

GenePOPS – Genetics and Public Policy Center

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# Pharmacogenetics: Is this Drug for you? Improving Patient Outcomes

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- Good News

- We understand disease and can subtype in most areas better than ever before
- We have more targeted drugs available than ever before
- We can tailor therapies for more people and more effectively than ever before
- Patients and physicians are more educated than ever before
- Diagnostic technology can detect more abnormalities earlier and more precisely than ever before

- Bad News

- Drug adverse reactions remain a major challenge for individual patients and health care system
- Drug compliance rates remain low
- Effective treatments not available for every subtype or disease
- New tools and drugs not being used consistently
- More education is necessary for health care providers and patients

- Traditional medical treatment has been empirical
  - Observation, action, and observed response
  - Repeated cycles as needed



*Trial and Error Medicine*

- In the past – best and only option available
- Today - Combination of clinical evaluation and quantitative testing successful – especially when it improves standard of care
- But fails when we settle for Trial and Error Medicine as the only option

# Improvements needed to improve drug efficacy



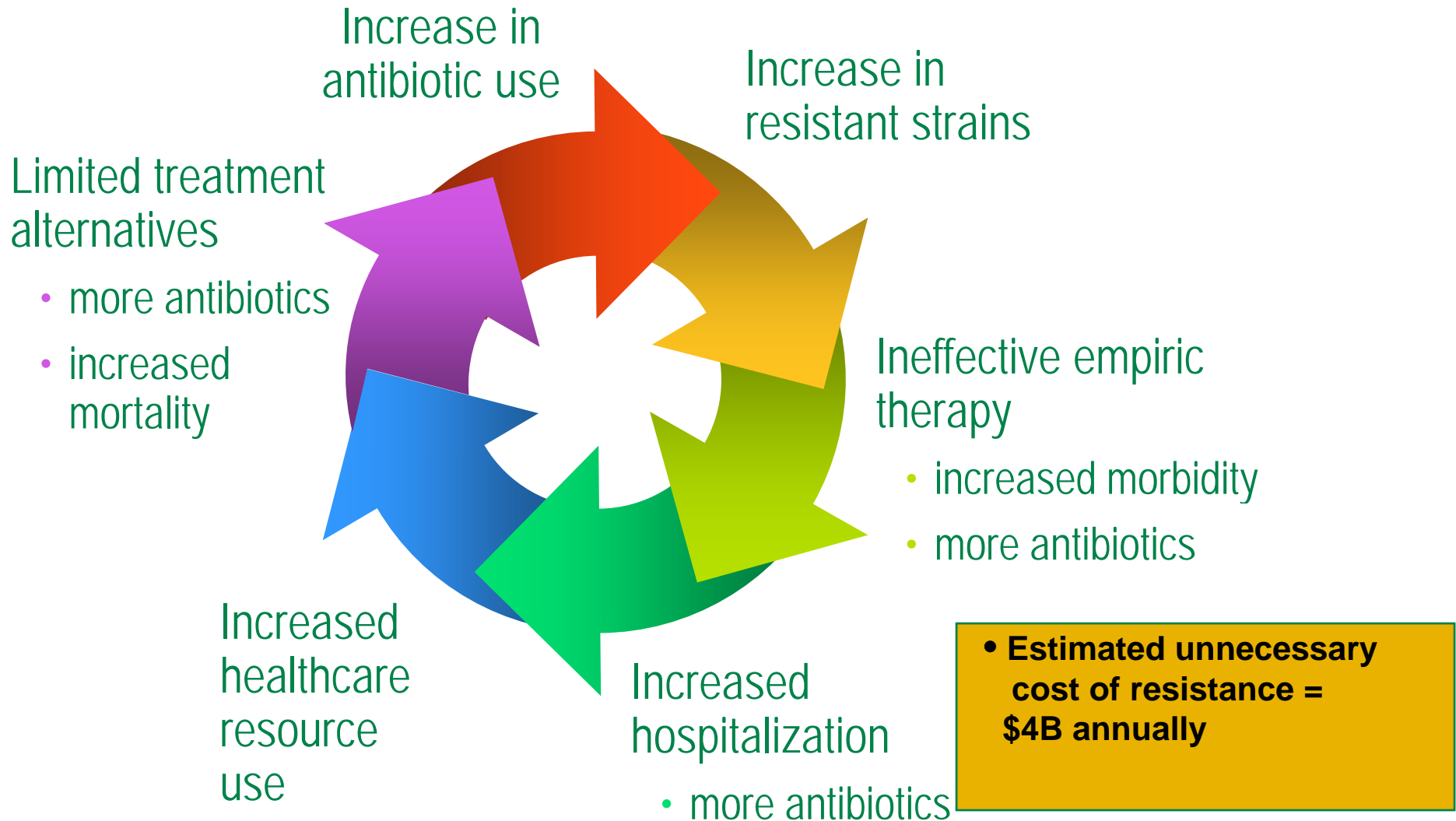
| Drug Class                                     | Frequency of Absent or Incomplete Efficacy (%) <sup>1</sup> | Total Market Size           | Cost to the Health Care System of Ineffective Therapy |
|--|---|-----------------------------|---|
| Angiotensin-converting enzyme (ACE) inhibitors | 10-30   | \$3.9B <sup>2</sup> (2003)  | \$390M-\$1.2B   |
| Beta blockers                                  | 15-25   | \$ 2.3B <sup>2</sup> (2003) | \$345M-575M   |
| Anti-depressants                               | 20-50   | \$11.7B <sup>3</sup> (2003) | \$2.3B-\$5.8B   |
| Statins  | 30-70   | \$12.6B <sup>4</sup> (2004) | \$3.8B-\$8.8B   |
| Beta agonists                                  | 40-70   | \$1.4B <sup>5</sup> (2004)  | \$560M-\$1B   |
| Oncology drugs                                 | 50-75   | \$22.8B                     | \$17.1B   |

