

# Careers in Clinical Trials and Epidemiology

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## Conflicts Relevant to this Presentation

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



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# Careers in Clinical Trials and Epidemiology

- **Why clinical research (trials, epi, outcomes)**
- **Career options/opportunities**
- **Training/mentorship**
- **Funding, \$\$, and COI issues**
- **Balance**



# **Why a Career in Cardiovascular Clinical Investigation?**

- **Heart disease globally increasing as population ages**
- **Medicare not sustainable in current form**
- **Promise of genomic advances is slow in translating into important new therapeutics**
- **Personalized medicine is obviously needed but surprisingly elusive**
- **Clinical research is increasingly complex, expensive, and difficult to integrate into clinical care**
- **Enormous gap between new knowledge and practice of medicine**



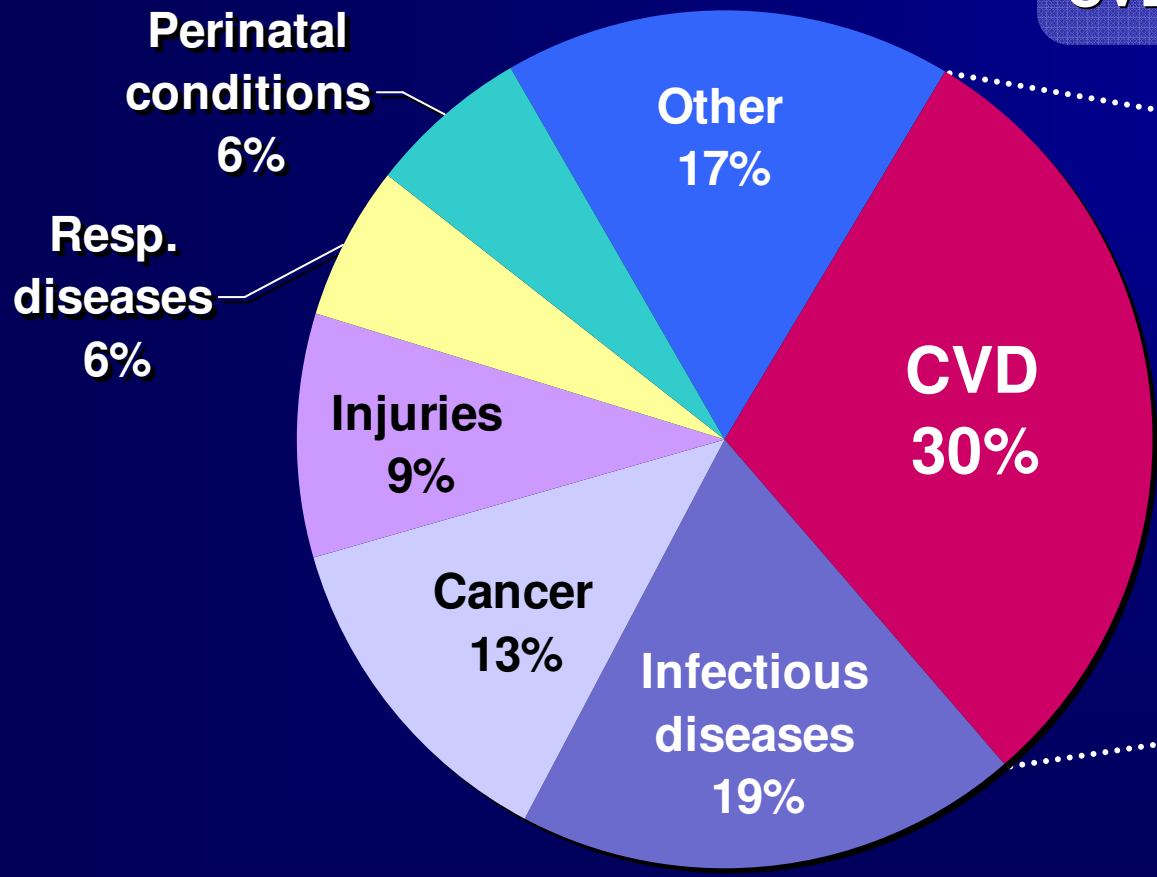
# Societal Forces Promoting Need for Evidence in Medicine

- Clinicians-Patients
  - Relationship between EBM and outcomes
- Marketing and labeling—FDA
  - Proving efficacy and safety
- Reimbursement—CMS, Major Insurers
  - Pay for Performance (Quality)
- Practice Guidelines—Performance Indicators
  - Role of professional societies

