

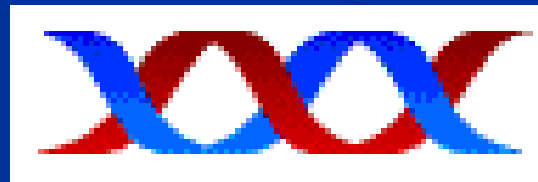
Measuring the Value of Genomic Diagnostics and Targeted Therapeutics: Implications for Patients and Public Policy

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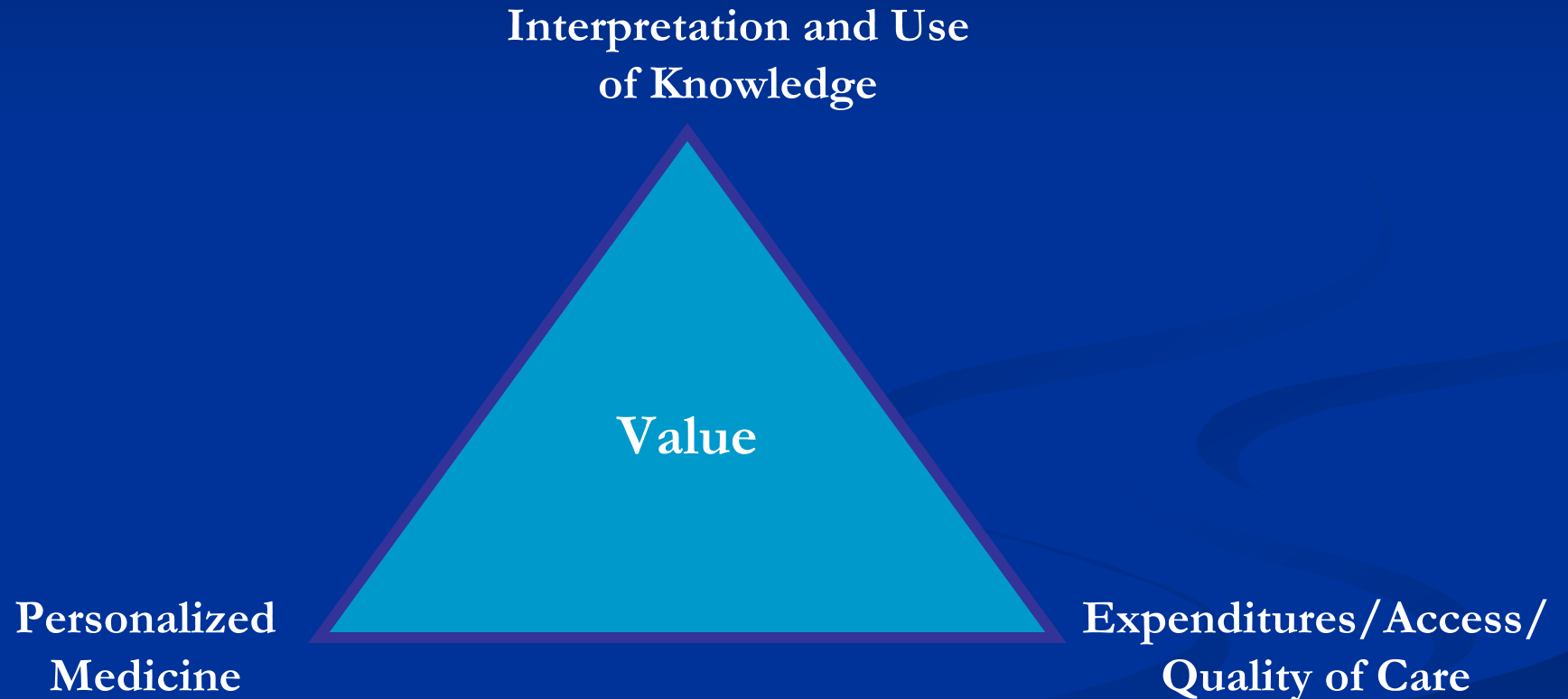
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Program in Personalized Medicine &
Targeted Therapeutics™

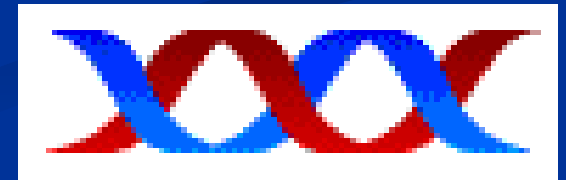
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The Emerging Trifecta of Forces Transforming Healthcare



