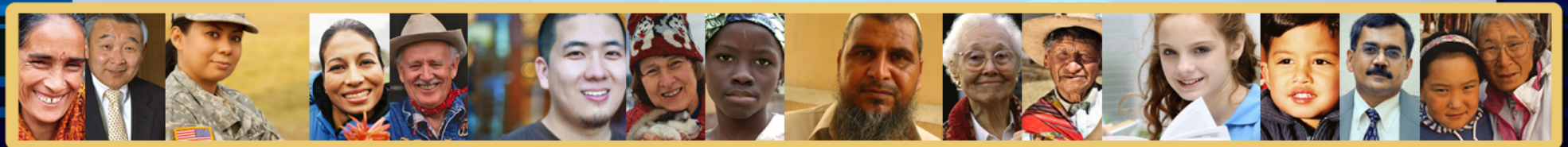27 October, 2015
Better Science, Better Health:
New Healthcare Models

Implementing Personalized Medicine, Determining Economic Value

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Empirical Medicine Success:
Improving Cardiovascular Death Rates
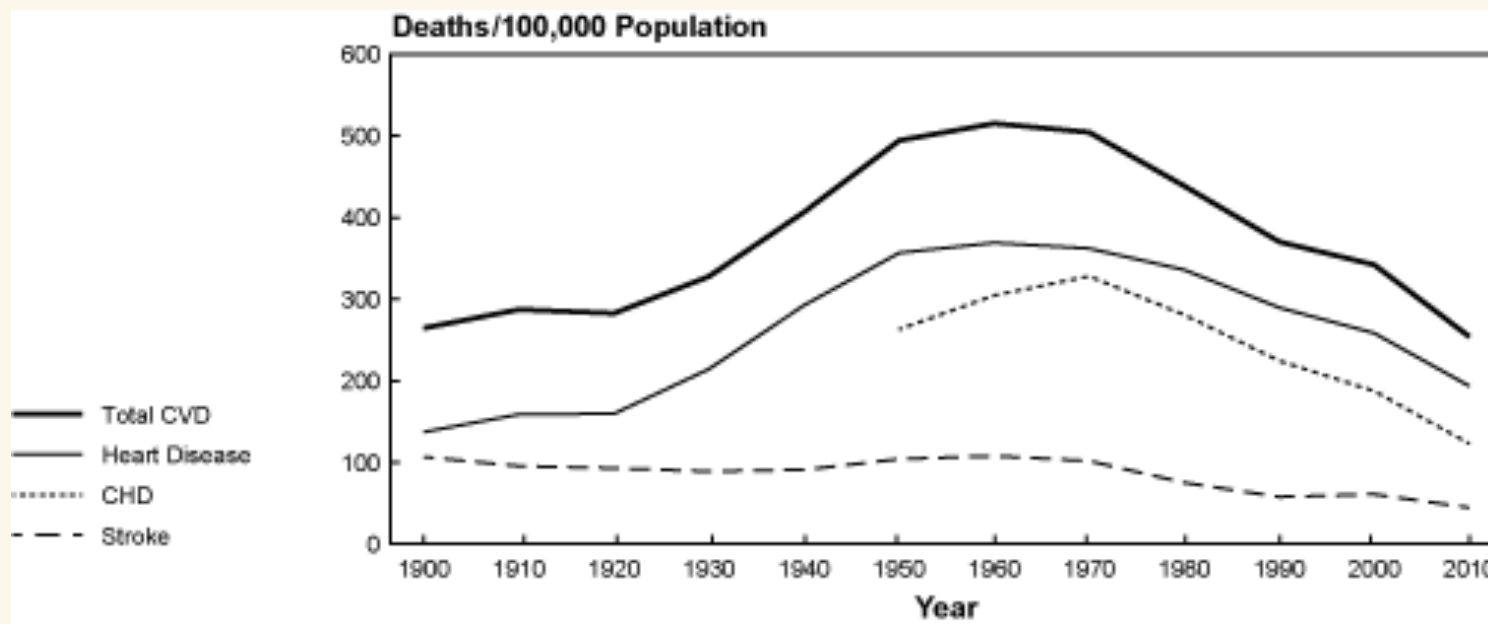
Source: Vital Statistics of the United States, NCHS

