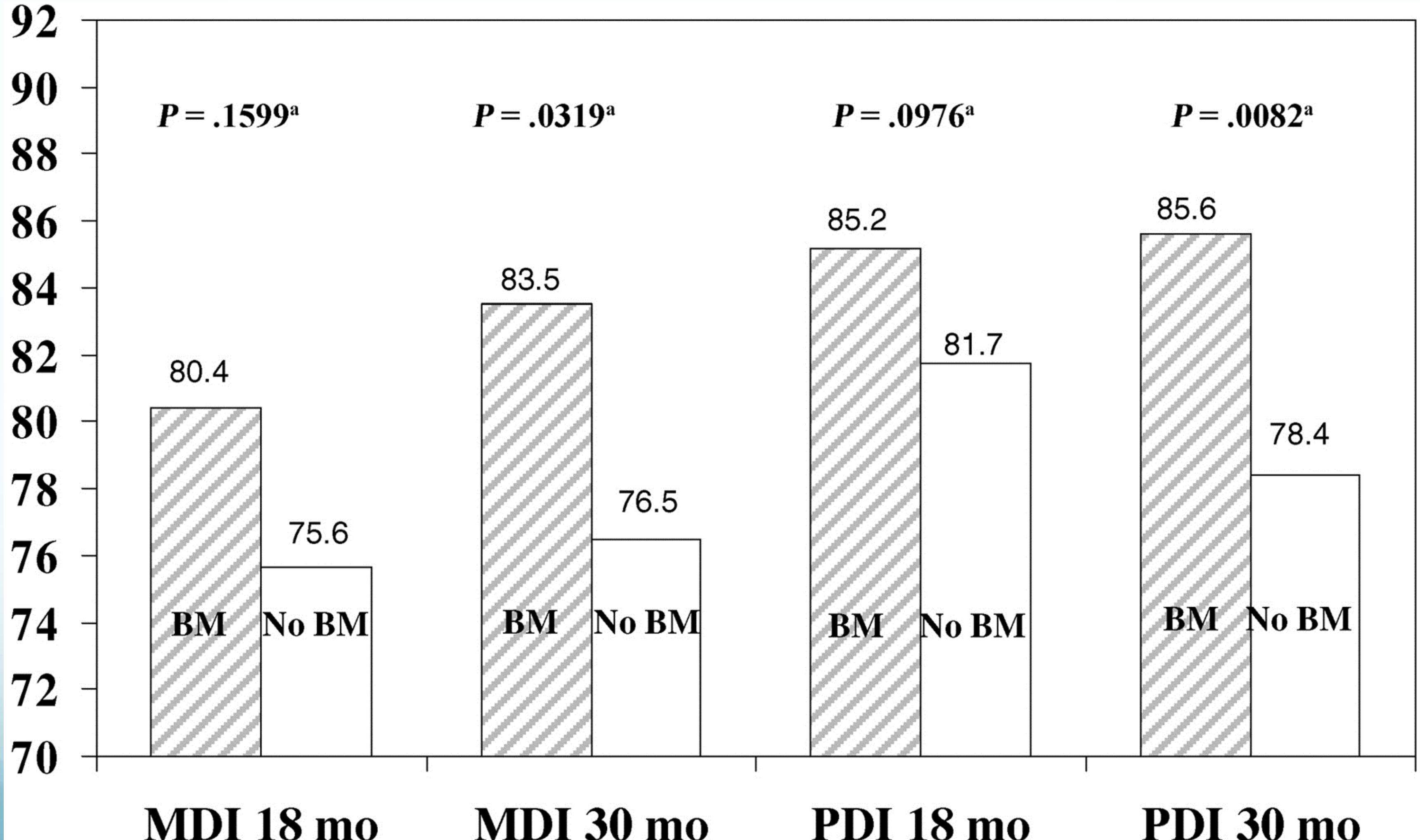
Meinzen-Derr J et al, *J Perinatol*. 2009

Every Ounce Counts!

- For every 10 mL/kg per day increase in breast milk
  - Mental Developmental Index increased by 0.59 points,
  - Psychomotor Developmental Index by 0.56 points,
  - Behavior percentile score by 0.99 points
  - Risk of rehospitalization between discharge and 30 months decreased by 5%.

Vohr B, *Pediatrics*, 2007

Mean, MDI and PDI Scores at 18 and 30 Months According to Any BM Feeding



Human Milk versus Formula- The Study that Got Everyone Talking

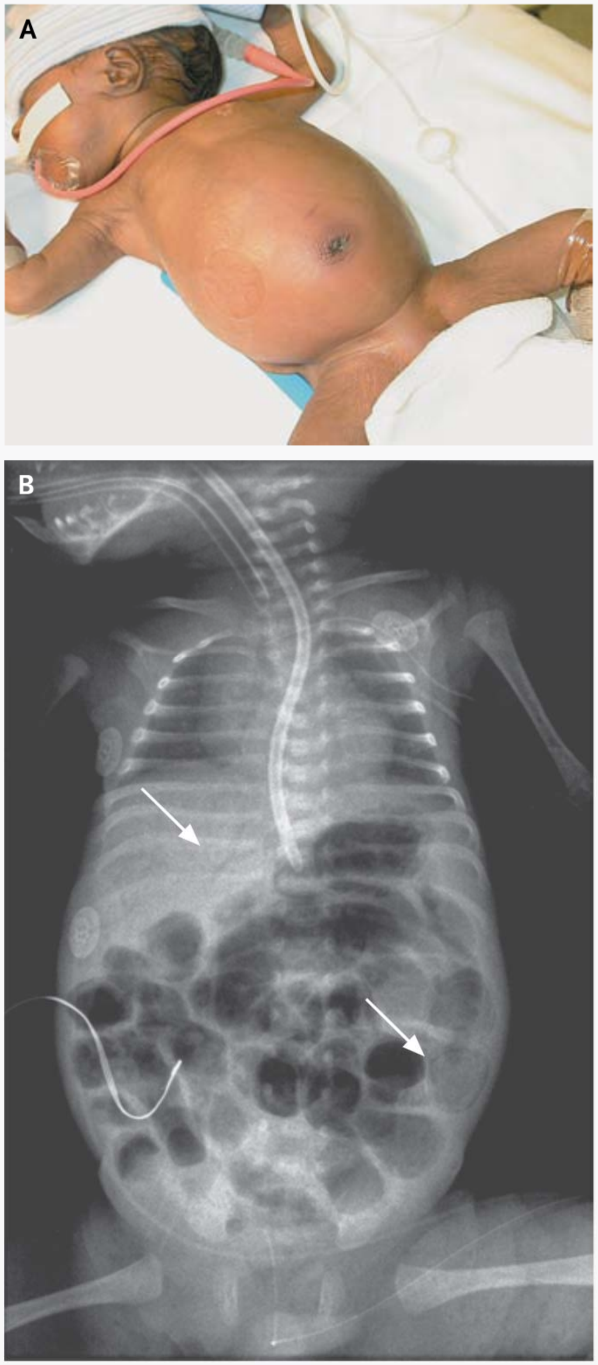
- 243 ELBW (mean wt 947-999 grams and gest. age 27$\pm$2 wks)
- Maternal Breast milk associated with
  - Decreased LOS, decreased incidence of late onset sepsis and NEC combined and decreased Mortality and NEC combined compared to donor milk and formula combined.
- Most recent study cited demonstrated that infants fed human milk with human milk based fortifier had 1.7% rate of NEC versus 15.3% incidence in those whose fortifier was bovine based milk
- Number needed to treat to prevent one case of surgical NEC was 8

