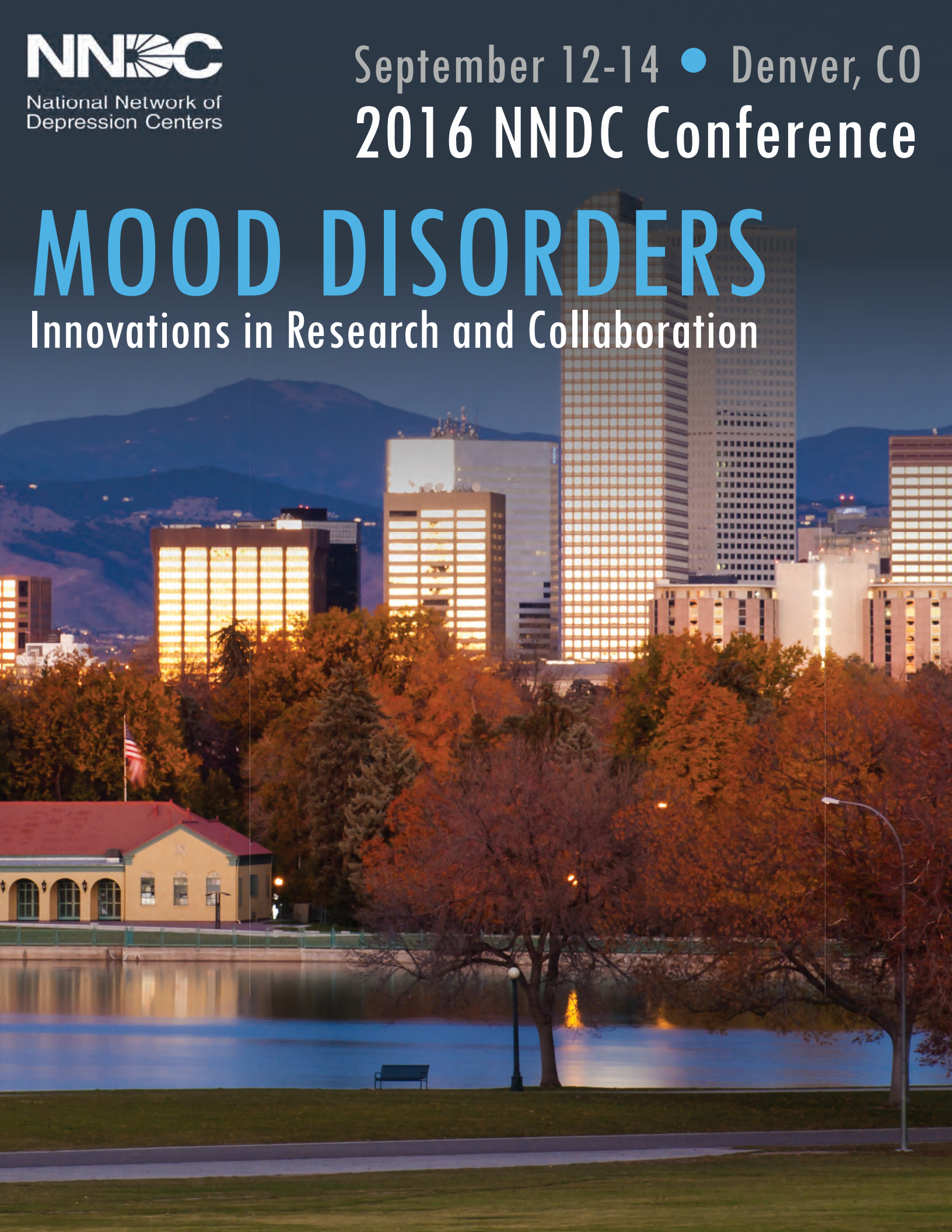
NNDC
National Network of Depression Centers

September 12-14 • Denver, CO

# 2016 NNDC Conference

# MOOD DISORDERS

## Innovations in Research and Collaboration



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PsychU
Improving mental health care... together

We would also like to thank George Wiegers for his generous support of the NNDC Annual Conference.

Helen and Arthur E. Johnson Depression Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

Special thanks go to the host of the 2016 NNDC Annual Conference, the Helen and Arthur E. Johnson Depression Center at the University of Colorado. The NNDC truly appreciates the support of the Colorado team throughout the planning process.

# Contents

# Acknowledgements

We would like to thank all of our speakers and facilitators for their contributions both to this conference and to their areas of study as a whole. We are proud to work with such highly respected and knowledgable clinicians, researchers, and advocates and hope to continue developing these and other relationships with some of the country's brightest minds in the future.

In addition, we thank the NNDC Conference Program and Planning Committees for putting together another engaging and innovative Annual Conference Program.

## Conference Program Committee

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Woodward-Chisholm Professor & Chair
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Last but not least, we'd like to thank our Summer Intern Gabi Guerra! Gabi is a sophomore at Stanford University and is considering a major in Psychology.

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National Network of Depression Centers

## Welcome to the 2016 NNDC Annual Conference!


**Frank deGruy, MD & Sagar Parikh, MD**
Conference Co-Chairs

We are thrilled to be hosting this year's event in Denver. There is much happening here and throughout Colorado that is of great interest on a national scale, including developing innovative collaborative care models, utilizing the latest technologies to improve quality and scope of treatment, and improving our understanding of how comorbidities of marijuana and tobacco use affect patients diagnosed with mood disorders. This year's program reflects the unique perspective that can be found here in Colorado and how we can work together as a Network to leverage the results of individual specialties for the overall improvement of treatment and understanding of mood disorders.

We are now at a tipping point, as NNDC Founding Chair John Greden likes to say – and he is right. The Network is growing, now up to 25 members with more on the horizon. The Mood Outcomes program, the NNDC's signature multi-site mood disorders patient registry, has launched at 6 sites and counting. We are increasing our presence in academic, public, and legislative domains. And we are forming more and more partnerships across the nation, and even the world. The NNDC is in precisely the right place to foster significant advances in treating and understanding mood disorders, to advocate for honest conversations about depressions and bipolar illnesses, and to promote and influence national and state level mental health legislation.

It is always a delightful challenge to put together content for these meetings – the collective knowledge of our member base could fill many more weeks of programming! What links the Network together, though, is innovation. NNDC members are part of some of the most innovative studies and clinical programs in the world. So that is where we started; this year's theme, "Mood Disorders: Innovations in Research and Collaboration," brings that NNDC core of innovation together with the local Colorado perspective. The result is a very interesting and exciting set of talks from both local and national experts.

We hope you learn new techniques and perspectives. We hope you connect with both NNDC members and partner organizations alike. But most of all, we hope you enjoy the content our speakers have prepared for you.

Thank you for joining us, as always.

The National Network of Depression Centers is pleased to welcome you to Denver! This year's theme is "Mood Disorders: Innovations in Research and Collaboration." The program committee has crafted the program to showcase the new tools and collaborations which we see in our future. We have top speakers this year in collaborative care and pharmacogenomics. Please join us and look to the future with your partners at the NNDC.

Ray DePaulo, MD - NNDC Chair

On behalf of the NNDC team, I hope you enjoy this year's Annual Conference. I know everyone involved with coordinating this event, from the planning and program committees to the speakers and poster presenters, put a lot of work into making sure it's a good one. Thank you for joining us – we hope to see you again next year!

Pat Rinvelt, MBA - NNDC Executive Director

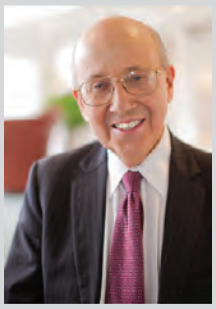
## Keynote Speaker • Jürgen Unützer, MD, MA, MPH

Professor and Chair
Psychiatry & Behavioral Sciences
University of Washington School of Medicine
uwpsychiatry.org

Director, AIMS Center
Advancing Integrated Mental Health Solutions
aims.uw.edu

Dr. Unützer is Professor and Chair in the Department of Psychiatry and Behavioral Sciences at the University of Washington. He holds adjunct appointments as Professor in the School of Public Health (Department of Health Services and Department of Global Health) and as Affiliate Investigator at the Group Health Research Institute in Seattle, WA. Dr. Unützer also directs the AIMS Center dedicated to 'Advancing Integrated Mental Health Solutions' and the IMPACT Program which has supportedthe development, testing and implementation of an evidence based program for depression treatment in more than 1,000 primary care clinics in the United States and abroad. IMPACT has been shown in randomized controlled trials to double the effectiveness of usual care for depression while lowering long-term health care costs. In recent years, Dr. Unützer's work has focused on developing local, regional, national, and global partnerships that support workforce development and capacity building in primary and behavioral health care. Dr. Unützer trained in Medicine (MD, Vanderbilt University), Public Policy (MA, University of Chicago), and Public Health / Health Services (MPH, University of Washington). He completed fellowships in Geriatric Psychiatry at UCLA and in Primary Care Psychiatry at the University of Washington.His work focuses on innovative models of care that integrate mental health and general medical services and on translating research on evidence-based mental health care into effective clinical and public health practice. He has over 250 scholarly publications and is the recipient of numerous federal and foundation grants and awards for his research to improve the health and mental health of populations through patient-centered integrated mental health services. His awards include the Beeson Physician Faculty Scholars Award from the American Foundation for Aging Research, the Gerald L. Klerman Junior and Senior Investigator Awards from the Depression and Bipolar Support Alliance, the Distinguished Scientist Award from the American Association of Geriatric Psychiatry, the Research Award from the Academy of Psychosomatic Medicine, and the Senior Health Services Scholar Award from the American Psychiatric Association.

## David Mrazek Lecturer • Richard M. Weinshilboum, MD



Mary Lou and John H. Dasburg Professor
of Cancer Genomics Research
Chair, Division of Clinical Pharmacology
Professor of Pharmacology and Medicine
Mayo Clinic College of Medicine

Dr. Weinshilboum received B.A. and M.D. degrees from the University of Kansas, followed by residency training in Internal Medicine at the Massachusetts General Hospital, a Harvard teaching hospital, in Boston. He was also a Pharmacology Research Associate at the National Institutes of Health in Bethesda, Maryland, in the laboratory of Nobel Laureate Dr. Julius Axelrod. Dr. Weinshilboum began his affiliation with the Mayo MedicalSchool and Mayo Clinic in Rochester, Minnesota, in 1972 where he is presently Professor of Pharmacologyand Medicine and Mary Lou and John H. Dasburg Professor of Cancer Genomics Research. Dr. Weinshilboum's career has been devoted to the development of "Precision Medicine", specifically, the use of genomics and other "omic" science to individualize drug therapy. He currently directs the Pharmacogenomics Program of the Mayo Center for Individualized Medicine and he is Co-Principal Investigator of the long-standing US National Institutes of Health (NIH) Pharmacogenomics Research Network Center at the Mayo Clinic. Dr. Weinshilboum has authored over 400 scientific manuscripts which address personalized drug therapy. A major area of investigation initially was the pharmacogenetics of drug metabolism but, in recent years, he has increasingly applied genome-wide pharmacogenomic techniques and "Next Generation" DNA sequencing to study individual variation in response to the drug therapy of breast cancer and depression. Dr. Weinshilboum has been the recipient of many awards and honors including an Established Investigatorship of the American Heart Association, a Burroughs Wellcome Scholar Award in Clinical Pharmacology Award, the Oscar B. Hunter Award of the American Society for Clinical Pharmacology and Therapeutics, the Harry Gold Award of the American Society for Pharmacology and Experimental Therapeutics, the Catecholamine Club Julius Axelrod medal, the Edvard Poulsson Award from the Norwegian Pharmacology Society, Distinguished Medical Alumnus Award from Kansas University Medical School and Mayo Distinguished Alumni Award. He has also served on the Advisory Councils for two US NIH Institutes, the National Institute of General Medical Sciences (NIGMS) and the National Human Genome Research Institute (NHGRI).