http://www.nhlbi.nih.gov/about/documents/factbook/2012/chapter4

Empiricial Medicine Success:
Lowering Cardiovascular Events with Statins

- Empirically prescribe to those displaying risk factors

5 Years

Avoid
1 Fatal
Event

Treat 83 People for 5 Years @ $1,000/yr — $415,000

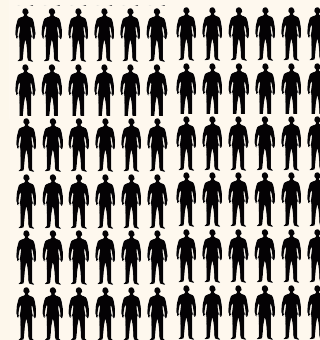Treat 83 People for 5 Years @ $120/yr with generics — $ 50,000
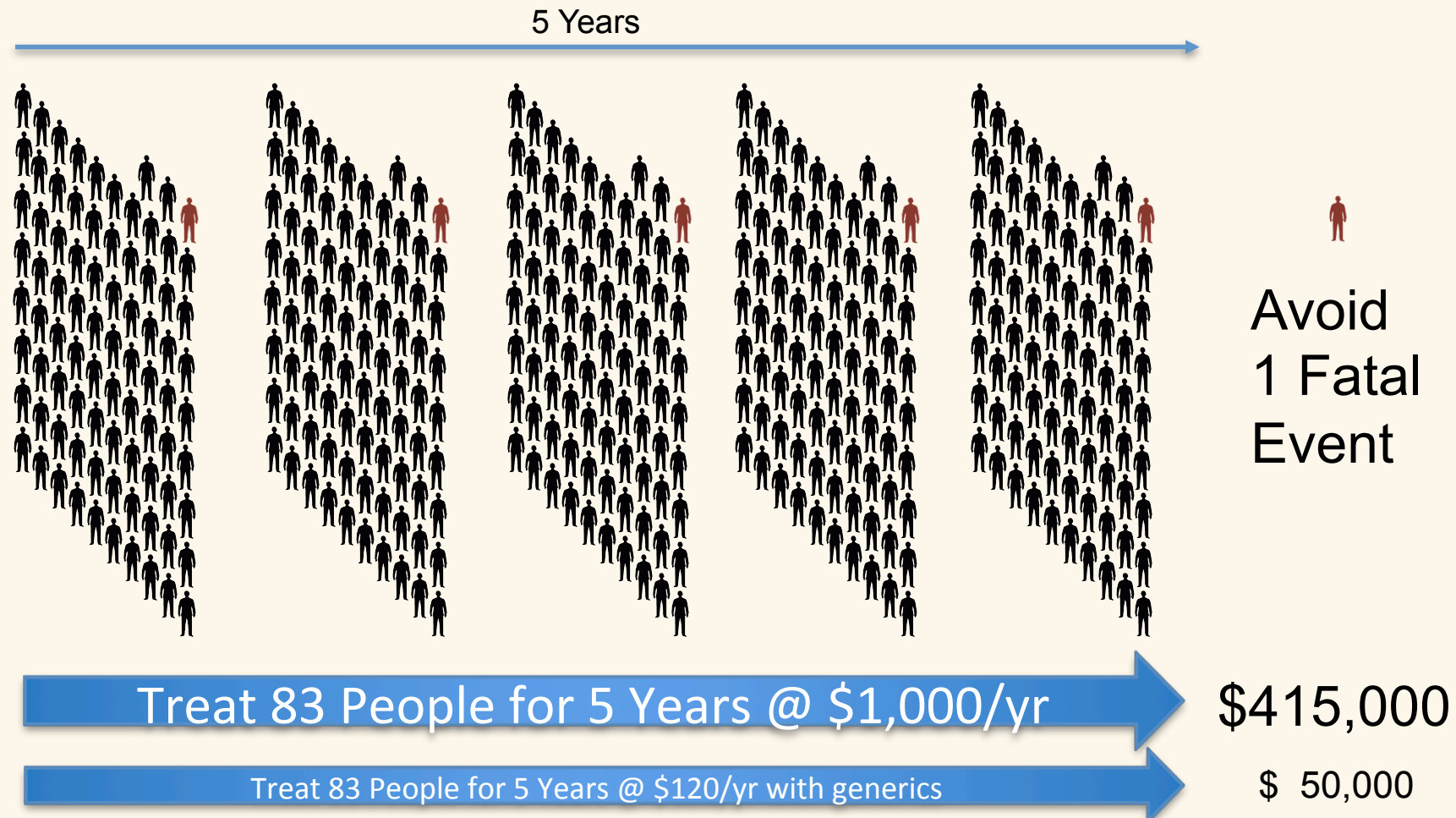
Classic Personalized Medicine:
Use a Molecular Diagnostic to Select Responders

- Targeted prescribing to those possessing proper profile

Higher response rate, But also higher price?

