Pricing of Therapeutics:
A Complex, Multidimensional Matrix

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The Strategic Landscape for Healthcare

- ageing society
- increased chronic disease burden
- economic sustainability
- shift from volume driven, fee-for-service to pay-for-performance
- more effective use of information for continuity of care
- improve outcomes at lower cost
- financial incentives for risk reduction
- precision (personalized) medicine

Pricing Increases in Prescription Drugs 2014 vs 2013 "The Medicare Drug Spending Dashboard"

- CMS report 21 Dec. 2015
- cost increases of >25% for 540 drugs covered by Medicare Part D
  - does not necessarily reflect rebates/discounts which cannot be disclosed by CMS
- 5 drugs with > 100% increase in cost-per-unit
- 80 drugs accounted for 33% of all Part D spending and 71% of all Part B prescriptions

Strategic Landscape for Healthcare

- Rx price as perceived threat to economic sustainability of quality care delivery
  - access
  - affordability
- particular concern over price of speciality Rx and projected growth trends

Speciality Drugs

- only 1% of all prescriptions but 31% total Rx spending
- $87.1 billion in 2012
- est. $192 billion in 2016
- projected $401 billion in 2020
- 20% CAGR

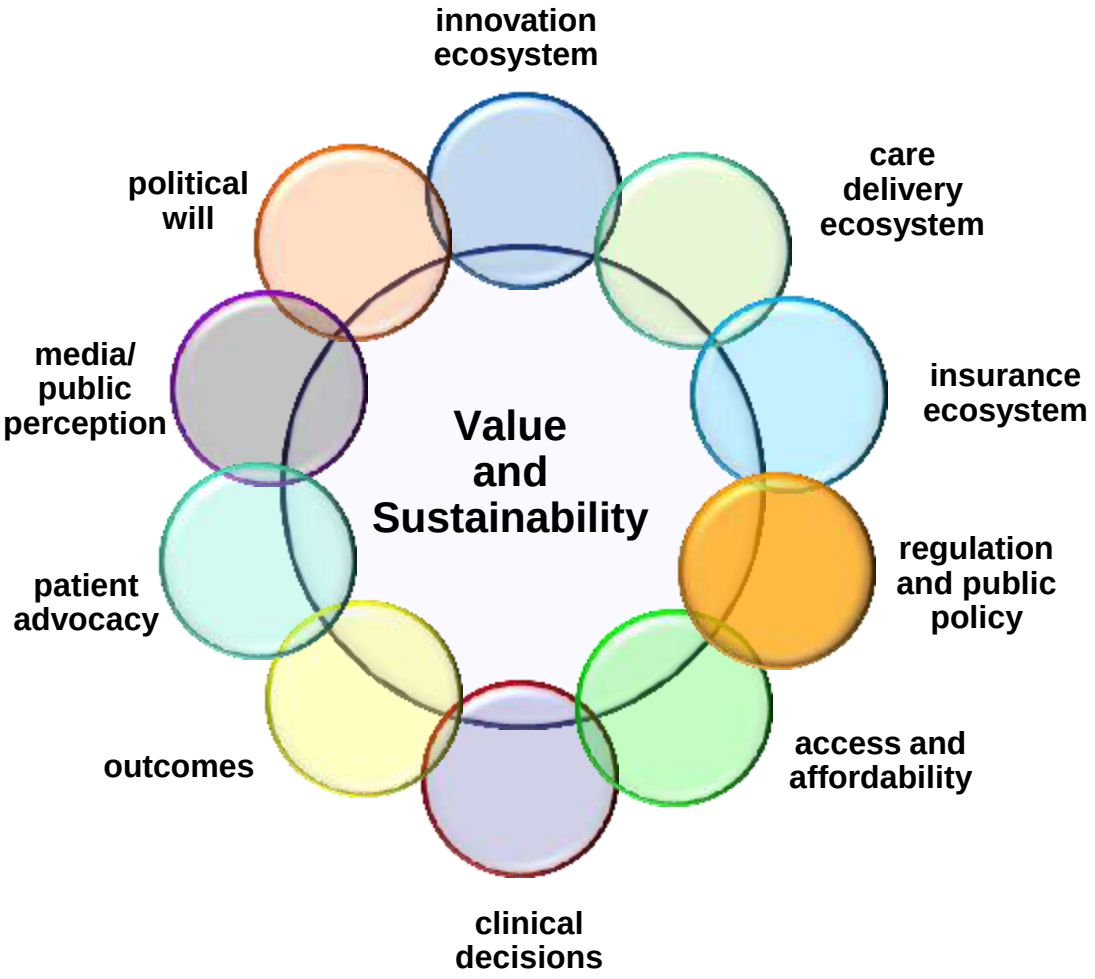
Waiting In The Wings

- gene therapy
  - Glybera (alipogene tiparvovec)
  - $1.22 million
- immuno-oncology cell therapies
  - individualized TIL, TCR, CAR therapies
  - estimated $1.5 to 2 million/patient
- immuno-oncology combination Rx
  - CTL4 + PD1-PDL1 inhibitors
  - $300,000 per treatment

Unidimensional Approaches to Complex, Multidimensional Problems: A Prescription for Flawed Conclusions, Ineffective Policies and Unintended Consequences

unidimensional

multi-dimensional



Industry Perspectives and Concerns

- 10-15 year R&D cycle: varied estimates of $1B to $2.6B per drug
- escalation of R&D cost without parallel gains in new product launches
- high attrition rates in clinical trials including advanced Phase III trials
- precision medicine, molecular profiling and stratification of major diseases into smaller cohorts
- growing reimbursement requirements to demonstrate clinical effectiveness (real world evidence)
- declining IRR on R&D spending
  - 10.5% (2010) to 4.8% (2014)
  - Deloitte and Thompson Reuters/Forbes 26 Nov. 2014


PRESCRIPTION MEDICINES:
COSTS IN CONTEXT
2015
PhRMA

Industry Critics

- sales and marketing budgets 1.2 to 2x higher than R&D investment in 20 largest companies
- direct-to-consumer advertising drives unnecessary Rx use
- lack of transparency in calculation of claimed R&D cost of $1 to $2.6 billion/product
- Rx products in US cost 1.5 to 3x more than in EU/Canada
- US pricing: “what the market will bear”

Industry Critics

- over investment in lower risk ‘me-too’ product classes versus higher risk, transformative innovation
- continued Rx price escalation despite entry of competitor products
- “pay-for-delay” arrangements to slow entry of generic competition to branded Rx
- ‘double dipping’: industry innovation based heavily on taxpayer funded research

Sudden Price Escalation in Generic Drugs

- industry consolidation and increased sole-source generics
  - Daraprim (Turing) 5000% increase from $13.50 to $750
  - Nitropress (Valeant) 312% increase from $257.80 vial to $805.61
  - Isuprel (Valeant) 820% increase from $4,489 to $36,811 for 25 pack 0.2 ml ampoules
- FDA backlog of 4300 generic applications

Consumer “Skin In The Game” ACA and Growth of Multi-Tier Formularies

- ‘closed’ formularies popularized in health exchange plans
- only cover a fraction of speciality drugs
- consumers carry full cost not on formulary list
- promote high deductibles and large co-pays


FREE 8mL
$0 CO-PAY
LARGER 8mL SIZE AVAILABLE
JUBLIA
(efinaconazole)
Topical Solution 10%


ADDERALL XR
Up to 75% off!
Save on ADHD Medication
ADDERALL XR Coupon
Drug Coupon


Pay as little as
$30* for Diclegis
(doxylamine succinate and pyridoxine hydrochloride) delayed-release tablets 10mg/10mg
Click Here to Download the Savings Offer Now!


