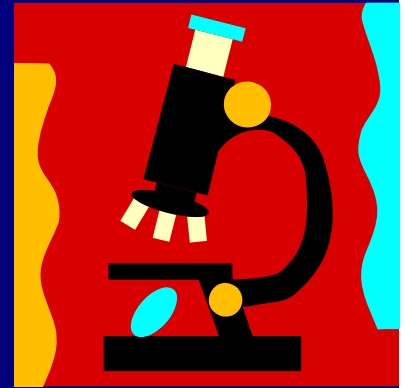


Sharing Best Practices in R&D Statistics: Focus on Health Research



Eric Buehrens
Executive Vice President and
Chief Operating Officer,
Beth Israel Deaconess Medical
Center, Boston

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Contents

- **Research Funding in the US**
- **Beth Israel Deaconess Medical Center and Harvard Medical School**
- **Research Overview**
- **How is Clinical & Translational Research Funded?**
- **Research Statistics for Hospital Management**



Who Funds Biomedical Research in the U.S.?

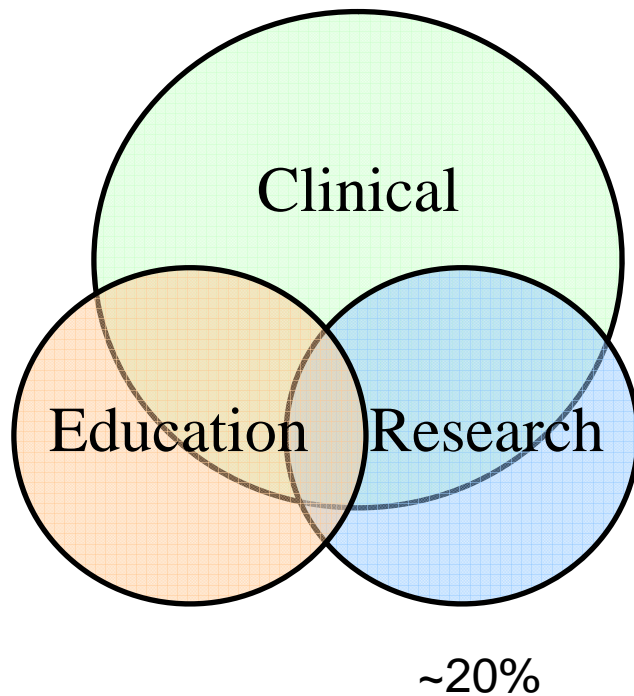
Industry*	\$ 74.8B
Federal Gov't	\$ 38.6B
NIH	\$ 29.3B
Other**	\$ 17.1B
Total	\$130.5B