Avoid adverse events and save critical time

Advancing Science Fragmenting Conditions into Many Molecular Types

- Combinations fragment even further
- And resistance evolves
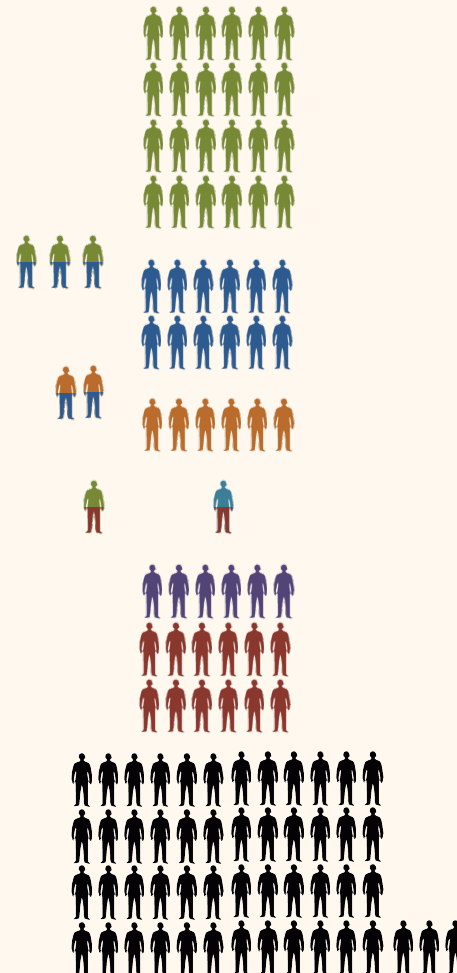
Is their an economic limit for development? For affordability?

Figure 4: Cancer organ of origin incidence with approved therapeutics for each
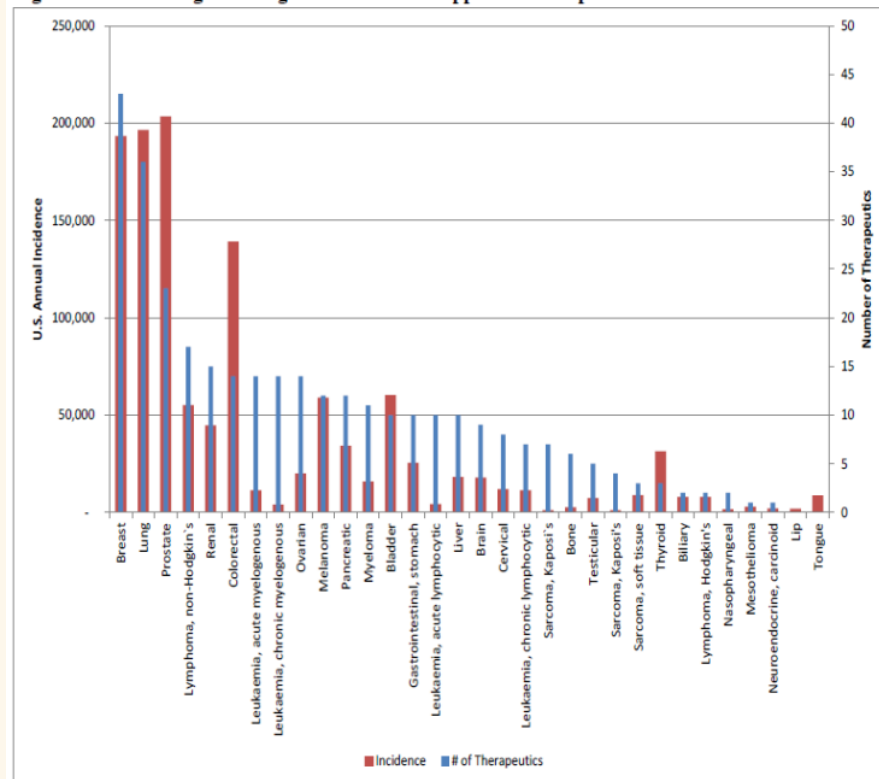
Figure 5: Bivariate regression of segment patient incidence and available drug therapies
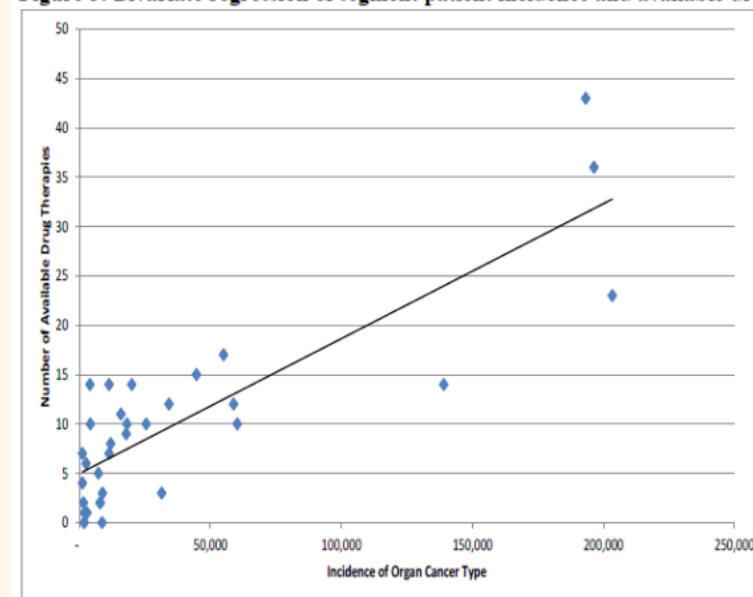
Trusheim MR, Berndt ER, Health Management, Policy and Innovation 2012

