Vignettes from the NCS

→ "One for the money, two for the show, three to get ready, four to go"
→ Donald Dudley, MD Obstetrics
→ Daniel E. Hale, MD Pediatrics
→ Louise O'Donnell, PhD Psychiatry
→ Pamela Wood MD Pediatrics
→ Doug Williamson, PhD Psychiatry
(Yes I can count)

Disclosures

→ Hale - grant support and speakers bureau Ibsen and Novo Nordisk
→ Dudley - consultant, Watson, Genzyme, March of Dimes
→ O'Donnell - none
→ Wood - none
→ Williamson – none

NCS is a Contract with the NIH

Presentation

→ Overview of the NCS
→ Formative Projects
  Developing and testing "field measures"
  → Pulmonary Function Assessment ("Pulmonary")
  → Physical Measures ("Ulnar")
  → Developmental Assessment ("Bayley")
  → Maternal Stress Measures ("Stress")
→ Why This Matters to You

Objectives

1. Explain the rationale and background for the NCS.
2. Briefly describe the pilot projects that are underway locally
   “I think it is a fantastic opportunity for you and your family to be part of a national project that is so important to the health of children over the next century”

President’s Task Force on Environmental Health Risks and Safety Risks to Children

→ 1998 Charge – Develop strategies to reduce risk of environmental exposures to children
→ Co-chairs – Secretary HHS, Administrator USEPA
→ Members – 7 more cabinet officers & Sr. staff
→ Many risks not clear or quantified
→ Need for additional study of effects of environmental exposures (broadly defined)
→ Consultation Jan. 2000 endorsed study: large, bold, multiple agencies, public private partnerships
→ New money would be required
PL 106-310
Children’s Health Act of 2000

(a) PURPOSE: . . . to authorize NICHD to conduct a national longitudinal study of environmental influences (including physical, chemical, biological, and psychological) on children’s health and development.

(b) IN GENERAL: The Director of NICHD shall establish a consortium of representatives from appropriate Federal agencies (including the CDC and EPA) to—

1. plan, develop, and implement a prospective cohort study, from birth to adulthood, to evaluate the effects of both chronic and intermittent exposures on child health and human development; and

2. investigate basic mechanisms of developmental disorders and environmental factors, both risk and protective, that influence health and developmental processes.

Line Item in US Budget: Funding is Year to Year

Increased Vulnerability to Environmental Exposures

→ Critical windows of vulnerability during development
→ Immature mechanisms for detoxification and protection
→ Differences in metabolism and behavior that may yield higher exposure in the same environments

Factors that Increase Exposures in Children*

<table>
<thead>
<tr>
<th>Factors</th>
<th>Infants</th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface Area : Body Mass Ratio (m²/kg)</td>
<td>0.067</td>
<td>0.047</td>
<td>0.025</td>
</tr>
<tr>
<td>Respiratory Ventilation Rate (ml/kg/m² lung surf. area/min)</td>
<td>133</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Drinking water intake (ml/kg/day)</td>
<td>43.5</td>
<td>35.5</td>
<td>19.9</td>
</tr>
<tr>
<td>Soil Ingestion (mg/day)</td>
<td>20</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Rate of lead absorption</td>
<td>42-53%</td>
<td>30-40%</td>
<td>7-15%</td>
</tr>
</tbody>
</table>

*Selevan et al. Environ Health Perspect 2000;108(suppl 3);451

Some Exposures of Concern

→ Solvents – alcohol, toluene, other
→ Food Additives – glutamate, aspartame, dyes
→ Infection in early life – H. pylori – gastritis; Chlamydia pneumoniae – coronary vascular disease
→ Head trauma – mild/moderate, age 0-14, 4/1,000
→ Witness violence – 3.3 million children
→ Neighborhoods – cohesion, collective efficacy
→ Poverty – 18% of children in poverty