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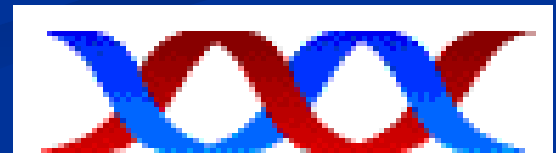


The Problem of 'Value' in Healthcare

- Different 'value' metrics for different stakeholders (patients, providers, payers, politicians)

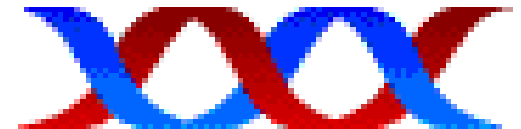


“You may believe that you’ve been overcharged, but remember you’ve been over-medicated.”



Objectives

- Provide an overview of pharmacogenomics and its clinical relevance
- Provide an overview of genomic diagnostics and therapeutic combinations
- Discuss approaches to measuring value



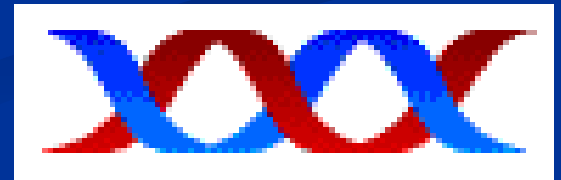
Personalized Medicine

- “Personalized medicine is the translation of the science of pharmacogenomics into clinical practice. Personalized medicine involves preventative, diagnostic and therapeutic interventions, with risk defined through genetics as well as clinical and family histories.”

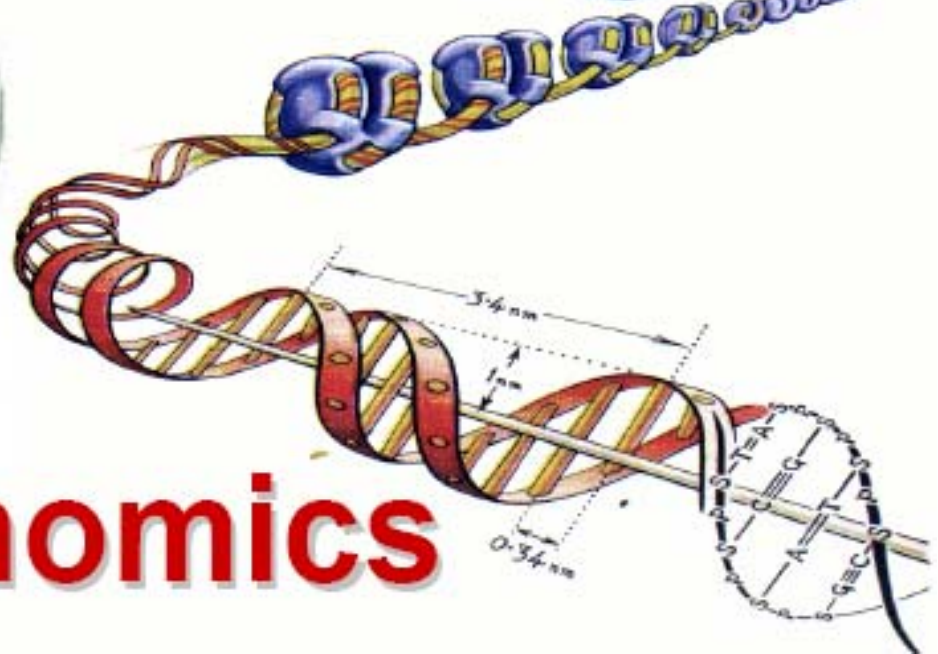
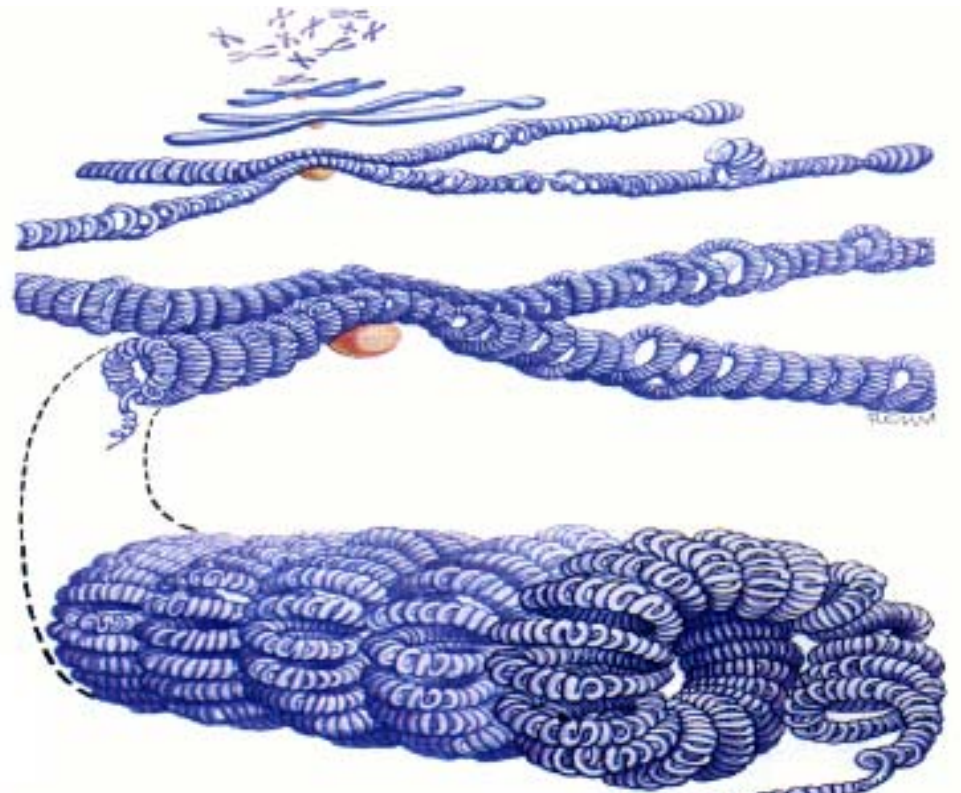
Issa, AM et al. *Personalized Medicine* 3(4): 421-427, 2006.