Targeted Cancer Therapies Face Transformed Economics

- The old rules for price and costs do not work for innovators

Large Cancer Indication
200K patients / yr

$20K Price *
40% Mkt Share * =

$625M
Net Cash Flow,
7 Years

6 Years
Adoption

$400M, 7 Years Dev't

20 Year Patent Life

$1,166M
Net Present Value

Stratified Cancer Indication
7K patients / yr

$400M, 7 Years, Dev't

$20K Price *
60% Mkt Share =

6 Years
Adoption

$33M Net Cash Flow,
7 Years

-$194M
Net Present Value
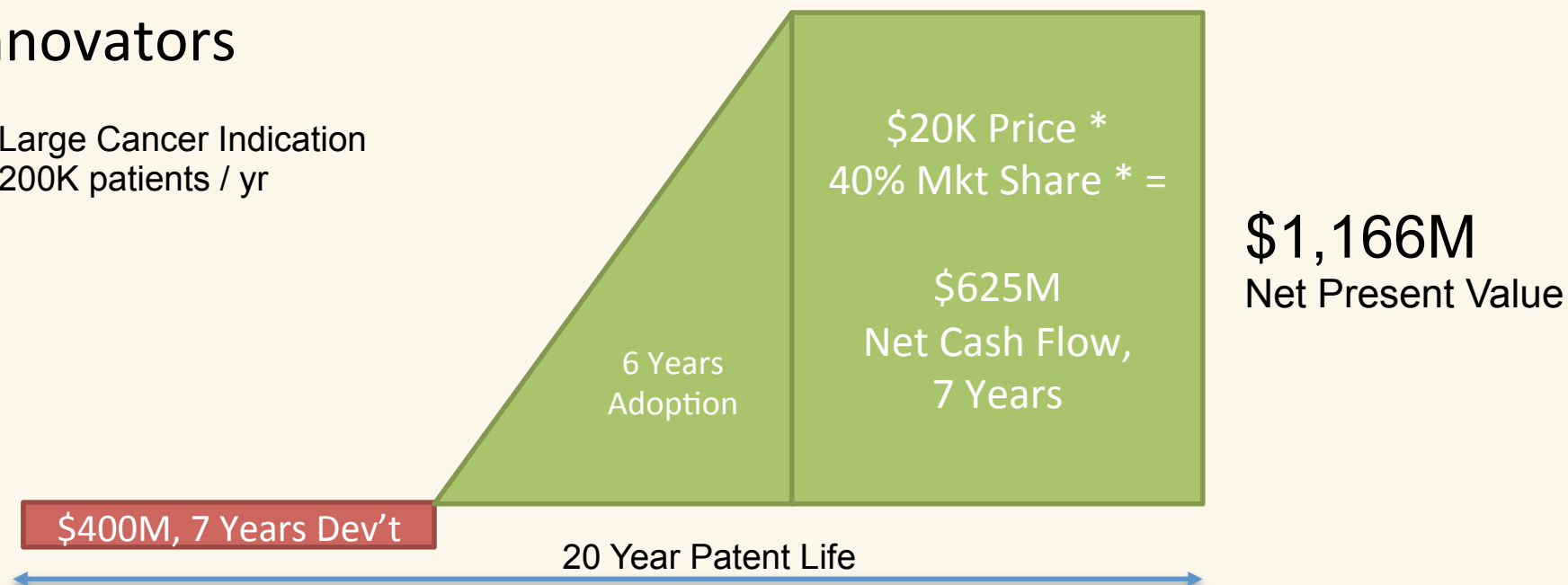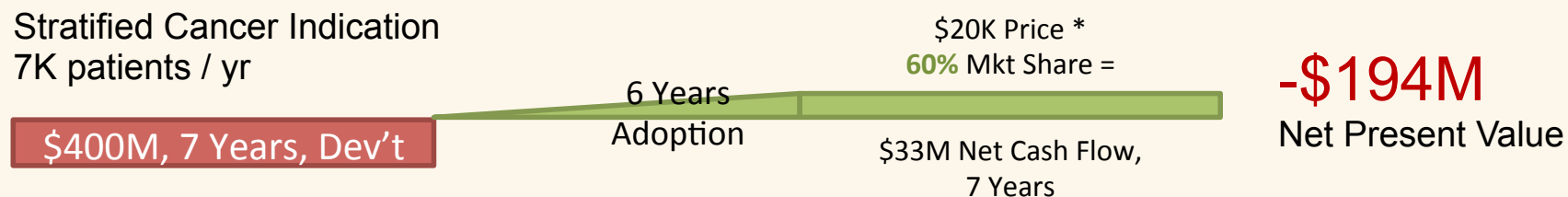
Adapted from Trusheim, Berndt: Economic Challenges and Possible Policy Actions to Advance Stratified Medicine, *Personalized Medicine*, 9(4)413-427June 2012

Could PM Life Span Shifts Provide Innovator Incentives?