<sup>1</sup> Ross JS & Ginsburg GS, *Am J Clin Pathol* 2003;119:26-36    <sup>2</sup> Datamonitor, August 1, 2005

<sup>3</sup> Global Industry Analysts, October 10, 2004    <sup>4</sup> Carnegie Research    <sup>5</sup> Specialty Pharmaceutical Pulse, SG Cowen, October 2005

# Wheel of Misfortune: Personalized medicine is not just for cancer

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# Time is of the essence

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| <b>Disease</b>                          | <b>1 Year Survival</b> | <b>5 Year Survival</b> |
|---|------------------------|------------------------|
| Lung cancer (small cell-non small cell) | 36-41%                 | 6-13%                  |
| Colorectal cancer                       | 60%                    | 39%                    |
| Chronic myeloid leukemia (CML)          | 73%                    | 37%                    |
| Heart failure (male-female)             | 76-72%                 | 41-55%                 |
| End stage renal disease                 | 78%                    | 38%                    |

<sup>1</sup>2005 USRDS Annual Data Report

<sup>2</sup>Levy, et. al., Long-term trends in the incidence and survival from heart failure, NEJM, 2002; 347(18):1397-402

<sup>3</sup>Cancer Perspectives U.S., 2004 Fourth Edition, DaVinci Healthcare Partners; NCI SEER data, average across all stages at Dx

- New “Traditional” medicine – Personalized
  - Observation, *test*, action, and *predictable* response
  - Repetition may not be needed



