

Clinical Research Collaborations in North Dakota

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Objectives

1. Brief overview of collaborative eating disorder research in North Dakota (1998 – 2021)
2. Overview of Collaborative Center of Biomedical Research Excellence (COBRE) Grant Application (2020 – 2021)

Eating Disorder Treatment Development

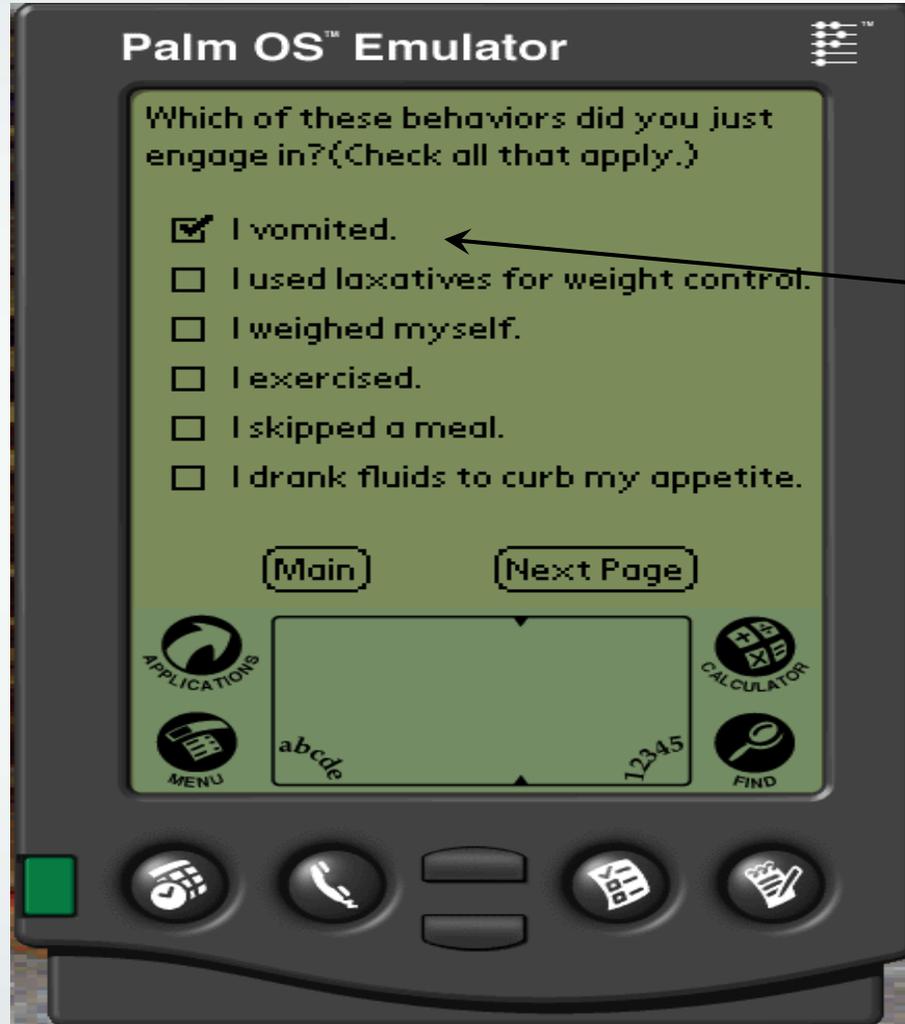
- Eating disorders represent one of the most (if not the most) lethal psychiatric disorders
 - Anorexia nervosa
 - Bulimia nervosa
 - Binge eating disorder
- Eating disorder treatments are moderately effective, intensive (hospital), and lengthy

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)



Real Time Assessment In the Natural Environment
By Neuropsychiatric Research Institute (NRI)

About ReTAINE

Contact Us

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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 smart phones, tablets or personal computers. ReTAINE is easy to use, economical and secure.

