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ADULT AND CHILD CENTER FOR OUTCOMES RESEARCH AND DELIVERY SCIENCE
UNIVERSITY OF COLORADO
CHILDREN'S HOSPITAL COLORADO

# Session Two: Improving Evidence Generation to Address Gaps in Serious Illness Care Research: Research Methodology/Study Design

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# Outline

- Current State, Gaps, & Opportunities
  - Study Design
  - Statistical Methods
  - Workforce & Training
- Specific opportunities
- Take-aways

# Study Design

## Current State

- Innovative trial designs
- Innovative cluster randomization techniques
- All stages of research maturity are represented in the literature
- Engaging patients & other stakeholders to learn what outcomes matter to them
- The PCRC & other groups made it possible to create multisite studies, connect & train researchers, and develop fully powered RCTs, CRTs

## Gaps

- Research cooperatives or collaboratives for facilitating multisite trials
- Reaching all relevant populations (diverse demographics, rural, barriers to accessing care, etc.)
- Pragmatic trials are unblinded with significant dropout or death

## Opportunities

- New U54 "Consortium for Palliative Care Research Across the Lifespan"
- Improving design to mitigate missing data & target outcomes important to stakeholders
- Make use of publicly available data & electronic health record (EHR) data

# Statistical Methods

## Current State

- Methodological advances in handling missing data
- Incorporation of SDOHs using census data
- Limited incorporation of EHR data in trials & use of NLP
- Causal mediation methods for evaluating mechanisms
- Dyadic analyses

## Gaps

- Too much missing data
- Use of older mediation methodologies & insufficient power to detect
- Insufficient power for CRTs, esp. non-inferiority
- Not enough focus on using existing data for research

## Opportunities

- Bayesian methods
- Contemporary mediation:
  - Coefficient methods
  - Potential outcomes
- Rethinking which outcomes to target on the causal pathway to reduce missing data & increase effect size
- Cross-disciplinary collaborations with computer science & biostatistics to make use of EHR data

# Workforce & Training: Collaborative Biostatisticians

**Current State**

- Strong biostatistics programs across the US
- Competition for students with Data Science and Computer Science programs
- NHLBI Summer Institutes in Biostatistics (SIBS)

**Gaps**

- **Too few collaborative biostatisticians**
- Few postdoctoral training programs in collaborative biostatistics

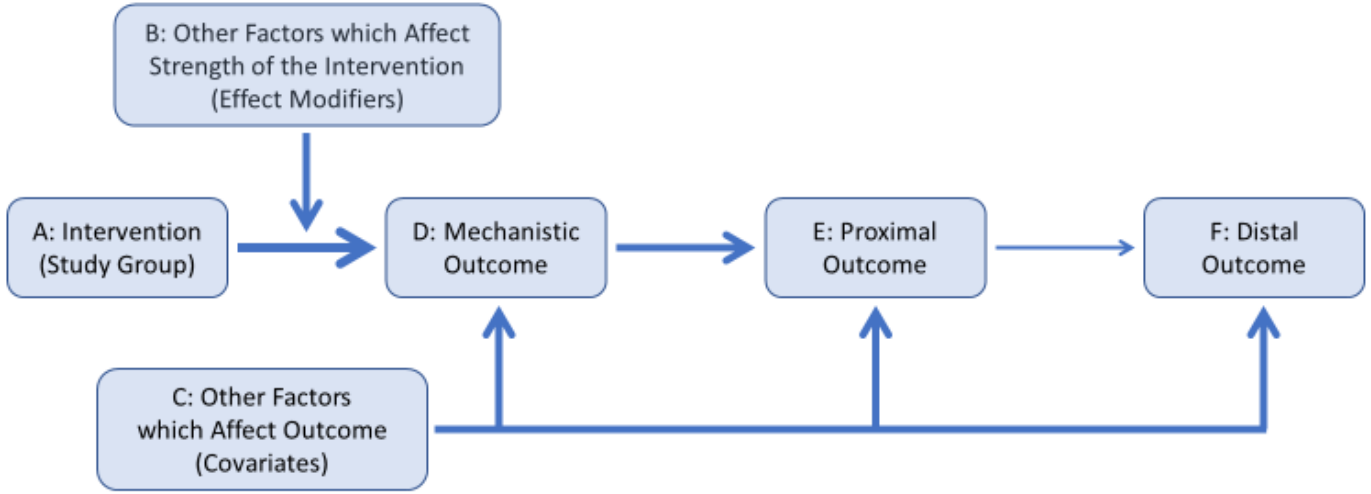
**Opportunities**

- Create centers for biostatistics resources & data coordinating centers (DCC)
- More NIH institutes investing in SIBS & postdoctoral training programs in **collaborative** biostatistics

# Opportunity: Clearly Define What Matters and **When**

- Can we reduce missing data if we focus on outcomes earlier in the causal pathway?
- What outcomes are important to stakeholders that can be impacted before patients decline?
- Be careful that non-inferiority conclusions are not type II errors
- Statistical methods for handling missing data should be last resort

