ASU Complex Adaptive Systems
ARIZONA STATE UNIVERSITY

# BIO 302:
# APRIL 29, 2014

## WEEK 15, LECTURE 1:
## THE FUTURE OF CANCER CARE


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**The Future of Cancer Care**

**Poses Many of the Same Challenges Facing US Healthcare At Large**

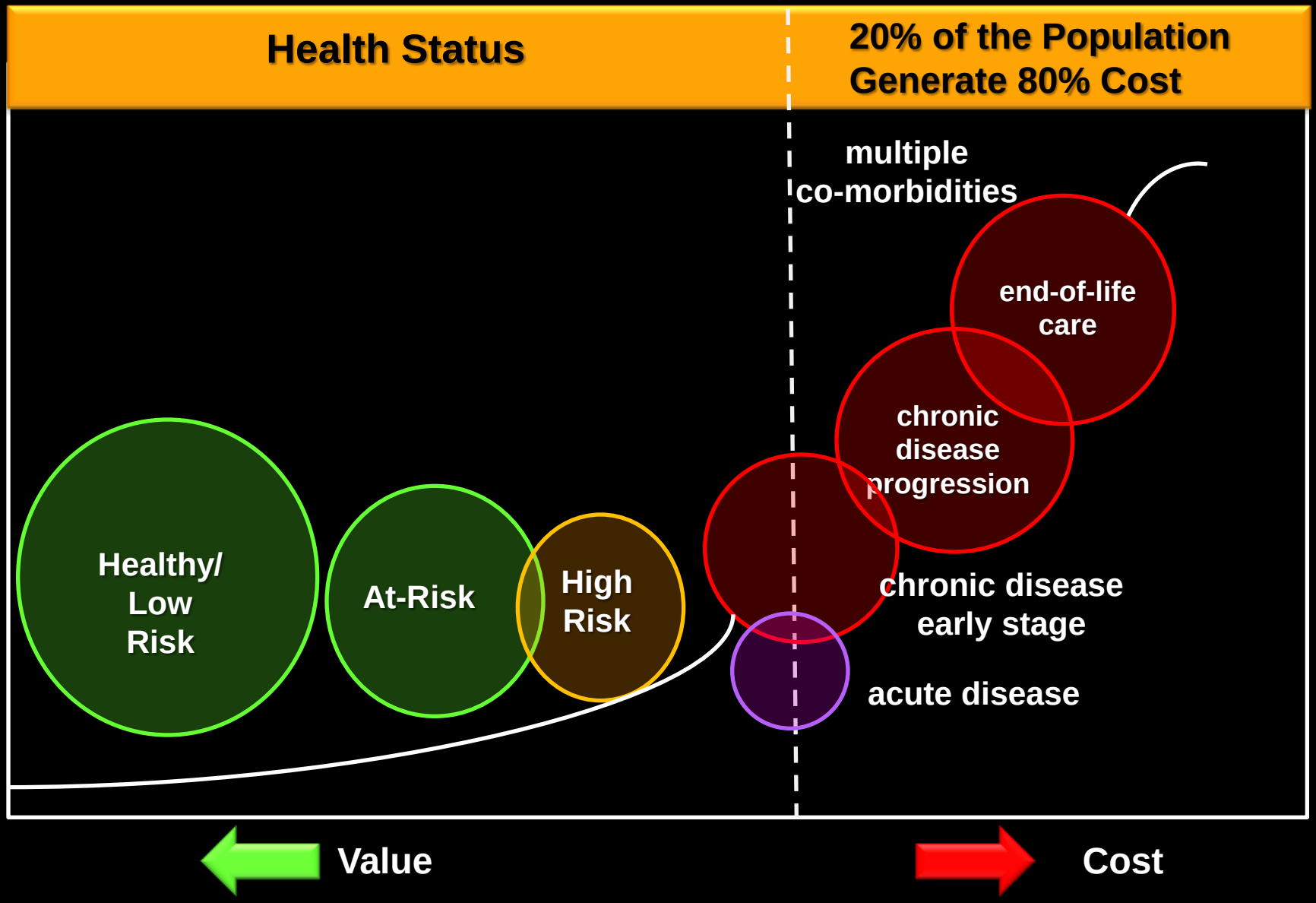
**Healthcare: An Expensive Menu Without Prices**

**Managing the Demands of an Aging Society and Chronic Disease Burden in an Era of Economic Constraint**

**Shift From a "Do More, Bill More" Healthcare System to Managing Individual Risk to Improve Health Outcomes and Control Cost**

**Sustainable Health: Societal (Economic) and Individual (Wellness)**

# The Economic, Social and Clinical Benefits of Proactive Mitigation of Disease Risk and Chronic Disease Co-Morbidities



# Top 25 Countries as % World Health Expenditures (= 90% of Global Health Expenditures)

1. United States: 40.1%
2. Japan: 8%
3. Germany: 5.9%
4. France: 4.7%
5. China: 4.6%
6. United Kingdom: 3.4%
7. Italy: 3%
8. Brazil: 3%
9. Canada: 2.8%
10. Spain: 2.1%
11. Australia: 1.6%
12. Netherlands: 1.4%
13. Russia: 1.2%
14. South Korea: 1.1%
15. Mexico: 1.1%
16. India: 1%
17. Switzerland: 0.9%
18. Belgium: 0.8%
19. Turkey: 0.8%
20. Sweden: 0.7%
21. Austria: 0.6%
22. Norway: 0.6%
23. Poland: 0.5%
24. South Africa: 0.5%

# US Healthcare (2014)

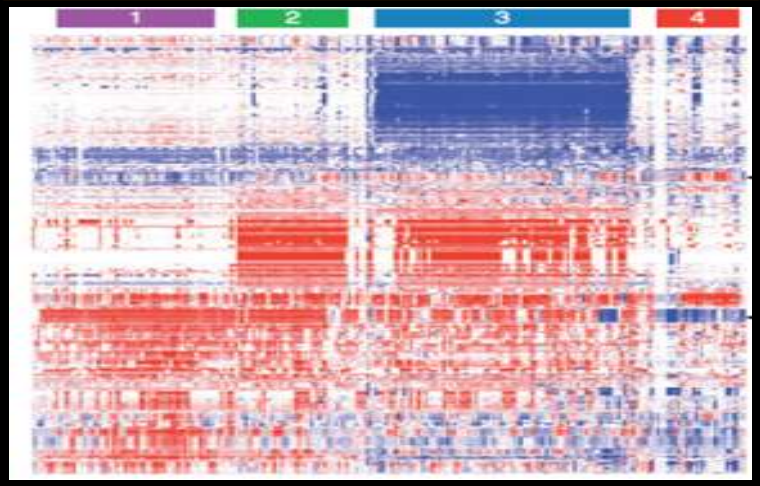
- $2.9 trillion enterprise (15% GDP) destined to grow to $5 trillion by 2020
- reactive ‘sickness’ system versus optimizing health (wellness)
- episodic ‘incident-based’ care versus integrated continuity of care
- multiple participants and stakeholders with divergent interests, aspirations and expectations
- passive consumers
- healthcare only industry in which new technologies constantly drive up the cost of care

# The Socio-Economic and Political Issues at the Core of the Healthcare Debate

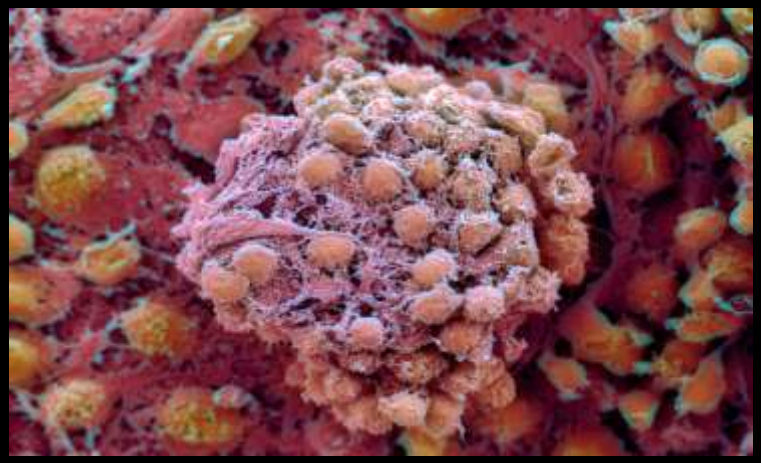
- infinite demand versus finite resources
- individual expectations for “cure” exceed technical capabilities or cost-effectiveness rules set by payers
- inadequate systems to generate robust evidence to evaluate improvement in clinical care and cost management
- polarizing national political debates with emotionally loaded sound-bites
  - rationing, denial of care, “like-Canada”, ‘death panels’

