Health Systems Adoption of Personalized Medicine: Promise and Obstacles

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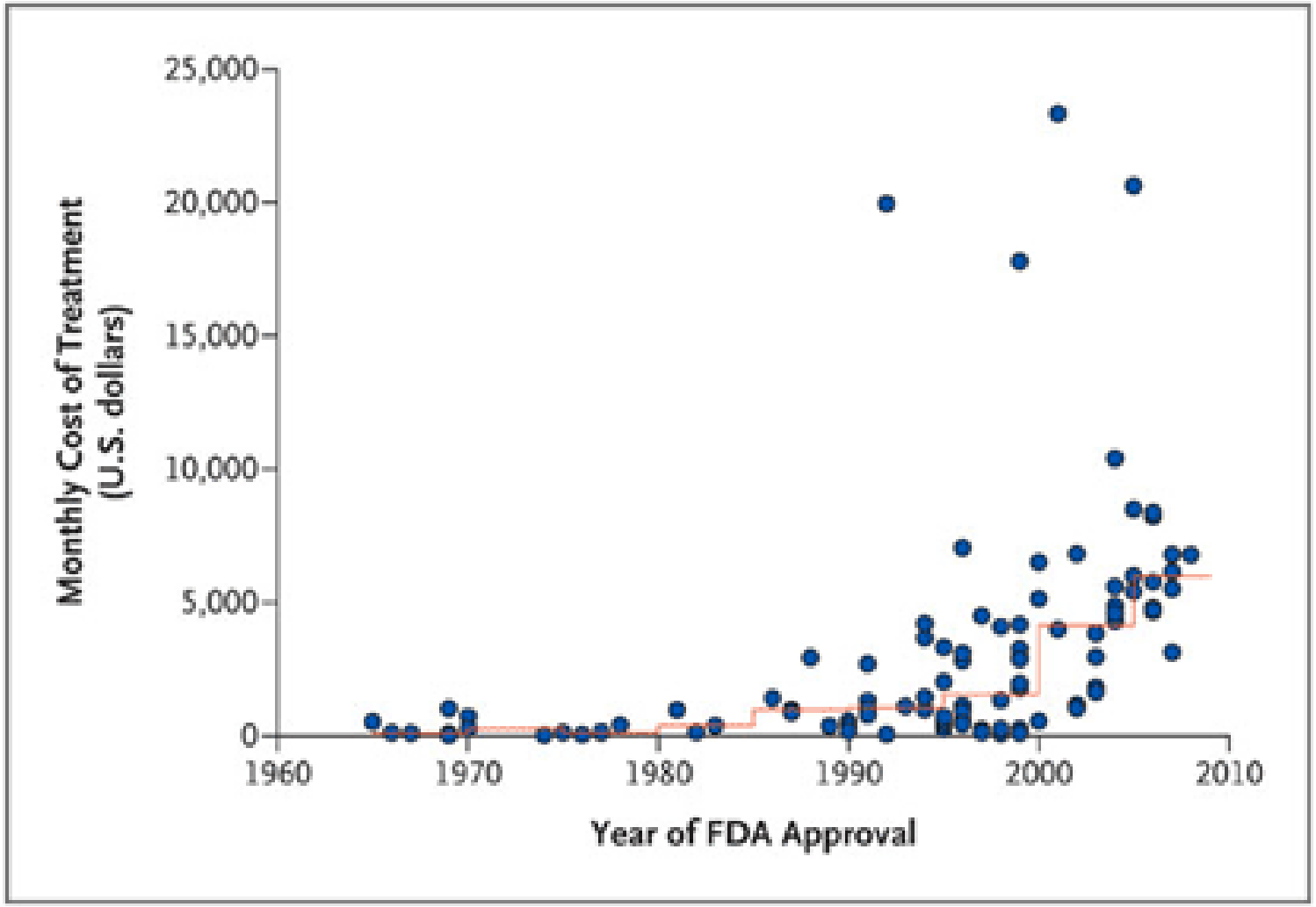
Cancer Pharmaceutical Pricing



