New research platforms are needed to speed development and deployment of CNS interventions

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Disclosures

• I have no personal financial relationships with commercial interests relevant to this presentation

• The views expressed are my own, and do not necessarily represent those of the NIH, NIMH, or the Federal Government
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In intervention development and refinement research at NIMH
Industry Retreats from CNS Space

Is Pharma Running Out of Brainy Ideas?
Recent cutbacks raise concerns about the future of drug development for nervous system disorders


“There are very few new molecular entities, very few novel ideas, and almost nothing that gives any hope for a transformation in the treatment of mental illness.”
– Thomas Insel, M.D.
The Problem: Development of New Therapeutics is Slow, Expensive, and Failure-Prone
Areas for improvement:

• Improve the speed and efficiency of clinical trials (design, launch, conduct)

• Capitalize on scientific innovations

• Improve selection, prioritization, support, and completion of clinical trials

• Expand participation among patients and physicians
Refocus CT priorities:

- Elucidate disease mechanisms and pathophysiological pathways
- Identify novel targets, validate target engagement to probe disease mechanisms
- Adopt innovative trial designs and funding mechanisms
- Emphasize scientific collaboration, standardization, and data sharing
“De-risking” Phases I and IIa

- Identify targets, validate engagement
- Interventions as probes
- Proof of clinical mechanism, POC
- Early signals of efficacy
Fast Fail Drug Development Paradigm

- NIMH FAST Contracts
- Small, “deep” trials
- Learn from wins & losses

- Autism Spectrum Disorders
- Psychotic Disorders
- Mood-Anxiety Spectrum

What about Later Phase Trials?

NIMH Practical Clinical Trials, 1998-2005

<table>
<thead>
<tr>
<th>CER Trial</th>
<th># Enrolled</th>
<th>Project Period</th>
<th>Total Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>CATIE</td>
<td>1,881</td>
<td>5 Years</td>
<td>$43M</td>
</tr>
<tr>
<td>STAR*D</td>
<td>4,041</td>
<td>7 years</td>
<td>$35M</td>
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<tr>
<td>STEP-BD</td>
<td>4,360</td>
<td>7 years</td>
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NIH Budget doubled between 1998 and 2003
Since then flat or reduced budgets force us to seek greater efficiency
How can we do more with less?
Practice-Based Research Networks

- Embedded within health care systems
- Large, diverse, representative populations
- Advanced health information systems
- Standardized assessment measures
- Integrated data repositories

? Improve speed/efficiency of clinical trials?
? Reduce overall costs of pragmatic trials?
? Increase impact of findings on practice?
? Reusable clinical trial infrastructure?
To explore possibilities and pitfalls:

• Michael S. Lauer, MD – National Heart, Lung, and Blood Institute
• Gregory Simon, MD – Mental Health Research Network
• Robert W. Dubois, MD – National Pharmaceutical Council
• Helena C. Kraemer, PhD – Stanford School of Medicine
• Thomas Laughren, MD – Massachusetts General Hospital