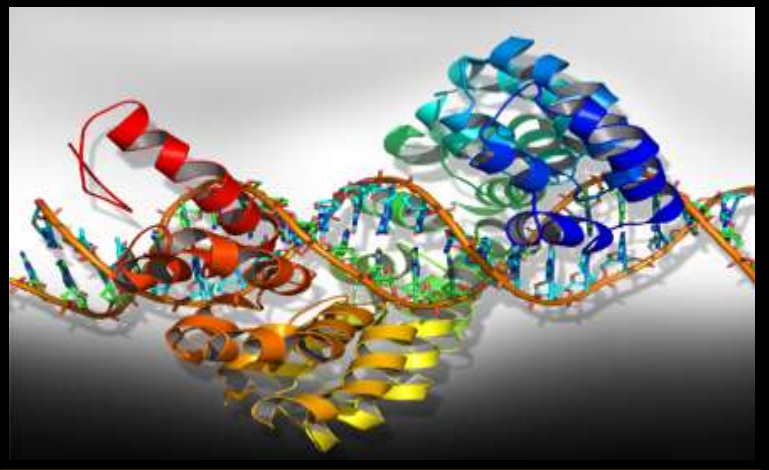
# New Vistas in Biomedical Innovation

**Molecular Profiling of Disease**




**Body Sensors and Remote Monitoring**



**Stem Cells and Regenerative Medicine**

**Genome Editing**

# The Real World

- innovation in science and technology alone is necessary but not sufficient
- adoption requires overcoming multiple barriers to adoption
  - existing competition/standard of care
  - cultural conservatism
  - financial disincentives
  - regulatory hurdles
- wide variation in adoption speed by different sectors
  - healthcare (10-30 years)
  - computing (1-2 years)
  - engineering (1-10 years)

# The Principal "'ics" in the Future Evolution of US Healthcare

- panOmics (profiling technologies)
- geriatrics (aging populations and chronic disease burden)
- informatics (big data and analysis)
- economics (value)
- ethics (societal)

# The Principal "'ics" in the Future Evolution of US Healthcare

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- ethics (societal)

**Politics:**
**Quick Fixes, Quick Wins and Ducking the Hard Questions**

Improving Clinical Outcomes

Health (Wellness) Versus Illness

Improving Clinical Outcomes

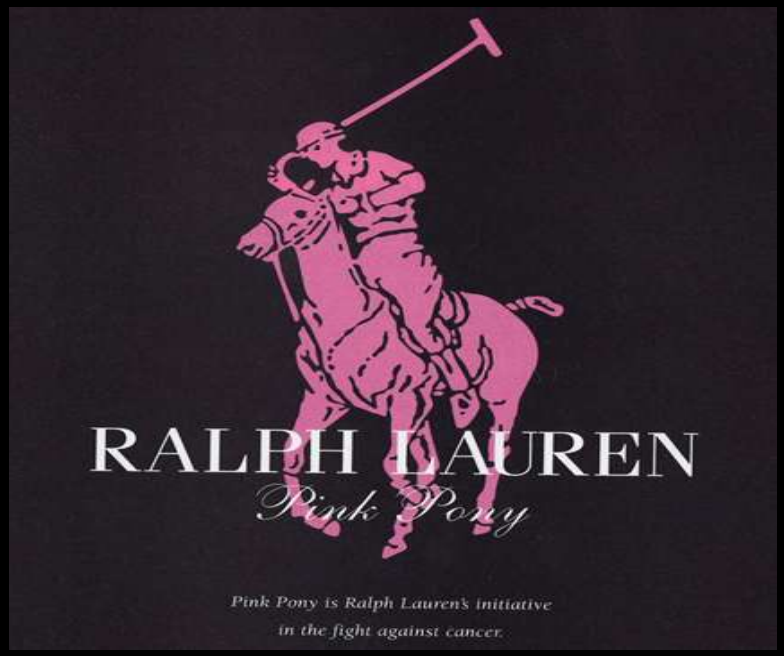
Health (Wellness) Versus Illness

VALUE

# “The War on Cancer”

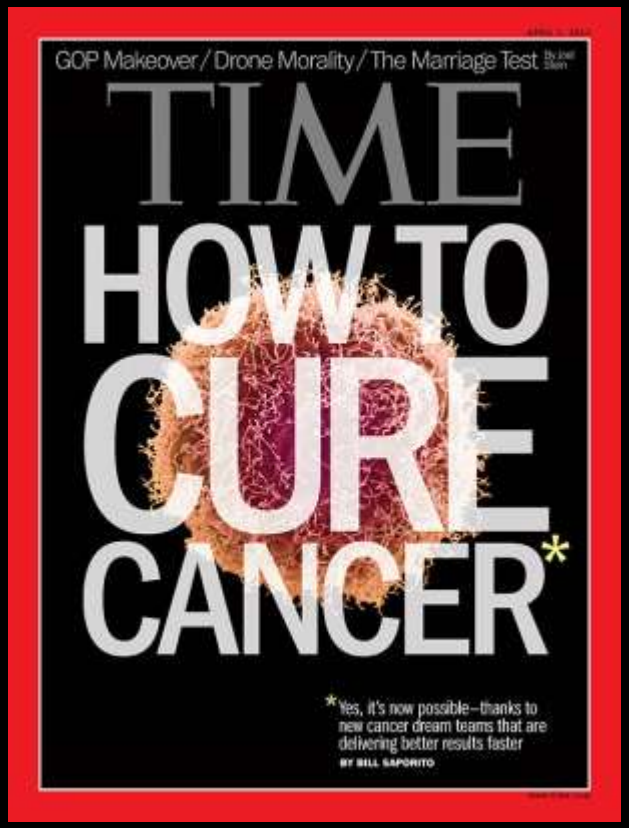
**President Richard Nixon signs the National Cancer Act December 23, 1971**

