HARVARD MEDICAL SCHOOL

Medicine at a Crossroads:
Informatics Driving Discovery and Improving Human Health

Alexa T. McCray, PhD

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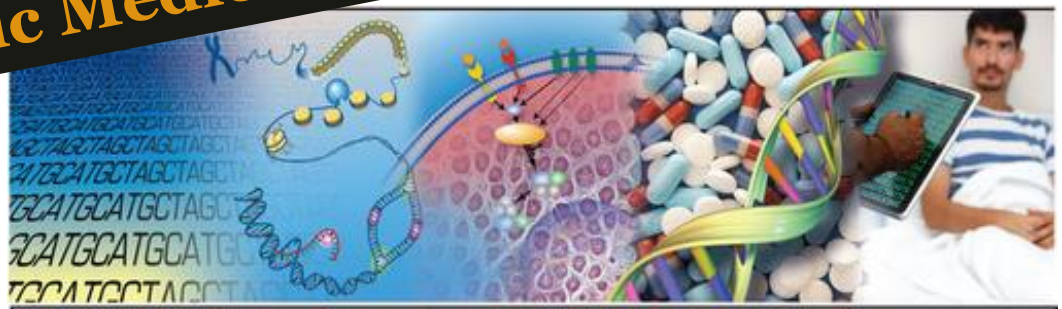
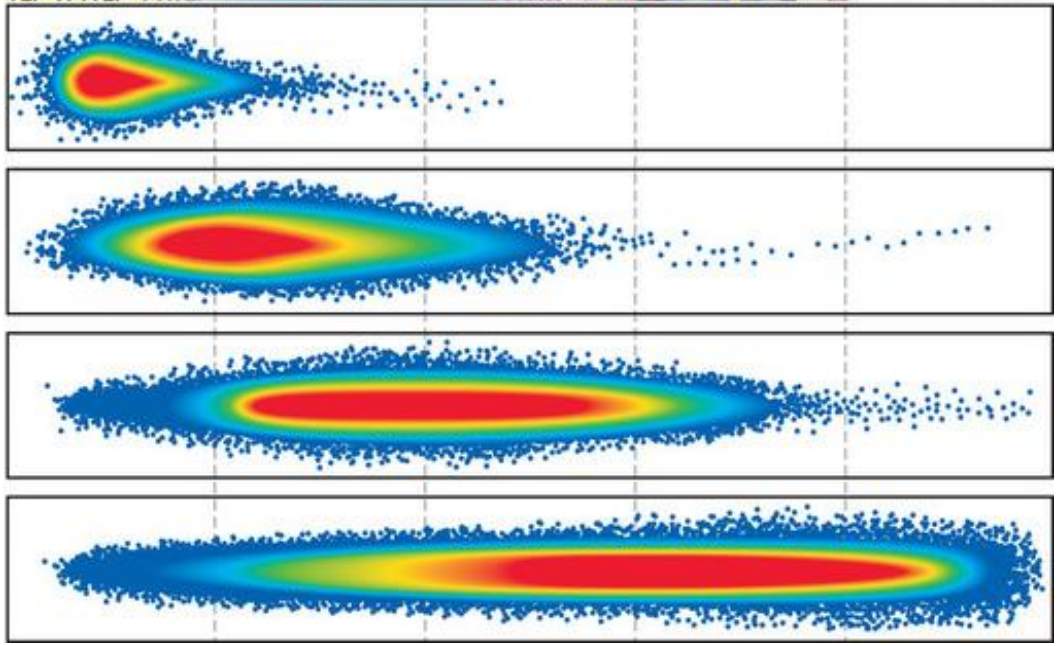
Society of Neurological Surgeons
June 9, 2013

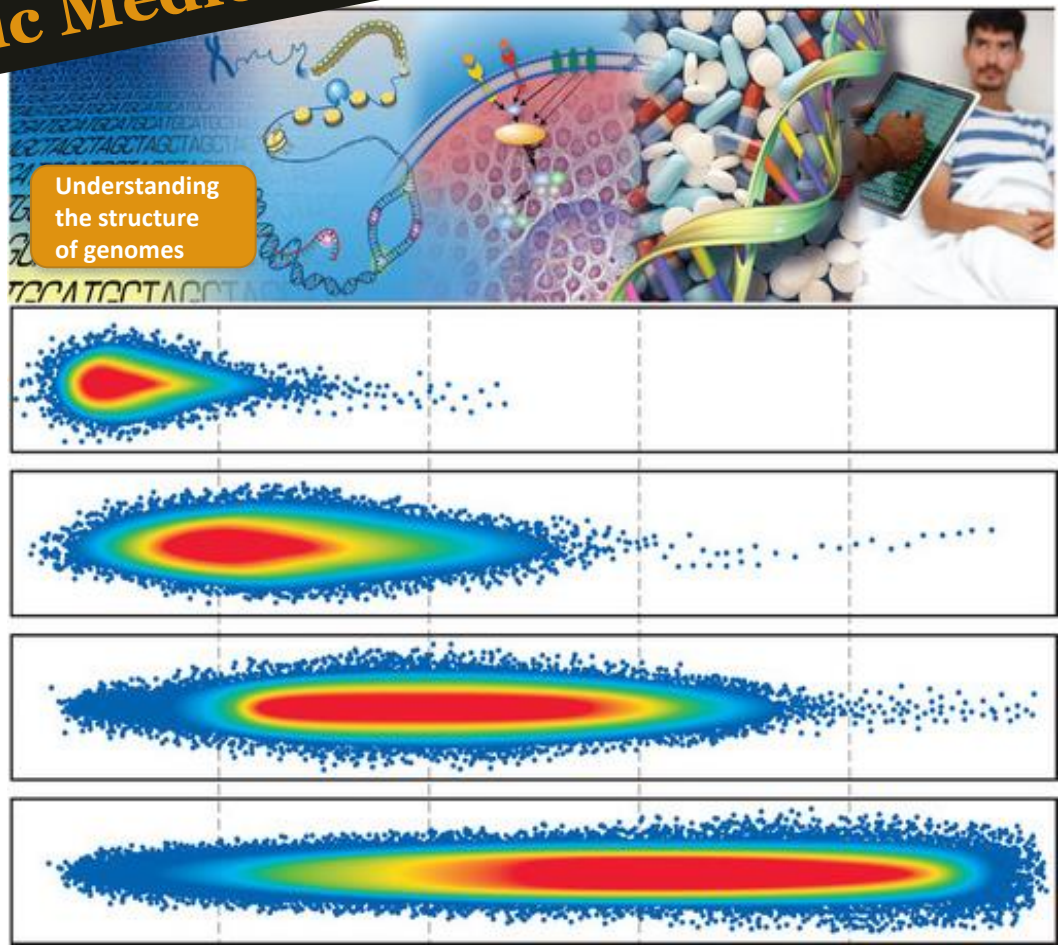
The Promise of Genomic Medicine





Green ED. *Nature* 2011; 470(10):203-13

The Promise of Genomic Medicine



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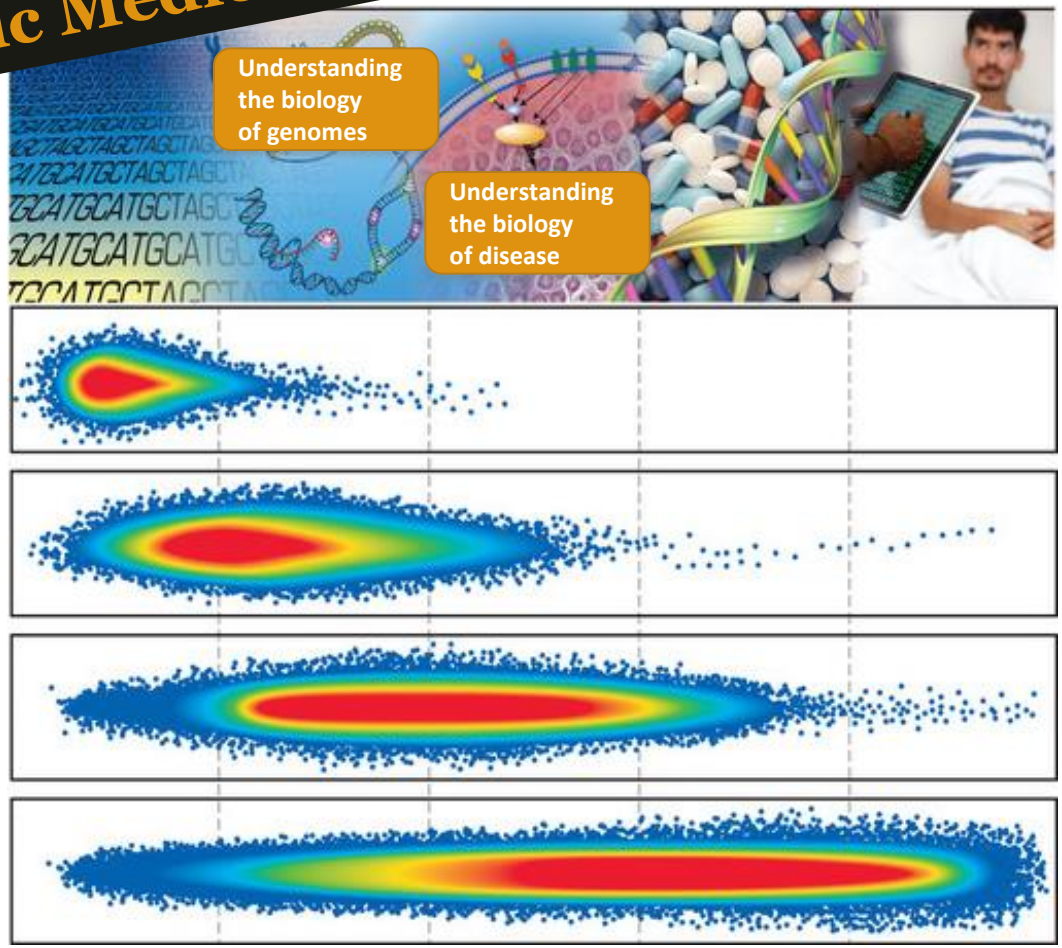
The Promise of Genomic Medicine



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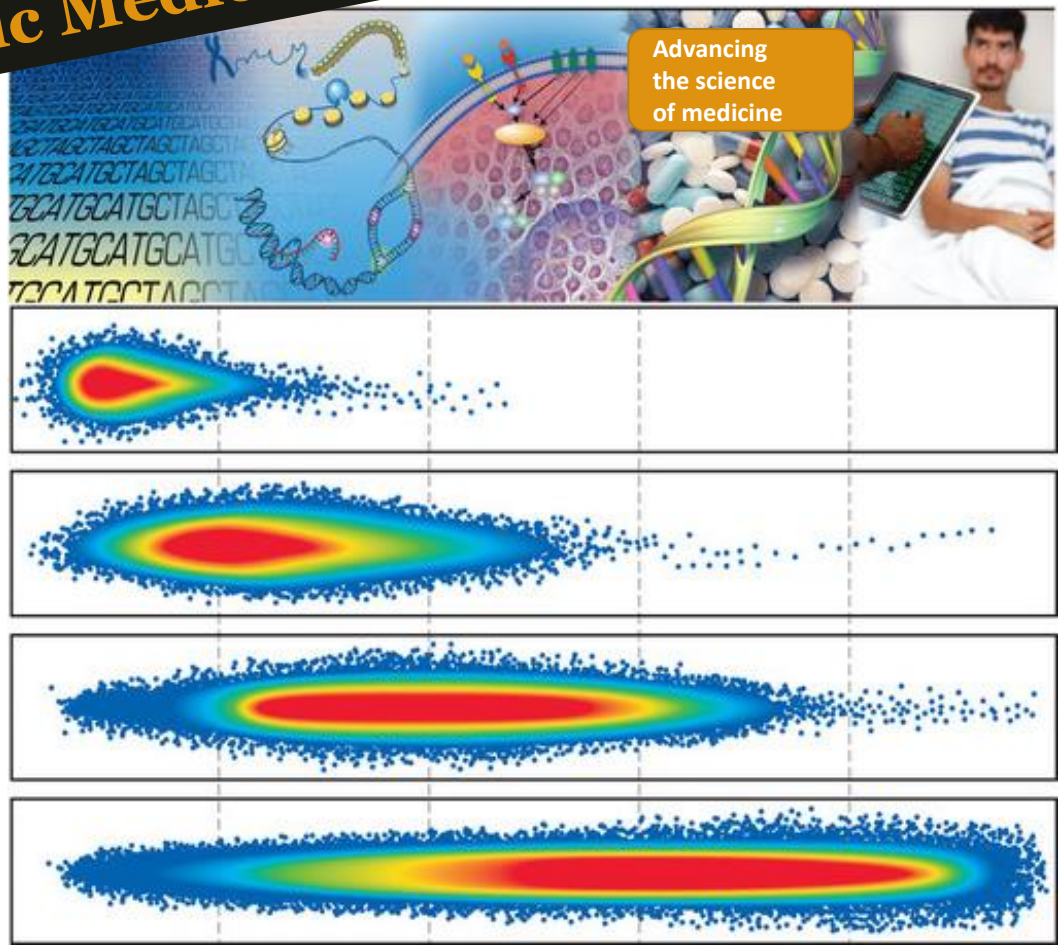
The Promise of Genomic Medicine