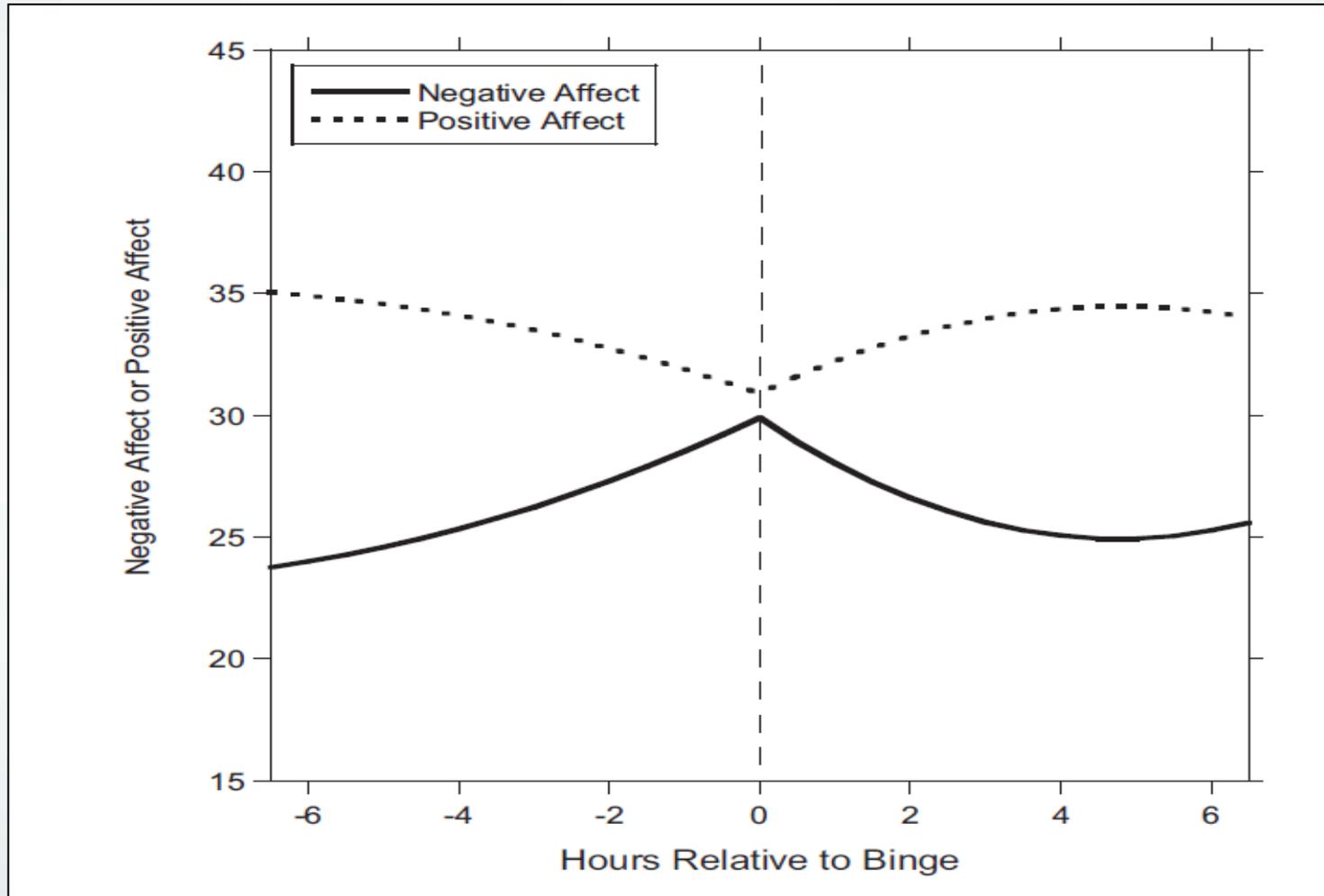
[CONTACT NRI TODAY](#) for more information or to schedule a demonstration.

[Retrieve User Login](#)

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**We learned a lot in these studies.
One example...**

Emotional States and Symptoms



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

S. A. Wonderlich^{1*}, C. B. Peterson², R. D. Crosby¹, T. L. Smith³, M. H. Klein³, J. E. Mitchell¹
and S. J. Crow²

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.