*Improved drug usage and targeted treatment*

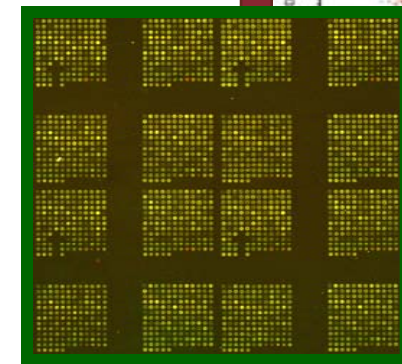
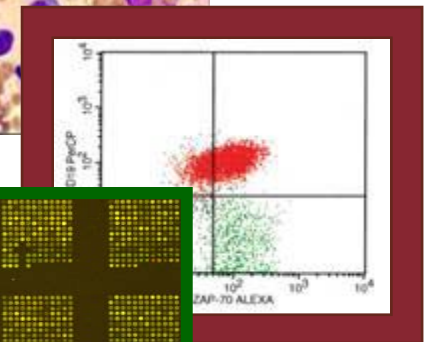
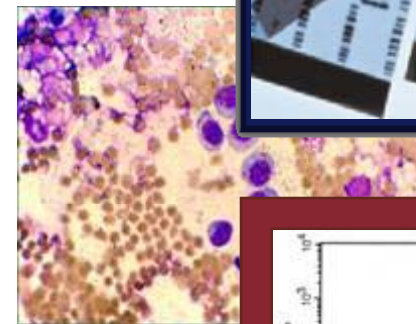
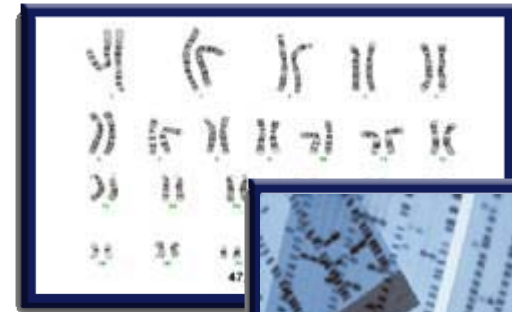
- Answers the question – Is this drug for you?
  - Combination of testing with treatment
  - It has evolved from hype, through controversy to growing acceptance



# Improvement in Testing allows Better Treatment Today & Tomorrow

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- **Past Practice – Macro Level Diagnostic Testing**
  - Disease defined by location and size
  - Tests differentiated disease from non-disease
- **Today – Micro Level Diagnostic and Prognostic Testing**
  - Disease defined by individual biology/DNA
  - Tests to subcategorize disease and:
    - predict outcomes of specific Rx
    - screen for adverse events
    - monitors disease
- **Emerging Tomorrow - Predictive Testing**
  - Add predictive testing for development of common diseases



The logo for Genzyme, featuring the word "genzyme" in a lowercase, white, sans-serif font. The logo is positioned in the upper right corner of a decorative header bar. The header bar has a dark grey top edge, a blue-to-green gradient background, and a light green bottom edge.

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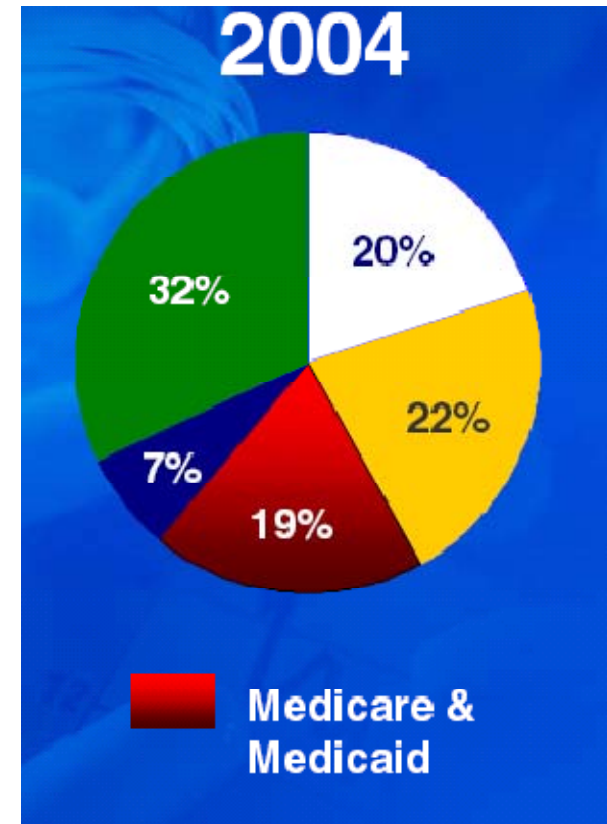
# The Honeymoon: High Expectations