* Pharma, Biotech, Devices

**Universities, States, Foundations

\$130B represents 5.5% of the \$2.4T spent on health
in the US in 2008

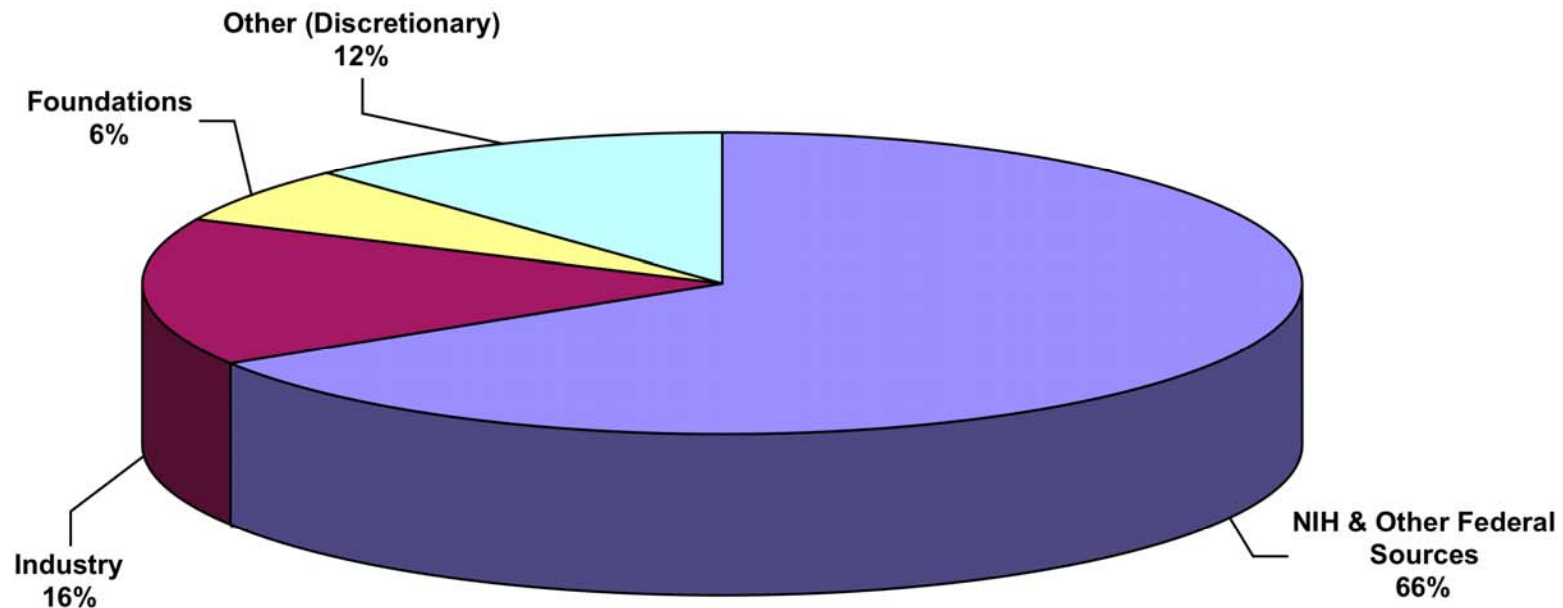
BIDMC's 3-Part Mission



The research mission of Beth Israel Deaconess Medical Center is to be a *world-class research institution* where *outstanding scientists* work to develop new knowledge for the *betterment of the health* of our local and extended communities. The research program strives to be renowned for its bench-to-bedside model of *translational research*, and for its *collaboration with industry* as a pathway for transferring the fruits of research into products that *improve the quality of life*.

Key BIDMC Research Statistics

\$225M in total research funding (18% of revenue)
4th in independent research hospitals nationwide



Approximately 10% of research activity is clinical research



Key BIDMC Research Statistics

- 1500 active & ongoing human research protocols
- Human subjects research program accredited by AAHRPP
- 350 active & ongoing animal research protocols
- Animal research program accredited by AAALAC
- 400,000 sf of research space
- 250 key principal investigators, 1600 other research staff



How the Harvard Model Differs

- U.S. research funding is typically awarded to and administered by universities and medical schools, not hospitals.
- In the Harvard Medical School system, hospitals are free-standing, financially independent entities that “own” and manage their own research portfolios, in addition to that of the medical school.
- Total funding = \$2.1B, hospitals = \$1.8B



Types of Research

- Basic – “Bench” or “Wet Lab” – Understanding fundamental functions of biology: clone a gene, study cell signaling, protein-to-protein interactions; yeast, fruit flies, mice
- Translational – “Bench-to-Bedside” – moving basic scientific discoveries from the lab to the patient care arena; mice, human tissue, diagnostic markers
- Clinical – Human Subjects – test a new drug or device, or a hypothesis about why a certain disease occurs; trial phases 1, 2 & 3
- Dry Lab - Epidemiology / Population Studies (distribution and determinates of disease and health in community cohorts) or Health Services Research



How is clinical & translational research funded?

- Federal (NIH)

- ☐ Favorable support of overhead @ $\pm 72\%$ of direct cost

- Industry – sponsored trials

- ☐ Often least restrictive, most comprehensive
- ☐ Conflict of Interest is closely regulated



How is clinical & translational research funded?