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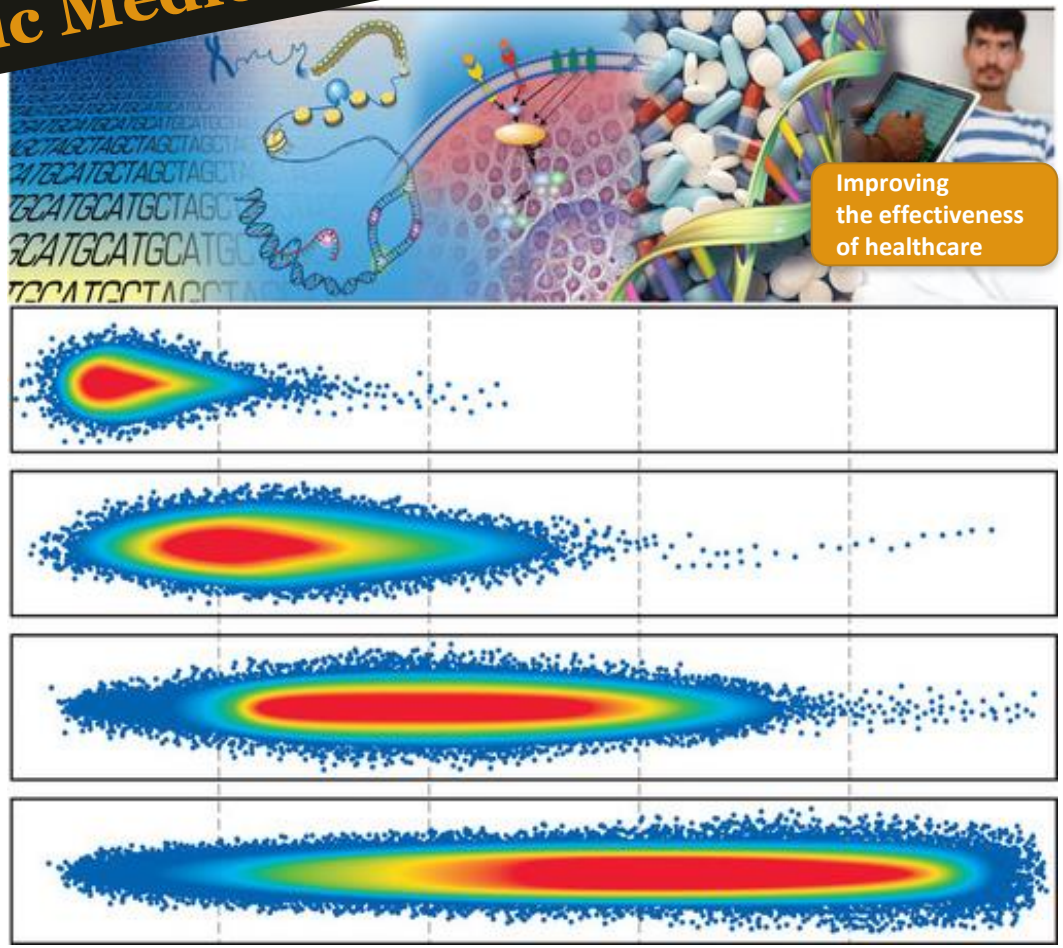
The Promise of Genomic Medicine



Green ED. *Nature* 2011; 470(10):203-13

The Promise of Genomic Medicine

- No longer is data generation the major bottleneck, rather
  - Computational challenges around
    - Data analysis
    - Data display
    - Data integration

Green ED. Nature 2011; 470(10):203-13.

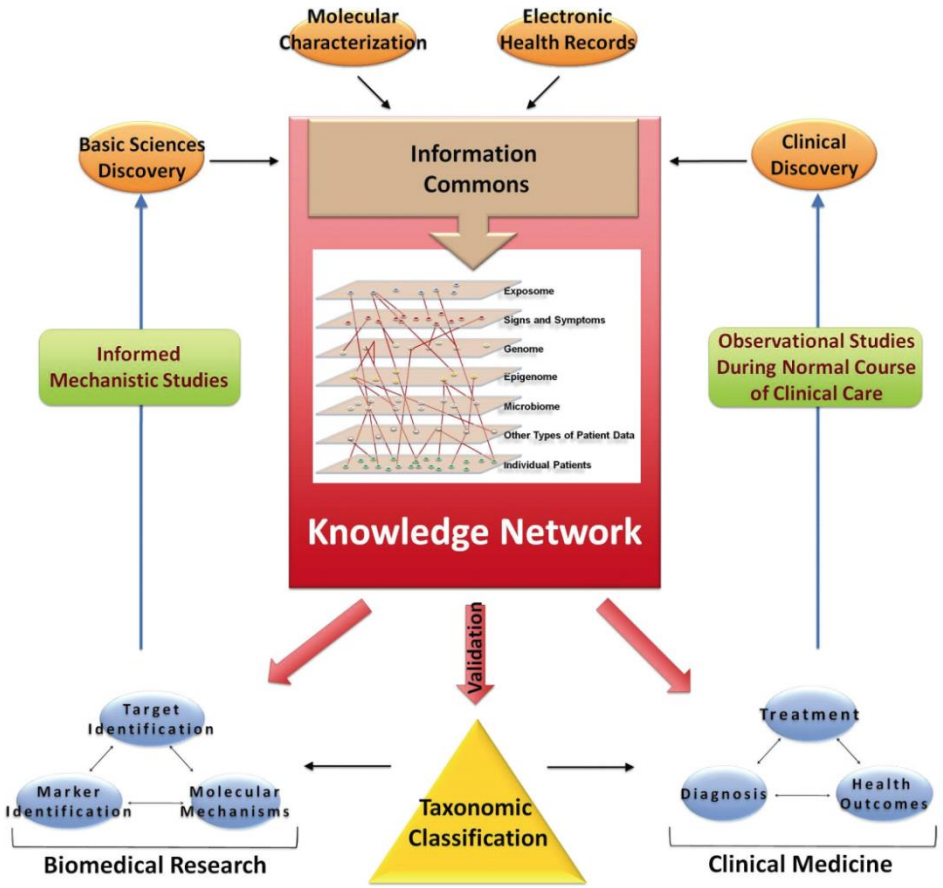
An Inflection Point

"Biomedical research and the practice of medicine, separately and together are reaching an inflection point: the capacity for description and for collecting data, is expanding dramatically, but the efficiency of compiling, organizing manipulating these data – and extracting true understanding of fundamental biological processes, and insights into human health and disease, from them – has not kept pace."

Toward Precision Medicine: Building a knowledge network of biomedical research and a new taxonomy of disease. National Research Council, 2011

