HealthCore®

Applied Pharmacoeconomics and Outcomes Research Forum

The New World of Biosimilars in the U.S.: Current Challenges to Inform Future Directions

Mark J, Cziraky, PharmD, CLS, FAHA, FNLA

Vice President of Research

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Key Discussion Points

- Challenges in our Current HealthCare System:
  - Cost, Quality and Coordination
  - Gaps in evidence impacting decision making
- Observational research designs utilized to address gaps in evidence
- Evaluation of biosimilars in the current and future healthplan environment
- Overview of Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

Key Challenges in U.S. Health Care System

Unsustainable Cost

20%
OF GDP BY 2021

$700B
WASTE ACROSS U.S. SYSTEM

2x
COST PER CAPITA VERSUS OECD NATIONS

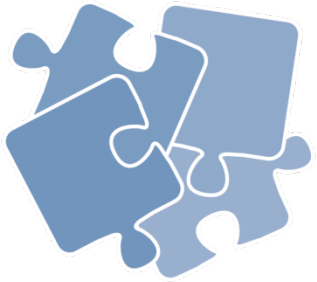
Variation in Quality

$210B
UNNECESSARY SERVICES

45%
CARE INCONSISTENT WITH RECOMMENDED GUIDELINES

3x
VARIATION IN HOSPITAL DAYS IN LAST 6 MONTHS OF LIFE

Lack of Coordination



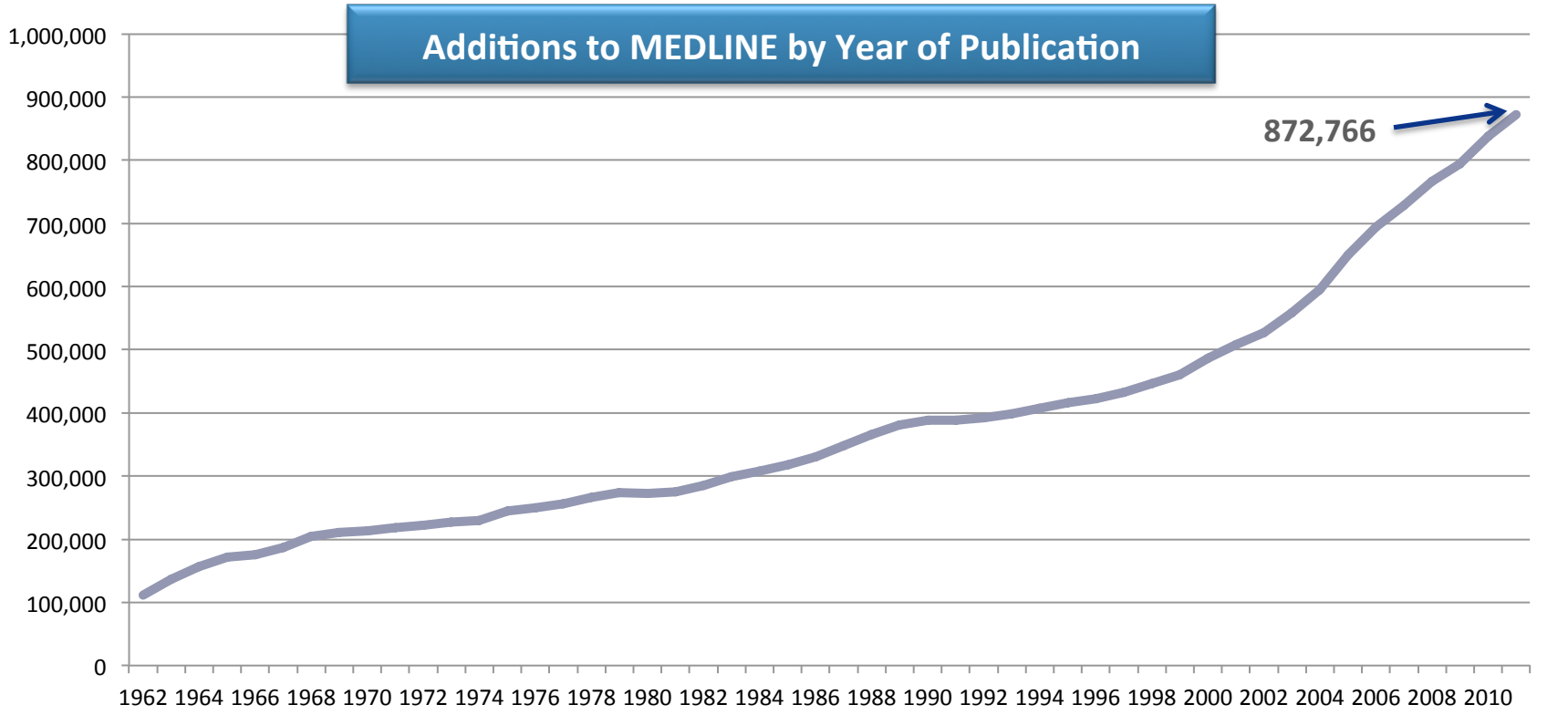