20 Year Patent Life

Stratified Cancer Indication
7K patients / yr

$400M, 7 Years, Dev't

6 Years
Adoption

$20K Price *60% Mkt Share =
$33M Net Cash Flow, 7 Years

-$194M
Net Present Value

Faster Development & Adoption

$200M,
4 Years

4 Years

12 Years

-$ 39M
Net Present Value

Incredibly Fast & Exclusivity

$150M,
3 Years

4 Years

$20K Price * **90%** Mkt Share =

$49M Net Cash Flow, 13 Years

$103M
Net Present Value

Balance Speed, Price & Competition

$200M
4 Years, Dev't

6 Years

$60K Price * 60% Mkt Share =
$33M Net Cash Flow, 7 Years

$195M
Net Present Value

Gleevec & Molecular Extension:
Can NGS Marker Matching Replace Clinical Trials?

- New imatinib indications entering market after 10 years
- 3 Biomarkers: Ph+, KIT, PDGFR rearrangements

Failed

CRC	Breast
NSCLC	Uterine
Ovarian	Malig. Gliomas
Thyroid	Sclero-doma
Head & Neck	PAH

Line/Demographic

Geography

Chronic	2009
Pediatric, Prior Tx	2002
Pediatric, Prior Tx	2002
New Diag.	2002

New Diag.

JPN

EU

| Ph+ CML, Prior Tx | KIT GIST, Prior Tx | DFSP | Ph+ ALL | PDGFR MDS/MPD, HES, CEL | D816V c-Kit Negative ASM |

2001   2002   2006   2006   2006   2006

Indication
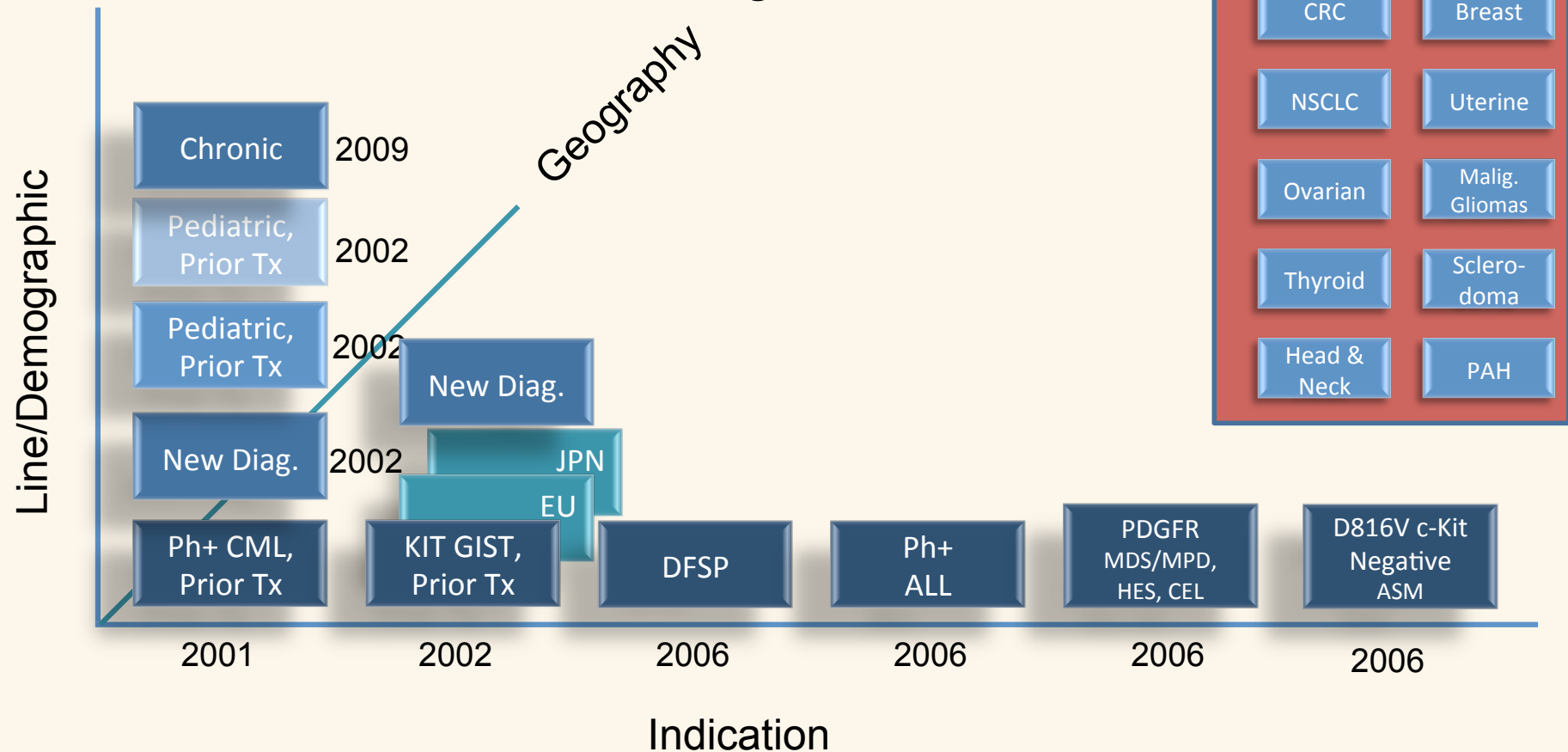
Companion Diagnostics Harness Variability to Link Science, Clinic, Markets and Ethics

