Clinical Research Collaborations in North Dakota

Stephen Wonderlich Ph.D.
Vice-President for Research, Sanford Health-Fargo
Chester Fritz Distinguished Professor
University of North Dakota School of Medicine and Health Sciences

February 17th, 2021
Objectives


2. Overview of Collaborative Center of Biomedical Research Excellence (COBRE) Grant Application (2020 – 2021)
Eating Disorder Treatment Development

• Eating disorders represent one of the most (if not the most) lethal psychiatric disorders
  – Anorexia nervosa
  – Bulimia nervosa
  – Binge eating disorder

• Eating disorder treatments are moderately effective, intensive (hospital), and lengthy
Local Basic Behavioral Science Collaboration (since 1998)

• Twenty years ago we needed a better understanding of the nature of EDs in real time and real world (what symptoms, when, under what conditions)

• UNDSOM, NDSU, Meritcare/Sanford personnel developed technology-based behavioral assessment system
  – Behaviors (symptoms)
  – Location
  – Stress
  – Cognition
  – Emotion
  – Eating

(Funded by NIMH MH059674, MH059674-5)
This was “cool” in 1998!

Check Boxes
Real-Time Assessment In the Natural Environment (ReTAINE)

ReTAINE is a highly effective tool for research organizations needing a secure system for collecting data from research participants in their natural environment.

ReTAINE stands for Real Time Assessment In the Natural Environment. The researchers at the Neuropsychiatric Research Institute in Fargo, North Dakota created this web-based system that allows researchers and clinicians to gather important information from individuals in their natural environment.

ReTAINE can be used to design customized assessments, can automatically signal participants to complete those assessments based upon individualized schedules, and it can collect and manage the data participants provide using their smartphones, tablets or personal computers. ReTAINE is easy to use, economical and secure.

CONTACT NRI TODAY for more information or to schedule a demonstration.
We learned a lot in these studies. One example...
Emotional States and Symptoms

![Graph showing emotional states over time](image)

- **Negative Affect**: Peaks around -2 hours relative to binge and drops to baseline at 0 hours.
- **Positive Affect**: Rises to a peak around 0 hours and remains high until 2 hours post-binge.
How to bring these findings to the clinic?

The strength of clinicians and scientists collaborating.
Integrative Cognitive-Affective Therapy for Bulimia Nervosa

A Treatment Manual

Stephen A. Wonderlich, Carol B. Peterson, and Tracey Leone Smith
with Marjorie H. Klein, James E. Mitchell, and Scott J. Crow

Guilford Press, 2015
A randomized controlled comparison of integrative cognitive-affective therapy (ICAT) and enhanced cognitive-behavioral therapy (CBT-E) for bulimia nervosa


1 Neuropsychiatric Research Institute/Department of Clinical Neuroscience, University of North Dakota School of Medicine and Health Sciences, Fargo, ND, USA
2 Department of Psychiatry, University of Minnesota, Minneapolis, MN, USA
3 Department of Psychiatry, University of Wisconsin, Madison, WI, USA

(Funded by NIMH MH098995, MH077571)
But how do we disseminate and implement?
2021 ICAT Learning Collaborative Marketing Plan

Learning Collaborative Presenters:
Stephen Wonderlich, PhD, FAED
Carol Peterson, PhD, FAED
Importantly, these collaborative projects can lead to bigger collaborative projects.
<table>
<thead>
<tr>
<th>Sanford Personnel</th>
<th>NDSU/UND Personnel</th>
<th>Other Institutions</th>
<th>Internal Advisory Board</th>
<th>Core Research and Educational Services</th>
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<tr>
<td>Steve Wonderlich, PhD</td>
<td>Ben Balas, PhD</td>
<td>Guido Frank, MD</td>
<td>Jonathan Geiger, PhD</td>
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<td>Ross Crosby, PhD</td>
<td>Colin Combs, PhD</td>
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<td>Lauren Schaeffer, PhD</td>
<td>Clayton Hilmert, PhD</td>
<td>Adrienne Juarascio, PhD</td>
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<td>Katie Gordon, PhD</td>
<td>Leah Irish, PhD</td>
<td>David Sarwer, PhD</td>
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<td>Clinical Research Training Program</td>
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<td>Gail Williams-Kerver, PhD</td>
<td>Jeff Johnson, PhD</td>
<td>David Warren, PhD</td>
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<td>Pilot Projects Grant Program</td>
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<td>Lora Black, RN, MPH</td>
<td>Michael Robinson, PhD</td>
<td>Joanna Steinglass, MD</td>
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<td>Kathy Lancaster</td>
<td>Jim Roerig, PharmD</td>
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<td>Lee Baugh, PhD</td>
<td>Paul Rokke, PhD</td>
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<td>Ryan Bosca, PhD</td>
<td>Kristine Steffen, PhD</td>
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Summary

- Local institutions have effectively collaborated on eating disorder research
- The research program has clinical utility and relevance
- In our experience health systems and universities are good collaborators
SANFORD RESEARCH

