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THE INTERNATIONAL SOCIETY FOR CNS CLINICAL TRIALS AND METHODOLOGY

The Future of Privately Funded CNS Clinical Research

Food for Thought

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The Questions

- Key influencing developments in policy
- Alignments/differences between:
  - Policymakers' data needs
  - Data being provided by clinical researchers
  - Data needed to improve public health
- Influence of policy stakeholders on future clinical research
- Can clinical research better support policy decisions
- What are meaningful endpoints to consumers, advocates, payers, and policymakers

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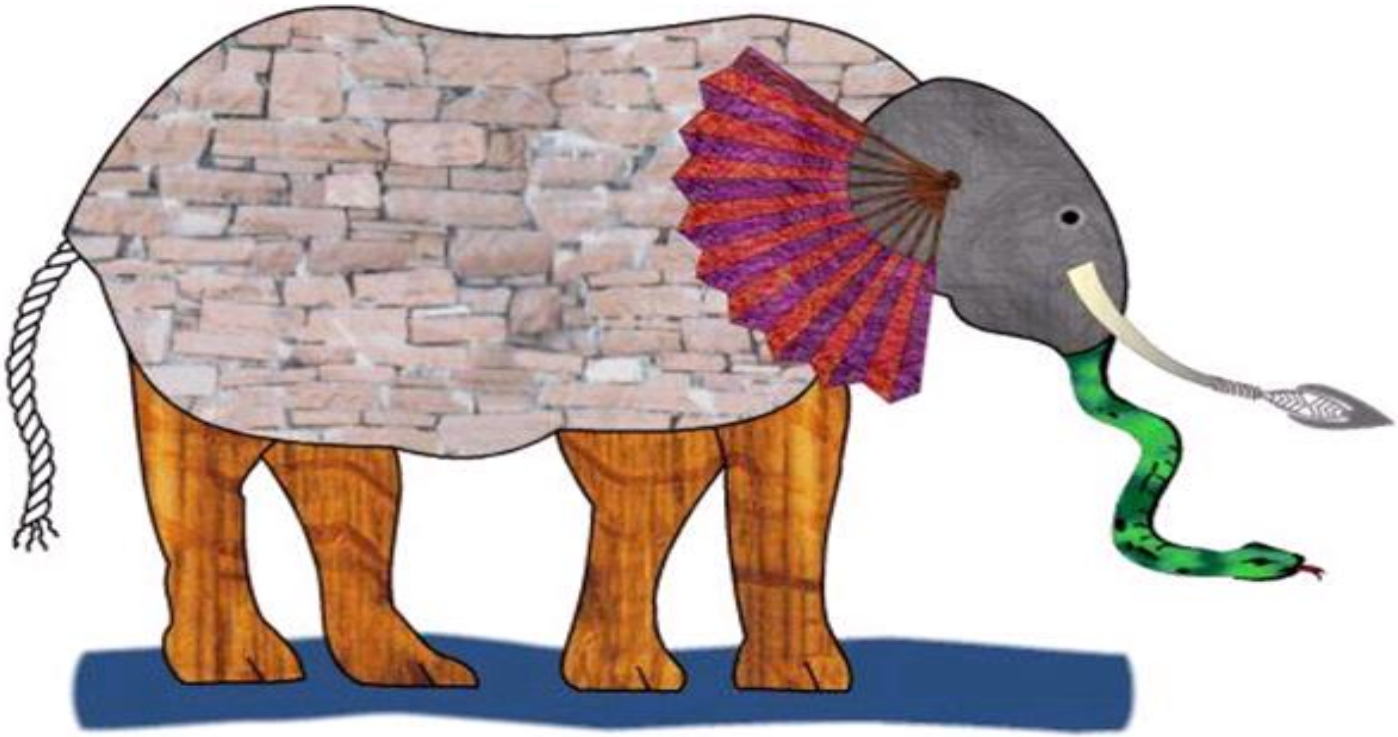
What Does the Future Hold?

THE BLIND MEN AND THE ELEPHANT



John Godfrey Saxe's (1816-1887) version of the famous Indian legend,

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Context

- Affordable Care Act
  - And whatever follows…
- Changes in Regulatory Environment
- Science Context
- Economic "Downturn" & Budget Crisis
- Changes in Market Access/Pricing Environment
- Alternative Opportunities / Needs
  - In Medicine
  - Outside of Medicine…

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Perspective

- Definition of “Privately Funded CNS Clinical Research”:
  - Non-Government and Non-Charity (?”Industry”)

- Consider This Perspective:
  - Much of this is the public’s own “discretionary” money
  - If they don’t pay Academic & Government researchers they go to jail (it’s called tax evasion)
  - But with their own money, used to pay “privately funded” research, they voluntary “vote with their feet” – voluntary funding of endeavors by market capitalization, mostly via professional “expert intermediaries”
  - They can often move the money quickly, typically not ideologically driven
  - They move resources (money) to where it is believed they will get the best return (Academic competition for government funds is fierce? Perhaps, but competition for funding is hardly unique…)
  - “They” are probably YOU (TIAA/CREF, Pensions, Mutual funds, Corporate Bonds, etc.)