A Bimodal Marker
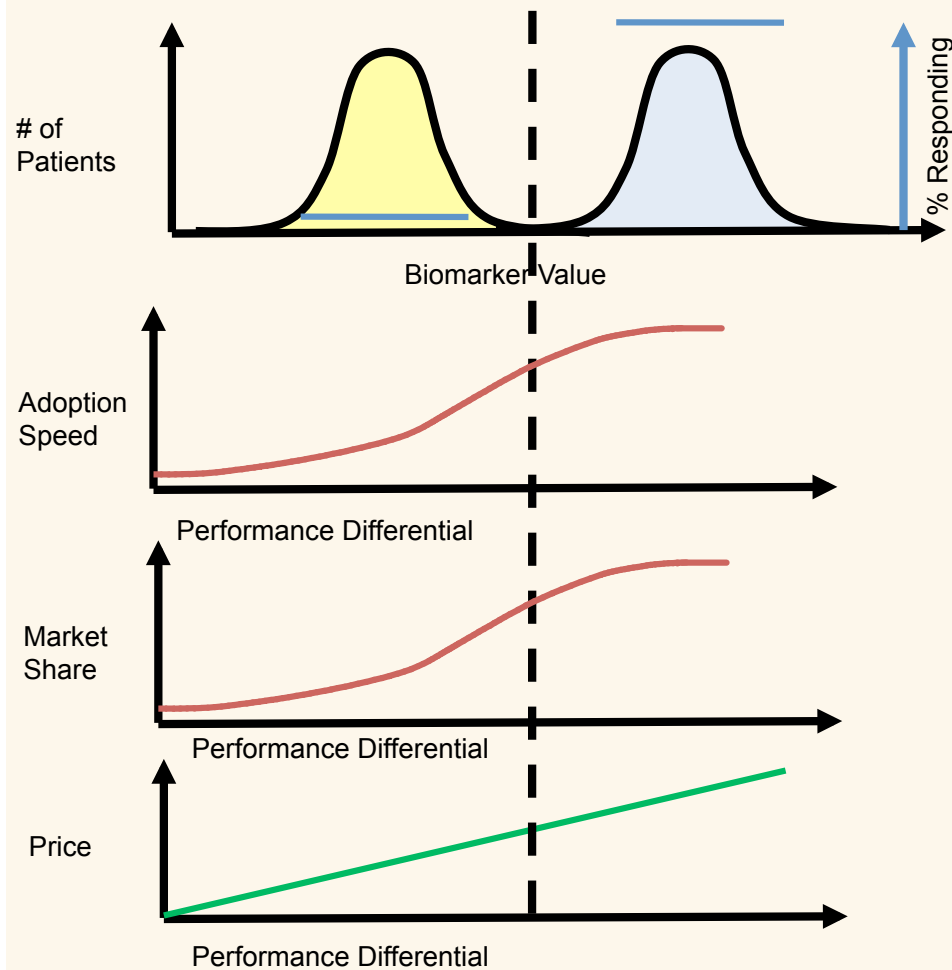
Overlapping Populations

Trusheim MR, Berndt ER,. NBER Working Paper 21233 June 2015

Trusheim: Determining Economic Value

Center for Biomedical Innovation

Massachusetts Institute of Technology

Competition Begins Early in Stratified Medicine

Most oncology targets have multiple compounds in competitive development

Cancer Therapies Launched or in Ph I, II or III, by Target
(Unspecified, Not Applicable and blank removed)