- Foundations (American Cancer, Juvenile Diabetes, etc.)
 - Often disease-specific
 - Poor support for institutional overhead (0-20%)
- Philanthropy – families and “grateful patients”
 - Large fraction of hospital fundraising



Research Statistics for Hospital Management

- Total Direct Research Revenue / year
- Overhead Cost Recovery rate
 - Varies widely by funding source
- $\text{Total \$} \times \text{OH \%} = \underline{\text{total indirect revenue}}$
- “Payer Mix” or ratio of funding from different sources
- “Portfolio Mix” or ratio of research enterprise devoted to bench, clinical, translational or “dry” research



Research Statistics for Hospital Management

- Our hospital aims to recover the direct cost of research through OH payments
 - Not non-research OH, not faculty recruitment
- Still leaves $\pm 20 - 30\%$ of total research costs unrecovered and subsidized by hospital clinical revenues
 - $\$225\text{M} \times 20\% = \$45 \text{ million / year}$



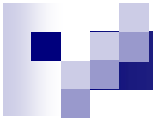
Research Statistics for Hospital Management

- Direct research cost = space occupancy cost + research admin cost
- $\text{Space \$} + \text{admin \$} \div \text{assigned sq. feet} = \text{"dollar density"}$
- Current enterprise target is $\pm \$212 / \text{NASF}$ or $\text{€}1844 / \text{meter}^2$
- Managed across enterprise, by dept.
- "Your money or your space!"



Lessons & Challenges

- Clinical & translational research requires an “ecosystem” of funding, institutional support, regulation and training
- Financial & resource management is important
- Bench scientists & physicians need training to be effective
- US system will be challenged by healthcare reform



End

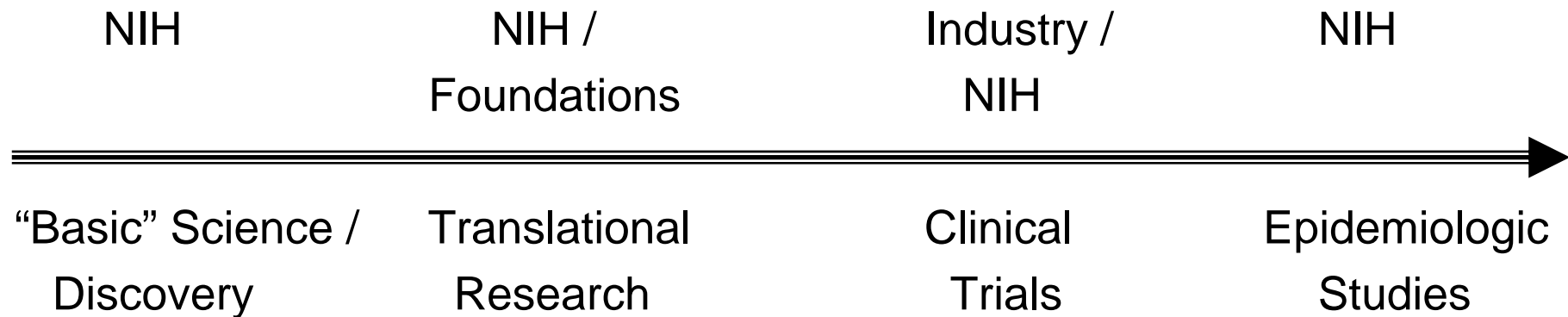


Preclinical science and translational medicine are different

■ *Extrinsic challenges*

- ☐ Not well-funded
- ☐ Lack of well-trained personnel
- ☐ Academic promotion policies lacking for those in translational research
- ☐ Availability of reagents to use in humans

The Research Continuum and IP Capture



Intellectual Property





Preclinical science and translational medicine are different

■ *Intrinsic challenges*

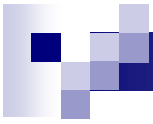
- Translation is not just an extrapolation to humans: humans and mice differ: outbred nature of population; different biology; humans can report events not typically sampled in a mouse
- Practical issues: difficult to access human tissue
- Demands on protocol design, management, etc;
- Long experimental times and expense
- Regulatory issues
- Conflicts of Interest
- Patient rights

(modified from Steinman and Mellman: Science 2004; Pober et al FASEB J 2001; Zerhouni 2005)



Why does translational medicine have to be interdisciplinary?