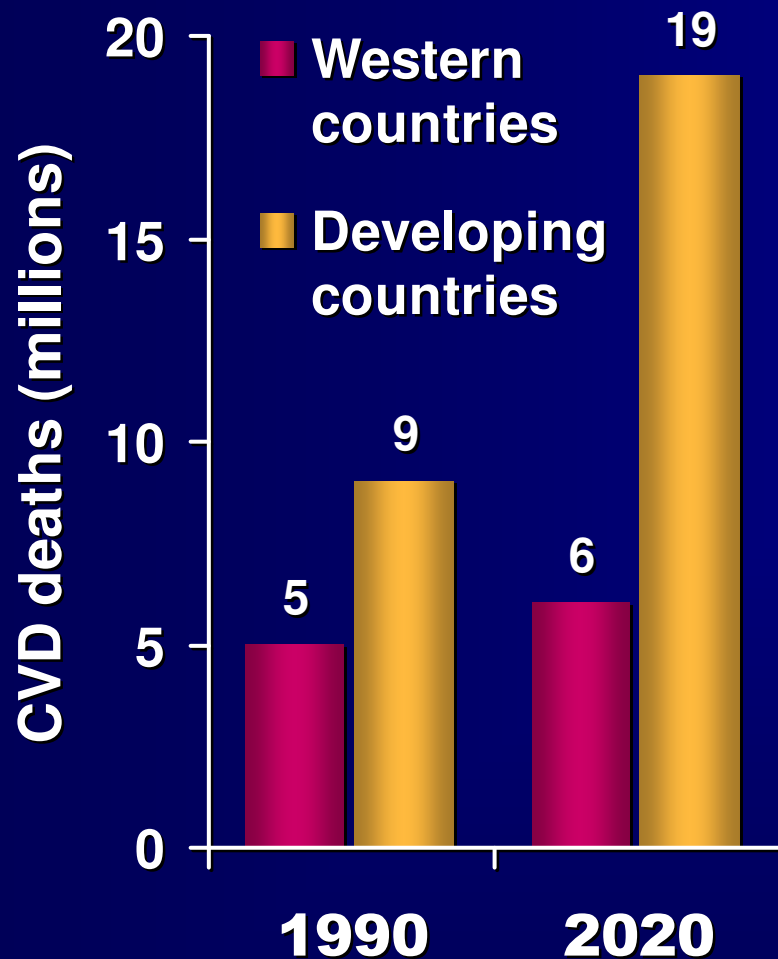


# CVD—A Global Epidemic

**2002**  
World pop.: ~6.12 billion  
Deaths: 56.6 million  
CVD deaths: 16.6 million



## Global Epidemic of CVD



**1990:** 25% of all deaths were from CVD.

**2020:** 40% of all deaths will be from CVD.

**In developing countries, MI and CVD deaths occur 10–20 years earlier.**

- CVD deaths < 70 y.o. in developing countries: 50%
- CVD deaths < 70 y.o. in Western countries: 20%



# Guidelines: Weighing the Evidence

- **Weight of evidence grades:**

**A** = Data from many randomized clinical trials

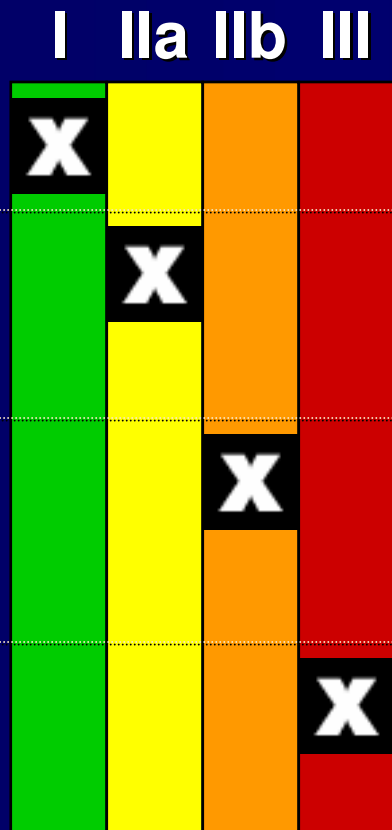
**B** = Data from single randomized trial or nonrandomized studies

**C** = Expert consensus





# Guidelines: Classes of Recommendation



**Intervention is useful and effective**

**Evidence conflicts/opinions differ but lean towards efficacy**

**Evidence conflicts/opinions differ but lean against efficacy**

**Intervention is not useful/effective and may be harmful**



CORRESPONDENCE



Rofecoxib, Merck, and the FDA

**Failing the Public Health — Rofecoxib, Merck, and the FDA**

Eric J. Topol, M.D.

**Raising the Safety Bar — The FDA's Coxib Meeting**

Susan Okie, M.D.

Analysis of 14 Trials Comparing Sirolimus-Eluting Stents with Bare-Metal Stents

Christ  
Mauriz  
Dietri

## Unanswered Questions — Drug-Eluting Stents and the Risk of Late Thrombosis

William H. Maisel, M.D., M.P.H.

Safety and Efficacy of Sirolimus-

**New  
England  
Journal of  
Medicine**

- Randomized trials of DES (for single simple lesions, stable patients) show less restenosis, a small (borderline significant) excess of late thrombosis, and no increase in death or MI
- Registries show increased late death, perhaps related to stopping clopidogrel
- Overall evidence suggests benefits outweigh risks for “on-label” use, and clopidogrel out to (at least) one year seems prudent

Christian Spaulding, M.D., Joost Daemen, M.D., Eric Boersma, Ph.D., Donald E. Cutlip, M.D., and Patrick W. Serruys, M.D., Ph.D.