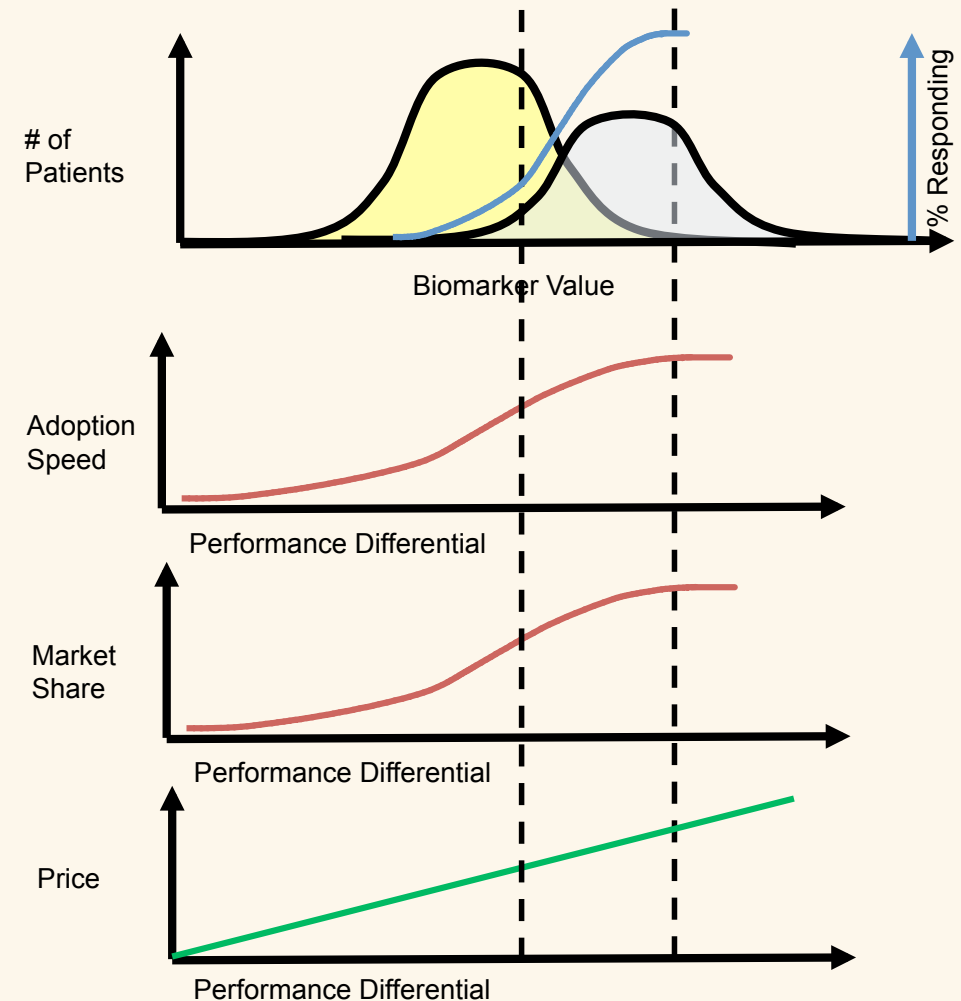For the 35 targets in Phase 3 with no approved products, only 12 of 141 compounds had no competitors for their target

(Chart labels: topoisomerases (DNA), tubulin, EGFR, HER2, MS4A1, topoisomerases (DNA), MET; Y-axis: Number of Therapeutics (0–40); X-axis: Targets (by # of Launched products then alphabetical); Legend: Launched, Phase I- III)

Authors' analysis of PharmaProjects pipeline database as of September 2014

Trusheim MR, Berndt ER,. NBER Working Paper 21233 June 2015

Center for Biomedical Innovation   October 2015   Trusheim: Determining Economic Value   11   Massachusetts Institute of Technology

Harnessing Variability Disrupts Price Comparisons

- Consider 3 identical medicines for a 100,000 patient cancer indication
- Each uses a different diagnostic strategy
- Recent published US oncology ICER of $138,582

Responders
33% of Population
12 months added OS

Non-Responders
67% of Population
0 months added OS

None | Max Responders | Minimize Non-Responders

# of Patients

Companion Diagnostic Score
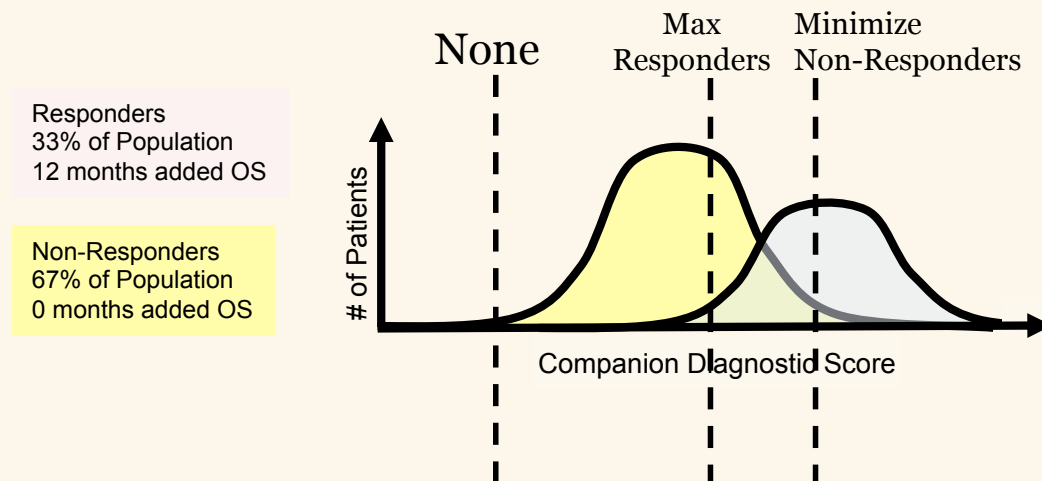
	None
RCT Efficacy (Months OS)	4.0
Price (ICER Based)	$46,000
Benefiting Patients	7,250
Treated Patients	21,750
Payer Cost	$1B