INNOVATING HEALTH CARE THROUGH CUTTING EDGE SCIENCE

OVERARCHING STRATEGY AND GOALS

• BUILD INFRASTRUCTURE CAPACITY TO CONDUCT VISIONARY RESEARCH WITH A FOCUS ON HEALTH IMPACT
• LEAD IN PROVIDING PATIENT FACING CLINICAL RESEARCH
• DEVELOP INNOVATIVE PROGRAMS INTEGRATING RESEARCH INTO HEALTHCARE
• CONTINUE DEVELOPMENT OF HUMAN CAPITAL DEDICATED TO RESEARCH AND SCIENTIFIC ADVANCEMENT
SANFORD HEALTH
INTEGRATED HEALTH SYSTEM WITH RESEARCH
FOUNDATION
<table>
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<tr>
<th>Category</th>
<th>Count</th>
<th>Notes</th>
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<tr>
<td>Scientists</td>
<td>46</td>
<td>New scientists supported by COBREs</td>
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<tr>
<td>Physicians</td>
<td>189</td>
<td>CBR, Hybrid positions, Invest. Initiated studies</td>
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<td>Staff</td>
<td>234</td>
<td>Clinical 44%, Basic 34%, CBR 6%, Admin/Animal 13%</td>
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<td>Publications</td>
<td>2923</td>
<td>Lifetime publications of SR scientists. 88/153 in 2019</td>
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<td>Major Awards</td>
<td>3 COBRES DaCCoTA NCORP 5 R Awards</td>
<td>SR maxed out on CoBRE awards. Replace as move into Phase 3. Add COBRE in CBR and R01s. Augment Govt grants with commercial.</td>
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<td>Treatment Approvals</td>
<td>&gt;15 in past 5 yrs.</td>
<td>Oncology and Gene Therapy</td>
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<td>Clinical Trials</td>
<td>&gt;300 Active</td>
<td>Moved from predominantly Oncology (&gt;60%) to 57% non-oncology</td>
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<td>Clinical Trial Accruals</td>
<td>&gt;3600 in 2019</td>
<td>Over 12,000 Sanford patients currently on a clinical trial</td>
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<td>Specialty Associated Working Group</td>
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<td>• Trauma</td>
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<td>Ortho Trauma</td>
<td>• Neurology</td>
<td>• Behavioral Health</td>
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<td><strong>Physician Lead</strong> (Currently Active PIs)</td>
<td>Dr. Noonan</td>
<td>Dr. Drofa</td>
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<td>Dr. Piatt</td>
<td>Dr. Timmerman</td>
<td>Dr. Hajek</td>
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<td>Dr. Timmerman</td>
<td>Dr. Hajek</td>
<td>Dr. Luis Casas</td>
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<td>Dr. Wonderlich</td>
<td>Dr. Griffin</td>
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<td><strong>Research Support</strong></td>
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<td>Directors/PMs</td>
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<td><strong>Executive Leads</strong></td>
<td>Dr. Garcia</td>
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# RESEARCH RESPONSE – COVID-19

## Basic/Translational
- **BIO-ID COVID-19 VIRUS CHARACTERIZATION**
- **LAB SUPPORT FOR COVID TESTING AND SERUM TESTING**
- **CHARACTERIZATION OF ANTIBODY RESPONSE WITH HEALTHCARE WORKER ANTIBODY STUDY**
- **BIOSTATS CORE SUPPORT (REGISTRY/PATIENT CARE DATA)**

## Clinical
- **FORMED COVID SPECIALTY ASSOCIATED WORKING GROUP (SAWG)**
- **EXPANDED TREATMENT OPTIONS WITH CLINICAL TRIALS ACROSS DISEASE SPECTRUM**
- **ADAPTIVE COVID-19 TRIAL TO RAPIDLY TEST THERAPY OPTIONS AND COMBINATIONS – INPATIENT AND OUTPATIENT STUDIES**
- **CELLULAR THERAPY CLINICAL TRIALS – FIRST IN NATION**
- **OUTPATIENT ANTIBODY INFUSION CREATION – OPEN IN TWO WEEKS, TREATED 1800+ TO DATE**

## Behavioral
- **BEHAVIORAL HEALTHCARE FOR HEALTHCARE PROFESSIONALS**
- **BEHAVIORAL HEALTH BRIDGE PROJECT WITH UND (RURAL MENTAL HEALTH)**
- **RESILIENCE TRAINING FOR HOSPITAL WORKERS**
Biobehavioral Research
A Collaborative Partnership in Research
Focused on Obesity and Bariatric Surgery

Kristine J. Steffen, Pharm.D., Ph.D.
Professor, Dept. of Pharmaceutical Sciences
School of Pharmacy/College of Health Professions
NORTH DAKOTA STATE UNIVERSITY &
Director of Biomedical Research
SANFORD CENTER FOR BIOBEHAVIORAL RESEARCH
In the news…