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Drugs and Genes



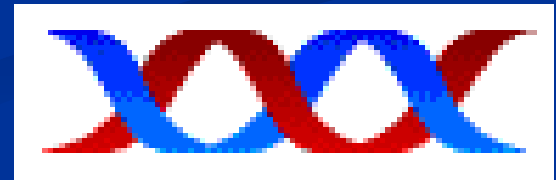
Pharmacogenomics

Clinical Relevance

- Can we predict who will derive an optimal response?
- Can we predict who will have a toxicity?
 - ❖ Host (patient) genotype determines optimal drug therapy approach
 - ❖ Disease (pathogen) genotype determines optimal drug therapy approach

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Diagnostics

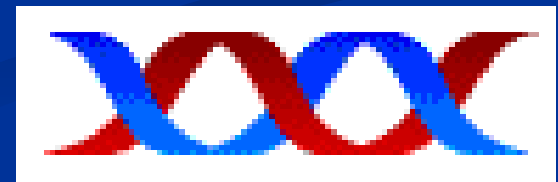
In vitro diagnostics:

- ❖ “Those reagents, instruments, and systems intended for use in diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.”

21 CFR 809.3

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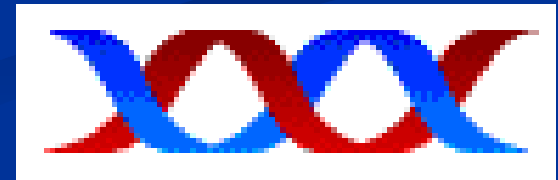


Molecular Diagnostics

- Risk Assessment Markers
 - ❖ Susceptibility to a disease which may or may not lead to development of the disease
- Screening Markers
 - ❖ Allow the discrimination between “healthy” and asymptomatic “disease” state by screening large populations
- Prognostic Markers
 - ❖ Once a disease state is established, enables prediction of the course of the disease to assist in determination of therapy (e.g. aggressiveness required)

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Genomic Diagnostics[©]

The use of genomic approaches to detect genetic sequences that are predictive of drug response, and that can be linked to a targeted therapeutic in an underlying cause-effect relationship.

Stratification



Predict response to drug & discriminate between responders and non-responders

Therapeutic Monitoring



Monitor efficacy of Tx once responder status is established

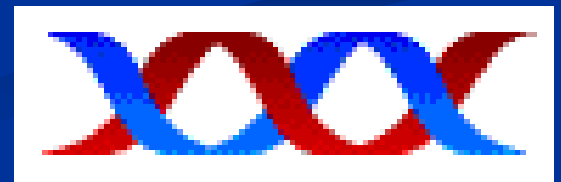


Targeted Therapeutics

Choices of therapeutic interventions for a specific disease or condition are guided by an understanding of relevant genetic variations between individuals with that disease and, when applicable, by the relevant molecular variations in the expression of that disease.