# Sincere Advertising and Advocacy or Cynical Hijacking of Public Generosity?

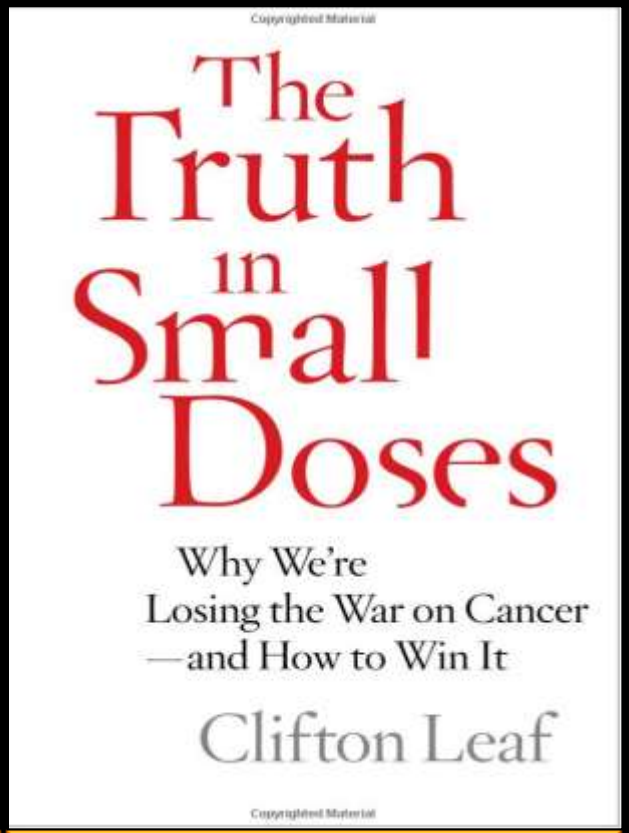





# Conflicting Messages



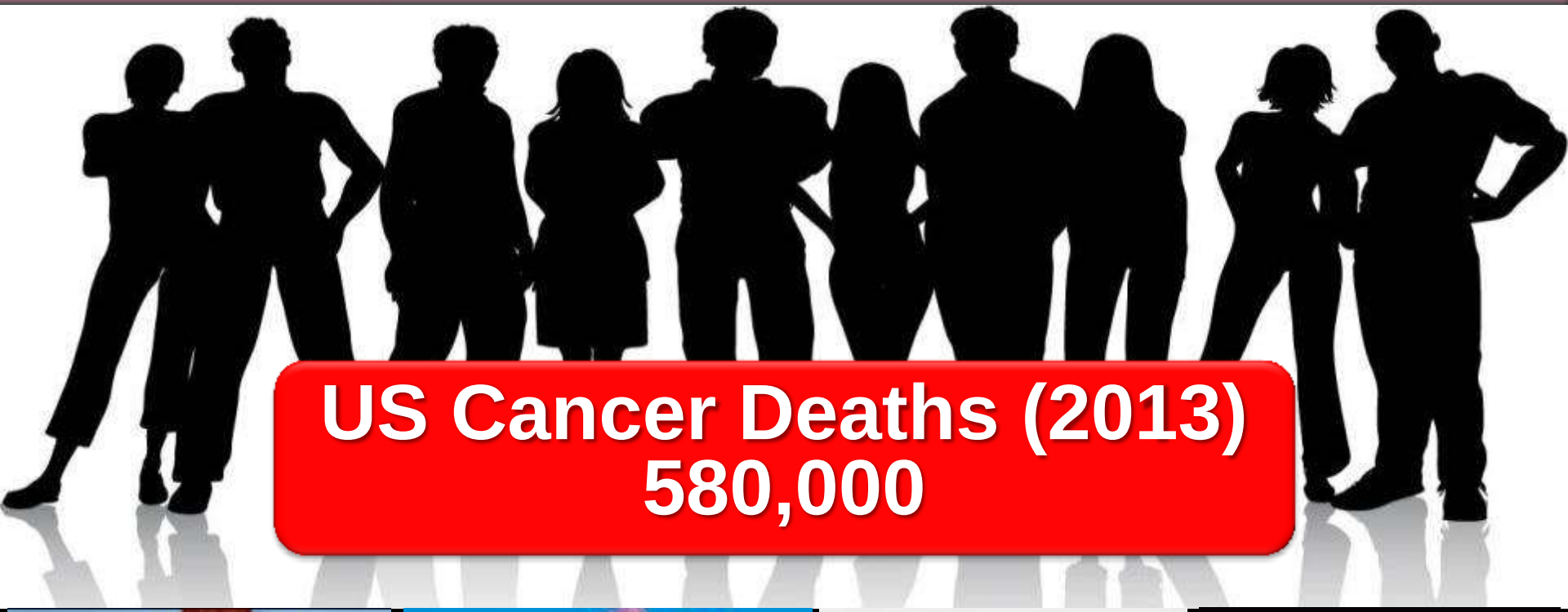

Hype



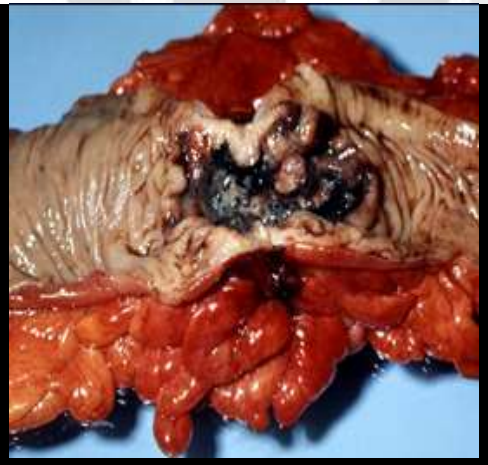

Balanced Critique

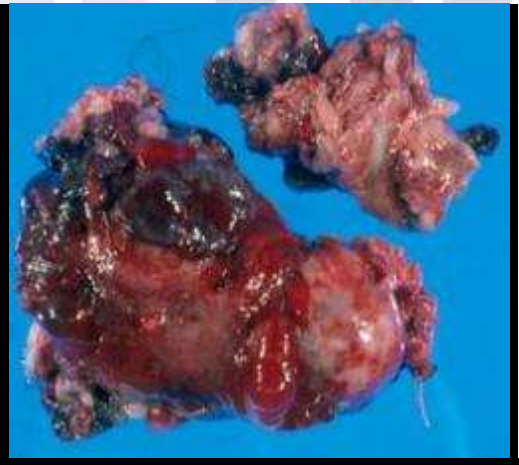

Reality

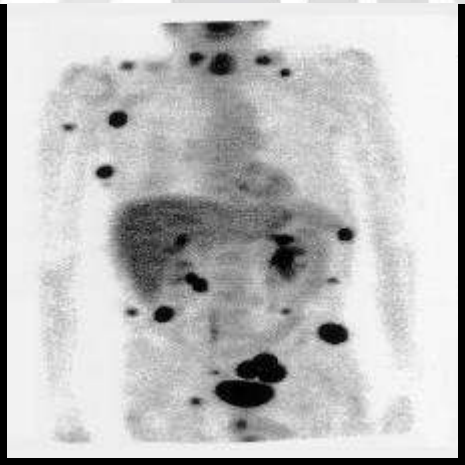
# An Unescapable Fact:
# Confronting the Clinical, Economic and Human Toll of Cancer

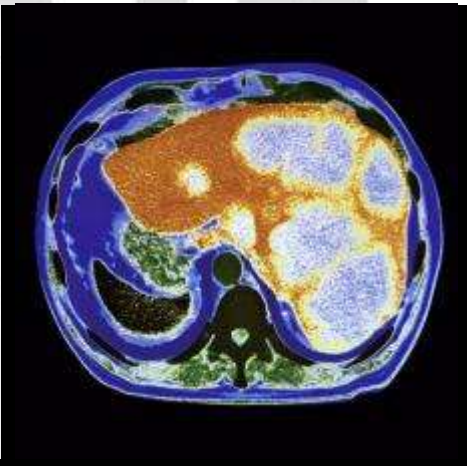


**US Cancer Deaths (2013)**
**580,000**









# US Cancer Prevalence Estimates 2010 and 2020

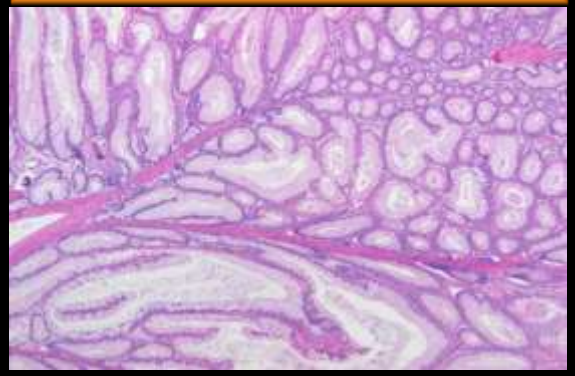
| Site | # People (thousands) 2010 | 2020 | % change |
|---|---|---|---|
| Breast | 3461 | 4538 | 31 |
| Prostate | 2311 | 3265 | 41 |
| Colorectal | 1216 | 1517 | 25 |
| Melanoma | 1225 | 1714 | 40 |
| Lymphoma | 639 | 812 | 27 |
| Uterus | 588 | 672 | 15 |
| Bladder | 514 | 629 | 22 |
| Lung | 374 | 457 | 22 |
| Kidney | 308 | 426 | 38 |
| Leukemia | 263 | 240 | 29 |
| All Sites | 13,772 | 18,071 | 32 |

From: A.B. Mariotto et al. (2011) J. Nat. Cancer Inst. 103, 117

# Challenging Questions Regarding Future Directions in Cancer Research and Clinical Oncology

# Cancer as a Complex Adaptive System: Emergent Phenomena and Tumor Progression (System State Shifts)

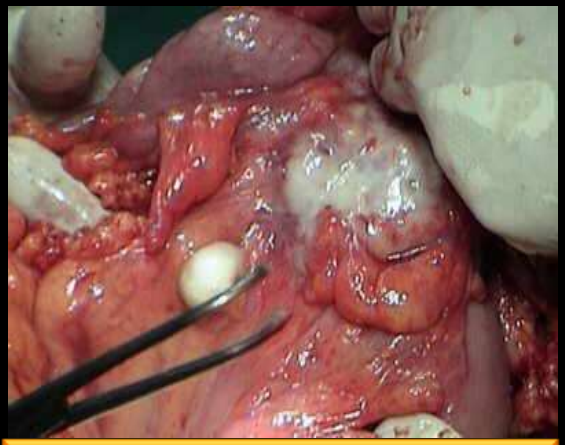
**Escape From Controls for Normal Tissue Architecture**



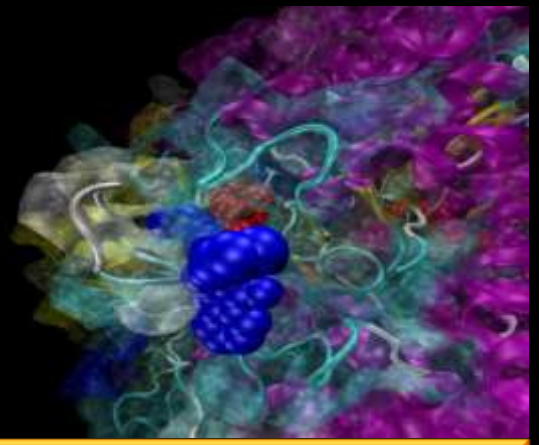
**Genome Instability and Emergence of Clonal Variants**

**Evasion of Detection/Destruction by Host Immune System**

**Use of Host Systems by the Tumor to Promote Progression**



**Invasion and Metastasis**



**Emergence of Drug-Resistant Clones**

# Confronting The Cancer Challenge

- need for more effective diagnosis and treatment of clinical disease (OS not just PFS)
- disease subtypes, tumor cell diversity (heterogeneity) and Rx selection
- metastatic disease (multiple locations)
- treatment resistance
- clinical impact (adverse quality-of-life) and cost of care
- post-treatment complications and supportive care
- end-of-life care

# The Biological Complexity of Cancer and the Design of Future Treatment Strategies

## Formidable Performance Requirements

- hit all clones
- hit all clones in multiple metastases in multiple body locations
- hit all new emergent Rx-resistant clones

**The Urgent Need for New Diagnostics and Molecular Profiling Tools for Improved Monitoring of Tumor Progression**

**From ‘Static Snap Shot’ at Initial Diagnosis to Dynamic Monitoring of Clonal Population Dynamics**

# Aspirations for Improved Cancer Diagnosis and Treatment

- earlier detection of disease progression/relapse due to Rx-resistance
- more agile switching of Rx combinations to counter emerging Rx-resistance (anticipatory therapy)
- better tests to assess the presence of minimal residual disease (MRD) and cancer dormancy