**Center of Biomedical Research Excellence
Sanford Center for Biobehavioral Mechanisms of Eating Behavior**

Sanford Personnel	NDSU/UND Personnel	Other Institutions	Internal Advisory Board	Core Research and Educational Services
Steve Wonderlich, PhD	Ben Balas, PhD	Guido Frank, MD UCSD	Jonathan Geiger, PhD UND	Research Assessment Core
Ross Crosby, PhD	Colin Combs, PhD	John Gunstad, PhD Kent State	Mark McCourt, PhD NDSU	Biostatistics Core
Scott Engel, PhD	Dan Friesner, PhD	Thomas Joiner, PhD Florida State	Dave Pearce, PhD Sanford	Human Subjects Core
Lauren Schaeffer, PhD	Clayton Hilmert, PhD	Adrienne Juarascio, PhD Drexel		Administrative Core
Katie Gordon, PhD	Leah Irish, PhD	David Sarwer, PhD Temple		Clinical Research Training Program
Gail Williams-Kerver, PhD	Jeff Johnson, PhD	David Warren, PhD U of Nebraska		Pilot Projects Grant Program
Lora Black, RN, MPH	Michael Robinson, PhD	Joanna Steinglass, MD Columbia		
Kathy Lancaster	Jim Roerig, PharmD			
Lee Baugh, PhD	Paul Rokke, PhD			
Ryan Bosca, PhD	Kristine Steffen, PhD			