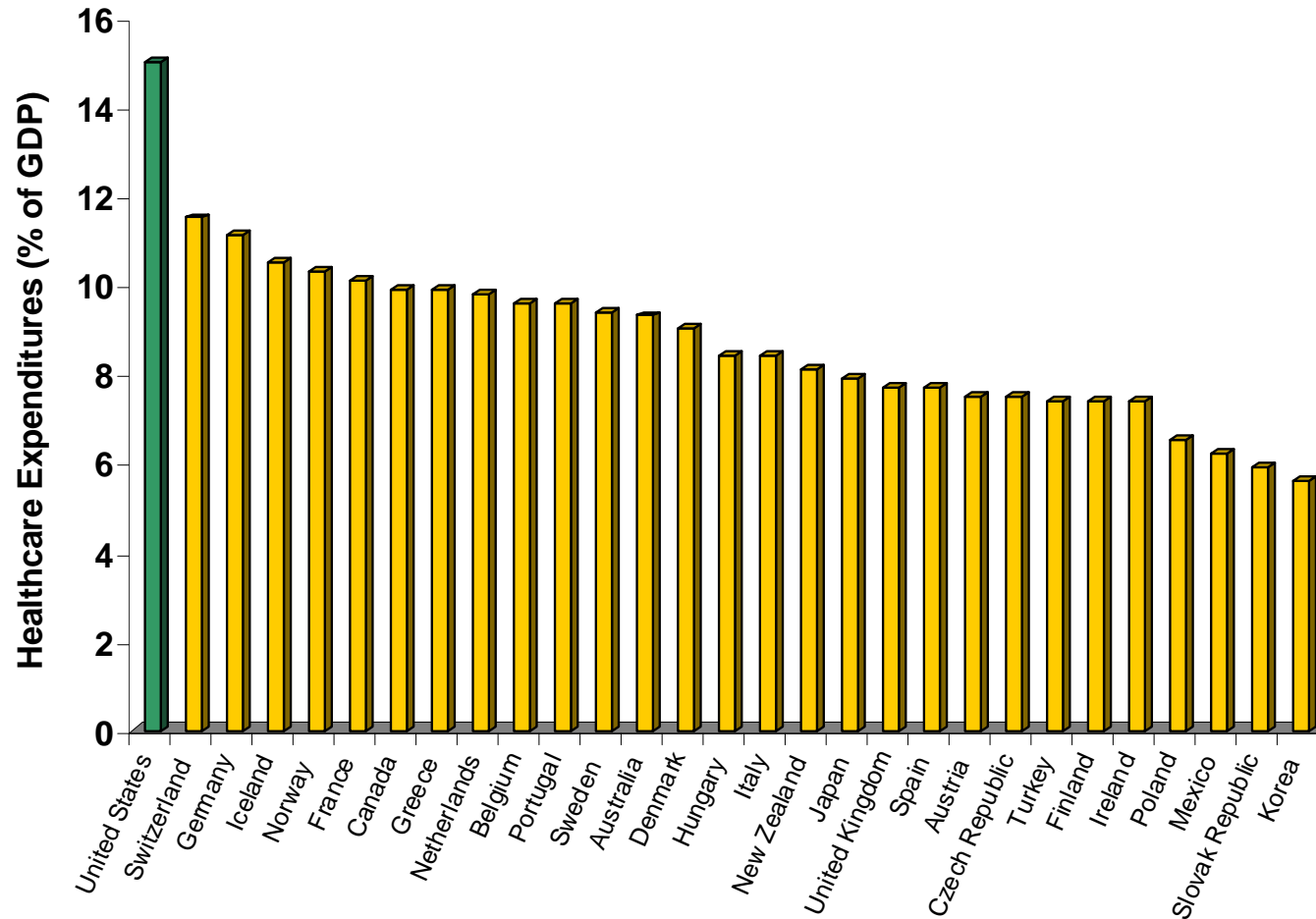
- "We expect that pharmacogenomics is going to **revolutionize** the way medicines are developed and prescribed...Bristol-Myers Squibb is committed to applying pharmacogenomics to new medicines and existing therapies **across our pipeline in every therapeutic area.**"  
*BMS (on deal with Millennium Predictive Medicine) 1999*
- "Novel drugs targeted to specific, common genetic variants will offer **unprecedented efficacy and safety** for the therapy of cancer and other important disorders."  
*Variagenics, 1998*
- "Medicine is going to change from a treatment-based to a prevention-based discipline."  
*Human Genome Sciences, pre-2000*