Sullivan S et al., *J Pediatr 2010*

Necrotizing Enterocolitis (NEC) The Scope of the Problem

- NEC is the most common cause of G.I. Emergency in the NICU
- It occurs in 5-7% of Very Low Birthweight Infants
- It occurs in 15% of ELBW (< 28 weeks and < 1000 grams)

Holman RC, et al, *Pediatr Perinata Epidemiol. 2006*
Hobar JD, et al. *Pediatrics. 2002*
Fitzgibbons SC, et al. *J Pediatr Surg. 2009*



Necrotizing Enterocolitis (NEC) Outcomes

-50% Mortality

-Short Bowel syndrome

-Cholestatic Liver Disease

-Sepsis

-Developmental Delay

-Prolong Hospital stay by 60 days

Neu J er al. *N.Eng J Med. 2011*

Breast milk protects against the development of necrotizing enterocolitis through inhibition of Toll-like receptor 4 in the intestinal epithelium via activation of the epidermal growth factor receptor

M Good[1,2], CP Sodhi[3,4], CE Egan[5,6], A Afrazi[5,6], H Jia[3,4], Y Yamaguchi[3,4], P Lu[5,6], MF Branca[5,6], C Ma[1,2], T Prindle Jr[3,4], S Mielo[5,6], A Pompa[5,6], Z Hodzic[5,6], JA Ozolek[7,8] and DJ Hackam[3,4]

Mucosal**Immunology,** 2015

BM is the Most Effective Strategy to Protect Infants against NEC

- BM reduced TLR4 signaling in wild type neonatal mice, not in mice lacking EGFR
- Selective removal of EGF from BM reduced protective properties
- Overexpression of TLR4 reversed protective effects of BM
- Protective effects of BM – inhibition of apoptosis and restoration of enterocyte proliferation

Necrotizing Enterocolitis (NEC): The Scope of the Problem

- 55% of births are covered by Medicaid (NEC occurs in 0.2%)
- Each Additional case of NEC costs the State of Texas
  - $60,000.00 per case of surgical NEC over 3 years of outpatient costs
  - $5000.00 per case of medical NEC over 6 months of outpatient costs
  - NEC costing the state $10 million additional outpatient costs per year

Ganapathy V, et al. *BMC Pediatrics. 2013*

Necrotizing Enterocolitis (NEC): The Scope of the Problem

Inpatient Costs

- 1 Surgical NEC case adds hospital charge of $186,200.00
- 1 Medical NEC case adds hospital charge of $73,700.00

In 2010 with 386,000 births and 55% covered by Medicaid

- Surgical NEC cases (127 patients) have added charges of $23 million/year
- Medical NEC cases (360 patients) have added charges of $26 million/year

Total added hospital charges in the state of Texas is $49 million/year!

Strategies to Prevent Necrotizing Enterocolitis

Table 2. Measures to Prevent Necrotizing Enterocolitis.*

Evidence of Efficacy and Safety	Evidence of Efficacy but Questionable Safety	Evidence of Efficacy in Animal Models but Not in Humans	Proposed Efficacy but Lacking Evidence
Breast-milk feeding	Enteral aminoglycosides	Anticytokines	Prebiotics (derived from plants and breast milk)
Nonaggressive enteral feeding	Probiotics	Growth factors	Microbial components and toll-like-receptor agonists
	Glucocorticoids		Glutamine, n-3 fatty acids
	Arginine		

* Adapted from Grave et al.[2] and Neu.[20]

Neu J, *Acta Paediatr. Suppl* 2005

Formula versus Donor Breast Milk for Feeding Preterm or Low Birth Weight Infants

Maria Quigley, William McGuire

- 9 trials, 1070 infants.
  - 4 compared standard term formula versus donor breast milk and 5 compared nutrient-enriched preterm formula versus donor breast milk.
- 2 recent trials - nutrient-fortified donor breast milk.
- No effect on post-discharge growth rates or neurodevelopmental outcomes.
- ***Formula feeding increased the risk of NEC: typical risk ratio 2.77 (95% CI 1.40 to 5.46); risk difference 4% (95% CI 2% to 7%).***

Cochrane Database of Systematic Reviews 2014

Table II. Clinical outcomes of study infants

	BOV	HUM
Parenteral nutrition, d*	36 (28, 77)	27 (14, 39)
Late-onset sepsis, n	19 (79%)	16 (55%)
NEC, n†	5 (21%)	1 (3%)
NEC surgery, n‡	4 (17%)	0
NEC and/or death, n†	5 (21%)	1 (3%)
Mechanical ventilation, d	24 (10, 75)	17 (2, 38)
Oxygen therapy, d	28 (21, 61)	20 (5, 32)
Retinopathy of prematurity, n	5 (21%)	8 (28%)
Death, n	2 (8%)	0

Values are median (25th, 75th percentile).
*$P = .04$.
†$P = .08$.
‡$P = .036$.