# Continuing Education Credit Statement

## ACCME

Amedco designates this live activity for a maximum of **8.0 AMA PRA Category 1 Credits™.** Physicians should claim only the credit commensurate with the extent of their participation in the activity.

### Approval Statement

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Amedco and the National Network of Depression Centers. Amedco is accredited by the ACCME to provide continuing medical education for physicians.

## APA

This course is co-sponsored by Amedco and the National Network of Depression Centers. Amedco is approved by the American Psychological Association to sponsor continuing education for psychologists. Amedco maintains responsibility for this program and its content. **8.0 hours**.

Professional Counselors in these 41 states can submit APA:

AK, AR, AZ, CA, CO, CT, DC, DE, FL, GA, IA, ID, IL, IN, KY, KS, ME, MO, MN, NC, ND, NH, NE, NJ, NM, NV, OK, OR, PA, RI, SC, SD, TN, TX, UT, VA, VT, WA, WI, WV, WY

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Addiction Professional in these 26 states can submit APA:

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Social workers participating in this course may receive up to **8.0 clinical continuing education clock hours**.

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MFT's in these 25 states can submit ASWB:

AK, AR, AZ, CA, CO, FL, IA, ID, IN, KS, ME, MO, NC, NE, NH, NM, NV, OK, PA, TN, TX, UT, VA, WI, WY

Addictions Professionals in these 19 states can submit ASWB:

AK, CA, CO, CT, GA, IA, IN, KS, LA, MO, MT, ND, NM, NV, OK, OR, SC, WA, WI, WV, WY

# Agenda

## Mood Disorders: Innovations in Research and Collaboration

### Monday • September 12

| | |
|---|---|
| 3:30 - 4:30 PM • Vail | NNDC Executive Committee Meeting |
| 5:00 - 8:00 PM • Vail | NNDC Board Meeting & Dinner |

### Tuesday • September 13

| | |
|---|---|
| 8:00 - 9:00 AM • Majestic | Breakfast |
| 9:00 - 9:30 AM • Majestic | Welcome & Opening Remarks<br>Ray DePaulo, MD - Johns Hopkins University<br>Frank deGruy, MD - University of Colorado Denver<br>Bruce D. Benson - President, University of Colorado |
| Session 1 • Majestic | Technological Advances in Mental Health Care<br>Facilitator: John Greden, MD - University of Michigan |
| 9:30 - 10:00 AM | "Advances in the Measurement of Mental Health" • NOT FOR CME/CE CREDIT<br>Robert D. Gibbons, PhD - University of Chicago |
| 10:00 - 10:30 AM | "Computer-Assisted Cognitive Behavior Therapy for Depression: Progress and Opportunities"<br>Jesse H. Wright, MD, PhD - University of Louisville |
| 10:30 - 11:00 AM | "Leveraging Telepsychiatry to Improve Access and Quality in the Treatment of Mood Disorders"<br>Jay H. Shore, MD - University of Colorado Denver |
| 11:00 - 11:30 AM | Beverage & Snack Break |
| Session 2 • Majestic | David Mrazek Lecture<br>Facilitator: Ray DePaulo, MD - Johns Hopkins University |
| 11:30 AM - 12:30 PM | "Precision Medicine and Major Depressive Disorder"<br>Richard M. Weinshilboum, MD - Mayo Clinic |
| 12:30 - 1:15 PM • Majestic | Lunch |
| Session 3 • Majestic | Mood Disorders and Comorbid Substance Use<br>Facilitator: Scott Langenecker, PhD - University of Illinois Chicago |
| 1:15 - 2:00 PM | "Innovation in Smoking Cessation Interventions in Mood Disorders"<br>Michael Ostacher, MD, MPH, MMSc - Stanford University |
| 2:00 - 2:45 PM | "Research on Cannabis Use and Comorbid Disorders Post-Legalization: Dazed and Confused?"<br>Kent Hutchison, PhD - University of Colorado Boulder |
| 2:45 - 3:15 PM | Beverage & Snack Break |

| | |
|---|---|
| Session 4 • Majestic | **Primary Care Integration**<br>Facilitator: Jacqueline Calderone, MD - University of Colorado Denver |
| 3:15 - 4:15 PM | "Achieving the Triple Aim: Can Collaborative Care Help Us Improve the Patient Experience, Improve Health Outcomes, and Reduce Cost"<br>Jürgen Unützer, MD, MPH, MA - University of Washington (Keynote Speaker) |
| 4:15 - 4:30 PM | "Integrated Care from the Primary Care Side of the River"<br>Frank V. deGruy III, MD, MSFM - University of Colorado Denver |
| 4:30 - 4:45 PM | "Changing Policy, Changing Payment, Changing Care: Fighting Fragmentation Through Integration"<br>Benjamin F. Miller, PsyD - University of Colorado Denver |
| 4:45 - 5:00 PM | **Break** |
| Session 5 • Vail | **Judged Poster Presentations** |
| 5:00 - 6:30 PM | Poster Presentations and Network Reception |
| 6:30 - 8:00 PM • Majestic | **Network Dinner**<br>Poster Awards Announced During Dessert |

## Wednesday • September 14

| | |
|---|---|
| 8:00 - 9:00 AM • Majestic | **Breakfast** |
| Session 6 • Majestic | **Novel Designs in Research**<br>Facilitator: Sagar V. Parikh, MD, FRCPC - University of Michigan |
| 9:00 - 9:30 AM | "Translating Research Into Practice: Pragmatic Research Designs"<br>Russell Glasgow, PhD - University of Colorado Denver<br>Whitney Jones, PhD - University of Colorado Denver |
| 9:30 - 10:00 AM | "Life in the Fast Lane: Study Design with Rapidly Acting Psychiatric Medications and in Acute Care Psychiatric Settings"<br>Cheryl McCullumsmith, MD, PhD - University of Cincinnati |
| 10:00 - 10:30 AM | "The Mood Outcomes Program: Status and Future Directions"<br>David Katzelnick, MD - Mayo Clinic<br>Peter Zandi, PhD - Johns Hopkins University |
| 10:30- 10:45 PM | **Break** |
| Session 7 • Majestic & Vail | **NNDC Mood Fair** |
| 10:45 AM - 12:15 PM | Progress Updates from NNDC Task Groups |
| 12:15- 1:00 PM | **Boxed Lunches for Carry Out**<br>Adjourn |

# Session Descriptions Tues Sept 13

## Session 1 Technological Advances in Mental Health Care

10:00 - 10:30

**"Advances in the Measurement of Mental Health" • NOT FOR CME/CE CREDIT**

Robert D. Gibbons, PhD
Blum-Riese Professor of Biostatistics
University of Chicago
adaptivetestingtechnologies.com

**Learning Objectives**

1. Understand the difference between diagnosis and measurement
2. Understand the difference between Classical Test Theory and Item Response Theory
3. Understand the fundamentals of Computerized Adaptive Testing

10:30 - 11:00

**"Computer-assisted Cognitive Behavior Therapy for Depression: Progress and Opportunities"**

Jesse H. Wright, MD, PhD (@JesswrightMD)
Professor and Kolb Endowed Chair in Outpatient Psychiatry
Director, University of Louisville Depression Center
University of Louisville

**Learning Objectives**

1. Describe empirical evidence for effectiveness of computer-assisted CBT for depression
2. Identify pros and cons of computer-assisted therapy (CCBT)
3. Recognize opportunities for improving access to effective psychotherapy for depression

11:00 - 11:30

**"Leveraging Telepsychiatry to Improve Access and Quality in the Treatment of Mood Disorders"**

Jay H. Shore, MD, MPH
Director of Telemedicine
Helen and Arthur E. Johnson Depression Center
University of Colorado Anschutz Medical Campus

**Learning Objectives**

1. Understand the current state of evidence for use of videoconferencing in psychiatric treatment
2. Learn about innovative models to leverage telepsychiatry in the treatment of mood disorders
3. Learn about clinical and administrative adaptation needed to successfully implement telepsychiatry services

## Session 2 David Mrazek Lecture

11:30 - 12:30

**"Precision Medicine and Major Depressive Disorder"**

Richard Weinshilboum, MD
Dasburg Professor of Cancer Genomics Research
Professor of Pharmacology and Medicine
Mayo Clinic College of Medicine

**Learning Objectives**

1. Understand the evolution of pharmacogenetics to pharmacogenomics to pharmaco-omics
2. Learn strategies for merging various "omics" datasets to gain understanding of MDD mechanisms and response to therapy

## Session 3 Mood Disorders and Comorbid Substance Use

1:15 - 2:00 **"Innovation in Smoking Cessation Interventions in Mood Disorders"**

Michael J. Ostacher, MD, MPH, MMSc (@RecoveryDoctor)
Associate Professor
Department of Psychiatry and Behavioral Sciences
Stanford University School of Medicine
Associate Director
Depression and Bipolar Research Program
VA Palo Alto Health Care System

**Learning Objectives**

1. Describe the differences in rates of smoking cessation in people with mood disorders compared to the general population
2. Describe novel interventions under study for smoking cessation in mood disorders

2:00 - 2:45 **"Research on Cannabis Use and Comorbid Disorders Post-Legalization: Dazed and Confused?"**

Kent Hutchison, PhD
Professor
Psychology and Neurosciences
University of Colorado Boulder

**Learning Objectives**

1. Understand the importance, nuances, and obstacles in studying the effects of cannabis on comorbid psychiatric disorders and health in general

## Session 4 Primary Care Integration

3:15 - 4:15 **"Achieving the Triple Aim: Can Collaborative Care Help Us Improve the Patient Experience, Improve Health Outcomes, and Reduce Cost?"**

Jürgen Unützer, MD, MPH, MA
Professor and Chair, Psychiatry and Behavioral Services
University of Washington
aims.uw.edu

**Learning Objectives**

1. Define and describe integrated behavioral health care
2. Describe the role of psychiatrists in collaborative care
3. Make the case for evidence-based integrated care programs to achieve the triple aim of healthcare reform
4. Apply principles of evidence-based collaborative care in diverse practice settings

4:15 - 4:30 **"Integrated Care from the Primary Care Side of the River"**

Frank deGruy III, MD, MSFM
Woodward-Chisholm Professor and Chair
Department of Family Medicine
University of Colorado School of Medicine

**Learning Objectives**

1. Describe the improvements of quality in primary care that resulted from integration
2. Describe 2 forms of integration that work in primary care

4:30 - 4:45 **"Changing Policy, Changing Payment, Changing Care: Fighting Fragmentation Through Integration"**

Benjamin F. Miller, PsyD (@miller7)
Eugene S. Farley, Jr. Health Policy Center
Department of Family Medicine
University of Colorado
farleyhealthpolicycenter.org

**Learning Objectives**

1. Discuss how fragmentation impacts behavioral health
2. Explain the solution found through behavioral health integration
3. Describe promising payment and policy recommendations in service to more robust behavioral health integration

## Session 5 Judged Poster Presentations

5:00 - 6:30 For poster abstracts, turn to page 14

# Session Descriptions Wed Sept 14

## Session 6 Novel Designs in Research

9:00 - 9:30 **"Translating Research Into Practice: Pragmatic Research Design"**

Russell Glasgow, PhD
Evaluation Hub, Department of Family Medicine
University of Colorado School of Medicine
re-aim.org

**Learning Objectives**

1. Identify limitations of traditional research designs
2. Discuss the 5 Rs to improve the relevance and applicability of research
3. Identify dimensions of the RE-AIM model for research translation
4. Use the PRECIS planning tool to plan research studies

9:30 - 10:00 **"Life in the Fast Lane: Study Design with Rapidly Acting Psychiatric Medications and in Acute Care Psychiatric Settings"**

Cheryl McCullumsmith, MD, PhD
Associate Professor
Director, Consultation Services
Associate Vice Chair for Hospital Services & Integration
Department of Psychiatry & Behavioral Sciences
University of Cincinnati Health

**Learning Objectives**

1. To understand issues in measuring effects of rapidly acting agents
2. To understand issues in acute care research

10:00 - 10:30 **"The Mood Outcomes Program: Status and Future Directions"**

David J. Katzelnick, MD
Professor of Psychiatry
Mayo Clinic
Peter Zandi, PhD
Professor, Department of Mental Health
Johns Hopkins Bloomberg School of Public Health

**Learning Objectives**

1. Learn the latest developments in building a learning health system for integrating clinical care and research on mood disorders
2. Learn about the challenges and solutions to implementing a patient registry on mood disorders

## Session 7 NNDC Mood Fair

10:45 - 12:15

Every year, NNDC Task Groups make positive contributions toward furthering research, diagnosis, treatment, and public policy on depression and bipolar illnesses. This year, four of the NNDC Task Groups (Electro Convulsive Therapy, Women and Mood Disorders, Telehealth, and College Mental Health) will hold exciting interactive sessions for knowledge translation during the Mood Fair. Interpersonal interaction rather than slide presentations is the main goal.