CHANTIX
(varenicline) TABLETS
Quit Smoking Now!
CHANTIX Coupon
Drug Coupon


CIALIS
COUPON
Pharmacy Instructions
Drug Coupon
NEVER EXPIRES
Member ID: Enter Year & Time
RxPCN: 7777
RxBIN: 610709
RxGRP: RXCOUPON
THIS IS NOT INSURANCE
Customer Service: 877-321-6755
Pharmacy Helpline: 800-223-2146
PharmacyCoupons.com


OXYCODONE
Coupon
Drug Coupon
NEVER EXPIRES
Member ID: 2H38DF233H
RxBIN: 610709
RxGrp: FDCUSXYC
Pharmacy Instructions:
THIS IS NOT INSURANCE
Pharmacy Helpline 800-223-2146 (Toll Free)
Customer Service 877-321-6755 (Toll Free)

Pharmaceutical Industry Discount Coupons/Cards 2015*

- estimated $7 billion in 2015 versus $1 billion in 2010 (IMS Holdings)
- cover some or all patient copay
- payer actions to exclude Rx with coupons from formularies
  - Express Scripts 80 drugs
  - CVS/Caremark 120 drugs
  - UnitedHealth Group 35 speciality drugs
  - 62% coupons are for Rx with low cost alternatives

*C. Koons and R. Langreth (2015) Bloomberg Business Week 28 Dec. 2015

The 340B Program

- established 1992 to offer Rx price discounts to hospitals with high percentage of low-income patients
- growth from 100 hospitals to 1700 (one third of US hospitals)
- all patients, uninsured and insured, can be treated with drugs purchased at 340B deep discounts
- unfair playing field versus private practices/clinics
- incentive trend for hospitals to acquire community practices and reclassify as hospital outpatient settings
- high cost of oncology drugs highly attractive to 340B institutions
  - single oncologist can generate up to $1 million in profit
- 340B Rx purchases are 46% of total outpatient Rx spend in US hospitals
- HRSA Mega-Rule (8/15) to limit abuses

Duke University Hospital
DUKE UNIVERSITY HEALTH SYSTEM

340B: A Huge Profit Generator*

- 2012 340B Rx purchase = $66 million
- sold to patients/payers = $136 million
- $70 million profit
- 67% 340B Rx for privately insured patients, only 5% to uninsured patients

* Oncology Times 25 Sept. 2014

Drug R&D and Pricing

Economics and Emotions

Do High R&D Investment and Risk Justify High Prices?

The Information Gap

"We don't have enough public information on the effectiveness of new drugs in the real world or about prices and rebate structures
We must increase the transparency of the information available about drug pricing and value."

Andy Slavitt
Acting Administrator, CMS
HHS Forum on Drug Prices, 20 November 2015
cited in Scrip 4 Dec. 2015 p.11

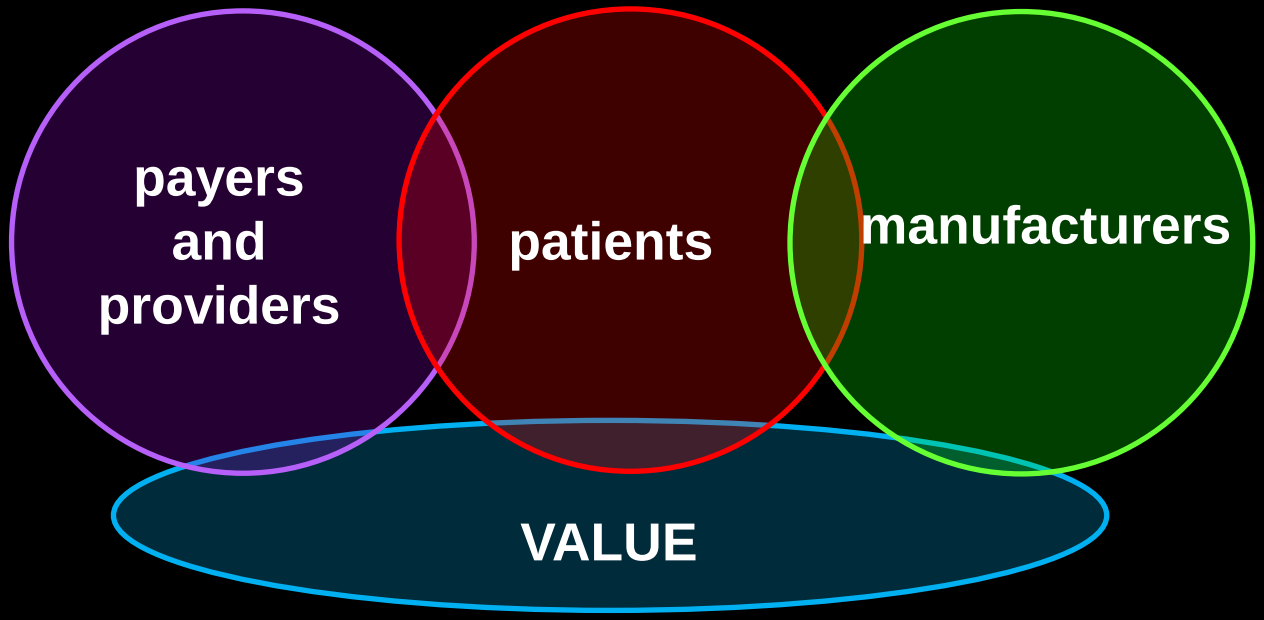
Transparency (or Lack of)

- R&D, production costs and pricing of Rx products (industry)
- all clinical trials data (industry, regulators?)
- criteria for creation of multi-tier formularies (pharmacy benefit management (PBM) companies, provider networks)
- evidentiary standards for selection of preferred Rx “clinical pathways” protocols (payers, providers)
- justification of wide variation in clinical care patterns and outcomes (physicians)
- access and facile integration of multiple data sources (patients)

“Price is what you pay.
Value is what you want.”

Warren Buffet

Aligning Diverse Interests and Incentives



- diverse constituencies with different incentives, expectations and definitions of “value”

Value Metrics

- effectiveness (endpoints and outcomes)
- safety (adverse events, prevalence and cost)
- quality and consistency of evidence
- comparators
  - standard of care, other modalities
- cost (unit, per year, per patient, combinations)
- access and affordability (patients, payers)
- patient preferences/QOL
- sustainability
  - economic (payers and delivery systems)
  - wellness (patients, consumers)

VARIATIONS ON VALUE

The **National Comprehensive Cancer Network** (NCCN), the **American Society of Clinical Oncology** (ASCO) and **Memorial Sloan Kettering Cancer Center** (MSKCC) have each developed tools to evaluate the cost of cancer drugs in the context of the benefits they provide. While all three tools use safety, efficacy and cost data, they differ in many of the other variables they consider as components of value. Another key difference is that while ASCO and MSKCC use drug price data to evaluate costs, NCCN asked oncologists to make a subjective assessment of "affordability" on a five-point scale that corresponds to a range between "very inexpensive" and "very expensive."

All three groups consulted patients, physicians, payers and drug companies during the development of the tools. MSKCC's Drug Abacus allows any user — whether a patient, physician, drug company, or payer — to adjust the weights assigned to each variable depending upon how important the variable is to that user. (A) MSKCC calls this variable "disease burden," which it defines as the estimated years of life lost due to the disease; QALYs = quality-adjusted life years; WAC = wholesale acquisition cost; ASP = Medicare-reported average sales price. *Sources: ASCO, NCCN, drugabacus.com*

	ASCO Cancer Value Framework	NCCN Evidence Blocks	Memorial Sloan Kettering Drug Abacus
Variables considered			
Efficacy	√	√	√
Safety/toxicity	√	√	√
Effects on patient-reported outcomes or other benefits	√	–	–
Quality of data	√	√	√
Consistency of data	–	√	–
Novelty	–	–	√
R&D costs	–	–	√
Rarity of disease	–	–	√
Years of life lost (A)	–	–	√
QALYs gained	–	–	√
Cost	√	√	√
Information sources			
Clinical data	Published studies	Published studies	Regulatory submissions
Cost	WAC (drug + supportive care)	Physician score of "affordability" ranging from "very inexpensive" to "very expensive" (drug + supportive care)	ASP (drug only)
Stakeholder input	Patients, industry, physicians, payers	Patients, industry, physicians, payers	Patients, industry, physicians, payers

Accelerated Demonstration of Clinical Effectiveness

Real World Evidence (RWE)

New Regulatory and Reimbursement Policies

Efficacy and Effectiveness

- clinical efficacy (randomized clinical trials and regulatory approval)
- clinical effectiveness (real world evidence post-approval)
- reimbursement decisions linked increasingly to demonstration of real world effectiveness
- need for new clinical trial designs
- new regulatory and reimbursement policies