Rationale

→ Converging factors
→ Increased vulnerability to environmental exposures in children in general
→ Exposures to some agents have caused serious developmental effects – lead, alcohol
→ Known current exposures of high frequency – pesticides, phthalates, etc
→ Existing studies limited in size & scope
→ Study needed to identify effects or assure safety
→ Longitudinal design to infer causality with multiple exposures and multiple outcomes
Study Concepts

→ Longitudinal study of children (to age 21), their families and their environment
→ National in scope
→ Environment defined broadly (chemical, physical, behavioral, social, cultural)
→ Study common range of “environmental” exposures and less common outcomes (n~100,000)
→ Environment & genetic expression

Measures Anticipated - Exposures

→ Environmental Samples: air, water, dust
→ Bio-markers for chemicals: blood, breast milk, hair, tissue, etc.
→ Interview and history
→ Serology and medical data
→ Housing & living characteristics
→ Family and social experiences
→ Neighborhood and community characteristics
→ Projected: 2-8 billion samples

NCS Sample

All Births in the Nation
→ ~4 million births in 3,141 counties
Sample of Study Locations
→ 101 Locations
Sample of Study Segments
→ Selection of neighborhoods
Sample of Study Households
→ All or a sample of households within neighborhoods
Sample of Study Women
→ All eligible women in the household

Study Locations

Segment Zip Codes

→ 78109 → 78211
→ 78023 → 78207
→ 78224 → 78237
→ 78209 → 78212
→ 78218 → 78216
→ 78227 → 78217
→ 78214 → 78240
→ 78223 → 78238
→ 78225 → 78245
→ 78241

Potential Impact on Health Outcomes

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>$14.5</td>
<td>3 – 7 %</td>
<td>$0.4 – 1.0</td>
</tr>
<tr>
<td>Obesity</td>
<td>$46.3</td>
<td>2 – 4 %</td>
<td>$0.9 – 1.9</td>
</tr>
<tr>
<td>Low Birth Weight</td>
<td>$13.3</td>
<td>4 – 7 %</td>
<td>$0.3 – 0.9</td>
</tr>
<tr>
<td>Mental Retardation</td>
<td>$51.2</td>
<td>2 – 5 %</td>
<td>$1.0 – 2.6</td>
</tr>
<tr>
<td>Injuries/Deaths from Aggressive Behavior</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor Vehicle Accidents</td>
<td>$50.0</td>
<td>3 – 7 %</td>
<td>$0.6 – 1.3</td>
</tr>
<tr>
<td>Violence</td>
<td>$24.3</td>
<td>0.5 – 1.5 %</td>
<td>$0.12 – 0.37</td>
</tr>
<tr>
<td>Impaired Cognitive Ability (1 IQ point)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mercury Exposure (50K at-risk newborns)</td>
<td>$0.8</td>
<td>5 – 15 %</td>
<td>$0.12 – 0.12</td>
</tr>
<tr>
<td>Nonpersistent Pesticide (90 percent of births)</td>
<td>$48.0</td>
<td>0.3 – 0.7 %</td>
<td>$0.15 – 0.34</td>
</tr>
<tr>
<td>Autism</td>
<td>$40.8</td>
<td>0.5 – 1.5 %</td>
<td>$0.2 – 0.6</td>
</tr>
</tbody>
</table>
Anthropometry

Daniel Hale, MD, Professor of Pediatrics

- Robert Danish, MD
- Michele Forman, PhD
- The NCS Staff, coordinated by Angela Garcia

Question

Child growth occurs in response to or is affected by the environment.

- Do components of body composition grow at different rates in response to environmental stimuli?
- How does the environment and genetic interaction influence child growth?

Aims

1. Correlate ulnar length in newborns, infants and children to age < six years and other parameters including length/height, weight, lower leg length, arm-splay and BMI, by ethnicity, age and gender.
2. Calculate the reliability and accuracy of traditional length/standing height with surrogate measurements
3. Identify field conditions under which these anthropometrics are reliably measured
4. Identify optimum training approach

Hypotheses

1. The length, width or circumference of a limb segment, when measured accurately, will serve as an acceptable surrogate measure of body length, height, or weight.
2. Limb segment length will be directly associated with total body length/height and will change with age.
3. There will be variability in the inter-observer reliability of measured segments.
4. There will be variability in measurements by specific tools for the same dimensions.
5. Total body (recumbent) length will be longer and more precisely measured than standing height.

