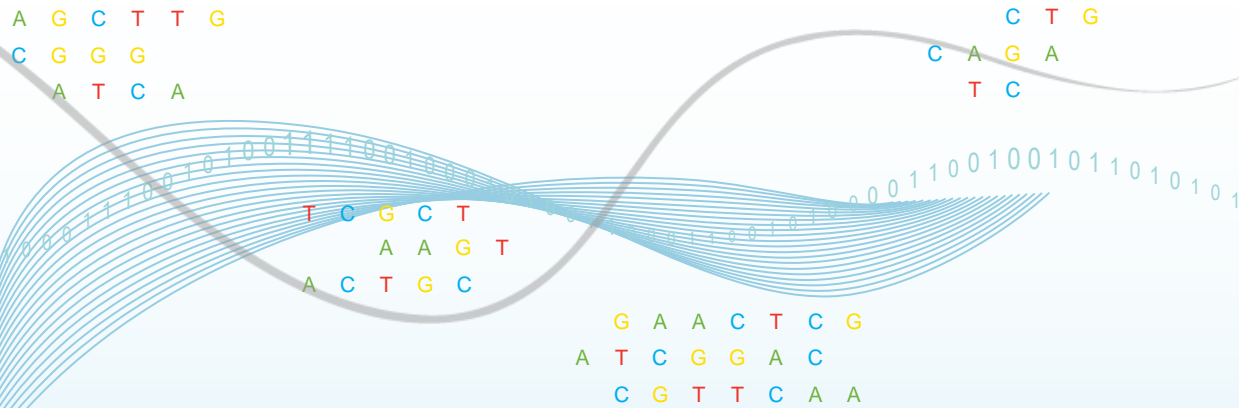


Biomarkers as Tools for Clinical Development: Expectations, Opportunities and Challenges: A Payer Perspective