- No one entity or person has the necessary expertise!
 - Basic science, clinical medicine, technology (engineering and physics), regulatory issues, ethical, etc...
- Therefore
 - Many barriers to be overcome: organizational, cultural, physical, technological, language, IP sharing
 - Training and mentorship is more difficult





Why now?

First time in human history that biology and medicine are becoming information rich...the convergence of two “events”



Genomics Revolution

IT Revolution

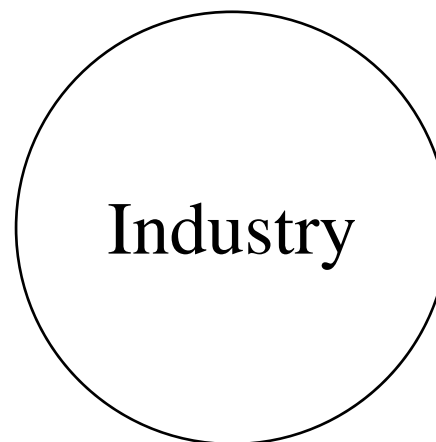
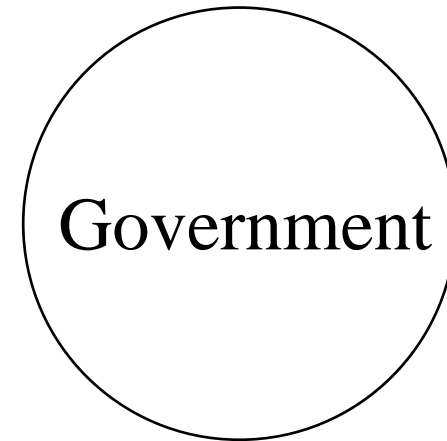
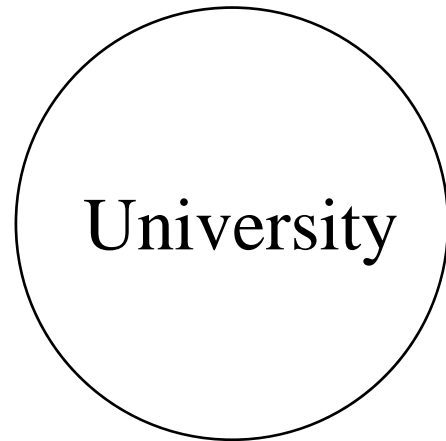
...plus some technologies

