CTSA 3.0
Special Populations Core

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What is a “Special Population”? 

Groups traditionally under-represented in health research 
- Pediatric populations (including adolescents and young adults) 
- Older adults 
- People with disabilities 
- People with rare disorders 
- Populations who have been under-served or under-represented in clinical research, including 
  - Racial/ethnic minorities 
  - Rural populations 
  - Sexual or gender minorities/LGBT communities 
  - Populations with low socioeconomic status
SPECIFIC AIMS of SP CORE

1. **Provide resources** to accelerate and amplify life course and disparities research

2. **Build workforce capacity** in life course and health disparities research

3. **Expand the professional network** of life course and disparities investigators
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<td>Partnership with Children’s Health Discovery Initiative and Translating Duke Health</td>
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Special Populations Core Pilot Program

Timeline

• Mandatory LOIs received **Sept 17**
• Invited Full Applications due: **Dec 4**
• Selection of Awardees: **Jan 2019**
• Funding Period: **March 1, 2019 – February 28, 2020**

Award: $25,000 for 12 months

Recruiting reviewers now
Research & Resources Survey 2018-19

- Survey of SOM, SON Faculty and Trainees
- Purpose: identify Duke researchers and resources for integrating special populations
- Survey domains:
  - Participant Department/expertise, position
  - Special populations researcher
  - Resources used (Duke, non-Duke; intend to use

Resource Categories
- Training
- Recruitment-related
- Existing data
- Measurement/Analytic
- Community Guidance
- Other
Registries and Datasets

- Follow up on Survey responses re: Registries and Datasets to develop list of these resources ("registry of registries")
- Collaborating with GetData@Duke, Phase 2 Steering Committee
- Ensure cataloguing features to identify special populations datasets
5 Ts Framework for Integrating Special Populations in Clinical Research

- 5 Ts Framework developed to support clinical research in geriatric populations
  - Bowling et al., submitted
  - CTSA/SP Core staff supported
- But the framework may be helpful for other special populations
### 5 Ts Framework for ISP *(working draft)*

| **Target population** | “At risk” or “real-world” population | - Avoid exclusions that limit study generalizability  
- Understand needs, historic barriers to research |
|-----------------------|--------------------------------------|-----------------------------------------------------------------|
| **Team**              | Research team  
Community members | - Engage with research experts in different fields experienced with target population(s)  
- Connect with community members, patients, caregivers |
| **Tools**             | Measurement tools validated for target population | - Choose appropriate measures of function, physical performance, patient-reported outcomes, etc.  
- Balance data collection and participant burden |
| **Time**              | Participant and study time | - Anticipate length of visit/timing adjustments – e.g., longer study visits for older populations, shorter visits for children, snacks/medications for long visits  
- Time of day – naps or school day, transportation availability |
| **Tips to accommodate** | Get Suggestions to engage target population effectively and sensitively | - Get tips for feasible research plan adjustments (e.g., transportation costs, extra time for visits or recruitment, outreach workers, tracking)  
- Communication accommodations or translations  
- Plan for retention and attrition rates in sample size/power |
One Way We are Already Partnering with CHDI: Durham Children’s Datamart

• Co-sponsoring CHDI project for TDH support
• Data pull of defined data elements from electronic health records from DUHS, Lincoln for more cost- and time-efficient access for IRB-approved research.
• CHDI/datamart analysts provide datasets in cost- and time-efficient manner (likely <1 week)
• Model may inform other special population Datamarts* (e.g., geriatric populations, rare disease patients)
Aim 3: Expanding the Professional Network

Let’s brainstorm... New opportunities for the SP Core and the CHDI to work together?
A Unique Birth Cohort Study

“The 1000 most studied people on Earth”

(These slides shared with enthusiastic permission from Drs. Terri Moffitt and Avshalom Caspi)
The Dunedin Study

<table>
<thead>
<tr>
<th>Age</th>
<th>Year</th>
<th>Number</th>
<th>Percent*</th>
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<tbody>
<tr>
<td>Birth</td>
<td>1972-73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1975-76</td>
<td>1037</td>
<td>100%</td>
</tr>
<tr>
<td>5</td>
<td>1977-78</td>
<td>991</td>
<td>96</td>
</tr>
<tr>
<td>7</td>
<td>1979-80</td>
<td>954</td>
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<td>1981-82</td>
<td>955</td>
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<td>1983-84</td>
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<td>13</td>
<td>1985-86</td>
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<td>1990-91</td>
<td>993</td>
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<td>21</td>
<td>1993-94</td>
<td>992</td>
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<td>26</td>
<td>1998-99</td>
<td>980</td>
<td>96</td>
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<tr>
<td>32</td>
<td>2004-05</td>
<td>972</td>
<td>96</td>
</tr>
<tr>
<td>38</td>
<td>2010-12</td>
<td>961</td>
<td>95%</td>
</tr>
<tr>
<td>45</td>
<td>2017-2019</td>
<td>800 and counting</td>
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*Percent assessed, of those who were alive at each age.
Multidisciplinary since the 70’s:
Vision, Hearing, Dental, Motor skills, Lung function
Longest Running Epidemiological Study of Psychiatric Disorders

- 35% of Dunedin cohort children had a first psychiatric diagnosis before the end of adolescence.
Age-3 Brain Health Assessment, 1975

- Exam by a pediatric neurologist
- Bayley Motor Skills test
- Reynell Receptive Language test
- Peabody Picture Vocabulary test
- Examiner-rated poor behavioral control
Age-3 Brain Health & Age-45 Gait Speed

![Graph showing the relationship between Age-3 Brain Health (z-scores) and GAITrite Velocity Z-Score. The graph indicates a positive correlation, with values increasing as brain health improves.](image-url)
Evolving Conceptual Models of Aging