Hybrid RCT/RWE Models

- robust PoC validated in smaller RCT (Phase II)
  - 4 years
  - efficacy
- early launch to capture RWE
  - 4 years
- two stage reimbursement
  - post-launch RWE generation
  - pay-for-performance based on RWE data
- potential for early commercial failure and product withdrawal if RWE insufficient/ unexpected safety issues

Real World Evidence of Rx Effectiveness

- standardization of systems and methods for data capture
- new technologies for real time data capture by remote monitoring
  - wearables, sensors, social media
  - direct uploading to EMRs
- improved integration of impact/value on patient preferences/QOL

Performance-Based, Risk Sharing Contracts

- Januvia (sitagliptin)/Janumet (plus metformin)
- reduction in HbA1C levels in T2 diabetes

- Rebif (interferon Beta-1a)
- reduction in ER visits/hospitalization in MS patients

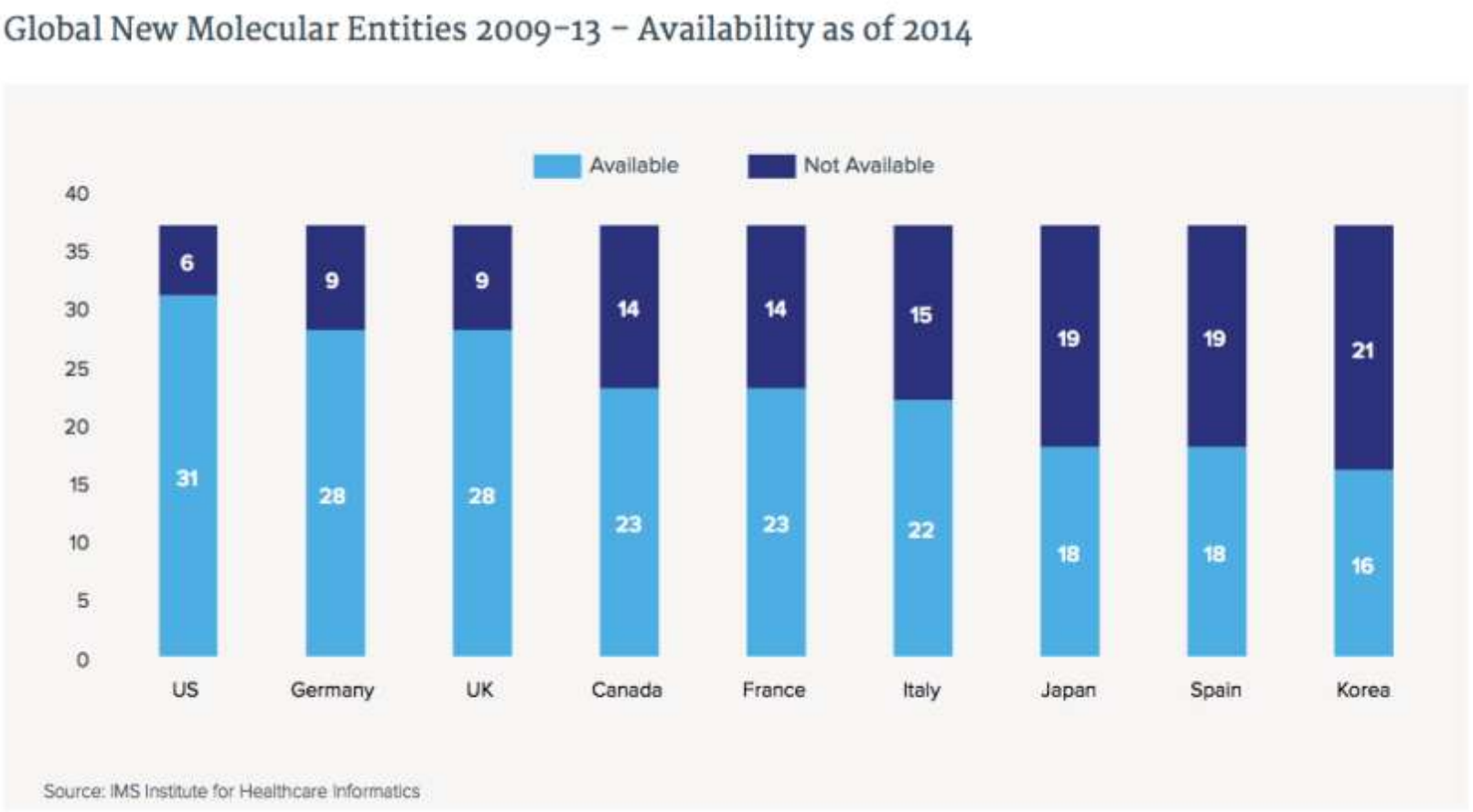
- Harvoni (sofosbuvir/ledipasvir)
- elimination of HCV genotype 1 in carriers

- Crestor (rosuvastatin)
- LDL cholesterol reduction

The Cost of Cancer (USA)

- 1 in 3 individuals affected in their lifetime
- average price of new cancer drugs has increased 5-10 fold over past 15 years.
- drug cost/additional year lived (inflation adjusted) risen from $54K (1995) to $207K (2013)
- all FDA approved anti-cancer drugs in 2014 and 2015 were priced over $75K/year and 85% over $100K/year
- trends in insurance coverage for OOP co-payments by patients has increased to 20-30% drug cost
- average annual US household gross income is $52K and $24.1K for Medicare beneficiaries
- US cancer patients more than twice as likely to declare bankruptcy versus other chronic diseases

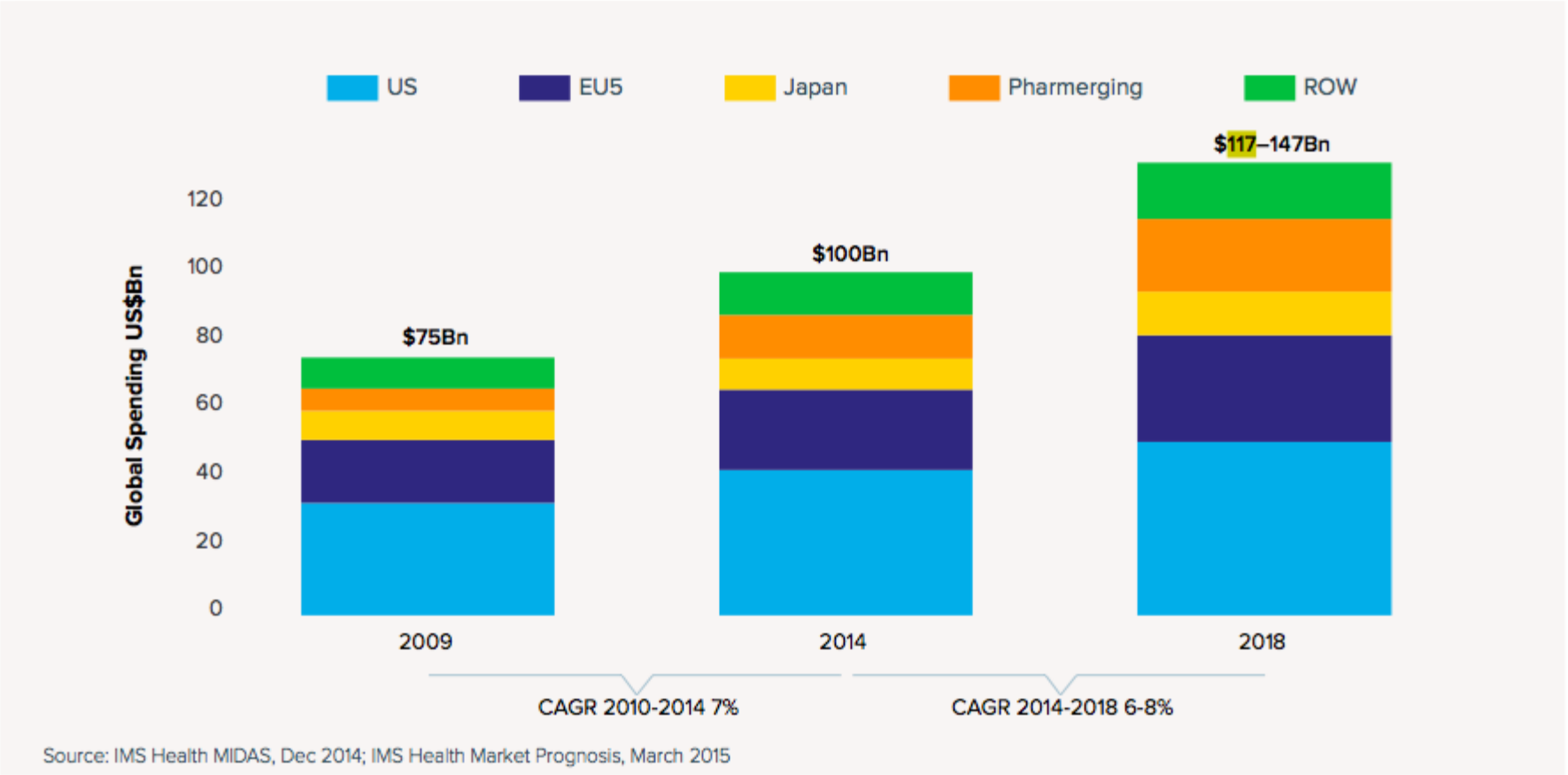
More Cancer Drugs Are Approved in the U.S. Than Anywhere Else



http://www.forbes.com/sites/matthewherper/2015/05/05/cancer-drug-sales-approach-100-billion-and-could-increase-50-by-2018/