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

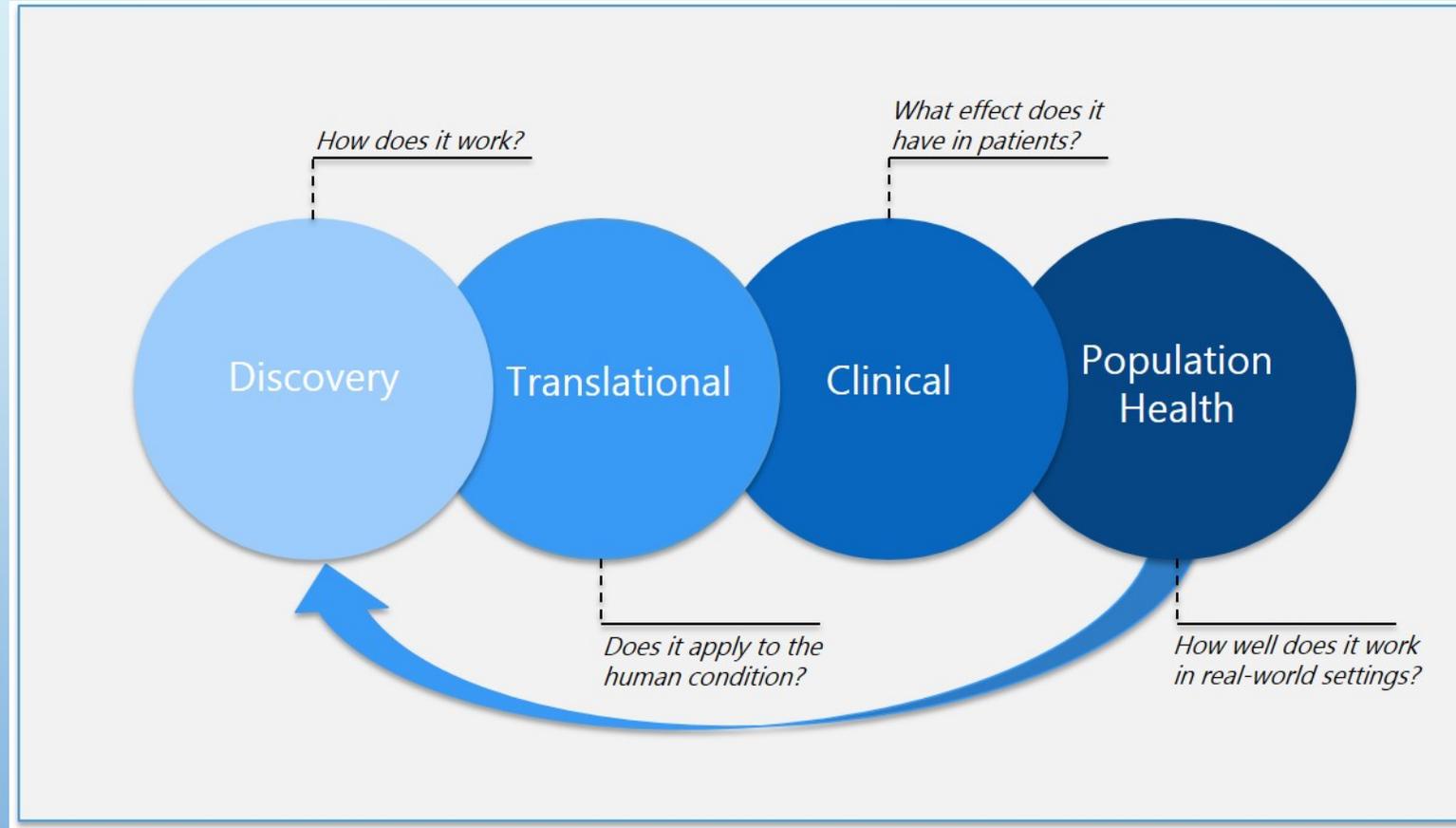
INNOVATING HEALTH CARE THROUGH CUTTING EDGE SCIENCE

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



Scientists	46	New scientists supported by COBREs
Physicians	189	CBR, Hybrid positions, Invest. Initiated studies
Staff	234	Clinical 44%, Basic 34%, CBR 6%, Admin/Animal 13%
Publications	2923	Lifetime publications of SR scientists. 88/153 in 2019
Major Awards	3 COBRES DaCCoTA NCORP 5 R Awards	SR maxed out on CoBRE awards. Replace as move into Phase 3. Add COBRE in CBR and R01s. Augment Govt grants with commercial.
Treatment Approvals	>15 in past 5 yrs.	Oncology and Gene Therapy
Clinical Trials	>300 Active	Moved from predominantly Oncology (>60%) to 57% non-oncology
Clinical Trial Accruals	>3600 in 2019	Over 12,000 Sanford patients currently on a clinical trial

SANFORD RESEARCH - 2020

Specialty Associated Working Group	SPORT	GOST	IGR	Diabetes	CV	WIPF
Specialties	<ul style="list-style-type: none"> • Sports Medicine • Podiatry • Orthopedics • Regen Medicine • Ortho Trauma 	<ul style="list-style-type: none"> • GI • Ophthalmology • Surgery • Trauma • Neurology 	<ul style="list-style-type: none"> • Imagenetics • Genetics • Rare Diseases • Pop Health • Outcomes • Behavioral Health 	<ul style="list-style-type: none"> • T1 Diabetes • T2 Diabetes • Endocrinology 	<ul style="list-style-type: none"> • Cardiology • Interv. Radiology • Vascular 	<ul style="list-style-type: none"> • Women's • IM/ID • Pediatrics • Family Medicine • Nephrology • Cystic Fibrosis
Physician Lead (Currently Active PIs)	Dr. Noonan Dr. Piatt	Dr. Drofa Dr. Timmerman	Dr. Wonderlich Dr. Hajek	Dr. Griffin Dr. Luis Casas	Dr. Kelly Dr. Haldis Dr. Stys	Dr. Benson Dr. Landeen Dr. Wallace
Research Support	Directors/PMs					
Executive Leads	Dr. Garcia	Dr. Garcia	Dr. Pearce Dr. Suttle	Dr. Wilcox	Dr. Cauwels	Dr. Suttle
HSD Leadership	Executive Directors and Clinic Directors as applicable					

