

What is a Biomarker, and what role do Biomarkers play in modern medicine?

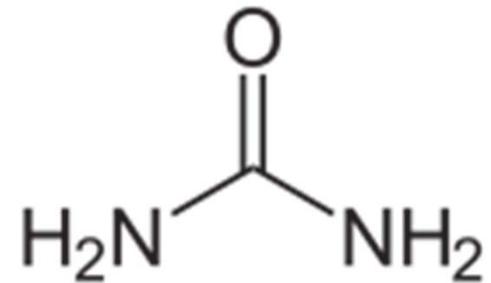
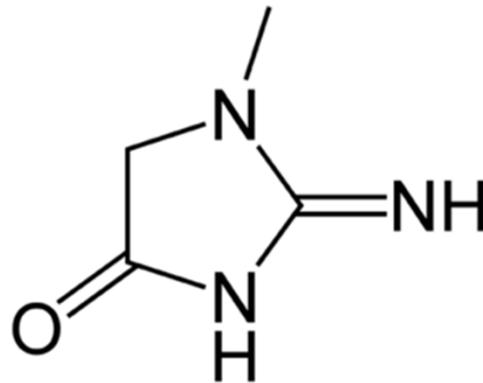
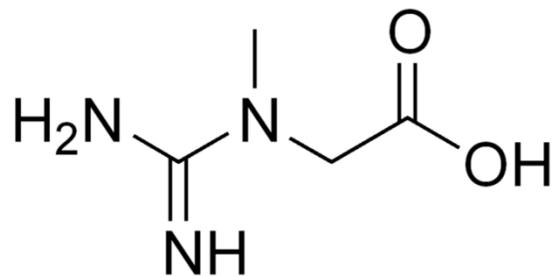
Arnold O. Beckman 30th Conference
November 5, 2013

Robert H. Christenson, Ph.D., DABCC, FACB
2013 AACCC President
University of Maryland School of Medicine
University of Maryland Medical Center
Baltimore, MD

WHAT IS A BIOMARKER?

Clips with Interviews

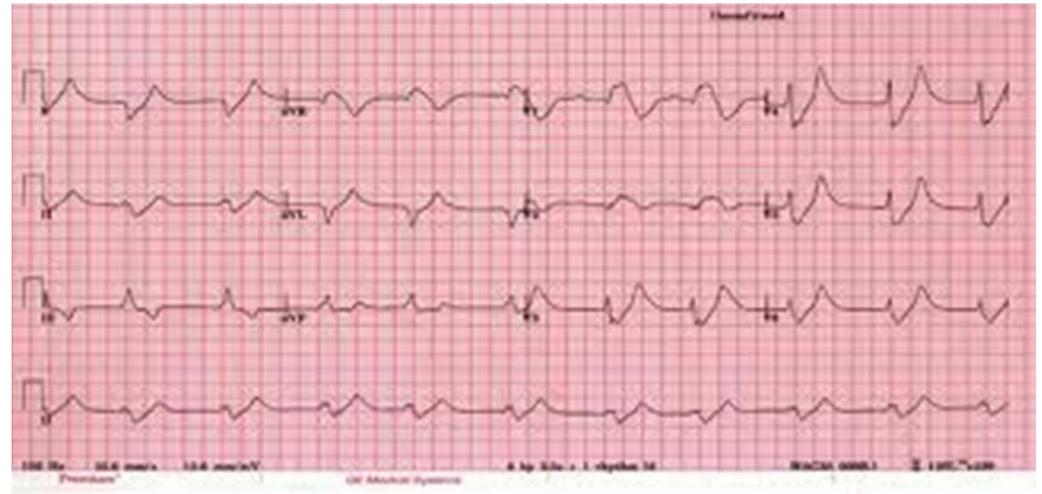
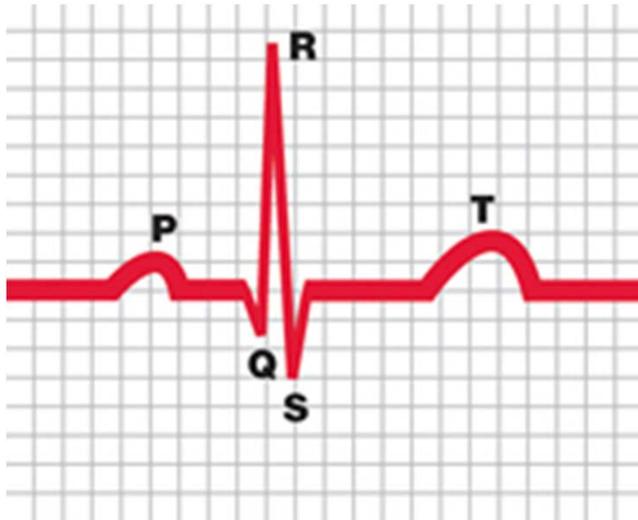
A biomarker, or biological marker, is in general a substance used as an indicator of a biological state.



Kayser–Fleischer rings (KF rings)



<http://www.wilsonsdisease.org/wilson-disease/kayserfleischerrings.php>



<http://en.wikipedia.org/wiki/Biomarker>

- In medicine, a **biomarker** is a measurable characteristic that reflects the severity or presence of some disease state. More generally a biomarker is anything that can be used as an indicator of a particular disease state or some other physiological state of an organism.

