NICHD-SACIM Report
July 9-10, 2014

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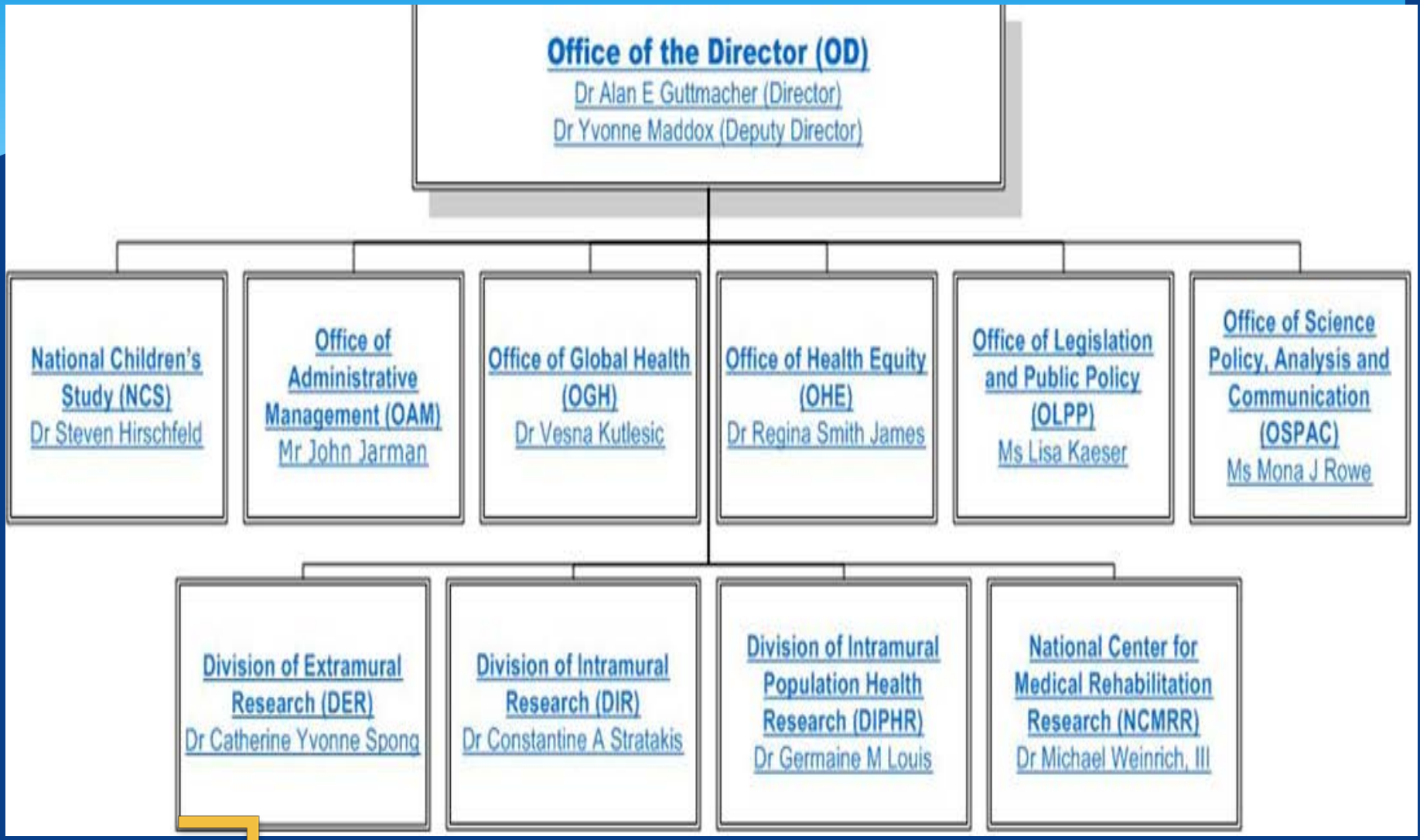
Eunice Kennedy Shriver National Institute of Child Health and Human Development