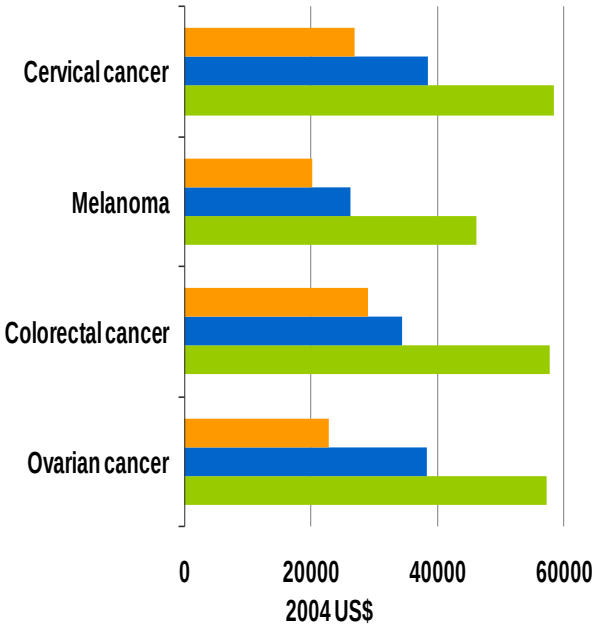
Bach P. NEJM 2009;360:626

Opportunities for Improved Molecular Diagnostics

Identify diseases at earlier, more curable stages

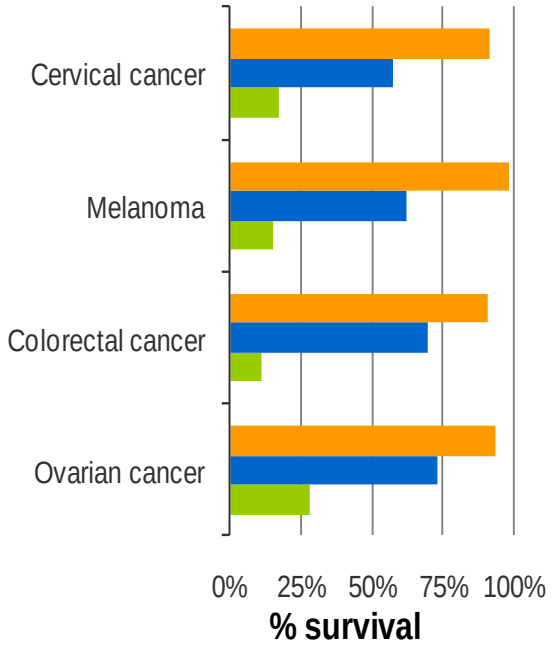
Estimated mean net costs of care in the last 12 months of life for US cancer patients aged 65+ years 1999-2003, by stage at diagnosis

Yabroff et al., J Natl Cancer Inst. 2008 May 7;100(9):630-41



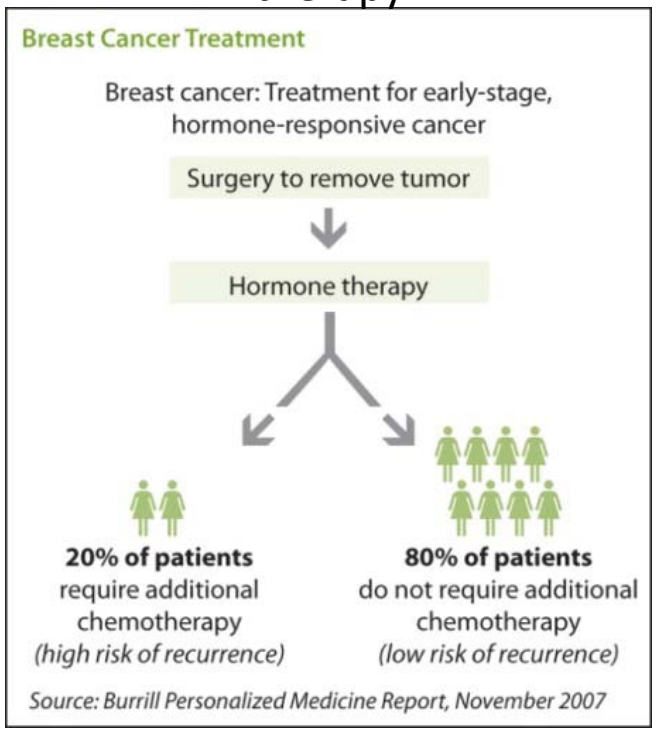
Five-year survival from diagnosis 2002-2006, by stage at diagnosis

NCI Surveillance Epidemiology and End Results



Stage at Diagnosis: Localized Regional Distant

Identify persons who will benefit from costly and toxic therapy



Issues for Personalized Medicine

- A huge number of new biomarkers are likely to be introduced over the next 5-10 years
  - Who will drive use – patients or clinicians?
  - How will clinicians know when it is time to use them?
  - How will health insurers know when they should pay for them?

Oncotype DX, Breast Cancer Assay - Mozilla Firefox

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http://www.oncotypedx.com/BREAST/index.aspx

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oncotype DX® Breast Cancer Assay

Make it part of the conversation.

How do you decide if chemotherapy is the right treatment choice? The Oncotype DX® assay is a first-of-its-kind diagnostic test that helps identify which women with certain types of breast cancer are more likely to benefit from adding chemotherapy to their hormonal treatment. It offers additional information about an individual's tumor that traditional technologies/tests do not capture. Armed with this and other information, patients and their doctors can make more informed, more *individualized* treatment decisions.

Patients & Caregivers
Is the Oncotype DX test right for you?

Professional Guidelines
ASCO and NCCN guidelines include recommendations for Oncotype DX assay usage.

Video
A complete step-by-step introduction to the Oncotype DX assay.

Oncotype DX Updates
12/15/09
Genomic Health Announces New Data Reinforcing Clinical Utility of Oncotype DX® in Multiple Breast Cancer Populations