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# JAMA

## May 14, 2007

- **“Off-label” use in 50-70% of DES cases and associated with about twice the risk of adverse events**
  - Observational data – but adjusted
- **Absolute risk is uncertain**
  - No randomized trials yet
  - Certain types of lesions and patients limited experience with BMS (L main, Bifurcation, ostial, multivessel CAD, etc)

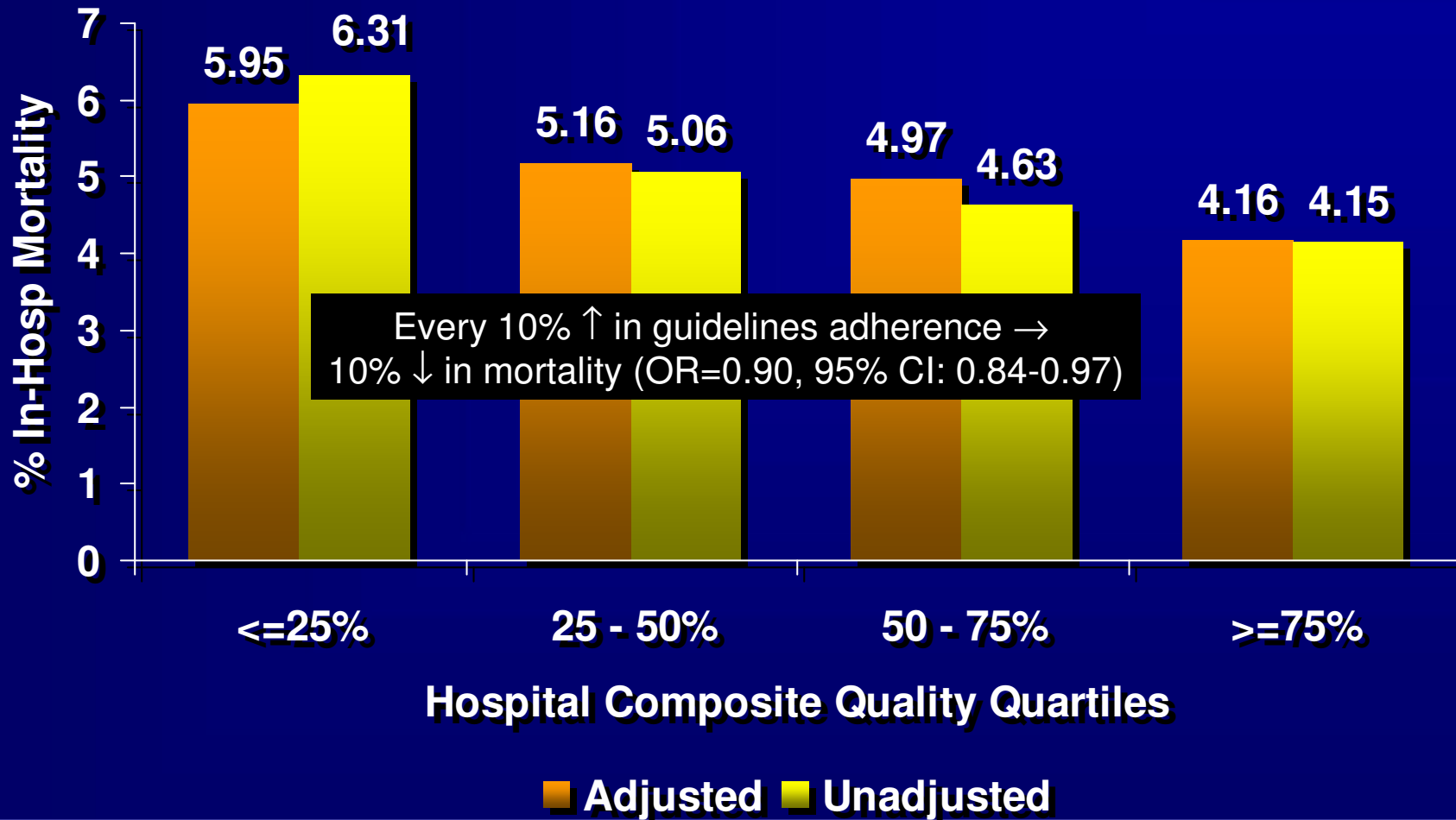
E. Magnus Ohman, MD

to detect events of rare frequency (usually less than 10%—as





# Hospital Link Between Overall Guidelines Adherence and Mortality



# CMS Pay For Performance (Quality) Pilot

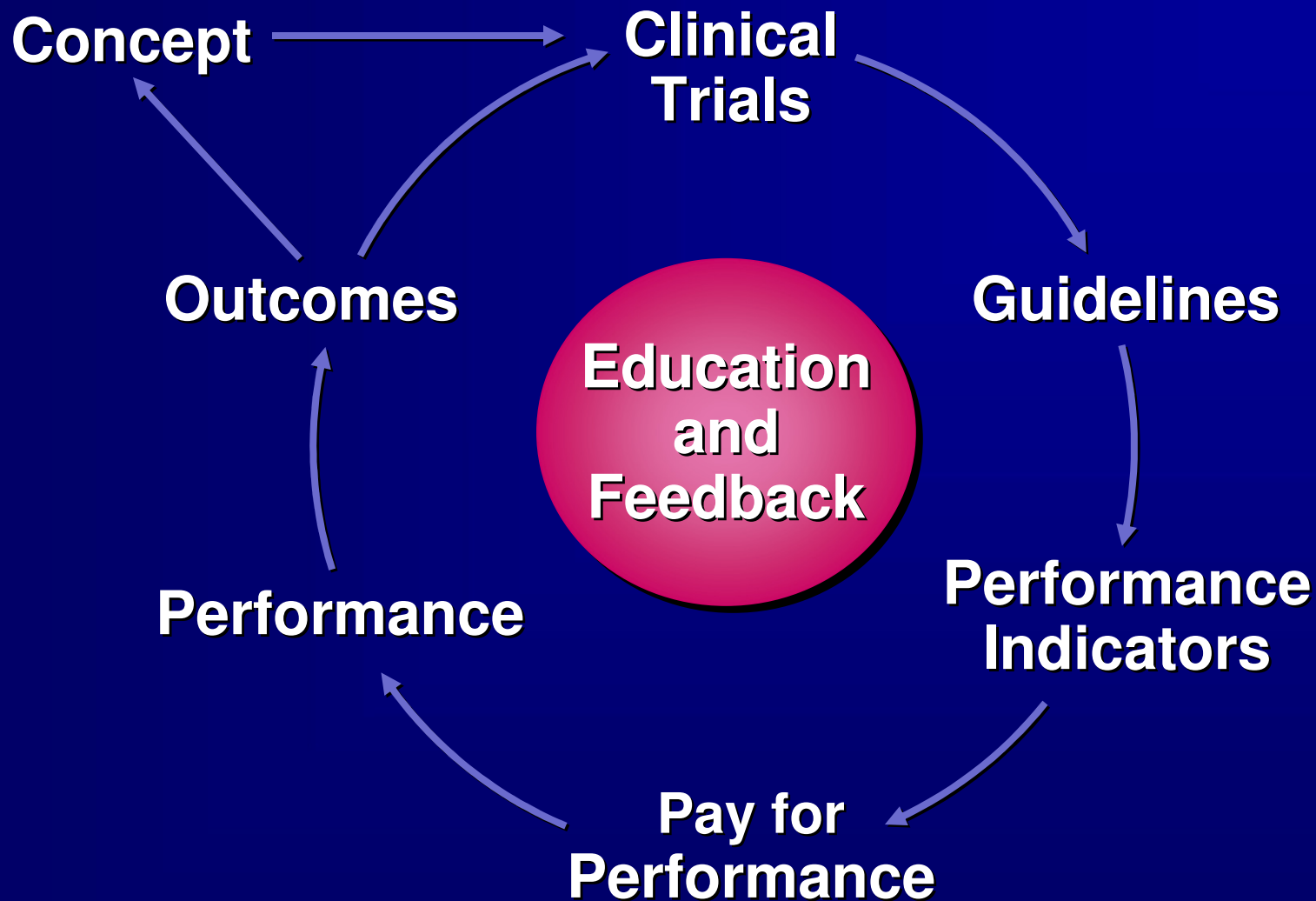
- CMS announced new pilot program to “pay for quality”
- 400 PREMIER hospitals
- 5 initial conditions (MI, CABG, CHF, pneumonia, hip/knee replacement)
- 35 health plans covering more than 30 million US patients have programs tying performance with bonus payments
- Mark McClellan, CMS Director, suggests that Pay for Performance based compensation will account for 20-30% of physician compensation in the next 5+ years

