EARLY BRAIN & BIOLOGICAL DEVELOPMENT: A SCIENCE IN SOCIETY SYMPOSIUM

The Pivot to Preemptive Treatments in Psychiatry

John S. March, MD, MPH
Director, Neurosciences Medicine
Duke Clinical Research Institute

June 1, 2011



Alberta family wellness initiative

Norlien Foundation

My Disclosures

- Advisory board: Alkermes, Inc., Avanir, Lilly, Pfizer, Shire
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- Research funding: Pfizer
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- Foundation: NARSAD, SRI
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- Promotional activities: None

http://www.dcri.duke.edu/research/coi.jsp

The Future Paradigm:

Transform Medicine from Curative to Preemptive

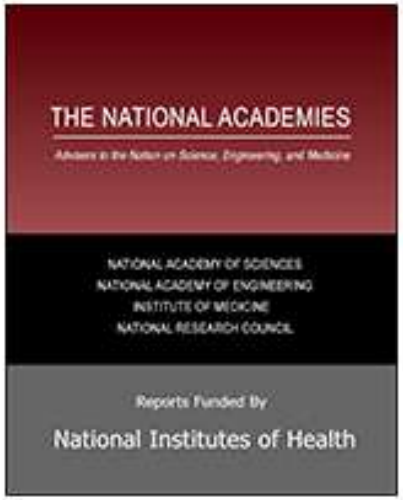
Predictive ⟷ Personalized ⟷ Preemptive

Topics

- What is meant by preemptive treatments?
- The four pivots to preemptive interventions:
  - Translational developmental neuroscience
  - Biomarkers and personalized medicine
  - Novel interventions and early phase clinical pharmacology
  - Prevention trials and comparative-effectiveness research

A preemptive approach promises to reduce morbidity and mortality by intervening early, before the full syndrome develops, and re-aligning the trajectory of development so the individual identified as at risk has the greatest opportunity for the best outcome.

Tom Insel, MD, NIMH Director



Preventing Mental, Emotional, and Behavioral Disorders Among Young People

Progress and Possibilities

National Research Council (US) and Institute of Medicine (US) Committee on the Prevention of Mental Disorders and Substance Abuse Among Children, Youth, and Young Adults: Research Advances and Promising Interventions; Edited by Mary Ellen O'Connell, Thomas Boat, and Kenneth E Warner.

Washington (DC): National Academies Press (US); 2009.
ISBN-13: 978-0-309-12674-8

"Prevention involves a way of thinking that goes beyond the traditional disease model, in which one waits for an illness to occur and then provides evidence-based treatment."

Preemption Requires:

- **A biologically-based theory of disease**
  - **Development (time) is integral**
- **Personalized predictive tools in the form of biomarkers or biosignatures**
- **Novel interventions that prevent or forestall illness**


"YOUR INSURANCE DOESN'T COVER THE SNIFFLES – COME BACK WHEN IT DEVELOPS INTO SOMETHING MORE SERIOUS."
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Definition of Prodrome

- Premonitory manifestation of the disease.
- Not a characteristic of the individual or their environment, or a causal agent of the disease
- May or may not continue to be manifest once the full disease appears.
- Prodromal symptoms may or may not manifest in different episodes.

Costello and Angold, J Ch Psychatr and Psych, 2010

THE JOURNAL OF CHILD PSYCHOLOGY AND PSYCHIATRY

ACAMH

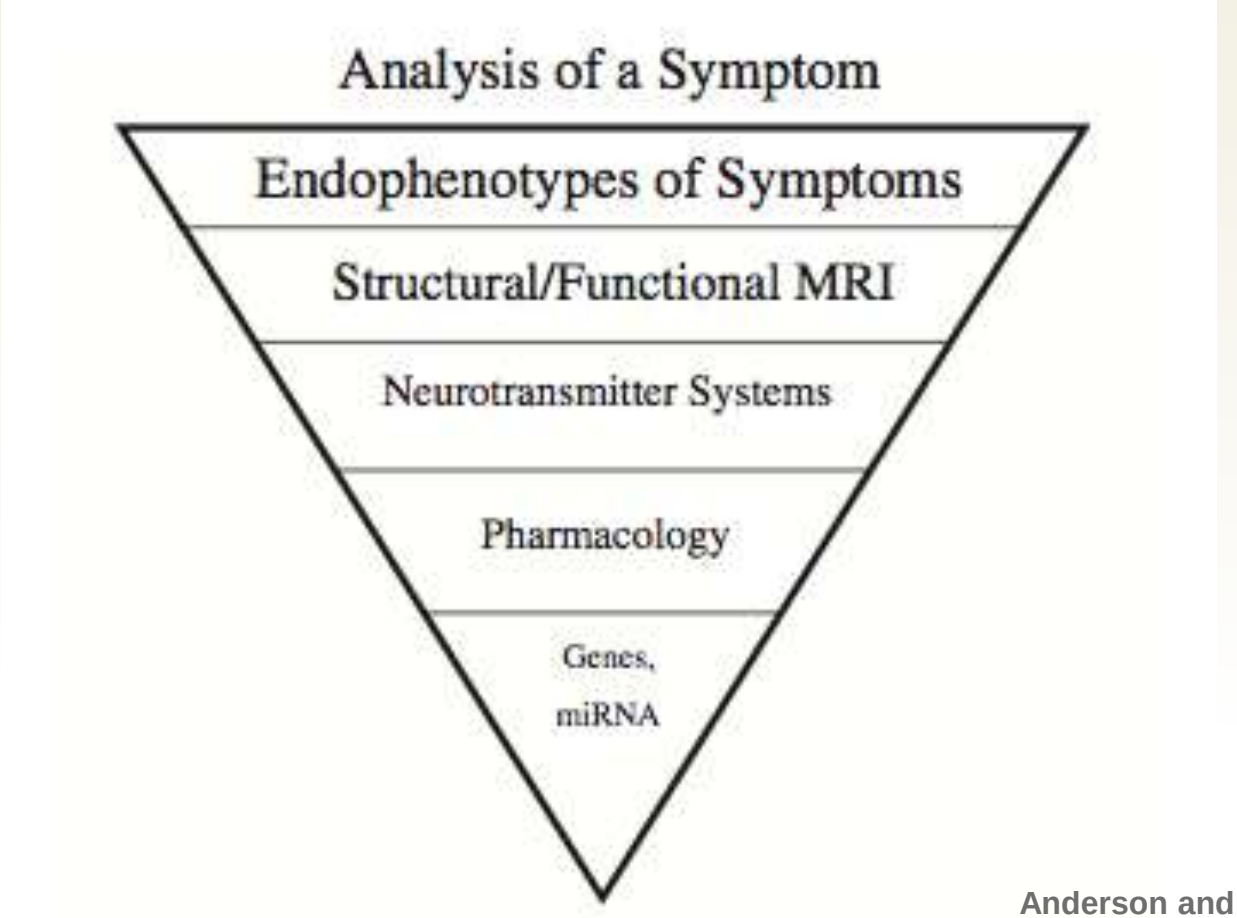
Journal of Child Psychology and Psychiatry 52:4 (2011), pp 476–503 doi:10.1111/j.1469-7610.2011.02376.x

Annual Research Review: New frontiers in developmental neuropharmacology: can long-term therapeutic effects of drugs be optimized through carefully timed early intervention?

Susan L. Andersen[1] and Carryl P. Navalta[2]

[1]Laboratory for Developmental Neuropharmacology, Department of Psychiatry, McLean Hospital, Harvard Medical School, Belmont, MA, USA; [2]Program for Behavioral Science, Department of Psychiatry, Children's Hospital Boston, Harvard Medical School. Boston. MA. USA

A Systems Approach to Disease Components



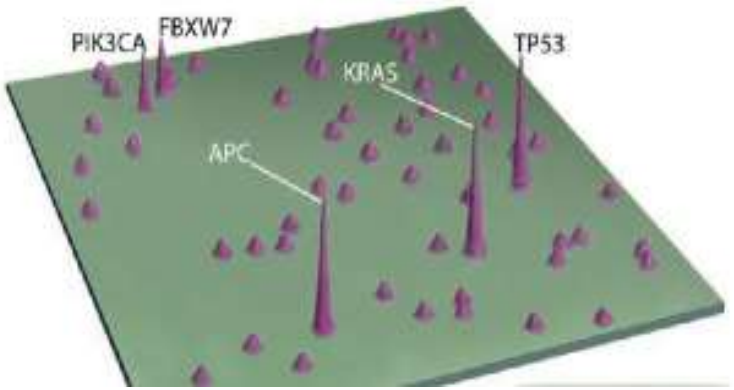
Anderson and Navalta, JCPP, 2011

The Genomic Landscapes of Human Breast and Colorectal Cancers

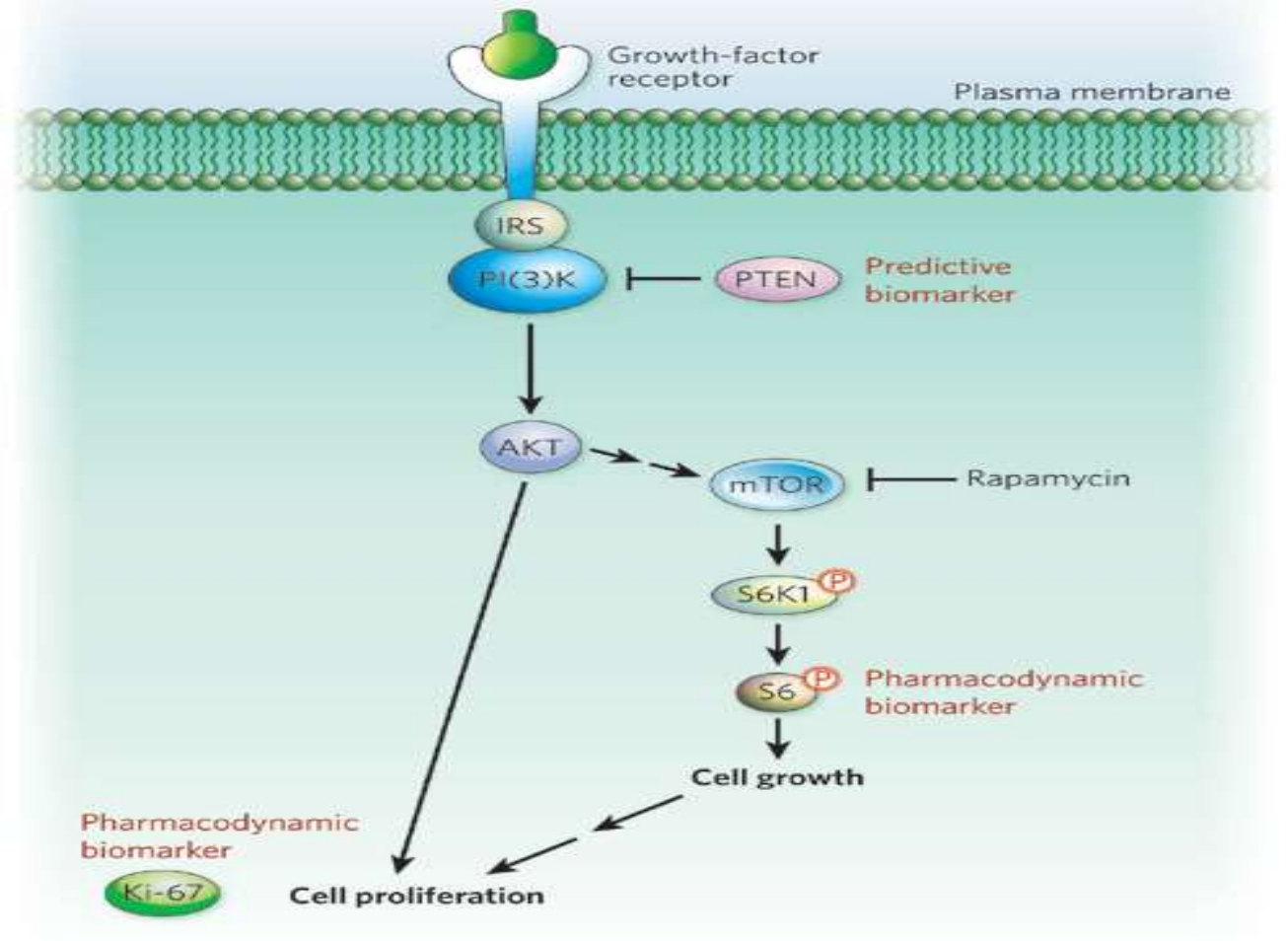
Laura D. Wood,[1*] D. Williams Parsons,[1*] Siân Jones,[1*] Jimmy Lin,[1*] Tobias Sjöblom,[1*†] Rebecca J. Leary,[1] Dong Shen,[1] Simina M. Boca,[1,2] Thomas Barber,[1‡] Janine Ptak,[1] Natalie Silliman,[1] Steve Szabo,[1] Zoltan Dezso,[3] Vadim Ustyanksky,[3] Tatiana Nikolskaya,[3,4] Yuri Nikolsky,[3] Rachel Karchin,[5] Paul A. Wilson,[5] Joshua S. Kaminker,[6] Zemin Zhang,[6] Randal Croshaw,[7] Joseph Willis,[8] Dawn Dawson,[8] Michail Shipitsin,[9] James K. V. Willson,[10] Saraswati Sukumar,[11] Kornelia Polyak,[9] Ben Ho Park,[11] Charit L. Pethiyagoda,[12] P. V. Krishna Pant,[12] Dennis G. Ballinger,[12] Andrew B. Sparks,[12§] James Hartigan,[13] Douglas R. Smith,[13] Erick Suh,[13] Nickolas Papadopoulos,[1] Phillip Buckhaults,[7] Sanford D. Markowitz,[1] Giovanni Parmigiani,[1‖] Kenneth W. Kinzler,[1‖] Victor E. Velculescu,[1‖] Bert Vogelstein[1‖]

AUTHORS' SUMMARY

How many genes are mutated in a human tumor? Answering this question would have seemed like science fiction just a decade ago. However, as a result of advances in technology, we have been able to answer this question in breast and colorectal cancers: There are ~80 DNA mutations that alter amino acids in a typical cancer. Examining the overall distribution of these mutations in different



AKT-mTOR: Cancer and Mental Illness



Topics

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  - Novel interventions and early phase clinical pharmacology
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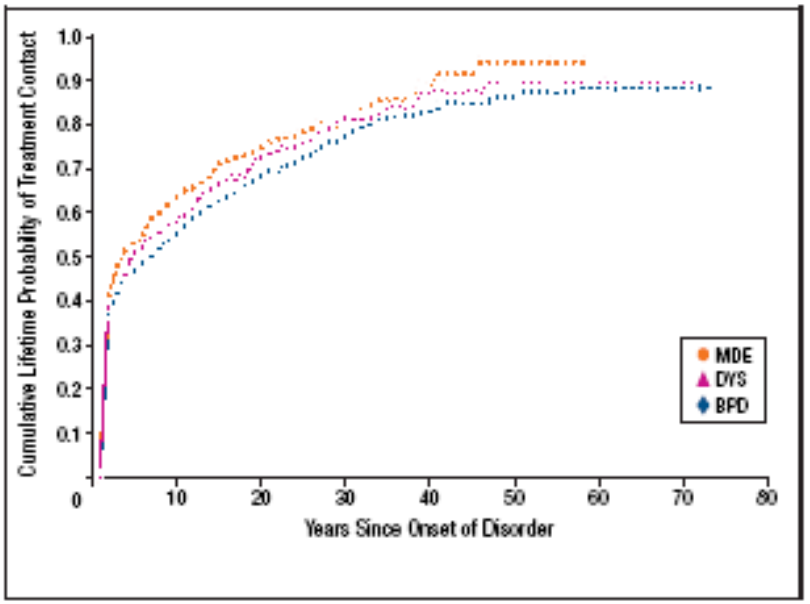
Age of Onset of First Mental Illness

> 75% early onset

Table 2. Lifetime Prevalence of *DSM-IV*/WMH-CIDI Disorders in the Total NCS-R Sample and by Age