Precision Medicine

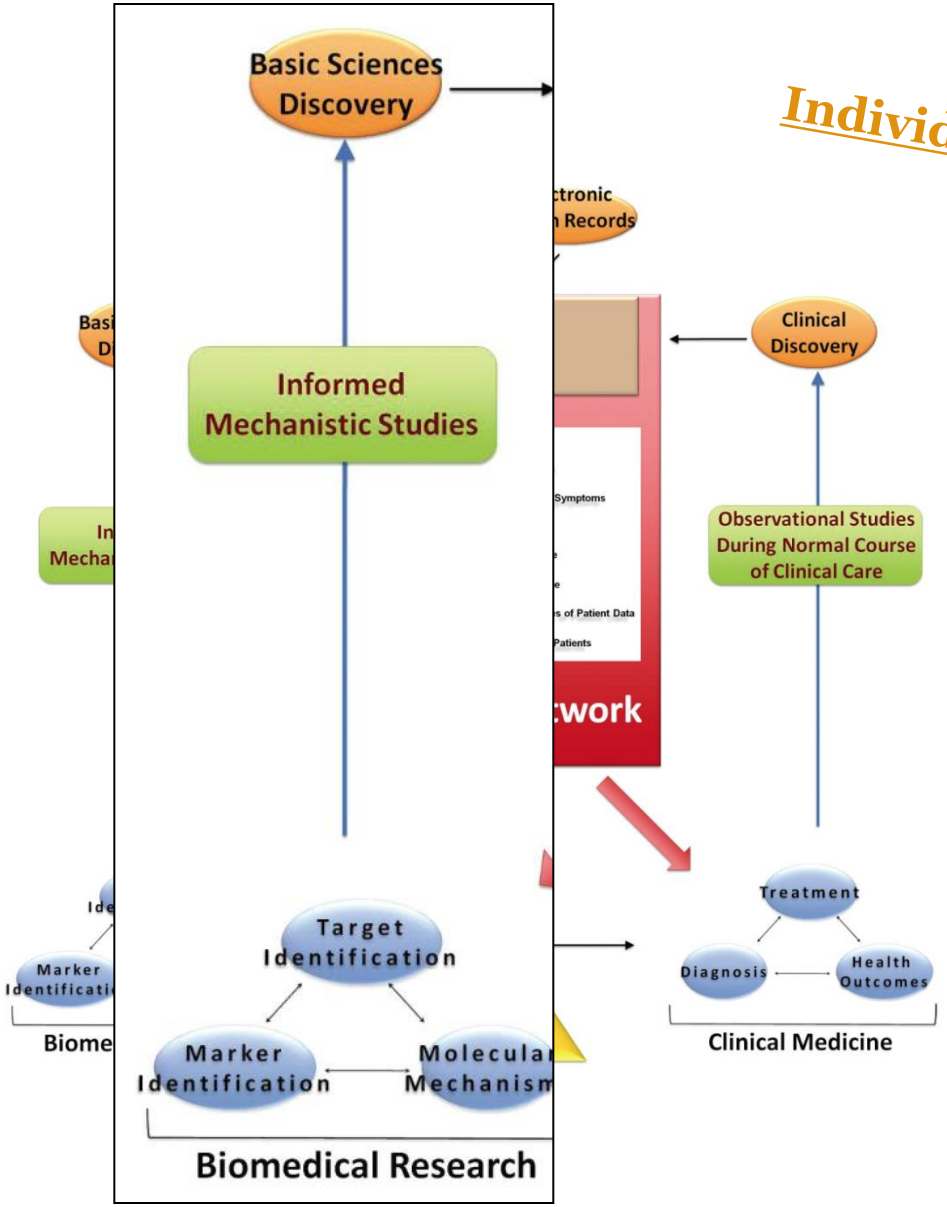
Individual-Centric



Toward Precision Medicine
National Research Council, 2011

Precision Medicine

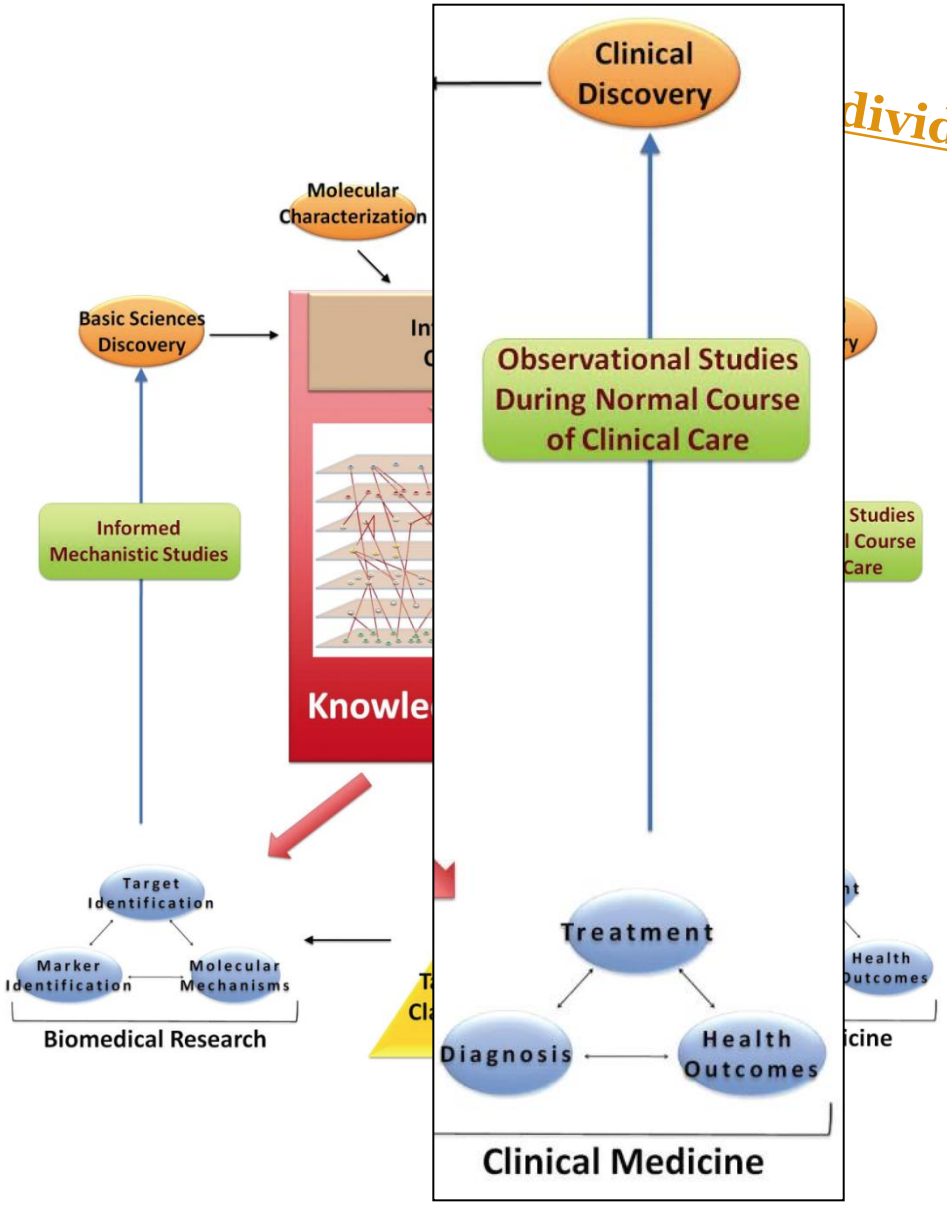
Individual-Centric



Toward Precision Medicine
National Research Council, 2011

Precision Medicine

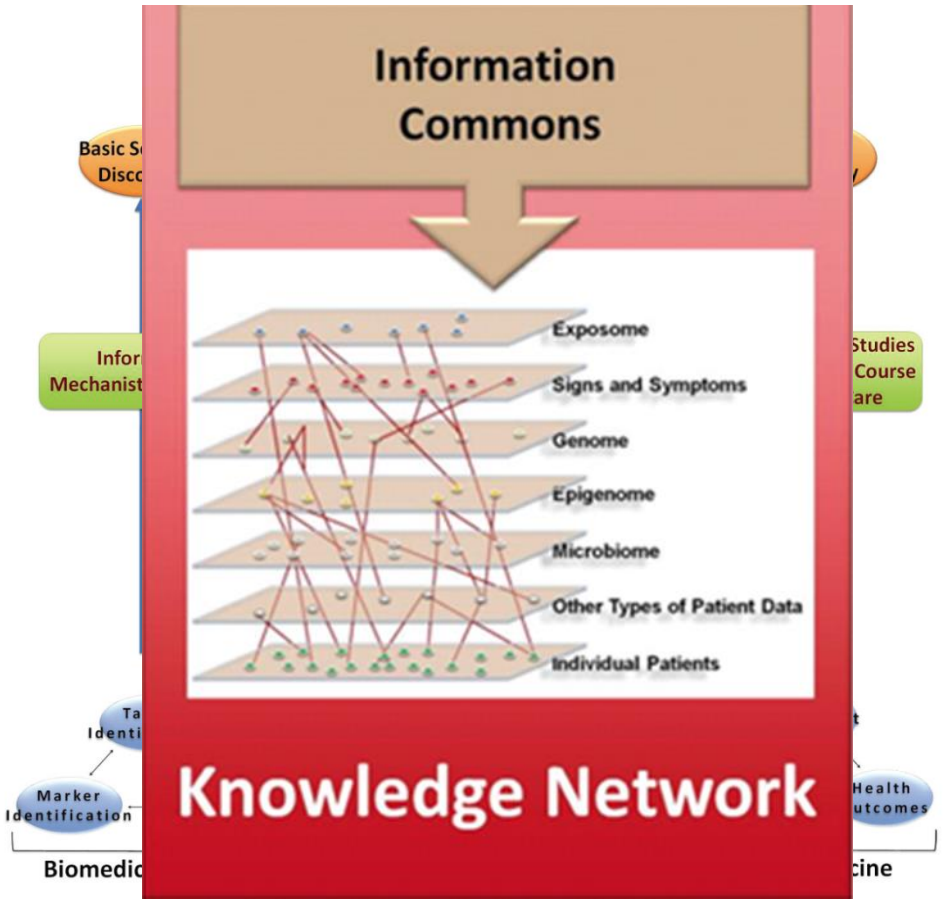
dividual-Centric



Toward Precision Medicine
National Research Council, 2011

Precision Medicine

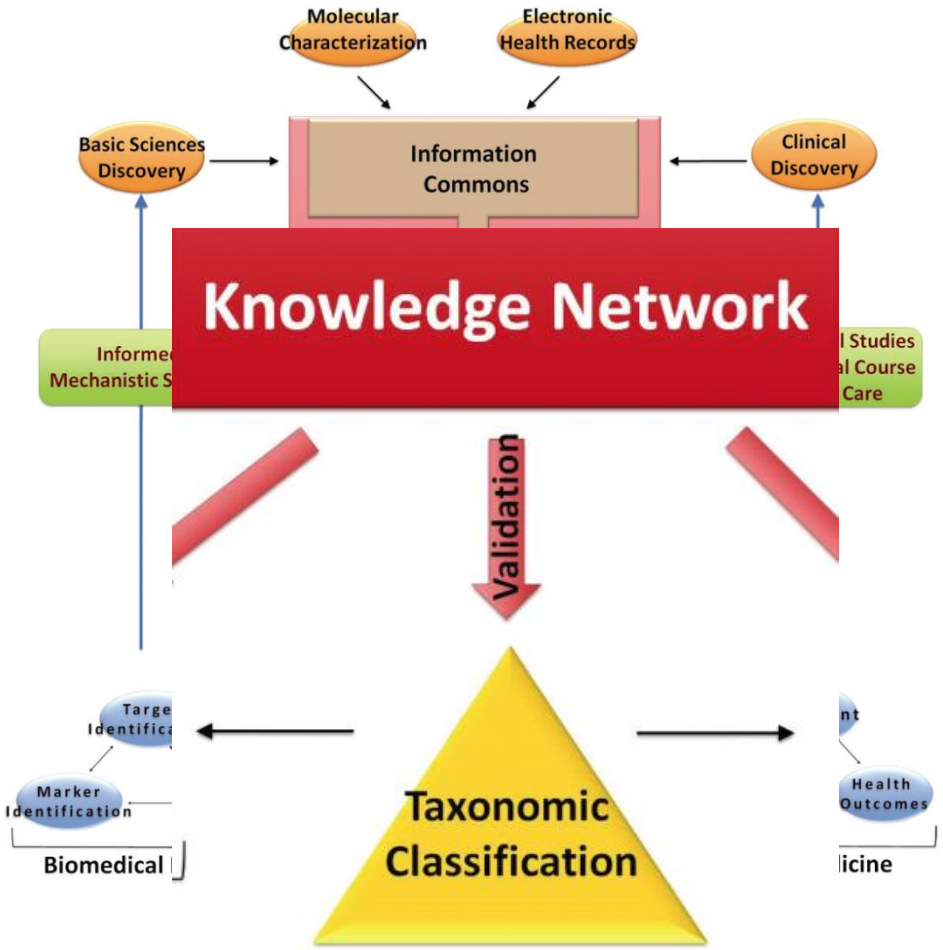
Individual-Centric



Toward Precision Medicine
National Research Council, 2011

Precision Medicine

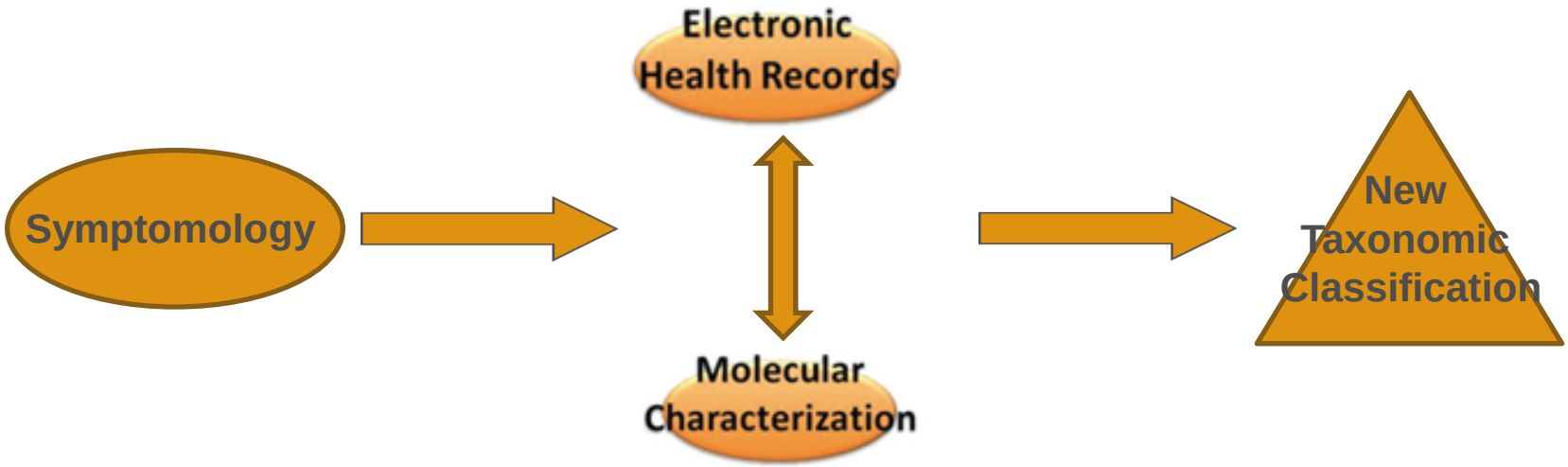
Individual-Centric



Toward Precision Medicine
National Research Council, 2011

A New Taxonomy of Disease

"Could it be that something as fundamental as our current system for classifying diseases is actually inhibiting progress?"