Design

- A one-point in time cross-sectional study (or a supplement nested within an existing prospective cohort study) of anthropometric status of newborns up to six-year-old children by age, gender, ethnicity, and study location.
- The study locations include nine study sites and may include measurements in the clinic and field (home, community center).

Eligibility Criteria

- Mothers: aged < 49 years.
- Infants and children: aged <6 years living with parent.
- Health status at measurement:
  - Afebrile
  - Not having suffered from an acute bout of diarrhea or other illness associated with weight loss within the past week
  - No acute illness within the past week.
Anthropometrics

- Ulnar length, width and circumference
- Length/height
- Weight
- Lower leg length
- Arm-span

Ulnar Length

- Calipers
- Grid (ages ≥ 3 m)
- Ruler

Forearm Width

- Grid ages ≥ 3 m
- Tape measure < 3 m

Length or Height

- Infantometer: ages < 36 m
- Stadiometer: ages ≥ 24 m
- Both: 24-36 months

Why This Matters to You

- Clinical
  - Children with disabilities
  - Children with casting or other impediments to height/weight measures
- Research
  - Field measurements with easily transportable equipment
  - A contemporary “gold standard”

“Two for the Show”

Bayley III Short Form

Louise O’Donnell, PhD
Assistant Professor, Psychiatry and Pediatrics

Nellie Springston, Research Associate

Collaborators:
- WESTAT
- Children’s Hospital of Philadelphia
- University of Washington
Goals
To create a measure of children’s developmental status that will:

- Serve as an anchor measure for comparison with other outcome measures in the NCS
- Evaluate the cognitive outcomes of at-risk children with negative exposure histories
- Compare NCS children’s outcomes to other studies of child development

Selecting a Measure
- Bayley Scales of Infant and Toddler Development, 3rd edition is the gold standard.
- Measures 5 domains: cognition, communication, motor, socio-emotional, and adaptive functioning
- Widely used and psychometrically robust
- Not amenable to field use or high volume of participants because it requires extensive training of staff and the time to administer is long (high respondent burden)

Goals
Psychometric Goals
- Target ages 6-, 12-, 18-, 24-, and 36-months
- Psychometrically rigorous (= full Bayley-III)
- Measure performance across the full ability distribution
Administration Goals
- Simplify basal and ceiling rules (as a developmental test, children only receive age-appropriate items)
- Reduce burden to participants and data collectors
- Demonstrate operational feasibility in the field

Process
- Obtain publisher agreement to develop Short Form
- Review data set from Bayley 3 development to identify questions and activities that provided the highest “bang for the buck” (reliability, specificity, ....)
- Review testing procedures to minimize cumbersome items & maximize operational ease

Experimental Design
- Four field sites
  - San Antonio, Philadelphia, Rockville, Seattle
- Sample size: 1,000 + test-retest sample (10%)
- Typically developing infants and toddlers
- Sample design emulates 2010 American Community Survey (census) data
  - Stratified by: Region, Gender, Age, Ethnicity/Race, Parent Education Level

Progress
- Bagley-III Short Form Developed
- Recruit Study Participants
- Recruited 20% of participants necessary
- We are actively looking for infants and toddlers to participate in the study.
  - One on one administration with parent present for approximately 30 minutes of time
  - Parents receive $25.00 gift card to HEB, books and a parent information sheet on activities to increase child’s functioning.
  - Testing here at UTHSCSA or other locations can be arranged
Likely Outcome/Expected Completion

→ Once testing is completed then the data will be compared against the larger standardization data.
→ If the form has adequate reliability and functionality it will used as a measure in the larger NCS study.