## A Statistician's Conceptual Framework




Samsa G, Colborn K, Olsen M, Pomann GM, Grambow S, Neely M, Troy J. *A Visual Tool to Help Develop a Statistical Analysis Plan for Randomized Trials in Palliative Care*. J Pain Symptom Manage. 2023 Jan;65(1)

# Opportunity: Leveraging Data

- Data collected as routine care are underutilized in serious illness and palliative care research
- Focus on patient reported outcomes is important, but data are difficult & expensive to collect
- Alternative outcomes:
  - Hospital-free days
  - Location of death
  - Visits to the hospital
  - Number of encounters with palliative care team
  - Using NLP to determine if goals of care were collected or achieved

# Opportunity: Centers for Biostatistics Support

- Many investigators spread throughout the US; few collaborative biostatisticians
- Not all institutions can build biostatistics capacity
- Collaborative centers for biostatistics support & DCCs are critical
- Training biostatisticians to be strong collaborators & skilled in methods unique to serious illness research is necessary
- Engage biostatisticians in R25 training programs
- Postdoctoral training programs in collaborative biostatistics
- Team science: psychometricians, computer scientists, biostatisticians

# Take-aways

- Pragmatic trials require many sites
- Design studies to mitigate missing data & incorporate data collected through routine care
- Engage interdisciplinary research teams to better integrate large, observational datasets & clinical notes
- Increase opportunities for biostatisticians to train alongside serious illness scientists to become effective collaborators & mentors

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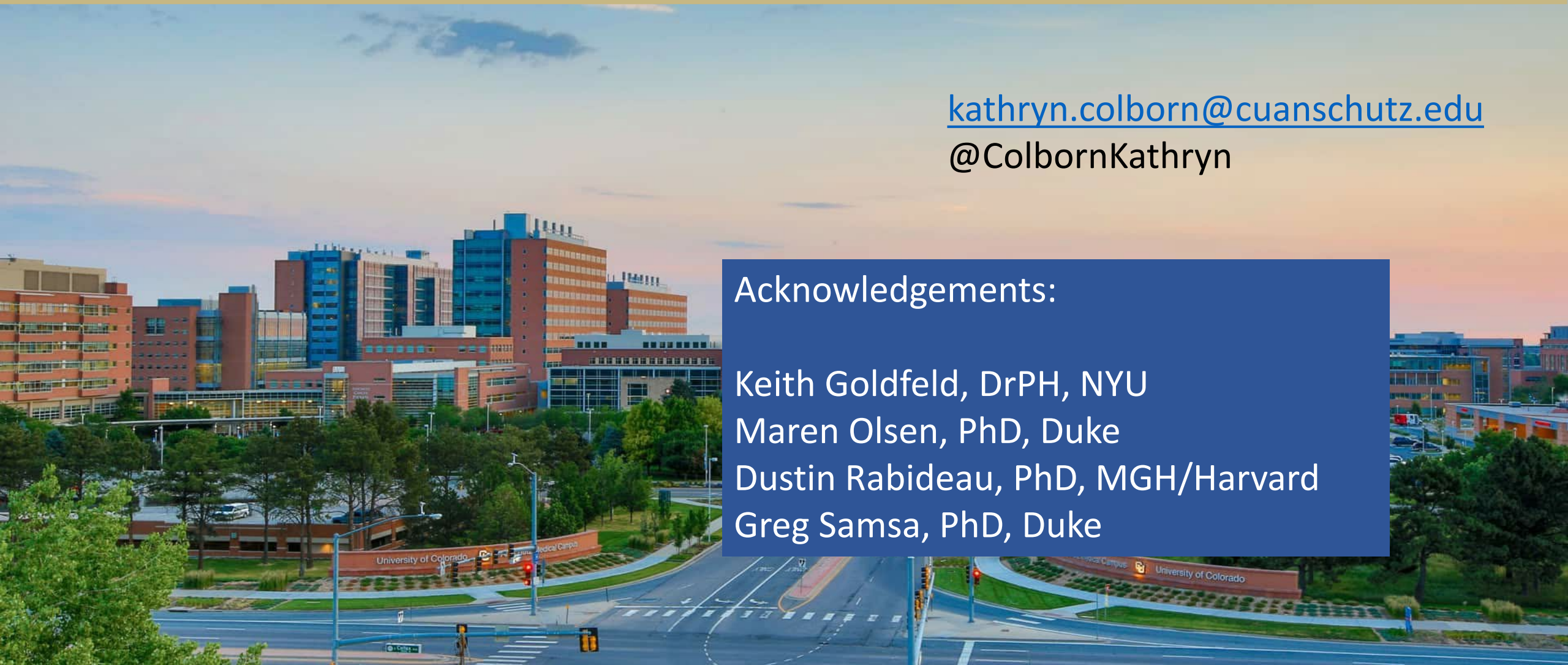


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