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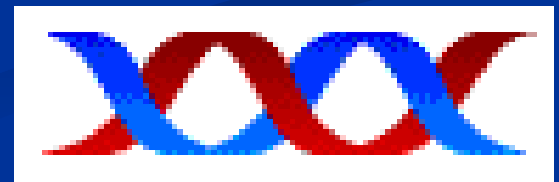


Anticipated Benefits

- Advanced screening for disease
- Improvements in the drug discovery and approval process
- Avoidance of serious adverse drug reactions
- More accurate methods of determining appropriate drug dosages
- Ability to uncover long-unknown correlations between ethnicity and efficacy
- Increased patient compliance
- Decrease in the overall, lifelong costs of health care, including shorter, lower-cost, end-of-life expenditures
- Improved outcomes and overall quality of life.

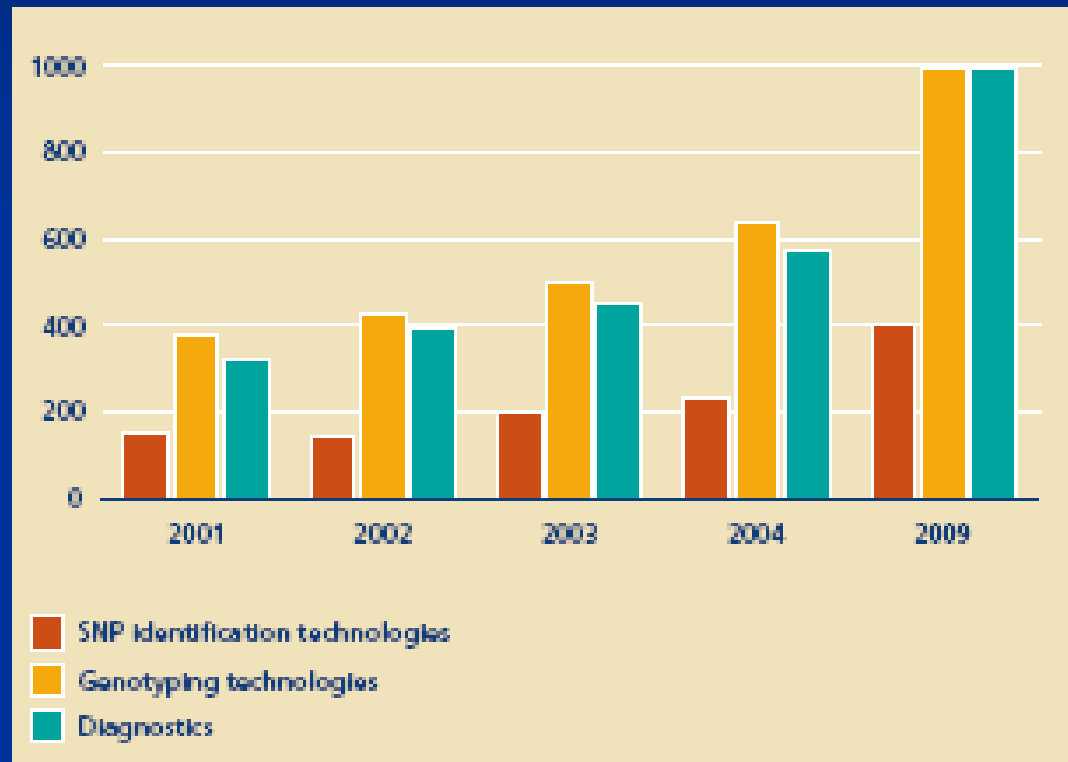
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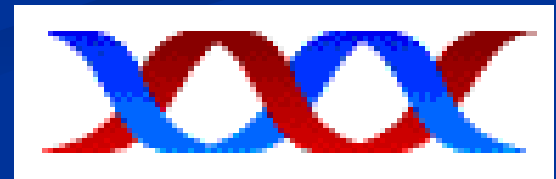
Worldwide market for Pharmacogenomic-based Therapies

USD
(Millions)



Adopted from the Business Communications Company, 2006

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Economics of *In Vitro* Diagnostics