Why This Matters to You

→ Research
  → Gold standard instrument used by psychologists to evaluate developmental delay
  → Short form will provide a reliable and time efficient measurement for selected age groups
  → Reduced participant burden
  → Reduced staff time and effort

“Three to Get Ready”

Spirometry in Preschool Children

Pamela R. Wood, MD, Professor of Pediatrics
• Ed Brooks MD, Professor of Pediatrics
• Jordan Kampschmidt, Research Associate

Background

• Need valid method to assess pulmonary function across entire age span (0-21 yrs)
• No one standard method for preschool children
  • Methods used: spirometry; tidal breathing; interrupter technique; forced oscillation; etc
  • Most testing done in lab setting by trained respiratory therapist

Challenges

• Difficulty in performing maneuver
• Exhalation is short (often <1 sec); cf. school-aged children (≥3 sec) and adults (≥6 sec)
• No standard age-appropriate predictive values

Literature review (all testing by respiratory therapists)

• [Eigen] n=259, 3-5 yrs; 82% completed valid test
• [Peasant] n= 164, 54% 3 yr olds cf. 89% 5 yr olds produced two acceptable curves
• [Gaffin] n= 248, 4-5 yr; 82% at least one acceptable test; 54% acceptable and reproducible; 29% at least one abnormal curve

Asthma Health Screening Survey

• Validated, brief parent questionnaire
• Scoring algorithm used to identify children with asthma vs “probable not asthma”
• Sensitivity 87%; specificity 84%; misclassification 14% (better than spirometry)
• High re-test reliability (kappa>.70)
• Spanish/English versions available
• Provides information on lung health over time
Purpose

Feasibility of implementing two different assessments of lung function in preschool children (spirometry; parent questionnaire) by trained lay fieldworker

Study Questions
- What % subjects provide acceptable results?
- Do spirometry results correlate with parent questionnaire; clinical assessment by specialist?
- Do questionnaire results correlate with specialist assessment?

Design

- Cross-sectional descriptive study
- Trained lay research assistant
- Setting: Head Start center (3-5 yrs)
- N=150 children (additional N=50 Lamar Co.)
  - Initial study visit: spirometry and questionnaires
  - N=25: repeat spirometry in 1 week
  - N=25: return for specialist visit
  - Probable asthma
  - Probable other resp. disorder, but not asthma
  - Probable healthy

Analysis

- Quality of data collected, reliability & validity
- Spirometry test-retest reliability
- Correlations:
  - spirometry and questionnaire
  - spirometry and specialist assessment

Enrolled Subjects’

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Bexar County</th>
<th>Lamar County</th>
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<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>American Indian/Alaskan Native</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Asian or Pacific Islander</td>
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<tr>
<td>White</td>
<td>27</td>
<td>20</td>
</tr>
<tr>
<td>More than one race</td>
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<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
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<tr>
<td>Not available</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>23</td>
</tr>
</tbody>
</table>

What This Matters to You

- Clinical
  - How reliable and consistent is the "gold standard" for assessing respiratory function (spirometry) in preschool children?
  - How does this compare to the more widely used questionnaire?

- Research
  - Can spirometry be taught to field staff?
  - Can spirometry be undertaken in the non-clinical environment?

“Four to Go”

Measurement of Maternal Life Experience (MOM-le)

Douglas E. Williamson, PhD

- Donald Dudley, MD
- Tabitha Wilhelm, Research Associate
Importance of Intrauterine Experience

- Susceptibility for many common disorders can be traced back to the intrauterine period of life.
- Timing of internal/external environment stress occurring during sensitive periods of cellular proliferation, differentiation, and maturation.
- Psychosocial stress and/or biological stress implicated as one salient condition that may underlie the long-term programming effects of the intrauterine environment.

Psychosocial Stress and Adverse Pregnancy Outcomes

- Increased stress associated with increased health risks during pregnancy.
- Increased risk for pre-term births and associated morbidity risks.
- Stress effects fetal programming resulting in transmission of epigenetic modifications.
- Recent evidence linking alterations in offspring’s telomere length predicted by maternal stress during pregnancy.