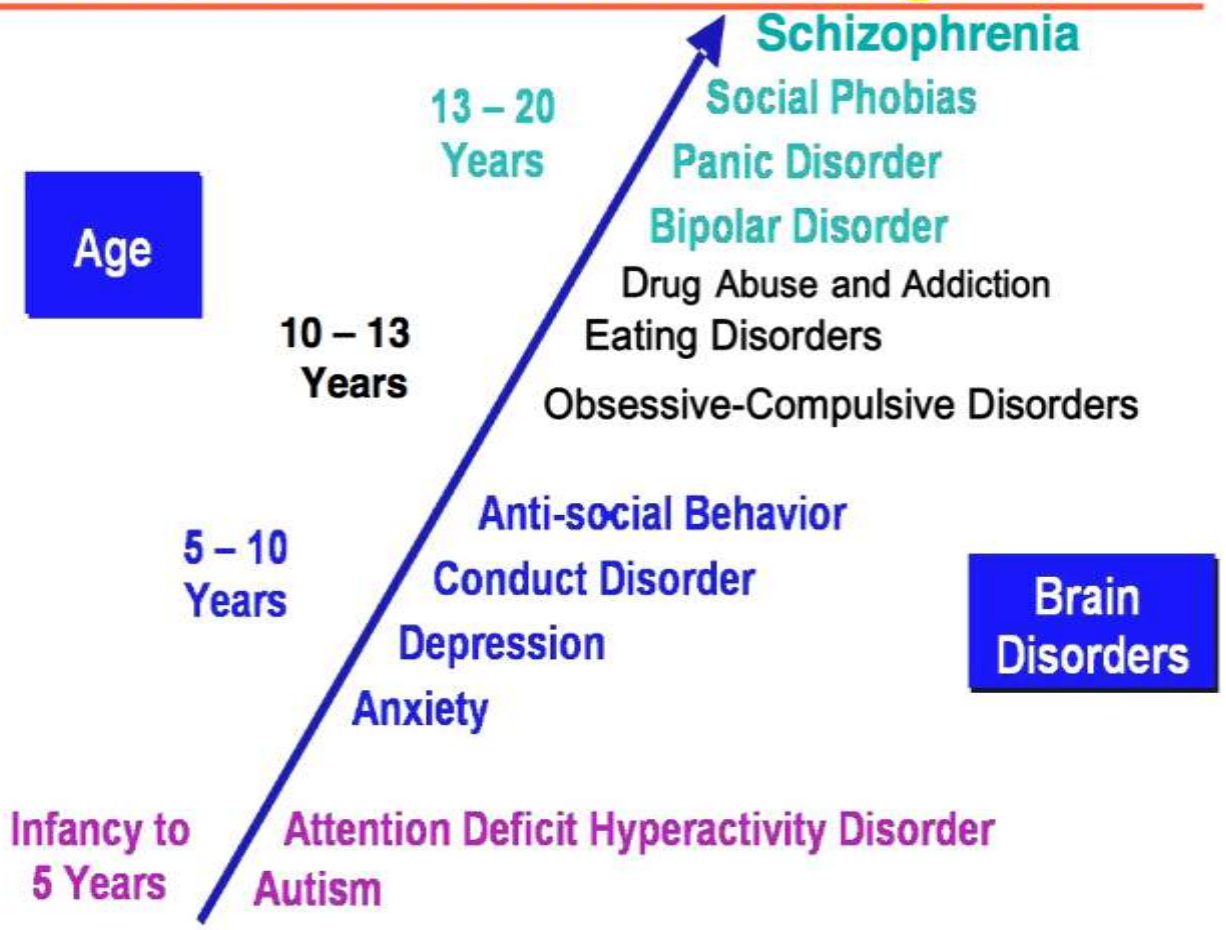
	Prevalence, % (SE)				
		Age, y			
	Total	18-29	30-44	45-59	≥60
Anxiety Disorders					
Panic disorder	4.7 (0.2)	4.4 (0.4)	5.7 (0.5)	5.9 (0.4)	2.0 (0.4)
Agoraphobia without panic	1.4 (0.1)	1.1 (0.2)	1.7 (0.2)	1.6 (0.3)	1.0 (0.3)
Specific phobia	12.5 (0.4)	13.3 (0.8)	13.9 (0.8)	14.1 (1.0)	7.5 (0.7)
Social phobia	12.1 (0.4)	13.6 (0.7)	14.3 (0.8)	12.4 (0.8)	6.6 (0.5)
Generalized anxiety disorder	5.7 (0.2)	4.1 (0.4)	6.8 (0.5)	7.7 (0.7)	3.6 (0.5)
Posttraumatic stress disorder‡	6.8 (0.4)	6.3 (0.5)	8.2 (0.8)	8.2 (0.9)	2.9 (0.5)
Obsessive-compulsive disorder§	1.6 (0.3)	2.0 (0.5)	2.3 (0.9)	1.3 (0.6)	0.7 (0.4)
Separation anxiety disorder	5.2 (0.4)	5.2 (0.6)	5.1 (0.6)	‖	‖
Any anxiety disorder¶	28.8 (0.8)	30.2 (1.1)	36.1 (1.4)	30.8 (1.7)	16.3 (1.6)
Mood Disorders					
Major depressive disorder	16.6 (0.5)	15.4 (0.7)	19.8 (0.9)	18.8 (1.1)	10.6 (0.8)
Dysthymia	2.5 (0.2)	1.7 (0.3)	2.9 (0.4)	3.7 (0.7)	1.5 (0.3)
Bipolar I-II disorders	3.9 (0.2)	3.9 (0.6)	4.3 (0.3)	3.8 (0.4)	1.0 (0.2)
Any mood disorder	20.8 (0.6)	21.4 (0.9)	24.6 (0.9)	22.8 (1.2)	11.9 (1.0)
Impulse-Control Disorders					
Oppositional-defiant disorder	8.5 (0.7)	9.5 (0.9)	7.5 (0.8)	‖	‖
Conduct disorder	9.5 (0.5)	10.9 (1.0)	8.2 (0.8)	‖	‖
Attention-deficit/hyperactivity disorder	8.1 (0.6)	7.8 (0.8)	8.3 (0.9)	‖	‖
Intermittent explosive disorder	5.2 (0.3)	7.4 (0.7)	5.7 (0.6)	4.9 (0.4)	1.9 (0.5)
Any impulse-control disorder	24.8 (1.1)	28.8 (1.7)	23.0 (1.3)	‖	‖
Substance Use Disorders					
Alcohol abuse	13.2 (0.6)	14.3 (1.0)	16.3 (1.1)	14.0 (1.1)	6.2 (0.7)
Alcohol dependence	5.4 (0.3)	6.3 (0.7)	6.4 (0.6)	6.8 (0.7)	2.2 (0.4)
Drug abuse	7.9 (0.4)	10.9 (0.9)	11.9 (1.0)	6.5 (0.6)	0.5 (0.2)
Drug dependence	3.8 (0.2)	3.9 (0.5)	4.9 (0.6)	2.3 (0.4)	0.2 (0.1)
Any substance use disorder	14.6 (0.6)	16.7 (1.1)	18.0 (1.1)	15.3 (1.0)	6.3 (0.7)
Any Disorder					
Any disorder¶	46.4 (1.1)	52.4 (1.7)	55.0 (1.6)	46.5 (1.8)	26.1 (1.7)
Two or more disorders¶	27.7 (0.9)	33.9 (1.3)	34.0 (1.5)	27.0 (1.6)	11.6 (1.0)
Three or more disorders¶	17.3 (0.7)	22.3 (1.2)	22.0 (1.1)	15.9 (1.3)	5.3 (0.7)

10 years to first treatment



Kessler, RS et al. Arch Gen Psychiatry. 2005;62:593-602
Wang PS et al. Archives of General Psychiatry. 62(6):603-13, 2005

Mental Disorders are Developmental



frontiers in PSYCHIATRY

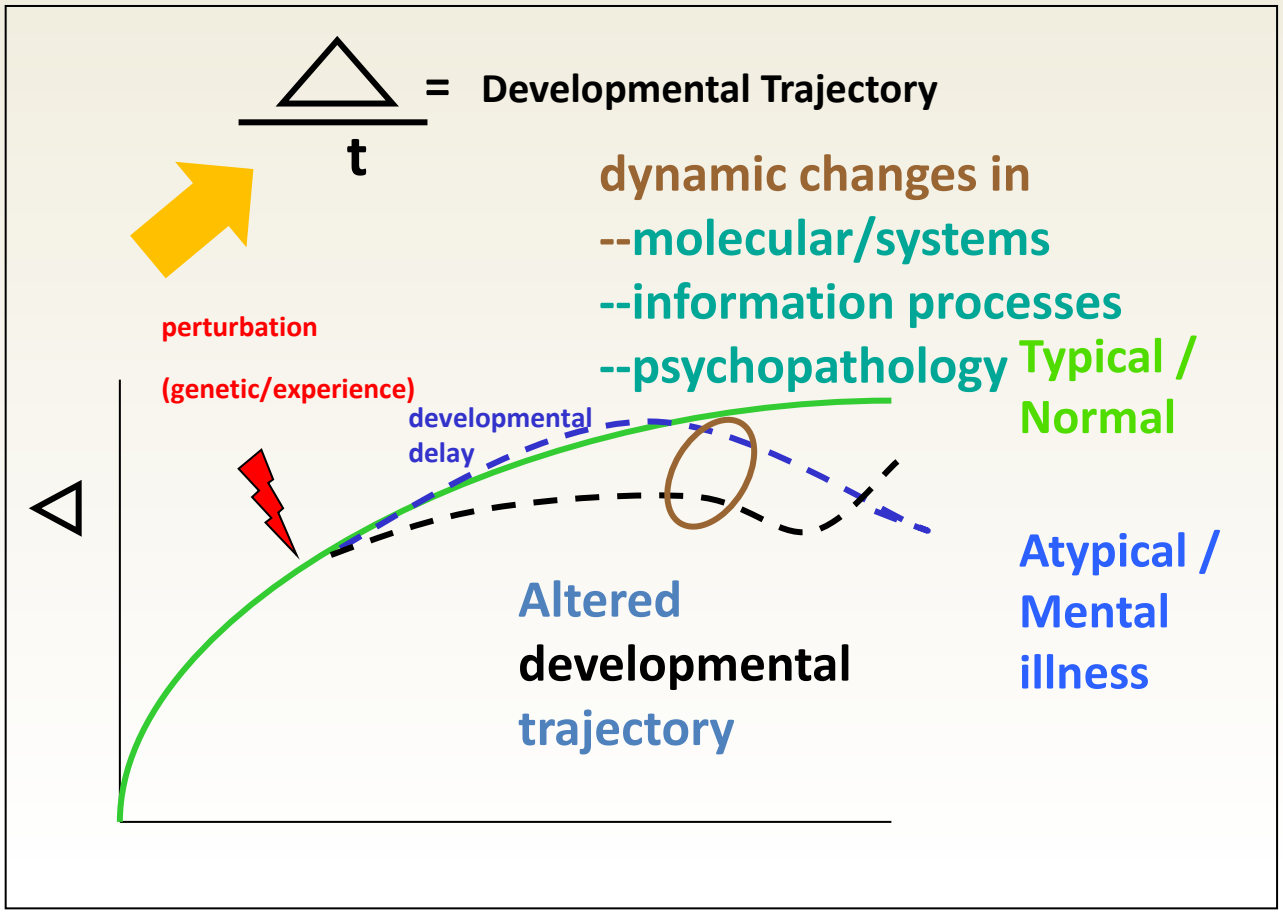
OPINION ARTICLE
published: 08 July 2010
doi: 10.3389/fpsyt.2010.00014

Grand challenges in child and neurodevelopmental psychiatry

E. Jane Costello*

Center for Developmental Epidemiology, Duke University Medical School, Durham, NC, USA
**Correspondence: elizabeth.costello@duke.edu*

"Prevention and development are intimately intertwined: only when we understand the developmental course of a symptom or disorder can we have a solid scientific underpinning for prevention…A well defined prevention trial will implicitly or explicitly test a developmental theory of disease."


= Developmental Trajectory
t
dynamic changes in
--molecular/systems
--information processes
--psychopathology
Typical / Normal
perturbation
(genetic/experience)
developmental delay
Atypical / Mental illness
Altered developmental trajectory
Fetal
Age 18
Time (t)

Editorial: Developmental neuroscience comes of age

James F. Leckman, John S. March

Article first published online: 15 MAR 2011

DOI: 10.1111/j.1469-7610.2011.02378.x

Issue

Journal of Child Psychology and Psychiatry

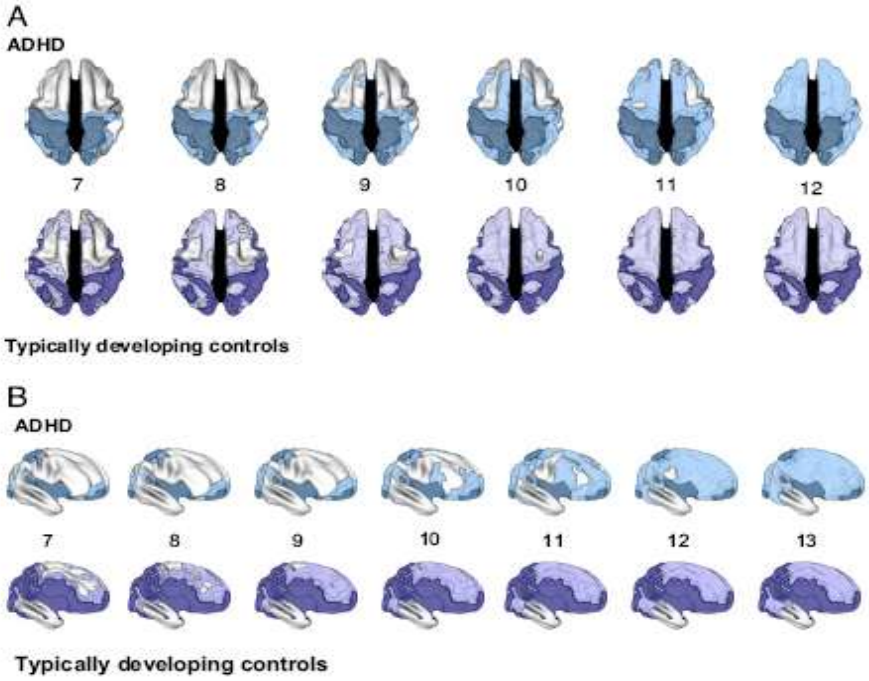
Volume 52, Issue 4, pages 333–338, April 2011

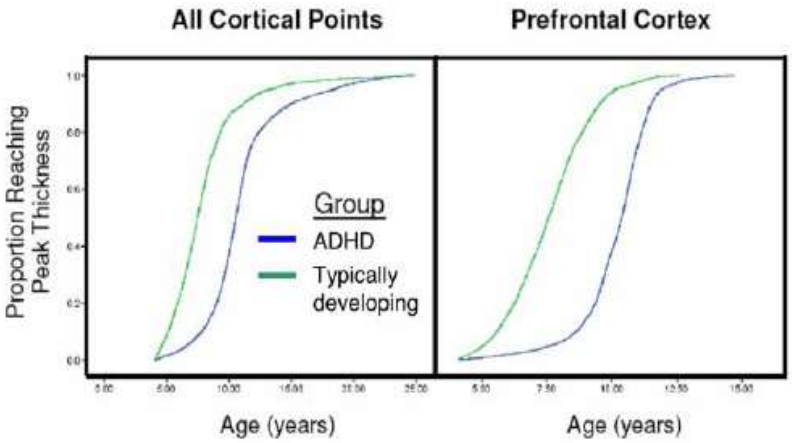
Mental disorders as brain disorders

Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation

P. Shaw[†‡], K. Eckstrand[†], W. Sharp[†], J. Blumenthal[†], J. Lerch[†], D. Greenstein[†], L. Clasen[†], A. Evans[§], J. Giedd[†], and J. L. Rapoport[†]