NIH *Eunice Kennedy Shriver* National Institute of Child Health and Human Development

Topics Covered

* Restructured NICHD
* SIDS, PASS and Dr. Kinney's work
* Safe-Sleep, bed-sharing workshop
* Breastfeeding and Human Milk research
* Other research:
  * Human Milk Biology; B-24; Generational effect of fetal nicotine exposure
* Evolving programs and ongoing research
* Liaison Activities (COFN, SMFM, ACOG, CoIIN)

NICHD Organization



12 Extramural Scientific Branches

Division of Extramural Research

Twelve Extramural Scientific Branches

*** Seven Branches support research that impact infant health & IMR**

- Child Development and Behavior Branch (CDBB)
- Contraceptive Discovery and Development Branch (CDDB)
- Developmental Biology and Structural Variation Branch (DBSVB)
- **Fertility and Infertility (FI) Branch** *
- **Gynecologic Health and Disease Branch (GHDB)** *
- Intellectual and Developmental Disabilities Branch (IDDB)
- **Maternal and Pediatric Infectious Disease Branch (MPIDB)** *
- **Obstetric and Pediatric Pharmacology and Therapeutics Branch (OPPTB)***
- **Pediatric Growth and Nutrition Branch (PGNB)** *
- **Pediatric Trauma and Critical Illness Branch (PTCIB)** *
- Population Dynamics Branch (PDB)
- **Pregnancy and Perinatology Branch (PPB)** *

Prenatal Alcohol in SIDS and Stillbirth Network (PASS)

* PASS funded by NICHD, NIAAA, and NIDCD
  * 2 clinical centers (Univ of South and University of Stellenbosch)
  * A Developmental Biology and Pathology Center (Children's Hospital Boston)
  * A Physiology Assessment Center (Columbia University),
  * A Datacenter (DM STAT)
* The network conducts community-linked studies to investigate the role of prenatal alcohol exposure in the risk for SIDS and adverse pregnancy outcomes, such as stillbirth and fetal alcohol syndrome (FAS) and how they may be inter-related.
* In high-risk communities of the Northern Plains and Western Cape, South Africa.

Prenatal Alcohol in SIDS and Stillbirth Network (PASS)

* The long-term goals are to decrease fetal and infant mortality and improve child health in these communities.
* The Network was recently re-competed, and is continuing enrolling in phase II, which aims to enroll 12,000 pregnant women.
* This prospective study will span early pregnancy through the first twelve months of infant life with assessments of fetal and infant autonomic function, neurobehavioral development, maternal and infant medical risks, and detailed assessments of prenatal alcohol consumption and fetal exposure.
* As of7/3/2014, 11,176 pregnant women have been enrolled.

PASS
&
Recent work by
Dr. Kinney's Group

**Coke's Hartebeest (*Alcelaphus buselaphus cokei*),
Kenya, EMBO Cover, 7 October, 2009**

Potential Asphyxia and Brainstem Abnormalities in Sudden and Unexpected Death in Infants

Bradley B. Randall, David S. Paterson, Elisabeth A. Haas, Kevin G. Broadbelt, Jhodie R. Duncan, Othon J. Mena, Henry F. Krous, Felicia L. Trachtenberg and Hannah C. Kinney

Pediatrics 2013;132;e1616; originally published online November 11, 2013; ɔeds.2013-0700

- **Prior work showed that many SIDS infants have deficits in the medullary serotonergic circuits that help to control breathing, heart rate, blood pressure and temperature control during sleep.**

- **Neurochemical analyses of medullary serotonin systems from 71 cases of SUID were grouped according to potential asphyxiating conditions in the environment**

- **The same abnormalities in medullary neurochemicals were found in the groups with and without potential asphyxiating conditions, and both of these differed significantly from control infants dying suddenly of known cause.**

Conclusions: No direct relationship between the presence of potentially asphyxia conditions in the sleep environment and brainstem abnormalities in infants dying suddenly and unexpectedly.