The Cancer Drug Market Just Hit $100 Billion And Could Jump 50% In Four Years

Global Oncology Market Forecast



Source: IMS Health MIDAS, Dec 2014; IMS Health Market Prognosis, March 2015

http://www.forbes.com/sites/matthewherper/2015/05/05/cancer-drug-sales-approach-100-billion-and-could-increase-50-by-2018/

Cancer Exceptionalism:

No Limits-Clinical or Economic?

What Represents a Meaningful Advance in Clinical Effectiveness?

Is There a Price Point That is Unacceptable Regardless of Long Term Value?

Can we continue to afford the high cost of anti-cancer drugs for modest gains in PFS/OS and limited QOL?

NICE National Institute for Health and Care Excellence

- cost-effectiveness analysis metrics
- QALY: Quality Adjusted Life Year

Health Technology Assessment
National Institute for Health and Care Excellence (NICE)

NICE
National Institute for Health and Care Excellence

- March 2000 to December 2014
- 36 negative recommendations on 141 Rx (26%)
- 24 negative recommendations for 57 oncology Rx (42%)
- 40% negative oncology Rx recommendations were for drugs approved by FDA

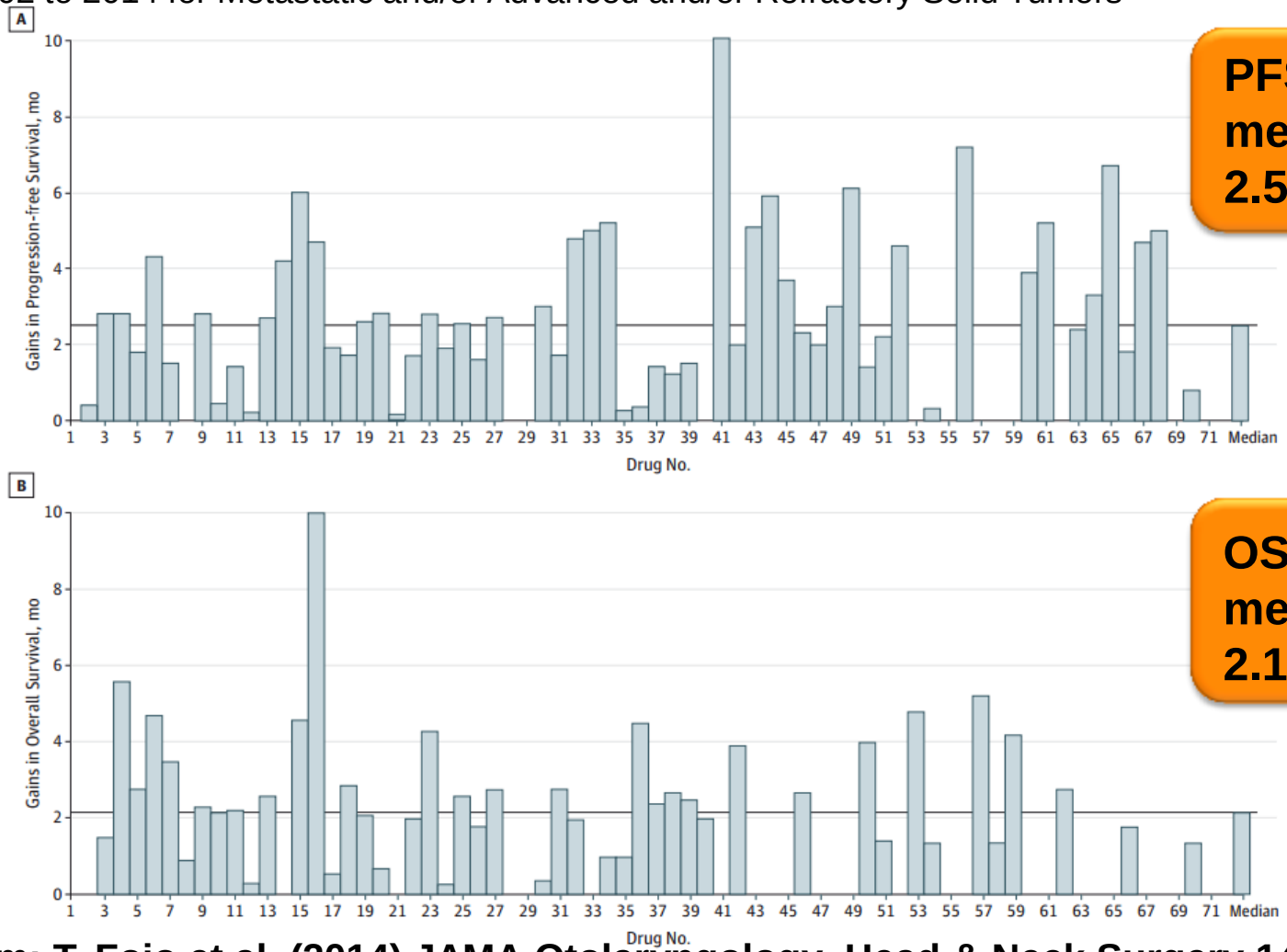
What Are We Willing to Pay for Added Months of Survival in Cancer?

Lifetime cost above standard care	If cancer is on par with other diseases ($150,000 per life year gained), months of added overall survival benefit needed	Treating cancer as worthy of much higher reimbursement ($250,000 per life year gained), months of added overall survival benefit needed
$50,000	4 months	2.4 months
$100,000	8 months	4.8 months
$150,000	12 months	7.2 months
$200,000	16 months	9.6 months
$250,000	20 months	12 months
$300,000	24 months	14.4 months
$350,000	28 months	16.8 months
$400,000	32 months	19.2 months
$450,000	36 months	21.6 months
$500,000	40 months	24 months

Source: Pink Sheet 13 Sept. 2010. Adapted from S. Ramsey FHCRC, ASCO 2010

Performance Comparison for New Anti-Cancer Drugs Approved 2002-2014 for Top Ten Pharmaceutical Companies

Gains in Progression-Free Survival (PFS) and Overall Survival (OS) for 71 Drugs Approved by the FDA From 2002 to 2014 for Metastatic and/or Advanced and/or Refractory Solid Tumors