Biochemical Marker

Applications of Biomarkers

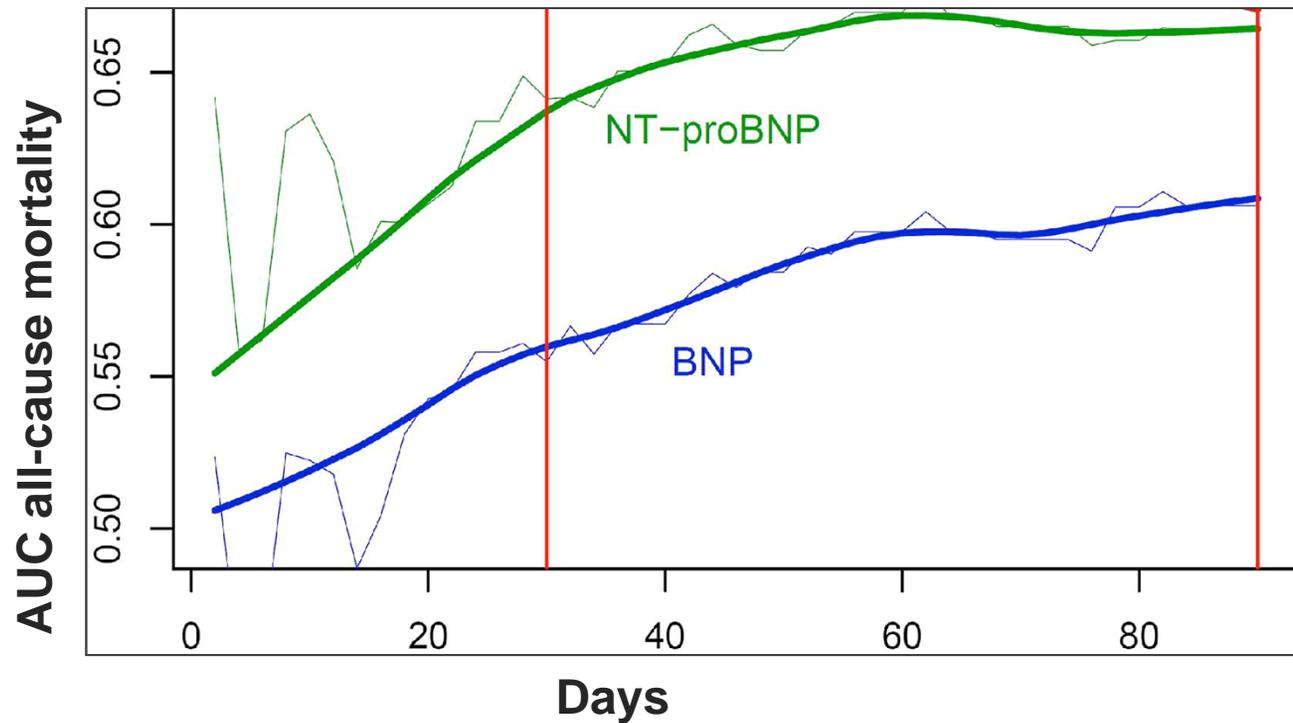
- Screen for disease
- Rule-in diagnosis
- Rule-out diagnosis
- *Assess prognosis*
- *Start intervention or treatment*
- *Adjust intervention or treatment*
- *Stop intervention or treatment*
- *Assess efficacy*
- *Assess compliance*

Fundamental Question

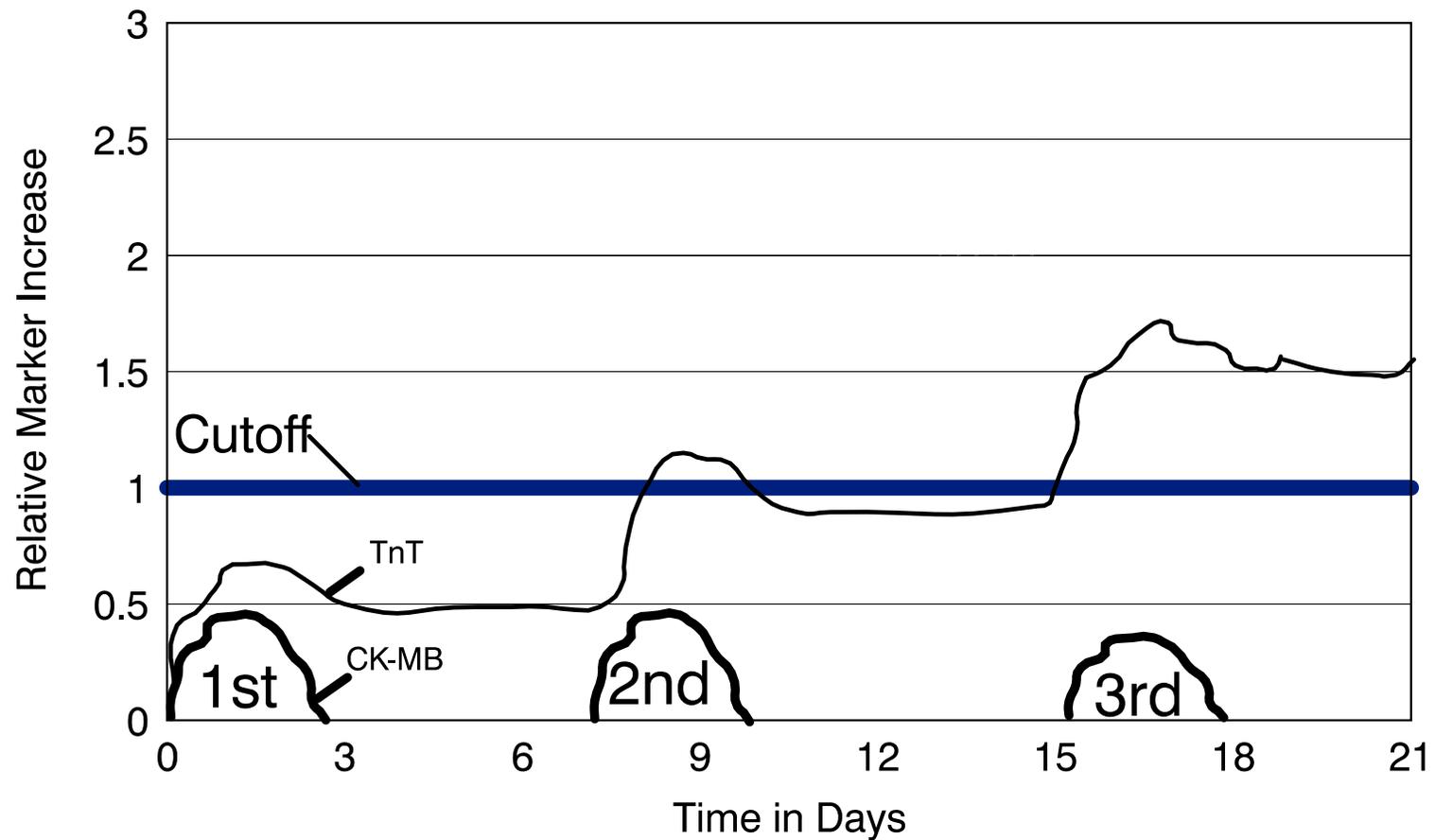
Do patients that have the biomarker measured have better outcomes compared to similar patients who do not have the biomarker measured?