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

**Off-Label/EUA
Clinical Use**

Trials

Approaches

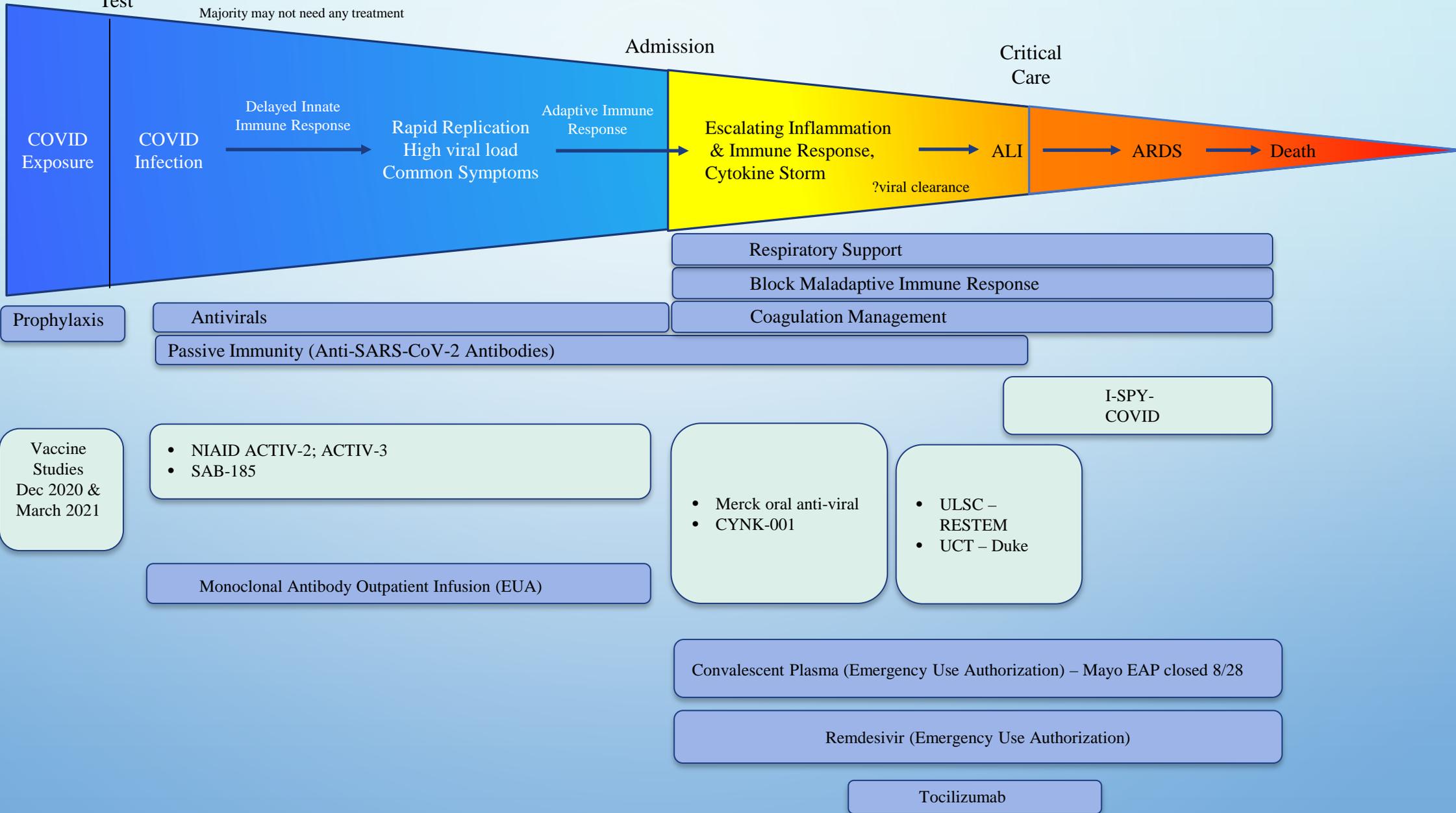
Clinical Stage

Surveillance

SURVIVE – HCW Antibody Surveillance Study

Positive
Test

Majority may not need any treatment



COVID Exposure

COVID Infection

Delayed Innate Immune Response

Rapid Replication
High viral load
Common Symptoms

Adaptive Immune Response

Escalating Inflammation & Immune Response, Cytokine Storm

?viral clearance

ALI

ARDS

Death

Prophylaxis

Antivirals

Passive Immunity (Anti-SARS-CoV-2 Antibodies)

Vaccine Studies
Dec 2020 & March 2021

- NIAID ACTIV-2; ACTIV-3
- SAB-185

Monoclonal Antibody Outpatient Infusion (EUA)

Respiratory Support

Block Maladaptive Immune Response

Coagulation Management

I-SPY-COVID

- Merck oral anti-viral
- CYNK-001

- ULSC – RESTEM
- UCT – Duke

Convalescent Plasma (Emergency Use Authorization) – Mayo EAP closed 8/28

Remdesivir (Emergency Use Authorization)