PFS median 2.5 months

OS median 2.1 months

From: T. Fojo et al. (2014) JAMA Otolaryngology–Head & Neck Surgery 140, 1225

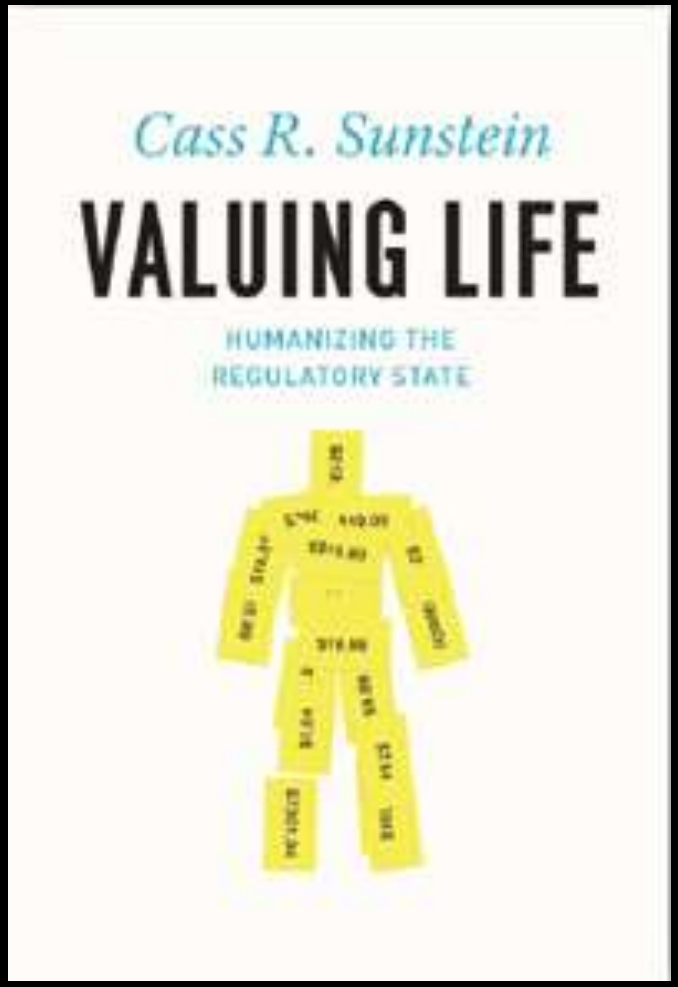
Hypothetical Scenarios for Indication-Based Drug Pricing

Drug and Indication	Median Survival Gain In Years	Current Monthly Price	Price Based On Indication With Most Value
Abraxane (Celgene)			
Metastatic breast cancer	0.18	$6,255	$6,255
Non-small cell lung cancer	0.08	$7,217	$2,622
Pancreatic cancer	0.15	$6,766	$448
Tarceva (Roche/Astellas)			
First-line treatment metastatic non-small cell lung cancer	0.28	$6,292	$6,292
Pancreatic cancer	0.03	$5,563	$1,556
Erbitux (BMS/Lilly)			
Locally advanced squamous cell carcinoma of head/neck	1.64	$10,319	$10,319
First-line treatment recurrent or metastatic squamous cell carcinoma of head/neck	0.23	$10,319	$471
Herceptin (Roche)			
Adjuvant treatment breast cancer	1.99	$5,412	$5,412
Metastatic breast cancer	0.40	$5,412	$905

Source: JAMA article by Peter Bach, Oct. 3, 2014

Adapted from: P. B. Bach JAMA (2014) 312, 1629 Pink Sheet 20 Oct. 2014

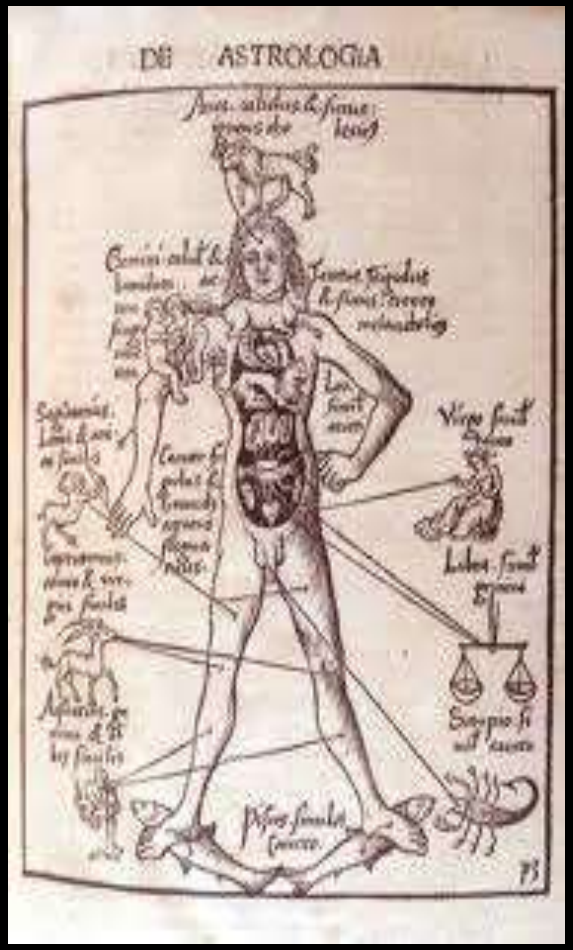
The Value of a Life

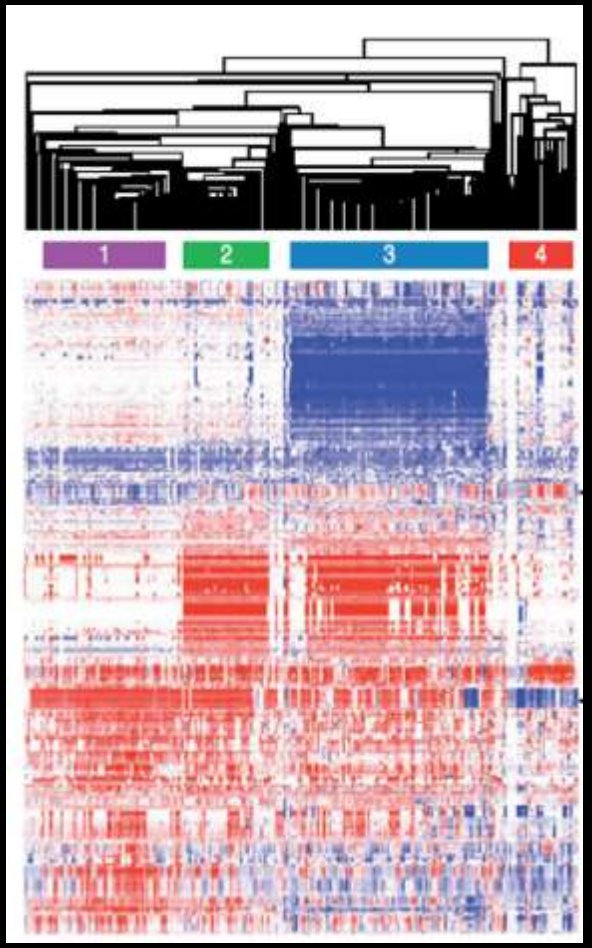


- the QALY is just a well researched number
- the value of a life is far more complex question

Paying for Precision Medicine

Medical Progress:
From Superstitions to Symptoms to Signatures





Population-Based Payment Models

- “one-size-fits all” regimens
- treating both responder and non-responder cohorts distorts cost-effectiveness calculus
- additional cost of adverse events from inappropriate exposure of non-responder cohorts to futile Rx

Reimbursement Policies for Precision Medicine

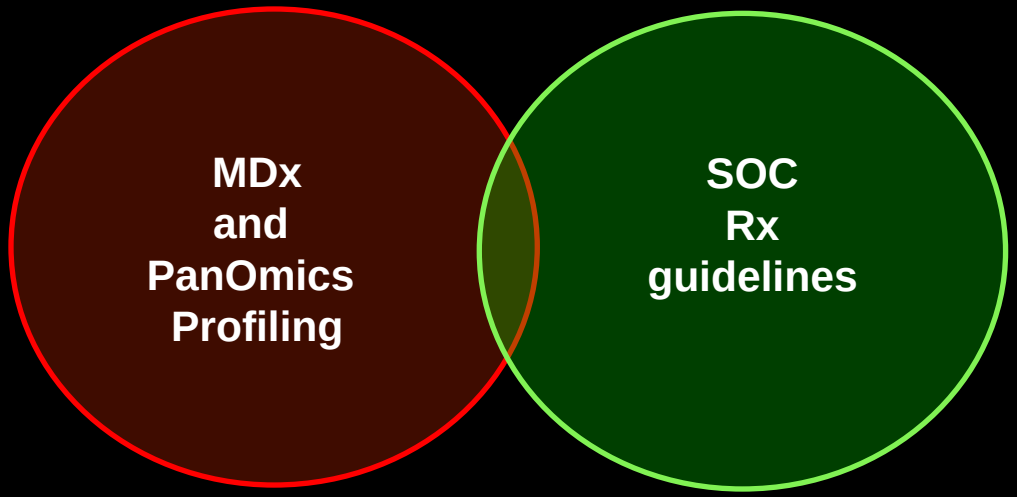
- Rx use targeted to ‘responder’ cohorts
- high Rx cost justified by positive (guaranteed?) treatment outcomes but in smaller patient cohorts
- obligate need for companion Dx and label restrictions
- current reimbursement policies for molecular profiling Dx as major barrier