19.6%
MEDICARE HOSPITAL READMISSIONS

$45B
ANNUAL COSTS FOR AVOIDABLE COMPLICATIONS

$91B
REDUNDANT ADMINISTRATIVE PRACTICES

Explosion in New Medical Evidence

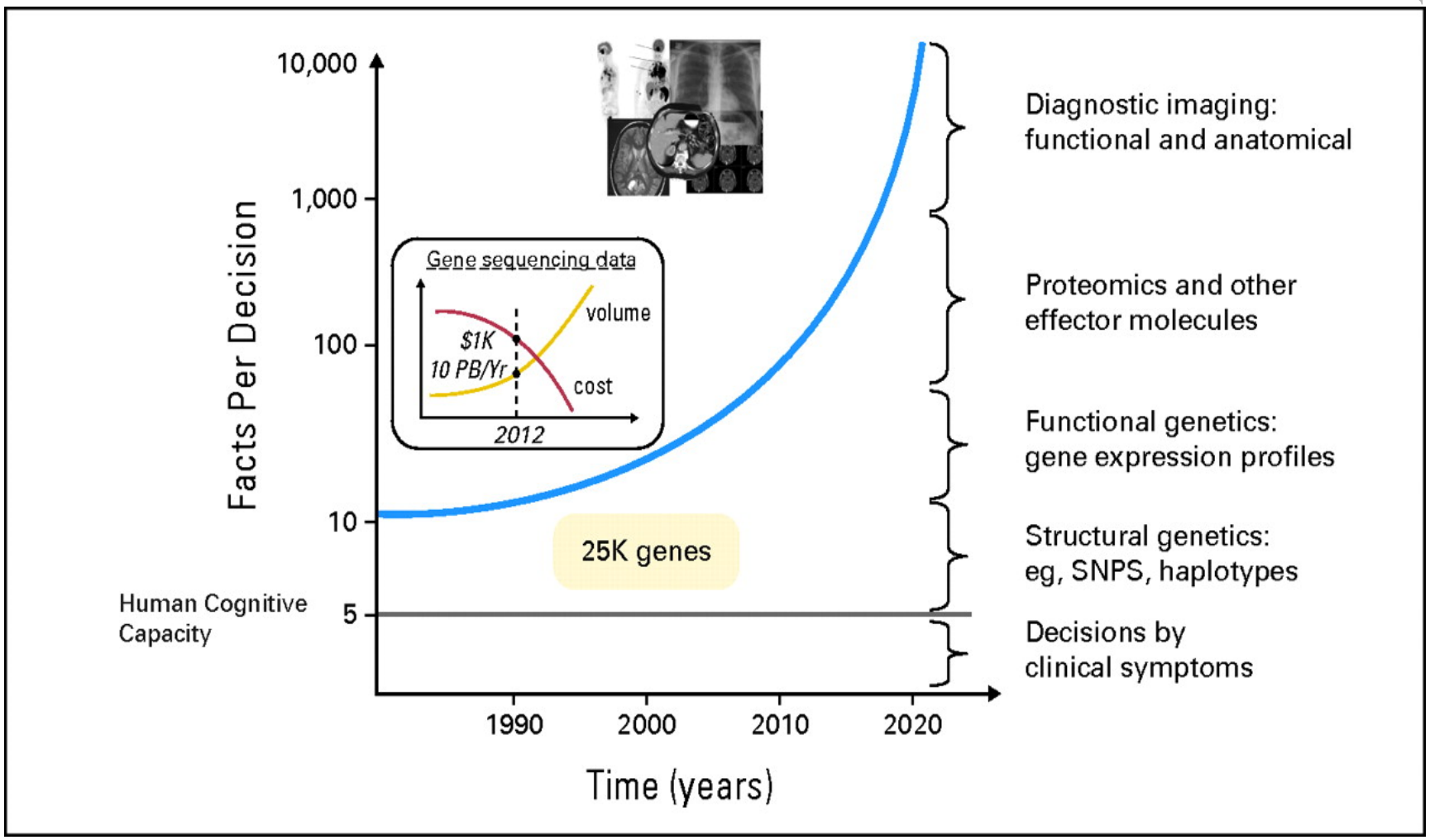
Last 50 Years



Currently houses more than 20 million citations
5,640 journals referenced in PubMed (as of July, 2013)
Represents 20-25% of the Journals in circulation

Source – National Library of Medicine

In the age of too much information…



Source: *JCO 2010*

Evaluation of Our Evidence Base

Example in Cardiovascular Disease

- A review of the level of evidence informing cardiovascular practice guidelines

Scientific Evidence Underlying the ACC/AHA Clinical Practice Guidelines

Pierluigi Tricoci, MD, MHS, PhD
Joseph M. Allen, MA
Judith M. Kramer, MD, MS
Robert M. Califf, MD
Sidney C. Smith Jr, MD

CLINICAL PRACTICE GUIDELINES are systematically developed statements to assist practitioners with decisions about appropriate health care for specific patients' circumstances.[1] Guidelines are often assumed to be the epitome of evidence-based medicine.