Natriuretic peptides for early prognosis

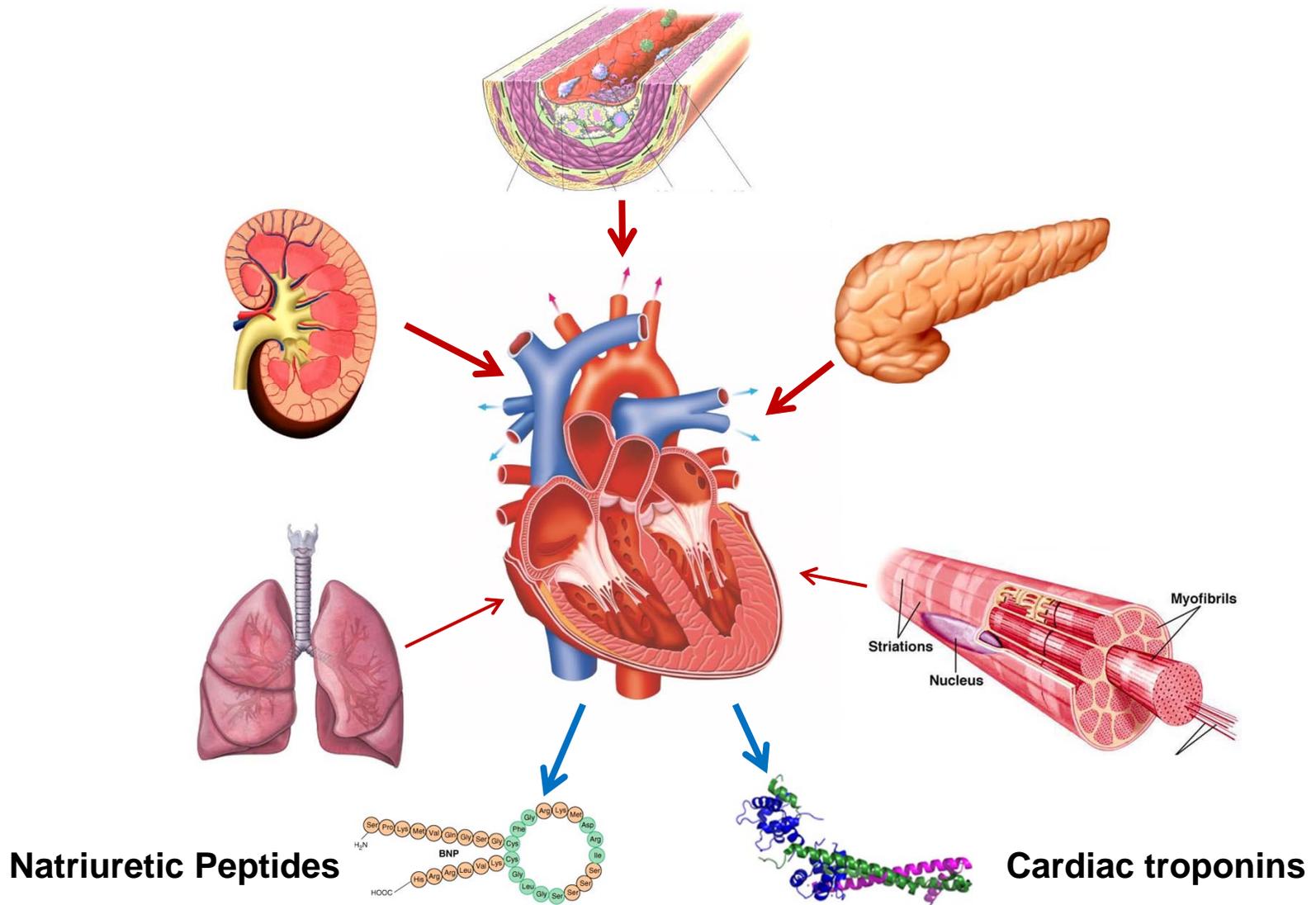
Results of the BACH study



Cardiac Troponin Cumulative Effect



Biomarker levels represent a summation of the influence of acute and chronic comorbidities