The Mood Fair consists of two parts:
Part 1) Similar to a featured poster session, the Task Groups will each have non-concurrent, 10-12 minute knowledge transfer talks to speak to the accomplishments and future directions of the Task Group.
Part 2) Table displays for each participating Task Group, where attendees can learn about the Task Group, ask questions, and develop new collaborations.

In addition, please join us for a discussion surrounding a newly proposed task group focused on Collaborative Care issues, starting at 11:30 am in the Vail room.

# Poster Abstracts

**1. The Right Antidepressant: Pilot Project of the Right 10K**

Ahmed T. Ahmed, M.B., B.Ch; Suzette J. Bielinski, Ph.D.; Nicholas B. Larson, M.S., PhD.; Jennifer St. Sauver, Ph.D.; Joanna M. Biernacka, Ph.D.; William V. Bobo, M.D., M.P.H.; Marin Veldic, M.D.; Simon Kung, M.D.; Richard Weinshilboum, M.D.; Liewei Wang, M.D., Ph.D.; Michelle Skime, M.S., CCRP; Scott Feeder, CCRP Mark A. Frye, M.D.

There is increasing recognition of pharmacokinetic/dynamic genetic variation and its contribution to treatment response and side effect burden. As there are more than 25 US FDA approved antidepressants, identifying the right drug, right dose, and right time utilizing genomic guided support tools gives the clinician and patient greater precision in treatment recommendations. In collaboration with the Pharmacogenomics Research Network (PGRN), Electronic Medical Record and Genomics (eMERGE), and the Mayo Clinic Center for Individualized Medicine, the RIGHT 10K pilot project identified 1013 patients from the Mayo Clinic Biobank. Initial review of the Right 10K (IRB 12-003371, PI Bielinski) data identified 318 patients [40% met international classification of diseases (ICD9) criteria for mood disorder (n=126 major depressive disorder, n=17 bipolar disorder)] who had been prescribed 1 or more conventional antidepressants [bupropion n=97, selective serotonin reuptake inhibitor (SSRI) n=285, serotonin-norepinephrine reuptake inhibitor (SNRI) n=109, atypical antidepressant n=160]. This initial survey of antidepressant data is the basis for this separate protocol focused on the Rochester Epidemiology Project (REP) for antidepressant response based on pharmacokinetic cytochrome p450 and pharmacodynamic genetic variation.

**2. rTMS modulates the limbic frontostriatal circuit in depression**

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**Background:** Repetitive transcranial magnetic stimulation (rTMS) modulates functional connectivity of cortical networks in depressed patients. Here, we investigated whether rTMS may also modulate frontostriatal functional connectivity in depression. **Methods:** 27 patients with treatment-resistant depression and 60 healthy controls underwent resting state fMRI (rs-fMRI). A seed-based analysis of functional connectivity (FC) used limbic, executive, and motor striatal seeds based on tractographic connectivity to ventromedial (limbic), dorsolateral (executive) and caudal (motor) frontal cortex (Cerebral Cortex. 2014 May; 24(5):1165-77). Patients underwent a 5-week course of rTMS over the left dorsolateral prefrontal cortex. HAMD-24 quantified depression severity and treatment response. Patients also were imaged with post-TMS rs-fMRI. FC was compared between patients and controls using a t-test and before and after rTMS in patients using a paired t-test, correcting for multiple comparisons. **Results:** Compared to healthy controls, depressed subjects showed frontostriatal hyperconnectivity in the limbic division and hypoconnectivity in the executive and motor divisions. rTMS appeared to affect only the limbic division. A comparison of FC before and after rTMS revealed a reduction in FC between the limbic striatal seed and a left orbitofrontal cluster near the subgenual anterior cingulate cortex (voxel-wise t-test, $p < 0.01$). This reduction overlapped with hyperconnectivity at baseline suggesting normalization of limbic frontostriatal connectivity after rTMS. **Discussion:** These results confirm previous findings that depression differentially affects limbic, executive and motor frontostriatal circuits. Further, it suggests that one candidate mechanism of rTMS for depression is that it modulates limbic frontostriatal connectivity.

**3. Differential mTOR activation, not GSK3, in peripheral blood distinguishes lithium responsive and non-responsive bipolar patients**

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Lithium remains the gold standard mood stabilizing medication for Bipolar Disorder (BD) worldwide. While available in most countries for more than 40 years, the mechanism of action that confers mood stabilization and/or reduction in suicidality remains relatively unclear. Developing personalized or individualized treatment approaches for bipolar patients

to best optimize outcomes will require greater delineation of the neurobiological mechanism underlying lithium response. Inhibition of glycogen synthase kinase 3 (GSK3) has repeatedly been shown to underlie the mood-related behavioral effects of lithium in preclinical rodent studies. GSK3 inhibition, in turn, directly modulates Wnt and PI3K/Akt signaling pathways in vivo and in vitro. Downstream of GSK3, mammalian target of rapamycin (mTOR) also plays a critical role in the behavioral actions of lithium, integrating cellular responses of both Wnt and PI3K/Akt pathways. These pathways contribute to cellular resilience, growth and plasticity processes thought to underlie antidepressant and mood stabilizing therapeutic outcomes in BD. GSK3 and mTOR have both been implicated in a number of important cellular functions critical to synaptic neurotransmission, plasticity, cell migration, survival, proliferation and plasticity. GSK3 and mTOR may also play a critical role in rapid antidepressant responses to ketamine, regulating both its behavioral and neurobiological effects, including establishment of long-term potentiation and new synaptic connections. Lithium treatment has also been shown to augment and extend these rapid antidepressant actions of ketamine through actions on GSK3 and mTOR, supporting a critical role for modulation of these signaling systems in its mood regulatory actions. The purpose of this study was to investigate the relationship between GSK3 and mTOR protein levels (total and phosphorylated) and lithium clinical response. The significant difference in phosphorylated levels of mTOR relative to no difference in total mTOR protein levels suggests increased overall mTOR activation in lithium non-responsive bipolar patients. Given all patients had been taking lithium >2 years at time of blood draw, this may reflect a limitation in the functional actions of lithium via this molecular substrate.

**4. The Bio-Psycho-Social Model and Primary Care: Uniting Telepsychiatry with a Robust Integrated Behavioral Health Service**

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The importance of behavioral health care integration into primary care is widely recognized. Both untreated and undertreated mental illness are major obstacles to achieving the quadruple aim of enhanced patient experience, improved population health, reduced health care costs and improved provider experience. Tele-psychiatry, in the form of live interactive video conferencing, has promise as a tool to facilitate integrated care between behavioral and medical treatments. The University of Colorado's Helen and Arthur E. Johnson Depression Center in partnership with the Department of Family Medicine have leveraged the use of tele-psychiatry into an integrated behavioral health service to most effectively conceptualize and treat the bio-psycho-social needs of our patient population. The innovation, which began in 2014, virtually embeds psychiatric providers into an existing integrated care team at a large local primary care PCMH academic residency practice. The service uses a cloud-based virtual telemedicine platform that is a real-time and video-based. The psychiatric providers offer three services which include: 1) E-Consults: Utilizing secure email to provide brief consultation and support psychiatric medication adjustments to primary care providers and the behavioral health team, 2) Consultations: Provider to provider, provider to team, and co-consultations with patients, and 3) Direct Psychiatric Care: Comprehensive psychiatric evaluation with continued coordination of care with the entire team. This presentation will provide a structured overview of the process used to develop and implement this service to guide others in developing similar programs. These steps include needs assessment, technology integration, work flow integration, and development of an array of protocols for systematic expansion and standardization of care. Lessons learned will be discussed including virtual integration apparatuses, continuous work flow modifications, and initial outcomes including service structure and utilization data.

**5. A comprehensive population health management approach to behavioral health issues in primary care**

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The impact of comorbid mental illness on medical morbidity, mortality and costs is well established. For many reasons, including stigma, lack of access to specialty mental health services, and patient preference, half of mental health care is delivered in primary care settings. To support this care, Partners HealthCare Population Health Management (PHM) undertook a multi-year initiative to promote behavioral health integration in primary care settings for its 950,000 primary care patients in more than 200 primary care practices organized into 10 health care management and delivery organizations in Eastern Massachusetts. There are two main components of the initiative. The first involved the rapid deployment of a broad set of services meant to support and improve the provision of care for persons with mild to moderate depression within primary care practices. Services include trainings, provider and patient resources, "curbside consultations" and referral assistance. The second component was a stepped implementation of the depression collaborative care model, an evidence-based integrated care model, within Partners primary care practices over several years. PHM simultaneously incentivized depression screening

and training. PHM is currently expanding this initiative to address anxiety and substance use disorders, and to expand the set of resources within the initiative. Routinely generated programmatic data is used to monitor implementation, and summarize adoption/utilization of the services over time and across the delivery system. By leveraging the stepped wedge implementation of collaborative care we will examine differences in clinical and cost outcomes across similar practices randomly assigned to early vs. later implementation time frames. In its first three years, the initiative has trained 830 providers from different disciplines in basic depression management. The virtual consultation service has assisted with more than 3000 cases. The depression collaborative care model was launched in 44 primary care practices; as of March 2016, 2514 patients had been referred, and 1,109 were formally enrolled in depression collaborative care. We anticipate evaluating the outcomes of depression collaborative care in 2017. Lessons learned include the challenges and importance of communicating frequently and extensively with local entities, achieving buy-in from primary care and psychiatry as well as the different disciplines that help provide behavioral health care, including voices from the "front lines," and adapting evidence-based models to fit local climates and utilize their unique resources. Next steps include quality improvement, data analysis and further expansion.

**6. Affective Personality Traits, Reward Behavior, and History of Major Depressive Disorder Predict Altered Functional Connectivity in the Ventral Striatum**

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**Background:** Studying remitted Major Depressive Disorder (rMDD) facilitates a better understanding of neural mechanisms for risk, given that confounding effects of active symptoms are removed. Disrupted resting-state connectivity has been reported in multiple networks in MDD. However, no study to date has specifically examined connectivity of the ventral striatum (VS), despite this region being highly implicated in reward and motivation. The present study therefore investigated resting-state functional connectivity of the VS in individuals with and without a history of MDD, and in relation to affective personality traits and reward responding. **Methods:** Forty-two individuals with rMDD and 28 healthy controls (HC) across two sites completed resting-state fMRI, the Behavioral Inhibition System/Behavioral Activation System Scale (including Reward-Responsiveness, Drive, and Behavioral Inhibition subscales), and the Monetary Incentive Delay Task (MIDT). Voxel-wise, whole-brain comparisons were calculated across and between groups for four seeds: the left inferior VS (LVSi), right inferior VS (RVSi), left superior VS (LVSs), and right superior VS (RVSs). **Results:** Compared to HCs, the rMDD group had less VSs connectivity in temporal and subcortical regions including the putamen and amygdala. VSi connectivity was positively correlated with trait Reward-Responsiveness in somatomotor regions. VSs connectivity showed positive correlations with trait Drive, particularly in the putamen, parahippocampal, and inferior temporal gyrus. VSs connectivity was negatively associated with trait Behavioral Inhibition in the anterior cingulate, frontal gyri, and insula. In relation to Reward-Responsiveness, amount of money won (AMW) on the MIDT was positively correlated with LVSi connectivity to the right anterior cingulate and with LVSs connectivity to the right caudate head. In relation to Behavioral Inhibition, AMW was negatively correlated with LVSi connectivity to the left superior frontal gyrus and left postcentral gyrus, and with LVSs connectivity to the right caudate head. **Conclusions:** Group connectivity differences emerged from the VSs rather than VSi. VSs showed associations with trait drive and behavioral inhibition, whereas VSi was related to reward-responsiveness. Reward task performance was associated with greater connectivity from the VS to striatal and frontal regions important in reward anticipation and reward sensitivity. Depression history, personality, and reward task behavior contribute meaningful and specific information about VS connectivity in understanding risk for MDD.