Context The joint cardiovascular practice guidelines of the American College of Cardiology (ACC) and the American Heart Association (AHA) have become important documents for guiding cardiology practice and establishing benchmarks for quality of care.

Objective To describe the evolution of recommendations in ACC/AHA cardiovascular guidelines and the distribution of recommendations across classes of recommendations and levels of evidence.

Data Sources and Study Selection Data from all ACC/AHA practice guidelines issued from 1984 to September 2008 were abstracted by personnel in the ACC Science and Quality Division. Fifty-three guidelines on 22 topics, including a total of 7196 recommendations, were abstracted.

Data Extraction The number of recommendations and the distribution of classes of recommendation (I, II, and III) and levels of evidence (A, B, and C) were determined. The subset of guidelines that were current as of September 2008 was evaluated to describe changes in recommendations between the first and current versions

JAMA. 2009;301(8):831-841

16

Current guidelines report levels of evidence

2,711

Total guideline recommendations

11%

Evidence classified as "A"

89% based upon a single trial or simply **expert opinion**

Origins in the Gap in Evidence

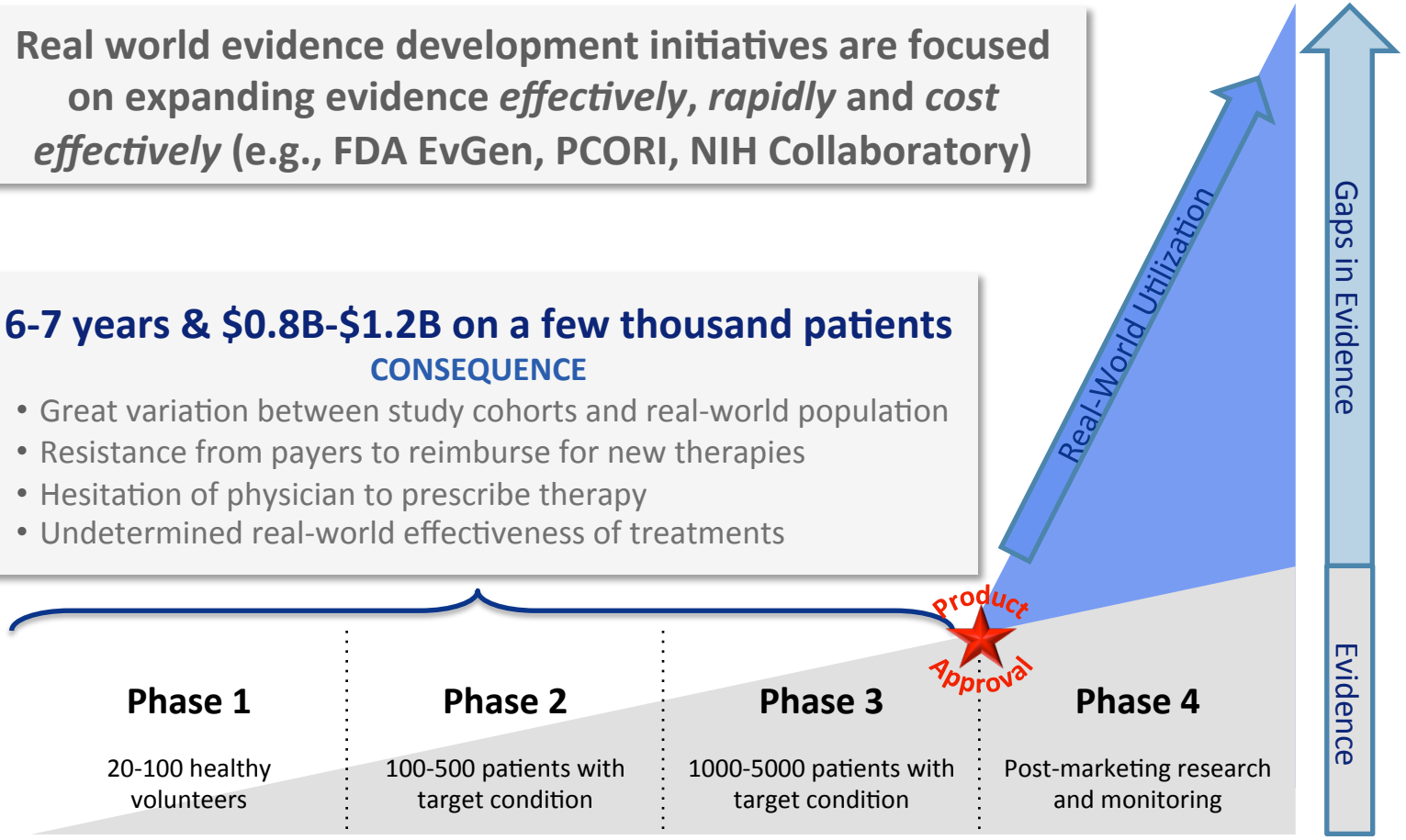
Real-world utilization quickly outpaces available clinical evidence