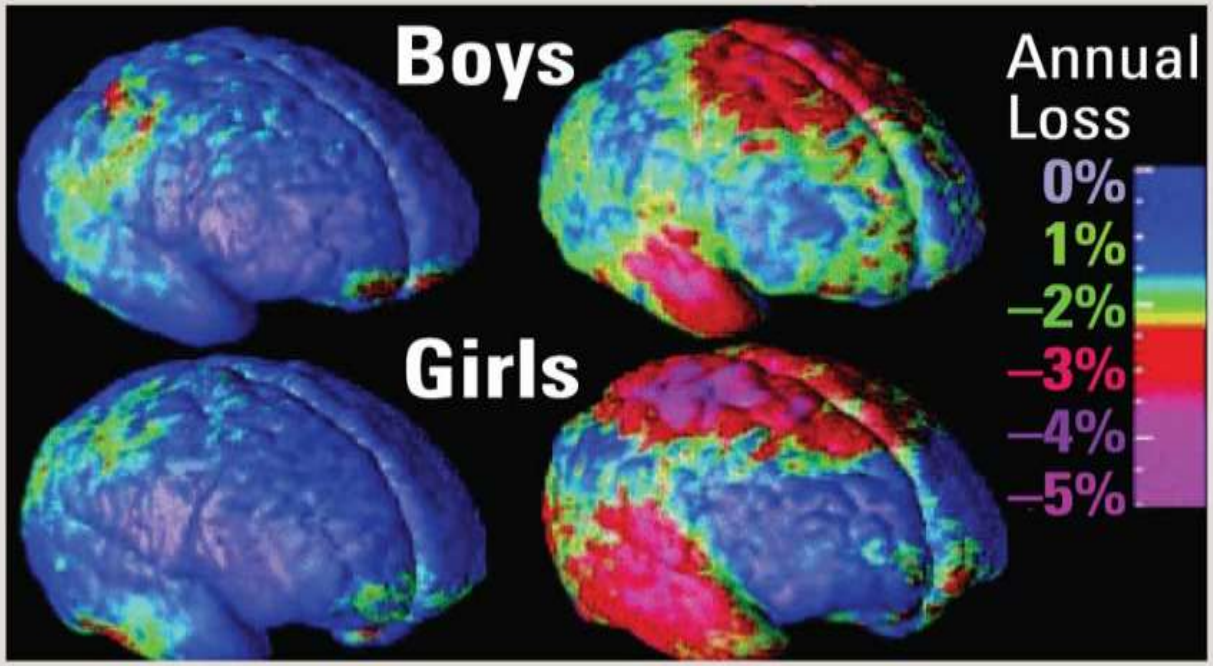
PNAS, 2007





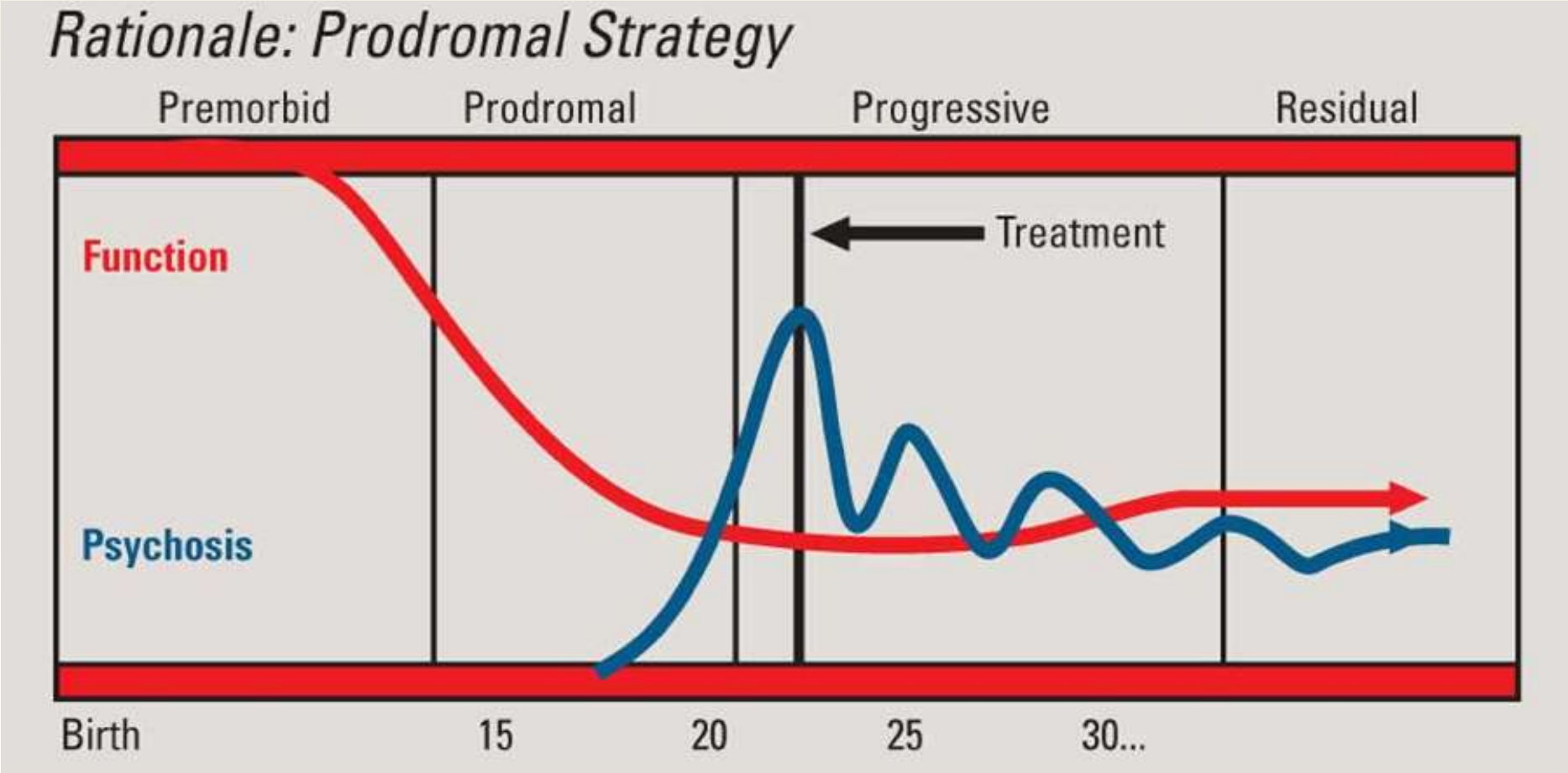
Schizophrenia may be a Disorder of Excessive Cortical Remodeling

Rate of Gray Matter Loss in Schizophrenia and Control Subjects[2]



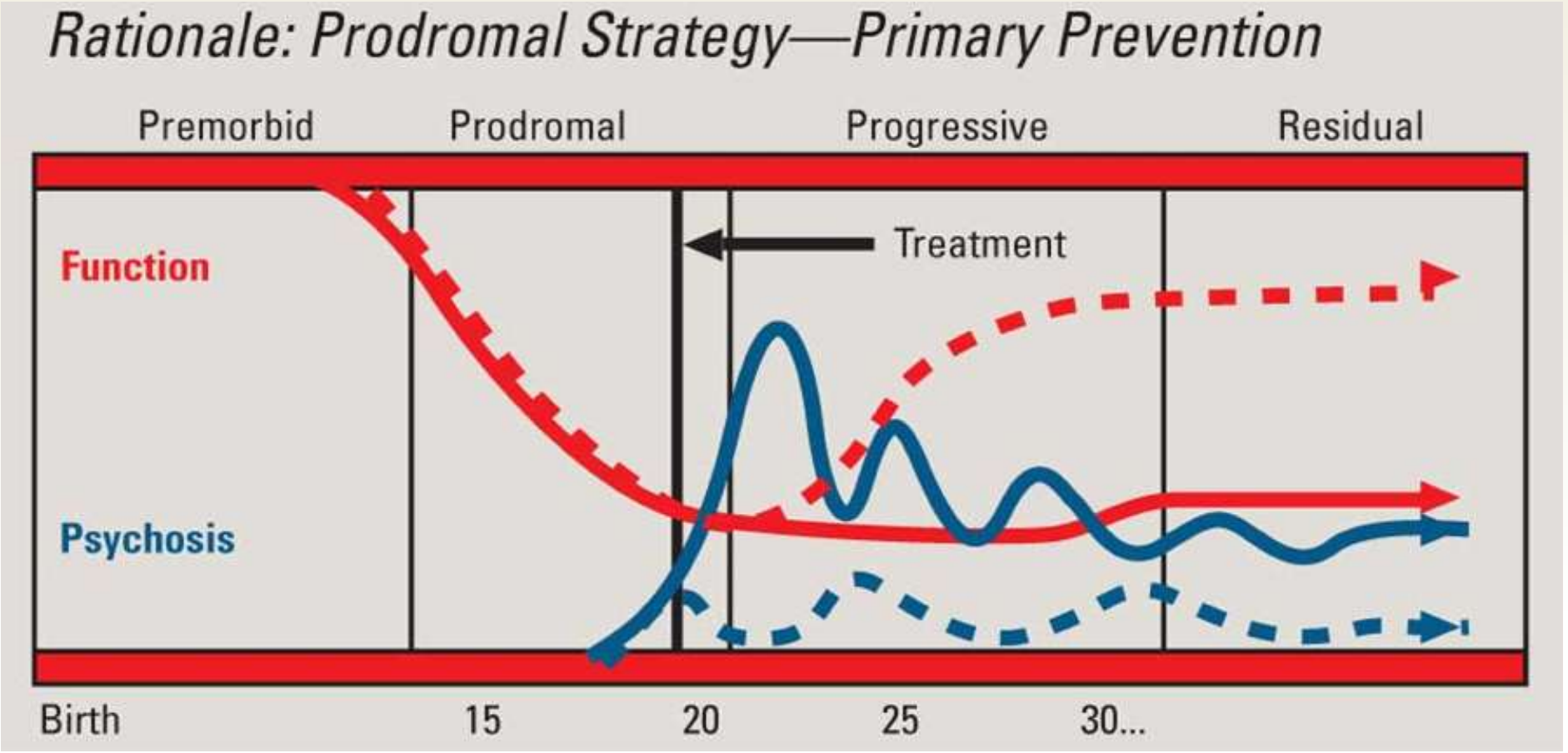
Vidal et al, 2006

Neuroprotection and Schizophrenia



Lieberman et al., CNS Spectrums, 2007; 12: 1-16

Neuroprotection and Schizophrenia



Lieberman et al., CNS Spectrums, 2007; 12: 1-16

Schizophrenia susceptibility genes: Current candidates

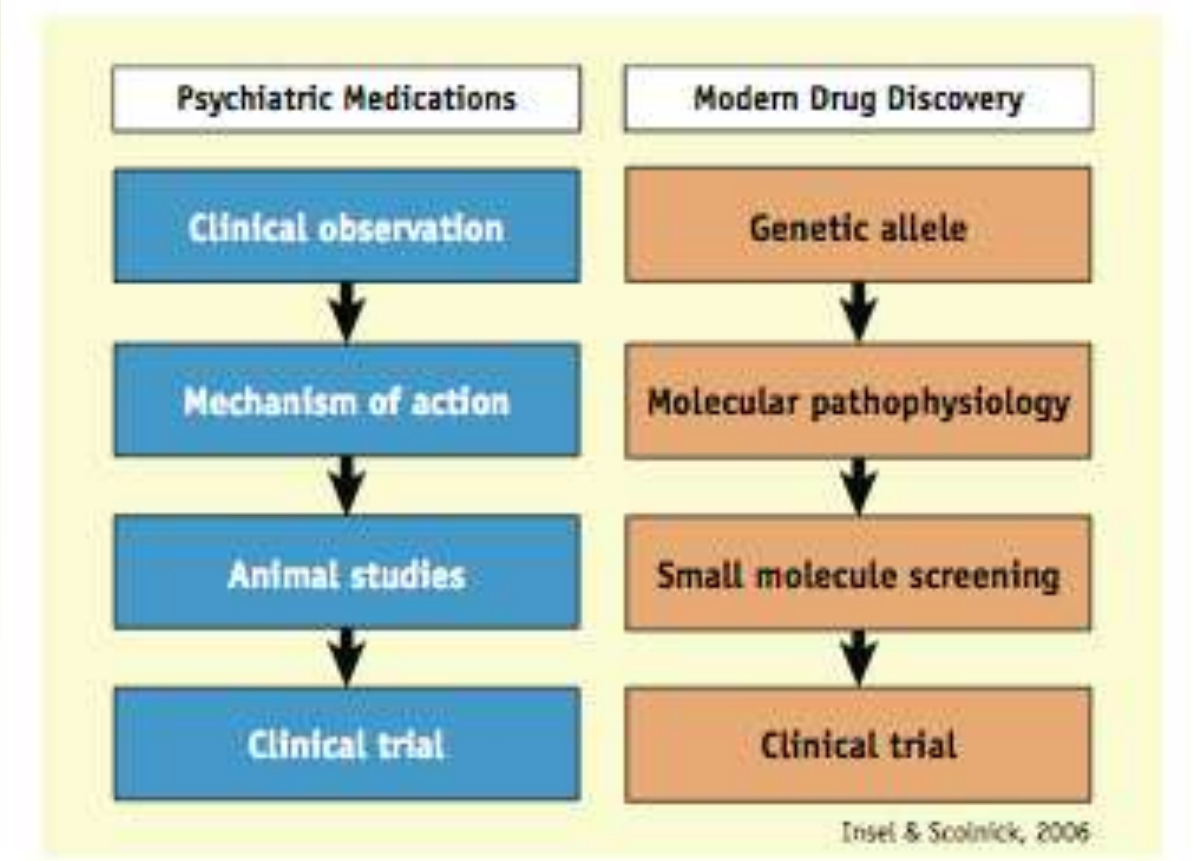
COMT (22q) (eight)*
GRM3 (7q) (four)*
GAD 1 (2q) (four)*
CNRNA7 (15q) (two)*
PPP3CC (8p) (two)*
Akt1 (two)
dysbindin (6p) (seven)*

neuregulin (8p) (*six*)*
G72 (13q) (three)*
MRDS1 (6p) (four)*
DISC1 (1q) (*three*)*
PRODH (22q) (two)

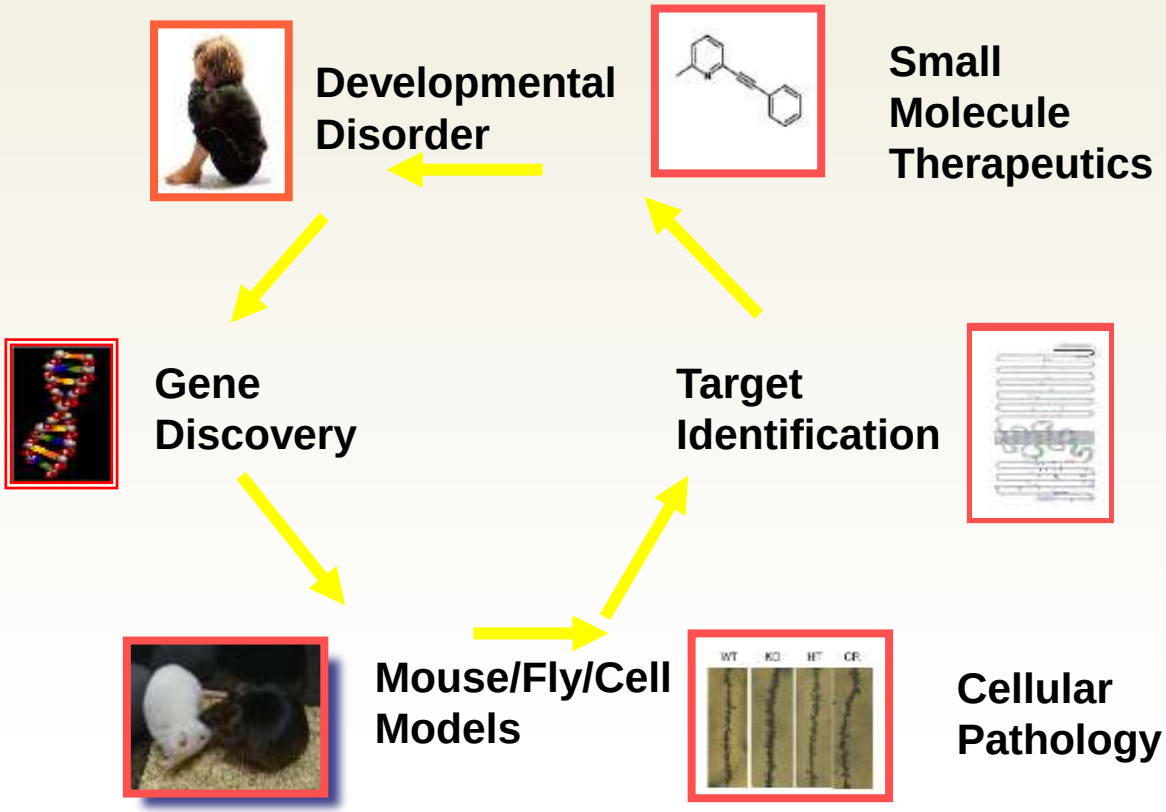
Rapoport / McClellan
Rare
Unique to individuals
Structural variants
Copy number variants
SLC1A3, neurodevelopment
Also autism / Bipolar