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genomic health

Recommendations Regarding Oncotype DX

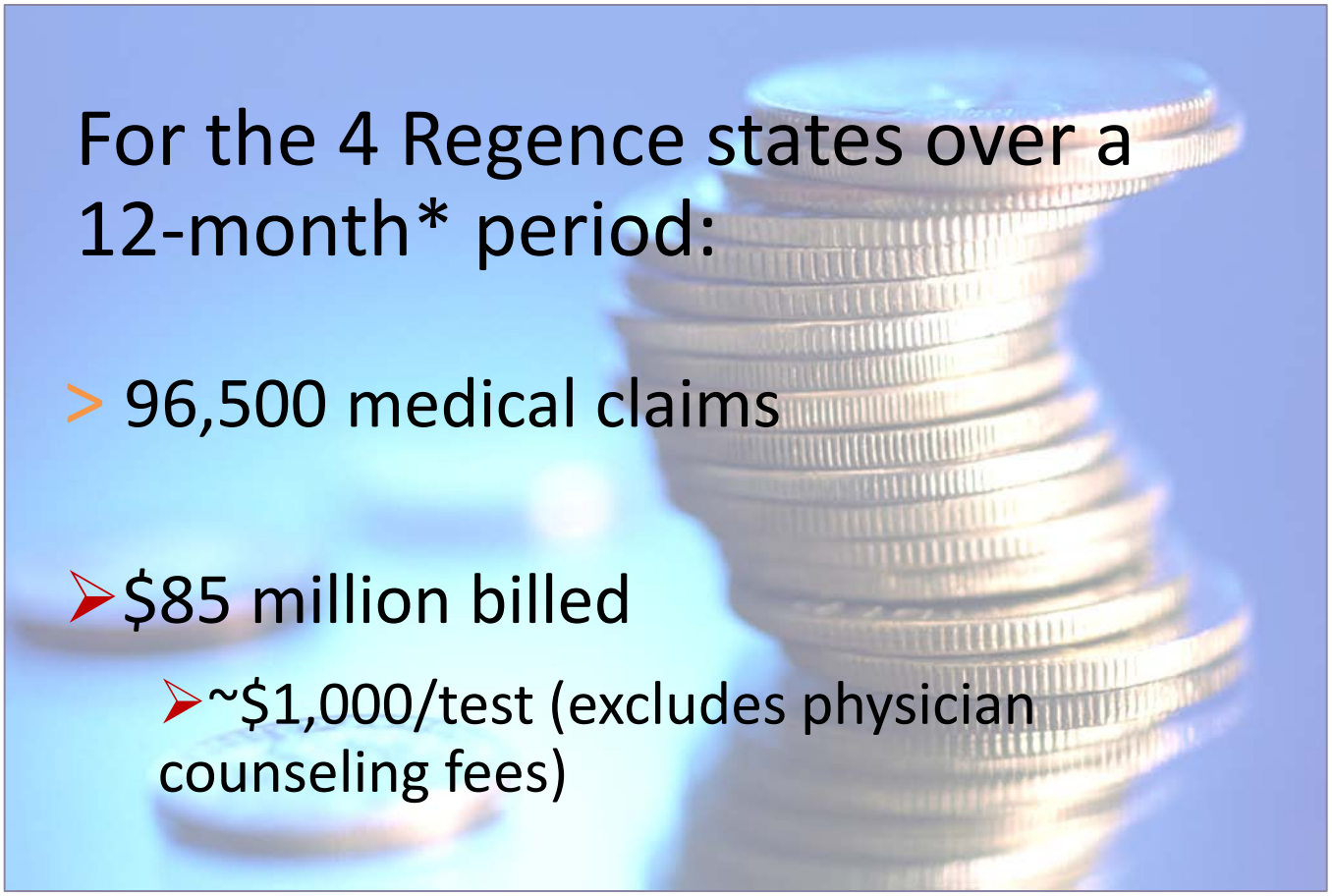
National Comprehensive Cancer Network

- …the Panel considers the 21-gene RT-PCR assay as an option when evaluating patients with primary tumors characterized as 0.6-1.0 cm with unfavorable features or > 1cm, and node-negative, hormone receptor- positive and HER2-negative (category 2B)

Evaluation of Genomic Applications in Practice and Prevention

- …insufficient evidence to make a recommendation for or against the use of tumor gene expression profiles to improve outcomes in defined populations of women with breast cancer

