EVIDENCE OF IMPACT: CASE STUDIES AND DATA SOURCES

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National Institutes of Health
Office of Science Policy
Grappling with Research Metrics and Outcomes

Data and Informatics Working Group

Draft Report to
The Advisory Committee to the Director

June 16, 2012

Assessing the Outcomes of NIH Research Spending:
Toward a Better Approach

August 2012

Research Management at the NIH: Report on
Current Practices, Needs and Possible Next Steps
of the IT Assessment

2010

Why Invest in Biomedical Research?
How to Frame Return on Investment Analyses:
Challenges and Tools

July 16, 2010

Environmental Health Perspectives
National Institute of Environmental Health Science

Conceptual Model of Comprehensive
Research Metrics for Improved Human Health
and Environment

2008

AGENDA
October 2, 2008
October 3, 2008
Overarching Recommendation of NIH’s Scientific Management Review Board

*Take a more coordinated and systematic approach to both better capture and communicate the value of NIH’s investments*
Specific Recommendations of NIH’s Scientific Management Review Board

- Develop **strategies to support or conduct assessments** of value, including through grants or contracts with external experts
- Seek **input from external experts** in the development of methods and tools to improve assessments of the value of biomedical research
- Adopt a **systematic approach to designing case studies** that can both illustrate the research process and illuminate the outcomes
- Determine a **process for strategically selecting study topics** that map to a conceptual framework including different translational pathways
- Oversee NIH efforts to **strengthen data** needed for assessing value
- Identify **promising analytical approaches**
Variety of Purposes and Audiences for Case Studies

- For the public:
  » Communicating complexity of scientific process
  » Providing accountability for NIH’s investments

- For NIH:
  » Understanding our outcomes
  » Identifying policy levers and strategies worth repeating
Case Study Features

1. Combine narrative with numbers to produce stories of impact with a strong data backbone

2. Trace the chain of evidence between scientific discoveries to impact

3. Identify diverse types of impacts, but privilege evidence of health impacts

4. Document data sources and identify “high value” data

5. Provide clear attribution by describing the contributions of NIH and other players in the biomedical enterprise
Investment by NIH & Others

- Identification of public health need and scientific opportunity
- Research initiatives
- Funding acknowledgments
- Funding amount (when feasible)

Research-to-Practice Milestones → Timeline

- Publications (basic to applied)
- Patents
- Industry licenses and development activities
- FDA approvals
- Clinical practice guidelines and recommendations
- Evidence of hand-off

Organized by Stream of Impact

- Health
- Knowledge
- Society
Impacts

**Society**
- Cost savings from improved interventions and health outcomes
- Industry/commercial activity from medical products and technologies
- New businesses/start-ups created

**Health**
- Number of people treated
- Lives saved
- Quality of life improvements
- Influence on follow-on FDA approvals, practice guidelines, health policy and services, etc.

**Science & Knowledge**
- Growth/emergence of new fields
- “Spillovers” to other lines of research
- Increased methodological and technological capabilities
- Award-winning work (Nobels, Laskers, *Science*’s top discoveries)
Case Study Topics

- Gleevec and molecular medicine
- Haemophilus influenzae Type B (Hib) vaccine
- Neurostimulation technologies: Past, Present, and Future
- Framingham Heart Study
Gleevec: A game-changing cancer treatment

- Gleevec is a kinase inhibitor approved in 2001 to treat Chronic Myelogenous Leukemia (CML)
- One of the first targeted, molecular-based cancer treatments

**THEN**

- In the 1950s, new techniques to study cells and the chromosomes within them were just starting to be developed; researchers began linking chromosomal abnormalities to specific human diseases.
- Until the 1990s, medications to treat cancer were limited to non-specific chemotherapy that killed many healthy cells in addition to cancerous cells.\(^1\)
- The standard chemotherapy treatment for CML was not very effective and could cause serious side effects.
- Industry had little incentive to invest in therapeutic development for rare diseases.

**The five-year survival rate for CML patients was less than 30%**.\(^1\)
**RESEARCH-TO-PRACTICE MILESTONES FOR GLEEVEC®**

For more information on the supporting evidence and research sponsors for the following milestones, see the Web appendix table.