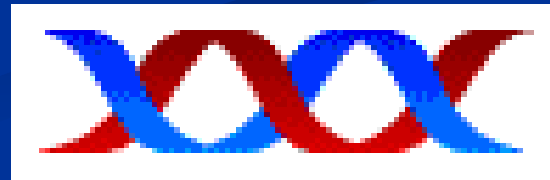
- Some 9 companies hold 80% of US market revenue of \$11.2 billion and \$28.6 billion global sales
- Current climate of diffuse regulatory oversight (CLIA; ASRs/“homebrew”)
- 5% of US hospital costs and 1.6% of prescription costs

BUT INFLUENCE

60 – 70% of health care decisions

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Herceptin[®]: The Business Case for Sub-dividing the Target Population

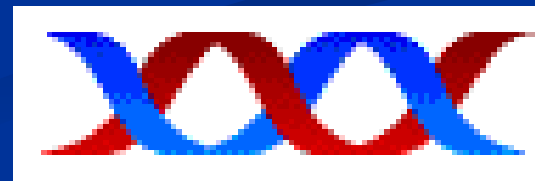
Trial Design	With HER2 neu	Without
# of patients	470	2200
Response rate	50%	10%
Years of follow-up	1.6	10

- Savings in clinical trial costs ~\$35 million
- Income from 8 year acceleration of product ~\$2.5 billion
- Access to drug from acceleration ~120,000 patients
- Recent success from adjuvant therapy – value extension.

*Source: Press & Seelig, Targeted
Medicine, New York, 2004*

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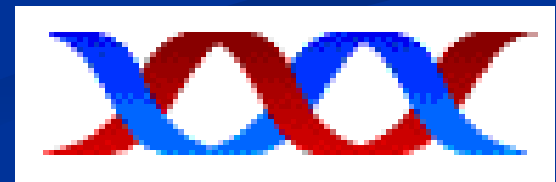
Roche's Amplichip[®]



- Chip measures alleles of CYP2C19 and CYP2D6.
- Tool to reduce under- and over-dosing.
- Estimated 20% reduction in adverse drug reactions.

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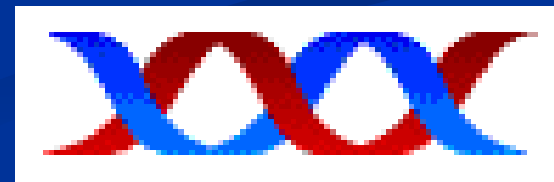


CYP 450 Testing (AmpliChip[®])

- AmpliChip[®] tests for CYP2D6 & 2C19 genotypes
 - ❖ Involved in metabolism of many drugs
- CYP2D6 testing could have high value
 - ❖ Relevant to ~196 million prescriptions and \$13.7 billion expenditures annually in US
- Limited data to assess impact and value of testing
 - ❖ Very limited data on clinical outcomes of testing
 - ❖ Uncertain what population is the “target”
- Drugs metabolized by CYP 450 generally do not have a narrow therapeutic index