Billing for Genetic Testing at Regence Blue Shield

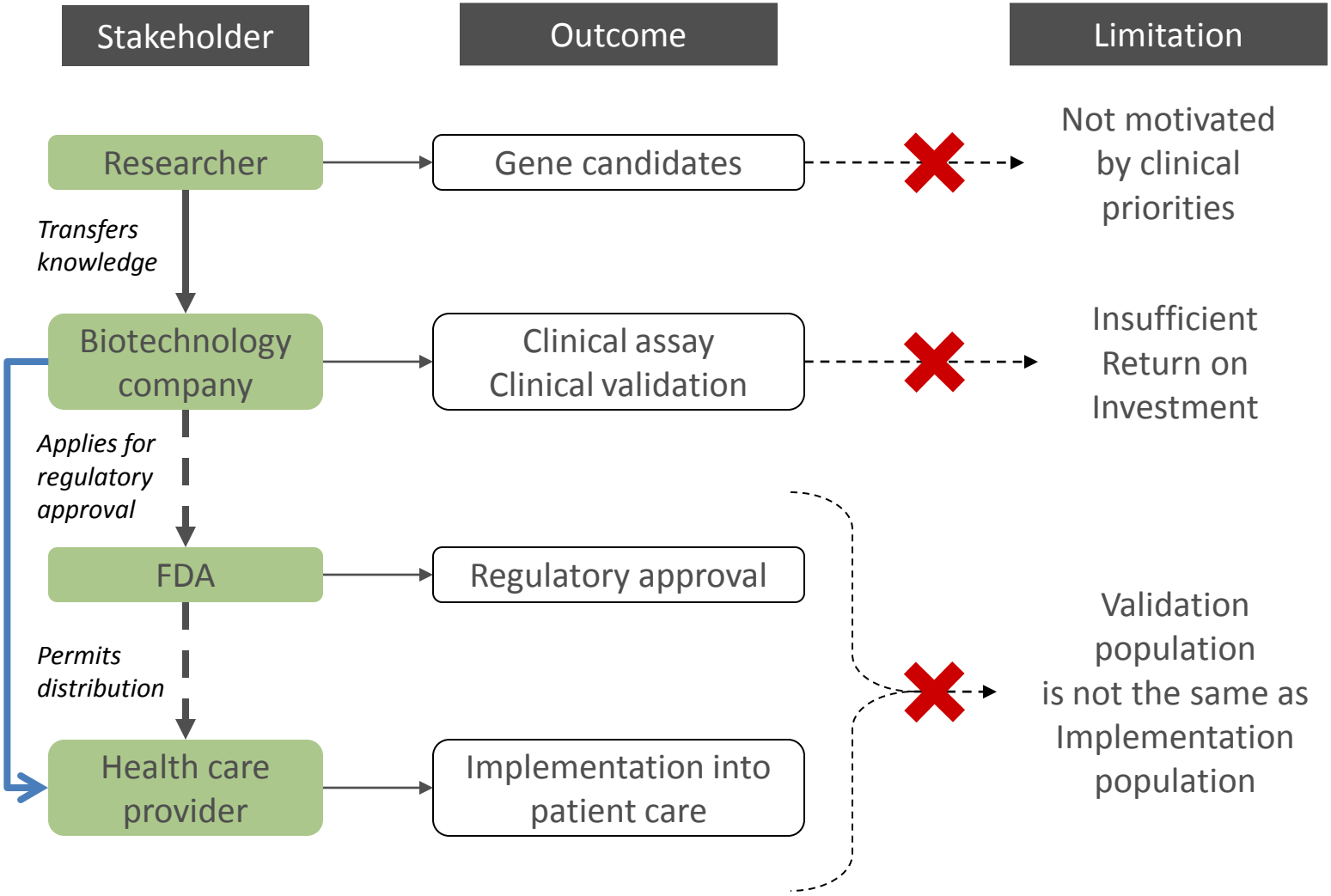


* Based on Oct 2007 – Sept 2008 Regence medical claims for genetic test CPT codes

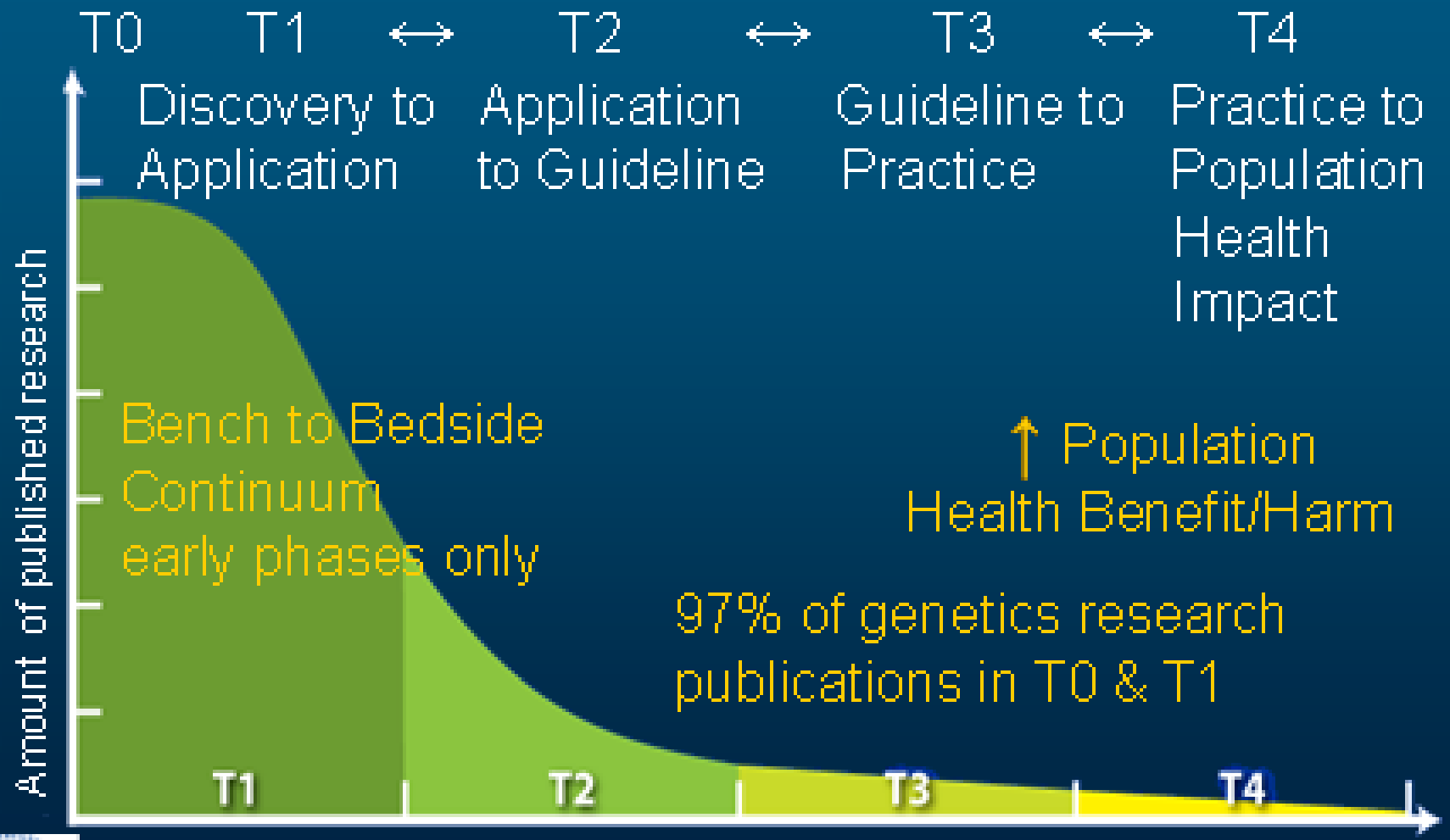
Testing and Personalized Medicine: Goals

- ***Analytic validity:***
  - *How accurately and reliably the test measures the genotype/phenotype of interest?*
- ***Clinical validity:***
  - *How consistently and accurately the test detects or predicts the intermediate or final outcomes of interest?*
- ***Clinical utility:***
  - *How likely the test is to significantly improve patient outcomes*
- ***Value:***
  - *Does the test influence care such that it represents good health value for money spent compared to not using the test?*