Technology Platforms:
Imaging
Genomics
Proteomics
RNAi

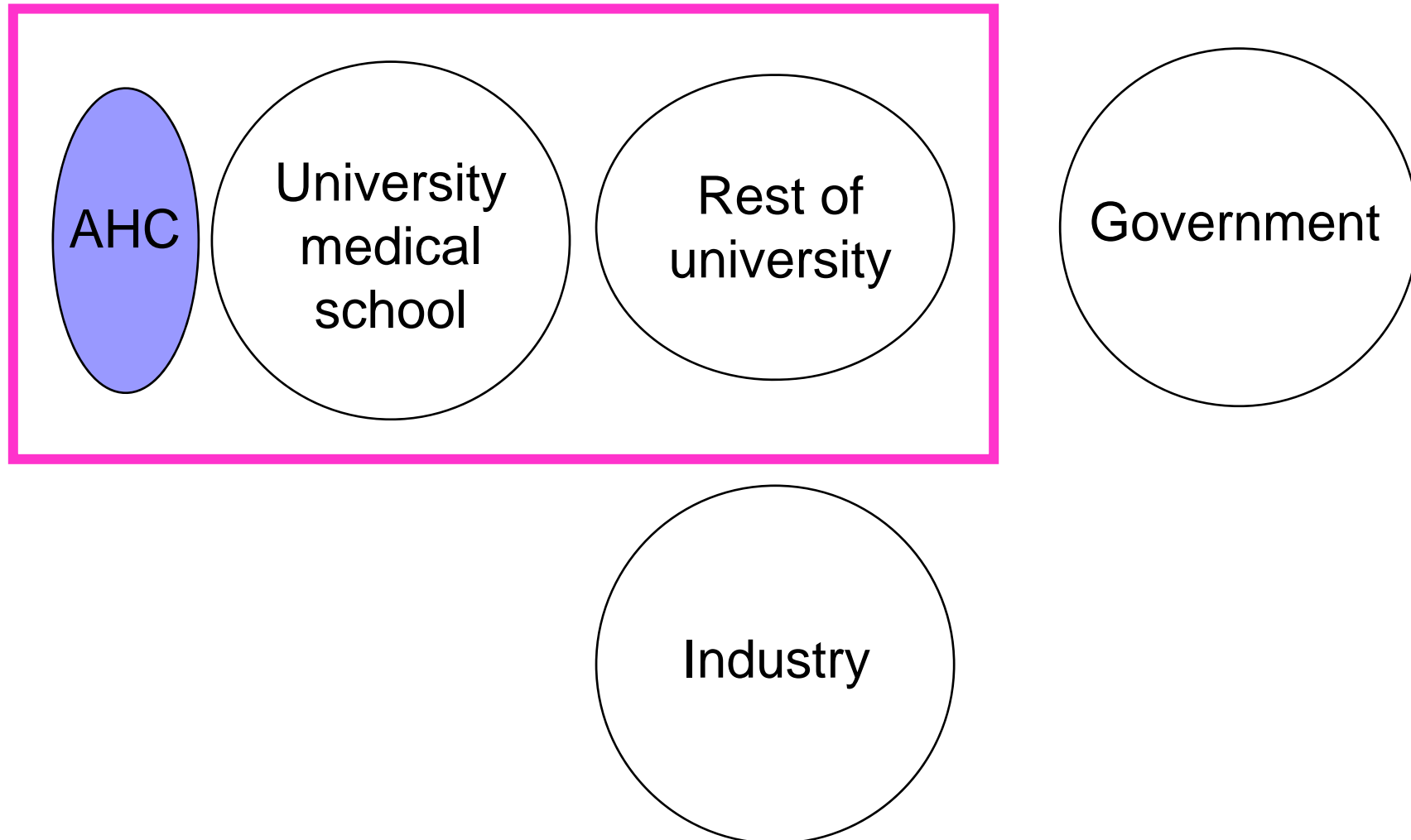
And sophisticated mathematical tools...



The players...



An academic health center (AHC) is key location for implementation





Why do this in an AHC?