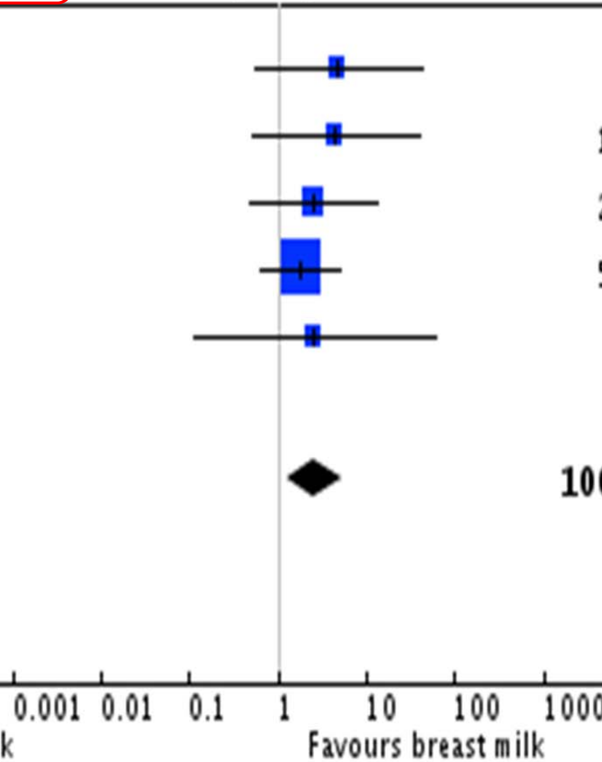
Cristofalo EA, Schanler RJ, Blanco CL, Sullivan S, Trawoeger R, Kiechl-Kohlendorfer U, et al. Randomized trial of exclusive human milk versus preterm formula diets in extremely premature infants. J Pediatr. 2013;163:1592-1595.

Human Breast Milk - Donor

Meta-analysis showed risk of NEC increased by 2.5 if fed formula vs. DBM

Study or subgroup	Formula milk n/N	Donor breast milk n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Gross 1983	3/26	1/41		8.1 %	4.73 [0.52, 43.09]
Lucas 1984a	4/76	1/83		10.0 %	4.37 [0.50, 38.23]
Lucas 1984b	5/173	2/170		21.0 %	2.46 [0.48, 12.49]
Schanler 2005	10/88	5/78		55.3 %	1.77 [0.63, 4.96]
Tyson 1983	1/44	0/37		5.7 %	2.53 [0.11, 60.39]
Total (95% CI)	**407**	**409**		**100.0 %**	**2.46 [1.19, 5.08]**

Total events: 23 (Formula milk), 9 (Donor breast milk)
Heterogeneity: $Chi^2 = 0.99$, df = 4 (P = 0.91); $I^2 = 0.0\%$
Test for overall effect: Z = 2.43 (P = 0.015)



Donor BM likely has protective effect against NEC as well

Quigley, et al. *Cochrane* 2008

Breast Milk Use in Premature Infants

SA Abrams et al. at Texas Children's Hospital

Compared 167 infants < 1250 grams fed human milk and donor human milk fortifier versus 93 infants who received human milk and cow milk based formula or fortifier

TABLE 2. OUTCOME OF STUDY INFANTS

	Group CM (n = 93)	*Group HM* (n = 167)	p *value*	*95% CI (difference)*
Mortality	7/93 (8%)	3/167 (2%)	0.04	0.3% to 13%
NEC	16/93 (17%)	9/167 (5%)	0.002	2.4% to 21.3%
Surgical NEC	11/93 (12%)	2/167 (1%)	0.0003	4.4% to 18.9%
Sepsis	32/93 (34%)	50/167 (30%)	0.46	−7.1% to 16.6%
TPN (median days)[a]	25	23	0.26	−2 to 5
Weight (g/kg/day)	13.6 ± 4.1	14.9 ± 7.2	0.11	−0.1 to 2.7
Length (cm/week)	0.89 ± 0.45	0.97 ± 0.35	0.12	−0.02 to 0.19
FOC (cm/week)	0.73 ± 0.23	0.77 ± 0.22	0.10	−0.01 to 0.11

[a]From the Kaplan and Meier[7] estimate.

CI, confidence interval; CM, milk containing cow milk-based protein; FOC, fronto-occipital circumference; NEC, necrotizing enterocolitis; HM, human milk fortified with a human milk protein-based fortifier; TPN, total parenteral nutrition.

Breastfeeding Medicine, 2014

Texas Data on Breast Milk Use in Premature Infants

Cook Hospital, Fort Worth, Texas

Results in reduction of NEC from 17.5% to 9.6%

Results in reduction in surgical NEC from 7.3% to 2.3%

University Hospital, San Antonio
Incidence of NEC in VLBW infants:
2002: 12% - started using Donor Milk
2004: 10%
2007: 7%
2009: 3.4% - Use of exclusive Human milk derived fortifiers

Human Milk Use - Magical Prevention of Morbidities and Amazing Cost Savings

- Premature Infants
  - Human Milk Use decreases the Incidence of
    - Bronchopulmonary Dysplasia
    - Brain Injury and Developmental Delay
    - Late Onset Sepsis
    - Necrotizing Enterocolitis

Economic Benefits and Costs of Human Milk Feedings: A Strategy to Reduce the Risk of Prematurity-Related Morbidities in Very Low-Birth-Weight Infants

Tricia J. Johnson, Aloka L. Patel, Harold R. Bigger, Janet L. Engstrom and Paula P. Meier