Take Home Message from the Collective Work from Dr. Kinney's Lab on SIDS

* Brainstem abnormalities were found in infants who died of SIDS regardless of potential asphyxiating conditions in the sleep environment.
* Most SIDS infants have an underlying developmental abnormality likely predisposing them to sudden death; we still do not know the exact mechanism by which risk factors in the sleep environment trigger death.
* This is important for ME and coroners to know because there is an increasing trend among them not to use SIDS as a cause of death but call them "positional asphyxia or suffocation."
* A positive correlation between the number of extrinsic risk factors (sleep position, bed sharing, face down or covered, minor illness within 48 hours) and serotonin binding was observed.
* It is important to continue to promote SAFE SLEEP messages.

Safe Sleep and Breastfeeding

Safe-Sleep, bed-sharing & breastfeeding

* Background and Issue
  * Potentially conflicting message: the benefits and risk of bed-sharing with regard to enhancing breastfeeding messaging, while not increasing the potential for infant death.
  * First ever workshop involving researchers from breastfeeding research and advocacy groups, and researchers from sleep/SIDS groups, including the respective AAP committees.
  * A pediatricians dilemma: How to balance the advice?

Safe-Sleep, bed-sharing & breastfeeding

* Despite AAP statements to the contrary, many women bed-share with their infants
* There are data to show that bed-sharing increases breastfeeding duration and exclusivity.
* There are data on the risk for infant death with bed-sharing
* But, the groups who work in breastfeeding and safe sleep topics have different perspectives on the relative merits/limitations of available data
* Breastfeeding and sleep researchers were invited to a meeting along with federal and non-federal professional partners.
* Purpose was to come up with a way to encourage safe sleep and breastfeeding while respecting those differences.

Safe-Sleep, bed-sharing & breastfeeding: Recommendations

Safe-Sleep, bed-sharing & breastfeeding: Recommendations

* Enhance the positive framing of messages.
* Craft messages that normalize breastfeeding. Promote breastfeeding as a package of benefits.
  * Reducing the risk of sudden infant death syndrome (SIDS) is one of the many advantages of breastfeeding.
* Tailor tips for different target audiences (e.g., grandmothers, who are often infant caregivers).
* Showcase testimonials of women (the successes and challenges) telling their personal stories about specific breastfeeding and safe infant sleep practices.
* Offer supporting statistics related to breastfeeding, safe infant sleep, and SIDS, when available.
* Disseminate materials that contain consistent messages.

A study with a potential for implementation

Effect of Primary Care Intervention on Breastfeeding Duration and Intensity

Karen Bonuck, PhD, Alison Stuebe, MD, MSc, Josephine Barnett, MS, Miriam H. Labbok, MD, MPH, Jason Fletcher, PhD, and Peter S. Bernstein, MD, MPH

Objectives. We determined the effectiveness of primary care–based, and pre- and postnatal interventions to increase breastfeeding.

Methods. We conducted 2 trials at obstetrics and gynecology practices in the Bronx, New York, from 2008 to 2011. The Provider Approaches to Improved Rates of Infant Nutrition & Growth Study (PAIRINGS) had 2 arms: usual care versus pre- and postnatal visits with a lactation consultant (LC) and electronically prompted guidance from prenatal care providers (EP). The Best Infant Nutrition for Good Outcomes (BINGO) study had 4 arms: usual care, LC alone, EP alone, or LC+EP.

Results. In BINGO at 3 months, high intensity was greater for the LC+EP (odds ratio [OR] = 2.72; 95% confidence interval [CI] = 1.08, 6.84) and LC (OR = 3.22; 95% CI = 1.14, 9.09) groups versus usual care, but not for the EP group alone. In PAIRINGS at 3 months, intervention rates exceeded usual care (OR = 2.86; 95% CI = 1.21, 6.76); the number needed to treat to prevent 1 dyad from nonexclusive breastfeeding at 3 months was 10.3 (95% CI = 5.6, 50.7).