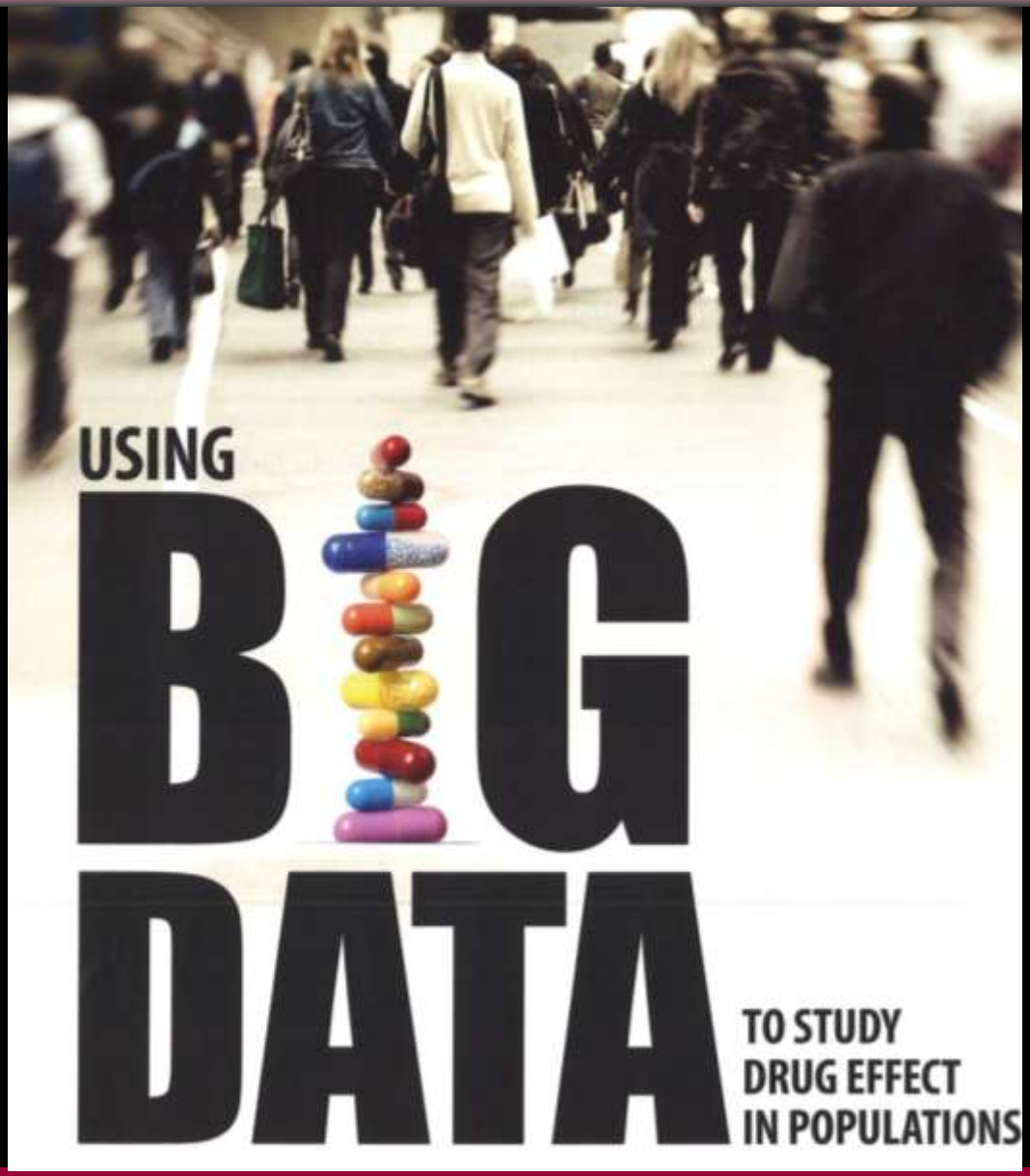
# Healthcare Information Systems

# 'Big Data' in Cancer Exemplifies MOOM (massive open online medicine)

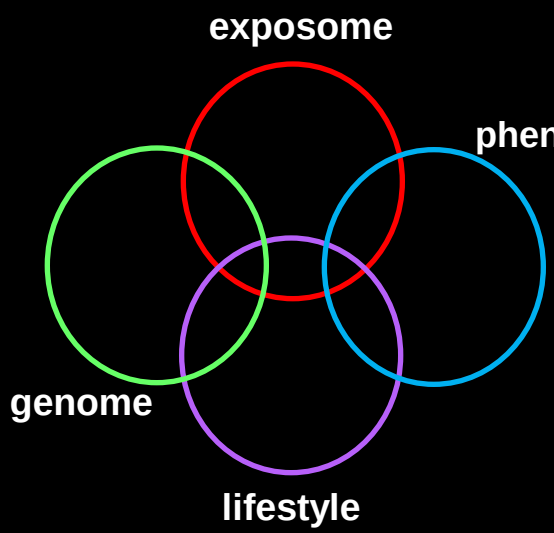
- Building a Transformation in Cancer Care
- “Cancer science and information technology are advancing rapidly, but the way we care for patients today cannot fully capitalize on those advances”.
- “Patients are increasingly presenting with “rare cancers,” more narrowly defined by their molecular characteristics, sometimes making the best course of treatment unclear”.
- “Today more than ever, oncologists need real-time decision support to help them provide the most effective treatments tailored to their patients’ unique biology and tumors”.

# “A Learning Healthcare System” (US Institute of Medicine)

- the urgent need for healthcare to adopt seamless integration of electronic health records
- data/metadata integration
- evidence-based care:  what works and what doesn’t
- increasingly accurate decisions and treatment selection
- enforcement of optimum clinical decisions (and patient compliance)


USING
BIG
DATA
TO STUDY
DRUG EFFECT
IN POPULATIONS

# Information-Based Services for Increased Precision in Managing Risk in Healthcare




data curation and analysis

risk identification and mitigation + decision-support tools

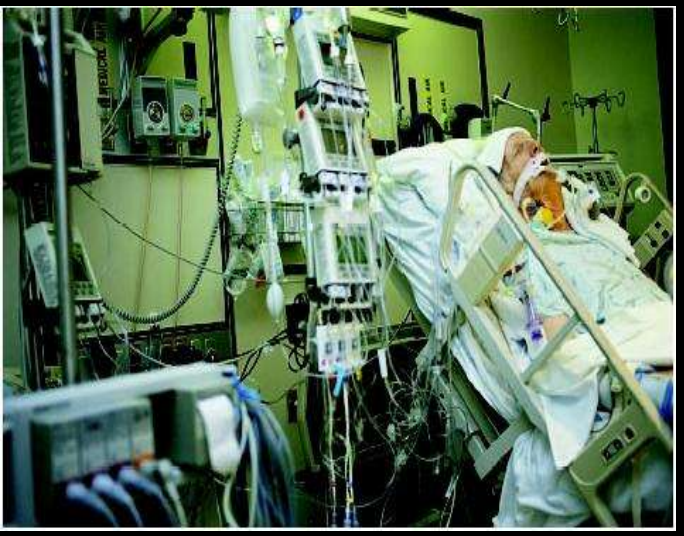
- earlier detection of disease
- rational Rx
- monitoring of health status
- predisposition risk
- risk pre-emption

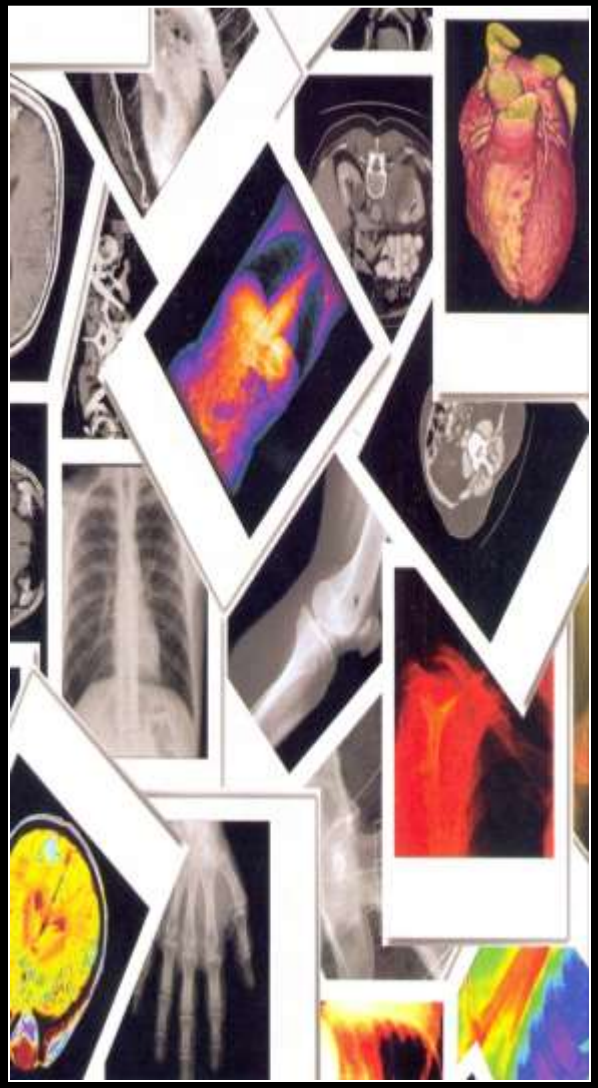
profiling

analysis

informed decisions

# How Much New Technology Can We Afford?





# The Quest for Affordable Care for Cancer and Other Chronic Diseases

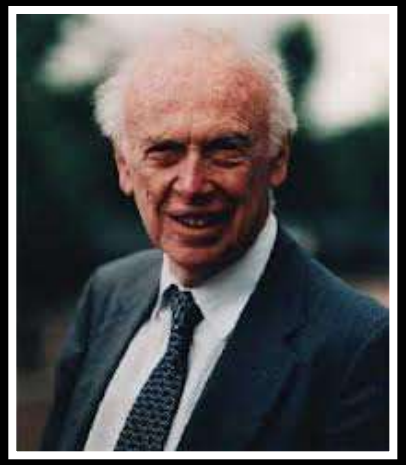
# The Difficult but Largely Ignored Central Questions in Oncology and Cancer Care Delivery