**7. Effect of Repetitive Transcranial Magnetic Stimulation on the Structural Connectome in Patients with Major Depressive Disorder**

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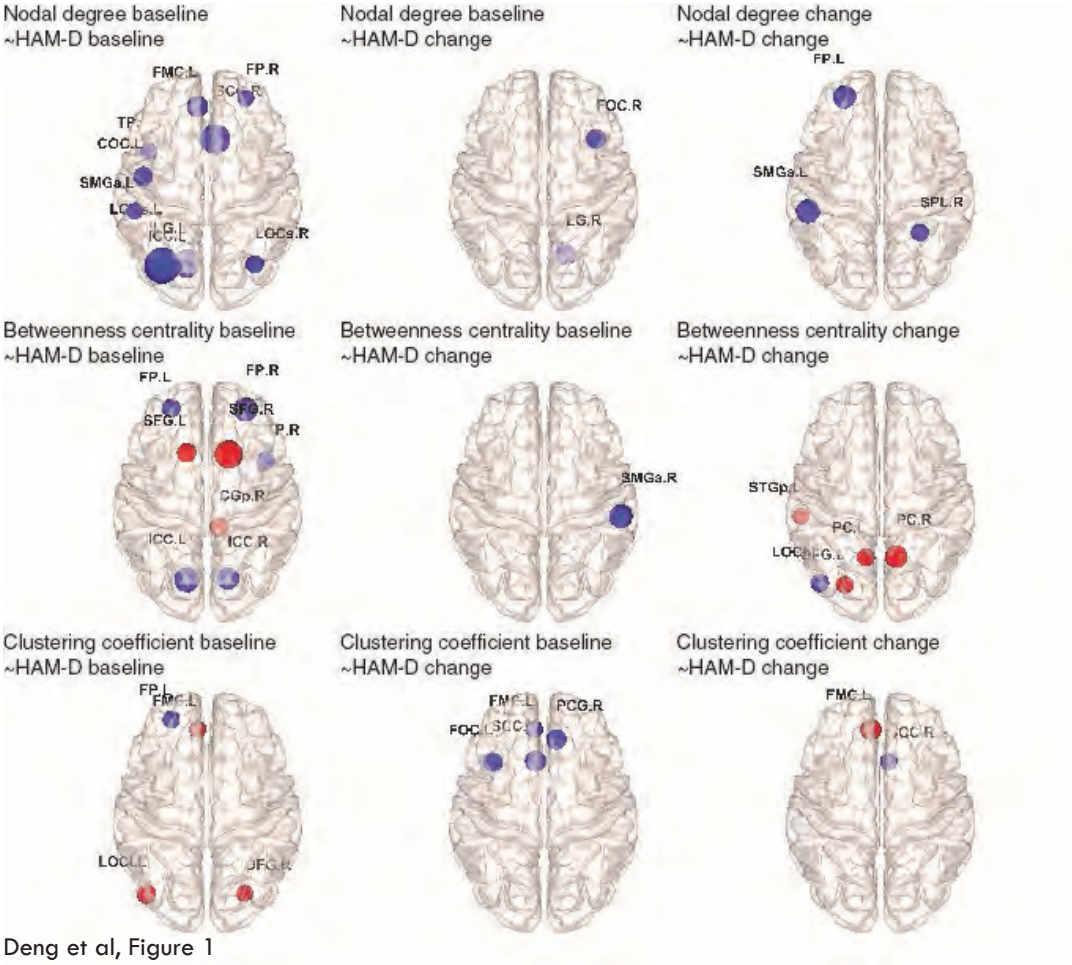
**Introduction:** Repetitive transcranial magnetic stimulation (rTMS) of the dorsolateral prefrontal cortex (DLPFC) is an FDA-cleared treatment for depression. Increasing evidence indicates that depression is accompanied by altered structural connectivity in the white matter. Here we assess the impact of rTMS treatment for depression on the structural brain connectome. **Patients & Methods:** The Institutional Review Board of Weill Cornell Medical College approved this study. 25 currently treatment-resistant depressed patients (age 21–68) participated in the study. Patients received daily 10-Hz rTMS over the left DLPFC 5 days/week for 5 weeks. Treatment response was assessed using the 24-item Hamilton Rating Scale for Depression (HAMD-24) at baseline and after the course of TMS. MRIs were acquired within 7 days prior to starting rTMS and within 3 days after the end of treatment. Diffusion tensor images were acquired using a single-shot spin echo imaging sequence. Nodes of the structural brain network were defined as the 96 anatomical brain areas in the Harvard-Oxford atlas. Whole brain

deterministic streamline generation was performed using the Euler delta crossings tracking algorithm. A weighted connectivity matrix was computed based on the number of streamlines traversing between pairwise cortical regions. Graph theory metrics were calculated to assess network integration (characteristic path length), distribution (network density), segregation (clustering coefficient, modularity), and nodal influence (nodal degree, betweenness centrality). **Results:** Figure 1 shows the distribution of nodes with properties that correlate ($p < 0.05$) with baseline and post treatment change in HAMD-24 score. The node size is proportional to the t-scores (blue: negative correlation, red positive correlation) in a linear regression with HAMD-24. A collection of nodes in the frontal pole, frontal medial cortex, subcallosal cingulate, and lateral occipital cortex (LOC) have baseline nodal degree, centrality, and clustering coefficient that are correlated with baseline HAMD-24. The post treatment change in centrality in the LOC and precuneus is correlated with change in HAMD-24. While we found regional changes, no global changes were observed post rTMS in the network metrics of density, characteristic path length, and modularity. No group difference was observed between treatment responders and nonresponders on these global network metrics. **Conclusion:** rTMS selectively modulates the white matter connectivity underlying key areas in the default mode network. Nodal properties of the structural connectome can potentially be useful biomarkers of depression severity and antidepressant treatment response.



Deng et al, Figure 1

**8. Implementing a new College Mental Health Program (CMHP) – An overview of the first 12 months**

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**Background:** In 2015, nearly 21 million students were enrolled in US colleges and universities. Due to early identification and treatment of mental illness in precollege youth, more students with mental health needs matriculate to undergraduate and graduate schools and often require continued care in these environments. The college setting provides unique opportunities for interventions in transition age youth that affect the life course and impact of mental illness. Therefore, academic medical centers can and need to participate in the development of novel, evidence-based CMHPs that improve the academic success and quality of life for their students. This abstract summarizes the demographics and clinical utilization patterns during the initial 12 months of a multi-disciplinary (.7 FTE Psychiatrist; .5 FTE Psychology/Social Work), collaborative CMHP, embedded within an academic Department of Psychiatry and augmenting an existing traditional campus-based Counseling

& Student Health Services program, at one west-coast public university (enrollment 33,000). **Method:** De-identified data was obtained via electronic health records (EHRs) of all students receiving care though our new CMHP from January - December 2015. **Results:** Demographics – 278 unique students identified by EHR to have been treated by our CMHP during this 1-year period (61% < age 25, 54% female, 50% Caucasian, 50% other ethnicities (13% Asian, 9% Hispanic)). Visits – In total, there were 1822 CMHP outpatient visits (mean 6.5 visits/student; 38 visits/week; 31 visits /FTE-week), 318 other medical visits and 103 total ER/inpatient visits. Mental health diagnoses included anxiety (179), depression (170), ADHD (117), sleep problems (50), substance use (47), bipolar disorder (42), psychosis (10) and "other" (70). Medical diagnoses included injury/poisoning (45), musculoskeletal (33), digestive (32), genitourinary (32), headache (24) and "other" (84). Medications prescribed by CMHP providers included psychostimulants (99), serotonin-selective reuptake inhibitors (96), bupropion (74), benzodiazepines (44), gabapentin (44), serotonin & norepinephrine reuptake inhibitors (34), antipsychotics (34), "other psychotropics" (30), "other antidepressants" (30) and mood stabilizers (21). ). The 30-day re-hospitalization rate was 10/278 unique students (3.6 %). Charges to CMHP totaled $470,157; total charges to the Health System were $2,378,315. Discussion: This new CMHP provided a high volume of clinical services to an ethnically diverse student population with significant mental health and other medical needs. Utilization based on visits/year and total charges suggests a high demand for CMHP services; despite their acuity and high demand, a 3.6% CMHP re-hospitalization rate is lower than that described in other cohorts. Future directions: Utilizing EHRs, we hope to collaborate with other CMHPs to create a multi-site database that can track students, especially those at higher risk, to assess longitudinal outcome measures.

**9. Low Barometric Pressure is Associated with Increased Completed Suicides**

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**Background:** Environmental factors can affect out biology. We have previously demonstrated that low barometric pressure is associated with an increase in the number of emergency psychiatric visits and assaults (Shory TJ, Piecznski N, Nair S, El-Mallakh RS: Barometric pressure, emergency psychiatric visits and violent acts. Can J Psychiatry 48:624-627, 2003). A previous analysis of suicides occurring in a single year did not have sufficient power to determine if there was an association between barometric pressure and completed suicide. **Methods:** Suicide data were obtained from the medical examiner's office of Jefferson County, Kentucky. Meteorological data were obtained from the Louisville Office of the National Weather Service. To limit the number of analyses, we only examined barometric pressure (inHg) (primary outcome variable), and Solar Radiation (MJ/sqm) and average air temperature (°F) (secondary outcome variables). Data were examined with Student's t-test. **Results:** There were a total of 714 suicides in Jefferson County in the 11 year period of January 2000 through December 2011. The average barometric pressure on days with a successful suicide was lower at 29.48 ± 0.038 inHg than in days without a successful suicide, 29.53 ± 0.0036 inHg ($P < 0.0001$, $t = 2.44$). Average daily temperature was not different (59.1 ± 0.67 vs. 58.1 ± 0.37 °F for suicide day vs. non-suicide day, respectively, $P = 0.63$, $t = 0.92$). Similarly, solar radiation, a measure of the extent of sunshine, was not different (6.95 ± 0.11 vs. 6.96 ± 0.06 MJ/sqm for suicide day vs. non-suicide day, respectively, $P = 0.09$, $t = 0.13$). **Conclusion:** Low barometric pressures are associated with changes in behavior that include increased emergency psychiatric visits, assaults, and completed suicides. Environmental variables may play a role in a wide range of human behaviors.