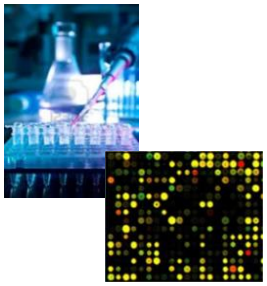
Toward Precision Medicine.
National Research Council, 2011:10

Heterogeneous Data Types

Realizing the Vision

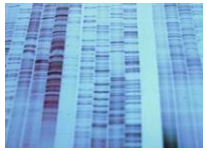
Basic Science Discovery

Laboratory

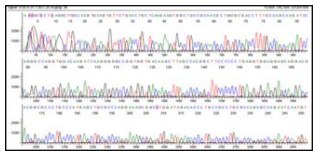


Text

Images

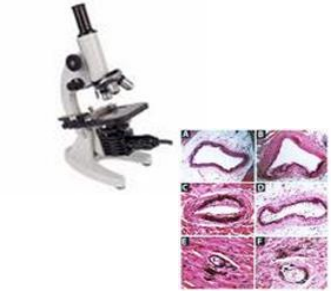


Signals



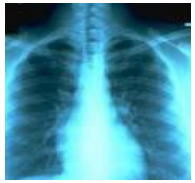
Clinical Discovery

Laboratory

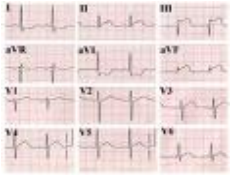


Text

Images



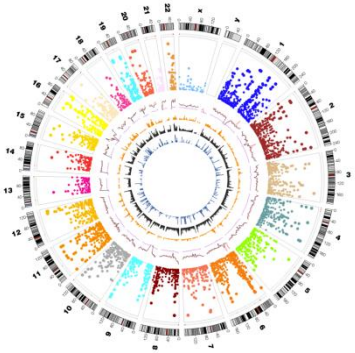
Signals



Varied Methods, Approaches & Tools

(BIG) Data Sources

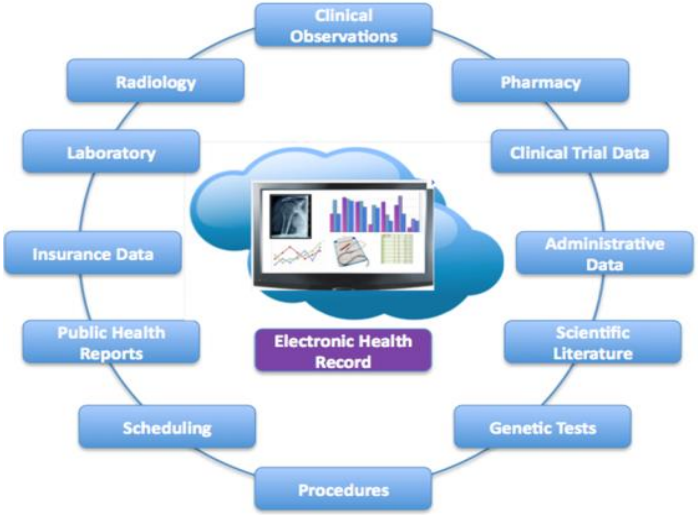
GWAS Data



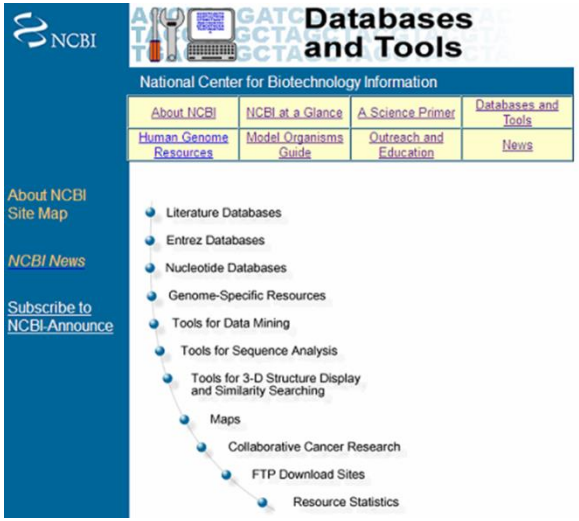
Biosensor Data

- Variation in level of
  - Structure
  - Curation (metadata)

Clinical Systems

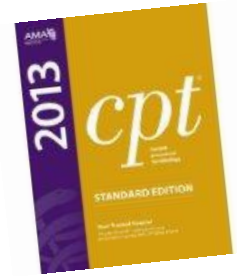


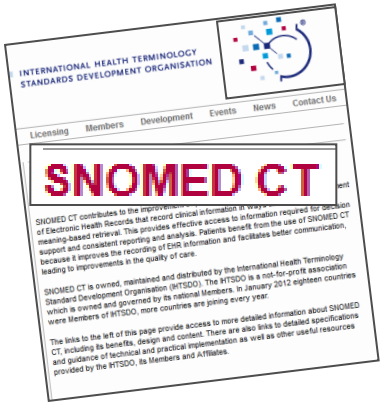
Public Databases

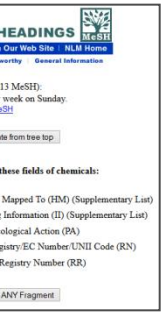


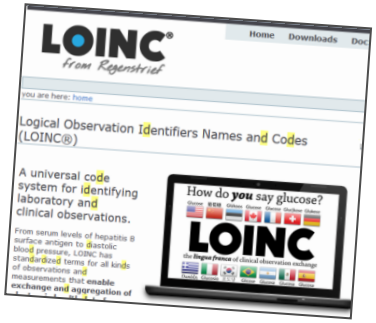
Social Networking Sites

Terminologies for Curating Biomedical Datasets



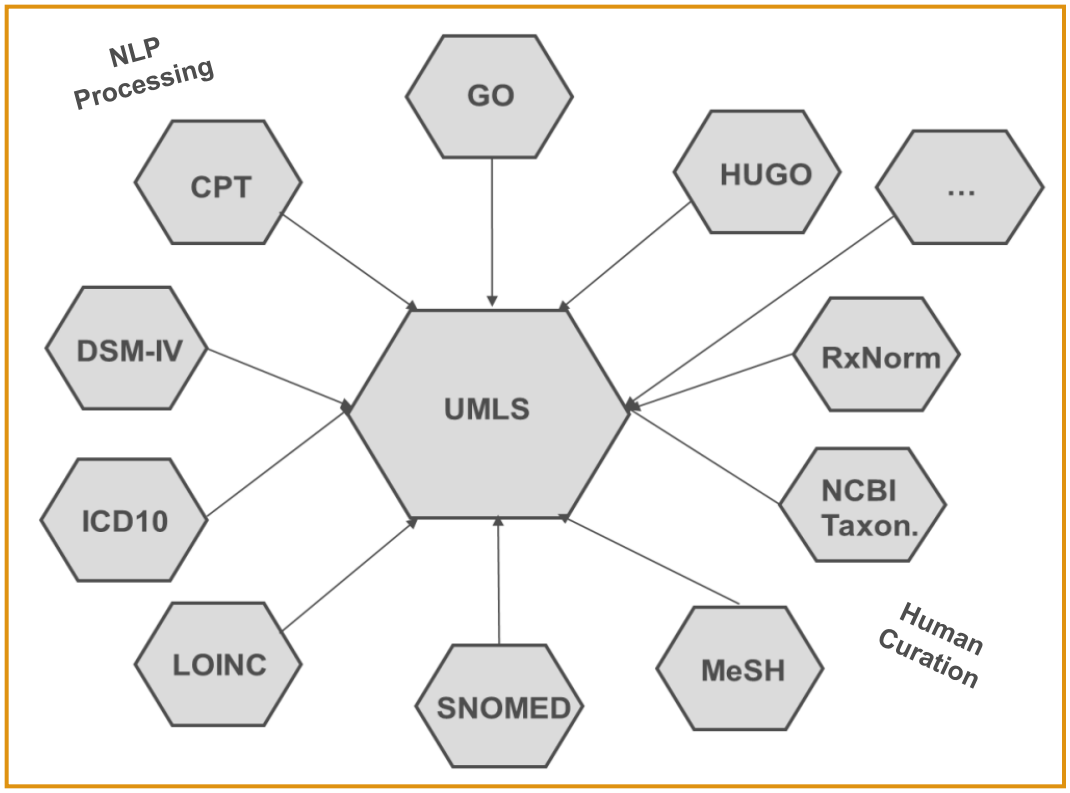






UMLS (Unified Medical Language System)

- Integrates > 100 existing biomedical terminologies



ClinicalTrials.gov

Informatics in Action

1997: Congress Passes Law (FDAMA) Requiring Trial Registration

The first U.S. Federal law to require trial registration was the Food and Drug Administration Modernization Act of 1997 (FDAMA) (PDF).

Section 113 of FDAMA required that the National Institutes of Health (NIH) create a public information resource on certain clinical trials regulated by the Food and Drug Administration (FDA). Specifically, FDAMA 113 required that the registry include information about federally or privately funded clinical trials conducted under investigational new drug applications (INDs) to test the effectiveness of experimental drugs for patients with serious or life-threatening diseases or conditions.

The information in the registry was intended for a wide audience, including individuals with serious or life-threatening diseases or conditions, members of the public, health care providers, and researchers.

1997 FDMA

2004 ICMJE

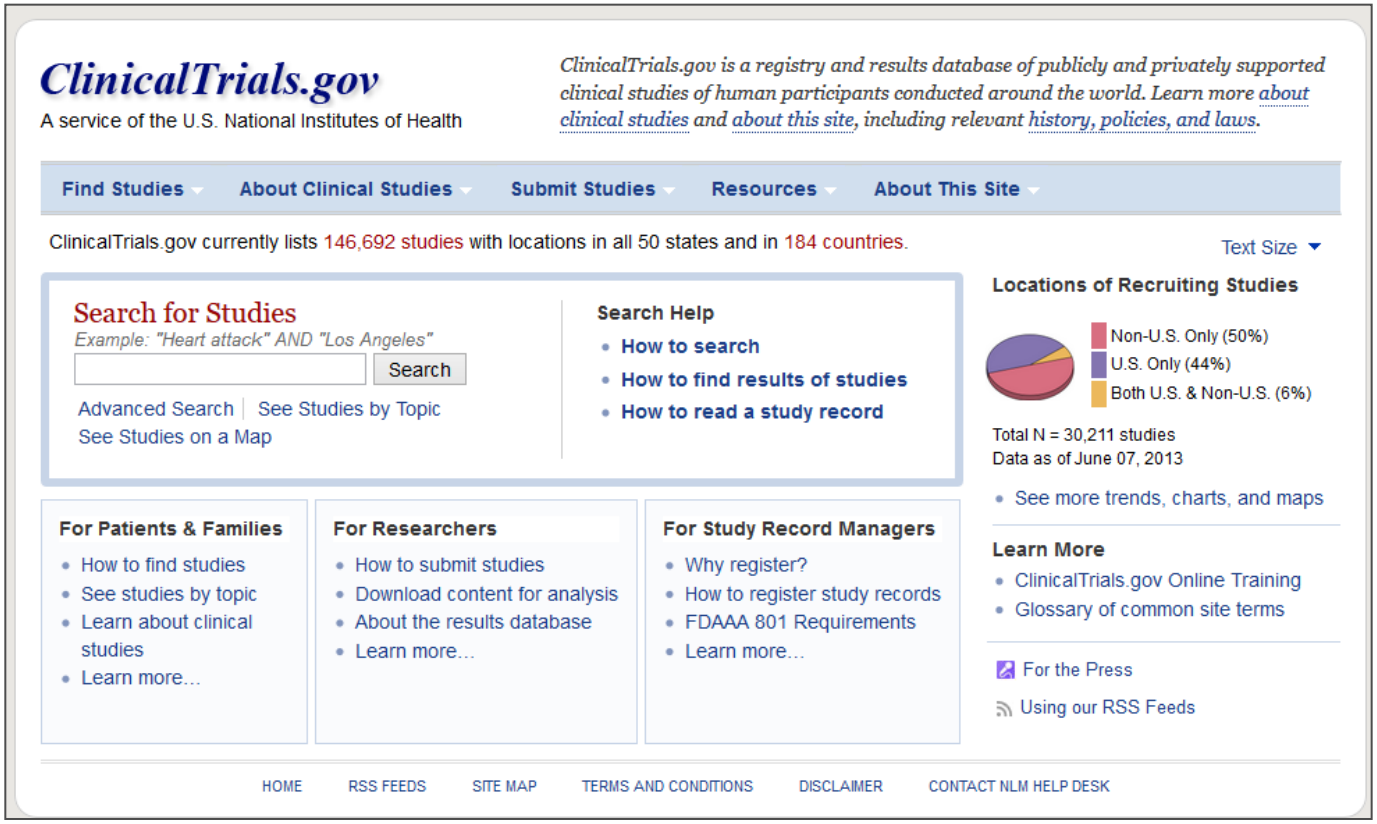
http://www.icmje.org/publishing_10register.html

2007: Congress Passes Law (FDAAA) Expanding ClinicalTrials.gov Submission Requirements

In 2007 the requirements for submission to ClinicalTrials.gov were expanded after Congress passed the Food and Drug Administration Amendments Act of 2007 (FDAAA) (PDF) Section 801 of FDAAA (FDAAA 801) requires more types of trials to be registered; additional trial registration information; and the submission of summary results, including adverse events, for certain trials. The law also included penalties for noncompliance, such as the withholding of NIH grant funding and civil monetary penalties of up to $10,000 a day.