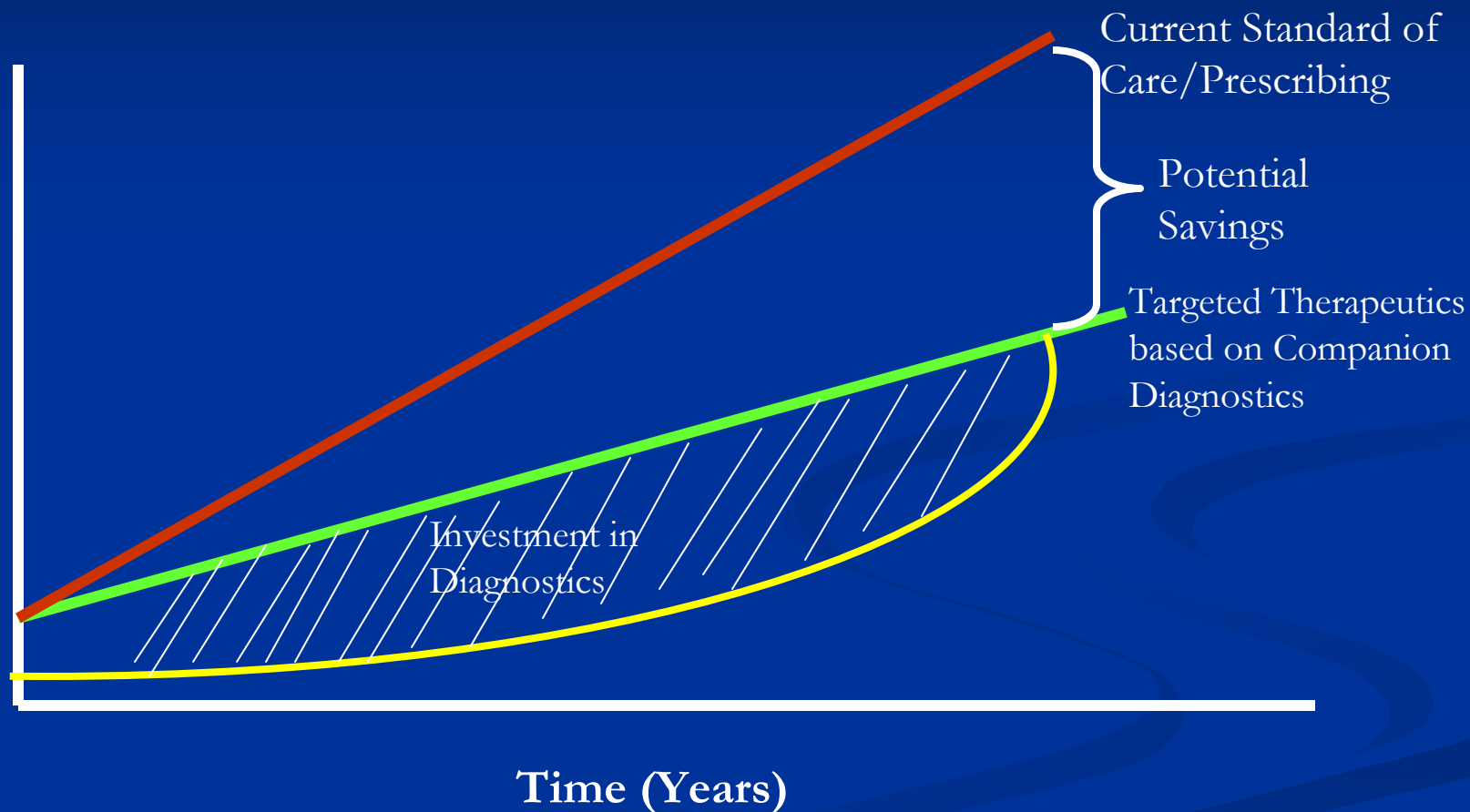
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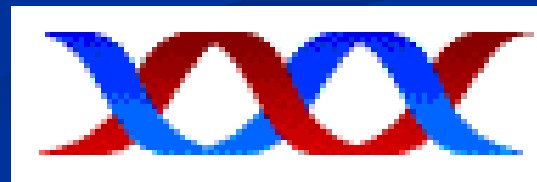
Shifting the Economic Paradigm

Health care
Expenditures
(\$)



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Measuring Value in Health Care: Economic Perspectives

- **Cost of Illness (COI)**
 - Measures economic burden of disorders
 - Can be used to calculate potential benefits of prevention
- **Cost Benefit Analysis (CBA)**
 - Health outcomes converted to currency (e.g. dollars)
 - Value of a “statistical life”
 - Productivity gains
 - Willingness-to-pay
 - Net benefit or benefit-cost ratio
- **Cost Effectiveness Analysis (CEA)**
 - Costs and effectiveness of alternatives compared using ratio of incremental costs to incremental effect.
- **Cost Minimization Analysis**
 - Outcomes of two or more comparators assumed equal
 - Assessment based solely on comparative costs
- **Cost-Utility (CU)**
 - Health outcomes expressed in life years or quality adjusted life years (QALYs), disability adjusted life years (DALYs), or health year equivalents (HYEs)
 - Cost per unit of outcome ratios can be derived that depict costs required to obtain one QALY

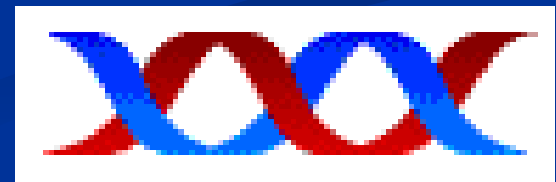


Measuring Value of Combined Genomic Diagnostics and Targeted Therapeutics: Economic Perspective

- **Cost Benefit Analysis (CBA)**
 - ❖ Measures Economic Outcomes
- **Cost-Effectiveness Analysis (CEA)**
 - ❖ Clinical outcomes
- **Cost-Utility**
 - ❖ Quality-adjusted life years (QALYs)

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Measuring Value of Combined Genomic Diagnostics and Targeted Therapeutics: Clinical Value Perspective

Assumptions:

- ❖ Clinical value of diagnostics depends on information leading to improved patient outcomes.
- ❖ The purpose of health care is to deliver value to patients.

