Mortality from Medical Causes

Peaks: 1965–1995
Currents: 2009–2012

- Suicide
  Peak: –
  Current: ~6,000

- Stroke
  Peak: ~20,000
  Current: ~30,000

- AIDS
  Peak: ~30,000
  Current: ~20,000

- Heart Disease
  Peak: ~1.1 Million
  Current: ~20,000

- ALL (Leukemia)
  Peak: ~75
  Current: ~25

Percent of Peak
U.S. suicide rate unchanged in 2 decades

Homicides have dropped from 9.8/100,000 in 1992 to 4.8/100,000 in 2010 (<15,000/yr)

SOURCES: Bureau of Justice Statistics (homicide); Centers for Disease Control (suicide)
U.S. Burden of Diseases: 291 diseases and injuries

Leading Categories of DALYs 2010

1. Neuropsychiatric Disorders
   - Mental and Behavioral Disorders: 13.6
   - Neurological Disorders: 5.1
   - Total: 18.7

2. Cardiovascular and Circulatory Diseases
   - Percent of Total U.S. DALYs: 16.8

3. Neoplasms
   - Percent of Total U.S. DALYs: 15.1

4. Musculoskeletal Disorders
   - Percent of Total U.S. DALYs: 11.8

5. Diabetes, Urogenital, Blood, and Endocrine Diseases
   - Percent of Total U.S. DALYs: 8.0

6. Chronic Respiratory Diseases
   - Percent of Total U.S. DALYs: 6.5

7. Other Non-communicable Diseases
   - Percent of Total U.S. DALYs: 5.1

The most disabling disorders before age 50

Cumulative DALYs (thousands)

- Mental and Behavioral Disorders
- Cardiovascular and Circulatory Diseases
- Neoplasms
- Musculoskeletal Disorders
- Diabetes, Urogenital, Blood, and Endocrine Disorders
- Chronic Respiratory Diseases

Age

The State of Mental Health in 2014

• Diagnosis limited to symptoms; detection late.
• Etiology unknown; prevention not well developed for most disorders.
• Treatment is trial and error – no cures, no vaccines.
Inconvenient Truth #1: We have failed to bend the curve for morbidity and mortality from mental illness.

Why?
Why have we failed to bend the curve?

Lack of Access

Broken “system”

Poor care

~60 million people in the US with any Disorder; 11-17 million “serious”

Sources:
NSDUH (2009); Kessler, Chiu, Demler, & Walters (2005); Wang, Lane, Olfson, Pincus, Wells & Kessler (2005); Merikangas, He, Burstein, Swendsen, Avenevoli, Case, Georgiades, Heaton, Swanson, Olfson (2011)
Why have we failed to bend the curve?

- Lack of Accountability – Who is responsible?
- Denial of illness
- Fragmentation of care
- Criminalization

The New York Times

Treatment, Not Jail, for the Mentally Ill

Published: January 31, 2013
Will more care bend the curve?

Sources:
GSS, NCS, NCS-R

From Sherry Glied
Will more care bend the curve?

IMS Health: millions of prescriptions in US market

A. Antidepressant prescriptions  
B. Antipsychotic prescriptions

Administrative data reveal more children in care system, more people on SSI, more payments for MH via Medicaid.
Inconvenient Truth #2:

More people getting more of today’s Rx but outcomes are not any better

If we are to bend the curve we must:
Not only improve access and quantity, we must improve options and quality.

Improving options and quality requires a different approach.
A Different Approach?

“The next great American project”
The Genomic Revolution

Cost per Megabase of DNA Sequence

Confirmed Psychiatric Gene Findings
PGCI 2011
9K cases
5 loci
PGC1 2011
9K cases
5 loci

PGC1 + Sweden 2012
14K cases
22 loci
PGC1 2011
9K cases
5 loci

PGC1 + Sweden 2012
14K cases
22 loci

PGC2 2013
31K cases
78 loci
Rank #3
PGC1 2011
9K cases
5 loci

PGC1 + Sweden 2012
14K cases
22 loci

PGC2 2013
31K cases
78 loci

PGC 2014
37K cases
108 loci
THE SUSPECTS
Based on new genetic findings, researchers have fingered the following cellular dysfunctions as playing a role in schizophrenia and/or bipolar disorder:

SCHIZOPHRENIA

- Oligodendrocytes and myelination
- Synaptic function
- Glutamate signaling
- Protein synthesis and cell growth
- Neuronal development

BIPOLAR DISORDER

- Circadian rhythms
- Chromatin remodeling
- Extracellular matrix proteins
- Cell surface proteins

BOTH

- Neurotransmitter release
- Calcium channel signaling
The Neuroscience Revolution

- Structural Connectivity
- Functional Connectivity
- Temporal Connectivity
  - Multimodal Integration

- Molecular Imaging
- New Molecular Imaging

Institutions:
- Wash U
- U Minn
- MGH
The Human Connectome
OCD as a Brain Disorder

Recurrent unwanted thoughts (obsessions) and/or repetitive behaviors (compulsions)
PTSD as a Brain Disorder

PERPETUATOR OF FEAR

Flashbacks, bad dreams, insomnia, frightening thoughts, avoidance, guilt, depression, hyperarousal
Depression as a Brain Disorder

GOVERNOR OF MOOD

Hopelessness, helplessness, suicidal thoughts, anorexia, loss of libido, sleep disturbance
Inconvenient Truth #3: In spite of progress, we still don’t know enough to ensure prevention, recovery, or cure for many people with SMI.

If we are to bend the curve, we must harness and direct the revolutions in genomics and neuroscience to:

- Transform diagnostics
- Transform therapeutics
Bending the curve with clinical neuroscience

Transforming diagnostics
From behavioral disorders to brain disorders:
  Diagnosis rooted in biology and behavior

Transforming therapeutics
From chemical imbalance to circuit dysfunction
  Treatments for circuit tuning
Diagnosis 2014

Symptoms only
Defined by consensus
Reliable but not valid

Heterogeneous
MDD: 256 combinations

Symptoms are late manifestations of brain disorders

Treatments focused on symptoms not cures
Transforming Diagnosis: PTSD

Fear Potentiated Startle Response

![Graph showing T-score difference for principal diagnosis and subtypes of PTSD and other anxiety disorders. The highest T-score difference is for single-trauma PTSD, followed by social phobia with circumscribed and specific phobias, and so on.](image)
Transforming Diagnosis: RDoC

Research Domain Criteria (RDoC) Project

Schizophrenia

Cognitive Deficits

Depression

Cognitive Systems Domain

Attention
Perception
Cognitive Control

Working Memory

Language Behavior
Declarative Memory

Behavior
Physiology
Circuits
Cells
Molecules
Genes

Units of Analysis

Social determinants

Insel et al., AJP 2010
Diagnosis 2024 (If RDoC Succeeds)

- Based on multiple factors
- Created via information commons
- Reliable, valid, and person-centered

Specific for an individual

Indicate risk and resilience

Tailored interventions/preventions
Treatments 2014

- Fragmented (medications vs psychosocial)
- Mostly focused on symptom control
- Access limited, adherence poor

Medications –
Little innovation,
Little R&D

Psychotherapy –
dose and duration
not known

Treatments depend on the provider not the patient
Promising Therapeutics

- Ketamine – Treating depression in 6 hours instead of 6 weeks.

- Family-focused Therapy – Treating anorexia nervosa by working with parents instead of removing parents.

- Deep brain stimulation to correct circuit dynamics in refractory depression.
Treatments 2024

- Preemptive and Personalized
- Person centered
- Network solutions not magic bullets

Engaging brain’s plasticity

Team-based with toolkit of options

Integrated with medical care
The Problem

Who wants to wait until 2024???
Schizophrenia - A Neurodevelopmental Disorder

Stage I: Risk
< 12 years

Stage II: Prodome
12 – 18 years

Stage III: Psychosis
18 – 24 years

Stage IV: Chronic Disability
> 24 years

Deficient myelination
Reduced inhibitory activity
Excessive excitatory pruning

Adapted from Insel, *Nature*, 2010
Schizophrenia - A Neurodevelopmental Disorder

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Deficient myelination
Reduced inhibitory activity
Excessive excitatory pruning

Adapted from Insel, *Nature*, 2010
RAISE: Recovery After Initial Schizophrenia Episode

- 2 Studies
- 22 States
- 36 Sites
- 134 Providers
- 469 Participants
- Policy relevant!