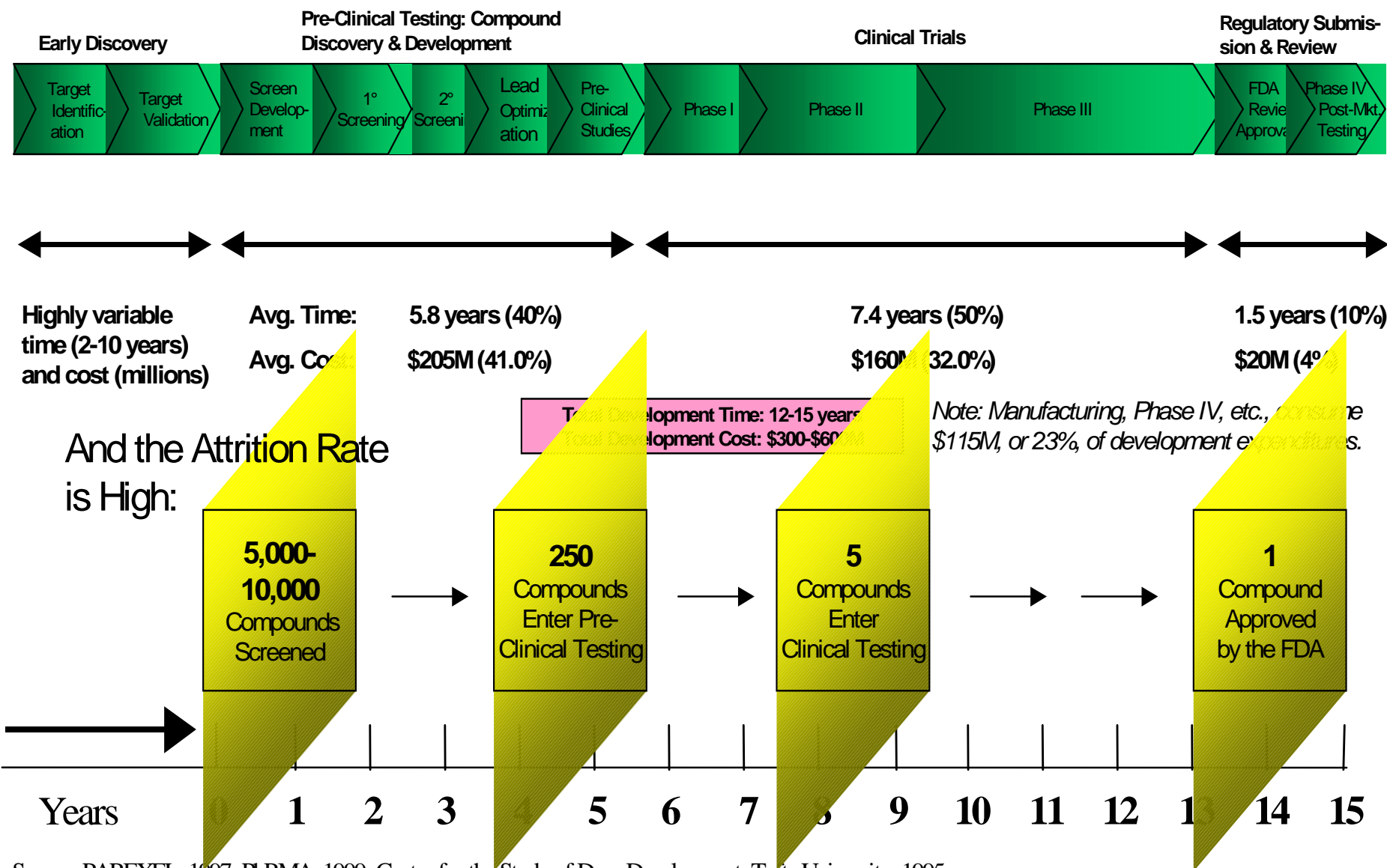
- Core **mission** – bring the benefit of scientific discoveries to patients
- Core **asset**: access to patient clinical information and to human specimens
- To attract patients - as a **differentiation tool** from other medical care providers
- Can take the **long view and can focus on unmet needs**, in contrast to industry
- **Return on investment** – if strategically focused in areas of clinical and basic science strength



What are the outcomes of translational medicine?

- ☐ Better **understanding** of disease pathophysiology
- ☐ Development of **new markers** for disease prediction, diagnosis, prognosis, and monitoring of efficacy and toxicity
- ☐ **New drugs**
- ☐ **New devices**

DRUG DEVELOPMENT IS INEFFICIENT: LENGTHY and COSTLY ...AND IT PUTS TOO MANY PATIENTS AT RISK!



Source: PAREXEL, 1997; PhRMA, 1999; Center for the Study of Drug Development, Tufts University, 1995.



Outcomes of translational medicine (con't)

- **New technologies** for improving the efficiency of the drug development process through
 - More “informative” clinical trials:
personalizing medicine: right drug at the right dose for the right patient at the right time...patient stratification
 - Novel readouts for monitoring therapy:
e.g. is a drug hitting its intended target, early markers for efficacy or relapse, etc.