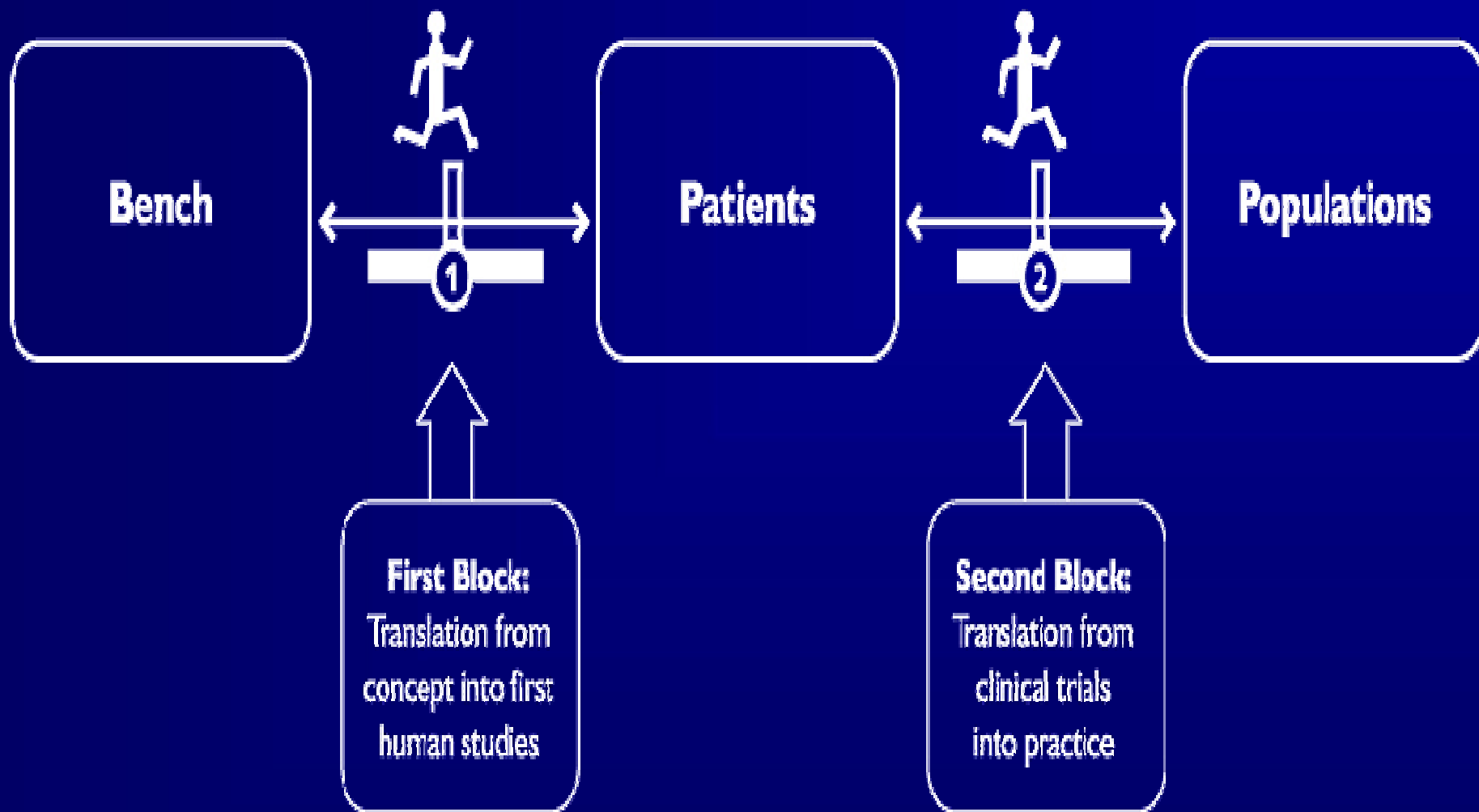
*-USA Today, July 11, 2003*

*-Wall Street Journal Sept 17, 2004*



# The Cycle of Clinical Therapeutics—New Model







## Six Medical Therapies Proven to Reduce Death

Therapy	Indication	# pts	Reduction in deaths		
			Relative	Absolute	C/E
Aspirin	MI	18,773	23%	2.4%	+++++
Fibrinolytics	MI	58,000	18%	1.8%	++++
Beta blocker	MI	28,970	13%	1.3%	++++
ACE inhibitor	MI	101,000	6.5%	.6%	+
Aspirin	2nd prev	54,360	15%	1.2%	+++++
Beta blocker	2nd prev	20,312	21%	2.1%	++++
Statins	2nd prev	17,617	23%	2.7%	++++
ACE inhibitor	2nd prev	9,297	17%	1.9%	++++
ACE inhibitor	CHF	7,105	23%	6.1%	+++++
Beta blocker	CHF	12,385	26%	4%	+++++
Spirolactone	CHF	1,663	30%	11%	+++++

*-Adapted from Granger CB and McMurray JJV. JACC 48:434;2006*

# The Clinical Researcher— An “Emerging” Species

Ralph Snyder

**T**HIS

chemistry,

physics, and microbiology provided the potential to trans-

form medi-

unscientific

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diseases at

**The discrepancy between current medical practice and the capabilities for improvement is greater now than at any time since the early part of the last century.**

**Through coordinated efforts, the medical community can help transform the clinical researcher from an endangered to an emerging species.**

Fueled by enlightened federal investments in biomedical

enterprise mo- relevance. This em is the criti- develop the evi- gies and moni- range of clinical analysis. With- out clinical research, the rational application of research dis-

re and person-

on of clinical

in this issue of

mines the role

er review pro- authors cite the on-repeated concern among clinical investigators that the NIH peer review process discriminates against clinical research.

# Clinical Research Career Opportunities

- Public Health
- Epidemiology
- Biostatistics
- Bioinformatics
  - Outcomes research
  - Quality of life
  - Cost-effectiveness
  - Health care policy assessment
- Designing trials
- Coordinating trials
- Enrolling patients



## **Fellow Training: Key Elements**

- **Didactic experience (assembling the tools: MPH, masters in clinical research, or simply courses)**
- **Practical experience (on a team, exposure/responsibility for various functions)**
  - Proposal development, sample size, budget, regulatory, operational planning, recruitment, data management
- **Analytic/writing experience (formulate question, design analytic plan, perform analysis, interpret, present, write)**
  - Writing is key
- **Culture valuing clinical research**
- **Mentor: motivator, advocate, advisor, role model**



# **Key Variables for Academic Success:**

## **An Informal Survey of Clinical Investigators and Fellows**

- 1. What characteristics do you see as most vital for the success of a new clinical investigator? For an established clinical investigator? List up to five for each.**
- 2. What is the ideal split of time between clinical work and research time for a new clinical investigator? For an established clinical investigator?**



# Key Variables for Academic Success: New Clinical Investigator

- **Mentorship, mentorship, mentorship...**
- **Resources: time and start-up funds**
- **Didactic training**
  - communication skills
  - research methods
  - regulatory requirements
- **Supportive culture (environment of research)**
- **Personal characteristics**
  - curious, focus, patience, perseverance, humility



# Identifying Mentors: Issues to Consider

- **Career role model**
- **Content expertise**
- **Methodological expertise**
- **Track record producing independent clinical researchers**
- **Interest in and time for mentoring**
- **Team mentoring**