- ClinicalTrials.gov: See the FDAAA 801 Requirements page
- NIH Office of Extramural Research: Frequently Asked Questions: FDAAA - Further Resources for NIH Grantees

2007 FDAAA



International Scope

Types of Studies

- Interventional Trials
  - Drug or Biologic
  - Behavioral
  - Surgical Procedures
  - Devices
- Observational Studies
- Device Trials

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world. Learn more about clinical studies and about this site, including relevant history, policies, and laws.

Find Studies | About Clinical Studies | Submit Studies | Resources | About This Site

ClinicalTrials.gov currently lists 146,692 studies with locations in all 50 states and in 184 countries.

Text Size

Search for Studies

Example: "Heart attack" AND "Los Angeles"

neurosurgery Search

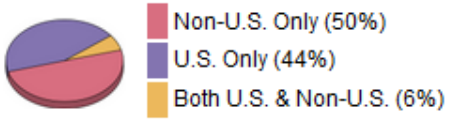
Advanced Search | See Studies by Topic

See Studies on a Map

Search Help

- How to search
- How to find results of studies
- How to read a study record

Locations of Recruiting Studies



Total N = 30,211 studies
Data as of June 07, 2013

- See more trends, charts, and maps

For Patients & Families

- How to find studies
- See studies by topic
- Learn about clinical studies
- Learn more…

For Researchers

- How to submit studies
- Download content for analysis
- About the results database
- Learn more…

For Study Record Managers

- Why register?
- How to register study records
- FDAAA 801 Requirements
- Learn more…

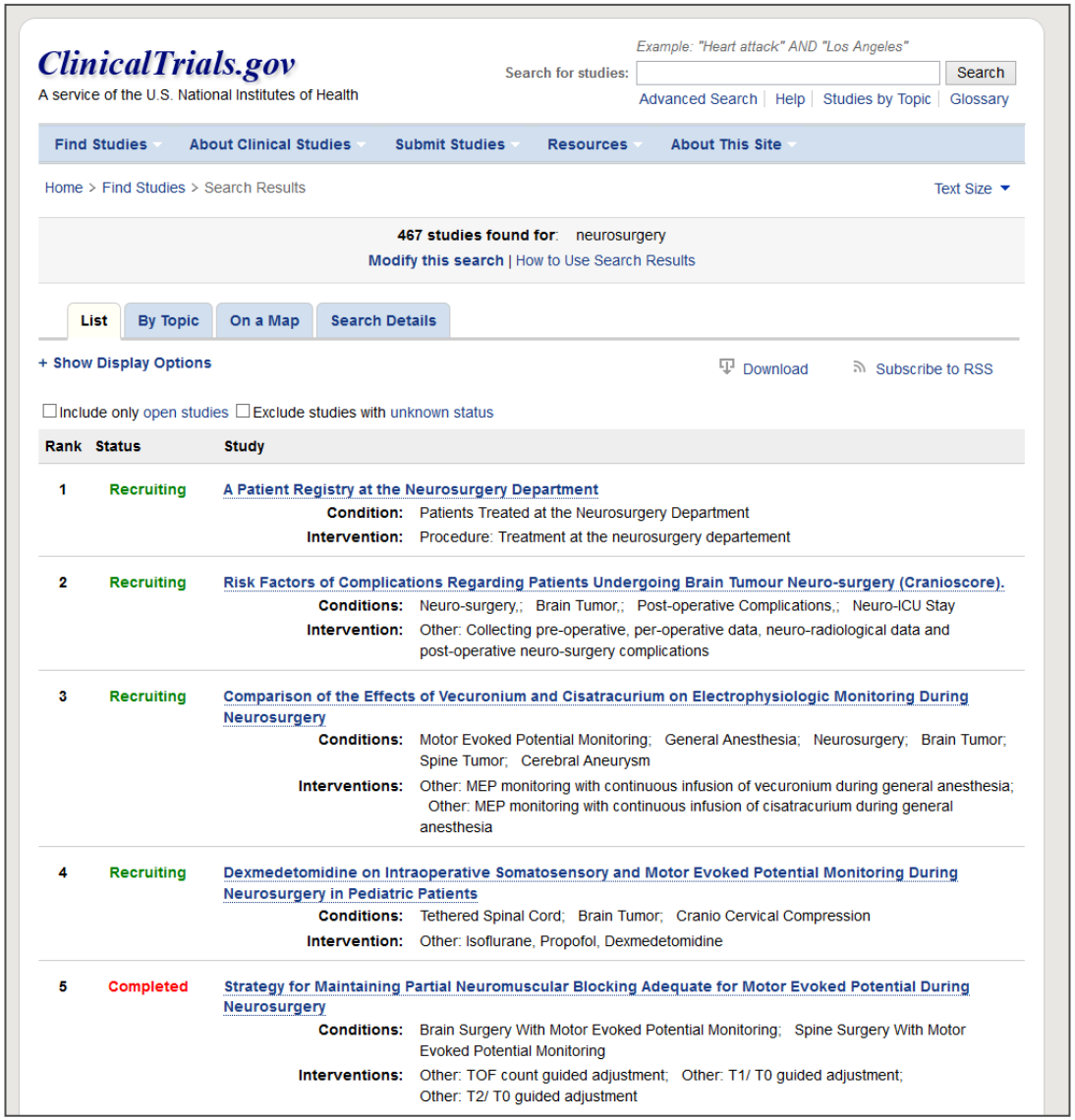
Learn More

- ClinicalTrials.gov Online Training
- Glossary of common site terms

For the Press

Using our RSS Feeds

HOME | RSS FEEDS | SITE MAP | TERMS AND CONDITIONS | DISCLAIMER | CONTACT NLM HELP DESK



ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Example: "Heart attack" AND "Los Angeles"
Search for studies: Search
Advanced Search | Help | Studies by Topic | Glossary

Find Studies | About Clinical Studies | Submit Studies | Resources | About This Site

Home > Find Studies > Search Results Text Size

467 studies found for: neurosurgery
Modify this search | How to Use Search Results

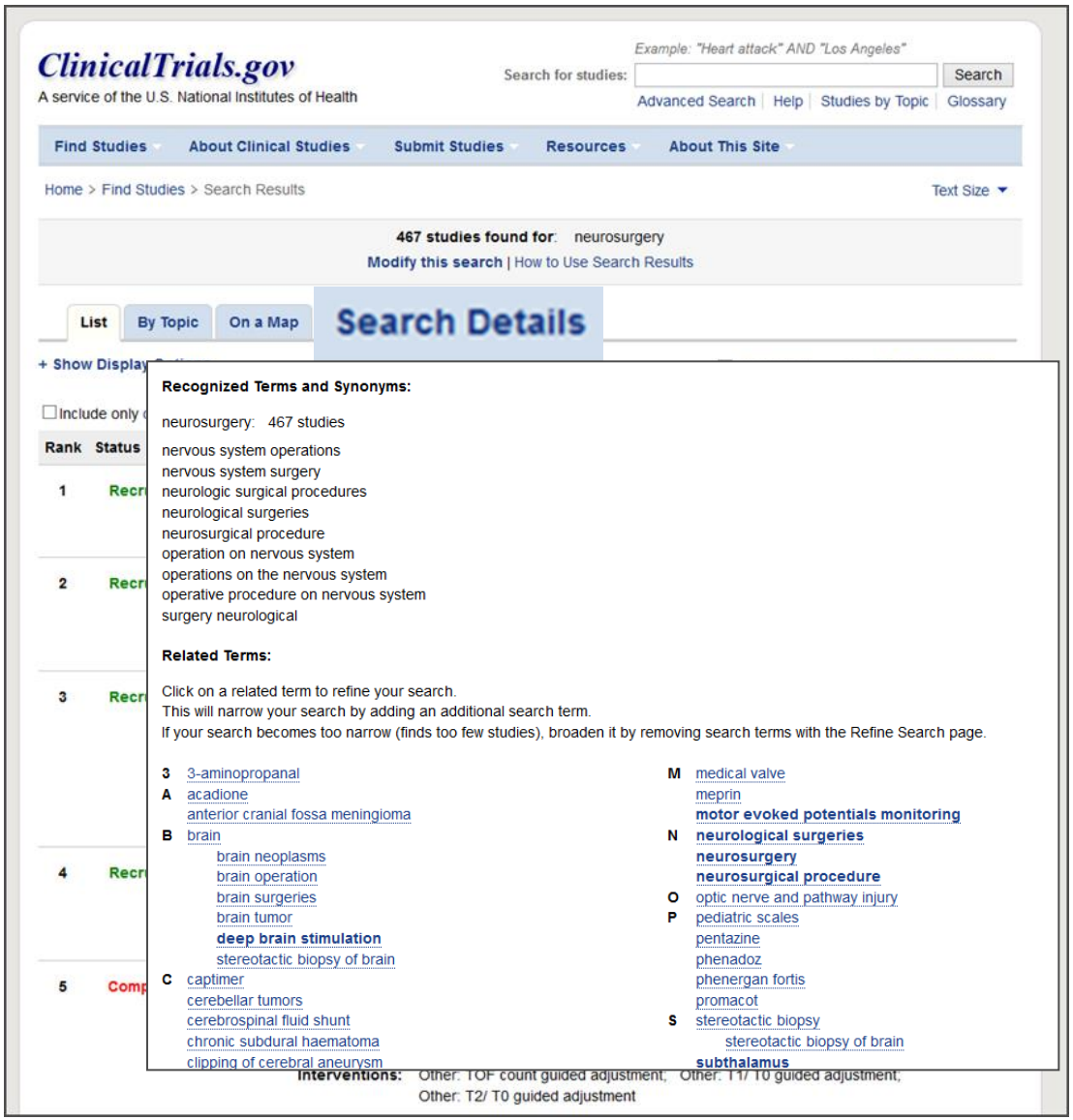
List | By Topic | On a Map | Search Details

+ Show Display Options Download Subscribe to RSS

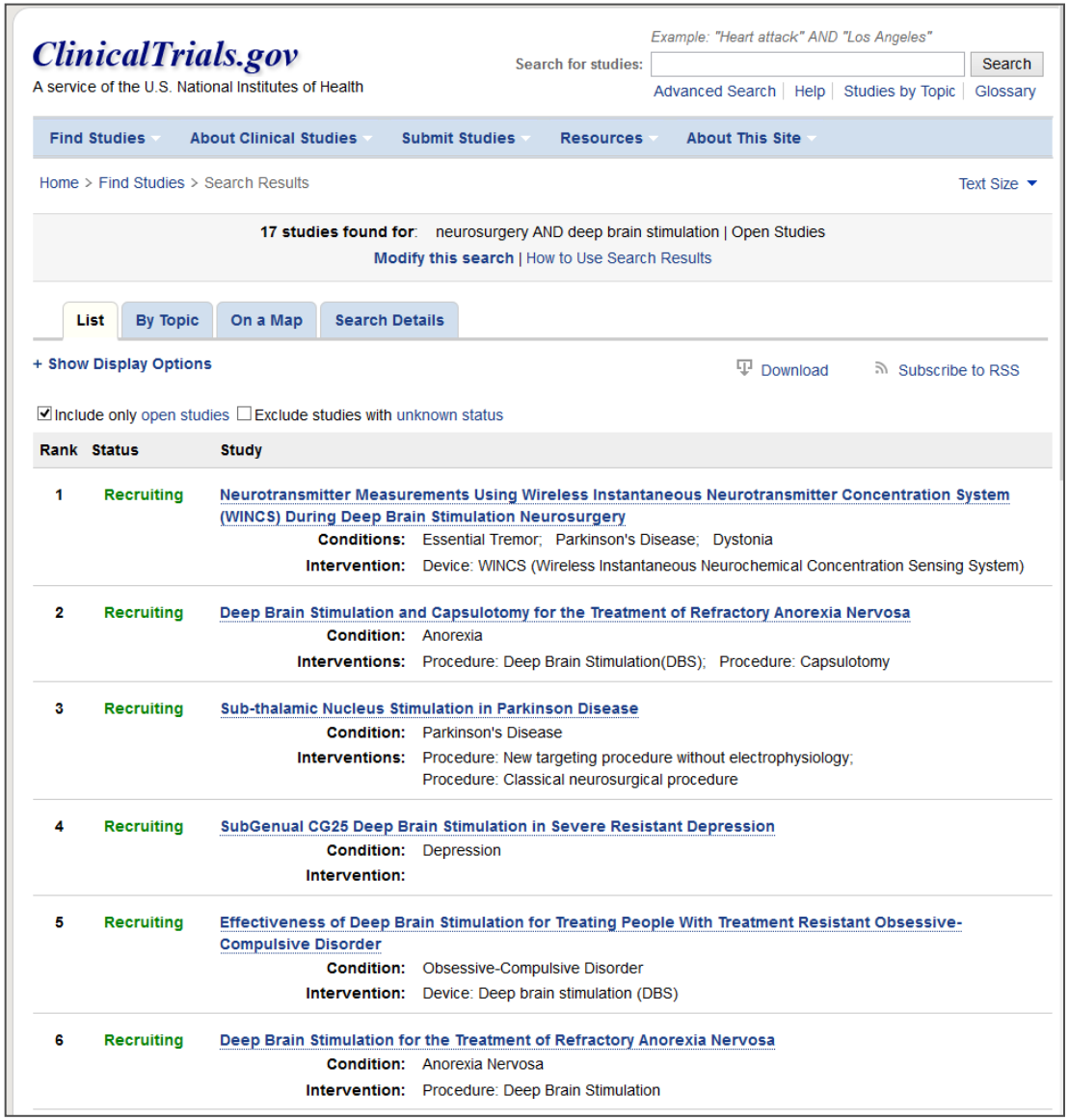
☐ Include only open studies ☐ Exclude studies with unknown status