* Number of positive samples worldwide

Pathways To Drug Development



Reverse Translation – The Molecular Medicine Cycle



Adapted from Tom Insel / Mark Bear

Seaside Therapeutics

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Improving lives of patients and their families

Home › Pipeline › Compounds

- Overview
- Compounds
- Additional Programs
- Clinical Trials

Compounds

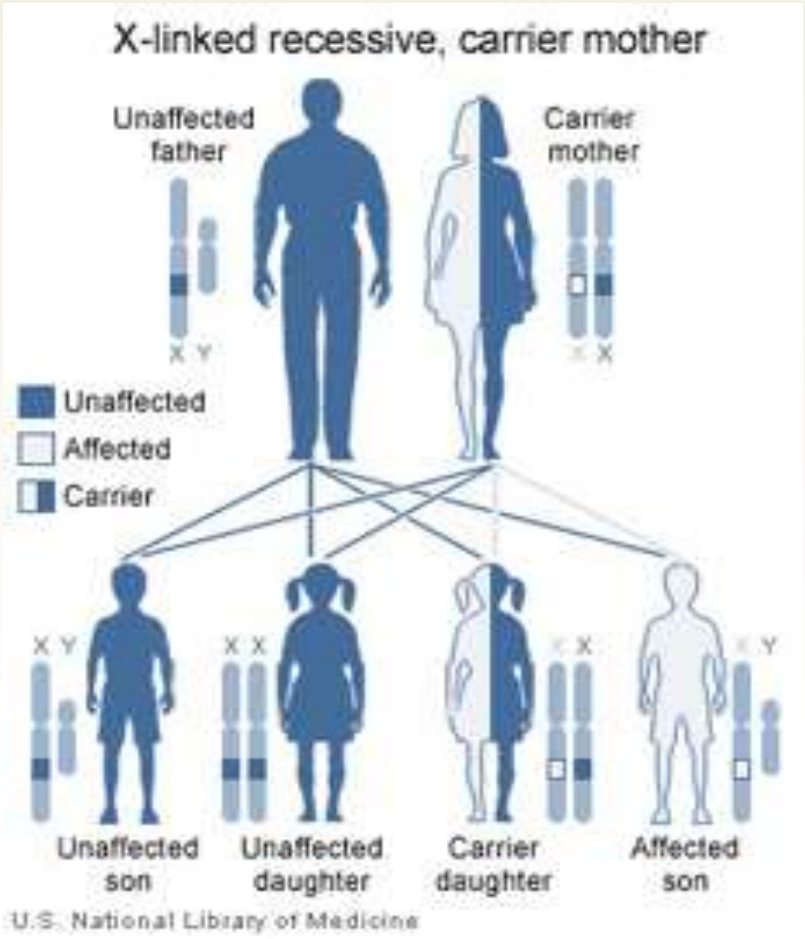
STX209

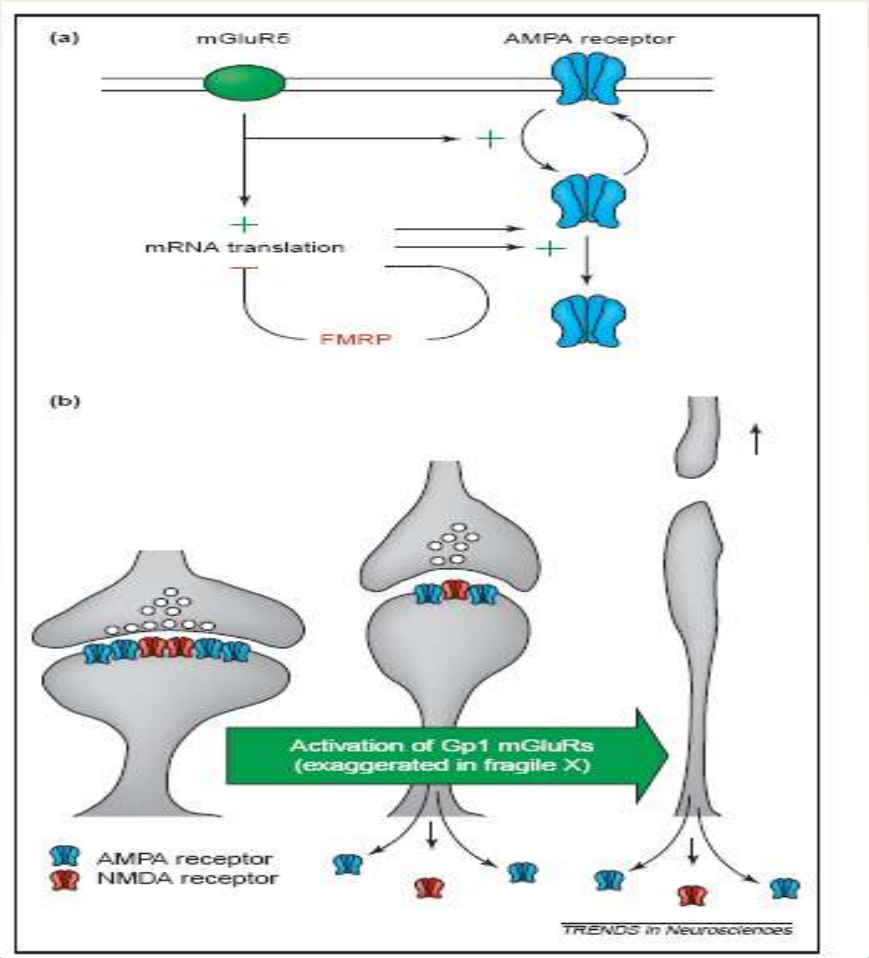
STX209 (arbaclofen) is a selective gamma-amino butyric acid type B (GABA-B) receptor against.

STX107

STX107 is a selective mGluR5 negative allosteric modulator (NAM).

Fragile X Syndrome





COMMENTARIES

Attention Bias Modification Training and the New Interventions Research

John S. March

As highlighted in a recent article by the National Institute of Mental Health (NIMH) director, Tom Insel, on transforming psychiatry as a clinical discipline, the age of symptomatic diagnosis and current generation treatments is passing; the age of interventions that emerge from the revolution in neuroscience has begun (1). The article in this issue of *Biological Psychiatry* on attention bias modification training (ABMT) by Hakamata *et al.* (2) from Daniel Pine's group in the NIMH Intramural Program provides a perfect example of the transformation of the interventions landscape.

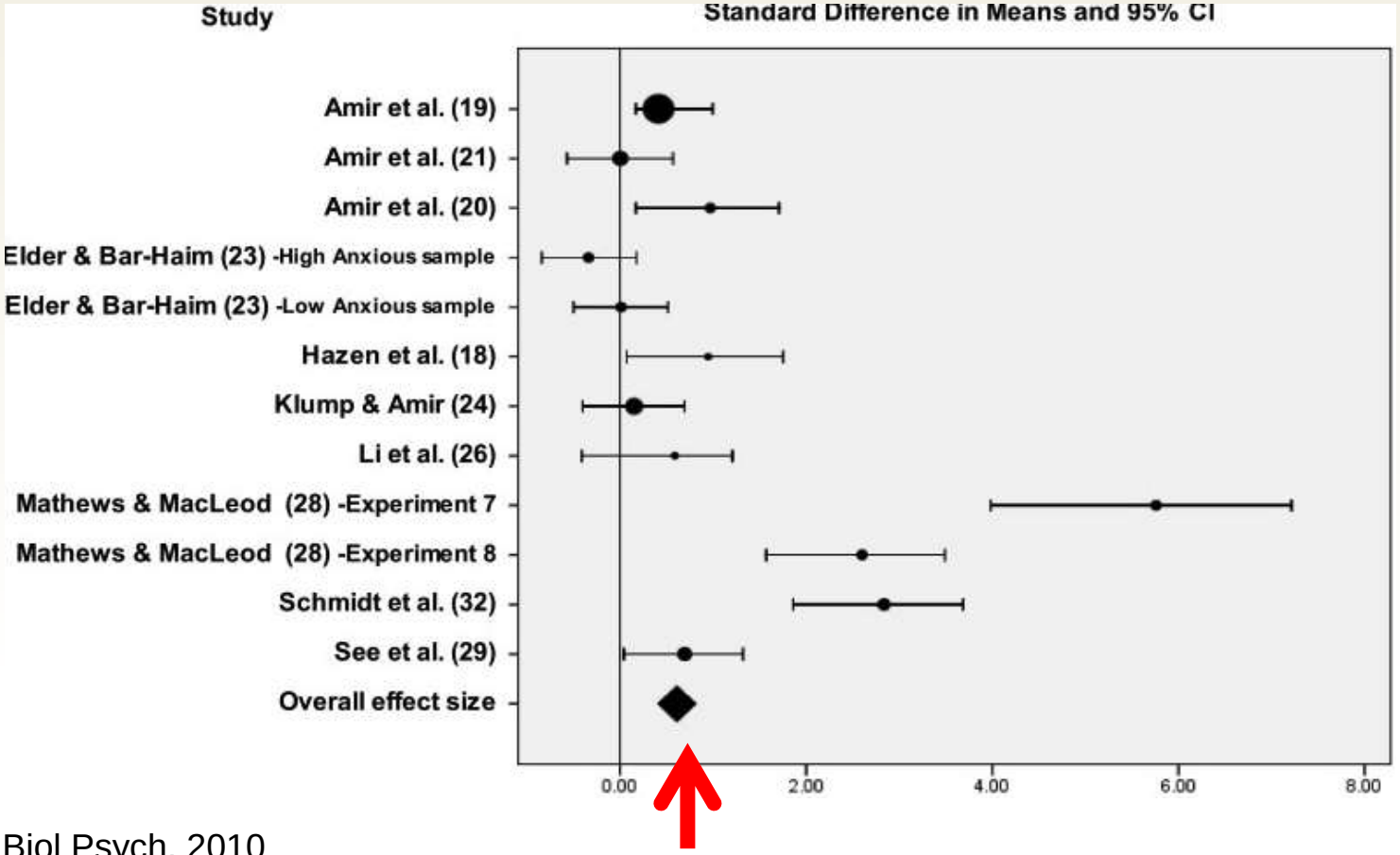
behind threatening and nonthreatening stimuli indexes attention bias for threat-related cues.

Attention bias modification training employs a variant of the dot probe task in which the probe replaces the neutral stimuli 100% of the time (4). Thus, the participant learns an implicit albeit intentional if-then rule: if both threatening and neutral stimuli are present, then attend preferentially to the neutral stimuli. The hypothesis is that to the extent that attentional biases have a causal role in the maintenance of anxiety, lowering attentional biases should improve anxiety in subjects given ABMT. Using state-of-the-

0006-3223/$36.00
doi:10.1016/j.biopsych.2010.10.007

BIOL PSYCHIATRY 2010;68:978–979

Attention Bias Modification Training



Pine et al., Biol Psych, 2010

National Advisory Mental Health Council Workgroup on Neurodevelopment

NIMH

Transformational Neuroscience and Mental Illness

Co-Chairs: Drs. John March and Pat Levitt

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Personalized Medicine

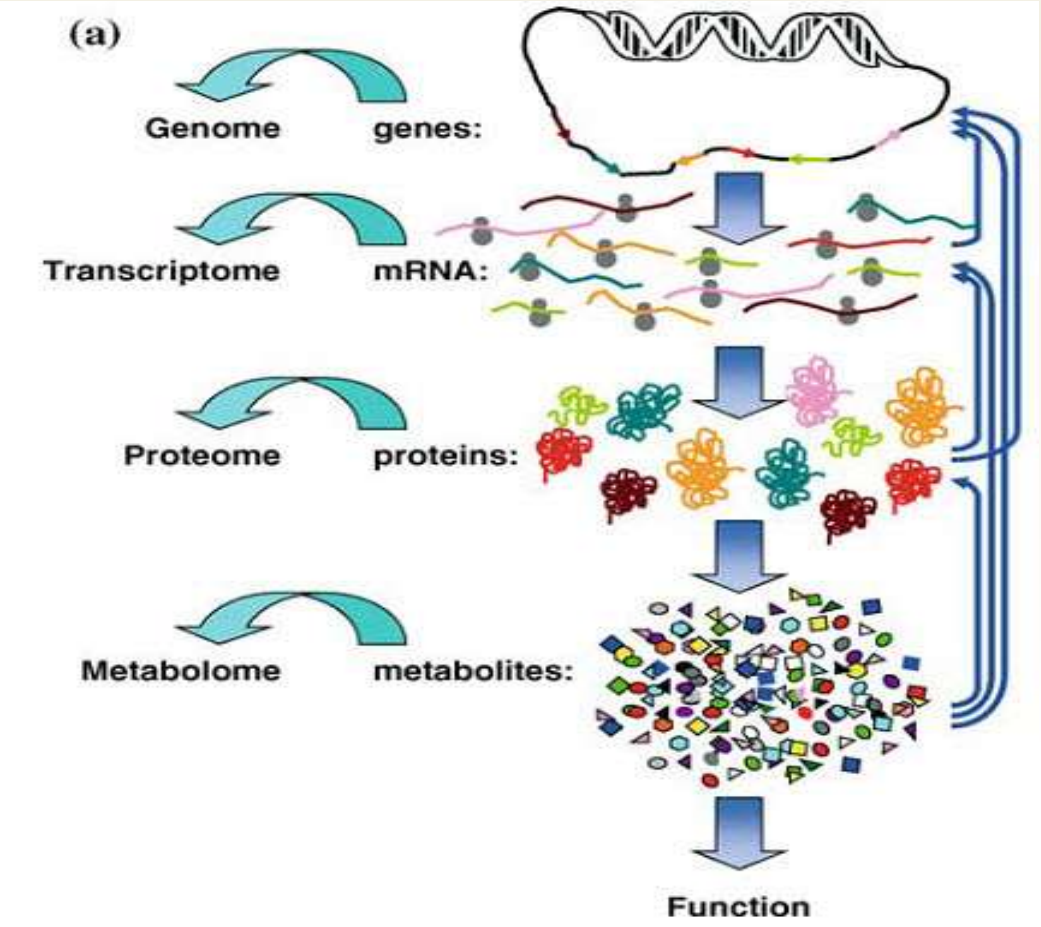
The US Congress defines personalized medicine as the "application of genomic and molecular data to better target the delivery of health care, facilitate the discovery and clinical testing of new products, and help determine a person's predisposition to a particular disease or condition."