# High-Quality Clinical Research: “It’s Not a Hobby”

- **Requires mastery of a diverse, multidisciplinary body of technical knowledge and skills**
- **Expertise often distributed throughout a group, instead of confined to a single individual**
- **Group members expert on certain functions, cross-trained on others**





# Career Myths and Realities: Didactic Training

- **Traditional view: clinical researcher needs to be expert clinician; statistician will run numbers**
- **Modern advice: get formal training in research methods, operations, quantitative methods**



# Didactic Training in Clinical Research: Core Elements

- **Biostatistics**  
(descriptive, estimation, hypothesis testing)
- **Principles of clinical research**  
(objectives, hypotheses, population, outcomes)
- **Clinical trials**  
(protocol, sample size, randomization, end points)
- **Ethical issues**  
(consent, conflict of interest, regulatory)
- **Research management**  
(budget, finances, project management, regulatory, etc.)



# **Didactic Training in Clinical Research: Elective Elements**

- **Advanced statistical topics**
- **Coordination of multi-center RCTs**
- **Molecular genetics of disease**
- **Computational genomics/proteomics**
- **Health services research**
- **Health economics**



# **Fellow Training: Predictors of Success in Clinical Research in Academic Medicine**

- **Enough experience to know if research makes you happy**
  - "when love and need are one"
- **Early exposure to research in fellowship**
- **"Protected time" and dedicated funding**
- **Transition plan at end of fellowship**
  - NIH awards, faculty transition positions
- **Passion**



# Key Variables for Academic Success: Established Clinical Investigator

- **Mentorship**
- **Funding**
- **Communication skills**
- **Networking ability**
- **Dedicated time**
  - balance administrative and clinical duties
- **Supportive culture**
  - ability to collaborate across disciplines



# Clinical Investigation Career: Myths and Realities

- **Traditional advice: working on large multi-center projects is a bad career move**
- **Modern advice: future impact projects will be large, collaborative endeavors, not single investigator initiatives**