Decades of the Human Life Course

Prior

1st → 2nd → 3rd → 4th → 5th → 6th → 7th → 8th → 9th

Disease → Disability, Frailty → Mortality

Newer

Early-life Adversity → Disease → Mortality

Innovative

Early-life Adversity → Accelerated Aging → Disease, Disability, Frailty → Mortality
Variation in pace of aging among 38-year-olds
Dunedin Team has operationalized the “Pace of Aging” Concept
Combine Change Slopes Across 18 Biomarkers Measured at Age 26, 32, and 38

\[
\text{Pace of Aging}_i = \sum_{B=1}^{18} u_{1iB}
\]

Scaled to Reflect Physiological Change per Chronological Year
1. The pace of biological aging can be measured in young adults as coordinated decline across organ systems

2. Measured aging predicts physical limitations, cognitive decline, and subjective face aging

Quantification of biological aging in young adults

Daniel W. Belsky,1,2,* Avital K. Caspi,3,4,* Karen M. Nessel,5 Harvey J. Cohen,6,7 William Kraus,6,7 Sandhya Ramakhr,6,7,8
Sarah E. Reiter,9 Andrea Strough,4,10 Ilana L. Hartog,10,11 Solomon Parnes,10 Morgan C. Leske,10 Jonathan B. Schaefer,10 Kuresh S. Patel,10
Edward J. Fratiglioni,10 Robert J. Kass,10 and Teresa M. Wolpoff,10,11

The pace of biological aging can be measured in young adults as coordinated decline across organ systems. Measured aging predicts physical limitations, cognitive decline, and subjective face aging. Measured aging is explained in part by lifestyle and genetic factors. Lifestyle factors that reduce measured aging include smoking, obesity, and physical inactivity. Genetic factors that increase measured aging include age, sex, and family history of disease. Measured aging is associated with a greater risk of mortality and disability in older adults. This suggests that measured aging is a useful biomarker for identifying individuals at risk of age-related diseases.
Collaborative Ideas with Longitudinal Data

1. Propose a new analysis using Dunedin data
2. Collect new data in ongoing longitudinal cohort (e.g., Kannapolis, Dunedin)
3. Aspirational Goal: Launch our own birth cohort?
   • Population Diversity
   • Novel Measures
   • Validate accelerated “Pace of Aging” concept
Aim 3: Expanding the Professional Network

Let’s brainstorm...

New opportunities for the SP Core and the CHDI to work together?
Expanded Newborn Screening

- Tandem mass spectrometry (MS/MS) has reduced several technical problems associated with previous screening technology
  - high false positive rates (by increasing specificity)
  - the expense of individual tests
  - the inflexibility of other methods
Tandem mass spectrometry (MS/MS) has reduced several technical problems associated with previous screening technology:

- high false positive rates (by increasing specificity)
- the expense of individual tests
- the inflexibility of other methods

Figure 3. Newborn screening with tandem mass spectrometry begins with the collection of blood, which is used to make spots on a cotton card. Small circles punched from the blood spots undergo laboratory processing that prepares the sample for analysis. Molecules from the sample are electrically charged by a technique called electrospray ionization before being introduced into one arm of a tandem mass spectrometer, the first mass analyzer, which can be tuned to pass selected ions into the central reaction cell. There, molecules of an inert gas, usually argon, collide with the ions, causing them to break apart. A second mass analyzer then separates the fragments. The abundance of different fragments provides a characteristic signature for abnormal metabolites. States must establish protocols for how to interpret results and how to treat sick children diagnosed in this way.
History of Newborn Screening in NC

- PKU (1967)
- Congenital Hypothyroidism (1979)
- Galactosemia (1988)
- Congenital Adrenal Hyperplasia (1989)
- Sickle Cell Anemia (1994)
- Expanded Newborn Screening (4/1999)
  - Amino Acid Profile (not all amino acids)
  - Acylcarnitine Profile
- Cystic fibrosis, adrenoleukodystrophy (2015-on)
Benefits of Newborn Screening

- 41 infants detected by NBS in NC with MCAD deficiency from inception in 4/97 to 6/02 (5 years)
- Incidence of 1 in 13,600 live births
- Outcome tracked through an IRB-approved protocol at UNC-Chapel Hill
- No deaths: Significantly improved morbidity and mortality compared to published cases of MCAD deficiency.

McCandless S et al., North Carolina Newborn Screening Advisory Committee, June 28, 2002, Raleigh, NC
Long-Term Follow-Up after Newborn Bloodspot Screening

- Newborns are tested for >30 congenital disorders
- Testing conducted by state public health laboratories
- NBS is a coordinated and comprehensive system:
  - Education
  - Screening
  - Follow-up
  - Diagnosis
  - Treatment
  - Management
  - Program evaluation
Expanded NBS: A National Priority

- All should be screened equally
- Screening should improve outcomes and save lives
- Screening is only as effective as the care it prompts
- Collaboration between screening, short-term, and long-term team members is critical to improved outcomes
- Data sharing is essential

Modified from Susan A. Berry, MD, University of Minnesota
Inborn Errors of Metabolism Information System

• Goals:
  o Develop a large scale follow-up record as a platform for research
  o Create a model for a national platform

• Started with one disorder (MCAD deficiency)
  o Developed demographic database
  o Developed condition-specific data elements

• Defined issues for short- and long-term follow-up
• Expanded to include other disorders
Inborn Errors of Metabolism Information System

- Planned together to have accessible information that is easy to maintain

- Documented consent to allow continuing contact, anticipating engaging subjects as participants in future research trials

- Duke was a site, now inactive IRB protocol

- Interest in resurrecting, expanding that effort?
Questions, Comments, Other Ideas?

Thank you!
EXTRA SLIDES