Conclusions. LCs integrated into routine care alone and combined with EP guidance from prenatal care providers increased breastfeeding intensity at 3 months postpartum. (*Am J Public Health.* 2014;104:S119–S127. doi:10.2105/AJPH.2013.301360)

Breastfeeding is associated with improved health outcomes for both mother and child.[1,2] All major medical organizations recommend exclusive breastfeeding for the first 6 months after birth, with continued breastfeeding for at least 1 year.[3,4] Nationally, 36% of infants born in 2009 were exclusively breastfed at 3 months and 16% at 6 months,[5] falling short of Healthy People 2020 targets of 46%, and 26%, respectively.[6] A recent study found that suboptimal breastfeeding rates incur $2.2 billion in direct pediatric medical costs each year.[7] There are also substantial disparities, with the lowest breastfeeding rates seen among non-Hispanic Black, younger, and less-educated mothers.[8]

Interventions are therefore needed to increase breastfeeding exclusivity and intensity, defined as the proportion of feedings that are breast milk. The United States Preventive Services Task Force (USPSTF) conducted a meta-analysis of randomized controlled trials of primary care–based breastfeeding promotion interventions. Interventions consistently increased rates of any and exclusive breastfeeding, although most findings were not statistically significant, and many studies were of poor quality.[9] Overall, systematic reviews supported the effectiveness of combined pre- and postnatal interventions,[8] scheduled, face-to-face visits,[10] and, for low-income women, on-going personal contact with a health professional.[11] In our previous trial, a pre- and postnatal intervention delivered by lactation specialists certified by the International Board of Certified Lactation Consultants (IBCLCs) had positive effects. However, IBCLCs were not a routine presence at prenatal care, intervention New York City. The present trials improve upon our previous work by integrating lactation consultants (LCs) into routine practice,[17] in combination with electronically prompted (EP) anticipatory guidance from prenatal care providers. We hypothesized that these interventions would increase breastfeeding intensity and exclusivity at 1, 3, and 6 months postpartum, compared with usual care.

METHODS

We conducted 2 separately funded single-blind randomized controlled trials at urban, medical center–affiliated prenatal care clinics in the Bronx: the Best Infant Nutrition for Good population. Research assistants recruited women during routine prenatal care from February 2008 to June 2010, with follow-up through September 2011. Enrollment was limited to English- or Spanish-speaking women aged 18 years or older, in the first or second trimester of a singleton pregnancy, without risk factors for premature birth, or maternal or infant conditions that would preclude or complicate breastfeeding (e.g., maternal HIV positive, infant congenital anomaly). The trials were described to prospective participants as studies to test the effect of patient education programs on infant feeding and health.

Eligible patients who signed informed consents were randomized using sequentially

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* Two trials, together had 4 arms:
  * Usual prenatal care
  * Prenatal and postnatal visits with lactation consultants (LC Alone)
  * Electronically-prompted guideline by prenatal care provider (EP-Alone)
  * Lactation consultants plus electronically guided prenatal care provider
* Participants: 941 women enrolled during the 1st or 2nd trimester. They were >18 years; singleton, otherwise healthy. Mostly low-income inner city cohort
* Intervention:
  * Usual Care: standard prenatal care, LC services when requested
  * LC: two prenatal and two postnatal visits/consultations & counseling
  * Providers were prompted with 5 questions to answer while completing patients' prenatal electronic medical records.

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Conclusions. LCs integrated into routine care alone and combined with EP guidance from prenatal care providers increased breastfeeding intensity at 3 months postpartum. (*Am J Public Health.* 2014;104:S119–S127. doi:10.2105/AJPH.2013.301360)

Bottom Line: ~ 15 to 20% more women were breastfeeding their infants more often, or exclusively at 3 months when lactation consultants were part of prenatal counseling, compared to routine care.