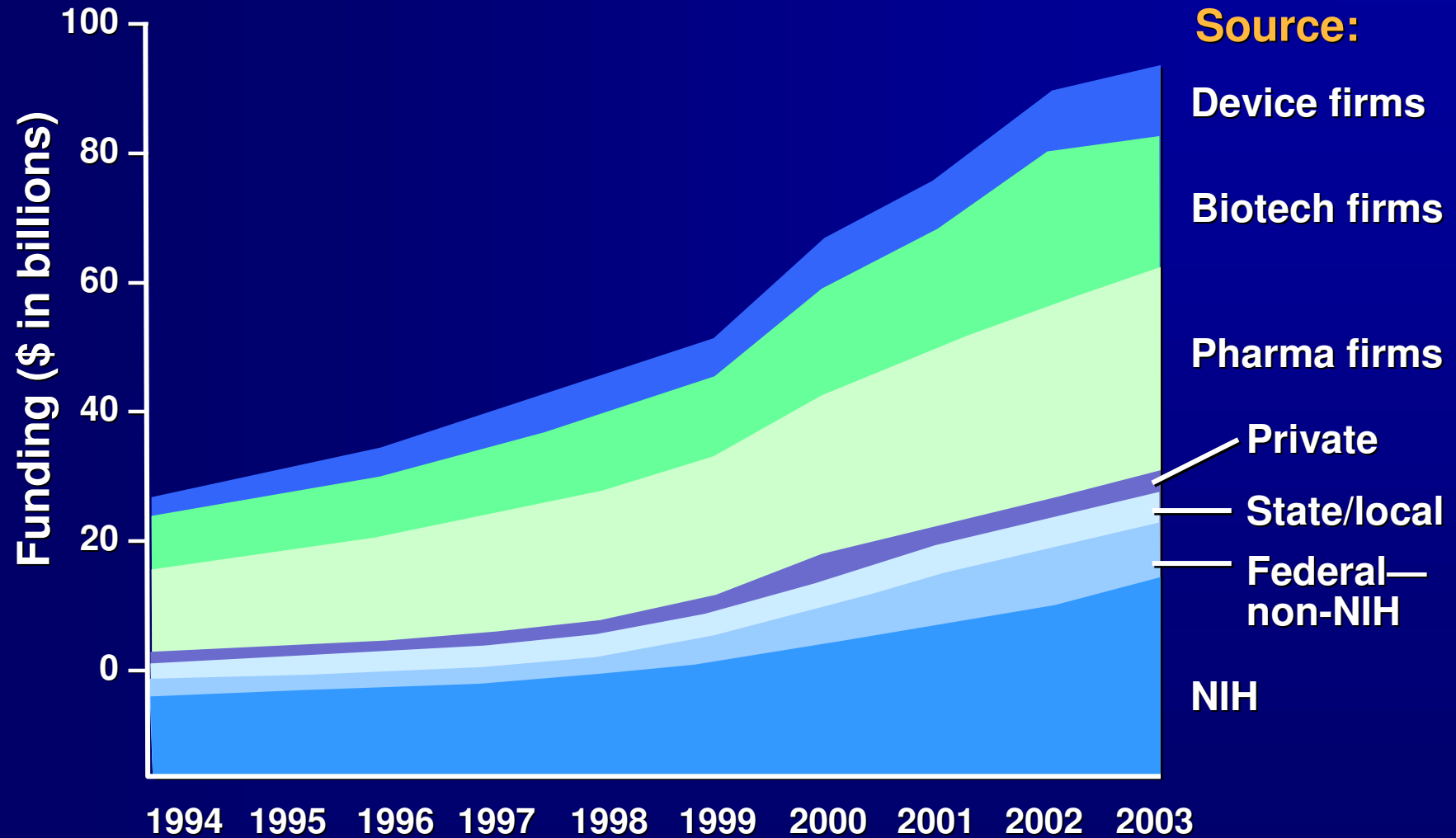


# Site Enrollment as Academic Involvement

- **Enroll patients**
  - access to therapies; better care
- **Look at protocol, science, volume, budget**
- **Creativity is in management**
- **Creation of systems: Coordinators, contracts, regulatory, negotiation, teaching**
- **Leverage success to broader role**
  - access to data; writing groups
  - steering committees



# Clinical Research Funding





## Alternative Sources of Funding—Bottom Line

- **Traditional NIH funding is the minority of research funding**
- **Alternative sources require different tactics**
- **Depending on your career aspirations, alternative sources may be preferable**
- **The best strategy is to find out what you are really passionate about, then develop the tactics to secure the funding you need!**