  - This market system, “worst except all the others”, dominates the Earth in 2011 and best creates wealth/health. It necessarily operates in a policy framework, parts of which are global and parts of which vary between or even within nations.

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Why Ask?

- A very large proportion of CNS clinical research investment is from non-government, non-charity sources
- Diverse research (and other) expertise specifically needed to develop a new drug resides largely in the private sector
- New treatments are very expensive & productivity is declining:
  - $1.8 Billion, 14 years, 25 projects, brings ONE new drug to market
    - Devices and other interventions may sometimes be less/faster
  - Total annual NIMH budget ~$1.4 Billion today
    - But vast majority of new CNS drugs of the past 35 years have not been brought to market by NIMH investment
    - Key NIMH mission in “basic science” (e.g., genomics & neural circuits)
- Because we care about improving care in mental health: patients, public health, even professional livelihood

Analysis: Neuroscience under threat as Big Pharma backs off

Fri, Feb 11 2011

By Kate Kelland, Health and Science Correspondent

LONDON (Reuters) - Scientists worried by waning commitment from major drugmakers to brain research warn the prospect for new drugs to treat diseases like Alzheimers is bleak unless regulators and governments find incentives fast.

Big Pharma is struggling to make money from neuroscience -- the science of how the brain works and affects behavior -- because research is proving unpredictable and costly at a time when companies are grappling with patent expirations and pressure to cut prices.

Experts in the field of neuroscience say moves by firms like GlaxoSmithKline, AstraZeneca and Merck to back away from some brain research and development (R&D) may sound its death knell in Europe and put it at risk elsewhere if nothing is done to recapture their interest.

They suggest companies could be encouraged to reconsider if they were given the option of sharing the risk of developing new drugs with publicly-funded research institutions, or if current patents were extended to ensure better returns on investment.

"If we think about a whole range of things from multiple sclerosis, to stroke, to Alzheimer's disease, to schizophrenia, to autism, we don't have effective treatments for any of them -- and the reason is that we don't really understand the basis of those diseases," said Colin Blakemore, a professor of neuroscience at Britain's respected Oxford University.

"The need for fundamental research that can be drawn on is the only hope for the development of new treatments."

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ECNP Summit on the future of CNS drug research in Europe

6-7 March 2011, Nice, France

ECNP, as one of the leading voices for neuropsychopharmacology and psychiatry in Europe, is very concerned about the pulling out or downsizing of neuroscience research in Europe by the pharmaceutical industry.

ECNP believes that European institutions can and must respond to this challenge immediately before the field suffers possibly irreparable damage.

In response to this crisis, ECNP, in conjunction with the EMA and EU, has organised this by-invitation-only summit. By means of this summit, ECNP hopes to develop a set of proposals to remediate the current situation and to secure a sustainable future for European neuroscience.

Organisers
Guy Goodwin, United Kingdom
David Nutt, United Kingdom

Director's Blog
March 30, 2010

Who Will Develop the Next Generation of Medications for Mental Illness?

Thomas Insel

In 2007 NIMH completed a series of practical trials to assess the effectiveness of currently available medications. With the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) trial for schizophrenia, the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study, and the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study, roughly 10,000 patients were studied at nearly 200 sites. None of these studies was perfect, but in aggregate they told us what we might have surmised from several worrisome public health indicators: the medications we have today, even when optimized within a research study, help some people get better, but too few completely recover. It is undeniable that we can improve outcomes for people with mental illness if we provide comprehensive evidence-based care. But, if we are honest with ourselves and our patients, we need to admit that today's treatments, both medications and psychosocial interventions, may be good but they are not good enough.