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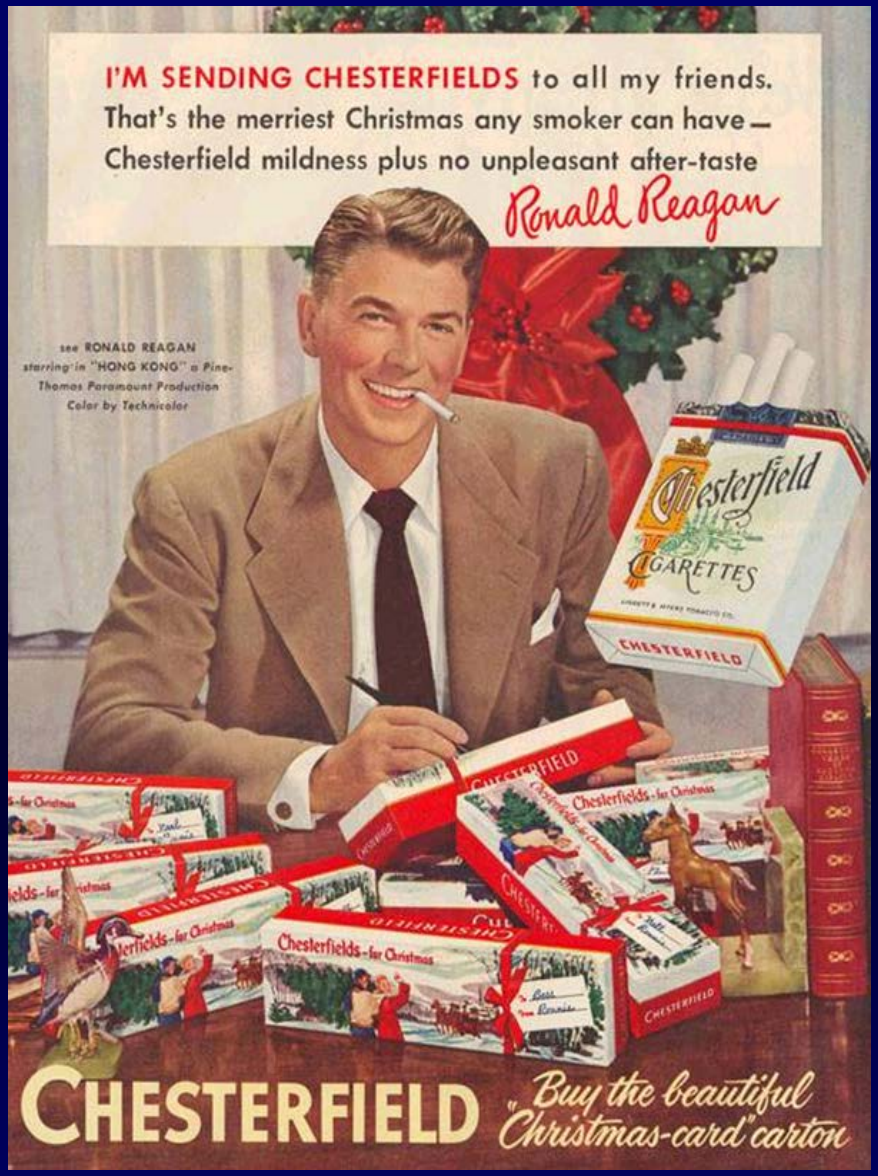
Breastfeeding & Role of Lactation Consultant

Basic Science and Translational Work

Research on Negative effects of Nicotine during Pregnancy

- Using nicotine as a proxy for maternal smoking, we have demonstrated that an asthma-like phenotype can be inherited by rat offspring for up to two generations, after the initial intrauterine exposure.
- We hypothesized that asthma transmission to offspring is not restricted up to F2 generation, but it also extends to subsequent generations.
- In this study, we show the findings to third-generation offspring, including abnormal pulmonary function, upper airway reactivity exclusively in males and to its effects on molecular functional markers
- These data, for the first time, demonstrate the transgenerational transmission of the asthma phenotype to F3 offspring following perinatal nicotine exposure of F0 dams.