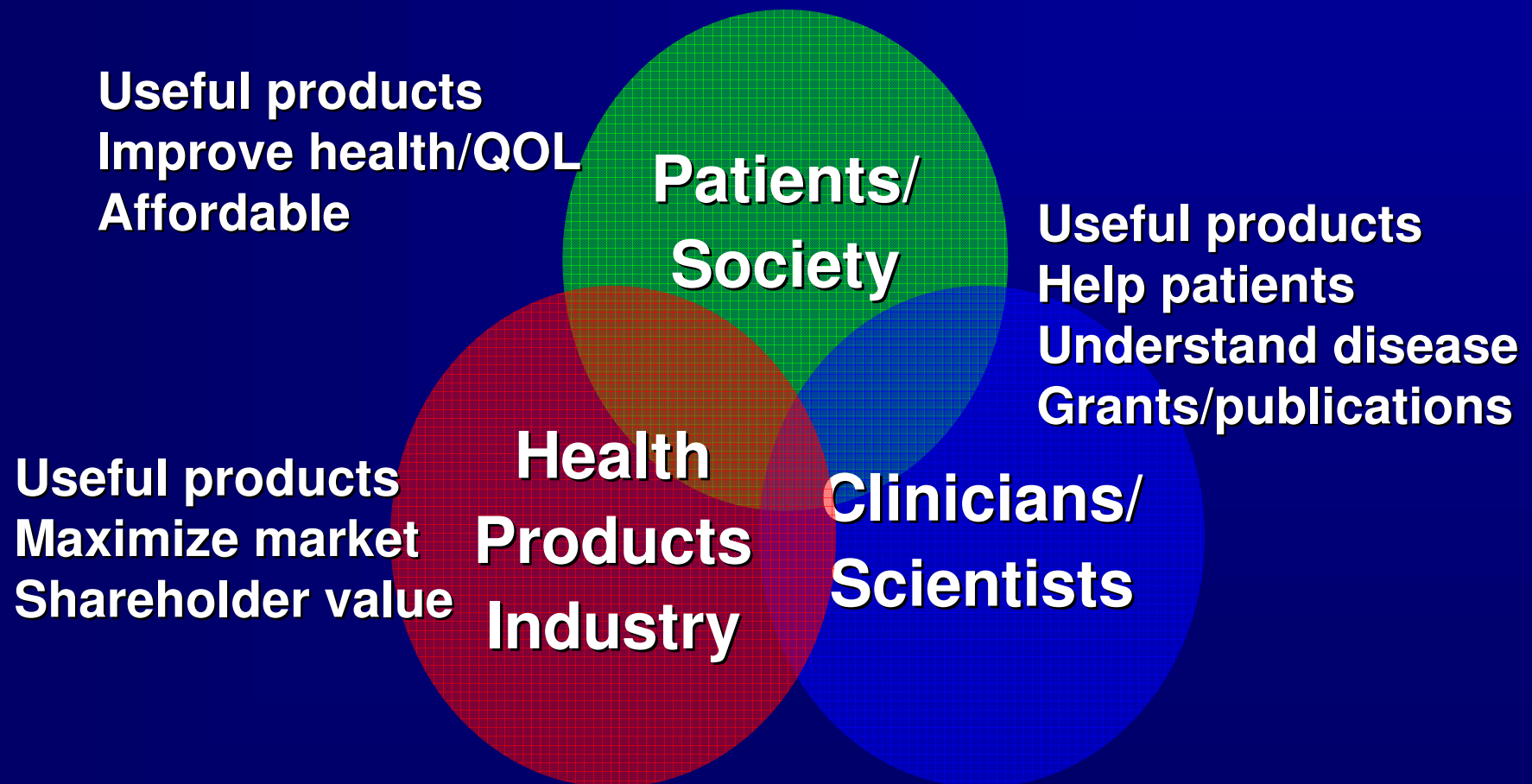


# Non-NIH Sources

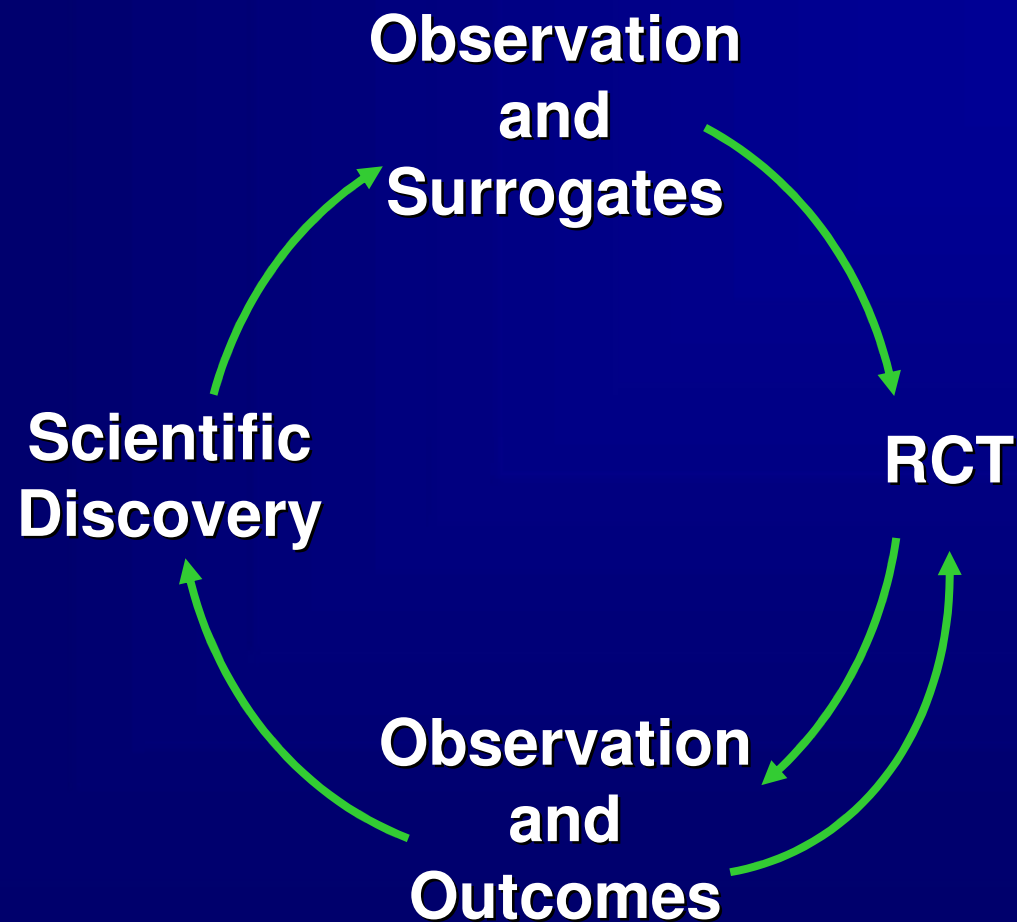
- **Other Federal Agencies**
  - AHRQ
  - CDC
  - CMS
  - VA
  - DOD
- **Medical Products Industry**
  - Pharma, biotech, devices
- **Foundations**



# Industry-Clinical Relationships in Research: Competing or Complementary Forces?



# The Cycle of Research Depends on the Clinician

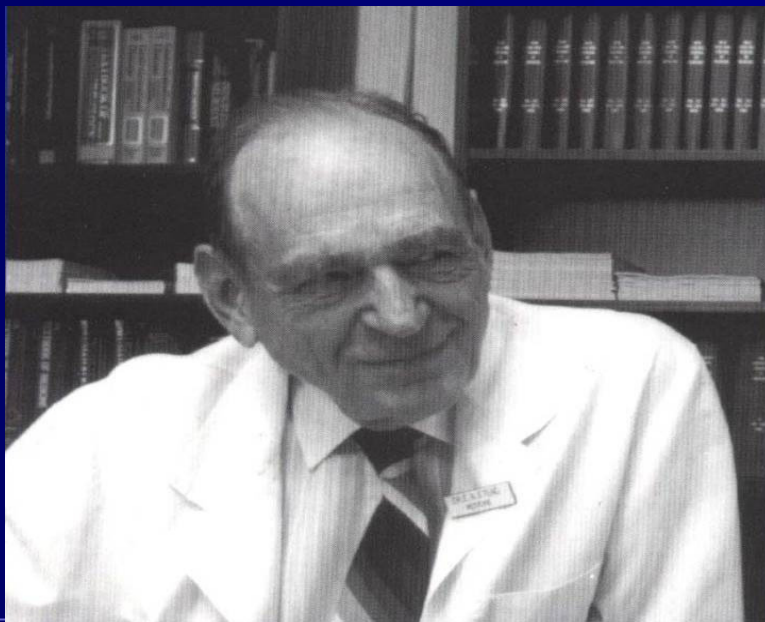


# Preparing for Clinical Research Career: Conclusions/Advice

- **Define your objective (“career specs”)**
- **Identify mentors**
- **Get didactic training**
- **Apprentice on a successful research team**
- **Do your own research projects**
- **Immerse yourself in culture of research**



**“There are those who wander around on the wards and those who are doctors. The difference is in having the data.”**



*-EA Stead Jr.  
Former Chair, DOM  
Founder, Duke CV Databank  
Founder, PA Profession*



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