How is Government Trying to Help?

- Re-engineered the national clinical research enterprise via the creation of the Clinical and Translational Science Awards (CTSA)
- A national consortium of medical research institutions working together to improve the way biomedical research is conducted nationwide. Consortium members share a common vision to reduce the time for laboratory discoveries to become treatments, to engage communities in clinical research efforts and to train clinical and translational researchers.
- Now includes 46 medical institutes across 26 states.



How is Government Trying to Help?

- 15 June 2010 New England Journal of Medicine article by Francis Collins, NIH Director and Margaret Hamburg, FDA Commissioner
- The NIH and the FDA will develop a more integrated pathway that connects all the steps between the identification of a potential therapeutic target by academic researchers and the approval of a therapy for clinical use. This pathway will include NIH-supported centers where researchers can screen thousands of chemicals to find potential drug candidates, as well as public–private partnerships to help move candidate compounds into commercial development.



Harvard Catalyst (CTSA)

- A shared enterprise of Harvard University, its ten schools and its eighteen Academic Healthcare Centers (AHC), as well as the Boston College School of Nursing, MIT, the Cambridge Health Alliance, Harvard Pilgrim Health Care and numerous community partners.
- Founded in May 2008 with a five year, \$117.5 million grant from the National Institutes of Health (Clinical and Translational Science Center) and \$75 million dollars from Harvard and its affiliates.
- Resources of the Harvard Catalyst are available to all faculties at Harvard regardless of their institutional affiliation or academic degree.



How BIDMC and HMS are Training the Next Generation

- KL2 Medical Research Investigator Training (MeRIT) Program
- Scholars in Clinical Science
- Clinical Investigator Training Program (CITP)
- International Translational Medicine Scholars Program



CITP: Summary

- Master's level program in clinical and translational investigation at Harvard Medical School
 - Funded through a partnership with Pfizer since 1993.
 - Master's Degree in Medical Science approved in 1997
 - Merck joined the program in 2004 as an additional partner.



CITP: Summary

- Provides the environment and the tools to facilitate the successful transition of senior fellows/junior faculty MDs to independent investigators pursuing careers in translational research
 - Focus on the laboratory/clinical interface (small “n” sample size)
 - Proof of concept
 - Concentration on utilizing technology appropriately to advance knowledge in disease states and/or developing measurement techniques that will facilitate drug discovery and drug development
 - “bench to bedside” and as importantly “bedside to bench”



Four Components of the CITP Educational Experience

- Intensive summer courses in biostatistics and study design
- Clinical Pharmacology course
- Weekly seminars in topics relevant to clinical investigation and translational research
- Mentor-based Research project



Differentiating CITP from Other Training Programs

- Integrated curriculum
 - Efficient (does not unduly extend years of training)
 - Allows fellows to work on projects while being presented with didactic material in seminars
 - Has sufficient academic rigor and requirements
 - Emphasizes integration of technology and outcome measurements



Differentiating CITP from Other Training Programs

- Preselected project and mentor
 - Improves likelihood of success with known mentor and guaranteed funding
- Funding
 - Salary support relieves burden on fellow and department
 - Training period a bridge toward independence



Measures of Success

147 graduates at academic medical centers, industry and regulatory agencies around the world:

- ☐ 2 Associate Directors of Program
- ☐ 1 GCRC Program Director
- ☐ Multiple Department Chairs.
- ☐ 11 graduates hold positions in industry
- ☐ Graduates in 10 countries



Select Translational Research Efforts at BIDMC

- Immune Tolerance Network (Turka)
 - A non-profit, government-funded clinical research consortium of researchers working together to establish new treatments for diseases of the immune system.
- The Co-Clinical Project: Informing clinical trials using preclinical mouse models (Pandolfi)
 - Mice receiving treatment in tandem with humans, in the hope that what is learned at the bedside can be integrated with results from the lab bench to speed up and streamline the development of cancer drugs.