**IDENTIFYING THE MOLECULAR TRIGGER OF CML (1914-1990)**

- **1914**
  - Biologist Theodor Boveri first had the idea that chromosomal abnormalities might play a role in tumor development, but no tools existed at that time to test his hypothesis.5

**DEVELOPING A TARGETED BCR-ABL KINASE INHIBITOR (1990-1996)**

- **1990**
  - NIH-funded researcher Dr. Brian Druker began developing model systems to study BCR-ABL kinase signaling and explore ways to inhibit it.15

- **1992**
  - Imatinib, the compound that would become Gleevec®, was first created, as part of a larger collection of compounds to test.17

**TESTING AND APPROVING A LIFE-CHANGING DRUG (1997-2015)**

- **1996**
  - Imatinib (Gleevec®) was shown to kill cancerous cells without harming healthy ones by blocking BCR-ABL kinase signaling.8

- **1997**
  - The FDA and Drug Administration Modernization Act® allowed the FDA to create a “Fast Track” mechanism that makes important new drugs available to patients more quickly.21

- **2001**
  - FDA granted “Fast Track” designation for Gleevec®, speeding up the review process because Gleevec® treated a serious condition with no known cure. FDA approved it only 10 weeks after the New Drug Application was submitted by Novartis.20

- **2006**
  - A follow-up clinical study found that after five years of continuous treatment, the vast majority of CML patients receiving Gleevec® remained cancer-free.24

**SCHEMATIC OF THE PHILADELPHIA CHROMOSOME FORMATION**

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- NIH indicates NIH-funded milestones
Health Impacts

CML Survival Rates Increased Dramatically after the Introduction of Gleevec®

Source: National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) Database

Source: Published literature (PubMed)

Five-year survival rates for CML patients treated with Gleevec® currently top 89%. 28
Knowledge Impacts

- First-in-class drug
- Stimulated an ongoing surge of new research
- 39 drugs targeting different kinds of kinases had been approved by the FDA

Source: Commentaries in published literature (PubMed)

Source: Manually compiled from FDA Center for Drug Evaluation and Research (CDER) data
Societal Impacts

- More than 15 major pharmaceutical companies have now pursued kinases as viable targets.

By the late 2000s, more than 100,000 CML patients worldwide had been treated with Gleevec®.

Source: Manually compiled from FDA Center for Drug Evaluation and Research (CDER) data

Source: Commentary in published literature
Lots of data – lots of sources

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Lessons Learned About the Data

• It is rarely feasible to estimate NIH’s dollar investment – influence of pivotal basic research is typically too diffuse to quantify

• Data blind spots: healthcare utilization, health statistics, and cost-effectiveness measures

• High need for comprehensive & structured Federal data
  » FDA metadata including citations in approval packages & clinical trials
  » AHRQ: national guidelines clearinghouse & evidence reports
  » FDA Orange Book; USPTO data (patent and non-patent references)
  » CMS healthcare utilization data; electronic health record data

• Linking “high-value” datasets to NIH grants
  » NIH Office of Extramural Research (OER) and Office of Portfolio Analysis (OPA)

• Sophisticated data aggregators could help semi-automate the process of identifying inputs, outputs, and impacts (e.g., OER’s ReTRACE tool)
Case Study Contributors

• **Gleevec and molecular medicine:**
  » OSP: Peter Reczek (Lead), Elizabeth Baden, Kristine Alexander, Laura Rosema, & Allison Lea
  » NCI: Jim Corrigan, Tracy Lively, Karen Parker, Maeva May
  » NIH Library: Josh Duberman

• **Hib vaccine:**
  » OSP: David Kosub (Lead)
  » NICHD: Sarah Glavin, Gitanjali Taneja
  » NIAID: Steve Zoha, Marie Parker, Jane Luckmuller, David Morens
  » NIH Office of History: Barbara Faye Harkins

• **Neurostimulation technologies:**
  » OSP: David Bochner (Lead)
  » NIDCD: Buck Wong, Laura Cole
  » NIBIB: Christine Cooper
  » NINDS: Paul Scott, Amy Adams, Ling Wong
  » NEI: Grace Shen, Matt Steinmetz, Dan Stimson
  » NIMH: Meredith Fox, Julie Frost Bellgowan

• **Framingham Heart Study (In Progress):**
  » OSP: Kristine Alexander, Joel Baumgart (Leads)
  » NHLBI: Paul Sorlie, Phyliss Sholinsky, Gina Wei, Sean Coady, Gaya Dowling
  » NIH Library: Chris Belter
Additional Resources

Learn more about the Office of Science Policy from our blog “Under the Poliscope”

http://osp.od.nih.gov/under-the-poliscope
Additional Resources

• For General Inquiries:
  SciencePolicy@od.nih.gov

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