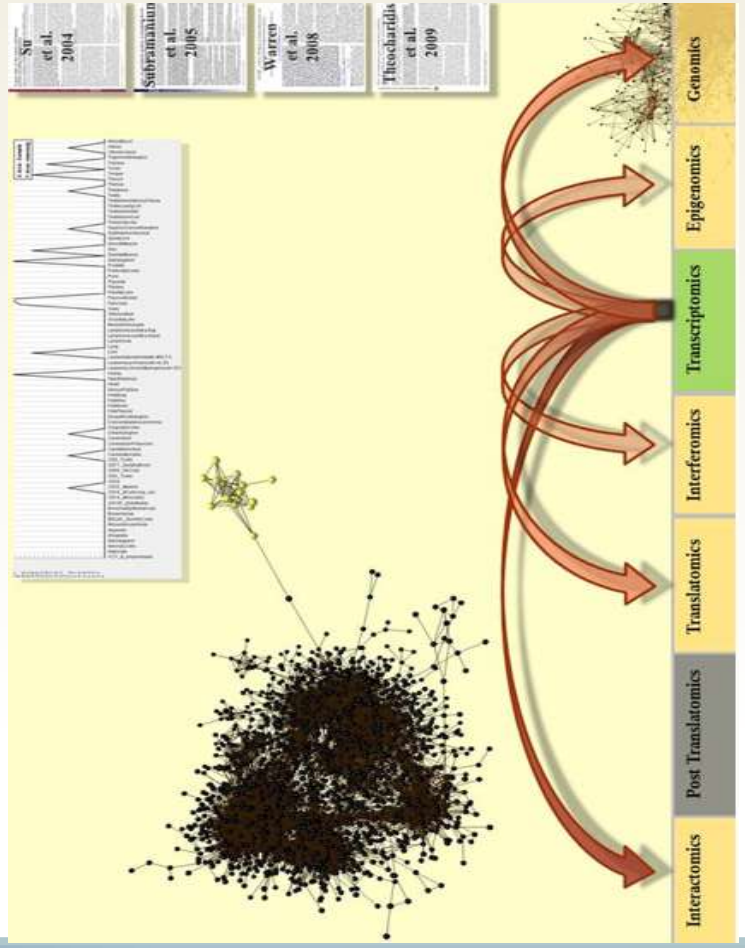
FDA Biomarker Definition

A biomarker is a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention

A biosignature is an optimized biomarker panel

-Omics Biomarkers / Biosignatures

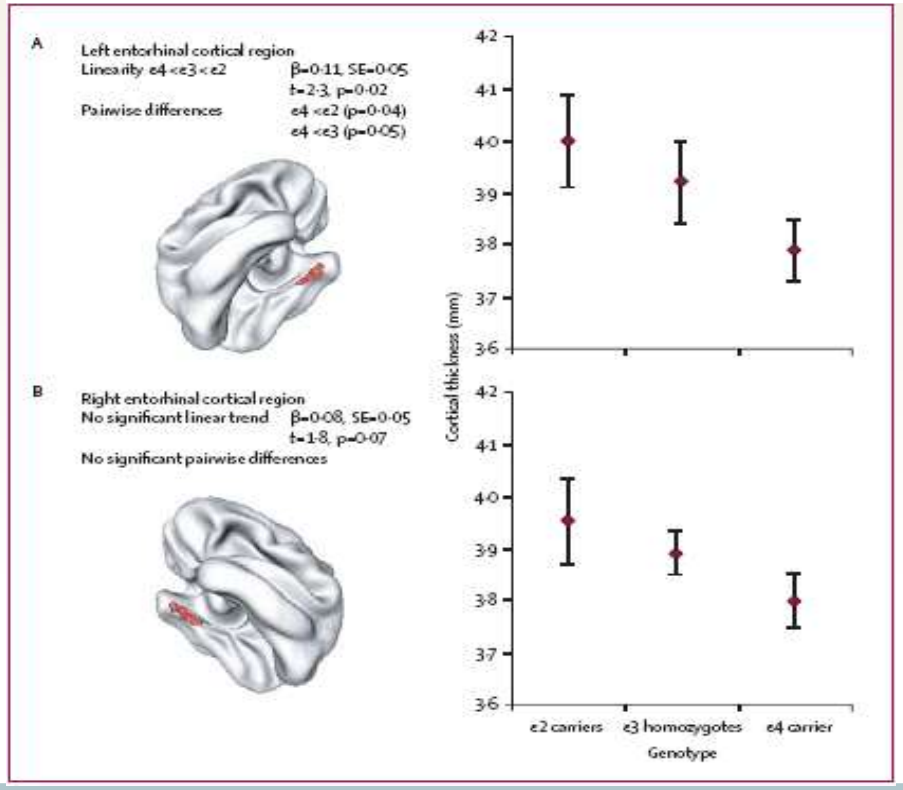


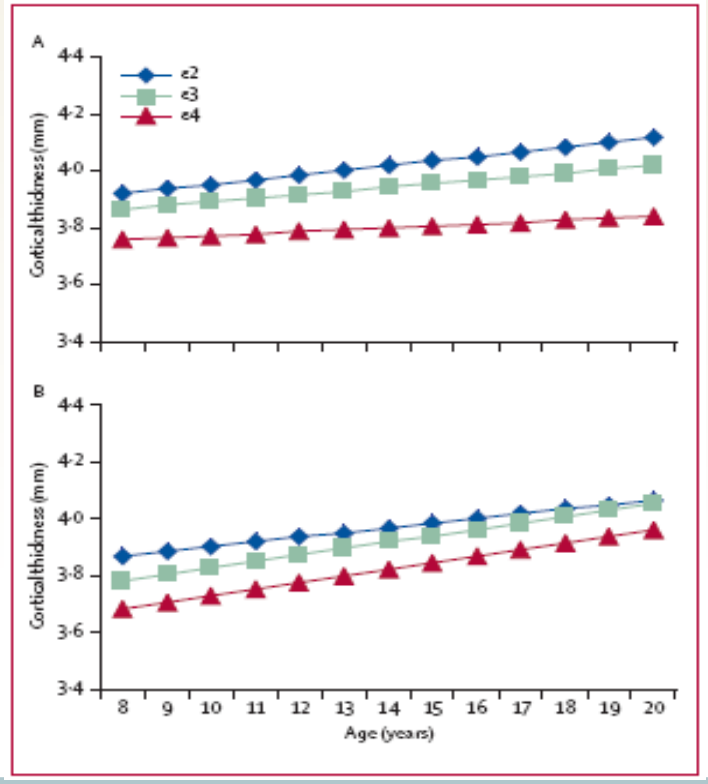


Alzheimer's: A Developmental Disorder?

Cortical morphology in children and adolescents with different apolipoprotein E gene polymorphisms: an observational study

Philip Shaw, Jason P Lerch, Jens C Pruessner, Kristin N Taylor, A Blythe Rose, Deanna Greenstein, Liv Clasen, Alan Evans, Judith L Rapoport, Jay N Giedd





Lancet Neurol, 2007

AJNR Am J Neuroradiol. Author manuscript; available in PMC 2010 February 12.
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Published online 2010 January 14. doi: 10.3174/ajnr.A1809.

PMCID: PMC2821467
NIHMSID: NIHMS173562

Combining MRI, PET and CSF biomarkers in diagnosis and prognosis of Alzheimer's disease

KB Walhovd,[1,2] AM Fjell,[1,2] J Brewer,[3,5] LK McEvoy,[3] C Fennema-Notestine,[3,4] DJ Hagler, Jr,[3] RG Jennings,[3] D Karow,[3] AM Dale,[3,5] and The Alzheimer's Disease Neuroimaging Initiative

^{11}C-PiB PET assessment of change in fibrillar amyloid-β load in patients with Alzheimer's disease treated with bapineuzumab: a phase 2, double-blind, placebo-controlled, ascending-dose study

Juha O Rinne, David J Brooks, Martin N Rossor, Nick C Fox, Roger Bullock, William E Klunk, Chester A Mathis, Kaj Blennow, Jerome Barakos, Aren A Okello, Sofia Rodriguez Martinez de Liano, Enchi Liu, Martin Koller, Keith M Gregg, Dale Schenk, Ronald Black, Michael Grundman

Summary

Background Carbon-11-labelled Pittsburgh compound B (^{11}C-PiB) PET is a marker of cortical fibrillar amyloid-β load

Lancet Neurol 2010; 9: 363–72

Utility of Biomarker Approach

No signs or symptoms, no known disease

- Risk-factor assessment (*susceptibility*)
- Presence of occult disease (*screening*)

Known or probable disease

Cause unknown

- Determine cause (*diagnosis*)
- Refine differential diagnosis

Cause known

- Disease extent or severity (*staging*)
- Predict natural history (*prognosis*)
- Predict response to intervention (*prediction*)
- Monitor disease course (*surveillance*)
- Assess response to treatment

Adapted from:

- **Harrison's Principles of Internal Medicine, 17th Edition. Editors; Fauci AS et al. The McGraw-Hill Companies.**
- **Whiting P et al. A review identifies and classifies reasons for ordering diagnostic tests. J Clin Epidemiol 2007; 981-9.**
- **Fischbach T. Manual of Laboratory & Diagnostic Tests, 7th Edition. Lippincott Williams & Wilkins: Philadelphia. 2004.**

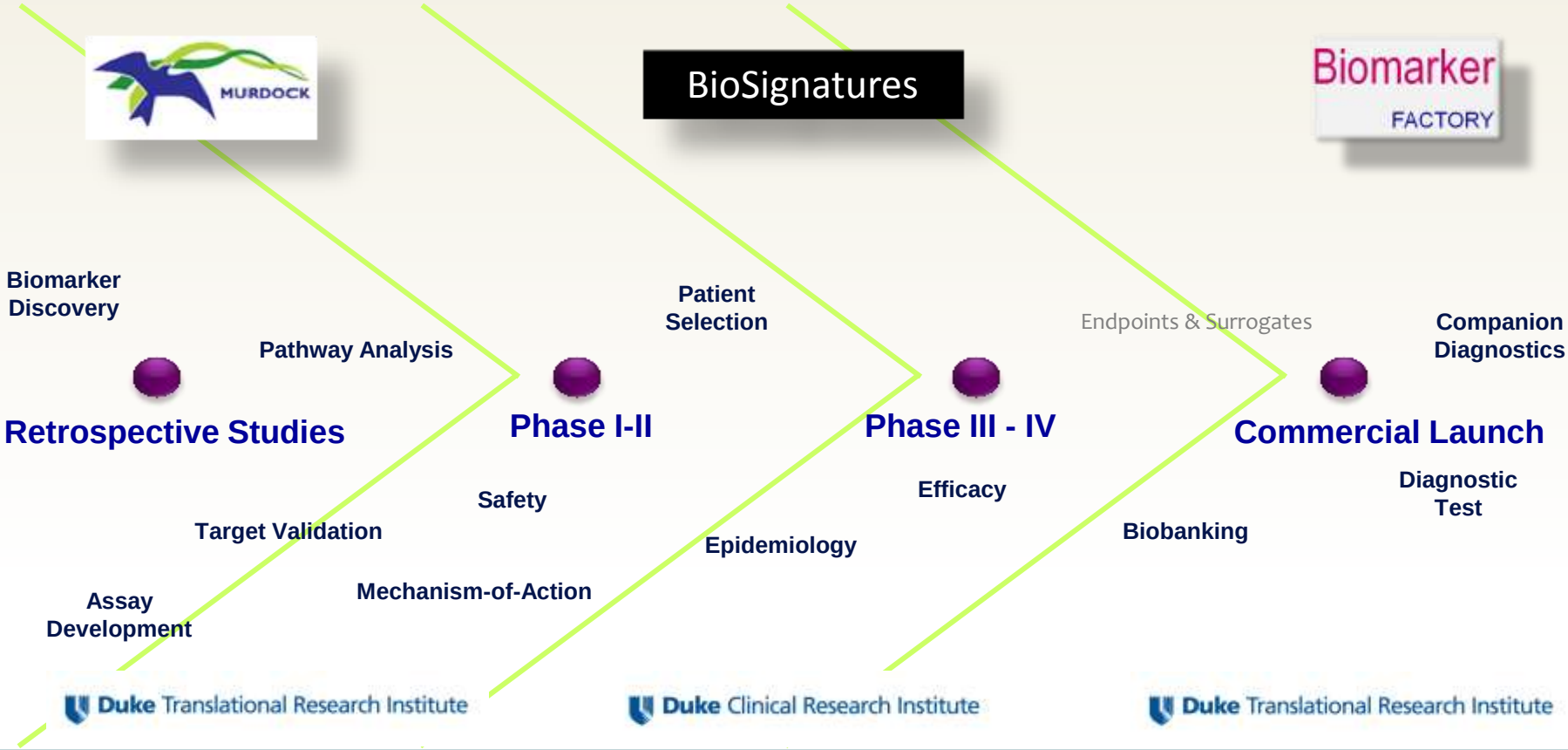
FDA: Biomarkers are Key to Efficient Drug Development

Biomarkers are the foundation of evidence based medicine--who should be treated, how and with what

Absent new markers, advances in more targeted therapy will be limited and treatment will remain largely empirical

It is imperative that biomarker development be accelerated along with therapeutics

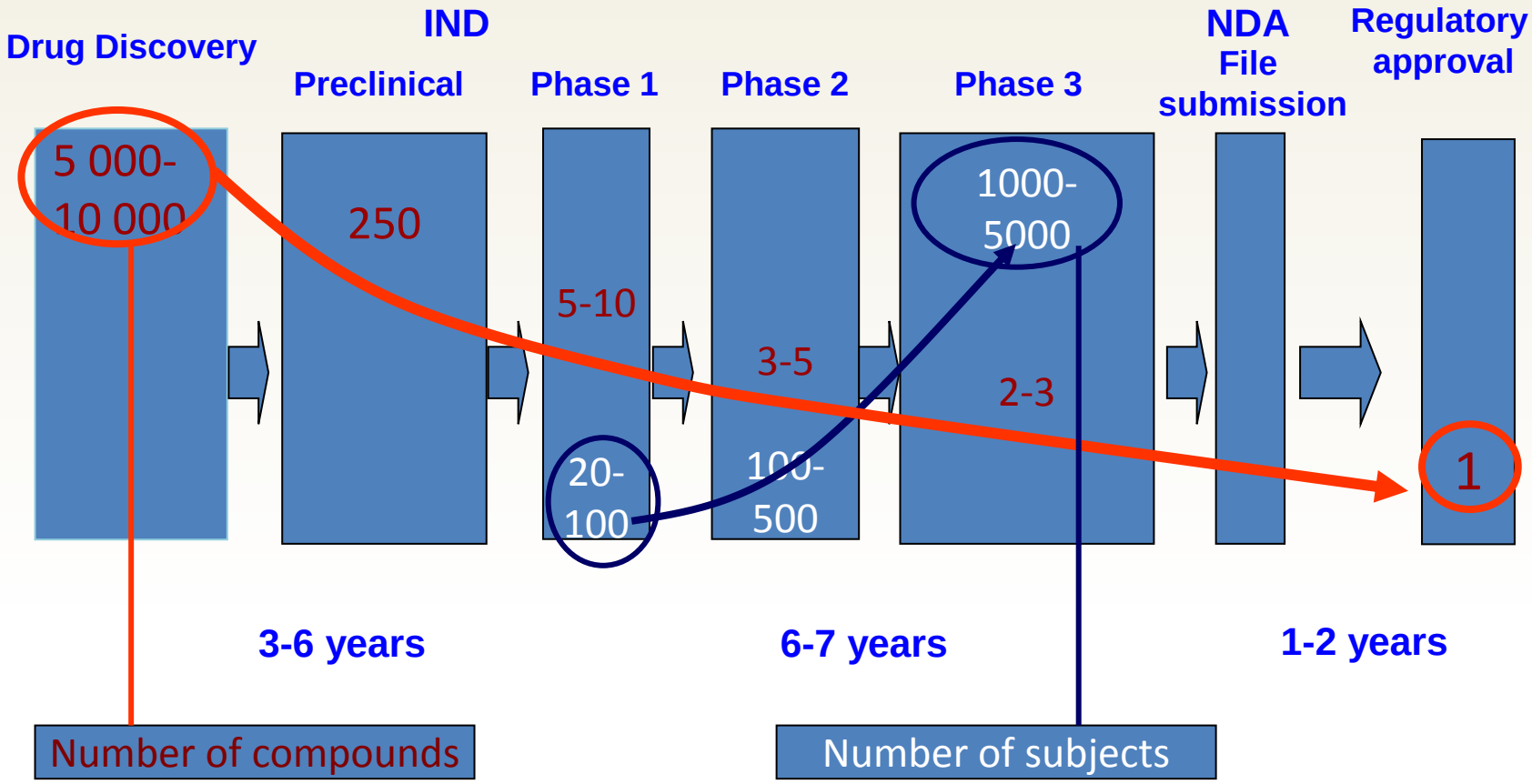
Biomarker-Driven Drug Development



Topics

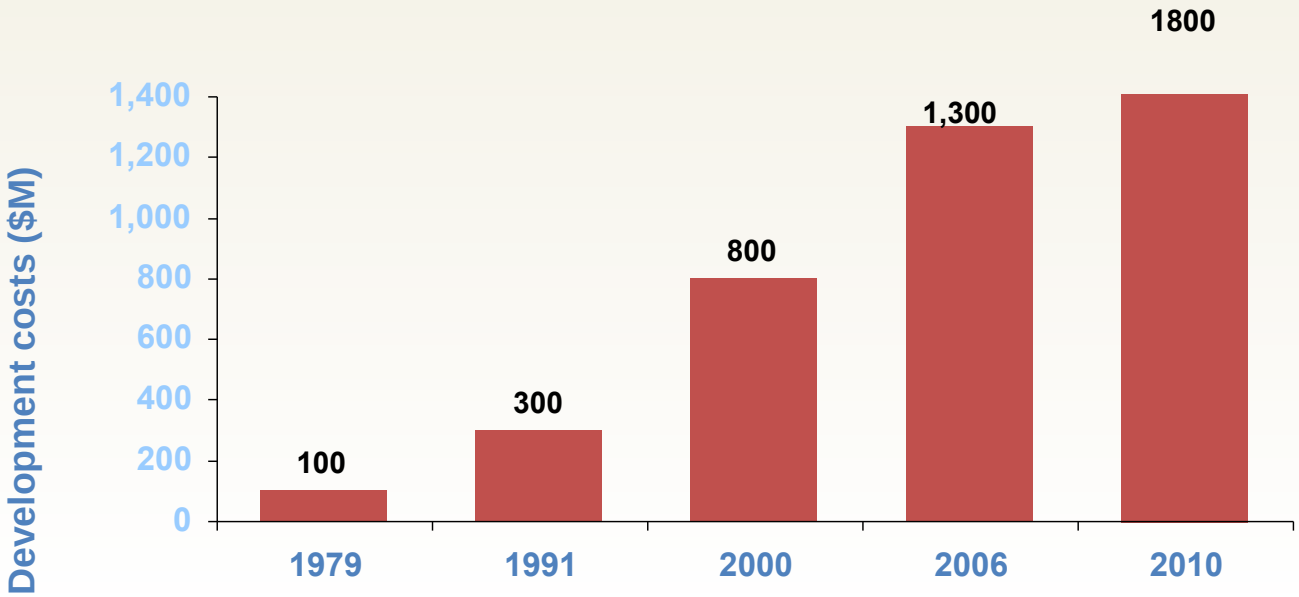
- What is meant by preemptive treatments?
- The four pivots to preemptive interventions:
  - Translational developmental neuroscience
  - Biomarkers and personalized medicine
  - Novel interventions and early phase clinical pharmacology
  - Prevention trials and comparative-effectiveness research