Value: Patient outcomes per dollar spent



Measuring Value of Combined Genomic Diagnostics and Targeted Therapeutics: Epidemiologic/Clinical Value Perspective

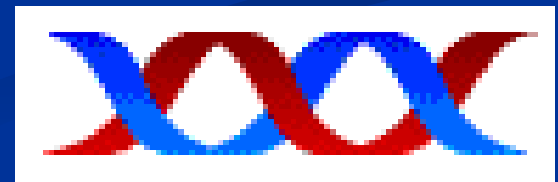
Important Features of a Diagnostic for Determining Value

The Diagnostic has to be:

- **Safer**
- **Cheaper**
- **More Specific** – capable of appropriately excluding more cases of non-response; Avoid unnecessary treatment
- **More Sensitive** – detects more cases of responders; Increase access to appropriate treatment

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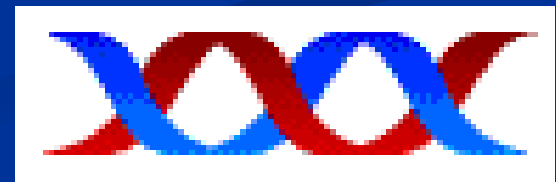


Some Principles for Delivering Value-Based Personalized Medicine

- Improvements in quality (in this case use of combined genomic diagnostics – targeted therapeutics) can lead to cost containment and reduction in healthcare expenditures
- Early detection and right diagnosis
- Delivery of right treatment to the right patient at the right time
- Less delays in delivery of care
- Slowing disease progression
- Reductions in adverse drug reactions

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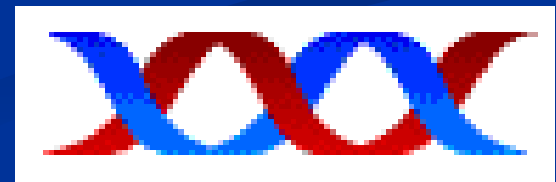


Policy Considerations: Barriers to Implementation of Combined Diagnostics - Drugs

- Uncertain clinical utility
- Lack of outcomes data
- Lack of integrated approach for improved detection, diagnosis and patient risk profiling
- Role of FDA in facilitating innovation/drug development
- Role of third party payers

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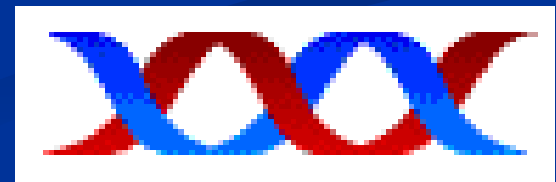


Reimbursement for Diagnostics

- Gaps in linking reimbursement to value
- Inadequate US Medicare coding and payment processes
- CPT codes out-dated & inadequate for diagnostics
- Need for third party payer involvement

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Policy Considerations: Drivers for the Implementation of Combined Diagnostics - Drugs

■ Efficacy/Value

- ❖ Current state of non-responsiveness of majority of drugs
- ❖ High costs

■ Safety

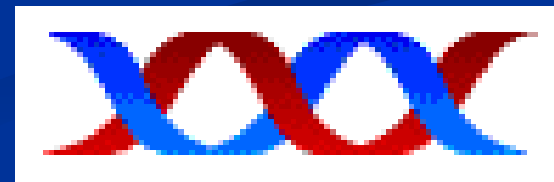
- ❖ Current concerns regarding ADRs
- ❖ Potential for preclinical toxicogenomics
- ❖ Potential for use in post-marketing pharmacovigilance