**10. Effects of nightly sleep, daily physical activity, and shift work on daily mood in first-year residents**

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**Background:** While short sleep duration, rotating shift schedules, and physical inactivity are recognized as important problems during residency, objective, real-time changes in these experiences and their relationships with mood are less understood. Aims: To understand how the change of sleep duration, sleep-wake timing and physical activity interact with the fluctuation of mood during first-year residency. Method: Mood of 29 first-year residents from the Intern Health Study's 2014-15 and 2015-16 cohorts was recorded daily by mood 24/7. Objective, real-time assessment of sleep parameters and physical activity of the same participants were measured using accelerometry-based fitbit. Data collection ranged from pre-internship across the first six months of the intern year. Linear mixed models were applied to test the relationships between these measures. **Results:** After internship started, first-year residents lost an average of 2.57 hours of sleep per week ($t=-2.52$, $p=.02$), with average wake-time 1.42 hours earlier than pre-internship baseline ($t=-3.13$, $p<.01$), and

had reduced physical activity by 11% (t=-2.76, p=.01). Correspondingly, mood decreased by 8% (t=-3.57, p<.01). A feedback loop emerged, with a night of short sleep leading to poor mood the next day (b=.12, p<.001), which, in turn, was associated with shorter sleep the next night (b=.06, p=.04). Interns slept less and reported poorer mood when their sleep-wake timing during internship deviated from their personal pre-internship baseline, irrespective of the deviation direction. Lastly, interns reported better mood on days with more physical activity (b=.03, p<.01). **Conclusions:** Shift work, sleep deprivation, and physical inactivity confer a challenging environment for intern mental health. Physician mood, sleep duration, and physical activity substantially decrease in the first months of internship, and internship enforces markedly earlier wake times, which are not accommodated by commensurate changes in bedtime. Efforts to increase sleep opportunity, improve exercise-compatibility of the work environment, and design shift schedules allowing for adequate opportunity to resynchronize the circadian system hold promise to improve mood in this depression-vulnerable population.

**11. Mood Symptom Trajectories and Correlation with Suicidal Behavior**

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Mood disorders affect roughly 15% of the general adult population, not limited to any age group or demographic, and have repeatedly been found to be a leading cause of disability worldwide. Patients with mood disorders are at an increased risk of suicidal behavior, with 10-15% of this population committing suicide. Regular monitoring of changes in mood symptoms may improve patient care and help identify those who are at risk for suicidal behavior. We sought to identify patterns in longitudinal trajectories of mood symptoms in patients with mood disorders that may correlate with and, hence, predict, such suicidal behavior. We analyzed data from the National Network of Depression Centers (NNDC) Clinical Care Registry, which includes data on patients with major depression and bipolar disorder receiving on-going care at one of 21 academic medical centers across the country. All patients provided informed consent and study procedures were approved by each local Institutional Review Board. Demographics, medical history, and self-report assessments, including the Patient Health Questionnaire (PHQ-9), Generalized Anxiety Disorder 7-Item Scale (GAD-7), Altman Self-Rating Mania Scale (ASRM), and Columbia Suicide Severity Rating Scale (CSSR-S), were collected at a baseline visit. The four self-report assessments were then collected at each subsequent clinic visit. Clinicians reviewed the results of these self-report assessments with the patients as part of a measurement based clinical care program, and the data was also captured in an NNDC KnowledgeBase for longitudinal research. We used SAS Proc Traj to identify latent classes of symptom trajectories based on repeated measures of the PHQ-9 and the GAD-7. We then sought to test whether certain of these classes were associated with greater suicidal behavior as assessed by the CSSR-S. Data on the PHQ-9, GAD-7, ASRM or CSSR-S were available for 4,905 observations from 1,428 patients who were seen in the clinic over time. Data on both the PHQ-9 and GAD-7 were present for 4,102 of these observations, with the remainder missing data on at least one measure. Of the 1,428 patients in the sample, 684 (approximately 47%) had at least one suicide measure from the CSSR-S. We analyzed the full data to identify different latent classes of trajectories on the PHQ-9 and GAD-7, and then used the subset of the sample with data also on the CSSR-S to test whether certain classes showed an increased risk of suicidal behavior. Mood disorders are a heterogeneous set of conditions with varying patterns of trajectories of mood and anxiety symptoms over time. This heterogeneity may reflect differences in etiology and influence clinical outcomes, including risk for suicide. In this work, we sought to identify those patterns that are correlated with suicidal behavior. This work may inform strategies for identifying patients who are at an increased risk of suicidal behavior based on the course of their symptoms, and in doing so it can help to achieve the mission of the NNDC, which is to improve the care we provide our patients with major depression and bipolar disorder.

**12. Risperidone Blocks the Antidepressant Response of Infralimbic Deep Brain Stimulation in Rat Model of Antidepressant Treatment Resistance**

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Dopamine plays an important role in depression and bipolar disorder. It is generally hypothesized that diminished dopamine output contributes to a state of depression whereas elevated levels of dopamine may precipitate mania and psychosis. Alterations in dopamine neurotransmission affect the synaptic expression of dopamine receptors. These receptors are therapeutic targets of antipsychotic treatments, which are used as adjunctive treatments in refractory mood disorders. We have previously demonstrated that deep brain stimulation (DBS) of mesocorticolimbic circuits induces an antidepressant response in animals non-responsive to tricyclic antidepressants and concurrently restores attenuated mesoaccumbens dopamine neurotransmission.

We hypothesized that blockade of dopamine receptors with antipsychotics, during deep brain stimulation (DBS), may impair the observed antidepressant actions of this emerging neuromodulation therapy. To test this, we utilized an animal model of antidepressant treatment resistance induced through daily administration of adrenocorticotrophic hormone (ACTH; 100µg/day, 15 days) in combination with high frequency DBS and risperidone (RIS). Antidepressant treatment response was determined through our primary measure of antidepressant response – immobility reduction in the forced swim test (FST), and validated using the open field test (OFT). Rats were divided into 7 groups: ACTH-DBS-RIS (n=8); ACTH-Sham-RIS (n=8); ACTH-DBS (n=8); ACTH-Sham (n=8); RIS (n=10); ACTH (n=11); and saline control (n=10). On day 14 and 15, treatment animals received 30 minutes of acute electrical stimulation (130Hz, 100µA, 90µsec) and/or RIS administration (1mg/kg; i.p.) followed by OFT (day 14) and FST (day 15). RIS significantly increased FST immobility duration alone and in combination with both DBS ($p<0.0001$) and Sham ($p<0.0001$). Results demonstrated that the antidepressant effects of IL DBS ($p=0.0272$) were blocked by RIS co-treatment. This suggests that DBS modulation of dopamine neurotransmission and consequent activation of dopamine receptors is critical to induction of the early antidepressant response. Further investigation is needed to elucidate the mechanisms through which DBS modulation of dopamine signaling contributes to its therapeutic effect. Importantly, the potential clinical implication of concurrent antipsychotic treatment during DBS for depression, particularly during recent clinical trials, should be assessed.

**13. A Clinical Study Investigating Biological Markers of Peripartum Depression**

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20% of pregnant women in the USA suffer from peripartum depression. The biological causes are not understood and no specific treatment is available. Evidence indicates that inflammation may cause depression, and peripartum depression may be a clinical subgroup where inflammatory mechanisms are important due to placenta biology. Inflammation is thought to induce depression through mechanisms partially acting on glutamate neurotransmission. The kynurenine pathway is induced by inflammation leading to production of metabolites acting on NMDA receptors and could be the link between inflammation and depression. The kynurenine pathway is expressed in the placenta regulating maternal tolerance to the fetus. We hypothesize perinatal depression patients will have increased inflammation and expression of kynurenine metabolites in blood and placenta. 7 healthy controls and 4 women diagnosed with depression were enrolled. Placental tissue was analyzed via Real-time PCR. 4 non-depressive and 4 depressive term placentas were studied to measure QUIN via GC-MS and IL-1B via mesoscale 6000. The expression of ACMSD (an enzyme of the kynurenine pathway) was higher in placenta from healthy controls than depressed women. There was a significant correlation between IL-1B and QUIN in term placenta (Pearson's R, $p<0.05$). This data indicates the enzyme ACMSD is present in term placenta and expressed to a lower degree in individuals with peripartum depression versus controls. QUIN expressed in the placental tissue correlates with the amount of IL-1B in the same tissue. This study shows that QUIN may be used as a biomarker for peripartum depression, possibly due to ACMSD dysfunction upstream.

**14. Increased plasma levels of circulating cell-free mitochondrial DNA in medication-free suicide attempters – associations with HPA-axis hyperactivity**

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Preclinical data suggest that chronic stress may cause cellular damage and mitochondrial dysfunction, potentially leading to the release of mitochondrial DNA (mtDNA) into the bloodstream. Major Depressive Disorder has been associated with an increased amount of mtDNA in leukocytes from saliva samples and blood, but no previous studies have measured plasma levels of free-circulating mtDNA in a clinical psychiatric sample. In this study, free circulating mtDNA was quantified in plasma samples from 37 suicide attempters, who had undergone a dexamethasone suppression test (DST), and 37 healthy controls. We hypothesized that free circulating mtDNA would be elevated in the suicide attempters and associated with hypothalamic pituitary adrenal-axis hyperactivity. Suicide attempters had significantly higher plasma levels of free-circulating mtDNA compared to healthy controls at different time points (pre- and post-DST) (all p-values <2.98E-12, Cohen's d ranging from 2.55-4.01). Pre-DST plasma levels of mtDNA were positively correlated with post-DST cortisol l

evels (rho=0.49, p<0.003). Suicide attempters may have elevated plasma levels of free-circulating mtDNA, which are related to impaired HPA-axis negative feedback. This peripheral index is consistent with increased cellular or mitochondrial damage. The specific cells and tissues contributing to plasma levels of free-circulating mtDNA are not known, as is the specificity of this finding for suicide attempters. Future studies are needed in order to better understand the relevance of increased free-circulating mtDNA in relation to the pathophysiology underlying suicidal behavior and depression.

**15. Pilot Study of a Brief Intervention for Medically Hospitalized Suicide Attempt Survivors**

Stephen S. O'Connor, Ph.D.[1], Michael Mcclay, B.A.[2], Shujah Choudhry, M.D.[3], Yaima Alonso, M.D.[3], Lisa Venanzi, B.A.[3], Stephen E. Nicolson, M.D.[3,4]

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3. Department of Psychiatry, Vanderbilt University Medical Center, Nashville, TN
4. Department of Psychiatry, Beth Deaconess Hospital- Plymouth, Plymouth MA

Suicidal patients are at increased risk for mortality in the period during and shortly after acute care emergency hospitalization. Multiple organizations (e.g., National Institutes of Health, The Joint Commission, and Department of Veterans Affairs) have called for improved continuity of care for suicidal patients transitioning through inpatient-to-outpatient clinical settings. The Teachable Moment Brief Intervention (TMBI) is a brief behavioral health intervention that was created specifically for early intervention in inpatient hospital settings following a suicide attempt and is informed by two evidenced-based approaches to suicide prevention: a) the therapeutic philosophy of the Collaborative Assessment and Management of Suicidality (CAMS) and b) the functional analysis of self-directed violence inherent in Dialectical Behavior Therapy (DBT). The TMBI represents the ideal vision of early intervention for hospitalized suicide attempt survivors by combining a patient-centered approach to treatment with a theoretically informed conceptual framework for suicide risk reduction. The TMBI was designed to magnify the cognitive and emotional constructs present shortly after a serious suicide attempt, namely to heighten the perception of risks and positive outcomes of the behavior, to deepen the appreciation of sense of self in relation to others, and to maintain the intensity of emotion present after an attempt. A pilot study is currently underway and involves N=69 patients admitted to Vanderbilt University Medical Center after a suicide attempt that were randomized to receive either the TMBI + care as usual (CAU) or CAU. Seven separate interventionists (five psychiatry residents, one social worker, and one mental health counseling graduate student) have been trained by the PI to deliver the intervention adherently to the intervention manual. Patients reported extremely high ratings of satisfaction with the TMBI (M = 3.84 (out of 4), SD = 0.16). We have completed recruitment and are currently conducting follow-up interviews at 1, 3, and 12 months. An overview of the conceptual model for early intervention after a suicide attempt, the 9 elements of the TMBI, an updated CONSORT chart and baseline demographic characteristics for all study participants will be presented on the finalized poster.