Rehan VK, et al: Perinatal nicotine-induced transgenerational asthma. Am J Physiol Lung Cell Mol Physiol. 2013; 1;305(7):L501-7.

Basic Science & Translational

Workshop: Human Milk Glycobiology

- Newburg DS, Grave G. Recent advances in human milk glycobiology. Pediatr Res. 2014 May;75(5):675-9. doi: 10.1038/pr.2014.24. Epub 2014 Feb 12. PubMed PMID: 24522101.

Birth-24 Dietary Guidelines

- Raiten DJ, Raghavan R, Porter A, Obbagy JE, Spahn JM. Executive summary: Evaluating the evidence base to support the inclusion of infants and children from birth to 24 mo of age in the Dietary Guidelines for Americans--"the B-24 Project". Am J Clin Nutr. 2014 Mar;99(3):663S-91S

Evolving Programs

- Human Placental Project: A major undertaking, groundwork is being laid out
- Pregnancy Registry
- Treatment of Neonatal disorders:
  - NEC; BPD; shock
  - TOP trial
- Active Initiatives:
  - Neonatal Resuscitation
  - Omics technology
  - Patient safety during perinatal and neonatal care

Human Placental Project: Placental Structure and Function in Real Time

- The placenta is the least understood human organ and arguably one of the more important, not only for the health of a woman and her fetus during pregnancy but also for the lifelong health of both. To address this lack of knowledge, the NICHD believes a concerted effort, the Human Placenta Project, would make substantial inroads.
- **Initial goals of the Human Placenta Project are to:**

- Improve current methods, and develop new technologies, for real-time assessment of placental development.
- Apply these technologies to understand and monitor, in real time, placental development and function in normal and abnormal pregnancies.
- Develop and evaluate non-invasive markers for prediction of adverse pregnancy outcomes.
- Understand the contributions of placental development to long term health and disease.
- Develop interventions to prevent abnormal placental development, and hence improve pregnancy outcome.

The Human Placenta Project

Bolger Center, Bethesda, MD: May 27-28, 2014.
http://www.nichd.nih.gov/about/meetings/2014/Pages/052814.aspx

NICHD Pregnancy Registry
Purpose, Goals, & Objectives

* To understand the natural history of pregnancy by asking women directly what is going on in their pregnancies.
* To learn: more about the range of physical and emotional experiences as well as alterations in behavior women have during pregnancy and after childbirth; the impact of these experiences on women's lives.
* The registry will use a crowd-sourcing, citizen science approach, asking women to enter information about their pregnancies throughout gestation via a website and mobile apps.
* In exchange, the site would send information about pregnancy back to these women including summarized data from the registry.
* De-identified data from the registry would be available for researchers
* Participants could be a potential pool of recruits for clinical studies
* Eligible women who self-identify as interested in participating in clinical studies, could be sent contact information about ongoing observational or interventional study opportunities.

NICHD Pregnancy Registry Workshop: June 30, 2014

What would it look like?

* Longitudinal
* Mobile/apps
* Tracking (e.g., weight)
* Feedback
* Links to information
* Clinical trial pool
* Research

Evolving programs and ongoing research (Others)

* Advances in neonatal disorders:
  * NEC; BPD, treatment of shock
  * TOP trial
* A few Initiatives:
  * Neonatal Resuscitation
  * Omics technology
  * Patient safety during perinatal and neonatal care

Liaison Activities

Liaison Activities
PPB Scientists Continue to Participate as Liaison to Professional Groups

* Committee on Fetus and Newborn (AA)
* Taskforce on SIDS (AAP)
* Committee on OB Practice (ACOG)
* Society for Maternal Fetal Medicine
  * Recent Activities
    * AAP-ACOG Committee Statements:
      * Delayed cord clamping
      * Immersion during labor and delivery
  * Combined Workshops: Periviable Births (2013)
  * Others are being planned for 2014-15

Thank You…