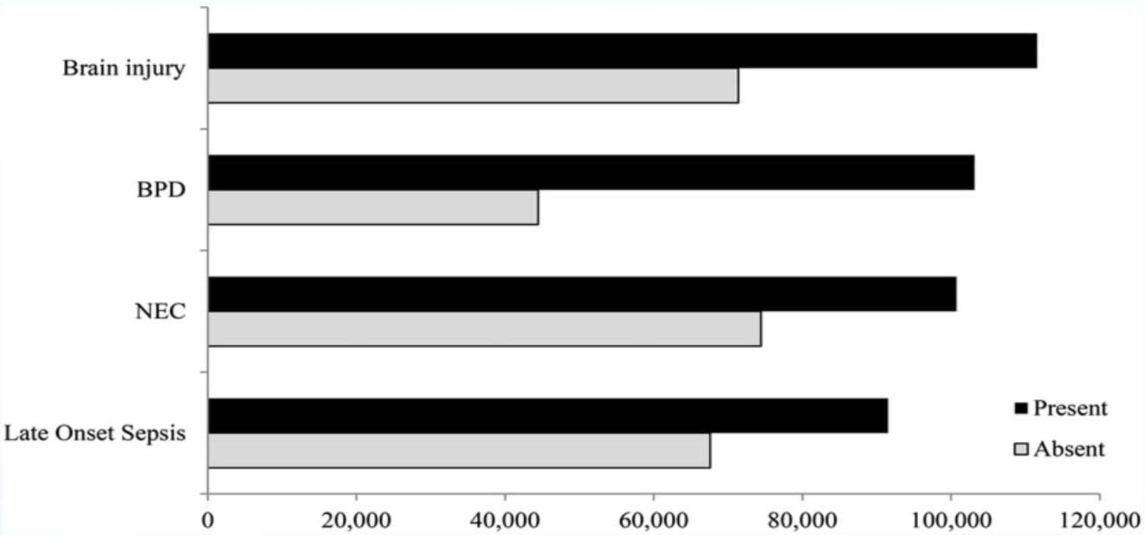


Figure 1: Competition of hospital direct costs with and without specific morbidity on 2009 US$, BPD, bronchopulmonary dysplasia, NEC, necrotizing enterocolitis

Impact of Human Milk on Costs of Preventable Morbidities in VLBW Infants

Authors	Type of costs	BW	Morbidity	Cost savings of HM	Year of costs
Ganapathy et al. (8)	Incremental cost due to reduction in NEC: HM bovine	≤1250 g	NEC	Bovine milk associated with \$8167 higher cost than HM	2011
Patel et al. (13)	Incremental cost, after controlling for sepsis: <25, 25–49.99, and ≥50 $mL \cdot kg^{-1} \cdot d^{-1}$	<1500 g	Sepsis	<25 $mL \cdot kg^{-1} \cdot d^{-1}$ HM had \$31,514 higher cost than ≥50 $mL \cdot kg^{-1} \cdot d^{-1}$ HM and \$20,384 higher cost than 25–49.99 $mL \cdot kg^{-1} \cdot d^{-1}$ HM	2010

[1] BW, birth weight; HM, human milk; NEC, necrotizing enterocolitis.

Adv. Nutr., 2014.

The Burden of Suboptimal Breastfeeding in the United States: A Pediatric Cost Analysis

Authors: Melissa Bartick, MD, MSC (Dept. of Medicine, Cambridge Alliance and Harvard Medical School) and Arnold Reinhold, MBA (Alliance for the Prudent Use of Antibiotics, Boston)

TABLE 2 Figures and Assumptions Used in Calculating Cost Impact for Each Disease (2007 Dollars)

	Type and Duration of Breastfeeding	OR in Favor of Breastfeeding	Overall Incidence	Treatment Duration, y	Cost
OM	EBF and any breastfeeding for 3 mo	0.77 for any breastfeeding; 0.5 for EBF	1.9 episodes in first year (reported data are for children 6–11 mo old)	NA	$156 direct case per episode; $291 total cost per episode
Gastroenteritis	EBF for 6 mo	0.36	0.222 ambulatory visits; 0.00298 hospitalizations in infants <1 y old	NA	$66 direct cost per outpatient visit; $2395 direct cost per hospitalization; $339 total costs per outpatient visit; $2668 total cost per hospitalization
NEC	Exclusively breast milk-fed for 3 mo	Risk ratio of 0.42	LBW infants: 0.00308 infants; VLBW infants: 0.0414	NA	LBW: $150 406 direct cost surgical NEC: $81 219 direct cost medical NEC VLBW: $260 506 direct cost surgical NEC; $140 858 direct cost medical NEC LBW: $155 845 total cost surgical NEC; $84 858 total cost medical NEC; VLBW: $265 945 total cost surgical NEC; $144 497 total cost medical NEC
NEC deaths	Exclusively breast milk-fed for 3 mo	0.42	LBW: 0.058 of NEC; VLBW: 0.20 of NEC	NA	$10 560 000 per case
Hospitalization for LRTI	EBF for 4 mo	0.28	0.0409	NA	$4338 direct cost per case; $4680 total cost per case
Deaths from LRTI	EBF for 4 mo	0.28	0.0000732	NA	$10 560 000
AD	EBF for 3 mo	0.68	0.165 cumulative incidence for first 2 y of life	6	$393 direct cost per y; $2131 direct costs per case; $787 total cost per y; $4263 total cost per case
SIDS	Any breastfeeding for 6 mo	0.64	0.00054	NA	$10 560 000
Childhood asthma	Any breastfeeding for 3 mo	0.73	0.127 cumulative incidence during childhood	10	$453 direct cost per y; $3633 direct cost for 10 y; $774 total cost per y; $6602 total cost per case
Childhood deaths from asthma	Any breastfeeding for 3 mo	0.73	0.00000273	NA	$10 560 000
Childhood leukemia	Any breastfeeding for 6 mo	0.81 for ALL; 0.85 for AML	0.0000321 for ALL (74% of cases) 0.0000113 for AML		$136 444 direct cost per case; $153 617 total cost per case
Deaths from leukemia	Any breastfeeding for 6 mo	0.81 for ALL; 0.85 for AML	10.1% mortality in ALL; 39.8% mortality in AML	NA	$10 560 000
T1D	Any breastfeeding for 3 mo	0.77 (average of 2 OR listed in AHRQ: 0.81 and 0.73)	0.000186	40, with 9-y latency	$4390 direct cost per y; $77 463 direct per case; $7378 total cost per y; $130 187 total cost per case
Deaths from T1D	Any breastfeeding for 3 mo	0.75	0.00000121	NA	$10 560 000
Childhood obesity	Any breastfeeding for 3 mo	0.93	0.176 by age 19 y	From midpoint of each age cohort to age 40 y	$1460 direct cost per y; $28 758 direct cost per case; $2285 total per y; $36 040 total cost per case

The Burden of Suboptimal Breastfeeding in the United States: A Pediatric Cost Analysis