**16. Metformin enhances antidepressant response rate to ketamine in a rodent model of antidepressant treatment resistance**

J.B. Price, C. He, S. Erhardt, L. Schwieler, W. Bobo, M. Frye, S. Tye

The mechanisms mediating the response rate for ketamine's antidepressant effect in treatment-resistant depression are not well understood. However, emerging evidence is pointing towards a neuroendocrine link between stress, depression, and metabolic dysfunction. In depression, chronic HPA-axis activation and allostatic overload ultimately impact cellular energy regulation through impairment of insulin sensitivity, glucose homeostasis, mitochondrial function, and downstream cellular metabolic pathways. As a consequence, an individual's capacity to function and respond to challenges at the cellular level is impaired. We have previously shown that activation of the insulin signaling pathway directly correlates with antidepressant response to ketamine in antidepressant-resistant rats. The main aim of this project was to determine the effect of metformin, a common treatment for type 2 diabetes, on ketamine's antidepressant response rate in these animals. Here, we examine the effects of metformin and ketamine co-administration on antidepressant behavioral response and peripheral levels of glucose and insulin in our preclinical model of antidepressant treatment resistance to determine assess potential for synergistic therapeutic effects. Rats were administered ACTH (100ug/day, 14 days) to establish a treatment resistant phenotype. Rats were administered either control vehicle saline or ketamine (10mg/kg) and/or metformin (200mg/kg). Rats were then subjected to forced swim testing. Before and after behavioral testing, blood was collected for measurement of glucose levels. Results demonstrate that metformin, when administered concurrently with ketamine, significantly reduced immobility during the forced swim test in rats pretreated with ACTH (p<0.001). This reduction in immobility matched the antidepressant effects seen in rats that responded to ketamine treatment alone. However, a critical difference was observed in the response rate when comparing ketamine only and ketamine+metformin groups. Specifically, the response rate for metformin with ketamine was significantly higher than for ketamine

alone ($p<0.05$). These animals also had significantly higher glucose levels relative to ketamine responders ($p<0.01$), ACTH controls ($p<0.05$), and naïve controls ($p<0.001$). Additionally, regressional analyses revealed a significant negative relationship between glucose and insulin following metformin and ketamine administration ($p<0.01$). These results suggest an important relationship between stress, insulin and glucose homeostasis, which may be a critical mediator of ketamine's antidepressant action. This presents the possibility that metformin may be a useful co-treatment to improve response rates to ketamine.

**17. A Pilot fMRI Study of Emotional Face Processing and Lithium Response in Bipolar Disorder**

Kelly Rootes-Murdy, Kara Glazer, Aparna Pisupati, Fernando S. Goes, Francis M. Mondimore, & Pamela Belmonte Mahon

Department of Psychiatry and Behavioral Sciences, Johns Hopkins School of Medicine, Baltimore, MD

**Background:** Bipolar disorder is largely treatable, with lithium commonly used as a first line treatment. However, there is no identified biomarker that can predict patient response to lithium. The goal of this project was to use functional magnetic resonance imaging (fMRI) to examine whether differences in activation to emotional face stimuli is associated with lithium response in patients with bipolar disorder. **Methods:** Participants with bipolar I disorder (N=11) were stabilized on lithium monotherapy and followed for up to two years to make a clinical determination of response to treatment, after which they underwent fMRI with an emotional faces task. Healthy comparison participants (N=17) were matched to cases on sex, age, and education. BOLD activation to fearful and neutral faces was analyzed using general linear models at the whole-brain level. A voxel wise threshold was set to $p<0.005$ and spatial extent cluster threshold of 20 voxels. **Results:** Compared with non-responders, lithium responders exhibited less activation in the parahippocampal gyrus (Tpeak=11.72) and insula (Tpeak =10.41) and greater activation in middle frontal gyrus (Tpeak =8.72). Both lithium responders and non-responders had less activation in cingulate cortex (Tpeak =4.67 and 3.80, respectively) compared to healthy comparison participants. **Conclusions:** This pilot study suggests lower parahippocampal and greater middle frontal activation when processing emotional faces may be indicators of response to lithium treatment in bipolar disorder. Changes in cortical and limbic activation should be examined further to determine whether they might also serve as predictors of response to lithium in patients with bipolar disorder.

**18. A Novel Context for Collaborative Care; Adapting Collaborative Care to Multidisciplinary Subspecialty care.**

Hilja Ruegg MD, Erin Thase PhD, Cheryl McCullumsmith, MD, PhD

University of Cincinnati, Department of Psychiatry and Behavioral Neuroscience, Cincinnati, Ohio

While collaborative care models provide excellent evidence based and efficient psychiatric care for primary care populations, academic medical centers serve populations not historically addressed in most collaborative care models, specifically subspecialty medical clinics. For many patients with complex multi-system disease these sub-specialty clinics are the de-facto primary care sites of care. These clinics often incorporate multidisciplinary services including social work, nutrition and multi-specialty medical care. In addition, those patients who additionally significant mental health co-morbidity also tend to be system 'super-utilizers'. In this setting, there is a need for mental health care to be more efficiently and reliably delivered for these vulnerable populations. Initial focus group meetings with subspecialty clinics in areas as diverse as cardiac transplant, cystic fibrosis, sickle cell anemia, obstetrics and infectious disease were held. We then examined needs and resources of each subspecialty group and adapted models of collaborative care interventions for psychiatric and substance use care tailored to each clinic setting. We regularly meet collectively across all subspecialty clinics to maintain fidelity to the collaborative care model and to share successes and challenges. This process has resulted in care manager placement in both the sickle cell clinic and cystic fibrosis clinic. Both subspecialty clinics are working on developing screening protocols and registries of patients. Processes for psychiatric consultation in place and being utilized. This approach represents a novel context for the implementation of the collaborative care model as well as the method to tailor and adapt its principles to fit into existing multidisciplinary teams caring for complex medical patients.

**19. Training for the Future: Innovations in Collaborative Care as a tool for training future physicians in multiple disciplines.**

Hilja Ruegg MD, Jocelyn Weber LPCC-S, Cheryl McCullumsmith MD, PhD

Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati, Cincinnati, Ohio

**Background:** Collaborative care provides quality evidence based psychiatric care to primary care populations, while reserving psychiatric time to address complex clinical concerns. While this model is gaining traction nationally, both psychiatry and their medical primary care trainees have limited exposure to these models of care. Integrating collaborative care in the academic medical training environment provides both unique challenges as well as opportunities for accelerating adoption of this model as trainees graduate and move into positions in the community. **Methods:** The Departments of Internal Medicine and the Department of Psychiatry jointly created a collaborative care pilot site embedded within the Internal Medicine Residency

primary care site. In the first year of implementation a Depression Care manager and supervising psychiatrist educated residents and faculty in depression screening, evaluation and referral through both individual 1:1 sessions and lectures. In the second year of implementation two senior level psychiatry residents each spent a month long elective with the collaborative care team, dividing their time between working with the Care Manager participating in initial care management evaluations and with the psychiatrist providing supervision and consultation. They attended clinic management meetings and provided education to the resident and faculty primary care providers. **Results:** This pilot project has now moved into a full permanent implementation phase with development of depression management skills for internal medicine residents. A standardized elective in collaborative care for psychiatry residents has been established. As a result of their exposure to the collaborative care model both graduating psychiatry residents who participated in the pilot project are pursuing careers that include a role as collaborative care psychiatrist. **Conclusions:** This pilot demonstrates that integrating collaborative care into the training experience for residents enhances multidisciplinary training and prepares professionals to use this model in the future.

**20. Transition Age Youth (TAY) Curriculum Development: Educating Future Providers on a Developmental Approach to TAY**

Brian M. Skehan, M.D., Ph.D., Daniel Kirsch, M.D.
Department of Psychiatry, University of Massachusetts Medical School, Worcester, MA

Young people transitioning to adulthood, roughly 16 to 30 years of age, are only recently recognized as a discrete cohort with important health and mental health vulnerabilities. This is the age when most mental health problems emerge yet we face critical service, training, and research gaps that limit our capacity to help. Training future psychiatrists to recognize and treat evolving mental illness in young people using a developmental approach is critical to early identification and treatment of those at risk. The evidence base informing our treatment approach to this population is limited. It is prudent to combine the clinical skills of experts in this field with the developmental knowledge of child and adolescent psychiatry to inspire trainees to broaden their clinical skill set and investigate new treatment modalities. Early identification and effective intervention by mental health services within this population will substantially decrease morbidity and mortality over the life span of these patients. Learning objectives in this new curriculum will be met through a combination of didactic lectures and clinical experiences under supervision of faculty that have extensive research and/or clinical expertise in caring for these youth. Clinical experiences will include observing, participating, and conducting psychiatric evaluations of youth referred from local colleges and community mental health centers by collaborating with both academic institutions and the state Department of Mental Health. A unique feature of this curriculum is it builds on a long-standing collaborative clinical partnership between an academic department of psychiatry and local and regional college and university counseling centers. This curriculum adds longitudinal resident and fellow elective clinical experiences incorporating multidisciplinary team work and education among these institutions. Further opportunities to participate in research projects focused on psychosocial interventions or clinical research looking at engaging youth and caring for this population may also be available for those interested through the Systems and Psychosocial Advances Research Center (SPARC) and the Transitions Research and Training Center under the supervision of Maryann Davis, PhD, the director of these programs. The goal of the College Mental Health/Transition Age Youth Curriculum is to provide both General Psychiatry and Child and Adolescent Psychiatry Residents with state of the art training in this underserved and increasingly important area and to inspire some to devote their careers to helping our young people.

**21. Attenuated Intrinsic Connectivity within Cognitive Control Network Among Individuals with Remitted Depression is Associated with Cognitive Control Deficits and Negative Cognitive Styles**

Jonathan P. Stange, Katie L. Bessette, Lisanne M. Jenkins, Katie L. Burkhouse, Amy T. Peters, Claudia Feldhaus, Natania A. Crane, Olusola Ajilore, Rachel H. Jacobs, Edward R. Watkins, & Scott A. Langenecker
1. University of Illinois at Chicago
2. University of Exeter

Many individuals with major depressive disorder (MDD) experience cognitive dysfunction including impaired cognitive control and negative cognitive styles. Functional connectivity MRI studies of individuals with current MDD have documented altered resting-state connectivity within the default-mode network and across networks. However, no studies to date have evaluated the extent to which impaired connectivity within the cognitive control network (CCN) may underlie known cognitive phenotypes for MDD, particularly when individuals are in a remitted state. In the present study, resting-state functional connectivity data were collected from 52 unmedicated young adults with remitted MDD (rMDD) and 47 demographically-matched healthy controls, using three bilateral seeds in the CCN (dorsolateral prefrontal cortex [dlPFC], inferior parietal lobule [IPL], and dorsal anterior cingulate cortex). Mean connectivity within the entire CCN was attenuated among individuals with rMDD, and this was most pronounced from the right dlPFC and right IPL to the six CCN seeds. In addition, connectivity

between CCN seeds and regions of interest that differed in rMDD was associated with several known cognitive risk factors for depression, including ruminative brooding, pessimistic attributional style, negative automatic thoughts, inhibitory control, and inhibitory processing speed. Furthermore, attenuated CCN connectivity mediated relationships between rMDD status and cognitive risk factors. Given that these cognitive markers are known predictors of relapse, these results suggest that connectivity within the CCN could represent a putative biomarker for trait phenotypes of depression risk.