Process of Drug Development

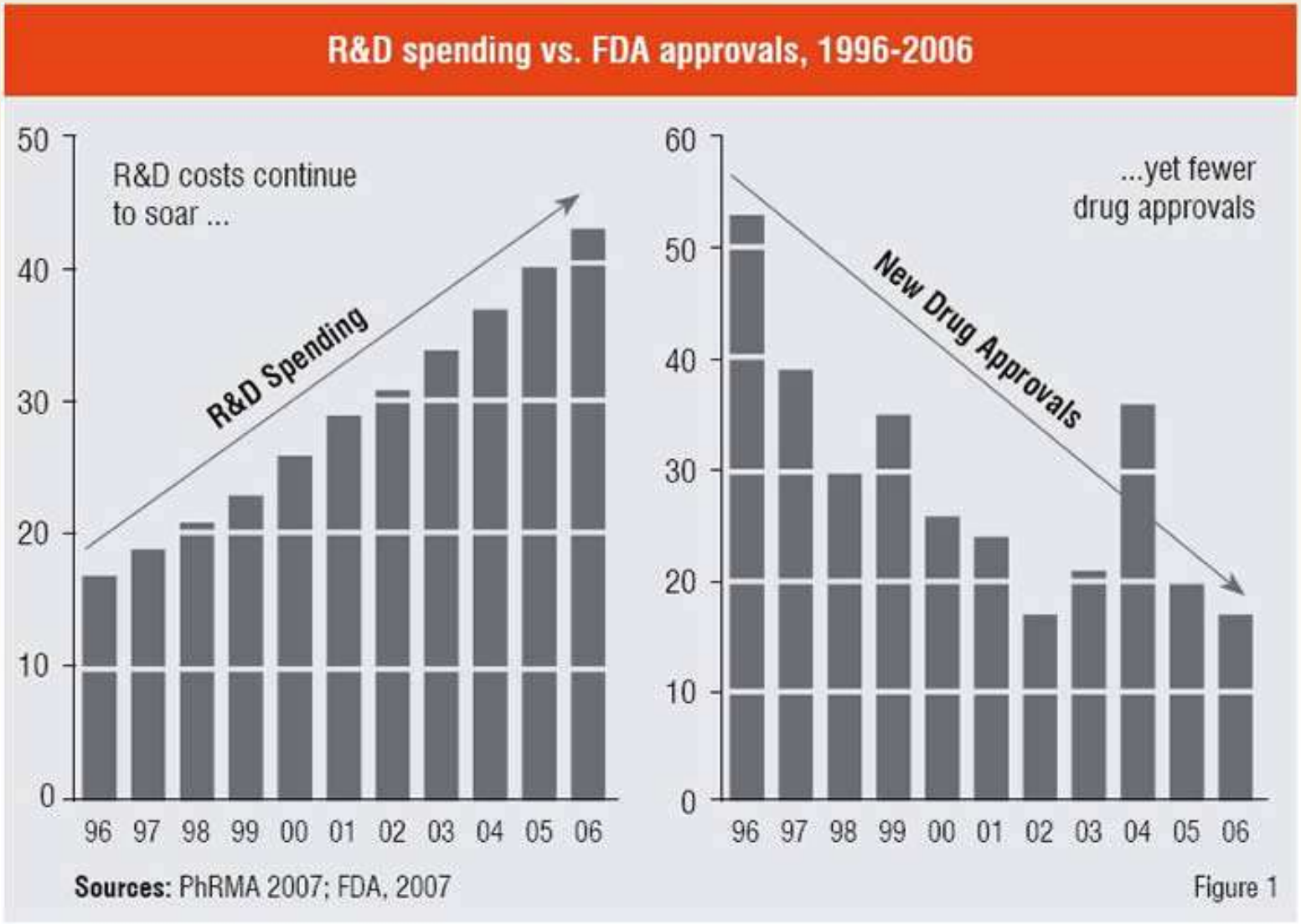


Average Cost to Develop a New Drug Single New Approved Drug

Drug Development Costs 1979–2010



Total industry includes members and non-members of PhRMA.
Source: PhRMA. Pharmaceutical Industry Profile


R&D spending vs. FDA approvals, 1996-2006
R&D costs continue to soar ...
R&D Spending
50
40
30
20
10
0
96 97 98 99 00 01 02 03 04 05 06
...yet fewer drug approvals
New Drug Approvals
60
50
40
30
20
10
0
96 97 98 99 00 01 02 03 04 05 06
Sources: PhRMA 2007; FDA, 2007
Figure 1

Mechanistically Novel New Medical Entities

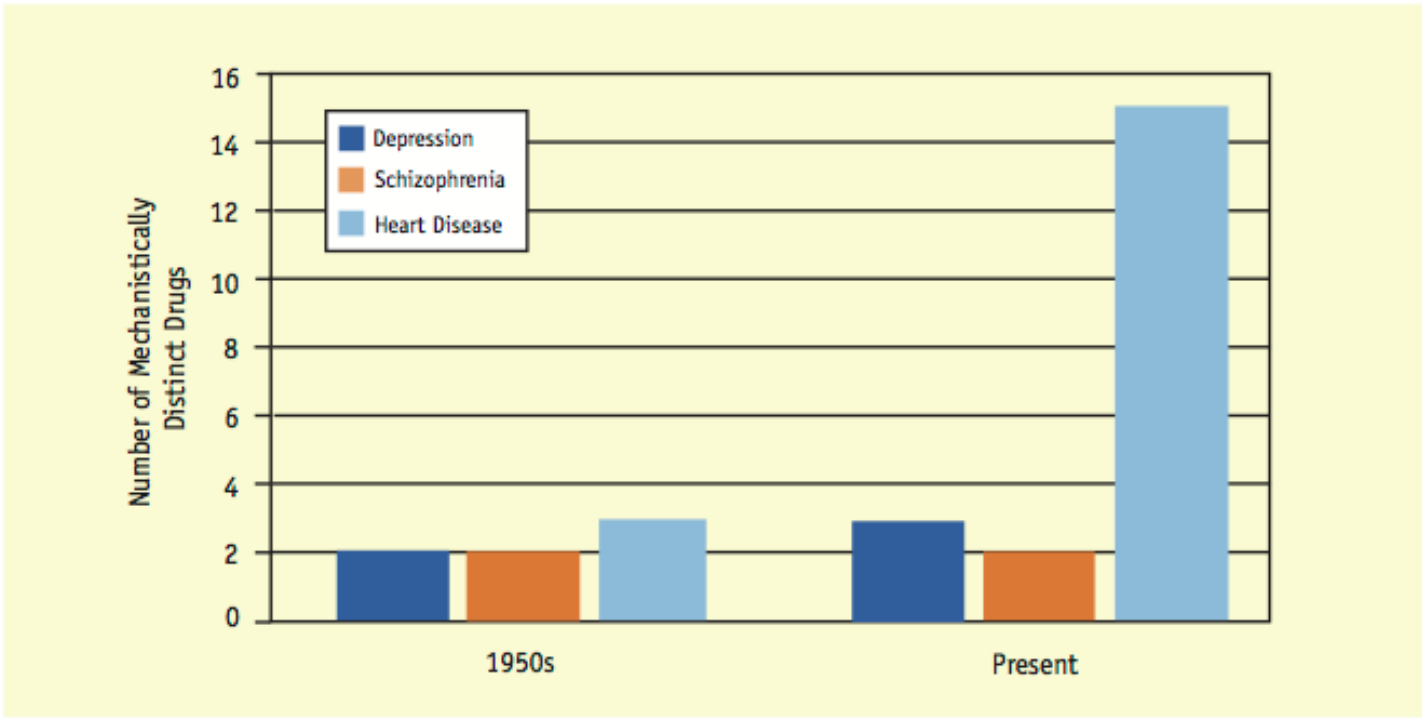
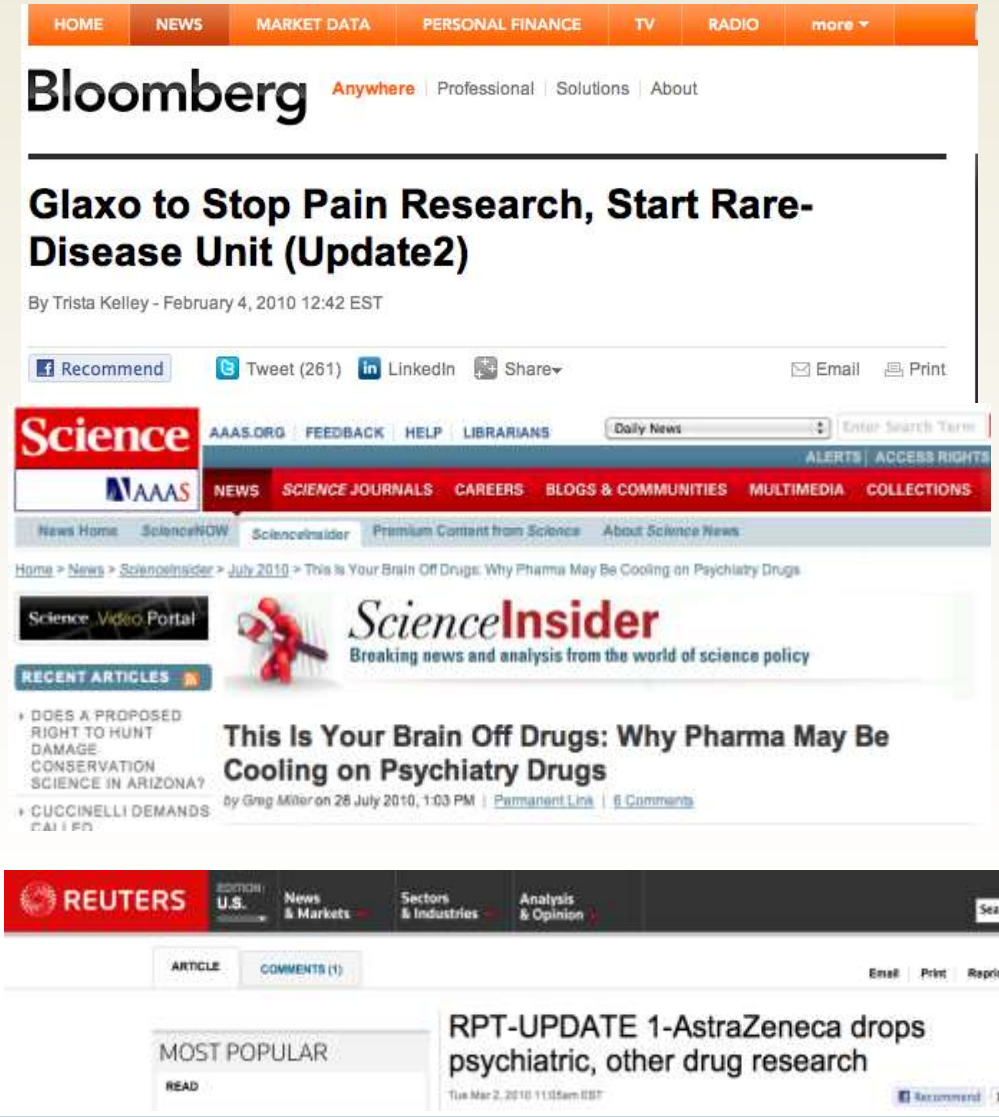


Figure 2. Drug development in the past 50 years.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ANALYSIS

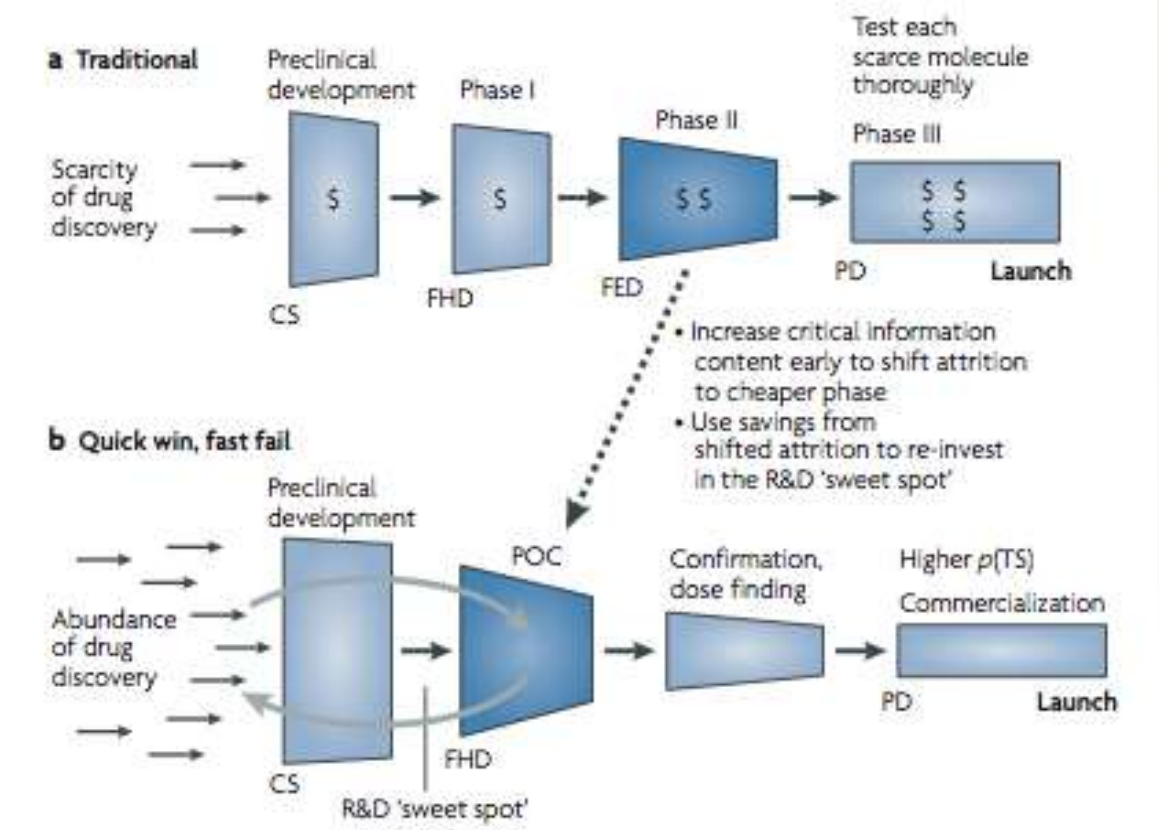
How to improve R&D productivity: the pharmaceutical industry's grand challenge

Steven M. Paul, Daniel S. Mytelka, Christopher T. Dunwiddie, Charles C. Persinger, Bernard H. Munos, Stacy R. Lindborg and Aaron L. Schacht

Abstract | The pharmaceutical industry is under growing pressure from a range of environmental issues, including major losses of revenue owing to patent expirations, increasingly cost-constrained healthcare systems and more demanding regulatory requirements. In our view, the key to tackling the challenges such issues pose to both the future viability of the pharmaceutical industry and advances in healthcare is to substantially increase the number and quality of innovative, cost-effective new medicines, without incurring unsustainable R&D costs. However, it is widely acknowledged that trends in industry R&D productivity have been moving in the opposite direction for a number of years. Here, we present a detailed analysis based on comprehensive, recent, industry-wide data to identify the relative contributions of each of the steps in the drug discovery and development process to overall R&D productivity. We then propose specific strategies that could have the most substantial impact in improving R&D productivity.