# Spending more and testing less

- Medicare & Medicaid represents 19% of the 2004 Federal Budget
- Continued growth expected (from 2005-2015)
  - Medicare = 9%
  - Medicaid = 8%
- Laboratory spending fell (Medicare Part B)
  - 40% reduction in real terms from 1984 to 2004



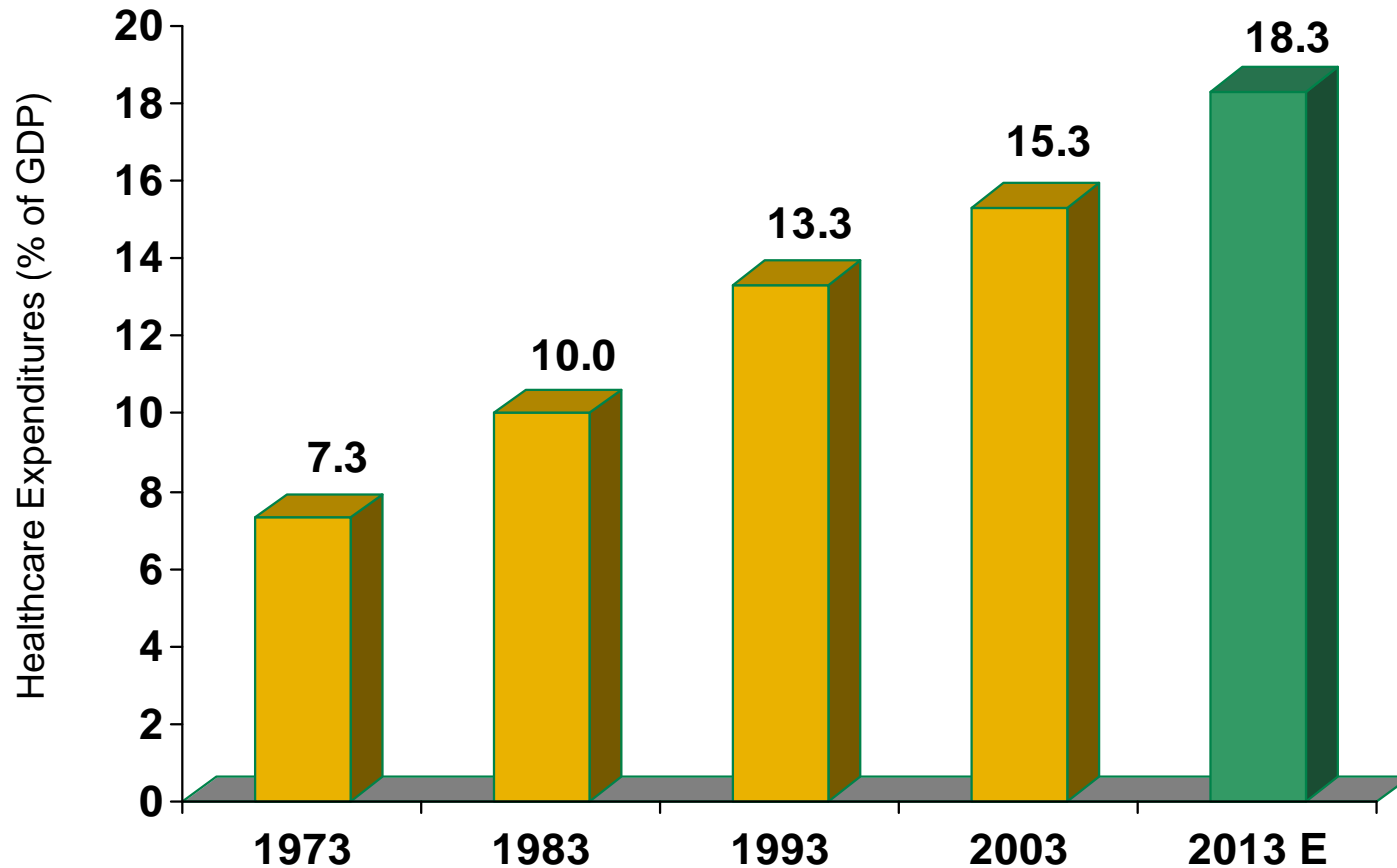
# The U.S. leads the world in total healthcare spending