TABLE 3 Excess Costs and Excess Deaths at Current Breastfeeding Rates Compared With Projected Costs if 90% or 80% of US Parents Could Comply With the Medical Recommendation to Breastfeed Exclusively for 6 mo

	Excess Costs Compared With 90% Compliance (Excess Deaths), 2007 $US	Excess Costs Compared With 80% Compliance (Excess Deaths), 2007 $US
Total	12 974 676 651 (911)	10 491 841 489 (741)
SIDS	4 725 328 464 (447)	3 722 074 013 (352)
NEC deaths	2 631 165 267 (249)	2 218 109 495 (210)
LRTI deaths	1 820 102 146 (172)	1 537 915 767 (146)
OM	908 793 396	765 766 295
AD	601 358 918	497 497 274
Childhood obesity	592 100 121	404 195 504
LRTI hospitalization	451 592 572	381 578 219
Childhood asthma	335 796 234	229 194 255
NEC	266 536 884	219 843 084
Childhood asthma deaths	216 869 872 (21)	148 022 294 (14)
Gastroenteritis	186 016 678	162 076 307
Childhood leukemia deaths	133 422 239 (13)	133 422 239 (13)
Childhood T1D deaths	95 231 472 (9)	64 999 258 (6)
T1D	8376 168	5717 067
Childhood leukemia	1986 220	1430 416

The Burden of Suboptimal Breastfeeding in the United States: A Pediatric Cost Analysis

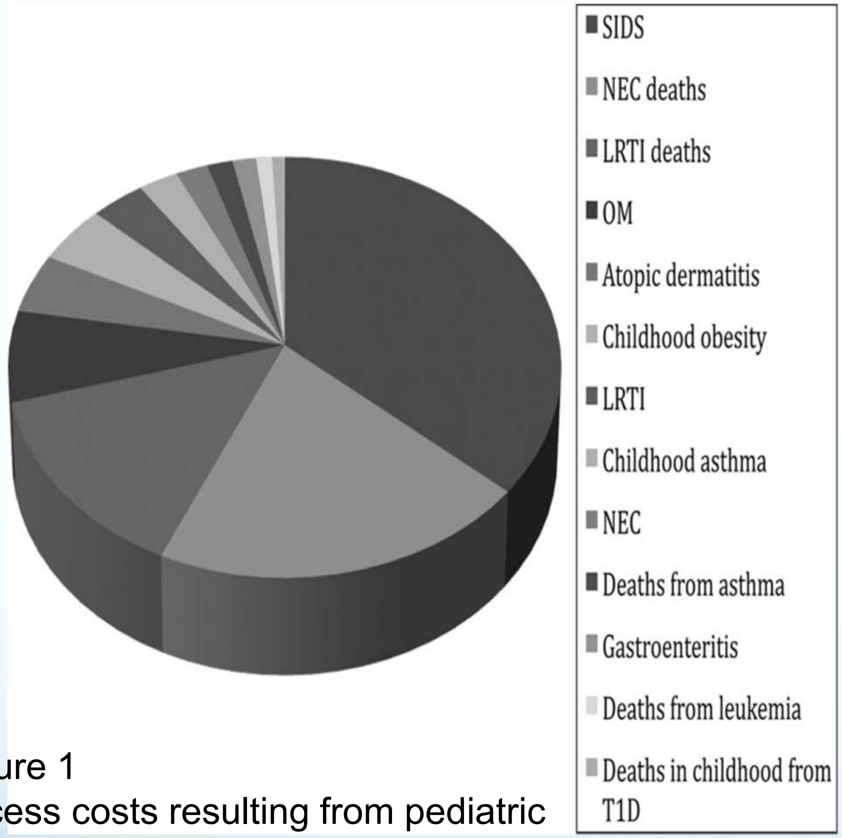


Figure 1
Excess costs resulting from pediatric disease at current breastfeeding rates compared with projected costs if 90% of U.S. families could comply with medical recommendations to breastfeed exclusively for six months (total $12.97 billion [2007 dollars]).

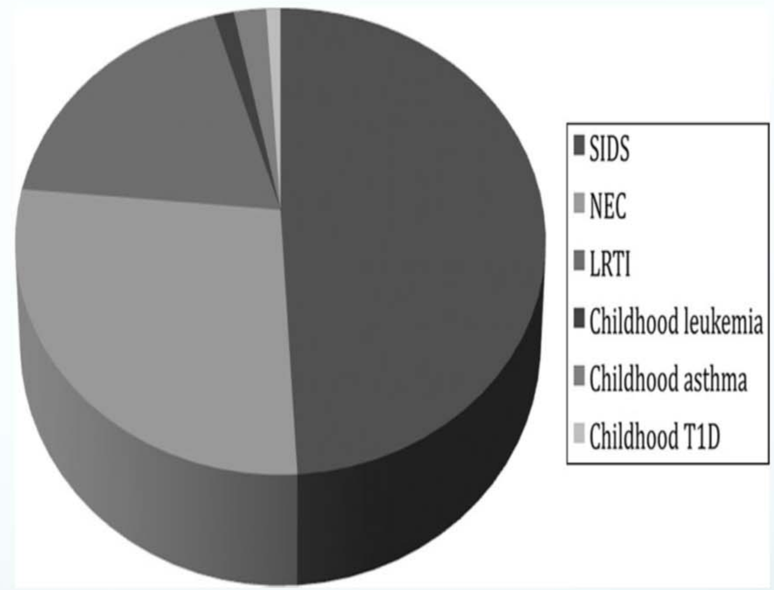


Figure 2
Excess pediatric deaths at current U.S. breastfeeding rates, compared with projected deaths if 90% of U.S. families could breastfeed exclusively for six month (total 911 deaths).