Criteria for Assessment of Novel Biomarkers

1. Can the clinician measure the biomarker?

1. Measure

2. Does the biomarker add new information?

2. More

3. Will the biomarker help the clinician to manage patients?

3. Manage

1. Measure

Criterion for “Prime Time” Biomarkers

1. Can the clinician measure the biomarker?

- *Accurate and reproducible assay*
- *Pre-analytical issues (including stability)*
- *Assay is accessible*
- Provision of high through-put and rapid TAT
- Reasonable cost

Circulation 2007;115:949-952

2. More

Criterion for “Prime Time” Biomarkers

2. Does the biomarker add new information?

- *Strong and consistent association between the biomarker and outcome or disease of interest in multiple studies*
- *Information adds to or improves upon existing tests*
- Decision-limits are validated in more than one study
- Evaluation includes data from community-based populations

Circulation 2007;115:949-952

3. Manage

Criterion for “Prime Time” Biomarkers

3. Will the biomarker help the clinician to manage patients?

- *Superior performance to existing tests*
- *Evidence that associated risk is modifiable with specific therapy*
- *Evidence that biomarker-guided triage or monitoring enhances care*
- Consider each of multiple potential uses

Circulation 2007;115:949-952

The Ideal Biomarker

| 2007 | 2012 |
|---|---|
| Sensitive and specific | Either highly sensitive (diagnosis) OR highly specific (treatment effect) |
| Reflects disease severity | Reflects abnormal physiology/biochemistry |
| Correlates with prognosis | Prognosis is <u>most</u> meaningful if level is clinically actionable |
| Should aid in clinical decision making | <u>Should</u> be used as a basis for specific “biomarker guided-therapy” |
| Level should decrease following effective therapy | “Bio-monitoring” <u>during</u> treatment is an effective surrogate of improvement |

Maisel, JACC 2012

Three Most Important Tasks

- Validation

- Validation

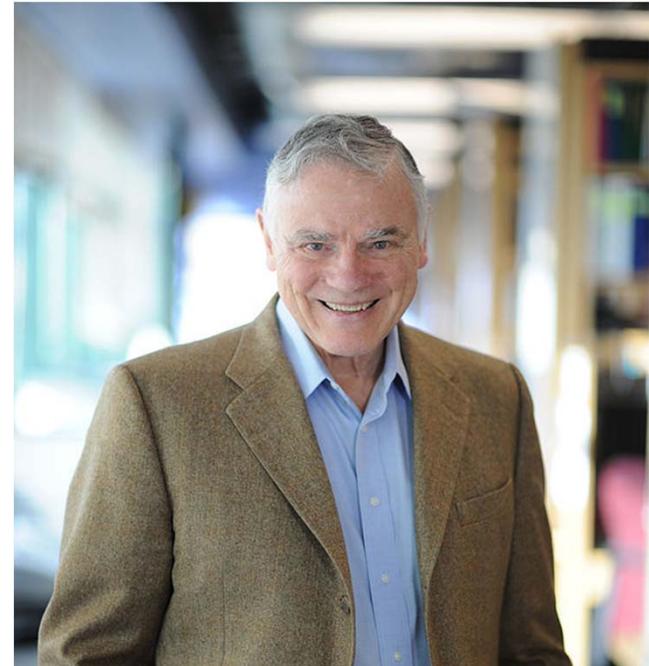
- Validation

What role do Biomarkers
play in modern medicine?

Leroy Hood, MD, PhD

world-renowned scientist, inventor, entrepreneur and visionary

- 4 P's from Personalized, Systems medicine, transforming technologies and the emergence of P4 medicine
 - predictive
 - personalized
 - preventive
 - participatory



AUGUST 18, 2009

Health Care Special Report

TIME



HEALTH CARE
SPECIAL REPORT

Paging Dr. Obama

- Exclusive interview
- Where's his prescription?
By Karen Tumulty
- Why Congress can't get it right
By Joe Klein
- PLUS A one-step graphic guide
to how a new plan would affect you