Tocilizumab

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

Los Angeles Times | ARTICLE COLLECTIONS

Gastric bypass and alcohol: mix with caution

March 10, 2011 | Melissa Healy, Los Angeles Times

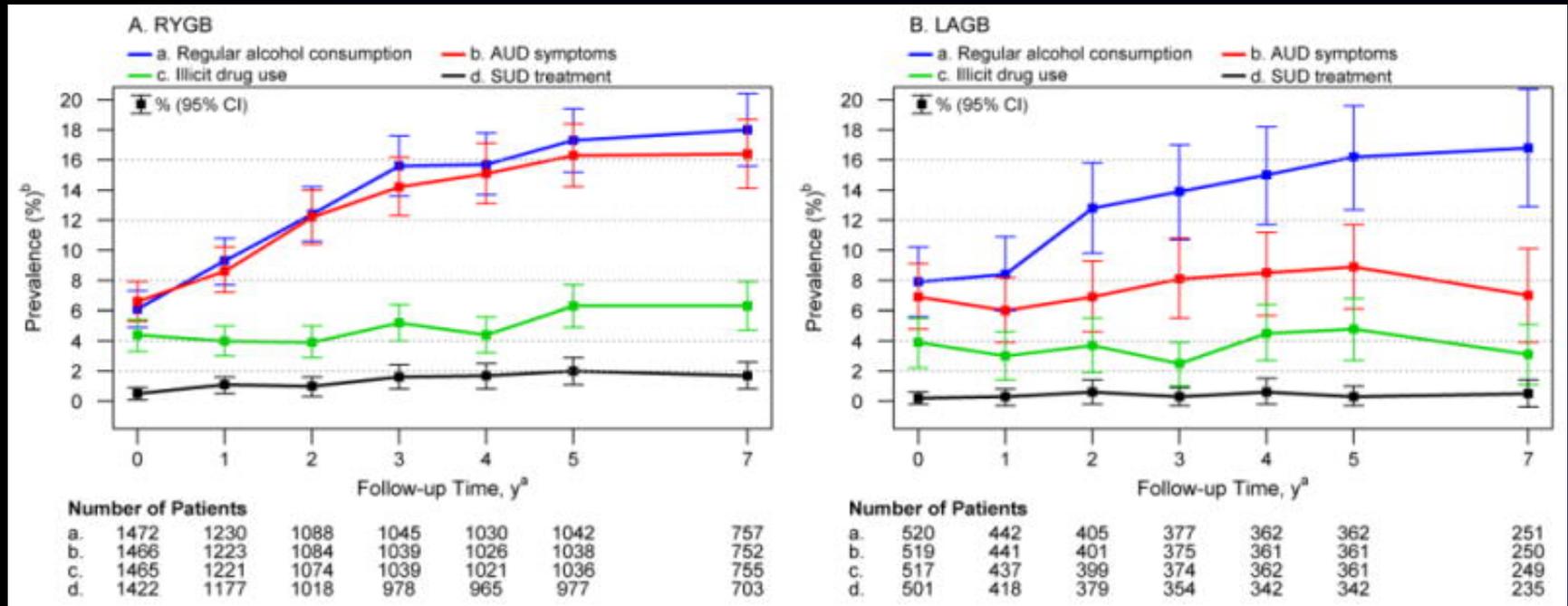
By CBS News Staff CBS News June 18, 2012, 2:33 PM