A Pricing and Reimbursement Dichotomy

Dx

Rx

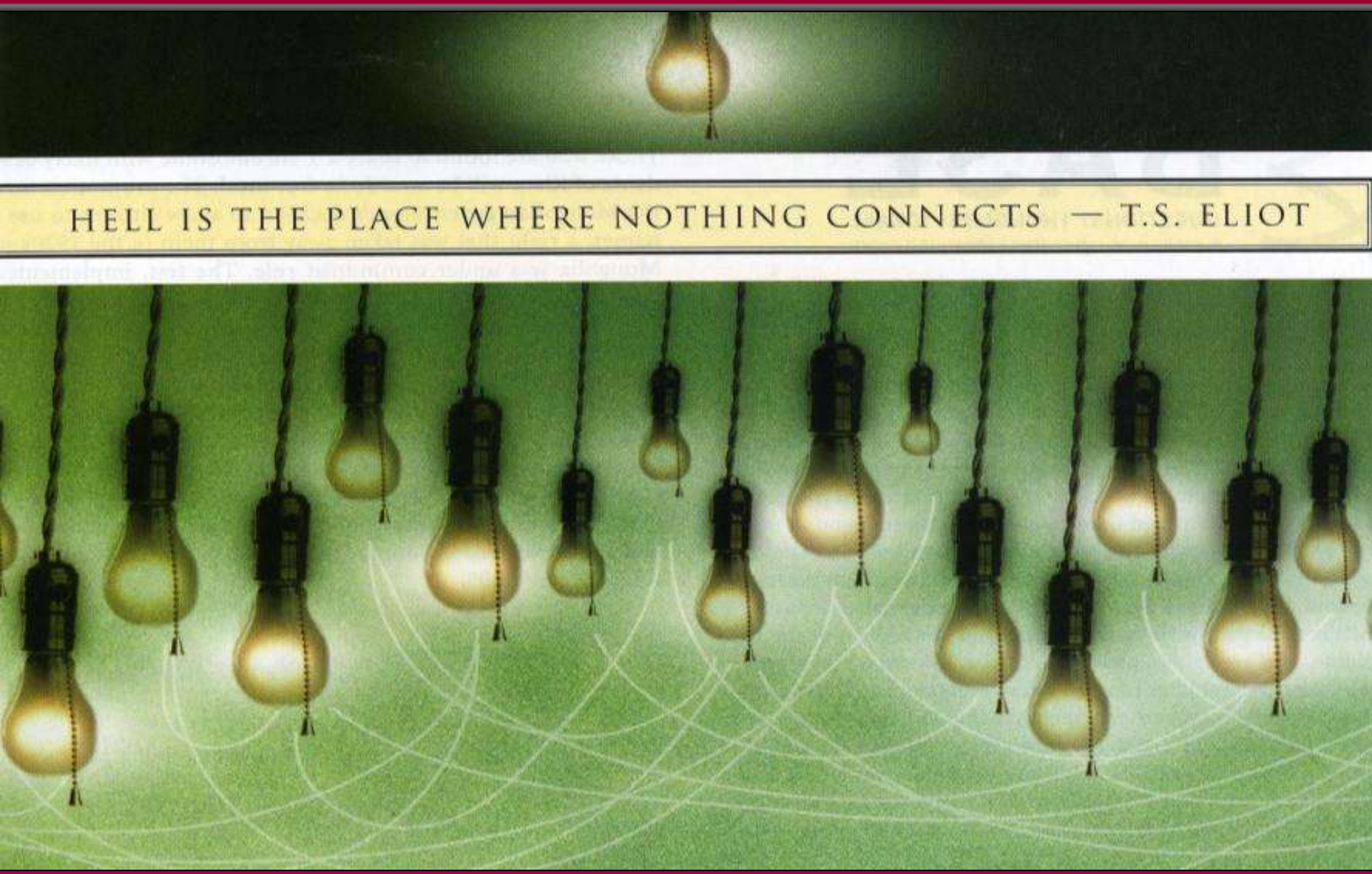
Conflicts and Contrasts in Reimbursement Policies and Clinical Utilization of Molecular Diagnostics (MDx) and Therapeutics (Rx) in Oncology

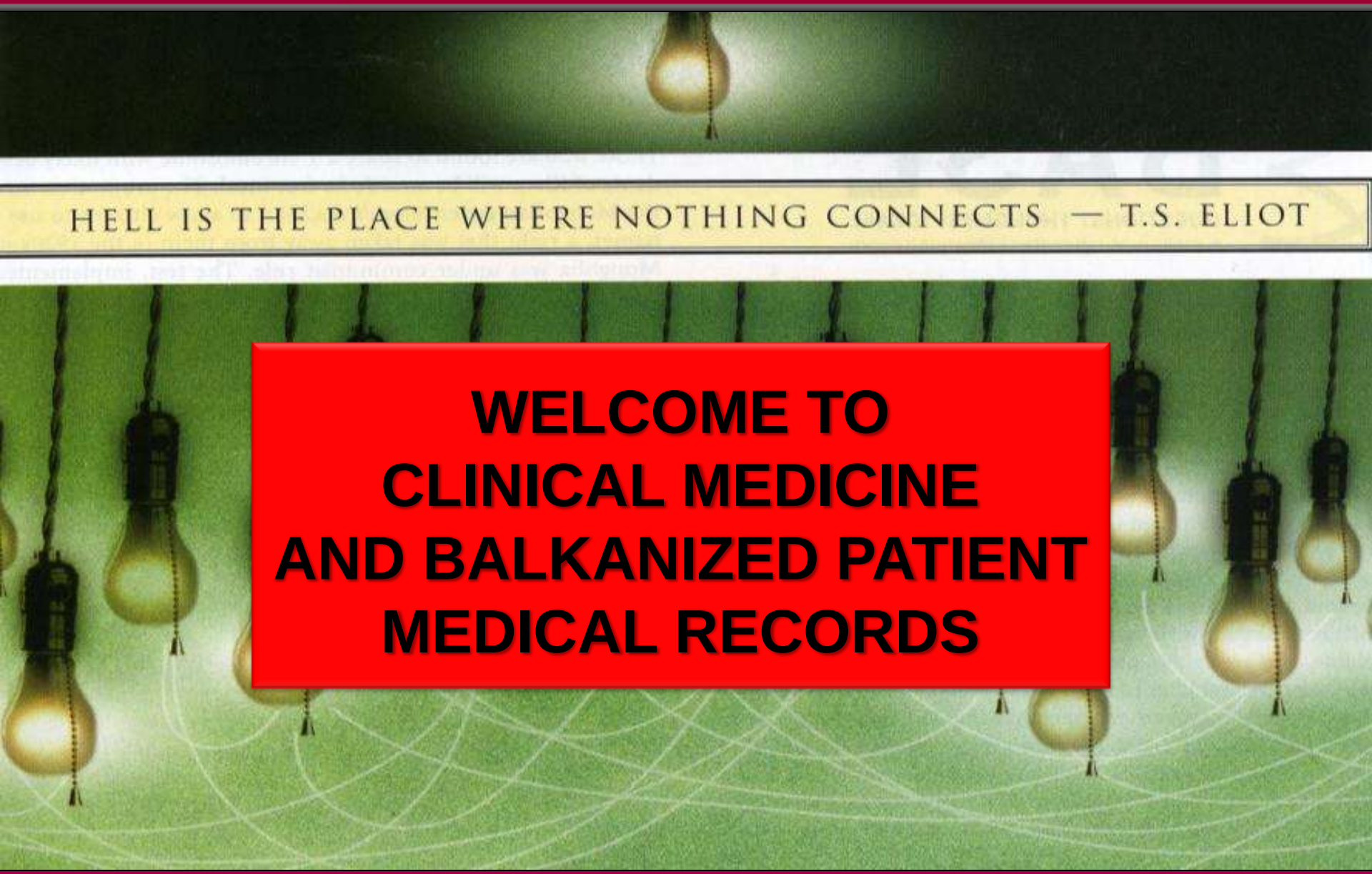


Cost-Based MDx	High Cost Rx Without Profiling For Presence of Rx Response Target
Precision Diagnosis and Rational Selection of Responder Patient	Propagation of "One-Size-Fits-All" Therapeutic Strategies With Limited Response Rates