The Association Between Breastfeeding and Childhood Obesity: A Meta Analysis

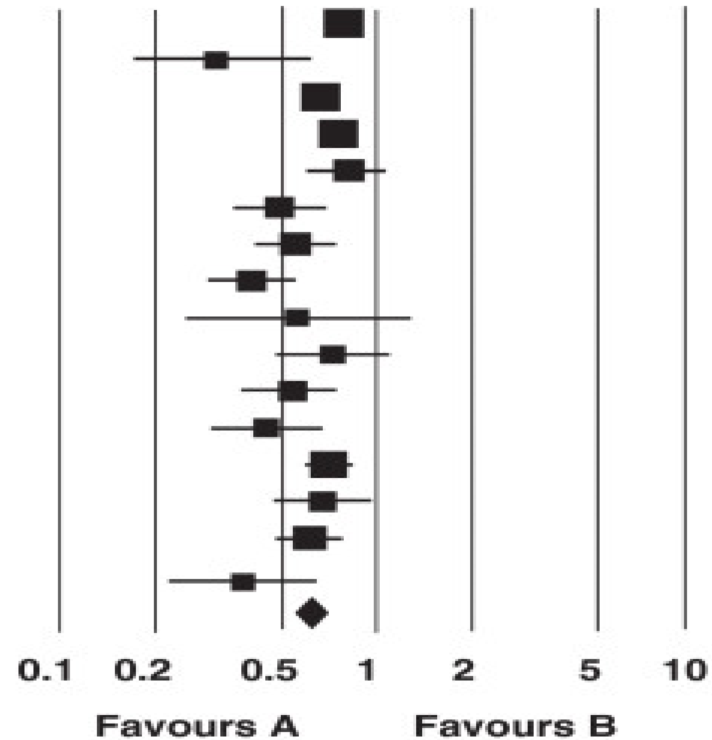
Jing Yan, Lin Liu, Yun Zhu, Guowei Huang, and Peizhong Peter Wang

Meta Analysis

Study name	Odds ratio	Lower limit	Upper limit
Armstrong 2002	0.78	0.70	0.87
Bergmann 2003	0.31	0.16	0.59
Gillman 2001	0.66	0.58	0.76
Hawkins 2009	0.75	0.66	0.85
Hediger 2001	0.81	0.61	1.08
Jwa 2014	0.49	0.35	0.69
Liese 2001	0.55	0.41	0.74
McCrory 2012	0.40	0.29	0.55
Novaes 2011	0.56	0.25	1.26
O'Challaghan 1997	0.72	0.48	1.09
Scholtens 2008	0.54	0.38	0.76
Scott 2012	0.45	0.30	0.67
Toschke 2002	0.70	0.59	0.84
Twells 2010	0.67	0.47	0.96
Von kries 1999	0.61	0.48	0.78
Zhao 2013	0.38	0.22	0.65
UOR (Random effects)	0.61	0.55	0.68

(Subgroup within study)

Odds ratio and 95% CI



Yan *et al. BMC Public Health* 2014, **14**:1267
http://www.biomedcentral.com/1471-2458/14/1267

Yan et al, *BMC Public Health*, 2014

Prevalence, Increasing Rate, and Long –Term Impact

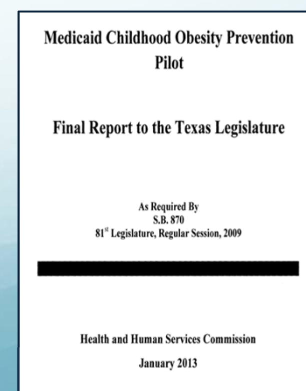
- 20.4 prevent of Texas children ages 10 to 17 are obese.
- Since 1980, the rate of obesity among U.S. children and adolescents tripled.
- Obese children have an 80 present chance of staying obese their entire lives.[2]

Costs Associated with Obesity

- Average health care spending for obese individuals was $1,429 or 41.5 percent higher than that of non-obese persons in 2006.
  Individuals with a BMI greater than 35 kg/M^2 represent 37 percent of the population but account for 61 prevent of the costs due to excess weight.
- A recent study of IBM's self-insured showed 2008 average per capita health insurance claims for obese children were $2,907 compared to $1,640 for non-obese children. Children with type 2 diabetes had average claims of $10,789. The study found that hospitalizations rates for obese children with chronic health conditions were up to 2.9 times higher than for non-obese children with no chronic conditions

Exclusive breastfeeding decreases adolescent obesity by 15-30%

Cost savings could be in the tens of millions of dollars


Medicaid Childhood Obesity Prevention Pilot

Final Report to the Texas Legislature

As Required By
S.B. 870
81st Legislature, Regular Session, 2009

Health and Human Services Commission
January 2013

Longer Breastfeeding is an Independent Protective Factor against Development of type 1 Diabetes Mellitus in Childhood

Diabetes/Metabolism Research and Reviews Vol 20 No. 2 pp 150-157, March/Apr 2004

Vaiva Sadauskaitė-Kuehne[1,2], Johnny Ludvigsson[2,],*
Žilvinas Padaiga[1], Edita Jašinskienė[1] and Ulf Samuelsson[2]

Results

Breastfeeding protects against diabetes among Swedish children

Exclusive breastfeeding > five months (OR 0.54, 0.36–0.81)

Total breastfeeding >7 (0.56, 0.38–0.84)

Breastfeeding protects against diabetes in Lithuanian children

Breastfeeding > two months (OR 0.58, 0.34–0.99)

Up to a 30% reduction in the incidence of type I diabetes

Early Infant Feeding and Risk of type 1 Diabetes Mellitus - A Nationwide Population-Based Case-Control Study in Pre-School Children

Rosenbauer JI, Herzig P, Giani G. Diabetes Metab Res. 2008 24(3):211-22.

Case-control review of 760 patients < 5 years of age
Newly diagnosed with type 1 diabetes during 1992-1995.
Compared with matched controls

Duration of breastfeeding and age at introduction of bottle-feeding were inversely associated with type 1 diabetes risk according to a dose-response relationship (trend test $p < 0.05$). Adjusted odd ratios (95% CI) for a long breastfeeding period and a late introduction of bottle-feeding (>or=5 month versus < 2 weeks) were 0.71 (0.54-0.93) and 0.80 (0.62-1.04), respectively.