**What is a meaningful advance in Rx effectiveness?**

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

# Cost of Recently Approved Anti-Cancer Drugs

- brenfuximab (Adcetris) $216,000/course
- ipilimab (Yervoy) $123,000/year
- cabazitaxel (Jevtana) $96,000/year
- sipuleucel-t (Provenge) $93,000/year
- vismodegib (Erivedge) $75,000/course
- petuzumab (Perjeta) $70,800/year
- vemurafenib (Zelboraf) $61,000/year
- abiraterone (Zimiga) $60,000/year
- premetrexed (Alimta) $30,000/course



**“I would like someone to declare war on cancer.**
**The NCI is an agency that is perpetuating**
**the old cancer establishment.**
**The FDA should not be approving drugs**
**that have only shown a three month survival benefit.”**

**Dr. James D. Watson**
**Nobel Laureate**
**2012 Celebration of Science**
**Washington, DC 7-9 Sept. 2012**
**cited in Scrip Intelligence 10 Sept. 2012**

# Phase III Studies Comparing Chemotherapy With or Without Bevacizumab as First-Line Therapy for Advanced Epithelial Cancers

| Neoplasm | Study | Bevacizumab Effect | |
|---|---|---|---|
| | | PFS (months) | OS (months) |
| Breast | ECOG E2100 | +5.9* | +1.5 |
| | AVADO | +0.8* | -1.1 |
| | RIBBON-1 | +2.9* | +7.8 |
| Ovarian | GOG 0218 | +0.9 | -0.6 |
| Lung | ECOG E4599 | +1.7* | +2.0 |
| Gastric | AVAGAST | +1.4* | +2.0 |
| Pancreas | CALGB 80303 | +0.9 | -0.1 |
| CRC | Hurwitz | +4.4* | +4.7* |
| | Saltz | +1.4 | +1.4 |

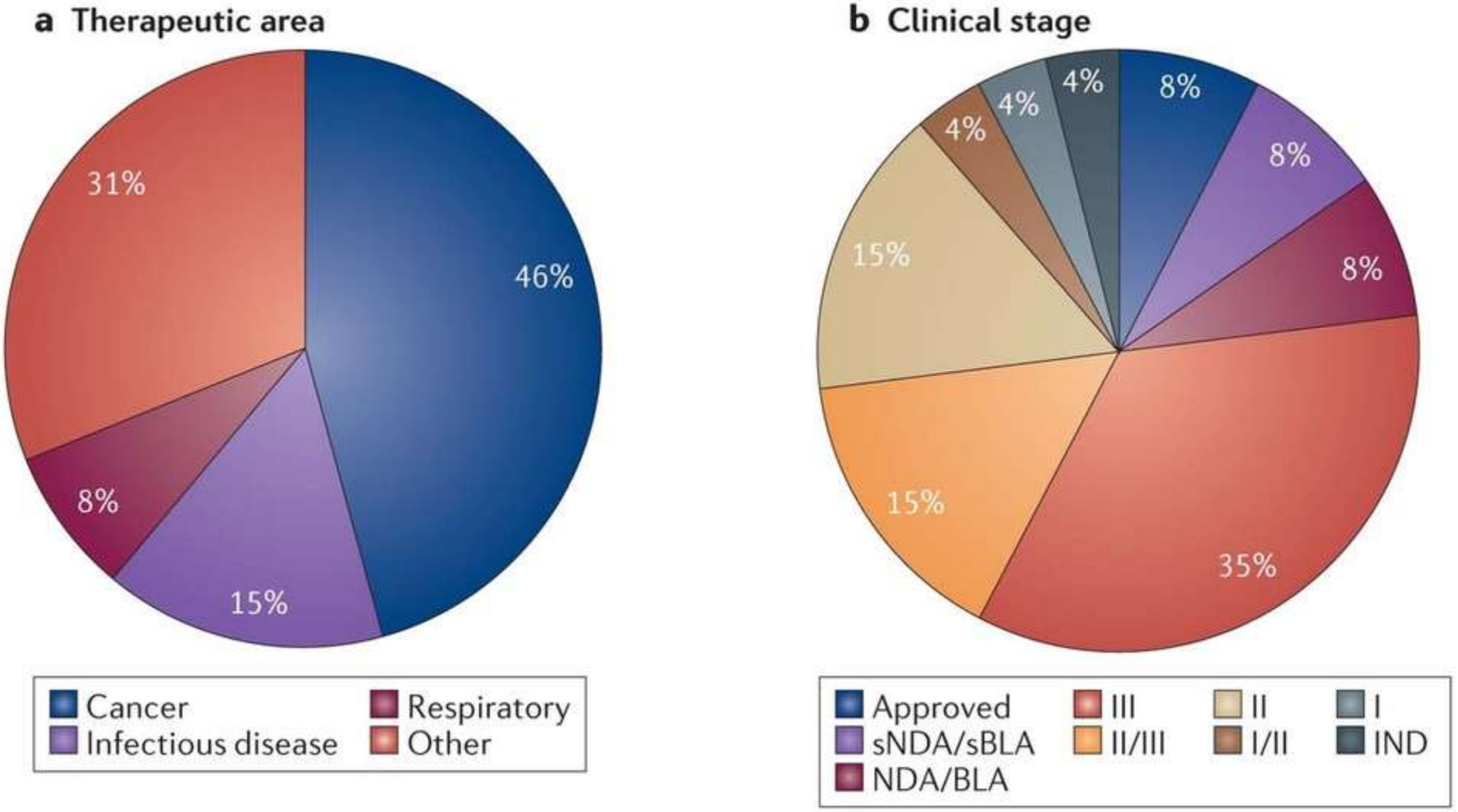
*Statistically significant

Adapted from: A. Ocana et al (2011) J. Clin. Oncol. 29, 254

**Are Regulatory Approval Hurdles Too Low for New Anti-Cancer Treatments?**

**Are Empathic and Political Considerations Diluting the Definition of “Breakthrough”?**

# Breakthrough Therapies: Class of 2012-13



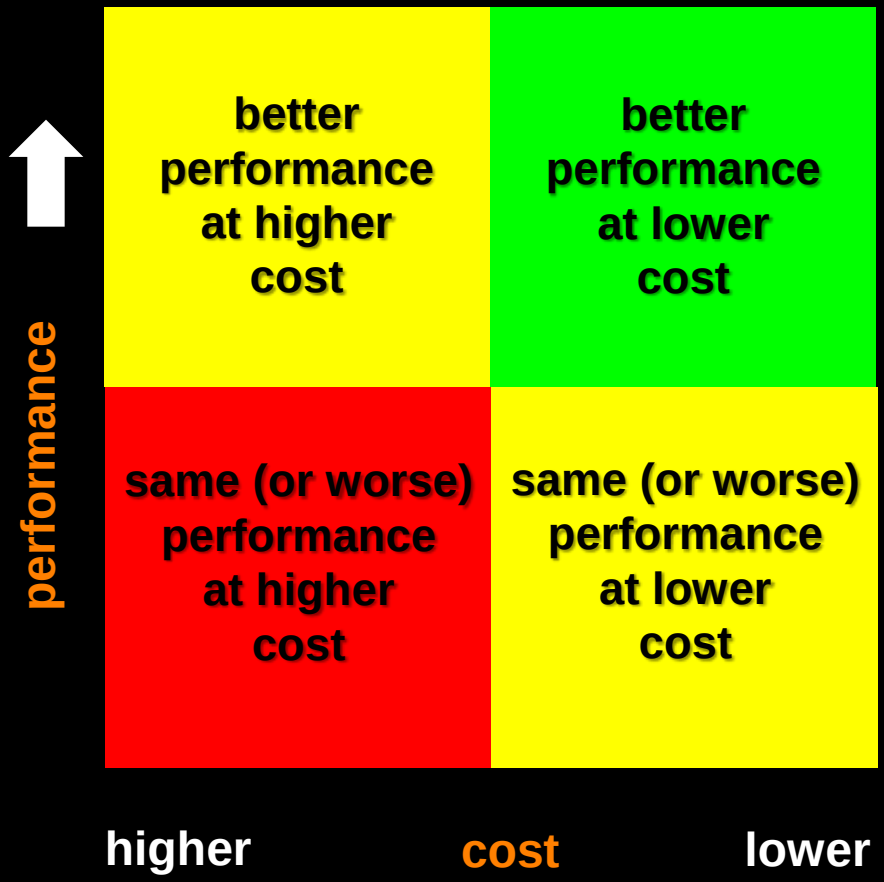

From: A. Mullard (2013) Nat Rev Drug Discovery 12, 891

Health Technology Assessment (HTA)

Defining What Works (and What Doesn't)

Defining Value

# Defining Value in Healthcare: A Complex Technical and Social Exercise



# Regulatory Criteria for Drug Approval


- safety
- efficacy


- safety
- efficacy
- cost-effectiveness
- separate review for regulatory approval (EU wide) and pricing (national)