Weight loss surgery tied to increase in drinking
Published October 16, 2012

Gastric bypass and alcohol: mix with caution
March 10, 2011 | Melissa Healy, Los Angeles Times

By CBS News Staff CBS News June 18, 2012, 2:33 PM

Gastric bypass surgery may double a patient's risk for alcohol problems
AUD Prevalence

- King et al., 2012 – LABS-2 Data - JAMA
  - AUDIT used to determine AUD
    - Preop: n=106 (7.6%)
    - 1Yr Post-op: n=101 (7.3%)
    - 2Yr Post-op: n=133 (9.3%)*
      - * statistically significant increase from baseline and from one year
  - 7.9% of participants without preoperative AUD had postoperative AUD
7-Year Follow-Up - LABS

King et al., 2017 - SOARD
Research in Fargo on AUD

• **R03, NIH, 2009**
  – Steffen & Engel
    • Ecological momentary assessment and laboratory Assessment to Evaluate the Development of AUD

• **R01, NIH, 2014**
  – Steffen (NDSU) & Engel (Sanford CBR)
    • Laboratory-based assessment of the pharmacokinetics and impairment associated with alcohol consumption.
Engel, Steffen, et al. 2020
Presented at the *Obesity Society* annual meeting

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**Reward**

Mean Reward

**Minutes from Administration**

- Blue line: Pre-Surgery
- Orange line: Post-Surgery

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**BAC**

Mean BAC

**Minutes from Administration**

- Blue line: Pre-Surgery
- Orange line: Post-Surgery
Where to Next…

• Mechanisms for this finding are currently largely unknown.

• Competing Continuation of R01

• Sanford Profile/NDSU funded collaboration
  – Drs. Steffen, Engel, Williams
  – Evaluating alcohol-related reward and naturalistic drinking patterns (SCRAM)
The “Microbiome”

• Trillions of microorganisms (microbiota or microbes) made up of thousands of species of bacteria, fungi, parasites, and viruses (aka “bugs”).
• Largest numbers are in the intestines – particularly the colon.
• Other organ systems have their own microbiome – it is not a phenomenon isolated to the intestine/gut.
• The microbiome consists of both symbiotic and pathogenic organisms.
  – Research is often focused on dysbiosis - unfavorable shifts in the microbiome due to disease, diet, drugs, etc.
“The microbes in the gut send messages in the brain and are able to influence cognition, mood, executive function, emotional regulation, stress response, pain, and social behavior.”

Adaes, 2019
NIDDK Funding -
1R01AA022336-01A1 & 3R01AA022336-01A1S1

- RFA issued by NIDDK - 2016
  - Psychosocial and Behavioral Mechanisms in Bariatric Surgery (R01)

- “Mechanisms that Predict Weight Trajectory after Bariatric Surgery: the Interactive Roles of Behavior and Biology” (R01DK112585-01)
  - Grant focused on the intersection of behavior and biology – “Biobehavioral”
• **Data Collection Centers & Investigative Team**
  - Sanford Center for Biobehavioral Research/North Dakota State University – Fargo, ND
    - Kristine Steffen (Grant PI)
    - Ross Crosby (Co-Investigator - Biostatistician)
    - James Mitchell (Co-Investigator - Bariatrics)
  
  - Cleveland Clinic Lerner College of Medicine at Case Western Reserve University – Cleveland, OH
    - Leslie Heinberg (Grant PI)
• Data Collection Centers & Investigative Team
  – University of North Carolina – Chapel Hill, NC
    • Christine Peat (Co-Investigator – Psychological Assessment)
    • Ian Carroll (Co-Investigator – Microbiome)
  – University of North Carolina – Charlotte, NC
    • Anthony Fodor (Co-Investigator – Metagenomic Sequencing)
  – Brown University, Providence, RI
    • Dale Bond (Co-Investigator – Physical Activity)
  – Kent State University, Kent, OH
    • John Gunstad (Co-Investigator – Cognitive Functioning)
What’s Next?

- Collaborative R01 in data analysis evaluating the relationship of the microbiome with Anorexia Nervosa
  - Partnership between UNC (Ian Carroll), Sanford CBR (Wonderlich) and NDSU (Steffen)

- Collaborative R01 focused on the intersection between behavior and biology between NDSU and Sanford CBR
  - Steffen, Engel, Schaefer, Williams, Crosby, Wonderlich
What’s Next?

• R01 Competing Continuation – June 2021
  – The microbiome appears related to weight outcomes…how?
  – Evaluate the combined contribution of the microbiome and behavioral variables to energy balance and weight outcomes following surgery.

• R01 Animal Study – October 2021
  – Collecting pilot data with Cleveland Clinic.
  – Colonize germ free mice with human microbiome to evaluate the impact on weight and psychiatric status.
Thank You!

Kristine Steffen, Pharm.D., Ph.D.
kristine.steffen@ndsu.edu