Does Breastfeeding Influence Risk of type 2 Diabetes on Later Life? A Quantitative Analysis of Published Evidence

The American Journal of Clinical Nutrition, 2006

Christopher G. Owens, Richard M. Martin, Peter H. Whincup,
George Davey Smith, and Derek G. Cook

Variable	No. of studies	No. of subjects breastfed, formula fed	Mean difference: Blood glucose	Mean difference: Serum insulin	OR of type 2 diabetes	*P* for difference between breastfed and formula fed	*P* for test for heterogeneity[2]
			mmol/L				
Glucose							
Infants	12	290, 270	−0.17 (−0.28, −0.05)[3]	—	—	0.005	0.169
Children and adults	7	4067, 1194	−0.01 (−0.04, 0.03)	—	—	0.679	0.245
Insulin							
Infants	7	140, 151	—	−2.86 pmol/L (−5.76, 0.04)	—	0.054	0.012
Children and adults	6	3855, 945	—	−3% (−8%, 1%)	—	0.127	0.402
Type 2 diabetes							
	7[4]	49 772, 26 972	—	—	0.61 (0.44, 0.85)	0.003	0.383
	5[5]	2579, 953	—	—	0.59 (0.40, 0.87)	0.008	0.280

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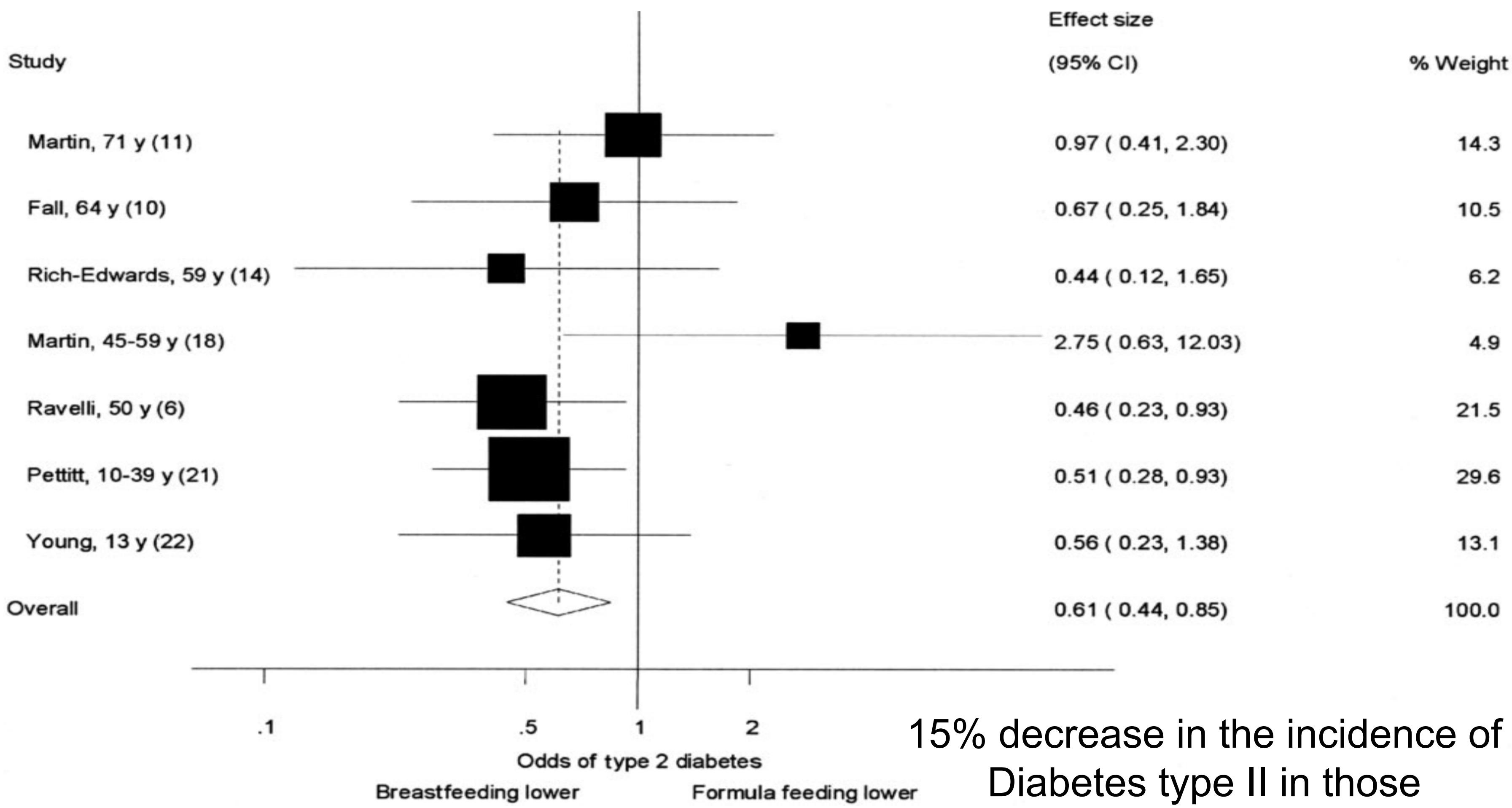


15% decrease in the incidence of Diabetes type II in those patients who are breastfed

Medical Expenditures for Diabetes-related Encounters, Fiscal Years 2010-2013 (STAR and Star PLUS)