Robert S. Epstein, MD, MS

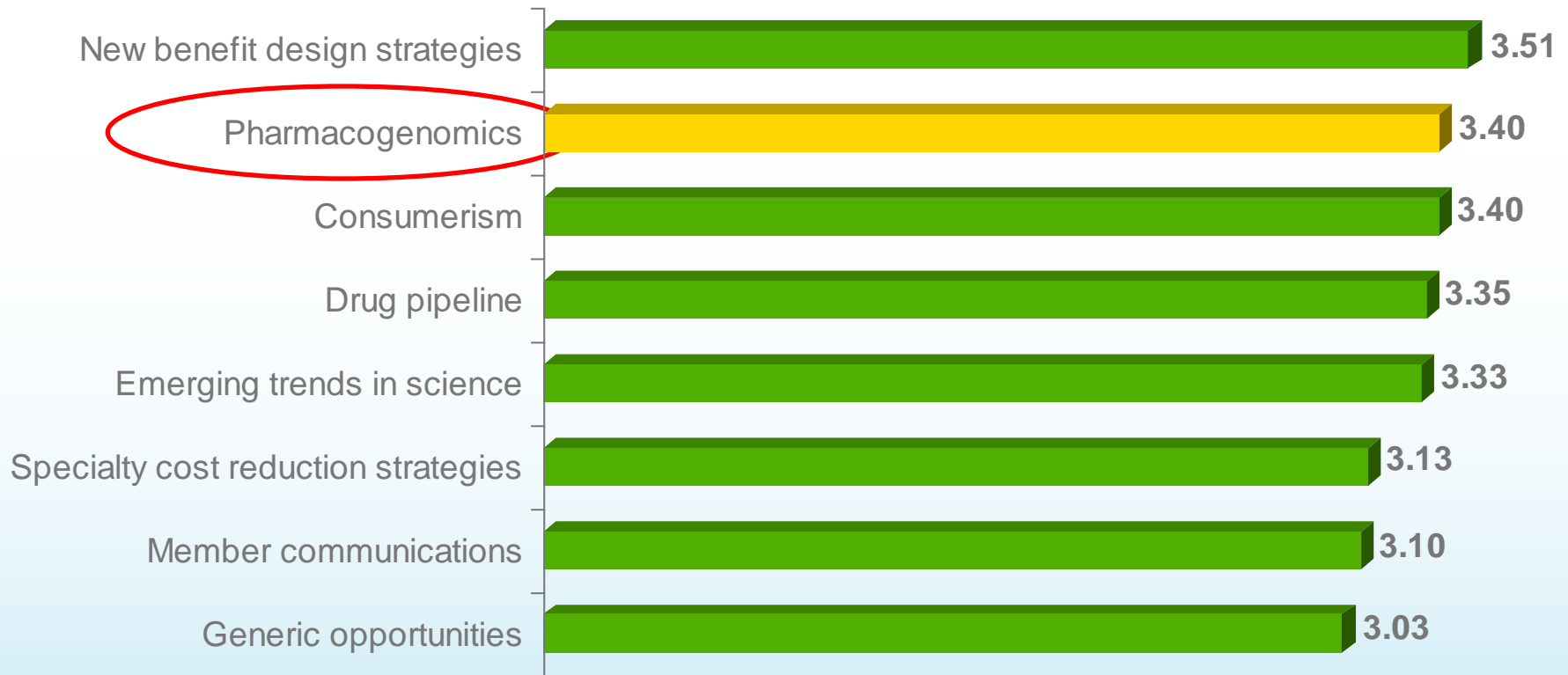
President, Advanced Clinical Science & Research