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

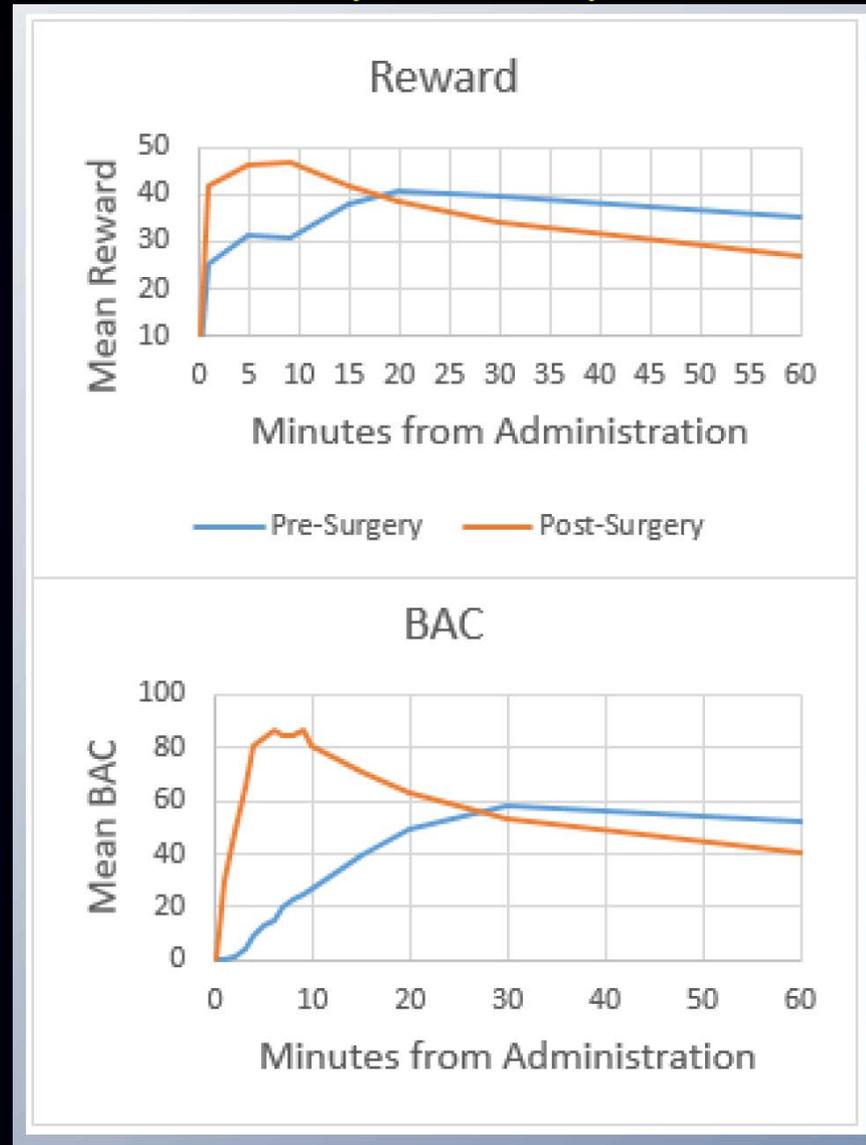
- R01, NIH, 2014

- 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



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)

Figure 9. 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.

Microbiome Gut-Brain Axis

“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.”

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”

1R01AA022336-01A1 & 3R01AA022336-01A1S1

- 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)

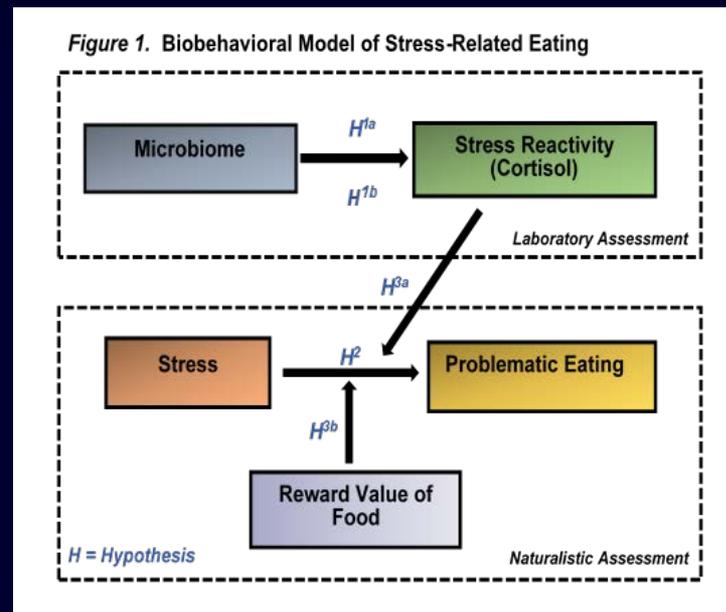
1R01AA022336-01A1 & 3R01AA022336-01A1S1

• 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!

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