Paul, Nat Rev Drug Disc, 2010

New Model



Paul, Nat Rev Drug Disc, 2010

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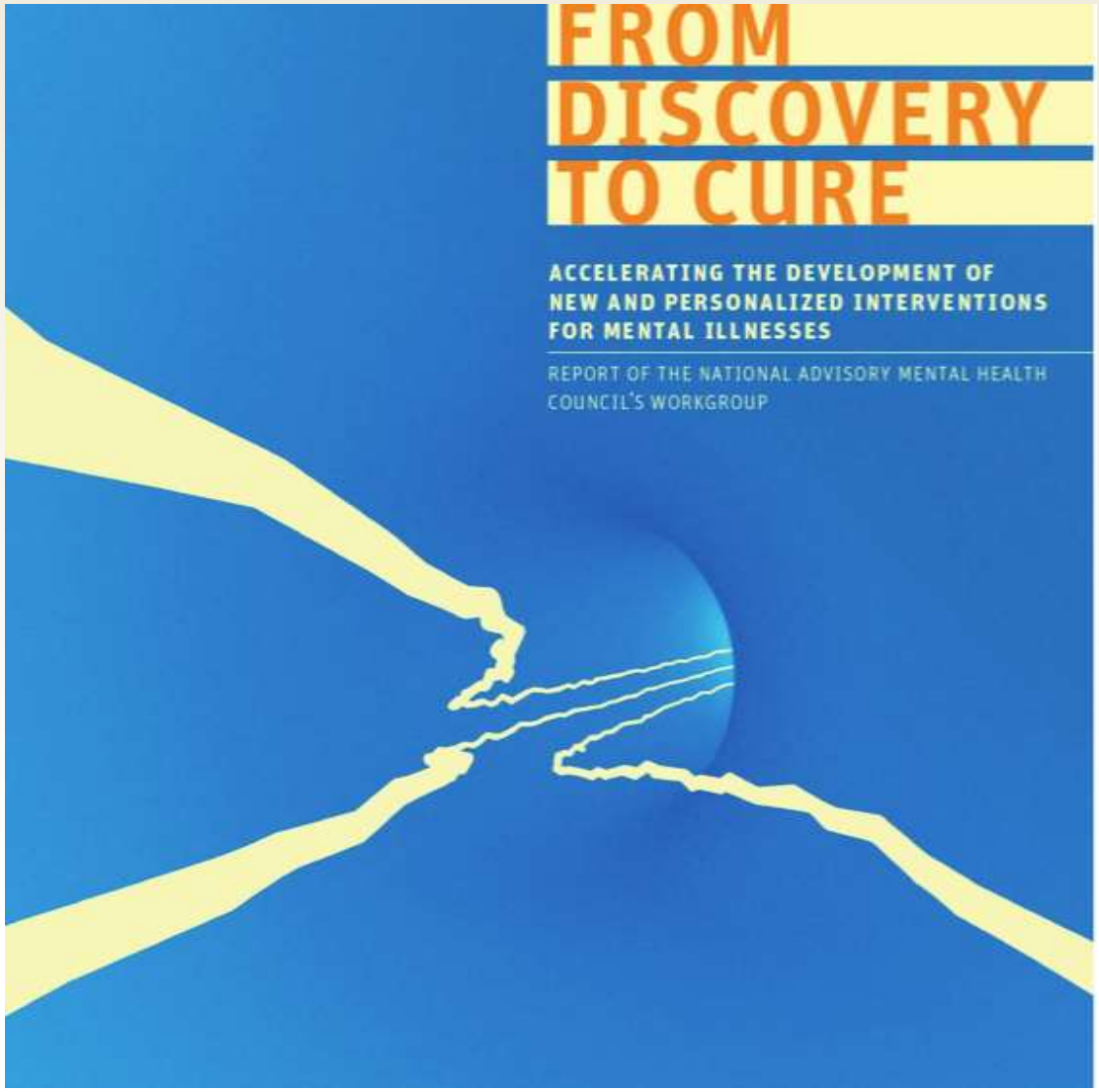

FROM
DISCOVERY
TO CURE
ACCELERATING THE DEVELOPMENT OF
NEW AND PERSONALIZED INTERVENTIONS
FOR MENTAL ILLNESSES
REPORT OF THE NATIONAL ADVISORY MENTAL HEALTH
COUNCIL'S WORKGROUP

The New York Times

Money & Policy

Federal Research Center Will Help Develop Medicines

By GARDINER HARRIS
Published: January 22, 2011

The Obama administration has become so concerned about the slowing pace of new drugs coming out of the pharmaceutical industry that officials have decided to start a billion-dollar government drug development center to help create medicines.

Topics

- What is meant by preemptive treatments?
- The four pivots to preemptive interventions:
  - Translational developmental neuroscience
  - Biomarkers and personalized medicine
  - Novel interventions and early phase clinical pharmacology
  - Prevention trials and comparative-effectiveness research

Explanatory Versus Pragmatic Trials

- **Some trials ask whether an intervention can work, under tightly-controlled, ideal conditions. We call these "Explanatory" or "Efficacy" trials.**
- **Other trials ask whether an intervention does work under the usual conditions that apply where it would be used. We call these "Pragmatic" or "Effectiveness" trials.**

U.S. Department of Health & Human Services • National Institutes of Health

NIH Consensus Development Program

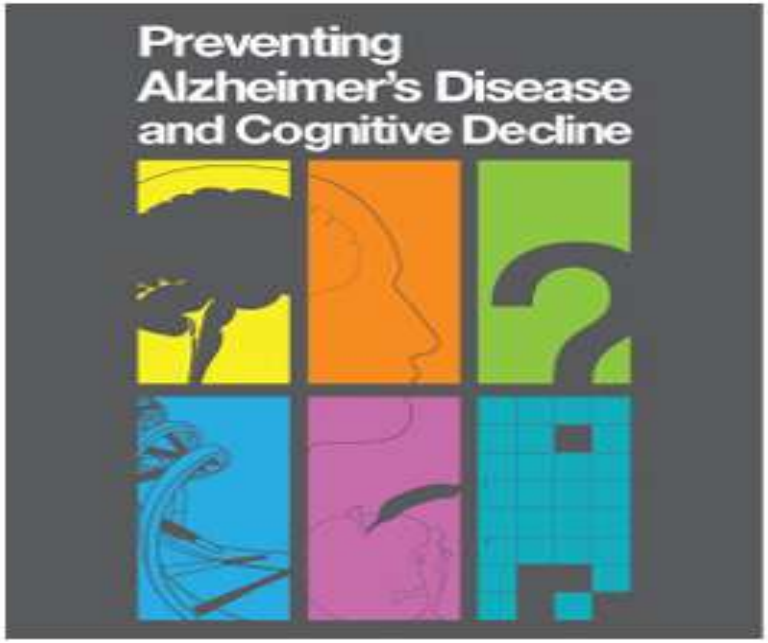
Pre-order This Statement

NIH State-of-the-Science Conference

Preventing Alzheimer's Disease and Cognitive Decline

April 26–28, 2010
Bethesda, Maryland

Return to Conference Home

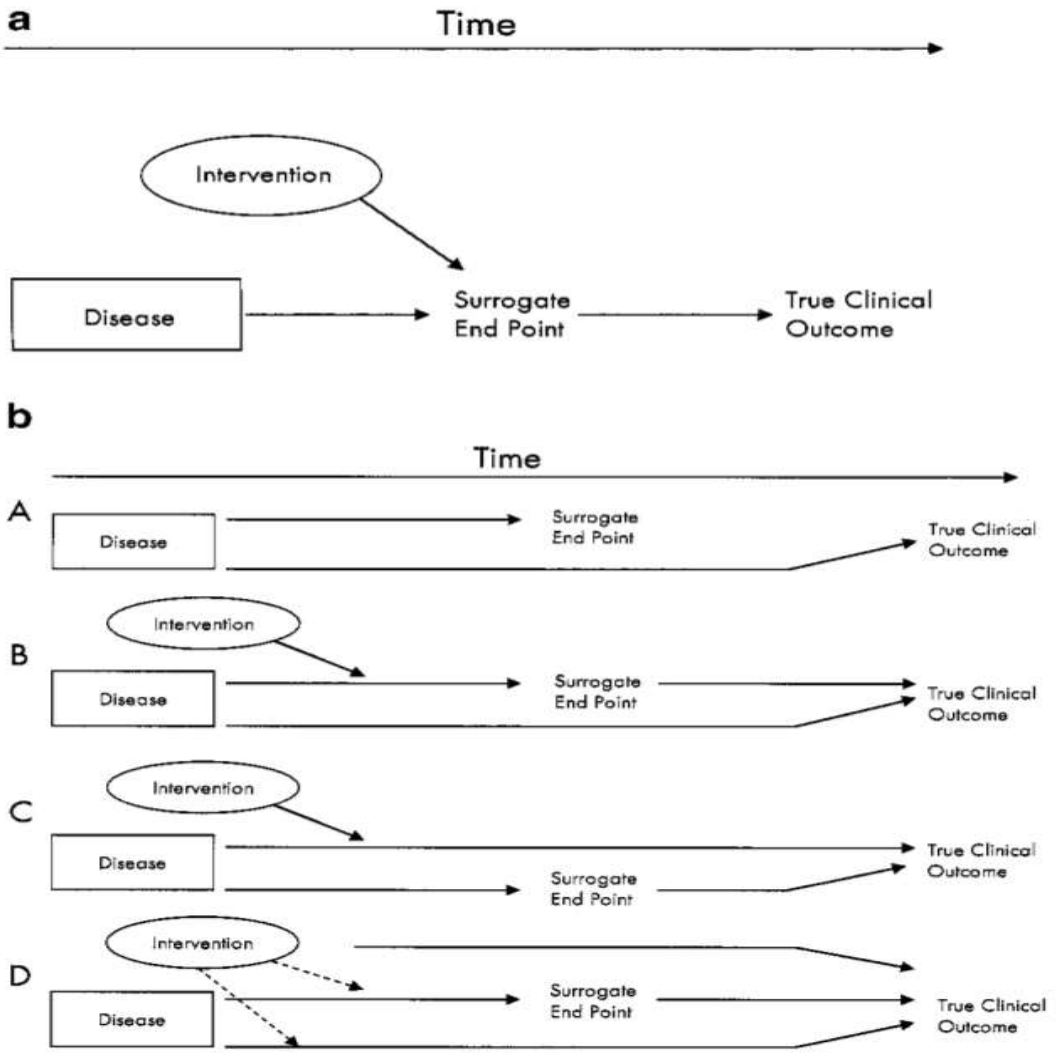


Final Panel Statement

For Printing and Download: [PDF Version-109KB]

Note: Documents in PDF format require the Adobe Acrobat Reader®. If you experience problems with PDF documents, please download the latest version of the Reader®.

An abridged version of this statement was also published in Annals of Internal Medicine: June 15, 2010, 152: 792-796.



Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
American Heart Association.
Learn and Live.

Lessons Learned From Recent Cardiovascular Clinical Trials: Part 1

David L. DeMets and Robert M. Califf

Circulation 2002;106;746-751
DOI: 10.1161/01.CIR.0000023219.51483.66

Definition and Purpose of CER

- CER is the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care.
- The purpose of CER is to help decision makers make informed decisions that will improve health care at both the individual and population levels.

Final Portfolio: 100 CER Priority Topics

TABLE 5-1 Recommended Research Priorities by Research Area

Category	Primary Research Area	Secondary Research Area	Total
Health Care Delivery Systems*	23	27	50
Racial and Ethnic Disparities	3	26	29
Cardiovascular and Peripheral Vascular	8	13	21
Geriatrics	2	19	21
Functional Limitations and Disabilities	2	20	22
Neurologic Disorders	6	11	17
Psychiatric Disorders	7	10	17
Pediatrics	1	15	16

What is CER?

Can include four types of CER:

- Data mining studies
- Observational studies
- Pragmatic / practical clinical trials
- Systematic reviews

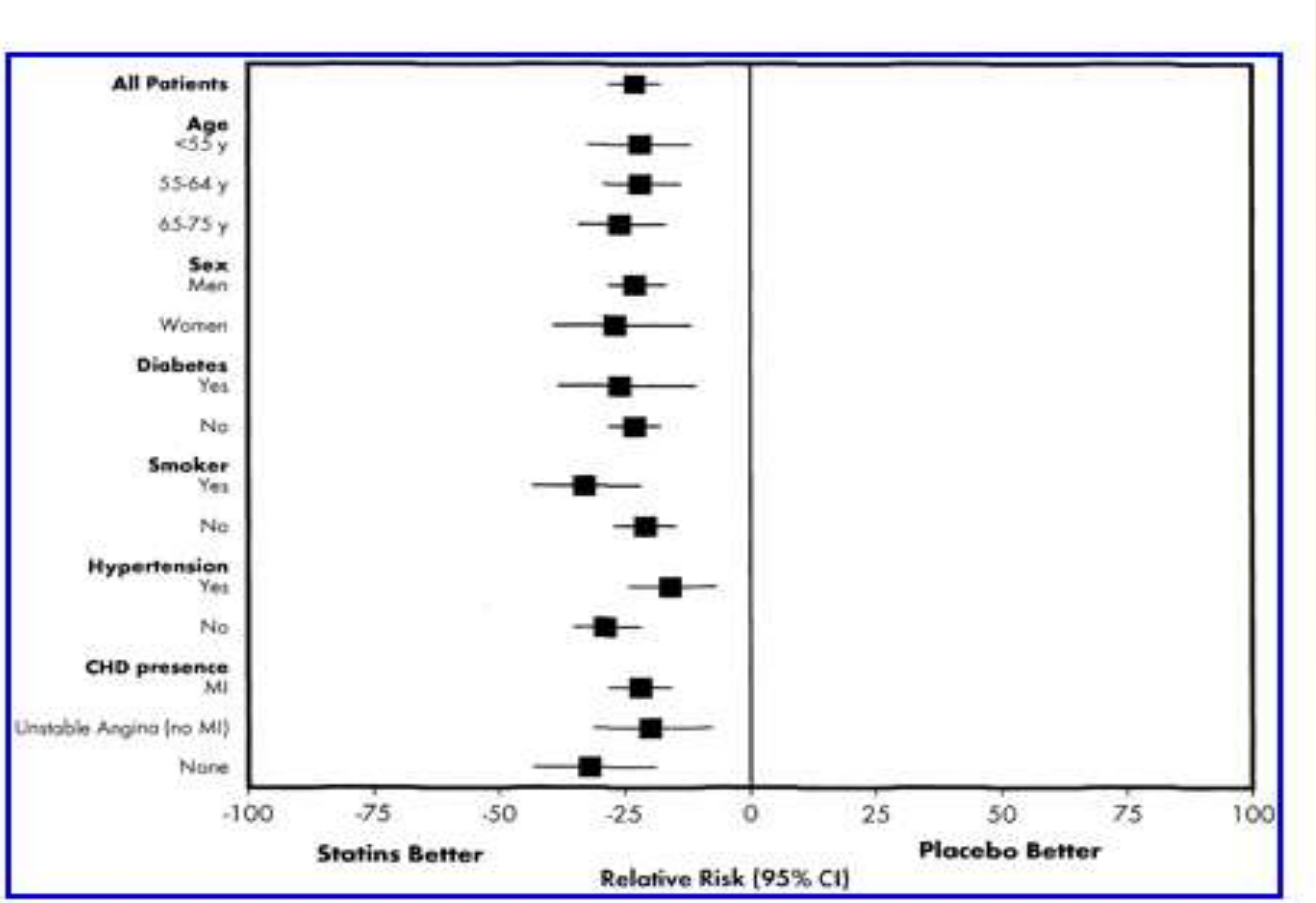
Things to Do On a PCT Network

- Inception cohorts (registries if use EHR)
- Active comparator trials
- Treatment addition or withdrawal trials
- Dynamic treatment regimes (adaptive designs)
- Population PK studies
- Stratify on subgroup, e.g age, gender, race, SES
- Traditionally excluded or rare populations
- Biomarker / Biosignature studies