Rank	Status	Study
1	Recruiting	A Patient Registry at the Neurosurgery Department **Condition:** Patients Treated at the Neurosurgery Department **Intervention:** Procedure: Treatment at the neurosurgery departement
2	Recruiting	Risk Factors of Complications Regarding Patients Undergoing Brain Tumour Neuro-surgery (Cranioscore). **Conditions:** Neuro-surgery,; Brain Tumor,; Post-operative Complications,; Neuro-ICU Stay **Intervention:** Other: Collecting pre-operative, per-operative data, neuro-radiological data and post-operative neuro-surgery complications
3	Recruiting	Comparison of the Effects of Vecuronium and Cisatracurium on Electrophysiologic Monitoring During Neurosurgery **Conditions:** Motor Evoked Potential Monitoring; General Anesthesia; Neurosurgery; Brain Tumor; Spine Tumor; Cerebral Aneurysm **Interventions:** Other: MEP monitoring with continuous infusion of vecuronium during general anesthesia; Other: MEP monitoring with continuous infusion of cisatracurium during general anesthesia
4	Recruiting	Dexmedetomidine on Intraoperative Somatosensory and Motor Evoked Potential Monitoring During Neurosurgery in Pediatric Patients **Conditions:** Tethered Spinal Cord; Brain Tumor; Cranio Cervical Compression **Intervention:** Other: Isoflurane, Propofol, Dexmedetomidine
5	Completed	Strategy for Maintaining Partial Neuromuscular Blocking Adequate for Motor Evoked Potential During Neurosurgery **Conditions:** Brain Surgery With Motor Evoked Potential Monitoring; Spine Surgery With Motor Evoked Potential Monitoring **Interventions:** Other: TOF count guided adjustment; Other: T1/ T0 guided adjustment; Other: T2/ T0 guided adjustment

Several hundred Neurosurgery Studies



UMLS-driven Search



ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Example: "Heart attack" AND "Los Angeles"
Search for studies: Search
Advanced Search | Help | Studies by Topic | Glossary

Find Studies | About Clinical Studies | Submit Studies | Resources | About This Site

Home > Find Studies > Search Results Text Size

17 studies found for: neurosurgery AND deep brain stimulation | Open Studies
Modify this search | How to Use Search Results

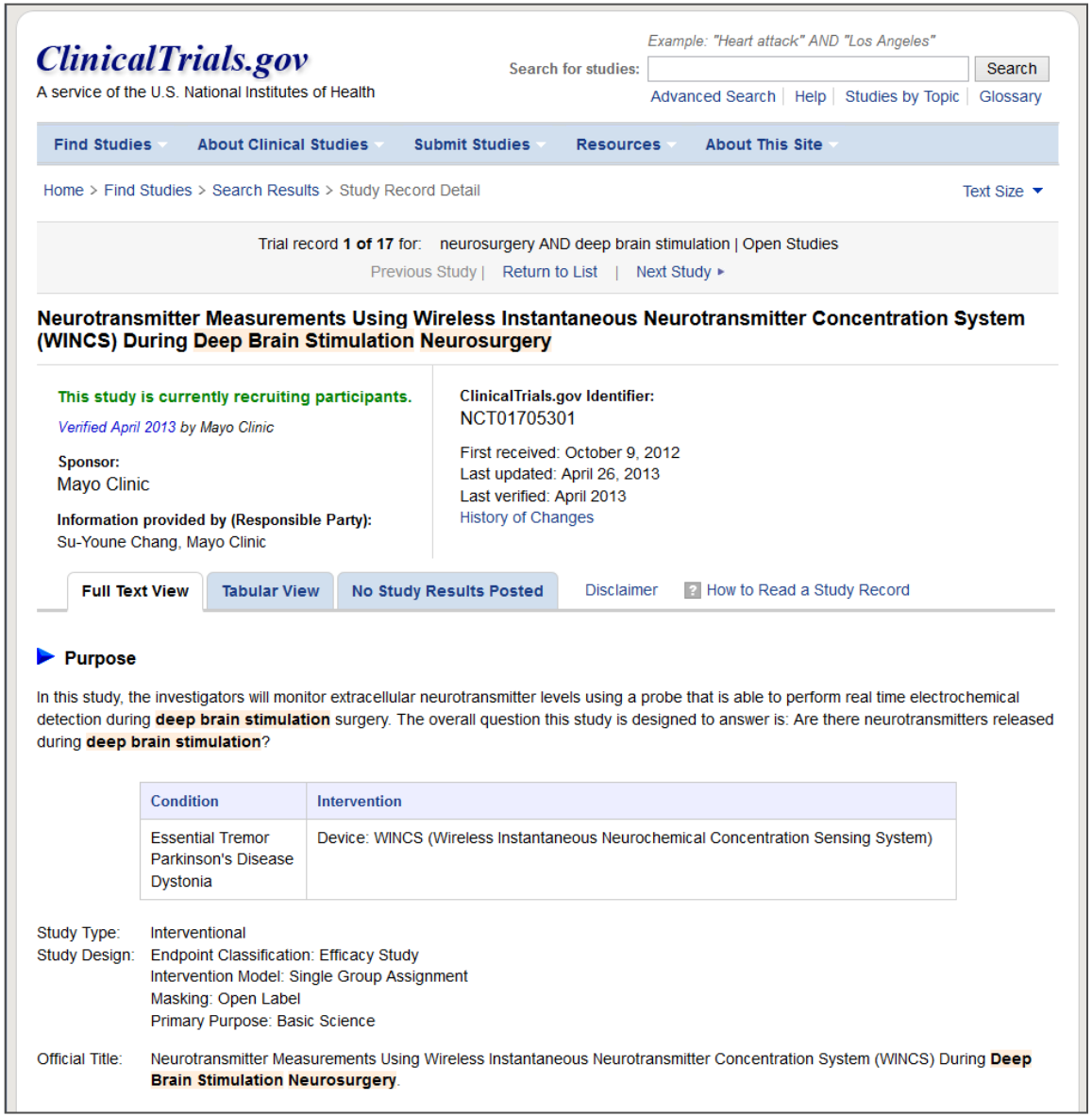
List | By Topic | On a Map | Search Details

+ Show Display Options Download Subscribe to RSS

☑ Include only open studies ☐ Exclude studies with unknown status

Rank	Status	Study
1	Recruiting	Neurotransmitter Measurements Using Wireless Instantaneous Neurotransmitter Concentration System (WINCS) During Deep Brain Stimulation Neurosurgery **Conditions:** Essential Tremor; Parkinson's Disease; Dystonia **Intervention:** Device: WINCS (Wireless Instantaneous Neurochemical Concentration Sensing System)
2	Recruiting	Deep Brain Stimulation and Capsulotomy for the Treatment of Refractory Anorexia Nervosa **Condition:** Anorexia **Interventions:** Procedure: Deep Brain Stimulation(DBS); Procedure: Capsulotomy
3	Recruiting	Sub-thalamic Nucleus Stimulation in Parkinson Disease **Condition:** Parkinson's Disease **Interventions:** Procedure: New targeting procedure without electrophysiology; Procedure: Classical neurosurgical procedure
4	Recruiting	SubGenual CG25 Deep Brain Stimulation in Severe Resistant Depression **Condition:** Depression **Intervention:**
5	Recruiting	Effectiveness of Deep Brain Stimulation for Treating People With Treatment Resistant Obsessive-Compulsive Disorder **Condition:** Obsessive-Compulsive Disorder **Intervention:** Device: Deep brain stimulation (DBS)
6	Recruiting	Deep Brain Stimulation for the Treatment of Refractory Anorexia Nervosa **Condition:** Anorexia Nervosa **Intervention:** Procedure: Deep Brain Stimulation

17 recruiting studies involving deep brain stimulation



ClinicalTrials.gov
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Example: "Heart attack" AND "Los Angeles"
Search for studies: Search
Advanced Search | Help | Studies by Topic | Glossary

Find Studies | About Clinical Studies | Submit Studies | Resources | About This Site

Home > Find Studies > Search Results > Study Record Detail Text Size

Trial record **1 of 17** for: neurosurgery AND deep brain stimulation | Open Studies
Previous Study | Return to List | Next Study ▸

Neurotransmitter Measurements Using Wireless Instantaneous Neurotransmitter Concentration System (WINCS) During Deep Brain Stimulation Neurosurgery

This study is currently recruiting participants.
Verified April 2013 by Mayo Clinic

Sponsor:
Mayo Clinic

Information provided by (Responsible Party):
Su-Youne Chang, Mayo Clinic

ClinicalTrials.gov Identifier:
NCT01705301

First received: October 9, 2012
Last updated: April 26, 2013
Last verified: April 2013
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

In this study, the investigators will monitor extracellular neurotransmitter levels using a probe that is able to perform real time electrochemical detection during **deep brain stimulation** surgery. The overall question this study is designed to answer is: Are there neurotransmitters released during **deep brain stimulation**?

Condition	Intervention
Essential Tremor Parkinson's Disease Dystonia	Device: WINCS (Wireless Instantaneous Neurochemical Concentration Sensing System)

Study Type: Interventional
Study Design: Endpoint Classification: Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Basic Science

Official Title: Neurotransmitter Measurements Using Wireless Instantaneous Neurotransmitter Concentration System (WINCS) During **Deep Brain Stimulation Neurosurgery**.

Trial Record
- Purpose
- Study Type
- Study Design
- Official Title

Resource links provided by NLM:

Genetics Home Reference related topics: dopa-responsive dystonia early-onset primary dystonia essential tremor Parkinson disease Perry syndrome

MedlinePlus related topics: Dystonia Parkinson's Disease Tremor

U.S. FDA Resources

Further study details as provided by Mayo Clinic:

Primary Outcome Measures:

- adenosine release in **brain** as measured by WINCS (Wireless Instantaneous Neurochemical Concentration Sensing System)recording device [Time Frame: 30 minutes] [Designated as safety issue: Yes]

  Pre, during, post DBS (deep brain stimulation)

Secondary Outcome Measures:

- dopamine release in **brain** as measured by WINCS (Wireless Instantaneous Neurochemical Concentration Sensing System)recording device [Time Frame: 30 minutes] [Designated as safety issue: Yes]

  Pre, during, post DBS (deep brain stimulation)

Estimated Enrollment:	45
Study Start Date:	January 2010
Estimated Study Completion Date:	January 2014
Estimated Primary Completion Date:	January 2014 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: WINCS WINCS (Wireless Instantaneous Neurochemical Concentration Sensing System), which is capable of wireless control and data transmission; and in addition is capable of detecting by fast scan cyclic voltametry (FSCV).	Device: WINCS (Wireless Instantaneous Neurochemical Concentration Sensing System) The experimental protocol will involve, after implantation of the DBS electrodes, the patient will have a single electrochemical recording electrode will be implanted along the same trajectory path as the electrophysiology and the DBS electrode

Eligibility

Ages Eligible for Study:	18 Years to 90 Years
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria
Inclusion Criteria:

Trial Record (cont.)