WWW.TIME.COM

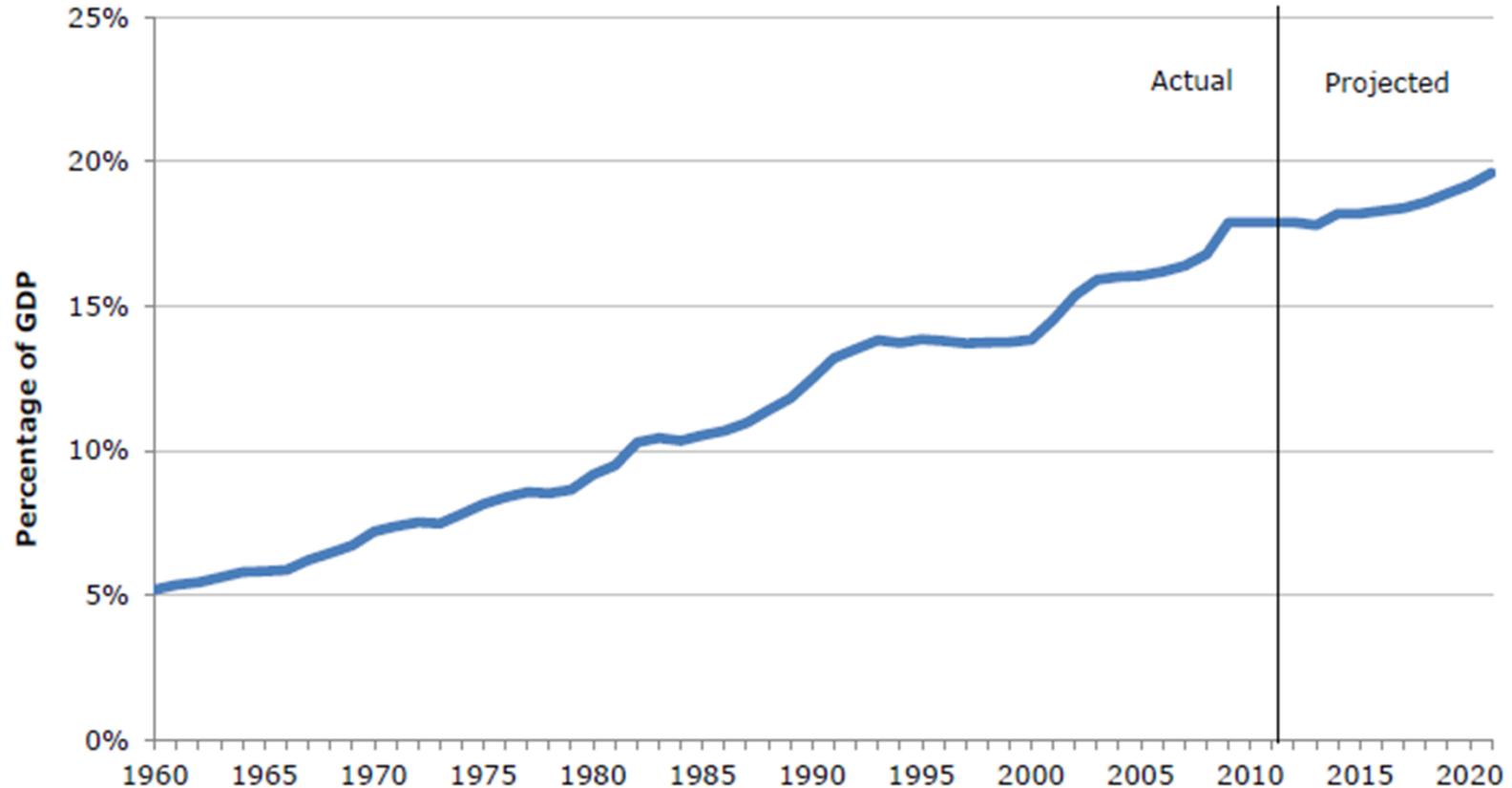
Health Care's Inconvenient Truth Unnecessary and Inappropriate Care

Many health care interventions* are of little or no benefit, and cause potentially uncomfortable, costly, and dangerous side effects and complications.

*Some of which are very expensive and invasive

Sources: IOM, RAND, Congressional Budget Office and medical journal publications 2001-20013