Current Model of Cancer Genomic Test Development

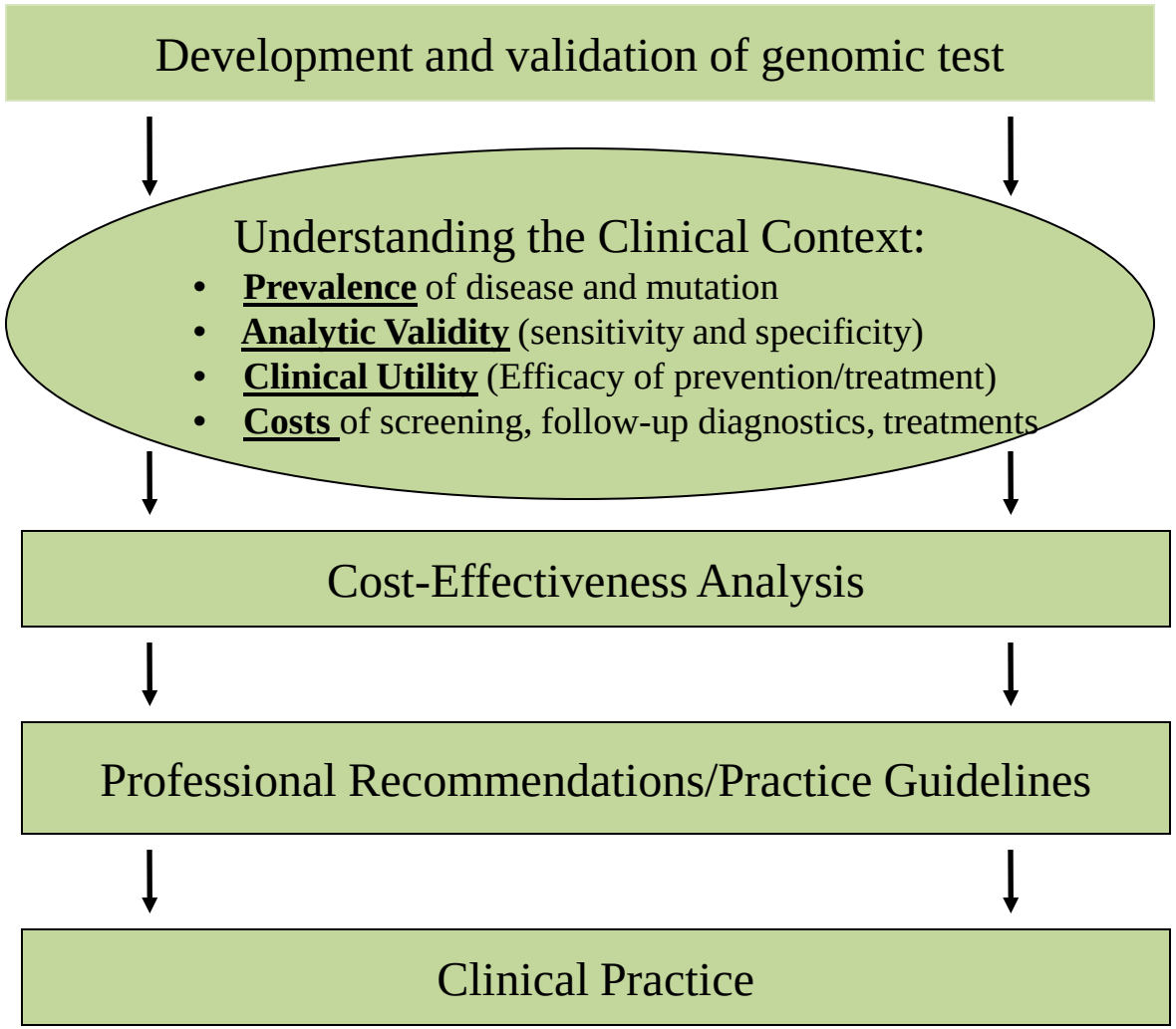


Currently, Limited Research for Evaluation & Implementation



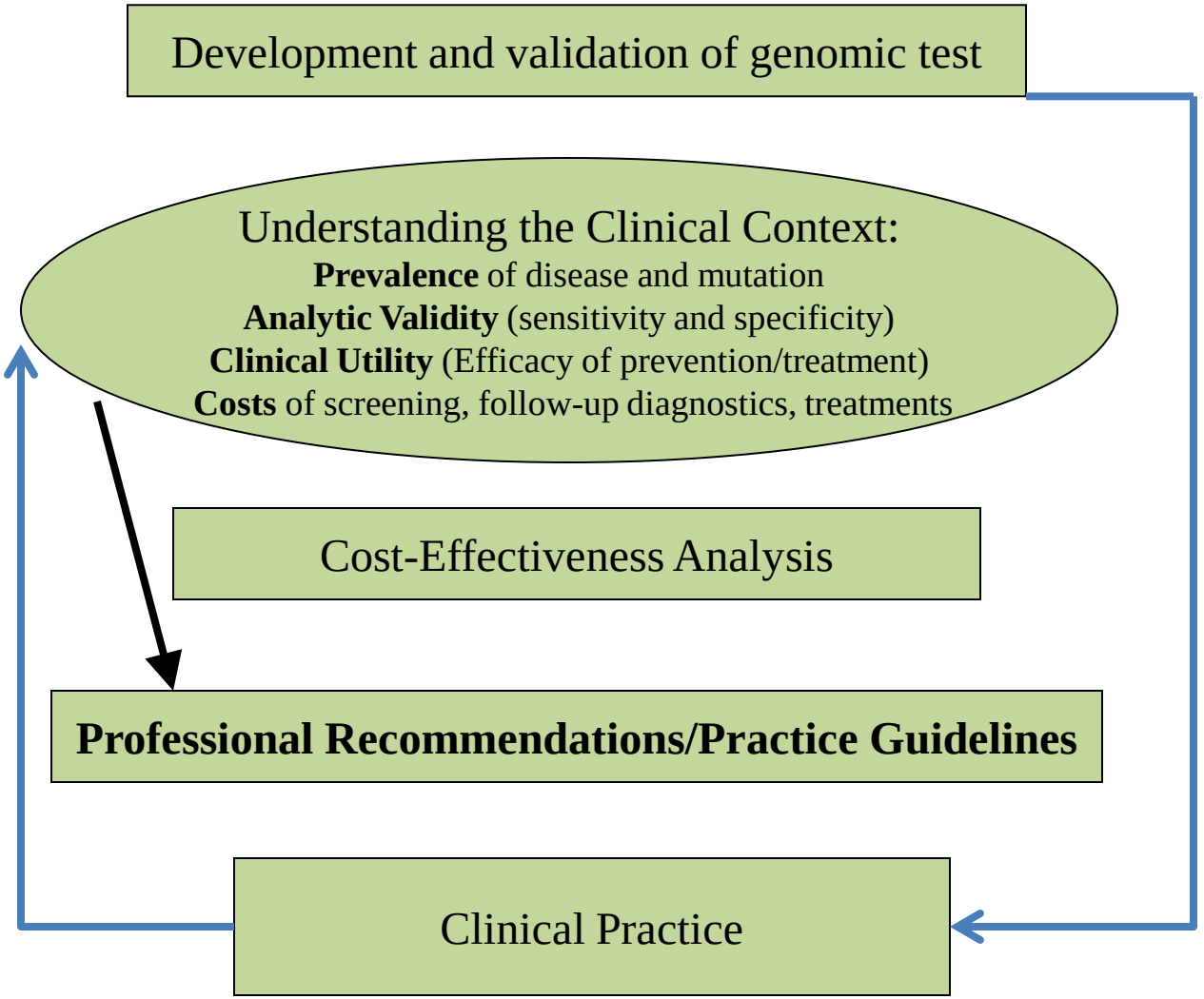
Khoury Genet Med 2007;9:665; Woolf JAMA 2008;299:211

Ideal Process for Evaluation of Genomic Tests



Adapted from: Col NF. Medical Decision Making 2003;23:441

Actual Process for Evaluation of Genomic Tests



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Lessons from Prostate Specific Antigen Testing

- Discovered 1970
- FDA approved 1994
- 30 million men tested annually
- Annual US expenditures for screening $3 billion
- Two studies evaluating the efficacy of screening published in 2009:
  - US: PSA screening did not lower prostate cancer deaths
  - Europe: absolute risk reduction in prostate death: 0.6%
  - For every man helped by PSA, 48 received unnecessary therapy

“The test is about 50 times more likely to ruin your life than it is to save your life”

Dr. Otis Brawley, chief medical officer of the American Cancer Society, commenting on the European Study

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cumulative Association of Five Genetic Variants with Prostate Cancer

S. Lilly Zheng, M.D., Jielin Sun, Ph.D., Fredrik Wiklund, Ph.D., Shelly Smith, M.S., Pär Stattin, M.D., Ph.D., Ge Li, M.D., Hans-Olov Adami, M.D., Ph.D., Fang-Chi Hsu, Ph.D., Yi Zhu, B.S., Katarina Bälter, Ph.D., A. Karim Kader, M.D., Ph.D., Aubrey R. Turner, M.S., Wennuan Liu, Ph.D., Eugene R. Bleecker, M.D., Deborah A. Meyers, Ph.D., David Duggan, Ph.D., John D. Carpten, Ph.D., Bao-Li Chang, Ph.D., William B. Isaacs, Ph.D., Jianfeng Xu, M.D., D.P.H., and Henrik Grönberg, M.D., Ph.D.

ABSTRACT

A Berg 2010