February 23, 2011

Apologies in advance

- Cover 65+ million US lives
- Payers we serve are diverse (employers, health plans, government entities)
- Perspectives are diverse – no single voice
- So these will be general themes

Payers' View of Pharmacogenetics



Source: Medco Poll of 700 clients, May 2008

Expectations for biomarkers

- Strong clinical and analytic validity
- If teamed with a pharmaceutical agent – something in the FDA approved label indicating its usefulness
- Lack of ambiguity across diagnostic laboratories
- Transparency of data supporting its test characteristics (e.g. negative predictive value)

Opportunities / Challenges

- Specialty society endorsement
- Comparative effectiveness studies (biomarker + intervention vs. usual care)
- Clinical utility studies (ie does the use of the biomarker make 'a difference' with the patient or clinician or both?)
 - > Some require these as RCTs
 - > Others consider 'real world' effectiveness
 - (may need both)

Example 1: Optimizing safety and efficacy

Medco-Mayo Warfarin Outcomes Study

■ *Hypothesis:*

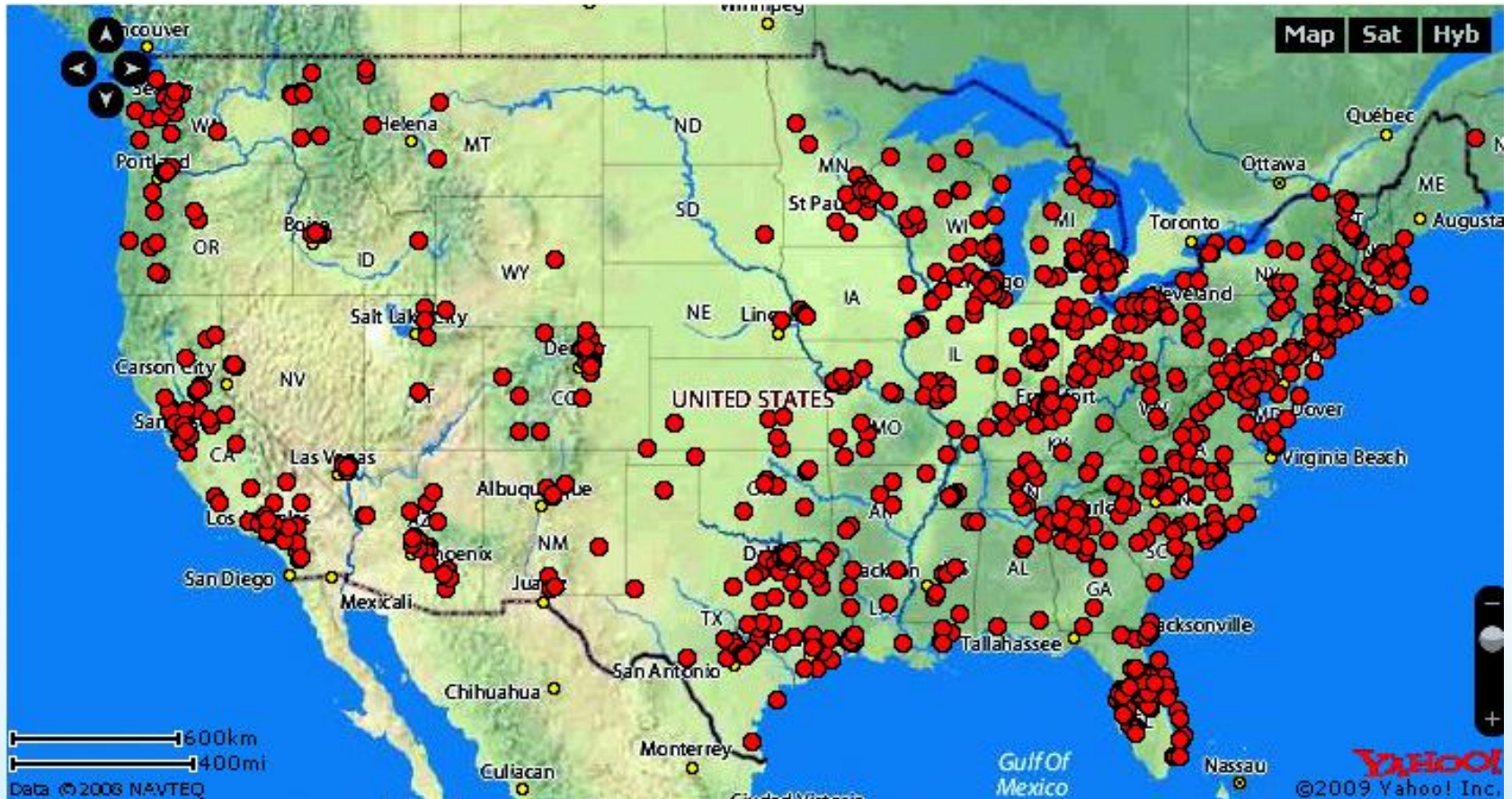
- > The use of CYP2C9/VKORC1 testing will reduce the risk of hospitalization during the first 6 months of warfarin treatment

■ *Design:*

- > Prospective observational cohort study with national community based sampling (quasi-experimental)