**22. If At First You Don't Succeed: A Case of Diagnosis-Refractory Catatonia**

Nuria J Thusius MD

Catatonia is a psychomotor disorder which occurs in those with medical as well as psychiatric disorders. We describe a unique patient with Bipolar disorder with a chief complaint of psychomotor slowing. Cerebrovascular fluid findings prompted to change her initial diagnosis of catatonia secondary to Bipolar disorder to autoimmune encephalitis, but after unsuccessful treatment with steroids, changed back to the original diagnosis. Our patient, a 48-year-old female Caucasian doctoral-level chemist with a 20-year history of Bipolar I disorder, presented to the ED after a 5-day change in her behavior, characterized by profound psychomotor slowing, decreased speech, "cautious" gait, flat affect, echolalic speech, waxy flexibility, and automaticity. She was admitted to a psychiatric unit for treatment of burgeoning catatonia secondary to Bipolar disorder. Diagnostic evaluation revealed cardiomegaly on chest X-ray and sporadic creatinine kinase (CK) elevations (peak CK 698 (normal range (NR) 38-146 U/l)). CBC and electrolytes were unremarkable. Quetiapine was discontinued, and she was treated with oral and then IM/IV lorazepam without improvement. ECT was pursued, but after her first treatment, she became dramatically more confused and agitated, with tachycardia (pulse 140), tachypnea (respiratory rate: 40), hypertension (blood pressure 168/110) and hyperthermia (temperature 38.2 C). Due to autonomic instability, she was transferred to the neurological intensive care unit. She was sedated with propofol and intubated. No acute intracranial pathology was demonstrated on head CT. Electroencephalography (EEG) demonstrated diffuse slowing, but no epileptiform discharges. Lumbar puncture (LP) showed an opening pressure of 22 cm H20 (NR 10-18 cmH2O), CSF glucose of 38 (with a serum 70-80s), normal cell counts and elevated protein at 145 (NR 0-35 mg/dl). Given LP and EEG results, she was diagnosed with a possible CNS autoimmune disorder and a six day course of IV methylprednisolone 250 mg every six hours was undertaken without success. Her creatine kinase (CK) continued to rise (from 24 to 328 U/l), and tachycardia, diaphoresis, tachypnea and rigidity worsened, prompting a change in her diagnosis to malignant catatonia. Her somnolence and oral intake worsened. Psychiatry consultation service recommended reinitiation of ECT, resulting in significant improvement after the first treatment. She was extubated after her second ECT. She completed four consecutive ECT with marked improvement and was subsequently transferred back to the Medical Psychiatry service, where lithium was reinitiated and lamotrigine added. Her paraneoplastic panel and NMDA receptor antibodies came back negative. Our patient offers a unique example of one with an established diagnosis of bipolar disorder and a first episode of malignant catatonia, with acute deterioration of mental status after her first ECT treatment and CSF changes on lumbar puncture, leading to misdiagnosis of autoimmune encephalitis. She demonstrated no response to a course of high dose steroids, but demonstrated significant improvement after ECT reinitiation.

**23. The STEDI clinic: Stabilization, Treatment, Evaluation, and Disposition. An innovative, patient-centered transition to outpatient psychiatric care.**

Raisa Tikhtman[1]; Arielle Tucker, M.S.[1]; Kim My Li[1]; Moeno Honda, L.I.S.W.-S.[1]; Cheryl McCullumsmith, M.D., Ph.D.[1]

1. Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati, Cincinnati, OH

**Case Report:** Ms. W, a 58-year-old woman with major psychotic depression, two previous suicide attempts, generalized anxiety disorder, and a traumatic brain injury, was referred to the STEDI clinic after a 16-day hospitalization for suicidal ideation. At her first STEDI clinic appointment two days after discharge, she expressed anxiety and confusion about establishing a permanent outpatient psychiatric provider. A licensed independent social worker (LISW) worked with Ms. W to ensure she remained psychiatrically stable and on track to comply with treatment recommendations. **Background:** Patients discharged from acute psychiatric settings lack resources to address the full scope of their psychiatric, substance use, social, and medical needs, catalyzing decompensation outside of the hospital setting. Because outpatient care is often limited by provider scarcity, mandating appointments be scheduled months in advance, patients turn to inpatient services to address their immediate psychiatric concerns. Few to no community services exist to support stabilization during the waiting period for outpatient care following psychiatric crisis. This study examined the feasibility of a specific STEDI (Stabilization, Treatment, Evaluation, and DIsposition) clinic model. **Methods:** A transitional STEDI clinic staffed by a LISW and psychiatrist was established at a large mid-western academic medical center. The STEDI clinic was designed based on qualitative needs assessments of patients and providers indicating a need for rapid follow-up after psychiatric crisis,

specific treatment modalities, and transportation. The resulting STEDI clinic model centered on patients being seen within two days of discharge and followed through in-person sessions, phone calls, or emails to ensure psychiatric stability until their first outpatient appointment. **Results:** 192 patients were referred to the STEDI clinic from acute psychiatric settings over the first six months of its implementation. Follow-up was achieved with 78% of patients, either directly, through collateral, or with a case manager, with a mean of 1.4 STEDI clinic interactions per patient. A patient-centered approach guided STEDI clinic management, allowing patients to reschedule as needed and specify preferred modes of communication. **Conclusion:** The STEDI clinic model is a promising solution to the current standard of care, which leaves patients stranded without access to stabilizing psychiatric services during the transition from inpatient psychiatry to outpatient care.

**24. Development of a Novel Patient-Centered Monitoring Strategy to Improve Patient Outcomes after Psychiatric Crisis**

Arielle Tucker, MS[1]; Raisa Tikhtman[1]; Kim My Li[1], Moeno Honda, LISW-S[1]; Cheryl McCullumsmith, MD, PhD[1]
1. Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati College of Medicine, Cincinnati, OH

**Background:** Quantifying treatment success in psychiatry has been hindered by heavy reliance on subjective provider assessments. Patient-centered and standard quality metrics are critical missing components of both routine clinical work and program evaluation. This project developed an innovative monitoring strategy to improve outcomes after psychiatric crisis using both traditional psychiatric measures and adaptive utilization of electronic health records (EHR) and is anchored by patient-centered, patient-driven goals and feedback. **Methods:** This multi-modal, patient-centered approach was modeled in the STEDI (Stabilization, Treatment, Evaluation, and DIsposition) clinic, which transitions patients from psychiatric crisis to permanent outpatient care. Each STEDI clinic session began with standardized depression and anxiety scales. Information was also integrated from the EHR, providing ongoing insight into the patient's evolving condition including medication status, medical illness, emergency room visits, and re-hospitalizations. Finally, the core assessment focused on patient driven goals and complete evaluation of needs and gaps in understanding using a Patient Understanding of Care Questionnaire. These assessments provided the basis for all treatment decisions. **Results:** The following patient case illustrates the efficacy of this monitoring strategy. Ms. S., a 65 y.o. woman with bipolar II disorder, was referred to STEDI clinic after a 7 day hospitalization for homicidal ideation and mixed mood symptoms. 1) Standardized scales showed irritability and anxiety were persistently high post-discharge, and Depakote was resultantly increased. 2) EHR review revealed that Ms. S had an emergency room visit right after discharge that she did not disclose; this information facilitated further coordination of her medical and psychiatric care. 3) Needs assessment revealed significant stress due to transportation barriers and guardianship of her granddaughter. Providers addressed these needs and enhanced Ms. S's compliance with treatment recommendations by creating a personalized care plan centering on her main goals of reducing homicidal thoughts and maintaining positive family relationships. **Conclusion:** This novel monitoring strategy consisting of standardized patient evaluations, EHR mining, and patient-centered metrics creates a comprehensive approach to adaptive patient-driven care after psychiatric crisis.

**25. A Comparator-Controlled Noninferiority Study of Computer-assisted Cognitive-Behavior Therapy for Depression: Efficacy, Durability and Cost Effectiveness**

Jesse H. Wright, Gregory Brown, Tracy Eells, Steven Wisniewski, Marna S. Barrett, Paul McCrone, G. K. Balasubramani, Michael E. Thase

**Introduction:** Although CBT has been shown to be an effective treatment for depression, its real world utility is limited by the availability of trained therapists and cost. To mitigate this factors, computer- and web-delivered models of this therapy (CCBT) have been developed and tested and show promise to reduce the cost and increase the accessibility of therapy. However, results of several recent studies and meta-analyses suggest that models of CCBT that do not include therapist support are not particularly useful for clinical populations with more severe depressive symptoms. We now report the final results of a two center study evaluating the efficacy, durability and cost-effectiveness of the Good Days Ahead model of CCBT, testing noninferiority versus conventional CBT. **Methods:**154 drug-free patients with major depressive disorder were randomly assigned to a 16 week course of therapy with either standard CBT or computer-assisted CBT (CCBT) using the Good Days Ahead program. The total amount of clinician time was reduced in CCBT to about 1/3 of the time in standard CBT (i.e., 5.5 hours versus 16.5 hours). Outcomes were assessed via self-report (BDI II) and independent raters (HAMD17) at baseline, weeks 8, and 16 and at 3 and 6 months post-treatment. Cost effective analyses took into account the costs of services received and work/social role impairment. **Results:** More than 80% of patients completed the 16 week protocol and rates were comparable in the two groups (CCBT: 79%; CBT: 83%). No significant differences in BDI II or HAMD17 scores were observed at any time point; CCBT met a priori criteria for noninferiority to conventional CBT at weeks 8 and 16. Intent-to-treat Remission rates also were similar in the two therapy groups (CBT: 48.5%; CCBT: 51.5%). Patients

in both groups maintained improvements throughout the follow-up and no remitted patients relapsed. **Conclusions:** Our findings indicate that this approach to CCBT, which blends web-delivered instructional modules with therapist feedback and support, is as effective as conventional CBT delivered by expert therapists. Moreover, as this model of CCBT achieved a rigorous standard of noninferiority with 11 hours less therapist time, it was significantly more cost-effective than conventional therapy. Future studies will focus on dissemination and optimizing therapist contact to maximize public health significance.

## Exhibitor Poster Abstracts

### 26. Assurex - Cost-Effectiveness of Combinatorial Pharmacogenomic Testing for Treatment-Resistant Major Depressive Disorder Patients

Lisa C. Brown, PhD[1], Michael Jablonski, PhD[1], Ilia Antonino PharmD[1], Bryan Dechairo PhD[1]

1. Assurex Health, Inc. Mason, OH

Historically, psychiatric pharmacogenomics (PGx) struggled to find significance relating genes to medication response and psychiatric outcomes. The simplicity of single gene testing often failed to predict patient response and therefore the clinical utility of PGx had been limited. However, the utilization of combinatorial pharmacogenomics which incorporates multiple genes involved in the metabolism and efficacy of individual medications, can accurately predict patient outcomes. This study used data from three prospective clinical outcomes trials of a combinatorial pharmacogenomic test, as well as published data from meta-analyses, to calculate the difference in quality-adjusted-life-years (QALYs) and medical costs between combinatorial pharmacogenomic testing and treatment as usual (TAU). Patients with treatment-resistant major depressive disorder (MDD) receiving combinatorial pharmacogenomic testing had 70% greater improvement in symptoms compared to TAU. Based on the positive data of combinatorial pharmacogenomic testing, QALYs was increased by 0.316 years. Combinatorial pharmacogenomic testing also substantially improved expected direct medical and indirect (worker productivity) savings compared to TAU. Patients using combinatorial pharmacogenomics testing were expected to save an average of $3,711 in medical costs over a patient's lifetime. Based on mathematical modeling of 10,000 possible simulations, there is 94.5% probability that combinatorial pharmacogenomic testing improves patient outcomes compared to TAU and is cost effective under a willingness to pay (WTP) threshold of $50,000/QALY gained. Furthermore, 74.7% of the simulations improved outcomes and reduced overall costs compared to TAU. Combinatorial pharmacogenomics testing is a valuable tool to aid clinicians in determining a tolerable and effective psychiatric medication for patients with treatment-resistant MDD.