- Resources
- Primary Outcomes
- Secondary Outcomes
- Estimated Enrollment
- Study Dates
- Eligibility

Exclusion Criteria:

- pregnant patients,
- prisoners,
- children (age less than 18), and
- any patients identified as unsuitable for these protocol by the Mayo DBS committee.

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01705301

Locations

United States, Minnesota

Mayo Clinic **Recruiting**
Rochester, Minnesota, United States, 55901
Contact: Debra Gorman, RN 507-266-3044 gorman.deborah@mayo.edu
Principal Investigator: Kendall H Lee, MD, PhD
Principal Investigator: Su-youne Chang, PhD

Sponsors and Collaborators

Mayo Clinic

More Information

No publications provided

Responsible Party:	Su-Youne Chang, PI, Mayo Clinic
ClinicalTrials.gov Identifier:	NCT01705301 History of Changes
Other Study ID Numbers:	09-007441
Study First Received:	October 9, 2012
Last Updated:	April 26, 2013
Health Authority:	United States: Institutional Review Board

Additional relevant MeSH terms:

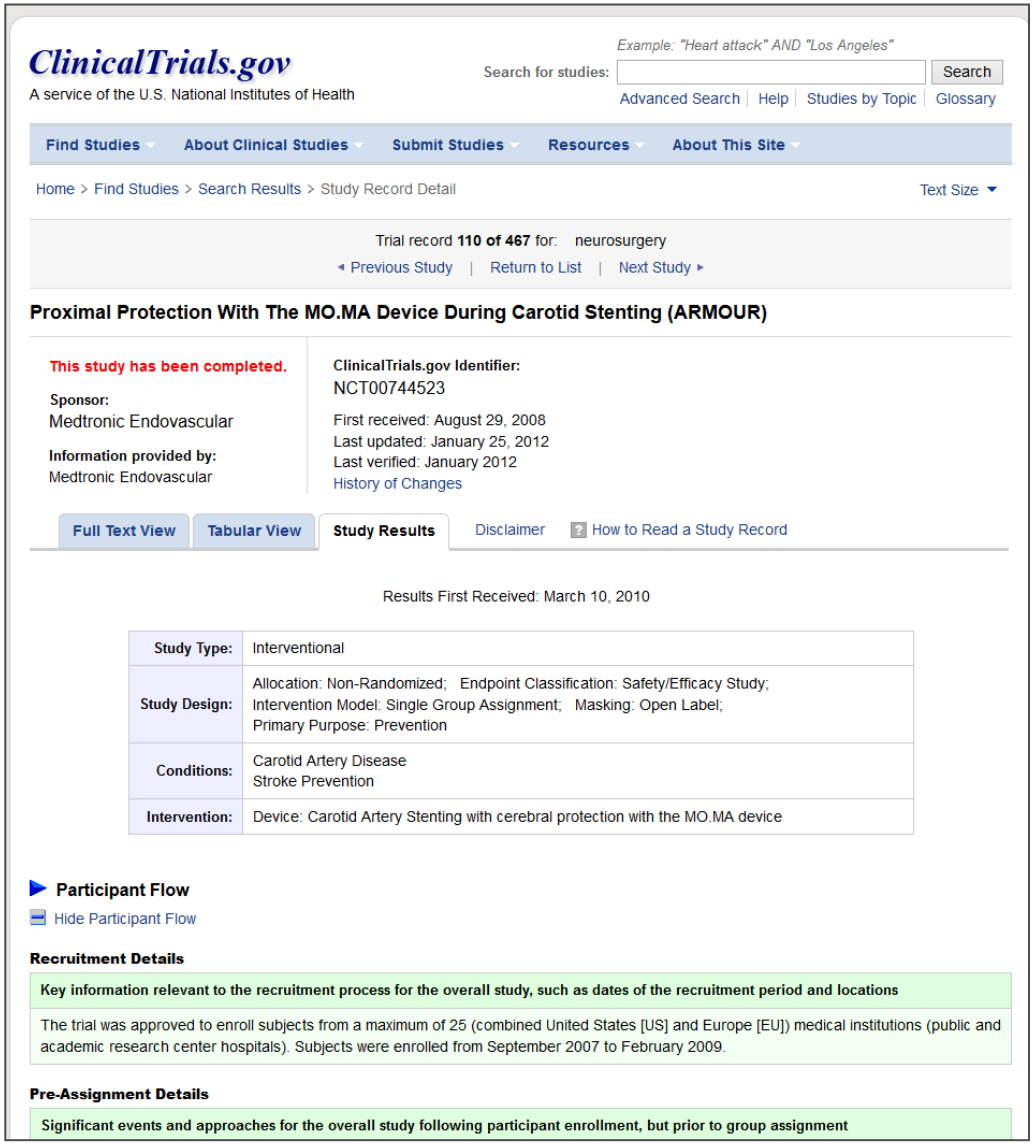
Brain Diseases
Dystonia
Dystonic Disorders
Parkinson Disease
Tremor
Essential Tremor
Dyskinesias
Neurologic Manifestations
Nervous System Diseases
Signs and Symptoms

Movement Disorders
Central Nervous System Diseases
Parkinsonian Disorders
Basal Ganglia Diseases
Neurodegenerative Diseases
Neurotransmitter Agents
Molecular Mechanisms of Pharmacological Action
Pharmacologic Actions
Physiological Effects of Drugs

ClinicalTrials.gov processed this record on June 06, 2013

Trial Record (cont.)

- Contacts
- Locations
- Sponsors
- More Information



ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Example: "Heart attack" AND "Los Angeles"

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Home > Find Studies > Search Results > Study Record Detail

Text Size

Trial record **110 of 467** for: neurosurgery

◂ Previous Study | Return to List | Next Study ▸

Proximal Protection With The MO.MA Device During Carotid Stenting (ARMOUR)

This study has been completed.

Sponsor:
Medtronic Endovascular

Information provided by:
Medtronic Endovascular

ClinicalTrials.gov Identifier:
NCT00744523

First received: August 29, 2008
Last updated: January 25, 2012
Last verified: January 2012
History of Changes

Full Text View | Tabular View | Study Results | Disclaimer | How to Read a Study Record

Results First Received: March 10, 2010

Study Type:	Interventional
Study Design:	Allocation: Non-Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Single Group Assignment; Masking: Open Label; Primary Purpose: Prevention
Conditions:	Carotid Artery Disease Stroke Prevention
Intervention:	Device: Carotid Artery Stenting with cerebral protection with the MO.MA device

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations

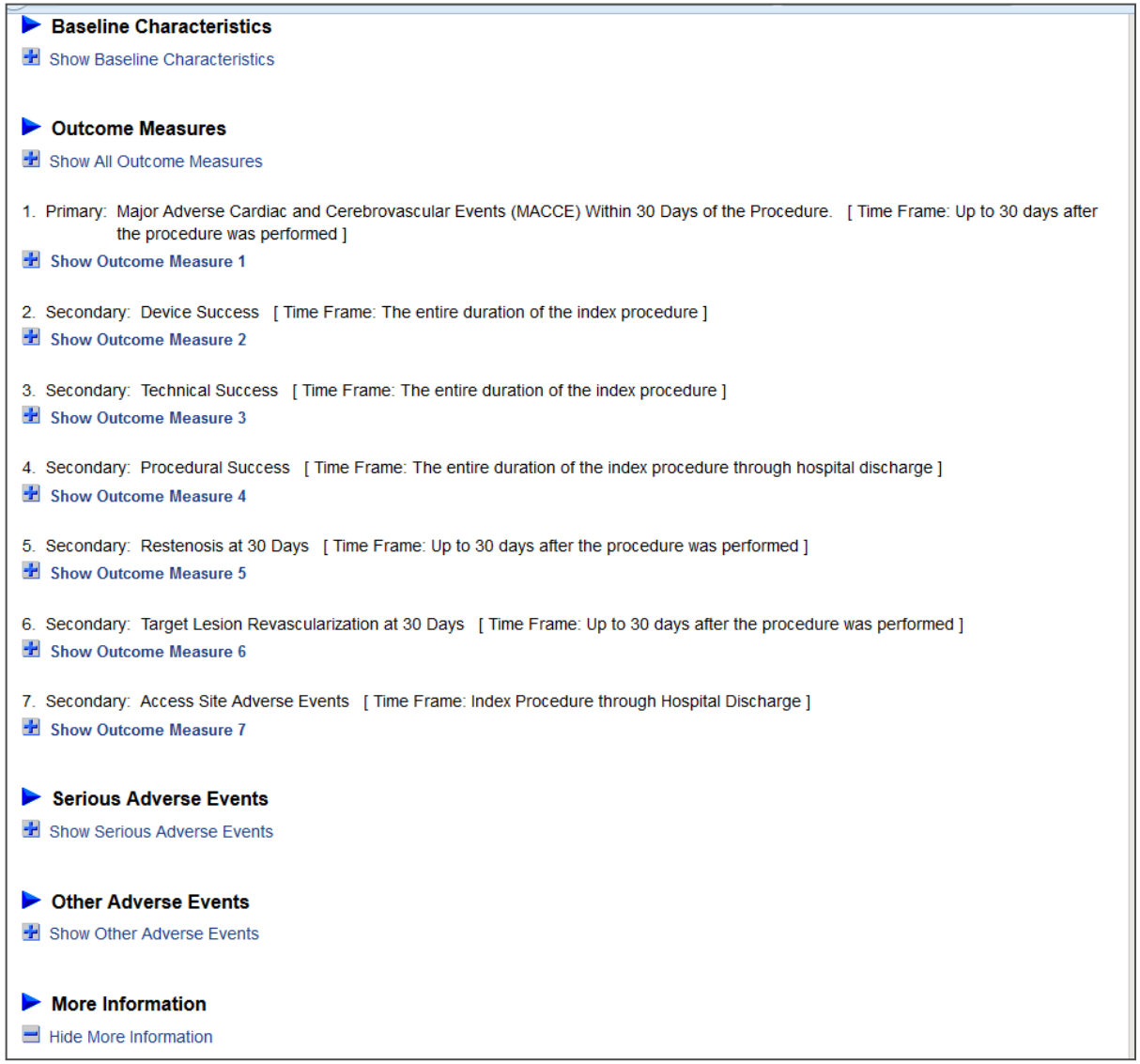
The trial was approved to enroll subjects from a maximum of 25 (combined United States [US] and Europe [EU]) medical institutions (public and academic research center hospitals). Subjects were enrolled from September 2007 to February 2009.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment

Results

- **Participant Flow**
  - **Recruitment Details**
  - **Pre-Assignment Details**
  - **Reporting Groups**



Results (cont.)

- Baseline Characteristics
- Outcome Measures
- Adverse Events
- More Information

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Index procedure through the 30 day follow-up visit.
Additional Description	No text entered.