SEM and Power

$$\sigma_M = \frac{\sigma}{\sqrt{N}}$$

CI $_{\text{population mean}}$ = +/- 2 [SEM]



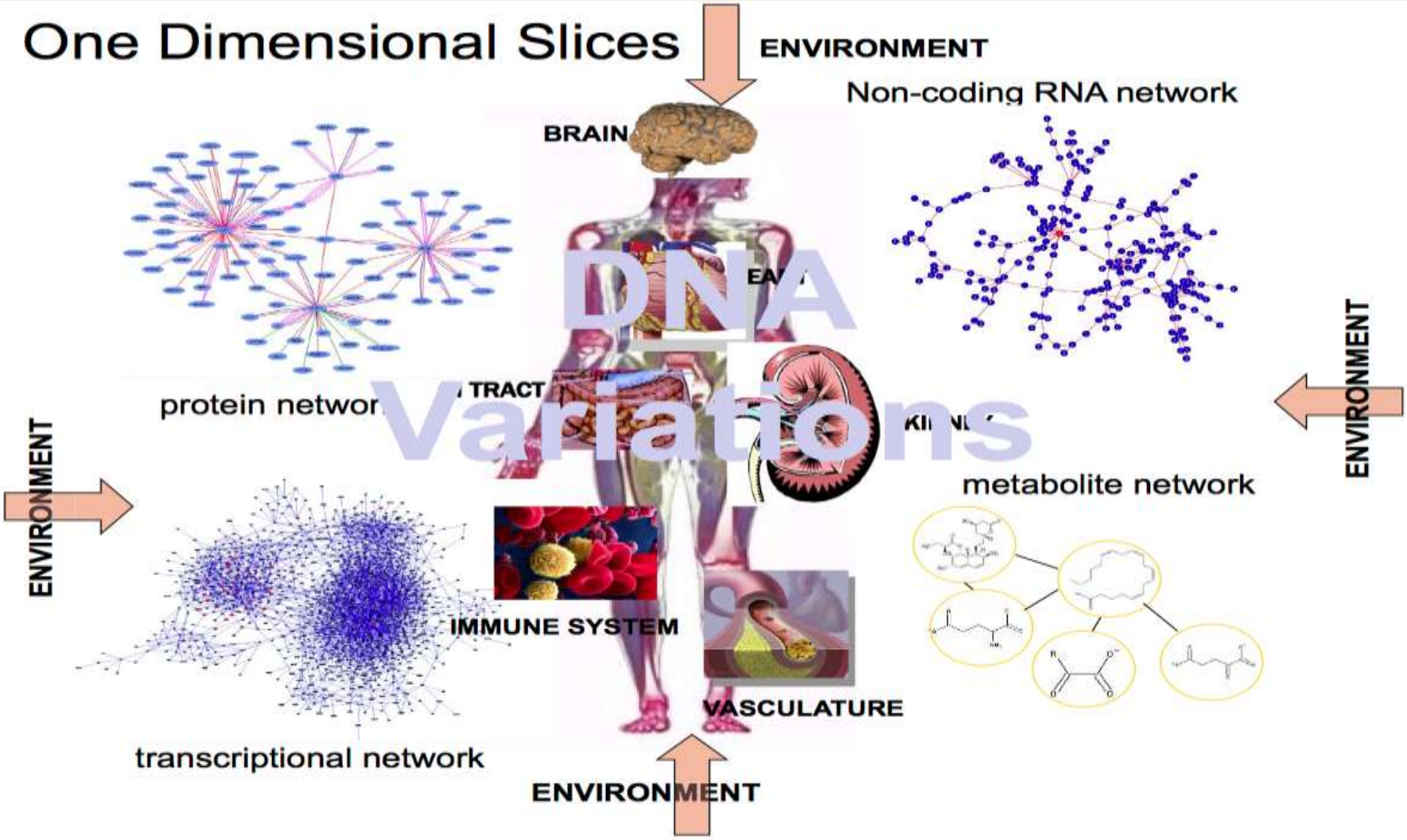
The NEW ENGLAND JOURNAL of MEDICINE

Perspective

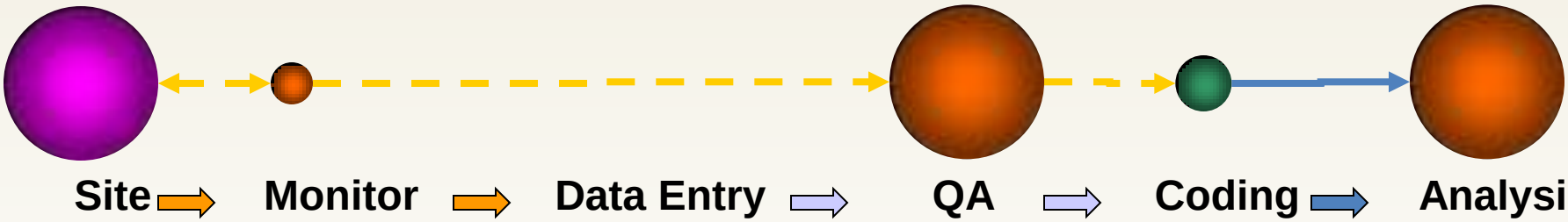
MAY 7, 2009

Does Comparative-Effectiveness Research Threaten Personalized Medicine?

Alan M. Garber, M.D., Ph.D., and Sean R. Tunis, M.D.


One Dimensional Slices
ENVIRONMENT
Non-coding RNA network
BRAIN
DNA
Variations
protein networ
TRACT
ENVIRONMENT
ENVIRONMENT
metabolite network
IMMUNE SYSTEM
VASCULATURE
transcriptional network
ENVIRONMENT

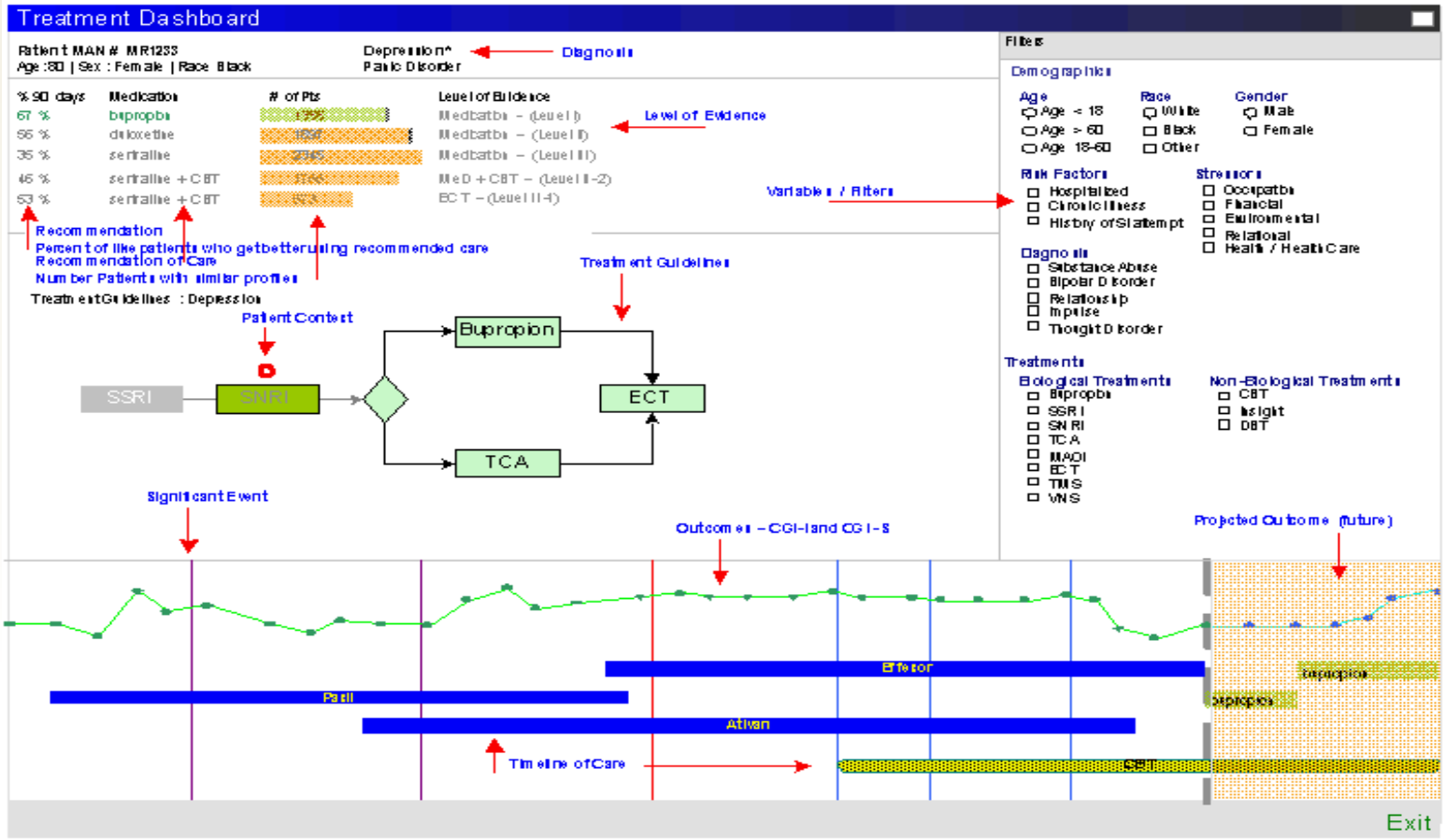
EMR-Based "Single Source" Data Entry



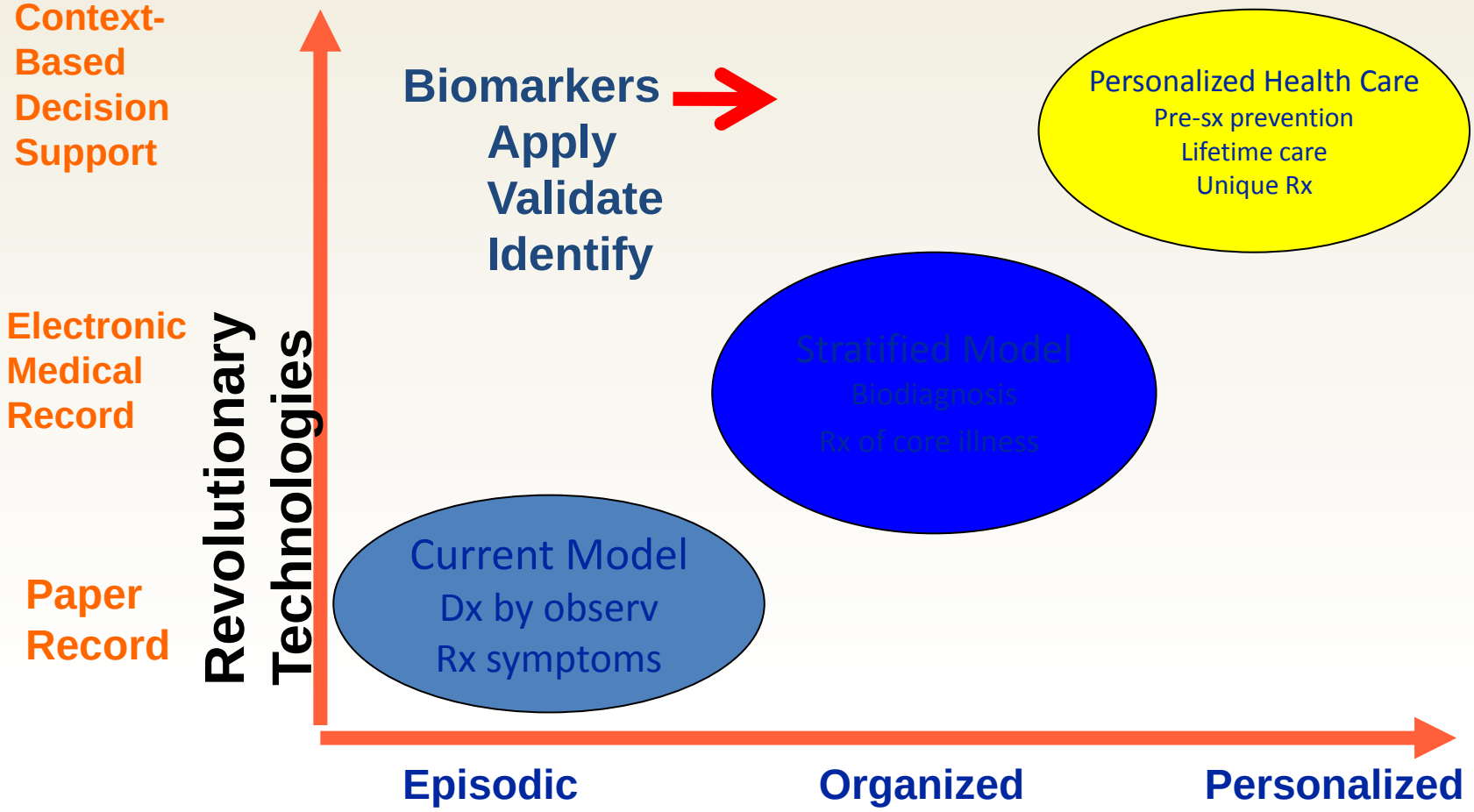
Data Driven Reasons: Why Single Source ?

- Eliminates Source Document Verification
- Eliminates redundant data entry
- Eliminates transcription errors
- Reduces queries and time spent on query resolution
- Provides richer data source
- Connects the data to the date/time of collection
- Builds in quality checks
- Allows for simple trials in clinical setting

Context-Based Decision Support



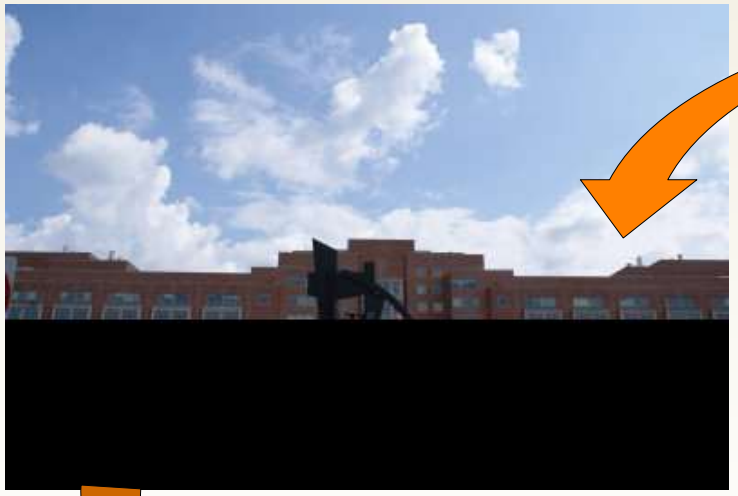
Mental Health Care in the -Omics Era



Adapted from Kovac, IBM 4/04

Heart Attack

NCI: A World Without Cancer



NIMH: A World Without Mental Illness