Building the Evidence Base for Improved Healthcare Quality, Performance and Priorities

Data, Data, Data


HELL IS THE PLACE WHERE NOTHING CONNECTS — T.S. ELIOT



WELCOME TO CLINICAL MEDICINE AND BALKANIZED PATIENT MEDICAL RECORDS


Healthcare delivery
of the future:
How digital technology
can bridge time and
distance between
clinicians and consumers
pwc


Healthcare's new entrants:
Who will be the industry's
Amazon.com?
pwc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Health Care Value: An Executive Primer
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CLOUD ADOPTION &
RISK IN HEALTHCARE
REPORT
Q2 2015
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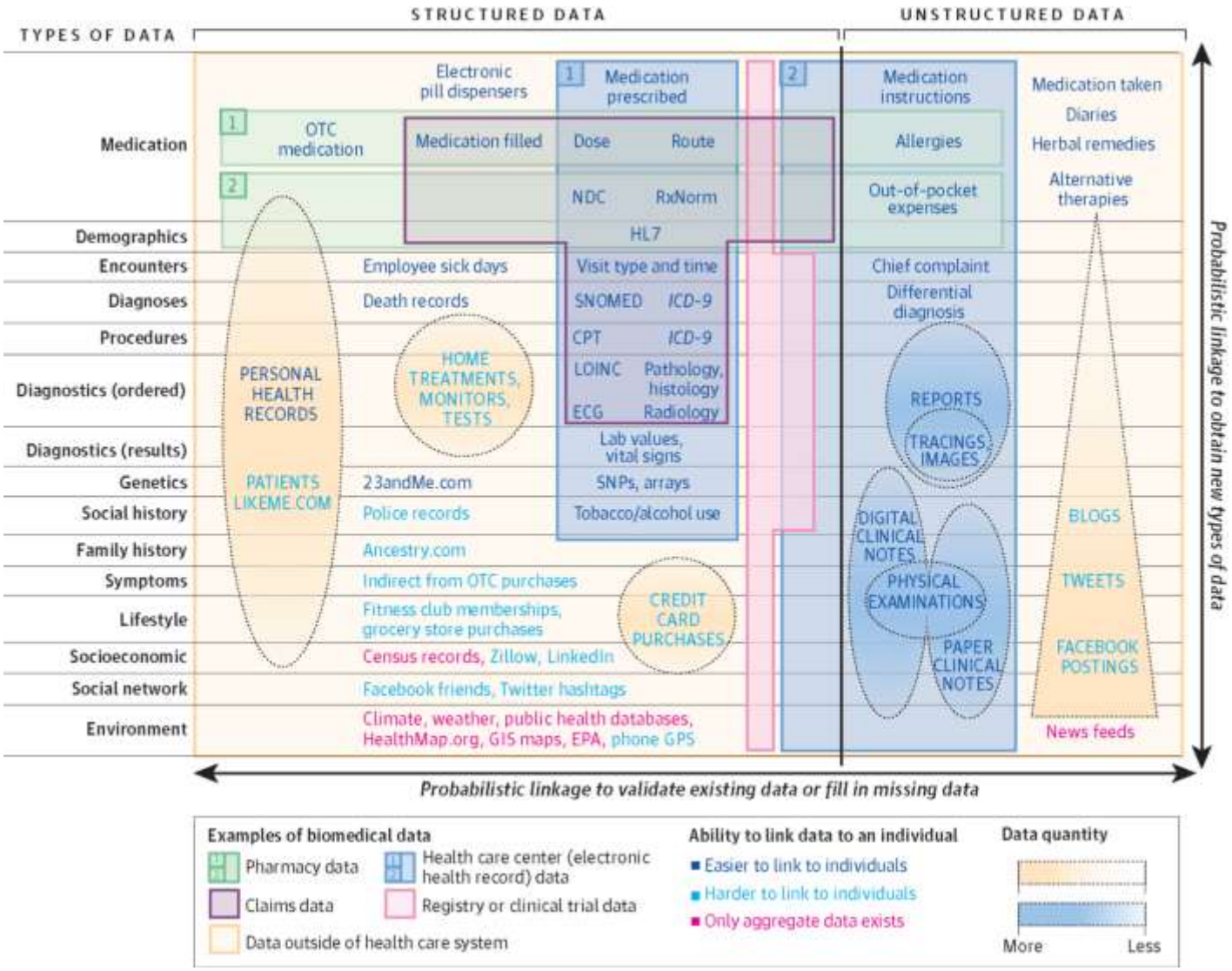
REAL WORLD
EVIDENCE AND
DIGITAL HEALTH:
PHARMA'S NEXT
FRONTIER


Transforming Health Care
Through Big Data
IHT


THE INFORMATION GENERATION
TRANSFORMING THE FUTURE, TODAY
Outlook Report
SPONSORED BY EMC²

The Diversity of High Value Data Sources in Healthcare: The Integration Challenge



G. M. Weber et al. JAMA. 2014;311(24):2479-2480. doi:10.1001/jama.2014.4228

Vaccines versus Viagra

Market Incentives and Innovation

Market Incentives and Innovation

- industry retreat from R&D investment in vaccines/anti-infectives
  - commodity markets-public health tenders (vaccines)
  - looming major vulnerabilities (antibiotic resistance, Ebola and other EIDs)
- fragmented pricing policies in EU and decision not to market in specific countries
- geographic shift of R&D investment
  - from EU to USA and Asia

Drug Discovery and Development: One of the Most Complex Intellectual and Logistical Exercises Undertaken by Modern Industry

"Fewer countries have discovered,
developed and registered drugs
to an international standard,
than have developed atomic bombs"