Reporting Groups

	Description
MO.MA Roll-In Cases	All subjects who were enrolled prior to the pivotal phase of the trial at each US site. All subjects who fulfilled the eligibility criteria and were screened and enrolled to undergo carotid stenting with cerebral protection with the MO.MA proximal flow blockage cerebral protection device
MO.MA Pivotal Subjects	All subjects who fulfilled the eligibility criteria and were screened and enrolled to undergo carotid stenting with cerebral protection with the MO.MA proximal flow blockage cerebral protection device

Serious Adverse Events

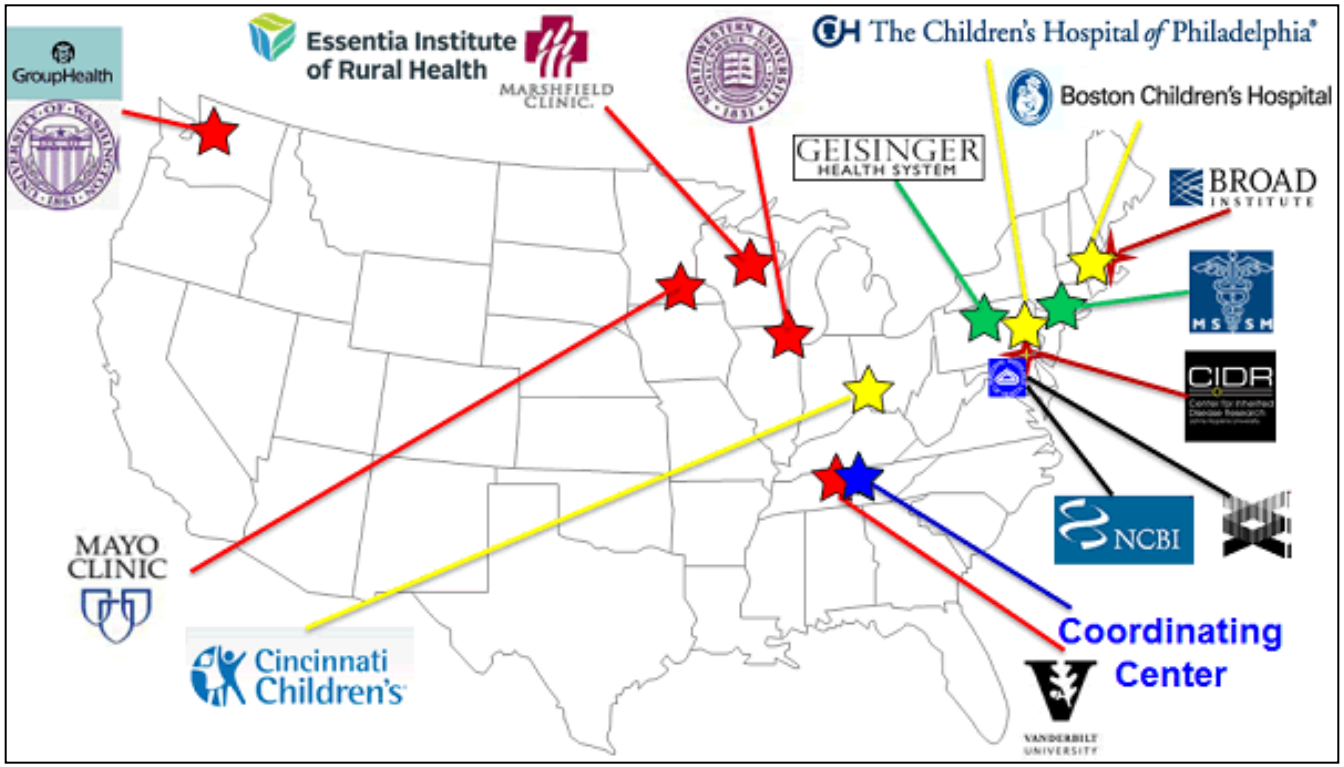
	MO.MA Roll-In Cases	MO.MA Pivotal Subjects
Total, serious adverse events		
# participants affected / at risk	11/37 (29.73%)	37/225 (16.44%)
Blood and lymphatic system disorders		
Anaemia [*1]		
# participants affected / at risk	0/0 (0.00%)	4/225 (1.78%)
# events	0	4
Coagulopathy [*1]		
# participants affected / at risk	0/0 (0.00%)	1/225 (0.44%)
# events	0	1
Cardiac disorders		
Bradycardia [*1]		
# participants affected / at risk	1/37 (2.70%)	2/225 (0.89%)
# events	1	2
Cardiac failure congestive [*1]		
# participants affected / at risk	0/0 (0.00%)	1/225 (0.44%)
# events	0	1
Cardio-respiratory arrest [*1]		
# participants affected / at risk	0/0 (0.00%)	1/225 (0.44%)
# events	0	1
Coronary artery disease [*1]		
# participants affected / at risk	0/0 (0.00%)	1/225 (0.44%)
# events	0	1

Results (cont.)

- Adverse Events

eMerge Consortium

Informatics in Action



Large-scale genomic data integrated with clinical workflow through EHR systems

http://www.genome.gov/27540473#al-2

Sharing Clinical Data

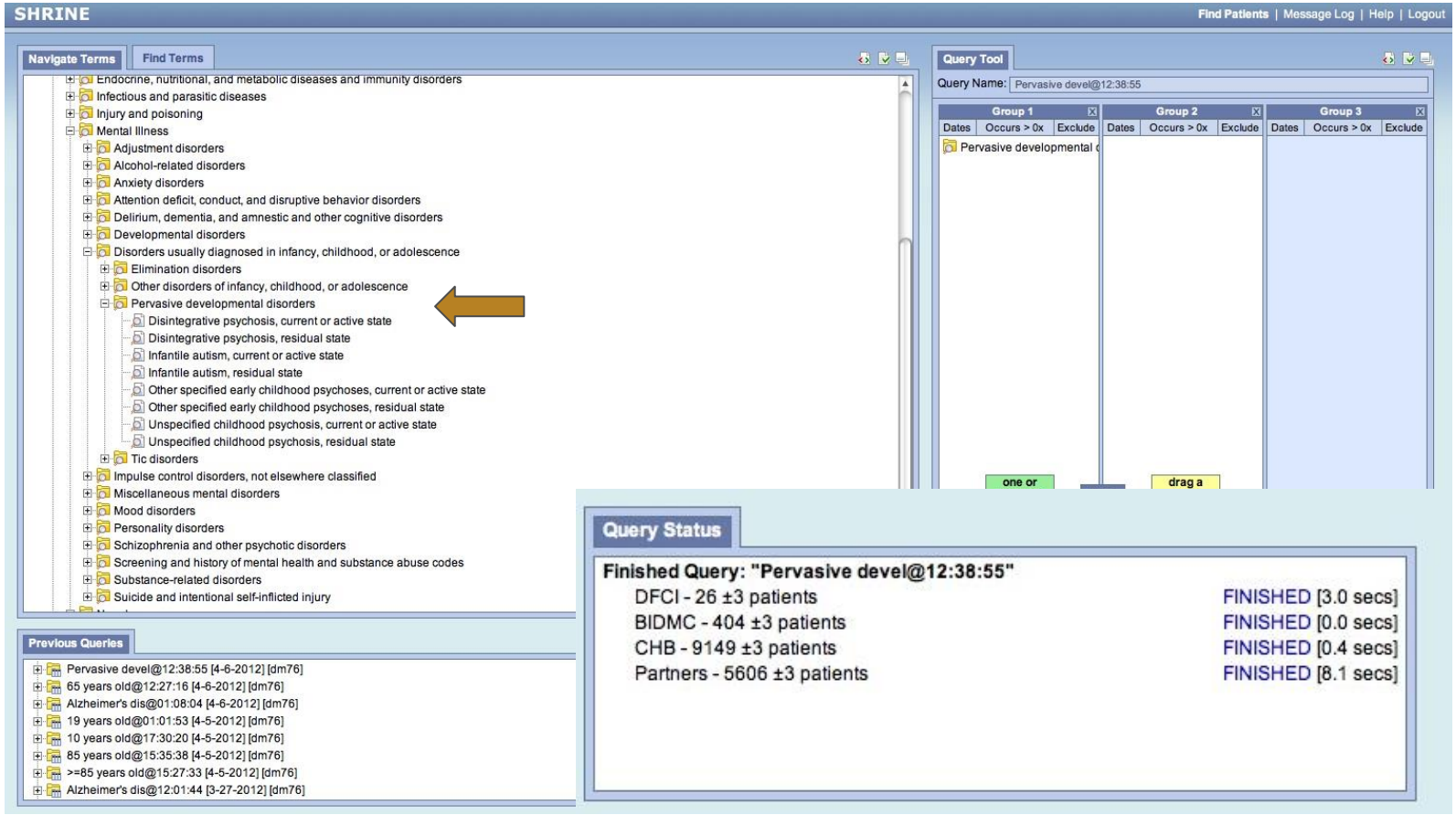
Informatics in Action

SHRINE (Shared Health Research Information Network)

- Query across multiple institutions for research purposes
- Objectives
  - Increase data set size for analysis and detection of patterns
  - Share routine clinical data – not disease specific
  - Increase pool of individuals for clinical studies
  - Demonstrate cooperation across traditionally competing institutions

http://catalyst.harvard.edu/services/shrine/

SHRINE Query Interface

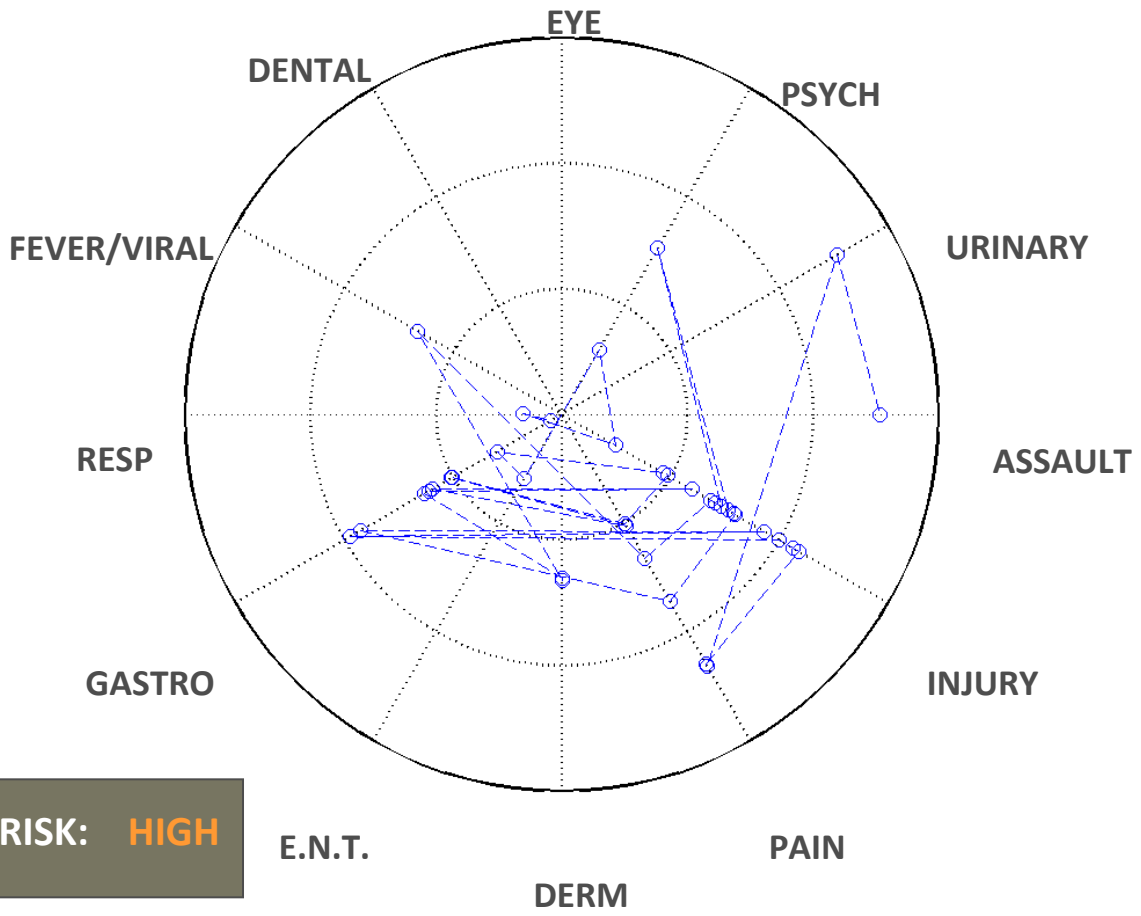


Query: What is the distribution of individuals with pervasive developmental disorders across 5 collaborating hospitals?

Electronic Health Data for Predicting Risk

Informatics in Action

Bayesian model used to predict a patient's risk of receiving a future diagnosis of abuse, based on the patient's diagnostic history.



Reis et al. BMJ 2009; Sep;339:b3677

Medicine at a Crossroads

- Petabytes of data are being collected
- Data need to be shared
- The data need to be stored, processed, filtered, visualized, integrated, and interpreted
- Social, legal, ethical, and economic issues need to be resolved