RESULTS

Multiple SNPs in each of the five regions were associated with prostate cancer in single SNP analysis. When the most significant SNP from each of the five regions was selected and included in a multivariate analysis, each SNP remained significant after adjustment for other SNPs and family history. Together, the five SNPs and family history were estimated to account for 46% of the cases of prostate cancer in the Swedish men we studied. The five SNPs plus family history had a cumulative association with prostate cancer (P for trend, 3.93×10^{-28}). In men who had any five or more of these factors associated with prostate cancer, the odds ratio for prostate cancer was 9.46 ($P=1.29\times10^{-8}$), as compared with men without any of the factors. The cumulative effect of these variants and family history was independent of serum levels of prostate-specific antigen at diagnosis.

A Berg 2010

ROC Curve — Area Under the Curve

- 0.58 — age, geography
- 0.61 — age, geography, family history
- 0.63 — age, geography, FH, 5 SNPs
- Reason: Odds ratios calculated against lowest-risk, will always give highest risk

A Berg 2010

Cost-effectiveness ratios for clinical and molecular subgroups, erlotinib in advanced nonsmall cell lung cancer

Characteristic	ICER, $ per life-year gained
Female	$120 671
Male	$96 601
Never-smoker	$39 487
Smoker	$504 911
Asian	$83 181
EGFR protein expression (+)	$63 805
EGFR protein expression (-)	$469 003
EGFR mutation Exon 19 deletion and/or exon 21 L858R mutation	$138 168
EGFR wild-type or other mutation	$87 994
KRAS mutation in codons 12 and 13	Best supportive care dominant
KRAS Wild type	$76 657
EGFR gene copy number High	$33 353
EGFR gene copy number Low	$109 792