RAISE Toolbox:
- Coordinated Specialty Care
- Person-centered treatment
- CBT-informed individual resilience training
- Family psycho-education
- Supported education / Supported employment
- Low dose antipsychotic medication
- Liaison with primary medical care providers

Orange color states = RAISE sites
Coordinated Specialty Care

Client

- Medication/Primary Care
- Psychotherapy
- Case Management
- Supported Employment and Education
- Family Education and Support
• Evidence-Based Treatments for First Episode Psychosis: Components of Coordinated Specialty Care

• RAISE Coordinated Specialty Care for First Episode Psychosis Manuals

• RAISE Early Treatment Program Manuals and Program Resources

• OnTrackNY Manuals & Program Resources

• Voices of Recovery Video Series

December, 2013

RAISE feasibility study completed

January, 2014

Congress required SAMHSA to implement RAISE-like treatment program (Coordinated Specialty Care) via Mental Health Block Grants in all 50 states

September 30, 2014

Every state will have a plan
Schizophrenia - A Neurodevelopmental Disorder

Adapted from Insel, *Nature*, 2010

[Diagram showing the development stages of schizophrenia with emphasis on myelination, excitatory synapses, and inhibitory synapses during different age periods: Stage I: Risk < 12 years, Stage II: Prodome 12 – 18 years, Stage III: Psychosis 18 – 24 years, Stage IV: Chronic Disability > 24 years.]

- Stage I: Risk < 12 years
  - Prefrontal excitatory synapses
  - Prefrontal inhibitory synapses
  - Myelination

- Stage II: Prodome 12 – 18 years
  - Deficient myelination
  - Reduced inhibitory activity
  - Excessive excitatory pruning

- Stage III: Psychosis 18 – 24 years
  - Deficient myelination
  - Reduced inhibitory activity
  - Excessive excitatory pruning

- Stage IV: Chronic Disability > 24 years
  - Reduced inhibitory activity
  - Excessive excitatory pruning

RAISE

CHR

REHAB

Adapted from Insel, *Nature*, 2010
Can we prevent psychosis?

Do we know who is at risk?

Yes!

- North American Prodrome Longitudinal Study (NAPLS) has followed 765 help-seeking individuals at risk for psychosis
- 81 (11%) transitioned to psychosis within one year
- 7 variables improve prediction from 11% to over 70%
Can we prevent psychosis?

Do we know how to prevent psychosis?

- CBT – yes; 50% risk reduction, but quality of evidence is “moderate”
- Antipsychotics – no
- Omega-3 Fatty Acids – maybe
- Targeted cognitive training – ???, but stay tuned
Cognitive Training: Using Brain Plasticity to Alter Circuits

- Attention (ADHD)
- Appraisal (anxiety)
- Social skills (autism)
- Memory (MCI)
- Exec Fcn (psychosis)

Improved Function

Source: Vinogradov et al, UCSF
Schizophrenia - A Neurodevelopmental Disorder

Adapted from Insel, Nature, 2010
What have we learned?

- Early intervention is critical
- Therapeutics = tuning circuits
- From magic bullets to “network solutions”
Inconvenient Truth #4 Science is slow. But we can use what we know already to bend the curve!

Long-term:
Develop precision medicine for mental disorders
Create a new generation of networked treatments
Integrate practice and research

Short-term:
Do what we know!
Bundle treatments together to optimize outcomes
Disseminate these innovations to those most in need
Inconvenient Truth #1 We have failed to bend the curve

Inconvenient Truth #2 Not just access and quantity, but options and quality.

Inconvenient Truth #3 We don’t know enough – science is essential for progress.

Inconvenient Truth #4 Science is a long-term solution, but there are short-term gains.

The path to better service is better science.
Thank you!

National Institute of Mental Health

Paving the Way for Prevention, Recovery, and Cure

www.nimh.nih.gov

Research = Hope