PRICES vary by 150% but VALUE is equal
(Better at higher price if any adverse events)

ICER: Incremental Cost Effectiveness Ratio
OS: Overall Survival

Trusheim MR, Berndt ER,. NBER Working Paper 21233 June 2015

Low Diagnostics Pricing
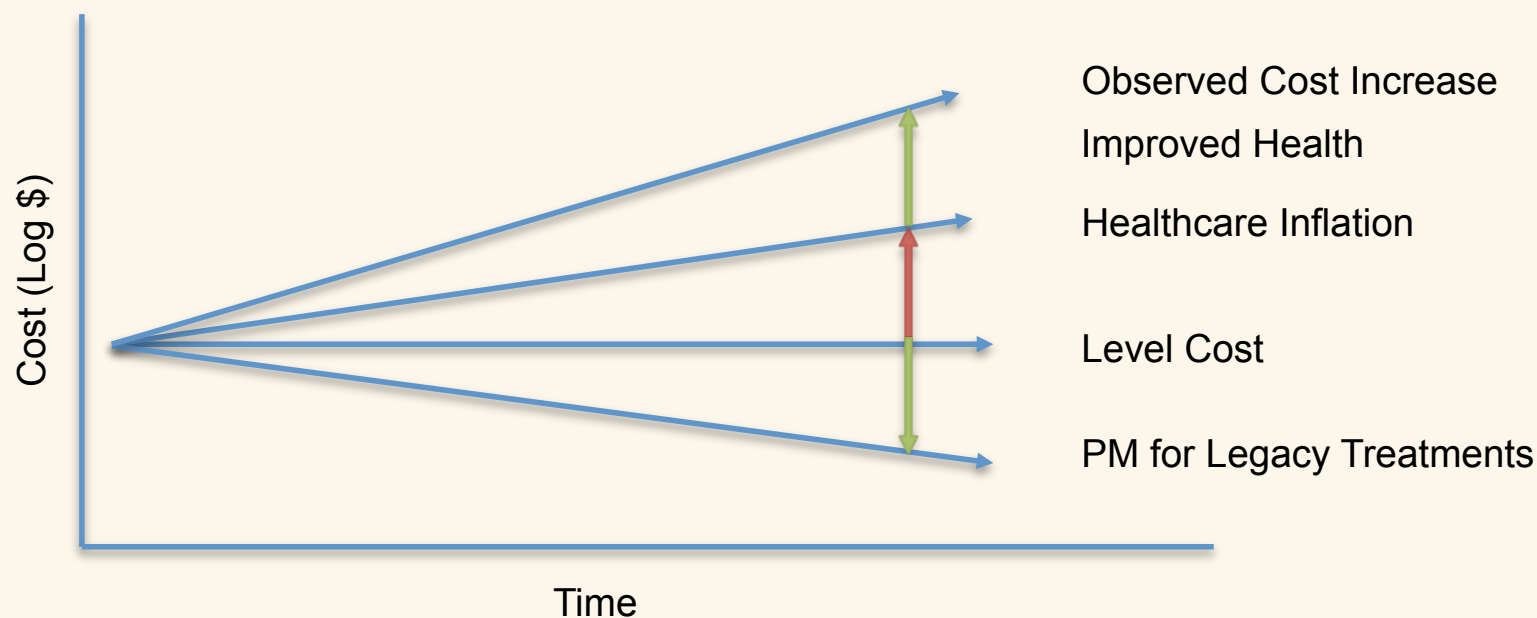# Limits Personalized Medicine to New Therapies

- Personalization enabled by diagnostic selection

- Diagnostics receive little of the value. Pricing dominated by cost based reimbursement with limited innovation protection (ie. power) for innovations

- Opportunities lost: Legacy treatment stratification
  - » Could reduce overall costs
  - » Neither diagnostics nor generic/original sponsors have incentives currently

Affordability for Payers and Society

- Pay for added health or for existing health cheaper?
- Challenge of effective treatments for large background prevalence conditions (Hepatitis C, Alzheimers?)
- Financing challenge of cures over chronic treatment
- Consider impact on non-healthcare areas?
  - » Absenteeism, productivity
  - » Caregiver costs: direct or workforce absence
  - » Social retirement, disability and other social program costs
- Value of compassion for orphan therapies and non-work force aged patients

Single Process to Explore Impact for all Stakeholders

- *Will I get better?*
- *Will I get access to new drugs faster?*
- *What are the risks?*
- *What are net health benefits? Social benefits?*

Patient / Public Health

- *Time & cost to market?*
- *Patient access?*
- *Evidence requirements?*
- *Financial returns and risk?*

Adaptive Biomedical Innovation

- *Aggregate & pharmacy costs?*
- *What clinical utility evidence exists?*
- *What are risks of overuse?*

Regulator

- *Evidence requirements for risk & benefit?*
- *Prioritization and staging of evidence generation across the product lifecycle and among regulators?*
- *Developing an adequate safety database?*