U.S. National Health Expenditures as a Share of the Economy (GDP), 1960-2021

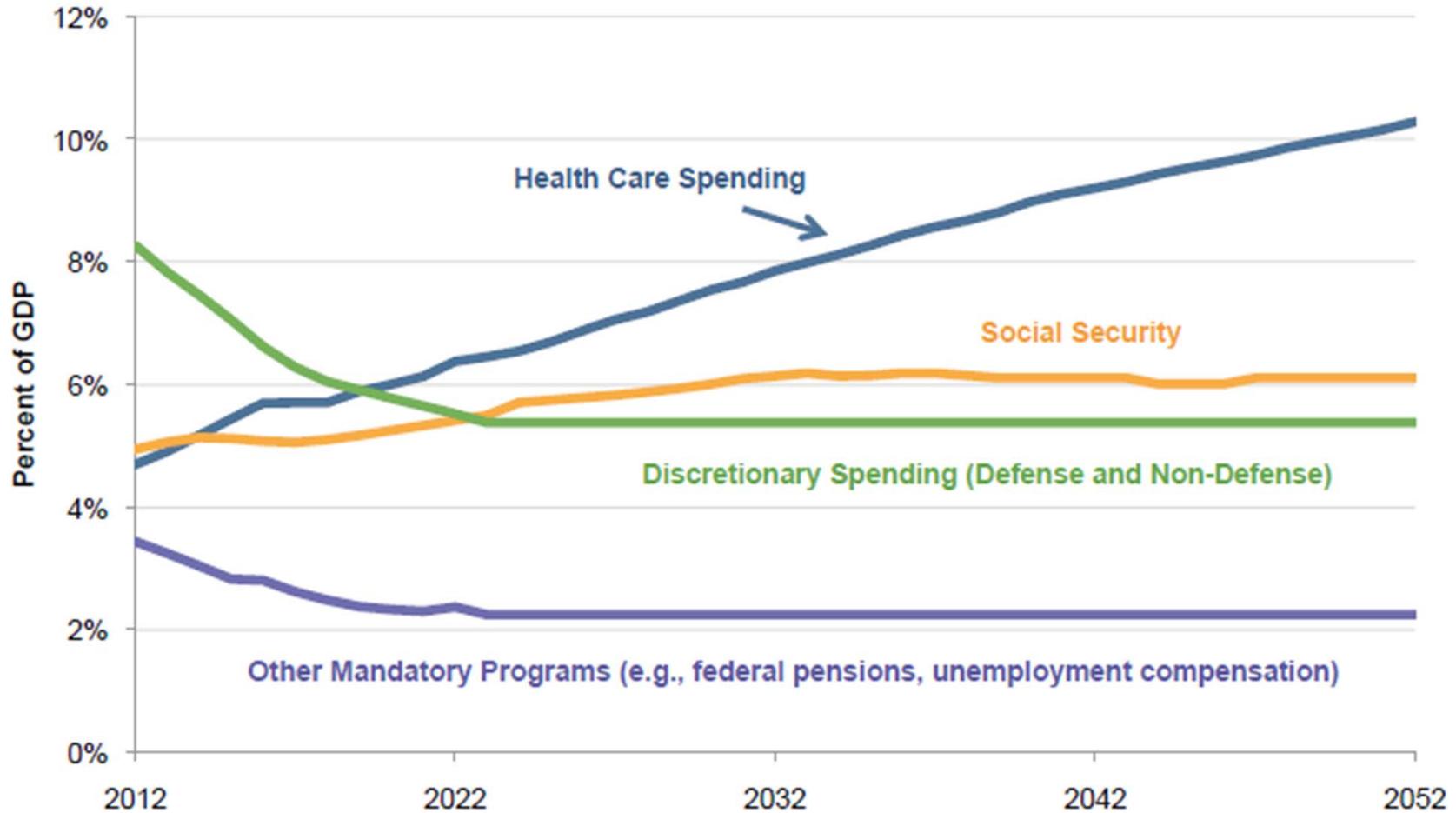


Source: Centers for Medicare and Medicaid Services.

Despite the highest per-capita spending in the world, the U.S. health care system fails to deliver commensurate value. In return for approximately \$2.8 trillion annually, millions of Americans receive care that is uncoordinated, unnecessary, or overpriced, while others receive little or no care at all.

Source: Bipartisan Policy Center, April 2013

Health Care Costs are the Primary Driver of U.S. Government Debt



Source: Congressional Budget Office's Alternative Fiscal Scenario (February 2013), additionally assuming that combat troops overseas decline to 45,000 by 2015 and that Hurricane Sandy funding is not allocated in future years; Bipartisan Policy Center extrapolations

Overspending can lead to this common U.S. health care system patient diagnosis (a financial condition)



Health Care Cost Drivers

- ❑ Fee-for-service reimbursement;
- ❑ Fragmentation in care delivery;
- ❑ Administrative burden on providers, payers and patients;
- ❑ Population aging, rising rates of chronic disease and co-morbidities, as well as lifestyle factors and personal health choices;
- ❑ Advances in medical technology;
- ❑ Tax treatment of health insurance;
- ❑ Insurance benefit design;
- ❑ **Lack of transparency about cost and quality, compounded by limited data enabling comparison of healthcare quality and outcomes to inform patients and clinicians to choose the best and most cost effective treatment;**
- ❑ **Cultural biases that influence care utilization;**
- ❑ Trends in health care provider and insurer market consolidation and competition;
- ❑ High unit prices of medical services;
- ❑ Health care legal /regulatory environment (medical malpractice, fraud, abuse)
- ❑ Structure and supply of the health professional workforce (scope of practice restrictions, trends in clinical specialization, and patient access to providers).

In Vitro Diagnostic Device

- Any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment, or system, whether used alone or in combination...
- ...intended for use *in vitro* for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information.

We in the lab are all about **information.**

Challenge: Connecting Laboratory Testing to Outcomes



The value of a lab test is reliant on linking the test information with management strategies, clinical actions and processes and that directly impact patient outcomes.

ACO

- Adverse Cardiac Outcomes?
- Ambulatory Care Outreach?
- Accumulated Cash Outlay?

Accountable Care Organization

- A group of healthcare providers who deliver coordinated care and chronic disease management, thereby improving the quality of care patients receive
- The organization's payment is tied to achieving healthcare quality goals and outcomes that result in cost savings.

What do in vitro diagnostics contribute? “right patient, right test, right time”

| Screening | Diagnosis | Prognosis | Treatment |
|------------------|-------------------------|--|---|
| - predisposition | - rule out - rule in | - risk assessment - venue of care - treatment stratification | - candidacy - adverse events - optimization - compliance |