### 27. Janssen - PeRSEVERe: A Study of Esketamine for the Rapid Reduction of the Symptoms of Major Depressive Disorder, including Suicidal Ideation, in Patients Assessed to be at Imminent Risk for Suicide

Carla M. Canuso, Jaskaran B. Singh, Maggie Fedgchin, Larry Alphs, Rosanne Lane, Pilar Lim, Christine Pinter*, Husseini Manji, Dong-Jing Fu*, Wayne Drevets

Neuroscience, Janssen Research & Development, Titusville, NJ *Presenting Author

**Background:** Major depressive disorder (MDD) is associated with an elevated rate of mortality, primarily due to suicide. The risk of suicide in those with MDD is about 20 times that of the general population, with over half of all suicides occurring in depressed individuals. While conventional antidepressants are often effective in treating depressive symptoms including suicidal ideation (SI), their delayed onset of action significantly limits their utility in the treatment of patients with MDD who are at imminent risk of for suicide. Recently, several studies of ketamine and esketamine have demonstrated that these agents can improve symptoms of depression in individuals with MDD within hours of administration. Additionally, preliminary studies of ketamine suggest it may have a similarly rapid effect in significantly reducing SI in patients with MDD. As such, Janssen R&D is developing intranasal esketamine for the rapid reduction of the symptoms of MDD, including SI, in patients who are assessed to be at imminent risk for suicide. **Methods:** PeRSEVERe is a recently completed 12-week, randomized, double-blind, placebo-controlled, multicenter Phase 2 study of intranasal esketamine in 68 adult patients with MDD who are assessed to be at imminent risk for suicide. Included patients had active SI and intent, and were in need of inpatient psychiatric hospitalization. The primary objective is to evaluate the efficacy of intranasal esketamine 84 mg compared with intranasal placebo in reducing the symptoms of MDD, including SI, as measured by the change from baseline on the MADRS total score at 4 hours post-dose on Day 1. Secondary efficacy objectives include the assessment of single and repeated doses of intranasal esketamine compared with intranasal placebo on the clinician's assessment of suicide risk as measured by the Suicide Ideation and Behavior Assessment Tool, and the patient's report of the severity in SI as measured by the Beck Scale for Suicide Ideation, through the end of the double-blind (DB) treatment and follow-up phases. Safety objectives include the assessment of transient perceptual changes, sedation, nasal tolerability, vital signs and suicidal thinking and behavior. The study consists of a 24-48 hour screening evaluation performed prior to the Day 1 intranasal dose, immediately followed by a

25-day DB treatment phase, and a 56-day follow up phase. Given the vulnerability of the patient population, the study was conducted in the context of standard clinical care, with all patients receiving standard antidepressant medication and initial in-patient hospitalization. **Results:** PeRSEVERe is the first multi-center, prospective, placebo-controlled trial of a rapidly acting antidepressant in patients with MDD who are assessed to be at imminent risk for suicide. The study, which was conducted at 11 centers in the United States, recently completed enrollment. Preliminary efficacy and safety results from the DB treatment phase will be available for presentation. **Conclusion:** PeRSERVERe is the first multi-center placebo-controlled study of a potential rapidly acting antidepressant in patients with MDD who are assessed to be at imminent risk for suicide. Should study results be positive, esketamine may offer hope and a new paradigm of treatment for depressed patients at risk for suicide.

**28. Otsuka - Effect of adjunctive brexpiprazole on cognitive and physical functioning in five exploratory, open-label studies in major depressive disorder**

Ross A. Baker, PhD[1], Peter Zhang PhD[1], Catherine Weiss PhD[1], Aleksandar Skuban MD[1], Emmanuelle Weiller PsyD2
1. Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, USA
2. H. Lundbeck A/S, Valby, Denmark

**Objective:** Fatigue and cognitive dysfunction are common in MDD. Brexpiprazole is a serotonin-dopamine activity modulator that is a partial agonist at 5-HT1A and dopamine D2 receptors, and an antagonist at 5-HT2A and noradrenaline alpha1B/2C receptors, all at similar potency. Brexpiprazole was approved in 2015 by the FDA for use as an adjunctive therapy to antidepressants for the treatment of MDD. We evaluated the effect of adjunctive brexpiprazole on cognitive and physical function assessed by the Cognitive and Physical Functioning Questionnaire (CPFQ). **Methods:** Five exploratory open-label studies were conducted in patients with MDD and inadequate response to antidepressant therapy (ADT), and 1) sleep disturbances [NCT01942733], 2) irritability [NCT01942785], 3) inadequate response to adjunctive treatment [NCT02012218], 4) anxiety symptoms [NCT02013531], or in, 5) young patients at work/school [NCT02013609]. Patients received ADT+brexpiprazole 1-3mg/day (target dose: studies 1 & 2: 3mg/day; studies 3-5: 2mg/day). The CPFQ is a patient-rated scale designed to assess cognitive and executive dysfunction including symptoms of fatigue. The CPFQ consists of 7 items, each rated on a scale from 1 -6; total score ranges from 7-42. The CPFQ was used in all 5 studies, with assessments at baseline and week 6 (studies 2-4), week 8 (study 1), and week 12 (study 5). The MADRS was used in all studies for assessment of depressive symptoms. **Results:** At baseline, mean MADRS total scores ranged from 28.3 (studies 1 & 5) to 30.3 (study 4). Improvements were observed in MADRS total scores in patients treated with ADT+brexpiprazole: changes from baseline to week 6 were: -14.2 (study 2) to -19.6 (study 4); week 8: -16.0; and week 12: -18.1. CPFQ total scores at baseline ranged from 26.1 (study 5) to 29.3 (study 3). Improvements were observed in CPFQ total scores in patients treated with ADT+brexpiprazole: changes from baseline to week 6 were: -7.7 (study 2) to -9.9 (study 4); week 8: -8.4; and week 12: -8.1. **Conclusion:** Baseline CPFQ scores indicated high levels of dysfunction in all 5 studies. Meaningful decreases from baseline, indicated improvements in cognitive function, and increased energy/alertness after adjunctive treatment with brexpiprazole, paralleled by similarly meaningful improvements in depressive symptoms.

# Local Resource Guide

## Urgent Care & Pharmacies

**Denver Adult Urgent Care Center**
7:00 AM - 10:00 PM
777 Bannock Street Pavilion A 1st Floor
Denver, CO
(303) 436-6000

**Denver Health**
**Emergency Room & Hospital**
777 Bannock Street Pavilion A 1st Floor
Denver, CO
(303) 436-6000

**Walgreens w/ Pharmacy**
5:30 AM - 12:00 AM
801 16th St
(303) 571-5314

## Convenience Stores

**Safeway**
757 E. 20th Ave
(303) 861-8169

**7-Eleven**
1560 Court Pl
(303) 534-5687
Open 24 Hours

## Transportation & Other Resources

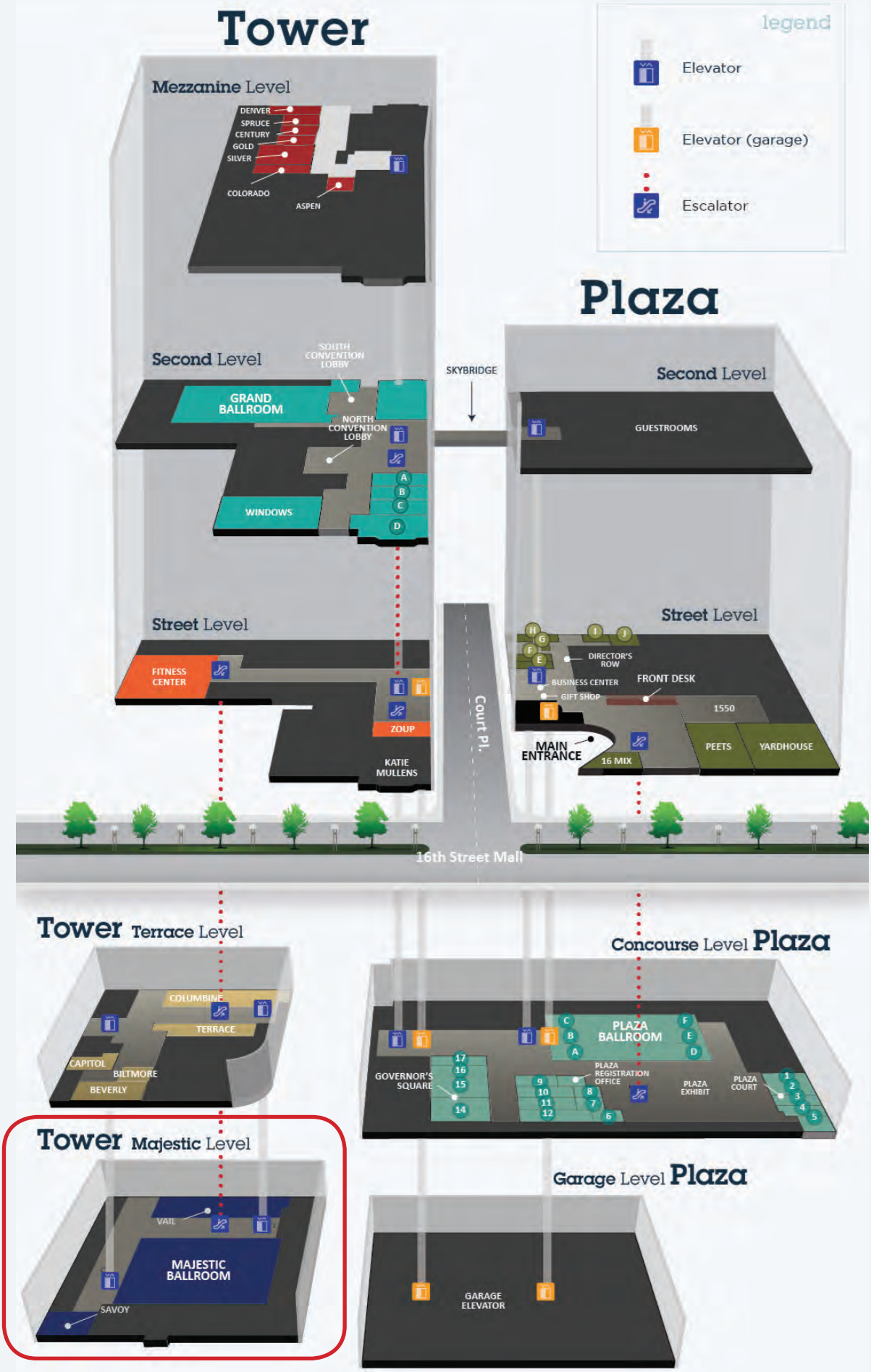
**Penfield's Business Center**
In the Sheraton
(303) 893-3333

**Denver Yellow Cab**
(303) 777-7777

**Metro Taxi**
(303) 333-3333

**RTD University of Colorado A Line**
Local train from Union Station in Downtown Denver to Denver International Airport (approx. 37 minutes travel time)
$9.00 one way fare to airport
www.rtd-denver.com/a-line.shtml

Sheraton


Tower
legend
Elevator
Elevator (garage)
Escalator
Mezzanine Level
DENVER
SPRUCE
CENTURY
GOLD
SILVER
COLORADO
ASPEN
Plaza
Second Level
SOUTH CONVENTION LOBBY
GRAND BALLROOM
NORTH CONVENTION LOBBY
WINDOWS
A
B
C
D
SKYBRIDGE
Second Level
GUESTROOMS
Street Level
FITNESS CENTER
ZOUP
KATIE MULLENS
Court Pl.
Street Level
H
G
F
E
I
J
DIRECTOR'S ROW
BUSINESS CENTER
GIFT SHOP
FRONT DESK
1550
MAIN ENTRANCE
16 MIX
PEETS
YARDHOUSE
16th Street Mall
Tower Terrace Level
COLUMBINE
TERRACE
CAPITOL
BILTMORE
BEVERLY
Concourse Level Plaza
PLAZA BALLROOM
C
B
A
F
E
D
GOVERNOR'S SQUARE
17
16
15
14
PLAZA REGISTRATION OFFICE
9
10
11
12
8
7
6
PLAZA EXHIBIT
PLAZA COURT
1
2
3
4
5
Tower Majestic Level
VAIL
MAJESTIC BALLROOM
SAVOY
Garage Level Plaza
GARAGE ELEVATOR

# The National Network of Depression Centers Annual Conference returns to Ann Arbor in 2017!


## Save the Date!

September 25-27, 2017