# UK National Institute for Health and Care Excellence (NICE)

NHS

National Institute for
Health and Clinical Excellence

NICE

National Institute for
Health and Care Excellence

# Cost Per Quality-Adjusted Life-Year (QALY)

| | |
|---|---|
| Switch to an aromatase inhibitor for early-stage breast cancer vs. continued tamoxifen | $22,900 |
| Prescribe trastuzumab for metastatic breast cancer vs. standard chemotherapy | $150,000 |
| Prescribe erlotinib for advanced pancreatic cancer vs. gemcitabine alone | $370,000 to $500,000 |
| Perform helical computed tomographic screening for lung cancer in 60-year old former heavy smokers vs. no screening | $2,300,000 |

From: G. Lyman (2013) The Oncologist 18, 752

# 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

# Payors' Changing View of Oncology Drugs

# Comparative Effectiveness Research (CER)

- generation and synthesis of evidence to compare benefits and harms of different healthcare services and treatment options
  - diagnosis
  - treatment
  - monitoring
  - delivery of care
- provide clinicians, patients, purchasers and policy makers with data for informed decisions
  - individual and population levels

**The Current Status of Cancer Care Delivery**

**Doing More, But Not Necessarily Doing Better**

**Buy and Bill: Oncologists' Financial Incentives Are Not Aligned With Quality of Care**

# The Unacceptable Status of Cancer Care

- unwarranted practice variation across the continuum of care
  - cancer outcomes vary regionally, nationally and internationally
- fragmented and poorly coordinated multi-speciality services
  - PCP, oncologists, pathologists, surgeons
  - inconsistent supportive care and survivorship care
- lack of proficient data migration and QA systems aligned across different parts of the delivery system

# Uneven and More Expensive Cancer Care

- Medicare payments up to 50% higher for Rx therapy given in hospital outpatient facilities versus Rx in community cancer clinics
  - medscape.com 12/26/13
- hospitalized patients also receive more expensive drugs than ambulatory patients

# The Unacceptable Status of Cancer Care

- failure to keep pace with advances in the molecular biology of cancer and integrate into SOC
  - community oncologists/HCPs versus academic medical centers
  - regulatory and reimbursement policies
  - clinical guidelines (SOC) and compendia
- refuge in anachronistic SOC guidelines and “one-size-fits all” Rx strategies based on histologic profiling (AP) taxonomy versus molecular profiling
  - slow pace of adoption of profiling and tumor subtyping for Rx selection
  - insufficient enrollment of stratified patients into investigational Rx trials

# Molecular Profiling and Rx Selection in Cancer Treatment

- should molecular profiling be conducted on all patients as SOC?
- should patients receive SOC if profiling indicates absence of molecular targets for the SOC regimen?

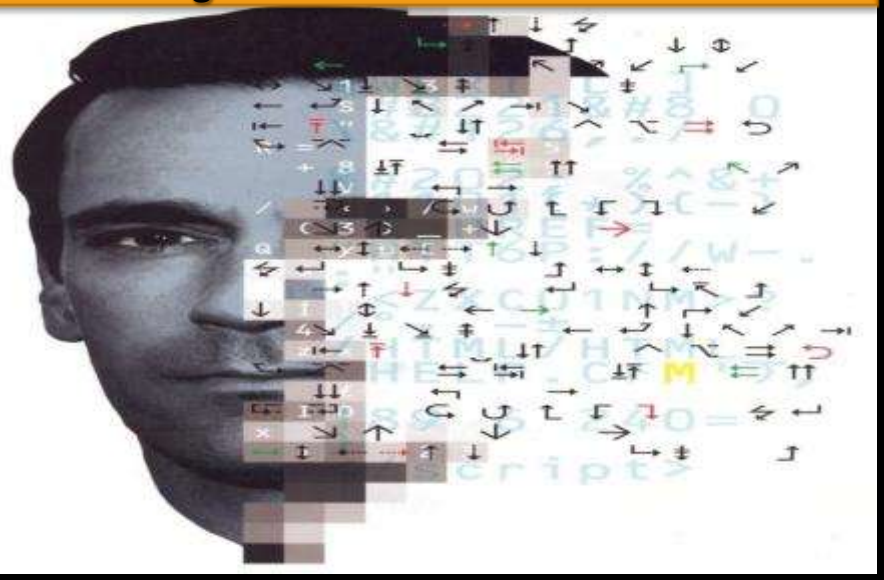
# Why Should Oncology Adopt Different Considerations for Rx Selection Than Other Clinical Disciplines?

- antibiotics aren't given to patients with a known antibiotic resistant bacterial infection
- HIV-positive patients are routinely profiled for Rx-resistance before Rx starts
- blood transfusions aren't given to people with incompatible blood groups
- influenza vaccines are designed to combat the current circulating influenza strains not some unknown strain(s)

# Technology Acceleration and Convergence: The Escalating Challenge for Professional Competency, Decision-Support and Future Education Curricula

## Data Deluge

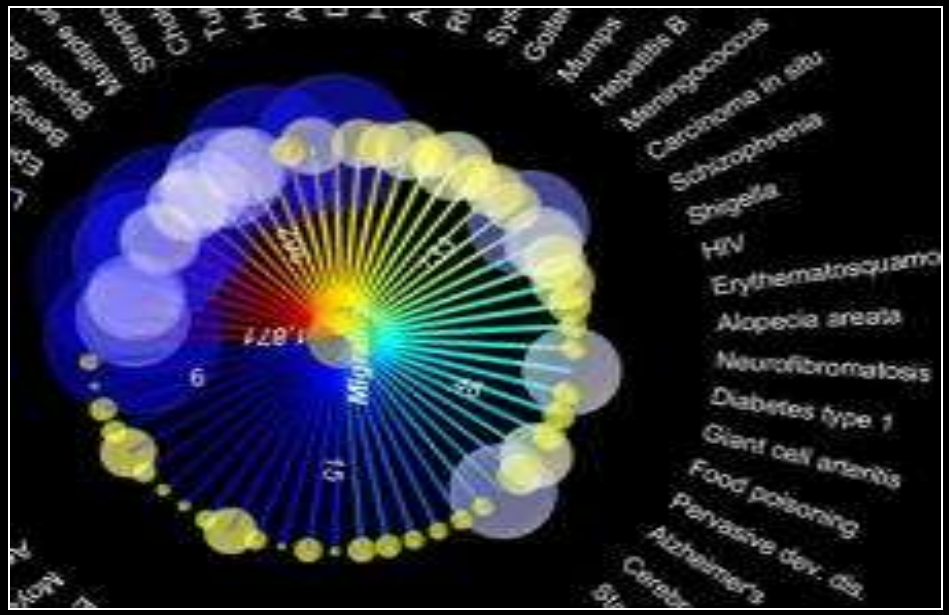
## Cognitive Bandwidth Limits

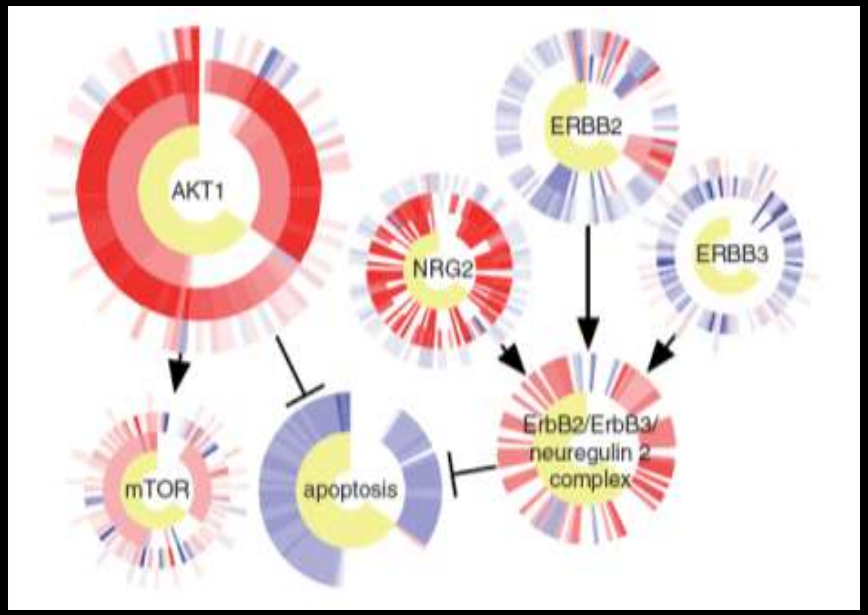


## Automated Analytics and Decision Support

## Facile Formats for Actionable Decisions

# The Growing Education and Knowledge Gaps in Comprehension of Molecular Medicine Concepts Among Healthcare Professionals