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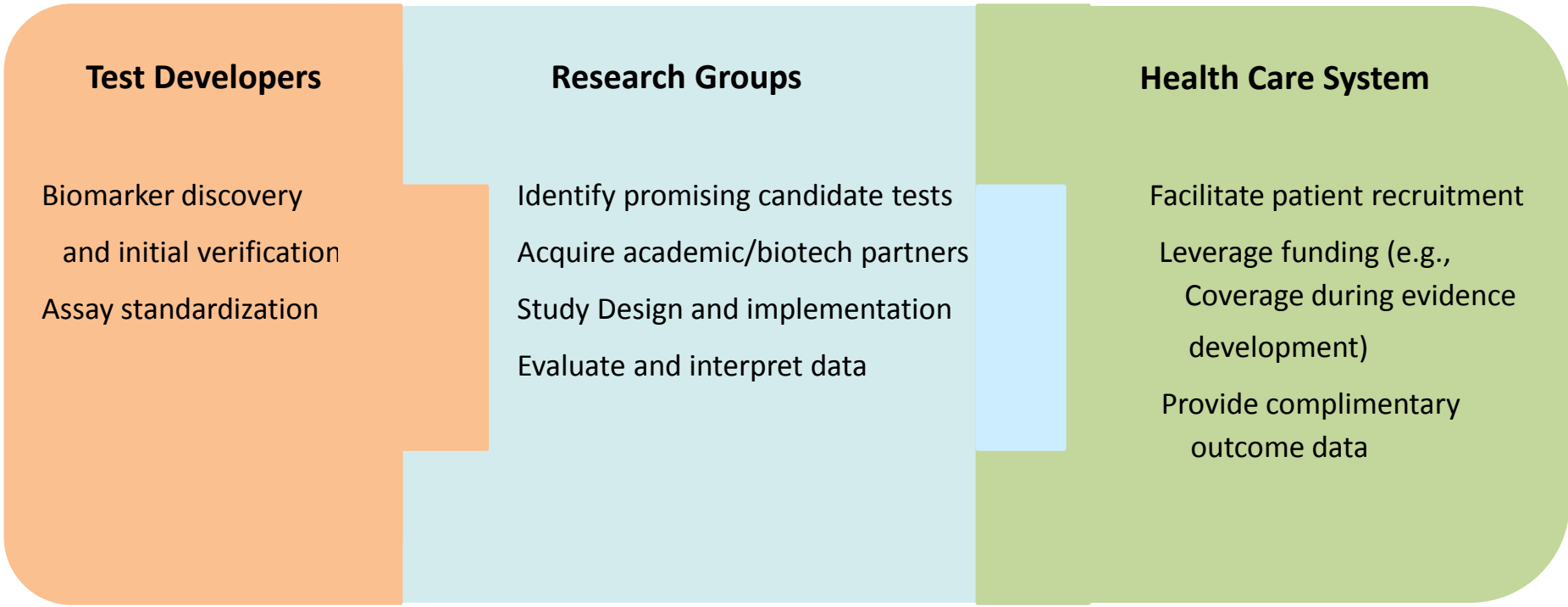
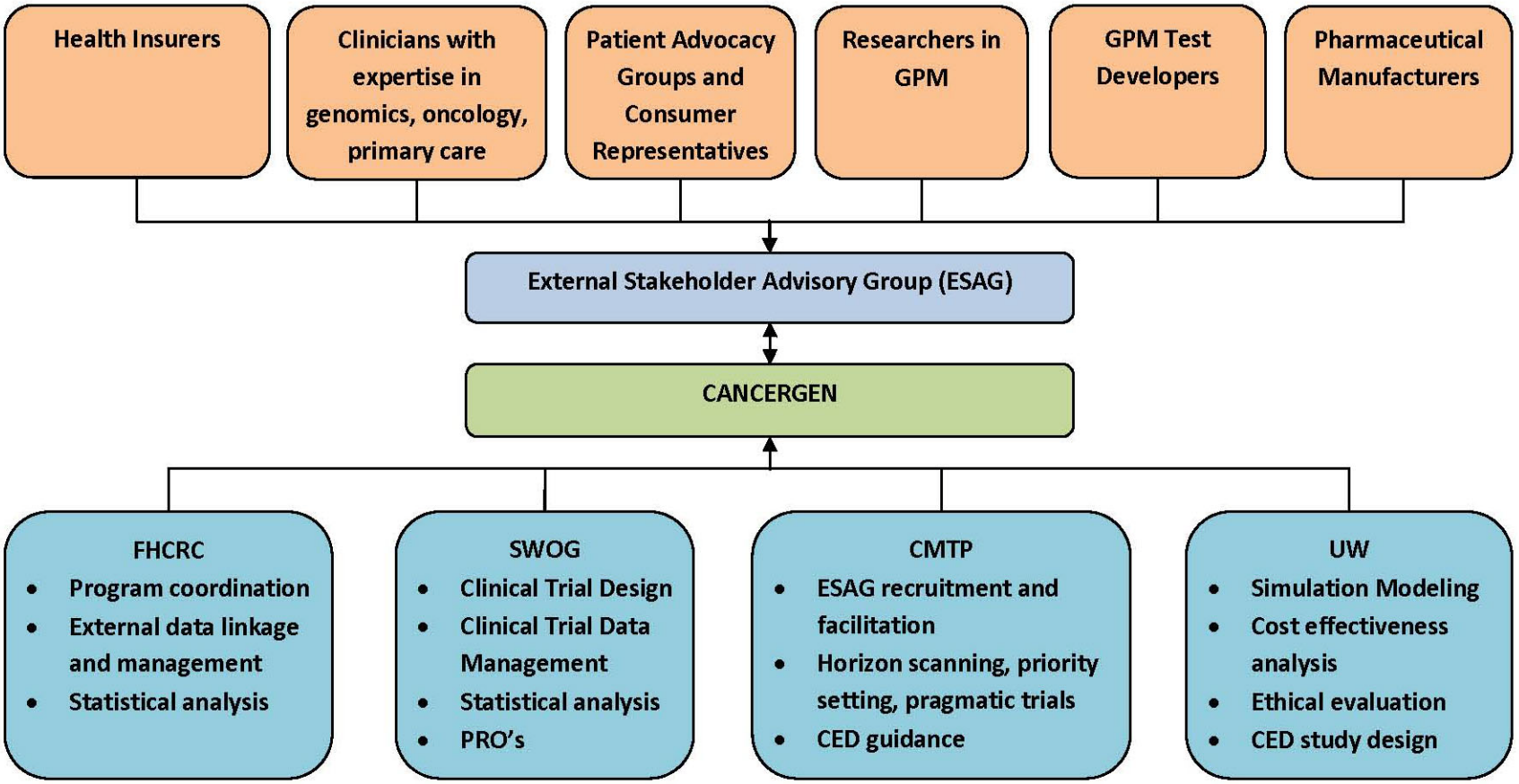
Ways Forward