Medco-Mayo Warfarin Study

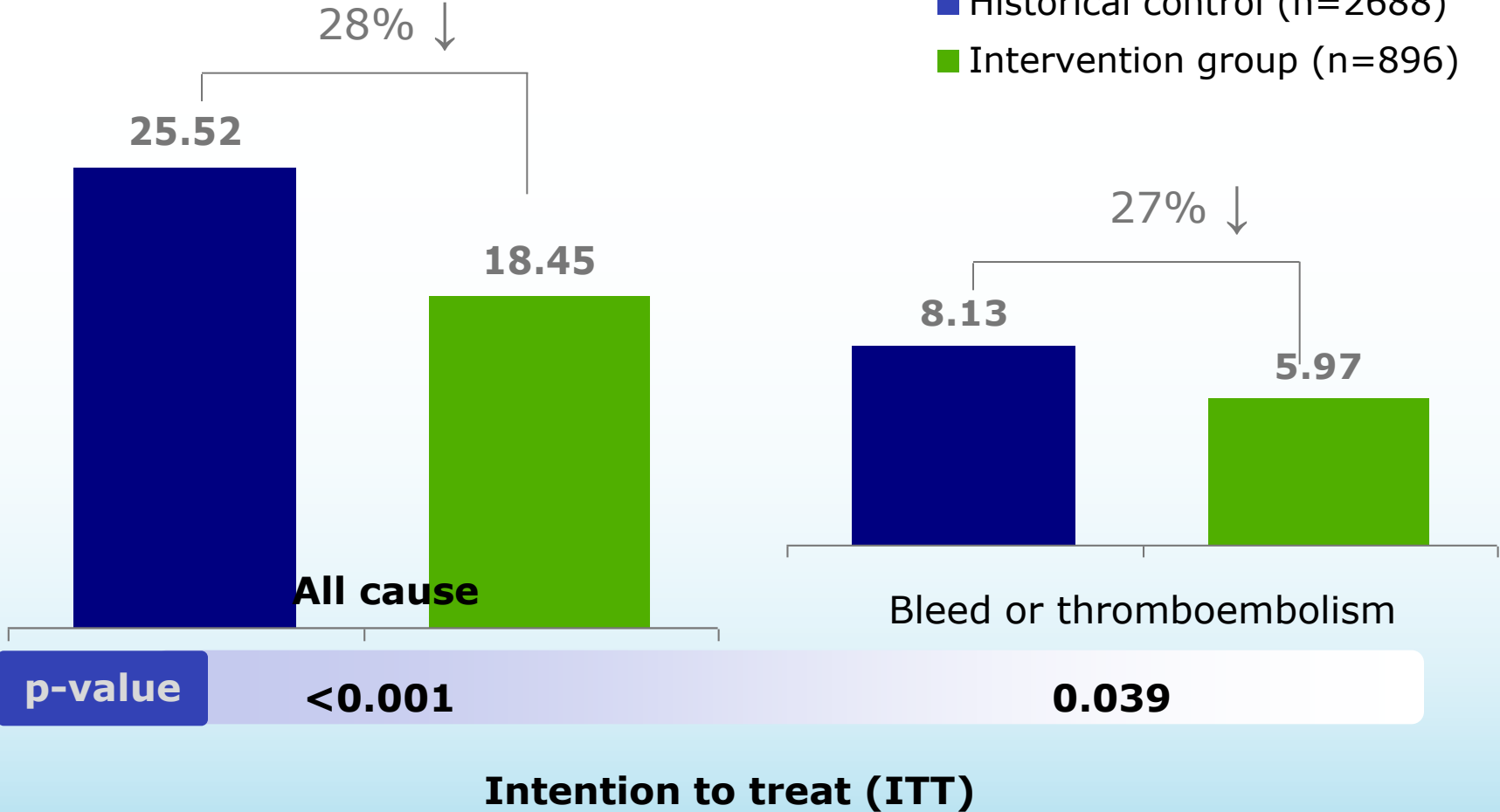
Power of Unselected Real World Enrollment Sites



80% of warfarin scripts not from specialized clinics/academic centers

Results: 6 month hospitalization rates

- Historical control (n=2688)
- Intervention group (n=896)



...what if ...