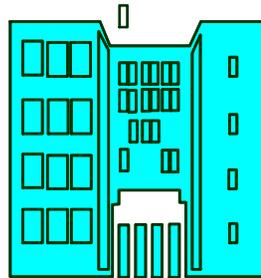
Continuum of Care



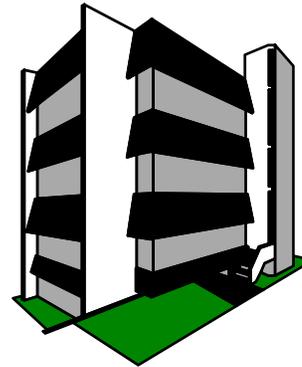
home



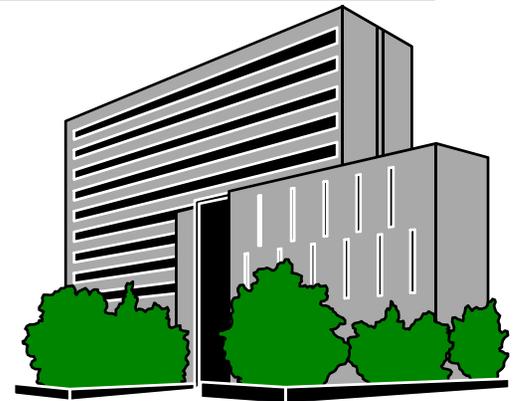
primary care center



Specialist
Physician Visit



Community
hospital



Regional/Tertiary
Medical Center

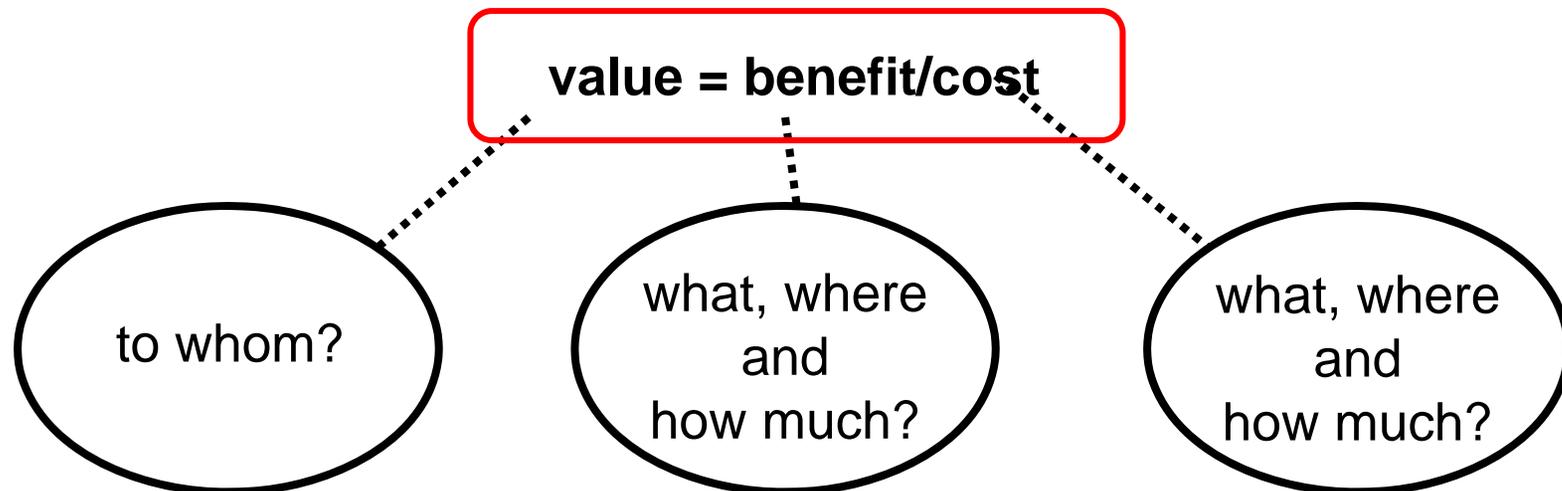
Fundamental Question

- *Do patients that have the diagnostic test measurement have better outcomes than patients who do not?*

Is the test valuable?

A Definition of **Value**

- The regard that something is held to deserve:
- importance or worth
- material or monetary worth
- the worth of something compared to its price



Reimbursement (Recovering Costs)

- Cost or value based?
- Unintended consequences
- Impact on care delivery
- Impact on health outcome
- Impact on innovation

Value-Based Reimbursement assessing the potential for diagnostics

- “...payment or reimbursement [should be] based on the economic value generated rather than on the short term marginal cost of supplying goods or service.”

Garrison et al 2011

Healthcare Reform: Changes to Reimbursement for 30-Day Readmissions

- ~20% of Medicare beneficiaries who are discharged from hospitals are re-hospitalized within 30 days (cost of > \$17 billion for unplanned readmissions)¹
- Recent national trends in risk-standardized 30-day readmission rates following HF hospitalization are ~24%²
- First two years of PPACA focus on HF, MI and pneumonia
- Potential to impact hospitals in the form of withheld Medicare payments³

1. Jencks et al. NEJM 2009; 360:1418-28

2. Ross et al. Circulation Heart Failure. 2010; 3: 97-103.

3. Patient Protection and Affordable Care Act of 2010, Pub. L. No. 111-148, 124 Stat. 119 (2010, March 23)

Penalties for Excess Hospital Readmissions

Patient Protection and Affordable Care Act (PPACA) Section 3025-3026

- **Affect CMS payments for hospitals beginning Oct-2012 for**
 - Heart Failure (>5% readmit for pneumonia)
 - Myocardial Infarction
 - Pneumonia (>7% readmit for HF) ¹
- **Penalty Calculation = (base operating DRG) X (Adjustment Factor)**
- **Adjustment Factor is greater of:**
 - Excess readmission ratio *OR*
 - Floor adjustment factor (1% in 2013, 2% in 2014, 3% in 2015)
- Percentages are calculated as aggregate for **all discharges**, not just for HF, MI, pneumonia²

1. Jencks et al. NEJM 2009; 360:1418-28

2. Thomson Reuters Resarch Brief, August 2010: Pending Changes to Reimbursement for 30-Day Readmissions

Using Laboratory Testing to Help Stratify Patients

- To help reduce readmissions, a key component of any cost-effective program is risk stratification.
- New biomarker tests can help clinicians understand the likelihood of a patient's readmission and may guide utilization of more aggressive treatment and compliance-improving protocols.

Role of New Biomarkers

- New biomarkers are available which can assist in the prognosis and aid in risk stratification for patients already diagnosed with HF, and may lead to earlier detection of treatment failure, compliance issues and therapeutic targets.