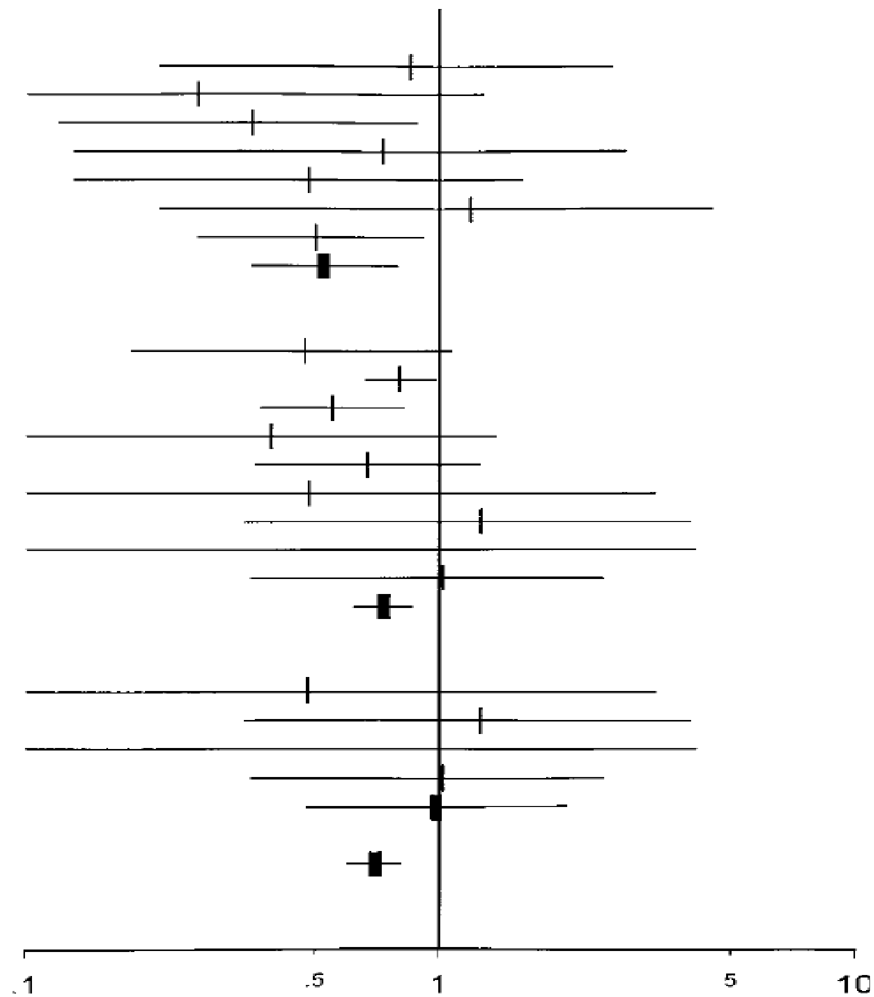
	Eligible STAR/ STAR+PLUS Clients	Percentage of Clients with Service	Number of Diabetes Clients	Number of Diabetes Encounters[1]	Encounters per Client	Amount Paid[2]	Amount Paid per Client	Amount Paid per Encounter[2]
FY2010								
STAR Age < 21	1,975,623	0.3%	5,223	29,100	5.57	$6,633,570.42	$1,270.07	$227.96
STAR Age >= 21	210,418	1.9%	4,007	16,338	4.08	$2,431,188.93	$606.74	$148.81
Total[3]	2,179,317	0.4%	9,200	45,438	4.94	$9,064,759.35	$985.30	$199.50
STAR+PLUS Age < 21	10,167	1.2%	127	967	7.61	$118,203.03	$930.73	$122.24
STAR+PLUS Age >= 21	180,363	15.3%	27,613	352,508	12.77	$98,827,343.40	$3,579.02	$280.35
Total[3]	190,147	14.6%	27,732	353,475	12.75	$98,945,546.43	$3,567.92	$279.92
FY2011								
STAR Age < 21	2,142,487	0.3%	5,390	33,144	6.13	$7,598,833.45	$1,405.11	$229.27
STAR Age >= 21	224,715	2.4%	5,408	22,059	2.06	$3,332,312.00	$310.47	$151.06
Total[3]	2,360,287	0.5%	10,733	55,203	5.14	$10,931,145.45	$1,018.46	$198.02
STAR+PLUS Age < 21	11,082	1.5%	163	1,112	6.82	$163,531.86	$1,003.26	$147.06
STAR+PLUS Age >= 21	275,017	13.7%	37,714	433,637	11.50	$117,374,647.26	$3,112.23	$270.67
Total[3]	285,605	13.3%	37,867	434,749	11.48	$117,538,179.12	$3,103.97	$270.36

2011…Potential cost savings of $15-17 million per year with just diabetes prevention
(if assume more conservative 15% decrease)

Breast-feeding and the Risk of Bronchial Asthma in Childhood: A Systematic Review with Meta-Analysis of Prospective Studies

Michael Gdalevich, MD, MPH, Daniel Mimouni, MD, and Marc Mimouni, MD

	OR	95% CI Lower	95% CI Upper
Positive family history			
Gruskay	0.85	0.21	2.62
Businco	0.26	0.03	1.28
Chandra	0.35	0.12	0.88
Hide	0.73	0.13	2.82
McConnochie	0.48	0.13	1.59
Fergusson	1.19	0.21	4.58
Marini	0.50	0.26	0.91
Subtotal	0.52	0.35	0.79
Negative family history or unstratified			
Wilson	0.47	0.18	1.07
Oddy	0.80	0.66	0.98
Tariq	0.55	0.37	0.82
Gordon	0.39	0.09	1.37
Wright	0.67	0.36	1.25
Gruskay	0.48	0.01	3.30
Hide	1.26	0.34	4.00
McConnochie	0.00	0.00	4.13
Fergusson	1.02	0.35	2.48
Subtotal	0.73	0.62	0.86
Children without a family history of atopy			
Gruskay	0.48	0.01	3.30
Hide	1.26	0.34	4.00
McConnochie	0.00	0.00	4.13
Fergusson	1.02	0.35	2.48
Subtotal	0.99	0.48	2.03
Total	0.70	0.60	0.81



Potential of a 20% decrease in asthma

J Peds, 2001

Texas Asthma Control Program Facts and Extrapolated Costs Savings with Increased Breastfeeding

In 2012, 25,158 hospital discharges were due to asthma

Asthma cost Texas $652.5 million

10,000 of those discharges were under the age of 18.

Breastfeeding has the potential to decrease the incidence of asthma and therefore hospitalization by 20% and thus decrease costs by $30 to $50 million

Final Take Aways

Human Milk is uniquely designed to benefit our infants and children.

The use of human milk is under recognized as an economic intervention to result in tremendous morbidity and mortality improvements for our patients.

Final Take Aways

Texas should consider that the small investments to promote human milk use (mother's own milk or donor) has far-reaching cost savings due to prevention of morbidities which cost Texas millions of dollars.

Texas should increase their promotion of human milk use in NICUs, newborn nurseries and in outpatient facilities to reap the tremendous benefit in morbidity and mortality.

Questions and Answers

Evelyn Delgado
Assistant Commissioner,
Division for Family & Community
Health Services, DSHS

Remote sites can send in questions by typing in the *GoToWebinar* chat box or email GrandRounds@dshs.state.tx.us.

For those in the auditorium, please come to the microphone to ask your question.

DSHS Grand Rounds
Fall Semester 2015

Wednesday, September 2, 2015

Wednesday, September 9, 2015

Wednesday, September 16, 2015

Wednesday, September 23, 2015

Wednesday, September 30, 2015