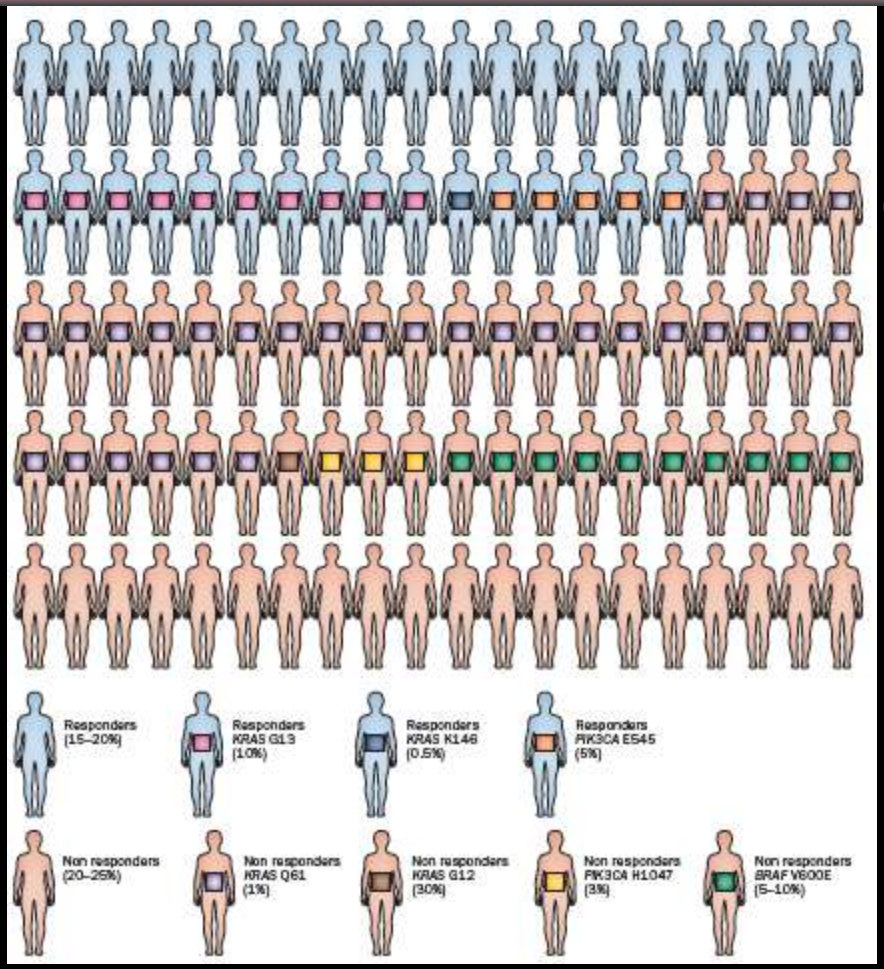
# Are Oncologists' Financial Incentives Aligned with Quality Care?

# Treatment At All Costs: How Far Should Treatment Go?

"Why do they put nails in coffin lids?
To stop oncologists having one last try….."

C. Chatfield
Prospect July 2012, p.16

# Molecular Diagnostics and Identification of Responder/Non-Responder Patients for Rational Rx




**Frequencies of Molecular Alterations in CRC and Responsiveness to Cetuximab or Panitumumab**

**From: M. Martini et al. (2012) Nature Rev. Clin. Oncol.**

**"The problem with all these tests, soon I'll have nothing (treatments) I can offer my patients"**

**"Eminent Oncologist" (journal's designation) Drug Discovery World. Spring 2011, p. 61.**

# Dangerous Arrogance?

"The problem with all these tests,
soon I'll have nothing (treatments)
I can offer my patients."

Eminent Oncologist
(journal's designation)
Drug Discovery World, Spring 2011, p.61

**So is it better to go ahead and prescribe Rx of no value?**
**- ethics?, malpractice?**
**- financial incentives?**

# Are Oncologists Financial Incentives Misaligned with Optimum Treatment?

- uncritical payer acceptance of high cost of new oncology drugs (US)
  - $50K-120K/year
- estimated 80% annual income for community oncologists tied to Rx use
- no incentives to select less expensive Rx or palliative care
- physician/payer refuge in slow pace of change in SOC guidelines to incorporate obligate molecular diagnostic profiling for Rx selection
- unacceptable levels of use of new Rx regimen(s) in last two weeks of life

# Reform in Current Oncology Drug Prescribing

- create new financial rewards to limit use of expensive drugs (particularly I.V.) and increased use end-of-life conversations/palliative care recommendations
- uncouple relationship between prescribing patterns and physician income
- new compensation and incentive schemes for clinical decisions and services that enhance/maintain QOL and reflect patient/family preferences

# Patients Often Do Not Understand the Goals of Cancer Treatment

# Cancer Care

- patients often do not understand goals of cancer treatment
- 70-80% believe treatment is curative and do not understand they had incurable disease (NEJM 2012, 367, 1616)
- patient ‘shut down’ and ‘denial’
  - how to best communicate difficult information and engage patients (and families) in care decisions

# The Vital Role of Patients and Patient Advocacy Organizations
















# Empowered Patients:
# Social Networking Sites (SNS) and Their Role in Clinical Care

- logical extension of rapid rise of web/apps in mainstream culture
- increasingly proactive and engaged consumers/patients/families
- more transparent information on treatment options
- improved recruitment of patients into investigational clinical trials

**The Need for Change in Physician-Patient Relationships**

**From Medical Paternalism in Decision-Making to More Inclusive Roles for Other Healthcare Professionals, Patients and Famililes**

# Certain Death in Uncertain Time: Balancing Hope and Harsh Reality in Terminal Illness

"I respect the seriousness of death
I've had many occasions to meditate on its intrusions.
….the way the message was delivered.
Frankly, it made me furious."

Sen. Edward Kennedy
True Compass. A Memoir. 2009

# The Too Often Overlooked Communication and Interaction Gap in Healthcare and Patient Safety

- "do you understand"
  - MD paternalism and patient timidity: a dangerous combination
- challenge for healthcare professionals
  - time = money but culture/training also a key factor
- the sociology of medical training and practice
  - hierarchical, authoritarian, paternalistic
- oncologists and patients often hold different perception of priorities
- inadequate focus by many physicians on team-based coordination in care delivery

# Physician (HCP): Patient Communications in Chronic and/or Terminal Illness

- clinical communication challenge of balance between ethical transparency and empathy
- the vulnerability of patients: "trust and surrender" and presumed "authoritative knowledge" of MDs/HCPs
- physicians/HCPs are rushed and stressed
- oncologists know, but often deny, the limited efficacy of many interventions
  - when to move from continued aggressive intervention to palliative care.
  - why do so many physicians chose "to go gently into the night (WSJ)".

**Palliative Care:**
**Treatment Without Curative Intent**

**Economic (Payors) and Evidence-Based Pressure for Increased Use of Palliation versus Repeated Aggressive Cycles of Different Rx Without Clinical Benefit**

# Factors Linked to Survival Benefit of Palliative Care in Cancer Patients

- limit futile Rx and impact of QOL and cost
- limit repeated testing and hospitalizations
- reduce physical symptoms due to disease progression
  - pain, nausea, CV complications
- reduce psychological symptoms
  - anxiety, depression, impaired cognition
- active engagement and education of patients and family members on value of palliative care versus aggressive intervention(s)

# Optimizing Palliative Care: A Team-Based Process

- physicians, nurse specialists, other HCPs
- physical therapists
- expertise in psychological support and spiritual care
- home-based care services
- ‘the family unit’

Approaching Death: Care At End of Life

Dying with Dignity

New Expectations for the Level of Intervention(s) in Late Stage Terminal Illness

# End-of-Life Cancer Care
## (N.E. Morden et al. (2012) Health Affairs 31, 786)

- wide variation in clinical practice in different care settings
- poor national compliance with National Quality Forum metrics
  - reduce rates of ICU use in last month of life
  - no new chemotherapy regimen in last 2 weeks of life
  - death at home or hospice versus hopsital/ICU

# “A Good Death”: Patient Preferences in End-of-Life Care

- ‘a good death’
- dignity
- death at home or hospice versus ICU and extended life support and intensive intervention
- fade away: state of unconsciousness induced by drugs

# Palliative Care:
# The Importance of Advance Care Planning

- clinicians often unaware of patient preferences at end of life
- patients with no expressed preference for place of death more likely to die in hospital