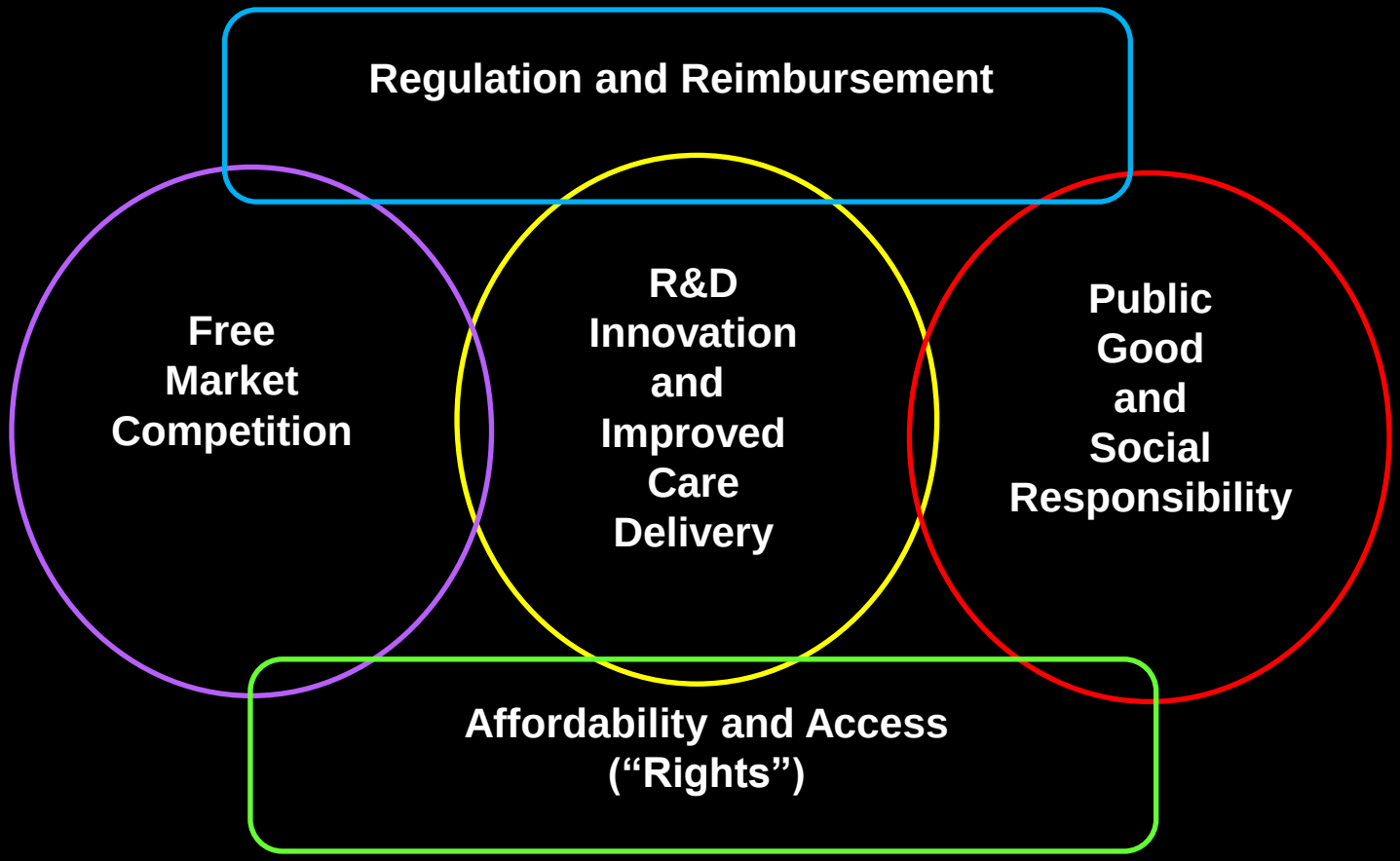
Chris Hentshel

Medicines for Malaria Venture: Lancet (2004) 363, 2198

(Bio)Pharmaceutical Innovation, R&D Investment and ROI

- limited productivity/innovation of state-sponsored R&D
- FSU/Russia
- China
- USA
  - JVAP, NIH

Balancing Conflicting Economic Incentives and Ethical Issues in Healthcare



The New Poster Boy for the Public Image of the Pharmaceutical Industry

Martin Shkreli, CEO, Turing Pharmaceuticals

Price Controls Solve the Problem!

Partisan Political Polemics

"Taxpayers who helped fund drug development
find themselves unable to afford
the cost of treatment."

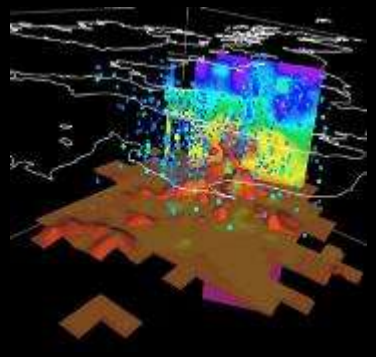
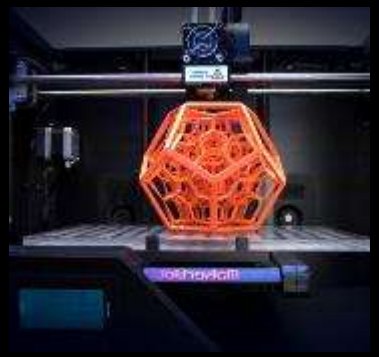
Rep. Jan Schakowsky (D.IL)

"These (biopharmaceutical) companies
grow their businesses
with the benefit of taxpayer-sponsored research
and then they turn around to gouge
the same taxpayers without whom
the drug may not even exist."

Rep. Rosa DeLauro (D.CT)

4 Nov 2015
The Affordable Drug Pricing Task Force (Democrats Only)

Why Focus on Pharmaceutical R&D as a Beneficiary of Taxpayer-Funded Research and Exclude Other Industrial Sector Beneficiaries?

Telcoms	GPS	Computing	Internet	Social Media
				
Novel Materials	**Geophysics**	**Robotics**	**3D printing**	**Biotechnology**
				

Taxpayer-Funded Research and Industrial Innovation

- fundamental research is a public good to stimulate industrial innovation for national competitiveness and prosperity
- long lag times for translation of fundamental research (science) into potential commercial use (technology)
- eventual use(s) often very different from those envisaged originally when research began
- intellectual pedigree of most major innovations is diffuse and always multi-factorial

How to Identify and Quantify the Contributions of Taxpayer-Funded Research to Commercial Products

- Bayh-Dole Act enables academic IP, licensing and revenue capture
  - major catalyst in creation of biotechnology sector
- intellectual lineages of conceptual or technological advances are diffuse and diverse
  - how to demarcate who funded what, when and who?
  - what were the intellectual precursors of the claimed ‘source’ of the innovation hijacked by industry?
- contemporary biomedical R&D is increasingly dependent on innovations originating in industry
- reciprocal industry entitlement to recoup investments based on public funded research that cannot be reproduced or failed to fully characterize the proposed Rx target?

“For Every Complex Problem There Is an Answer That is Clear, Simple and Wrong.

- H.I. Mencken

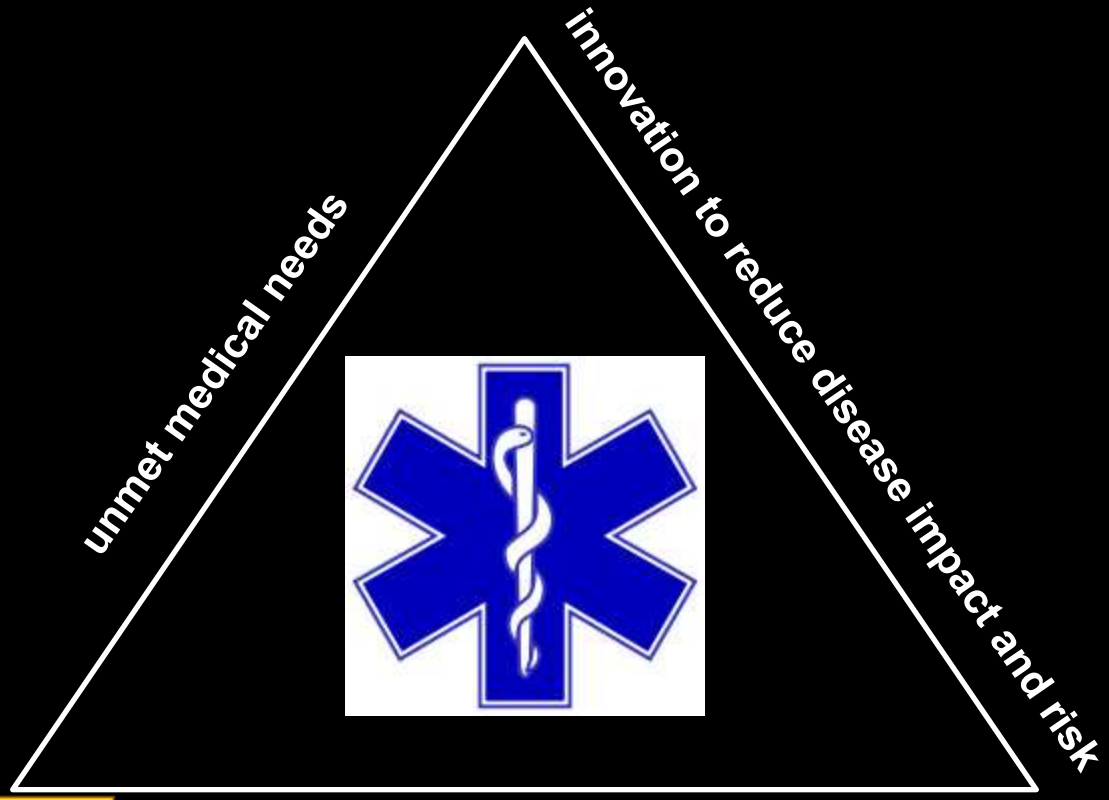
Moving Beyond Ill-Informed Political Populist Grandstanding to Comprehensive and Rigorous Analysis of an Urgent Problem

- complex multi-dimensional problem
  - multiple constituencies
  - diverse interests and incentives
  - multi-modality care and demarcation of respective costs/value contributions
  - need for robust standardized metrics for effectiveness and outcome metrics
- provide evidence base to counter flawed, unidimensional political/media attacks
- foundation for rational policy and economic alignment:
  - patients, payers, providers, manufacturers
  - sustainable health system

The Healthcare Challenge: Sustaining Innovation, Improving Outcomes and Reducing Cost

Improved Outcomes

clinical, economic, quality-of-life



Innovation and Demonstrating Value

infinite demand versus finite resources

Access to Affordable Care

Slides available @ http://casi.asu.edu/