Clearly, developing a new generation of medications of truly novel compounds with far greater efficacy and greater effectiveness will require a new, rational basis for therapeutic development based on understanding mechanisms responsible for disease, identifying targets through which these mechanisms can be altered, and building the pipeline to create innovative medications. The good news is that research elucidating the neurobiological bases of disorders is revealing new targets for drug development for depression, schizophrenia,

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Publications by the Director

Selected publications by NIMH Director Thomas Insel

Posts by Topic

Disorders

- Attention Deficit Hyperactivity Disorder (ADHD) (3 Items)
- Autism (4 Items)
- Bipolar Disorder (1 Item)

- "NIMH will not be able to replace pharma"
- NIMH-supported science could yield tools that would re-incentivize industry to invest (e.g., "quick win-fast fail" lead compounds)?
- Need to free up funds by making clinical research more efficient
- Hard choices between "new medications" and optimizing existing ones

The Perfect Storm: *CNS Drug Development in Trouble*

Andrew A. Nierenberg, MD

"For every complex problem there is an answer that is clear, simple, and wrong".

H.L. Menken

The high cost and high risk of central nervous system (CNS) drug development coupled with decreased opportunities for pharmaceutical companies to recoup their investments and may free up some resources required to make a major investment. But limits in the NIMH's funding clearly indicate that, as we set priorities, hard choices will need to be made between investing in new medications and attempting to optimize the use of existing ones".[1]

Pharma's retreat from CNS drug development, coupled with woefully inadequate funding

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The Perfect Storm: *CNS Drug Development in Trouble*

Andrew A. Nierenberg, MD

More efficient clinical research* will not solve the problem. Hope is in the ACA initiative for CER to sustain CNS clinical research.**

*also n.b. “quick win/fast fail”, *Nature Reviews Drug Discovery* **9**, 203-214 (March 2010)

**To be funded by a new tax/fee on health insurers from 2012 forward

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Policy Domains Impacting Privately Funded CNS Clinical Research

More Than ACA At Work…

(+) RETURN

- Access
- Reimbursement
- Price
- Patent Protection

(-) COST / RISK

- Risk – science-related
- Risk – non-science related
- Cost of Research
- Cost of Commercialization
- Opportunity Cost

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Relevant Policy Domains: More than ACA

RETURN

- Access
- Reimbursement
- Price
- Patent Protection

COST / RISK

- Risk – science-related
- Risk – non-science related
- Cost of Research
- Cost of Commercialization
- Opportunity Cost
  - Other therapeutic areas
    - Immunology, Cancer, etc.
  - Non-medical
    - Alternative Energy, Climate Change, Fresh Water, Food Security, Biodiversity, Consumer, etc.

For Private Investment in CNS:
- Acceptable/Encouraging Perception
- "At Risk" Perception
- Discouraging Perception

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Policy Stakeholders Influence CNS Clinical Research

- Government policy drives many incentives and disincentives for private investment generally and for specific CNS clinical research behaviors
  - Changes in specific behavior may result (e.g., ICH, EU regulation concerning active comparator has stimulated a change in CNS research) OR may simply tip the balance for/against making an investment at all
  - "Thumbs on the Scale" – but don't control all factors…
    - Burden of regulation (pre- and post-launch)
    - Patent protection
    - Tax incentives/disincentives
    - Payment systems
    - Many, many, others…
  - Note geographic policy variation can drive geographic choices!
- Stakeholders may encourage specific research supporting policy decisions
- Stakeholders may encourage specific research of ideological interest or in response to political exigencies

A Research Spectrum

- Discovering New Approaches
- Proof of Possibility
  - ‘Efficacy’ (e.g. placebo) research
- Breakthrough/Transformation
- Role of Serendipity

- Optimizing Existing Approaches
- Realizing the possibility
  - Effectiveness & CER
- Incremental Improvement
- Often Benefits from Efficiency Mindset

Private funding has been applied across the spectrum, when risk/return have been commensurate

Government funding is also across the spectrum, with tilt toward the left side

Arguably, the right side has been chronically underserved

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(+) Cures Acceleration Network

(+) A Growing Quality Enterprise

(+) Information Technology

(-) Declining Pharm Investment

- Products

- End-Services

- Systems/ Processes

PCMH, ACO…

(+) Patient Centered Outcomes Research Institute

(+) CER funding

(+) Needs/Demands of Payers

(+) Economic and Demographic pressures

(+?) Non-pharm private funds

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Reasons for Hope

- Enormity of Unmet Need
- Strength of Advocacy
- Growth in Global “Middle Class”
- Advancing Understanding of Biology
- Individual Altruism

The Future of Privately Funded CNS Clinical Research

Stimulated Thought. Broadened Perspective.

And Illuminated Part of the Truth…

…And so these men of Indostan
Disputed loud and long,
Each in his own opinion
Exceeding stiff and strong,
Though each was partly in the right,
And all were in the wrong!

…They prate about an Elephant
Not one of them has seen!