Real world evidence development initiatives are focused on expanding evidence *effectively*, *rapidly* and *cost effectively* (e.g., FDA EvGen, PCORI, NIH Collaboratory)

6-7 years & $0.8B-$1.2B on a few thousand patients

CONSEQUENCE

- Great variation between study cohorts and real-world population
- Resistance from payers to reimburse for new therapies
- Hesitation of physician to prescribe therapy
- Undetermined real-world effectiveness of treatments

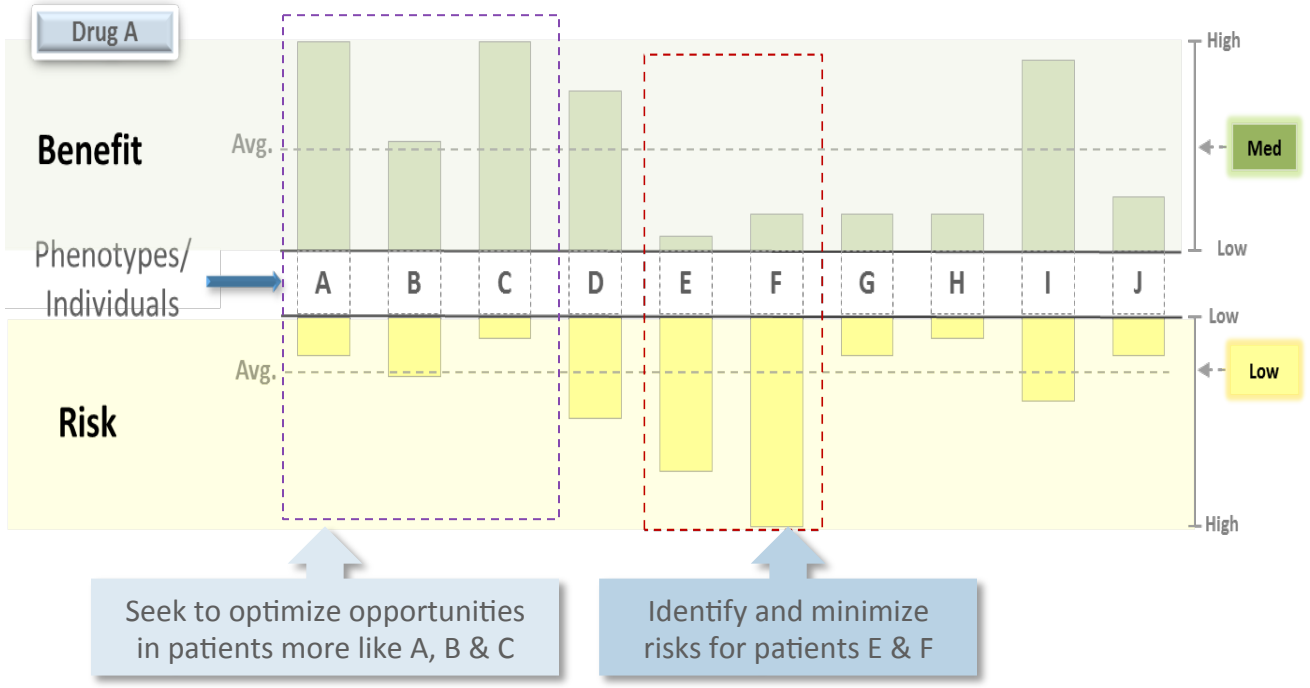


Precision Medicine

Knowing in whom treatments work is critical for population health

Traditional clinical trials can help determine if a product is relatively safe and effective for regulatory approval

- Rarely can RCTs provide detailed answers that address payer concerns and emerging population health metrics that require more targeted interventions



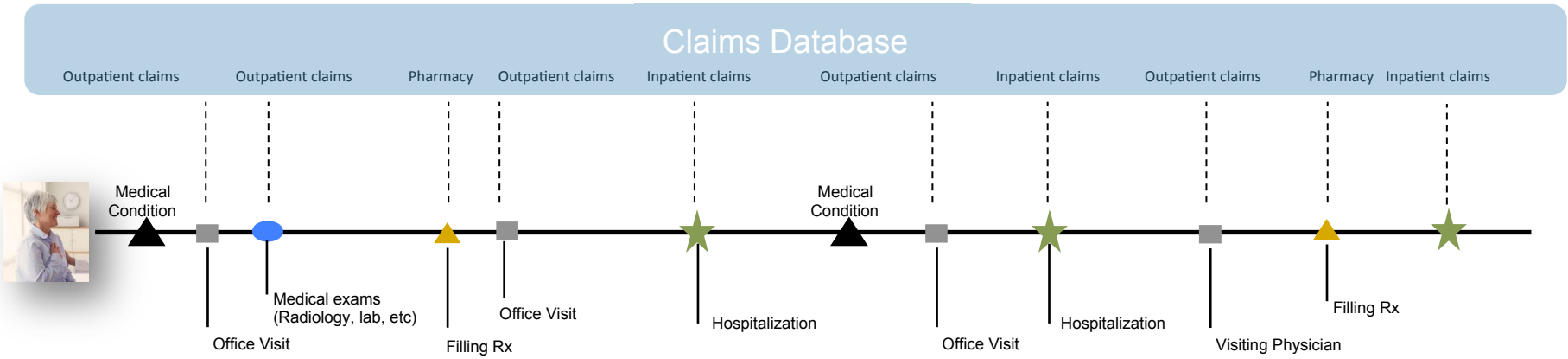
Observational Research Designs to Fill Evidence Gaps

A focus on Pragmatic Clinical Trials

Common Types of Observational Research

- Retrospective Database Analysis
- Large Simple Trials
- Registries
- Prospective Observational Study
- Pragmatic Trials

Value of a Retrospective Claims Database Analysis



Data sources with complete claims capture on the individual provides:

- A very good overview of the patient's exposure to the healthcare system
- Good proxy(ies) for medical conditions and procedures performed
- Reasonable measure of clinical outcomes, though PPV is highly variable
- A good history of drug exposure and utilization
- Very good source for assessing healthcare costs, overall and segment

PCT

Pragmatic Clinical Trials are designed to inform clinical and health policy decisions by evaluating the risks and benefits of health interventions in real-world, clinical practice settings.

Pragmatic Trials to Fill Evidence Gaps

When do you need a PCT?

- To create evidence of the value of a new therapy or intervention
- To provide evidence regarding the placement of a new therapy or intervention in the treatment paradigm
- To provide evidence of effectiveness of a therapy or intervention in real-world practice

What can be learned from a PCT?

- How are treatments used in clinical practice
- How effective a treatment is in a non-RCT population
- Supplementing the evidence from the RCT studies

Pragmatic Trials vs Randomized Controlled Trials

	Randomized Controlled Trial	vs	Pragmatic Trial
Tests if the Intervention Works Under	Ideal Circumstances		Real-World Circumstances
Conducted in	Controlled Setting		Usual Clinical Practice
Comparator	Placebo		Standard Care
Inclusion Criteria/ Patient Population	Extremely Restrictive		Minimally Restrictive
Treatment Regimen	Fixed and Protocol Driven		Flexible and Patient-Oriented
Goal	Regulatory Approval		Reimbursement Approval and Success in the Marketplace

Evaluating Biosimilars

A Commercial HealthPlan Perspective

Outcomes-Based Formulary Management

General Approach

Consider the complete burden of disease

Clinical Burden

Epidemiology

Natural History of Disease

Total Cost of Care

Productivity Impact

Quality of Life Impact

Leverage the formulary process to improve patient outcomes:

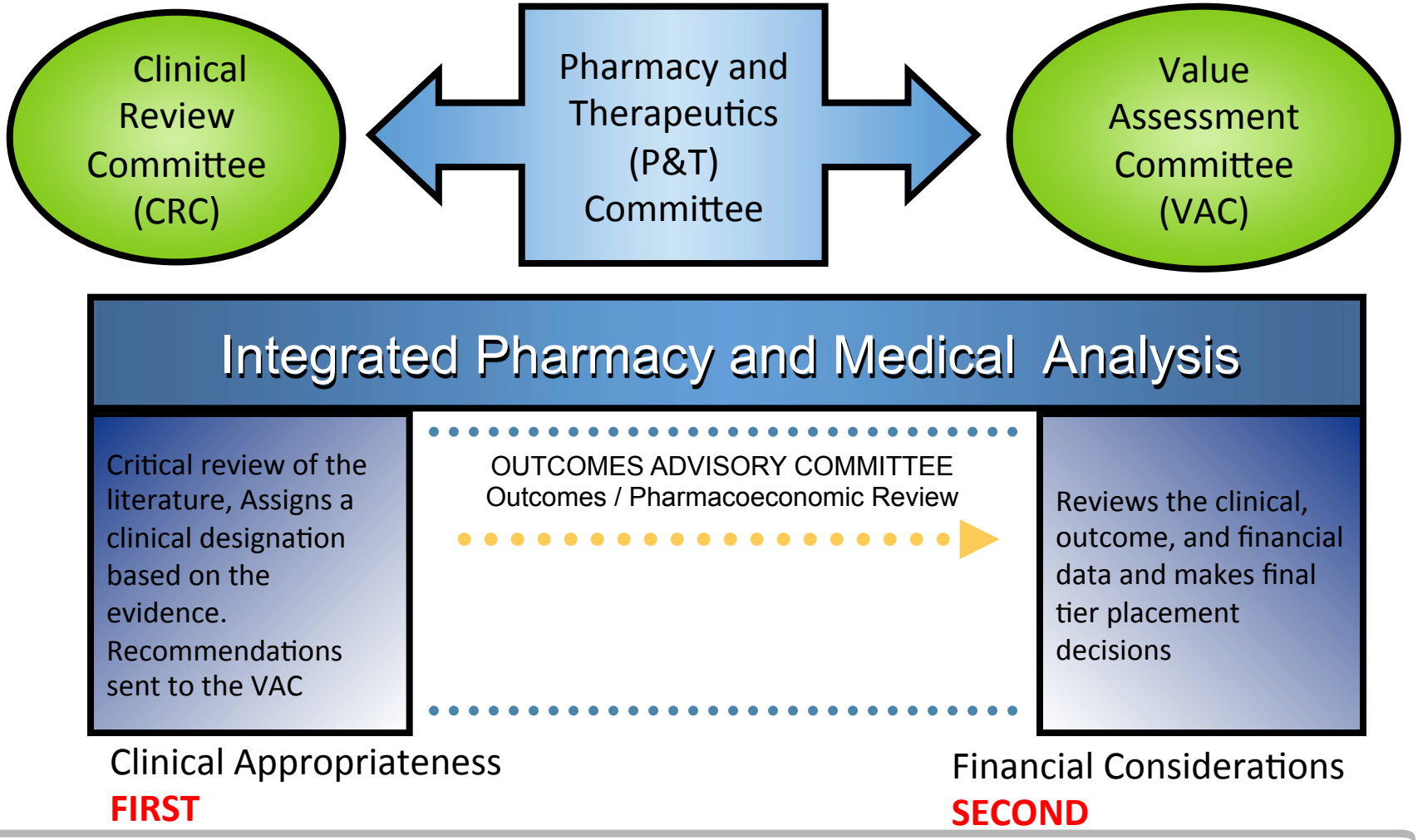
Improve Quality of Care
(clinical status, quality of life)

Reduce Total Cost
(pharmacy, medical, ancillary, home health, nursing home, etc.)

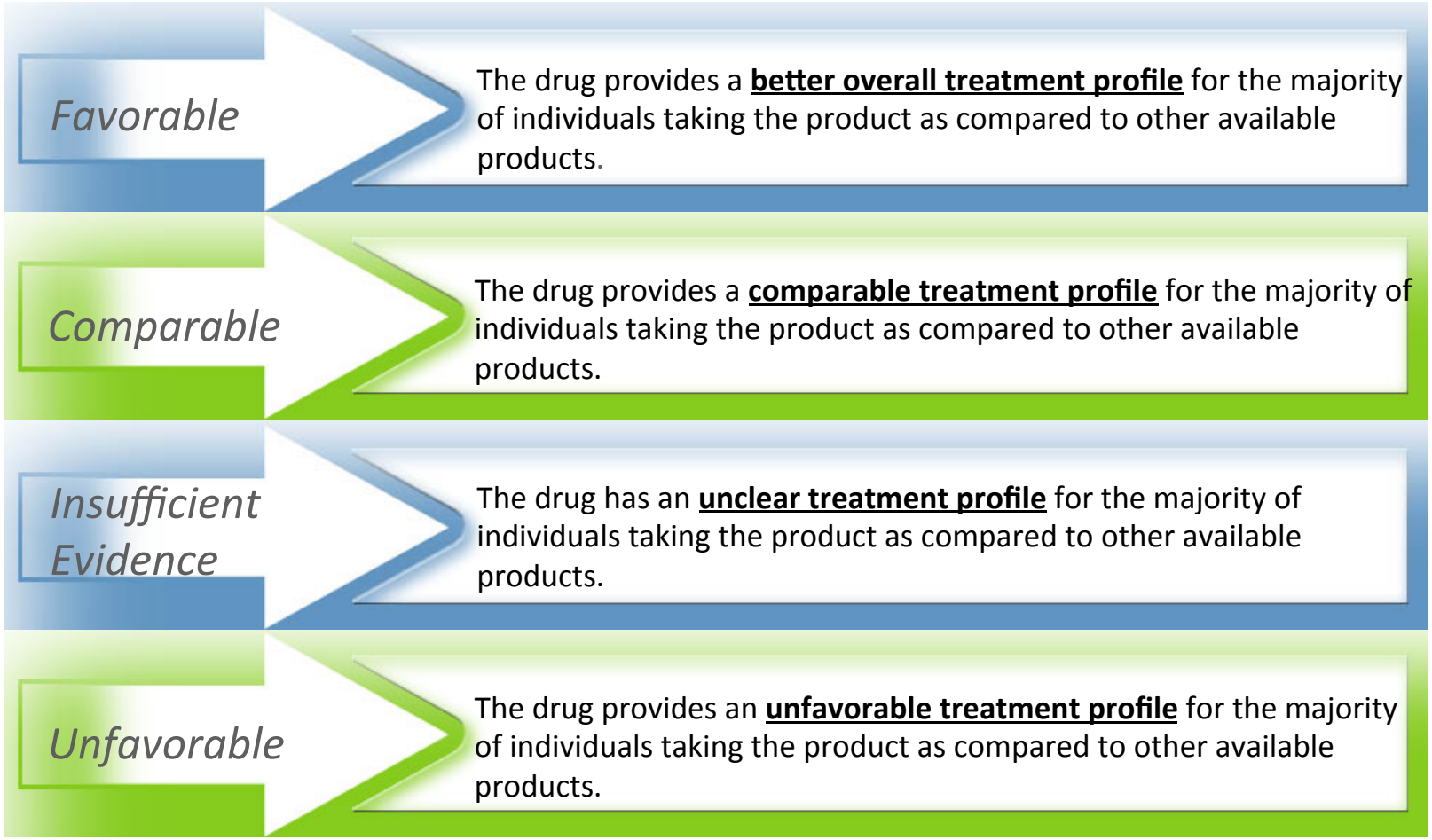
Optimize Value of Care
(cost effectiveness)

Improve Productivity

P & T Process and Committee Overview



Clinical Review Committee Designations



Clinical Review Committee – Clinical Comments

Substantive clinical comments about the products under review or issues pertaining to the therapy of a disease the drug(s) is/are used to treat.

Clinical Comments:

- May highlight important safety, efficacy, or clinical attribute concerns
- May be used to provide further detail supporting a *Clinical Designation*
- May be used to further differentiate important clinical points between products given the same *Clinical Designation*
- Emphasize key clinical concerns in the treatment of a disease state pertaining to the choice of drug therapy

Pharmacoeconomic and Outcomes Data

- How well does the drug perform in the real world (effectiveness vs. efficacy)?
- Are we achieving the outcomes we expect based on clinical trial data?
- Is the drug being used properly (right patient, dose, duration, etc.)?
- Are there quality of life or productivity benefits?

Efficacy vs. Effectiveness

	Efficacy (Clinical Trial Data)	Effectiveness (Real-World Data)
Objective	Does it work under **ideal** circumstances	Does it work under **usual** circumstances
Setting / Design	Controlled clinical trial	Real-world clinical practice
Purpose	Regulatory approval (FDA)	Drug performance in real-world
Intervention or treatment	Fixed regimen	Flexible regimen
Comparator	Placebo	Active comparator/usual care
Subjects	Homogenous/highly selective (stringent inclusion/exclusion criteria)	Heterogeneous / any subjects
Compliance	High	Low to High
Outcomes	Clinical endpoints (e.g. BP, HbA1c, LDL)	Example: Cardiovascular events, hospitalizations; moving to clinical endpoints
Internal Validity	High	Low
External Validity (generalize to other populations)	Low to medium	Medium to high

Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

Overview of BBCIC Surveillance Strategy

- With the advent of the new science of biosimilars in the U.S., physicians, patients and other stakeholders will have questions about the safety and effectiveness of these products, similar to what was experienced with the introduction of generics more than a generation ago.

- As biosimilars come to market, **the BBCIC will actively monitor biosimilars and their innovator products, using anonymous data from more than 100 million patients.**
  - The BBCIC will use well tested data and analytic methods (which FDA has spent $150M developing) to help ensure the safe passage of biosimilars. This improves the efficiency and cost-effectiveness of post-marketed observational studies
  - BBCIC's multi-stakeholder model allows for a larger voice with more credibility. A consortium of MCOs, IDNs, PBMs, medical societies, researchers & biopharma is less easily ignored

Scientific Partners Bring Expertise

Lead – HPHC Institute

Data and scientific partners

Scientific partners

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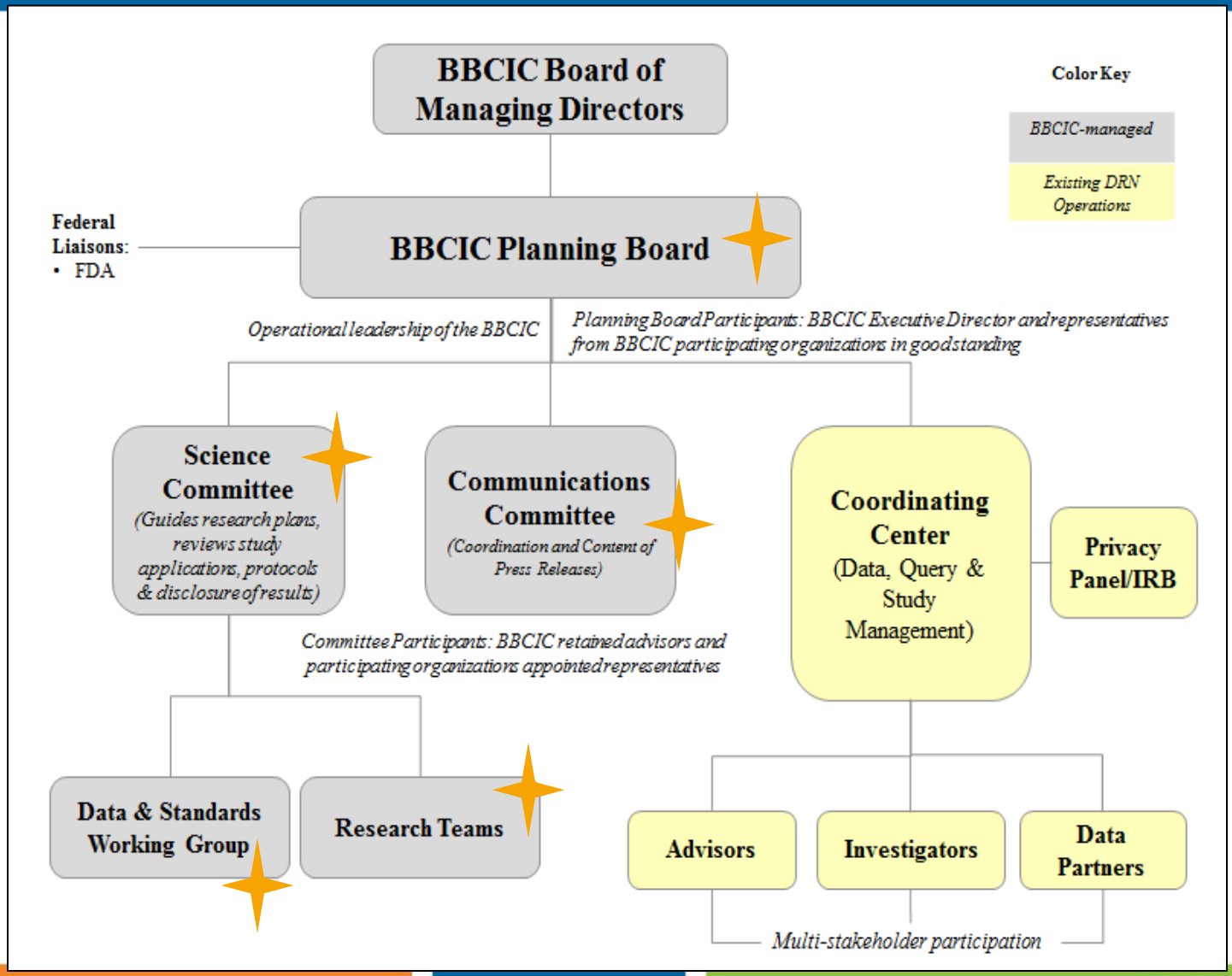
BBCIC Progress to Date

- Consortium officially kicked off in June 2015
- Governance approved October 2015. The BBCIC uses a ***transparent organized process*** to characterize patient populations and generate evidence for biologics
- 16 founding participants including Managed Care Organizations, Integrated Delivery Networks, PBMs & Harvard-Pilgrim Health Care Institute

AbbVie • Aetna • Amgen • Anthem-Healthcore • ApoPharma • Boehringer Ingelheim • Express Scripts • Group Health Cooperative • Harvard Pilgrim Health Plan • HealthPartners •Hematology Oncology Pharmacy Association (HOPA) • Henry Ford Health Systems • Merck • Momenta • Optum • Pfizer Inc. • Sandoz

- Public representatives on Planning Board: ASCO (Miller), American College of Rheumatology (Curtis), National Health Council (Perfetto)
- Research plan started February 2016
- 3 Research Protocols approved by Science Committee Jun-Aug 2016; Results are expected in the next 4-6 months

BBCIC Governance Overview



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Q&A