# End-of-Life Care

**Assisted Death:**
**the most perplexing issue in medical ethics, law and religious discourse on end-of-life care**

# US Healthcare

**Healthcare: An Expensive Menu Without Prices**

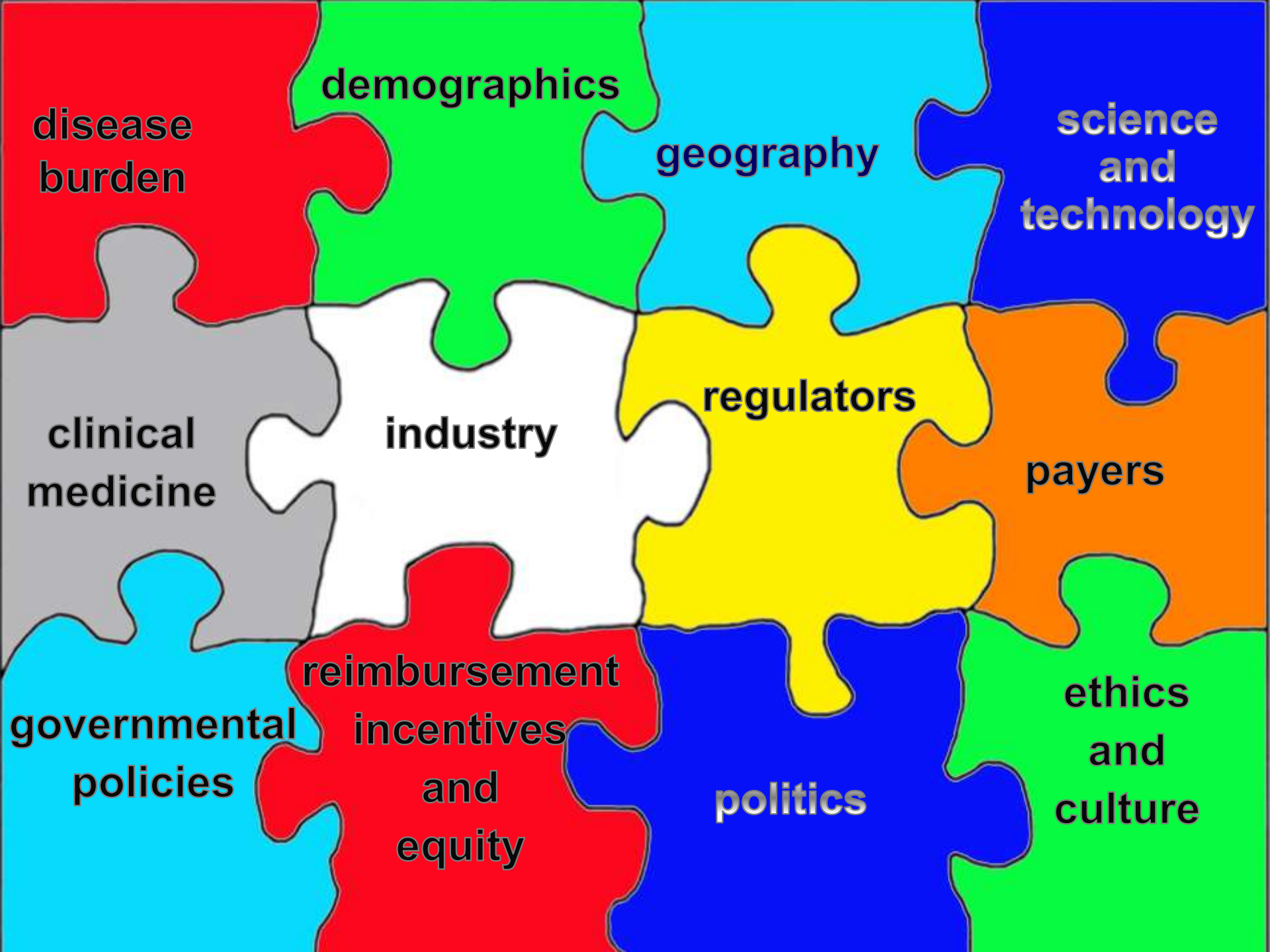
**Managing the Demands of an Aging Society and Chronic Disease Burden in an Era of Economic Constraint**

**From a "Do More, Bill More" Healthcare System to Managing Individual Risk for Improved Health Outcomes and Cost Control**

**Sustainable Health: Societal (Economic) and Individual (Wellness)**

# The Core Elements in Healthcare: Better Decisions for Better Outcomes

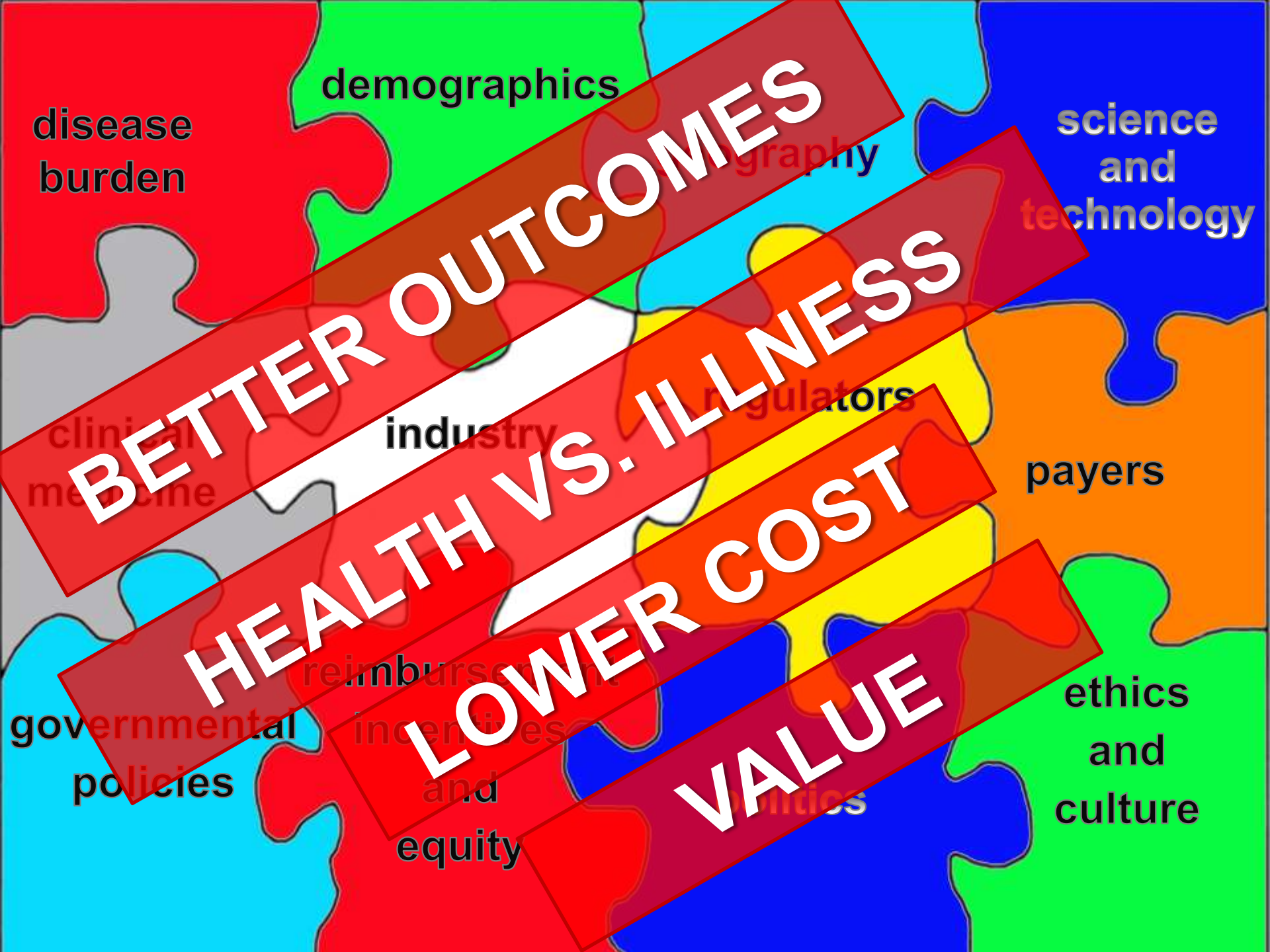
# US Healthcare:
# A Complex, Multi-Dimensional Ecosystem with Diverse Stakeholders and Conflicting Incentives


disease burden
demographics
geography
science and technology
clinical medicine
industry
regulators
payers
governmental policies
reimbursement incentives and equity
politics
ethics and culture

**Healthcare:**
**A Complex, Multi-Dimensional Ecosystem with Diverse Stakeholders and Conflicting Incentives**

**US Healthcare:**
**An Economically Unsustainable Enterprise**

**US Healthcare:**
**Radical Realignment of Patterns of Care Delivery to Achieve Better Outcomes and Control Cost**


disease burden
demographics
science and technology
BETTER OUTCOMES
HEALTH VS. ILLNESS
LOWER COST
VALUE
industry
payers
governmental policies
ethics and culture
equity

# Cost Control in Healthcare

- shift from fee-for-service (do more-bill more) to bundled episode of care or capitation independent of services provided
- new analytical approaches and metrics for “socially optimal amount of care”
  - benefits of intervention must equal or exceed their cost
- challenge for valuation of technology innovations whose benefits may not be fully assessable today but will likely increase over time

# Improving Healthcare Using Data

- better data on where money is spent and outcomes
- many MDs don’t often know (or care) about the cost of recommended actions
- evidence-based tracking of waste, error and failure to adopt best practices
- greater awareness and access of patients/families of treatment options and performance outcomes of different providers

# The Challenge of Cultural Conservatism

# Discarding What Doesn't Work

Choosing Wisely®

*An initiative of the ABIM Foundation*

American Society of Clinical Oncology

ASCO

American Society of Clinical Oncology

**Five Things Physicians and Patients Should Question - 2013**

http://www.asco.org/sites/www.asco.org/files/asco_choosing_wisely_top_five_list_2013.pdf

# “Choosing Wisely”

- launch of the “Choosing Wisely” and “Top Five” initiatives
- recognition by professional medical societies of need to abandon procedures/treatments of no proven value
- enforcement by payors
- awareness and rejection by patients/families

# The Rise of Precision (Molecular) Medicine and Information-Based Medicine

- knowledge of disease mechanisms at the molecular level
- molecular profiling of patients and rational Rx selection and agile adjustment
- large scale data capture and analysis for evidence-based assessment of what works and what doesn't
- consistency and enforcement of evidence-based procedures/processes for better outcomes

**Better Decisions**

**Better Outcomes**

**Better Allocation of Finite Resources**

**Better Cost-Effectiveness**

# The Future of Healthcare in 140 Characters In 2030

- healthcare is transparent
- computerized decision tools dominant diagnosis and treatment selection
- healthcare services are integrated from cradle to grave
- patients are empowered but must take greater responsibility for sustaining that health
- healthcare is not MD (physician)-centric but provided by multi-disciplinary (the new MD)-centric teams

ASU Complex Adaptive Systems

ARIZONA STATE UNIVERSITY

# BIO 302: