

National Institute of Mental Health Intramural Research Program Impact of Red Team Report



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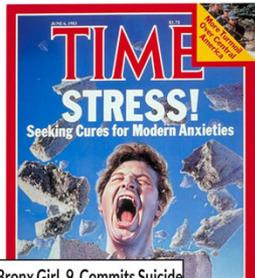
National Institute
of Mental Health

Outline

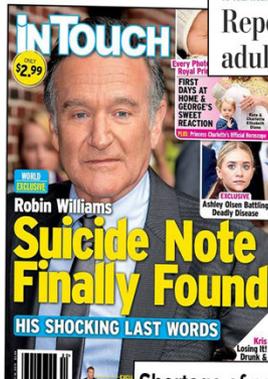
- **About NIMH**
- **NIMH IRP Clinical Program**
- **Impact of Red Team Report**
- **Current Challenges**

Mental Illnesses Touch Us All

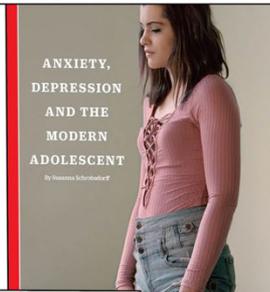
UPenn student kills herself by jumping in front of a train - marking the TENTH suicide at the university in just three years



Bronx Girl, 9, Commits Suicide



To Your Health
Report: More than half of mentally ill U.S. adults get no treatment



Shortage of psychiatric hospital beds shortchanges American children

Boy, 9, Kills Himself After Enduring Months Of Bullying, Family Says



Kate Spade death: Mental illness 'doesn't discriminate'



Depression is on the rise in the US, especially among young teens

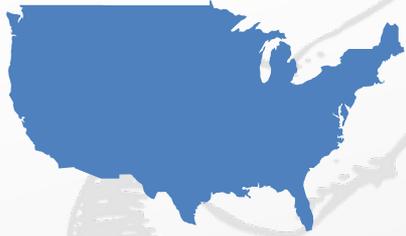


'Thinking of Ways to Harm Her'
New Findings on Timing and Range of Maternal Mental Illness

State suicide rate tops national average



US Burden of Mental Illness



18% of adults



20% of children



50% of all lifetime cases of mental illness begin by age 14



Estimates suggest that **only half** of people with mental illnesses receive treatment



The average delay between onset of symptoms and intervention is **8-10 years**



- 1 provider/529 individuals with a mental illness



Education & Employment

- 0.8% of students are identified as having an ED IEP¹⁰
- 5-6 million people lose, fail to seek, or cannot find employment



Insurance/Cost

- 50% of adults with a disability with untreated need did not receive treatment because of costs



Homelessness & Incarceration

- 1 in 5 people experiencing homelessness had a serious mental illness
- 14.5% of men and 31% of women in jails have a serious mental health condition.
- 70% of youth in contact with the Juvenile Justice System meet criteria for a mental illness



Health & Mortality

- 68% adults reported having at least one general medical disorder
- 44,000+ Americans die each year from suicide



Cost

- 3rd most costly medical condition
- \$300 billion + direct and indirect financial costs associated with mental illness



About NIMH



- The National Institute of Mental Health (NIMH) is the lead federal agency for research on mental illnesses.
- NIMH supports more than 3,000 research grants and contracts at universities and other institutions across the country and overseas.
- NIMH intramural research programs support approximately 600 staff working on the NIH campuses.



NIMH Mission

MISSION

To transform the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure.

www.nimh.nih.gov

Research = Hope



NIMH Strategic Plan for Research



Objective 1:

Define the mechanisms of complex behaviors

Objective 2:

Chart mental illness trajectories to determine when, where, and how to intervene

Objective 3:

Strive for prevention and cures

Objective 4:

Strengthen the public health impact of NIMH-supported research

Research Priorities



- **Short-term Goals: Suicide Prevention**
 - Identify implementable evidence-based practices and knowledge gaps
- **Medium-term Goals: Neural Circuits**
 - Develop technologies to interrogate neural circuits, and ultimately improve the understanding and treatment of mental health disorders
- **Long-term Goals: Computational Psychiatry**
 - Develop computational perspectives and approaches to improve the understanding and treatment of mental health disorders



NIMH Intramural Research Program (IRP)

41 Research Groups on the NIH Campus

- 22 basic, 19 clinical
- Many levels of analysis (genes-cells-systems-behavior)

Budget approximately \$181.9M FY18

- ~251 Trainees at all levels (postbac, predoc, postdoc)
- ~447 scientific, clinical and administrative staff

Eleven shared core resources

- Neurophysiology Imaging Facility
- Magnetic Resonance Spectroscopy Core
- Functional MRI Core Facility
- Magnetoencephalography Core Facility
- Scientific and Statistical Computing Core
- NIMH Human Brain Collection Core
- Statistical Genomics and Data Analysis Core
- Transgenic Core Facility
- Instrumentation Core
- Rodent Behavioral Core
- Systems Neuroscience Imaging Resource



NIMH Intramural Program Goals



- **To nurture the most creative science** that uses cutting-edge, cross-disciplinary approaches to explore how genes, cells, circuits and systems operate in the healthy brain and how they are altered in mental disorders
- **To address critical areas and gaps in basic & clinical research** that would be hard to address without stable long-term funding
- **To evolve common themes and coordinating mechanisms** between the clinical & basic research
- **To ensure that an outstanding and diverse group of young scientists and clinicians are inspired** to continue to undertake high risk, innovative research
- **To encourage collaborative science and the exchange of ideas** by facilitating partnerships with researchers everywhere

IRP Collaborations with External Partners (FY17)

41

- Faculty who list extramural collaborators

461

- Extramural collaborations listed

210

- Different non-NIH institutions

9

- Average number of external collaborating institutions per investigator

Fostering Collaborative Science: Mechanisms for Intramural-Extramural Interactions

Bench to Bedside Awards (1-3 per year)

U01 Grants

research project cooperative agreements that allow extramural labs access to CC resources

BRAIN Initiative Grants

Lasker Scholar Awards (1)

CRADAS amendments FY17 (5)

Data Transfer Agreements FY17 (15)

Formal Collaborative Agreements FY17 (5)

Participation in **Outside Consortia** (genomics, tissue banking)

Outline

- **NIMH IRP Clinical Program**

Clinical Center is a rare resource for implementing placebo controlled studies

- Outstanding staff/patient ratios
 - Expertise to support patients through medication washout and drug free periods
- Ability to support extended length of stay without insurance barriers
- Highly monitored environment
- Rigorous inclusion/exclusion
- Multi-modal, extensive characterization

NIMH Clinical Center Activity



- **20 Adult Psychiatry inpatient beds**
 - Treatment Resistant Depression/Neurobiology of Suicide
 - Schizophrenia
- **4 Child/Adolescent Psychiatry inpatient beds/ 2 day hospital beds**
 - Adolescent Depression
 - Severe Mood Dysregulation Disorder
- **Outpatient Clinics (sample protocols)**
 - Puberty Study
 - Behavioral Endocrine Studies (premenstrual, perimenopausal, post-partum)
 - Irritability, Anxiety, ADHD, Autism
 - Rare Genetic disorders-Williams Syndrome, Phelan-McDermid, Fragile X
 - Psychiatric Epidemiology Studies

NIMH Successes

- Characterization of Disorders
 - Irritability/Disruptive Mood Dysregulation Disorder
 - Childhood Onset Schizophrenia
 - Pediatric Obsessive Compulsive Disorder
 - Premenstrual Dysphoric Disorder (PMDD)
- Development of Treatments
 - Lithium, Clomipramine, Clozapine, Ketamine
- Debunking Myths
- Pathophysiology
- Drug Development
- Public Health Crises
 - Major Depression
 - Suicide

Importance of Placebo to NIMH Studies

Clinical Trials efficacy studies:

- Fluoxetine's efficacy in PMDD (one of two studies used to get FDA approval for fluoxetine in PMDD) thus establishing insurance coverage of a treatment for PMDD
- Clomipramine effective in Obsessive Compulsive Disorder (OCD)
- Clozapine effective in children with psychosis
- Effects of estradiol in perimenopausal depression -now replicated in 2-3 trials

Importance of Placebo in NIMH studies

Pathophysiology

- First demonstration under controlled conditions of the neuropsychiatric effects of anabolic steroids in men
- Brain imaging studies needed placebos for women so they were blinded to what hormone they were receiving
- Use of ketamine as a proof of principle-rapid acting antidepressants are possible within hours

Outline

- **Impact of Red Team Report-NIMH Experience**

The Red Team Report April 2016

REDUCING RISK AND PROMOTING PATIENT SAFETY FOR NIH INTRAMURAL CLINICAL RESEARCH

DRAFT REPORT

April, 2016

The Clinical
Center
Working
Group
Report to
the
Advisory
Committee
to the
Director,
NIH

SPEAK
UP
FOR
SAFETY



The safety of NIH Clinical Center patients, visitors and staff is our highest priority.

If you have concerns about your care or see an unsafe condition, please tell us.

Dial the NIH Clinical Center
Anonymous Safety Hotline
1-866-444-8811



Patient Safety-Right Path?

NIMH Practices in Place

- Monthly Patient Safety and Quality Meetings-increased participation since Report, required Branch level projects

Since the Red Team Report

- Promotion of team member to Director of Patient Safety & Quality, NIMH
- Daily Participation in Clinical Center Huddle
- Implementation of New Protocols- use of Failure Modes & Effects and Analysis

Neurobiology of Suicide (2016)

- Evaluate environmental risks
- Prepare for staffing needs due to high acuity (1:1) / volume
- Ensure staff training around detecting suicide risk

Electroconvulsive Shock Therapy (2018)



NIMH Contributions to NIH and Clinical Center Safety since the Red Team Report

- Integration of NIMH PET laboratory with CC cGMP PET facility
- Working with Office of Research Support and Compliance on transition of INDs to CC
- Implementation of Suicide Screening in Clinical Center Medical Patients
- Continued improvements in Human Subjects Protections
- Distressed Trainee Resources

Ask Suicide Screening Questions (ASQ)

Ask the patient:

1. In the past few weeks, have you wished you were dead? Yes No
2. In the past few weeks, have you felt that you or your family would be better off if you were dead? Yes No
3. In the past week, have you been having thoughts about killing yourself? Yes No
4. Have you ever tried to kill yourself? Yes No

If yes, how? _____

When? _____

If the patient answers **Yes** to any of the above, ask the following acuity question:

5. Are you having thoughts of killing yourself right now? Yes No

www.nimh.nih.gov/asq





ASQ Toolkit Summary

ASQ TOOLKIT

The ASQ toolkit is organized by the medical setting in which it will be used: **emergency department, inpatient medical/surgical unit, and outpatient primary care and specialty clinics.** All toolkit materials are available on the NIMH website at www.nimh.nih.gov/asq. Questions about the materials or how to implement suicide risk screening can be directed to Lisa Horowitz, PhD, MPH at horowitzl@mail.nih.gov or Debbie Snyder, MSW at DeborahSnyder@mail.nih.gov.

Emergency Department (ED/ER):

- ASQ Information Sheet*
- ASQ Tool*
- Brief Suicide Safety Assessment Guide
- Nursing Script
- Parent/Guardian Flyer
- Patient Resource List*
- Educational Videos*

Inpatient Medical/Surgical Unit:

- ASQ Information Sheet*
- ASQ Tool*
- Brief Suicide Safety Assessment Guide
- Nursing Script
- Parent/Guardian Flyer
- Patient Resource List*
- Educational Videos*

Outpatient Primary Care/Specialty Clinics:

- ASQ Information Sheet*
- ASQ Tool*
- Brief Suicide Safety Assessment Guide
- Nursing Script
- Parent/Guardian Flyer
- Patient Resource List*
- Educational Videos*

***Note: The following materials remain the same across all medical settings. These materials can be used in other settings with youth (e.g. school nursing office, juvenile detention centers).**

- ASQ Information Sheet
- ASQ Tool
- ASQ in other languages
- Patient Resource List
- Educational Videos

www.nimh.nih.gov/asq

Current Collaborators

Screening for Suicide Risk in the Medical Setting



NIH Community

National Institute of Mental Health

Human Research Subjects Protections Toolkit

Version 9, June 20, 2018

Developing SECTION **1** **Protections**

- How to Design a Program
- Assessment Description
- Monitoring Description

NIH Distressed Trainee Toolkit

Resources

To Support the Supervisor and the Distressed Trainee

NATIONAL INSTITUTES OF HEALTH 

OITE 301-496-2427 training.nih.gov

- o Career Services
- o Educational Counseling & Advising

SUPERVISOR SUPPORT
Consultation and training to support quality mentorship and resolve workplace issues

TRAINEE SUPPORT
Graduate/professional school advising, career exploration, wellness programs, interpersonal skills development, cultural adaptation, mentor/mentee relationships



Office of
Intramural
Research
Training &
Education

EAP 301-496-3164* ors.od.nih.gov/sr/dohs/EAP

- o Mental Health Professionals
- o Confidential
- o Voluntary

SUPERVISOR SUPPORT
Supervisory consultation, crisis intervention, assistance referring trainees to EAP

TRAINEE SUPPORT
Short-term counseling, crisis intervention, community resources & referral



Employee
Assistance
Program

*Phone and face-to-face consultations

Civil 301-402-4845 hr.od.nih.gov/hrguidance/civil

- o NIH Human Resources

SUPERVISOR SUPPORT
Consultation to clarify nature of the problem, mitigate workplace difficulty, refer to appropriate resources & establish interventions

TRAINEE SUPPORT
Resource for disruptive or dangerous behaviors, intimidation, threats, workplace violence, domestic violence, harm to self or others



Civil
Program

Ombudsman 301-594-7231 ombudsman.nih.gov

- o Consultation
- o Coaching
- o Mediation
- o Facilitation

SUPERVISOR SUPPORT
Coaching and conflict resolution design and implementation, confidential discussion of personal and interpersonal issues, identify work-related problems, policy and procedures concerns

TRAINEE SUPPORT
Neutral, confidential, independent resource, coaching, problem-solving



Office of
Conflict
Resolution

OMS 301-496-4411

Occupational Medical Service
ors.od.nih.gov, 301-496-1211 (after hours)



24/7, Medical Emergencies, CCBldg 10, OP6
Evaluations for abrupt behavior change, substance abuse, injury, illness

Police



24/7, Emergency Law Enforcement

NIH Police Main Bethesda Campus
911 landline, 301-496-9911 mobile
Non-emergency, 301-496-5685

Local Police All other NIH facilities
9-911 landline, 911 mobile

Flyer for Trainees & Supervisors, March 25, 2017



Outline

- **Current Challenges**

Pharmaceutical Development Service Manufacturing Timeline

May, 2015

- FDA inspects PDS (sterile manufacturing) and Intravenous Admixture Unit (IVAU)
- Issues FDA Form 483 (Inspectional Observations) for both areas
- NIH CC stops sterile manufacturing & begins remediation for IVAU
- Outsourcing critical sterile products begins

Aug, 2015

- Consultants perform review of all PDS areas and IVAU
- Deficiencies found in PDS sterile processing, non-sterile processing, and Analytical Unit
- Non-sterile processing limited by risk analysis (e.g. placebos, over-encapsulation, solutions)
- Limited assay work for ongoing projects
- Outsourcing sterile and non-sterile products

April, 2016

- Non-sterile manufacturing completely halted
- PDS manufacturing space to become Interim-IVAU
- Outsourcing expands

Summary of Obstacles

- Contracting-complex and time consuming
- Many external pharmacy sources are cost prohibitive (2-3x a Principal Investigator's supply budget)-smaller ICs lack financial resources to pay high cost of using outside vendors
- Hard to find company for some products (e.g. syringes, hormone patches)
- **Identified, selected and contracted outside pharmacy fails FDA GMP inspections as well**
- Product quality issues- needed analysis for FDA not done, some drug inconsistencies identified, repeat testing needed
- **DELAY in developing new treatments**

Unintended Consequences for NIMH of Closure of Pharmaceutical Development Service

- Some PIs have stopped designing placebo controlled double blind trials
 - Difficulty conducting medication trials in youth
 - Plans to do a estrogen study in post-partum psychosis on hold due to concerns it is too risky to undertake given the hurdles with drug supply
- PIs have redirected efforts to only non-drug trials:
 - Cognitive Behavioral Therapy
 - Neuromodulation
 - Transcranial Magnetic Stimulation Electroconvulsive Shock Therapy
- Possible further negative impact on Pharma psychiatric drug development

Thank you