- Partnerships
- Better evidence
- Risk sharing

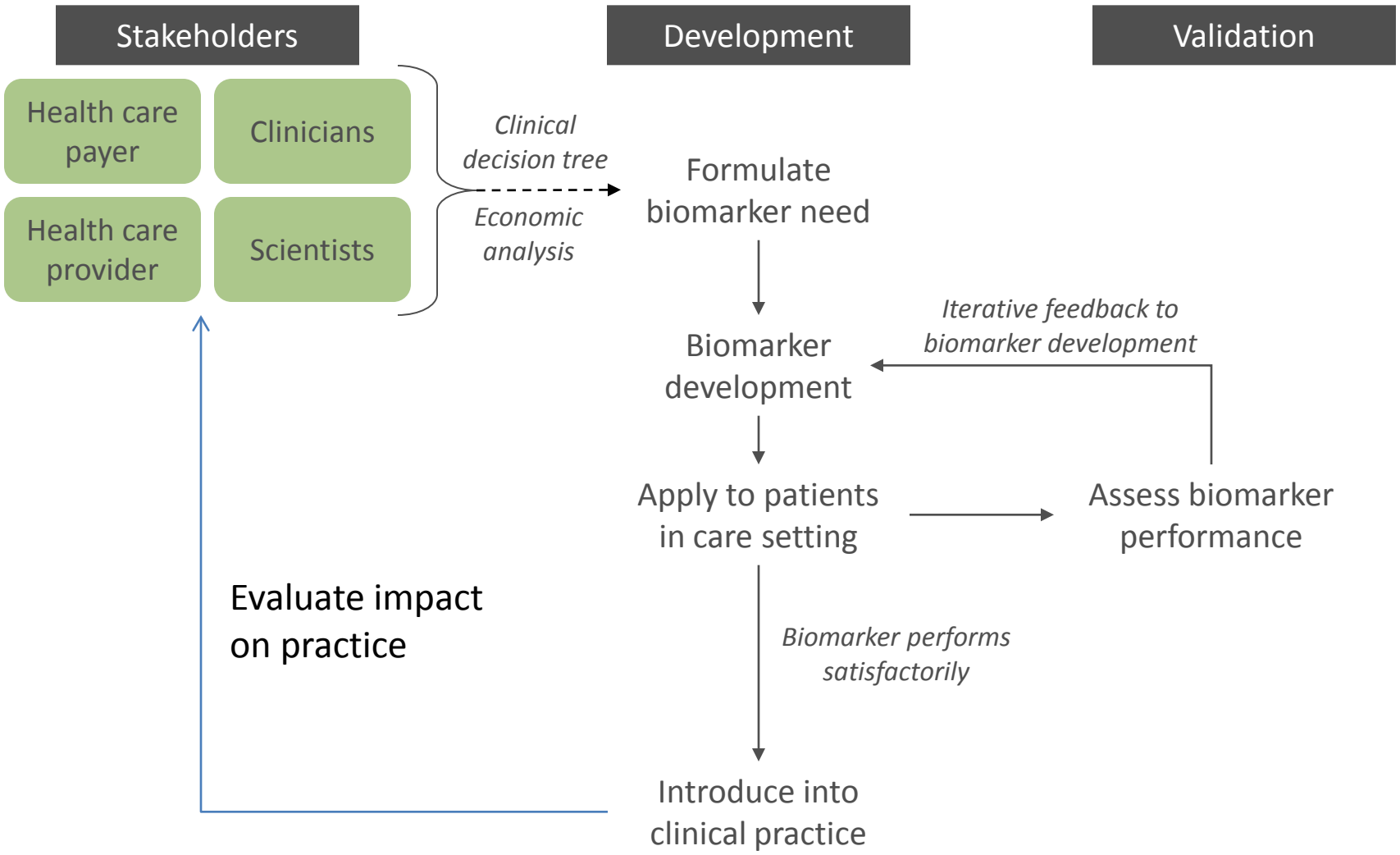
Risk Sharing: Partner Contributions



CANCERGEN Structure



Shared Model of Diagnostic Development



Summary

- There is no guarantee that PM will bend the health care cost curve or improve patient outcomes
  - Current incentives poorly aligned with generating high quality evidence
  - Limited investment in translational science
- Partnerships spanning the spectrum from developer to health system offer the best chance of directing discoveries that both improve outcomes and provide value
  - Focus on the health system perspective at the earliest point of development