Source: Organization for Economic Cooperation and Development Health Data, October 2005

# Health expenditures will continue to absorb an increasing share of GDP and the Federal Budget

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Source: The Centers for Medicare & Medicaid Services, Office of the Actuary

Source: Unsustainable Trends Necessitate Reforms to Control Spending and Improve Value, Health Care Working Group, July 22, 2005

# Society can't afford low efficacy

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# Industry missing benefits with status quo genzyme

- Pharmaceutical Industry
  - Reduce Clinical Trial costs
  - Reduce adverse events
  - Demonstrate real value for drug
  - Achieve sustainable commercial advantage
  - *Challenge - focus on markers early*
    - *Need to involve diagnostics expertise in pre-clinical, if possible, but certainly before Phase II*
- Payor Industry
  - Improve patient care and reduce costs
    - Eliminate ineffective treatment costs by appropriately using diagnostics to ensure right patient at the right time

# Impact of Diagnostic Tests



## Contribution of Selected Diagnostic Tests to Avoidable Adverse Events, Deaths and Costs

| Disease/<br>Condition | Diagnostic<br>Test      | Use   | Annual Avoidable<br>Events   | Annual Avoidable<br>Deaths | Avoidable<br>Costs |
|-----------------------|-------------------------|---|--|----------------------------|--------------------|
| Diabetes              | HbA1c level             | Manage glucose levels                         | 14,000 heart attacks, strokes, or amputations                        | 4,300-9,600                | \$573 million      |
| Colorectal cancer     | Fecal occult blood test | Rule in risk for cancer                       | 20,000 cases of colorectal cancer diagnosed/treated at a later stage | 4,200-6,300                | \$191 million      |
| Heart disease         | Cholesterol test        | Assess risk for heart disease or heart attack | 14,600 major coronary events   | 6,900-17,000               | \$ 87 million      |

*\*Adapted from: The state of health care quality: industry trends and analysis. Washington, DC: National Committee for Quality Assurance, 2004.*

## ➤ FDA

- ❑ Insist on diagnostic links that decrease side effects and improve efficacy with new therapies

## ➤ Payors

- ❑ Demand diagnostics to manage drug costs and improve patient care
- ❑ CMS approval for targeted drugs depends on efficacy

## ➤ Pharmaceutical Companies

- ❑ Reduce drug failures in late clinical trials (and on the market)
- ❑ Increase efficacy - show real value of drug

## ➤ Patients

- ❑ Improved care – more effective treatments with fewer side effects

## ➤ **Diagnostics – Turn the Hype into Reality**

- ❑ **3% of the costs – 70% of the medical decisions**
- ❑ **Make new drugs work**
  - ❑ More than 50% of cancer drugs in development today are targeted and will need diagnostics to determine use
- ❑ **Save money**
  - ❑ Reduce ineffective use of drugs and treatments
- ❑ **Save lives**
  - ❑ Give physicians information to better use options available
- ❑ **Deliver on the promise**
  - ❑ The right drug to the right patient at the right time

# The Golden Years: Acceptance As Is



Though the early hype over-stated the impact...

| <b>Hype</b>  | <b>Reality</b>   |
|--|--|
| Complete Responses   | Improved probability of response   |
| Certainty of Safety  | Lower likelihood of severe side effects  |
| Effects every therapeutic area                                   | Starting in cancer and growing;<br>metabolism of blockbuster drugs                               |
| Precludes need to treat disease; new focus on preventing disease | Still treating disease, but choosing The Right Treatment for the Right Patient at the Right Time |

**...Personalized Medicine provides real value TODAY**

- **to patients**
- **to physicians**
- **to bio/pharma companies**
- **to the overall healthcare system**

# Personalized Medicine Gaining Momentum Facts and Figures

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