Purpose

- To develop an optimized measures of self-reported stress in pregnancy scale.
- Determine the association between self-reported stress, and stress biomarkers (CRH, CRP, EBV, serum cortisol, hair cortisol, and salivary cortisol).
- Evaluate how stress biomarkers, cytokines, and genetic polymorphisms are linked to self-reported stress.

Design

- Socio-demographically diverse population of 500 pregnant women (English speaking).
- Adult women 18 years of age and older with a singleton intrauterine pregnancy (woman is pregnant with a single fetus).
- Initial assessment 2nd trimester (14’0 to 20’6 weeks gestation).
- Assessed again in 3rd trimester (28’0 to 32’6 weeks gestation).

Measures

- Panoply of psychosocial stress self-reports and interviewer-based interview.
- Collection of blood samples for genetic markers of the HPA axis and peripheral stress markers (e.g. CRH CBP) as well as inflammatory markers.
- In-home saliva sampling for cortisol measures (wake-up, 30-minutes, and bedtime over two days).
- Hair samples to validate their use in cortisol measures as an index of stress.
- Assessments at 2nd and 3rd trimesters in 500 pregnant women across study centers.
“Pregnancy Stress” Projects

- QUEX 01.1: Development of an Optimized Measure of Chronic Stress in Pregnancy: data-reduction project to create an optimized measure of psychosocial stress during pregnancy validated against biological markers of maternal stress. Lead Center – Greater Chicago Study Center
- QUEX 01.2: Evaluating Psychosocial Stressors in Pregnant Women. Lead Center – BEXAR Center
- QUEX 01.3: Selection and validation of self-report and biological measures of maternal stress using ecological momentary assessment (EMA) methodology. Lead Center – the Southern and Central California Study Center, Orange County Location
- QUEX 01.4: Biological moderators of cortisol activity. Lead Center – the Southern and Central California Study Center, Orange County Location
- QUEX 01.5: Validation of cortisol in hair samples for quantification of long-term cortisol exposure in pregnant and non-pregnant women. Lead Center – Pacific Northwest Center (PNW NCS)

Study Centers

<table>
<thead>
<tr>
<th>MOM-is Study Sites</th>
<th>Principal Investigators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown University</td>
<td>Maureen Phipps</td>
</tr>
<tr>
<td>Children’s Hospital of Philadelphia</td>
<td>Jennifer Culhane</td>
</tr>
<tr>
<td>Northwestern University</td>
<td>Ann Borders, William Grodman</td>
</tr>
<tr>
<td>Tulane University</td>
<td>Emily Harville</td>
</tr>
<tr>
<td>University of California, Irvine</td>
<td>Pathik Wadhwa</td>
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<tr>
<td>University of Minnesota</td>
<td>Pat McGovern</td>
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<td>University of Pittsburgh</td>
<td>Hyagriv Simhan</td>
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<tr>
<td>UTHSCSA</td>
<td>Douglas Williamson, Donald Dudley</td>
</tr>
<tr>
<td>University of Washington</td>
<td>Shirley Beresford</td>
</tr>
</tbody>
</table>

Recruitment Efforts

- Waiting for OMB!!!!!!!!!
- UTHSCSA leads stress interview consensus panels via Skype
- Identified recruitment sites at MARC and UHS Downtown
- N=3 women recruited locally at UTHSCSA during 2nd trimester as of 2/1/2012
- N=10 women recruited across all sites

Why This Matters to You

Clinical
Identifying increased morbidity risk associated with psychosocial stress likely to result in changes in clinical care (e.g. stress reduction) during pregnancy

Research
The measurement of psychosocial stress in the NCS study, as informed by this formative project, will yield insight into the relation between stress and health across development for years to come

What’s Next?

- Main Study start date now projected for 2013
- Actively recruiting for the Spirometry and Ulnar Study
- Awaiting OMB approval for Bayley and Maternal Stress Study (but generating lists of potential participants and locations)

Call 210-567-7599 or Come By and See Us