■ Policy

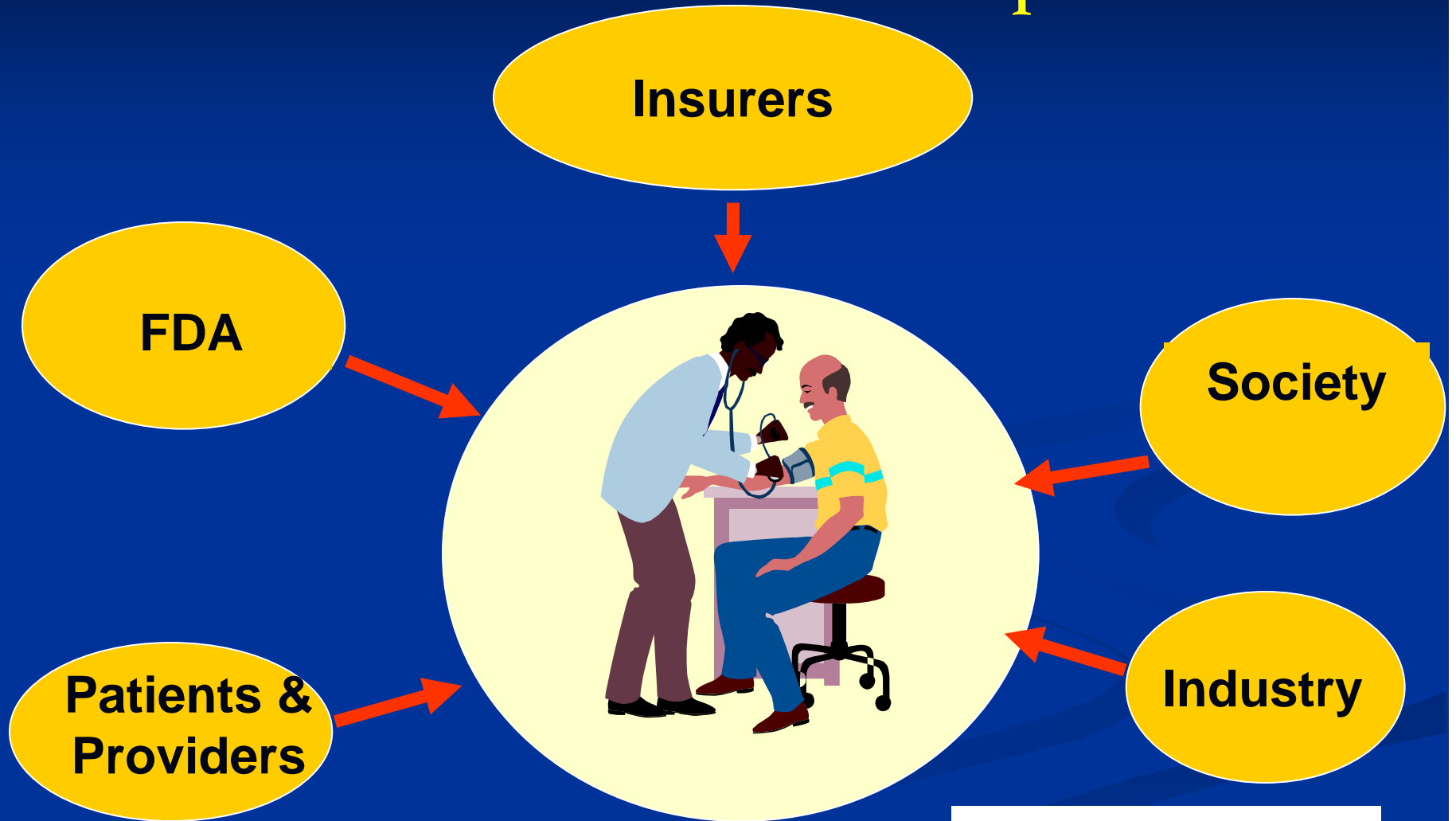
- ❖ Role of CMS
- ❖ Role of FDA
- ❖ Public expectations

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Challenges to Implementing Personalized Medicine: Stakeholder Perspectives



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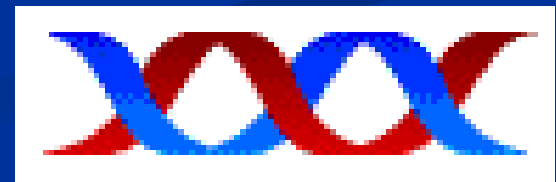


Challenges to Integration of Genomic Diagnostic-Targeted Therapeutic Combinations into Clinical Practice

- More widespread availability of diagnostic tests
 - Turn-around time, IP issues, FDA approval
- Evidence of clinical utility and cost-effectiveness
 - Threshold for PPV/NPV compared to cost of disease/AEs
- Interpretation of results by healthcare providers
 - Clinical judgment necessary; need for education
- Reimbursement by CMS, Blues, HMOs...
 - Affordability limits impact on health of segments of population

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How We Can Succeed in Moving Personalized Medicine Forward into Routine Clinical Practice & Consistent Healthcare Delivery



“Skate to where the puck is going, not to where it is.”

~Wayne Gretzky

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