PRESS RELEASE

Oct. 16, 2012, 8:00 a.m. EDT

Walgreens WellTransitions(SM) Provides Discharge Services to Help Hospitals and Health Systems Reduce Readmissions

Government penalties now being imposed for preventable hospital

The WellTransitions(SM) program offers a number of services, including:

- **Medication review** - pharmacists review patients' prescriptions upon admission to the hospital and at discharge; check for potential interactions and simplification of medication regimen

Walgreen's New Medication Management Program May Foreshadow Similar Models for Clinical Laboratory Services – Pamela Scherer *McLeod*



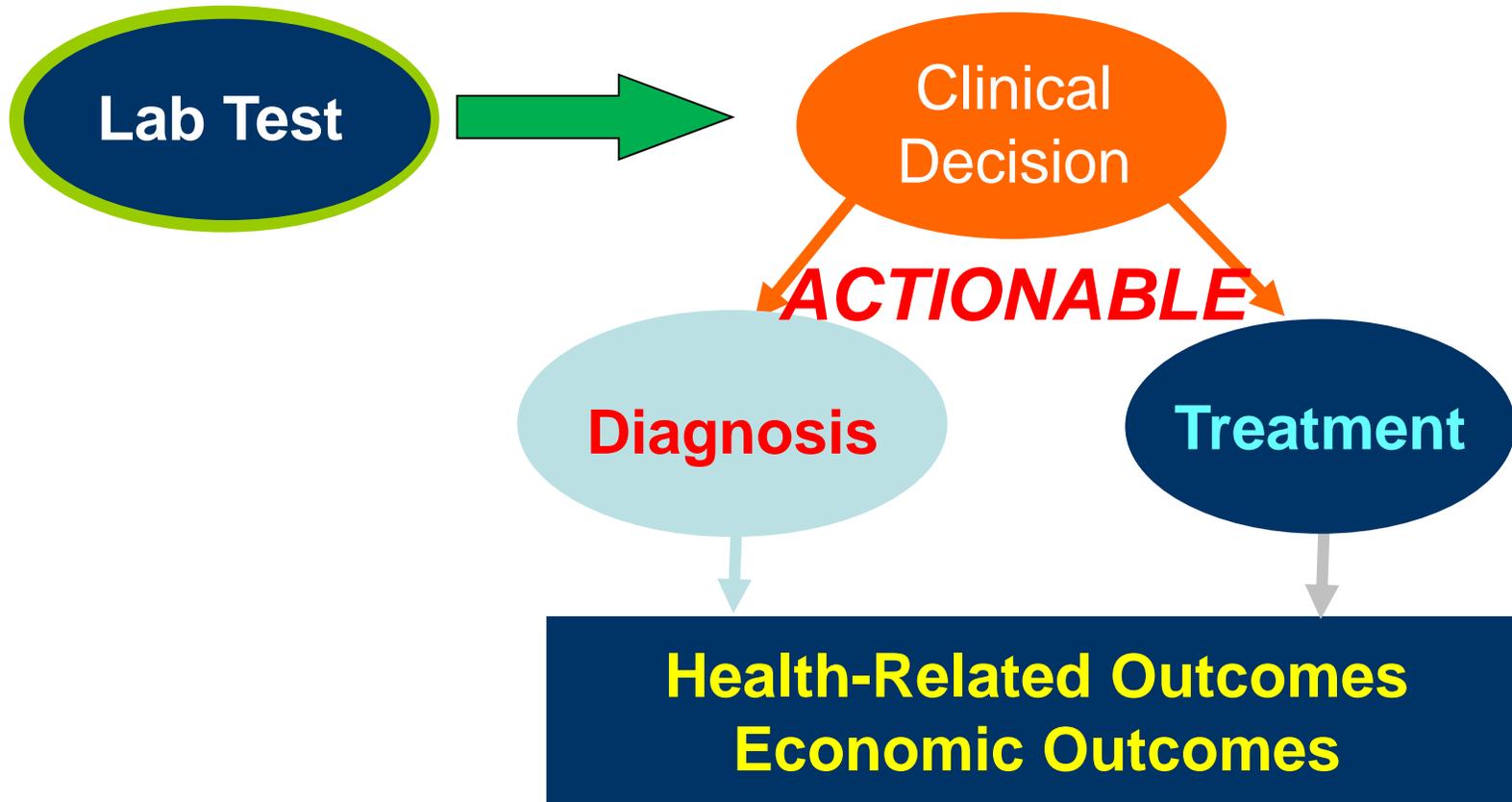
- Walgreen's program could be a forerunner of many innovative, cost-saving approaches to **coordinated care**
- **Laboratories:** It is not difficult to imagine the possibility of a national medical laboratory company **adopting a pharmacy care type model.**
- Clinical laboratories should develop relationships with national pharmacy chains to **track patients' medical laboratory testing needs** at discharge and in the following weeks.

Walgreen's New Medication Management Program May Foreshadow Similar Models for Clinical Laboratory Services – *Pamela Scherer McLeod*



- Clinical laboratories could identify which patients have **not received their ordered discharge lab tests.**
- Track patients whose post-discharge **laboratory test results indicate that some clinical action or follow-up is required to help prevent readmission.**
- Collaboration between a pharmacy and a clinical laboratory that identifies **patients failing to comply** with their post-discharge regimen would be an innovative example of **integrated clinical care.** It could help the patient to **avoid falling into the gaps** that currently exist between different types of healthcare providers.

Challenge: Connecting Laboratory Testing to Outcomes



Evidence in Action! NOT Evidence Inaction!

Thank you!