800,000 patients start new on warfarin per year

65,000 (8%) hospitalized due to bleed or embolism

\$10,000 per hospitalization → \$650 million

30% reduction → savings of \$195 million

\$200 per genotyping test

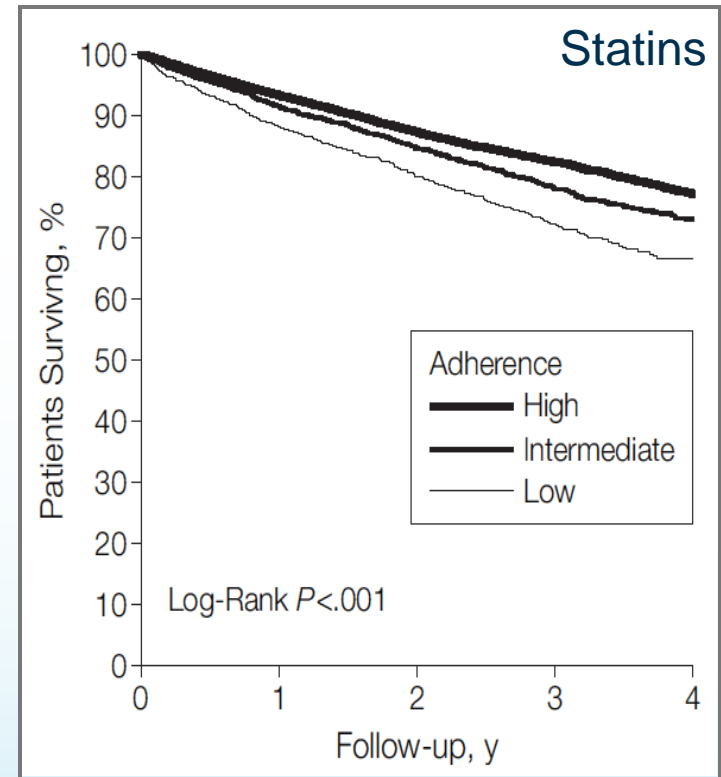
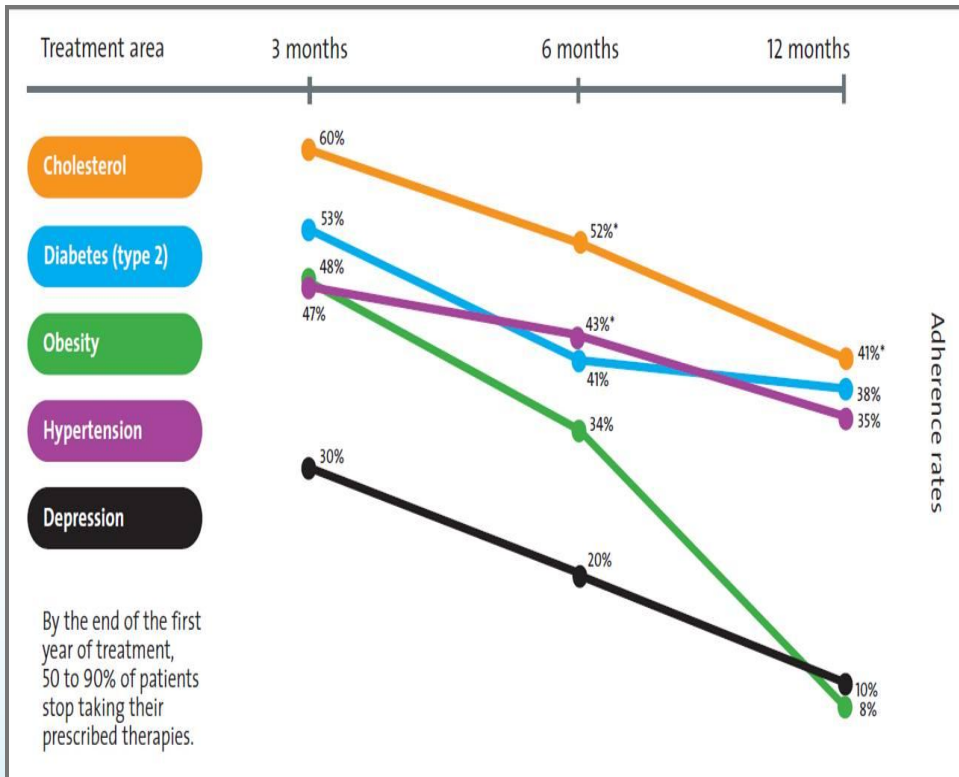
\$160 million for genotyping all new patients

→ cost-effective to neutral

But what about:

- *Patient better served*
- *Indirect costs*
- *All cause hospitalizations*

Example 2: Impacting Adherence



Medco data, various sources

Rasmussen et al. JAMA 297:177-186

Can providing genetic information about disease susceptibility help increase adherence rates?

ORIGINAL ARTICLE

Effect of Direct-to-Consumer Genomewide Profiling to Assess Disease Risk

Cinnamon S. Bloss, Ph.D., Nicholas J. Schork, Ph.D., and Eric J. Topol, M.D.

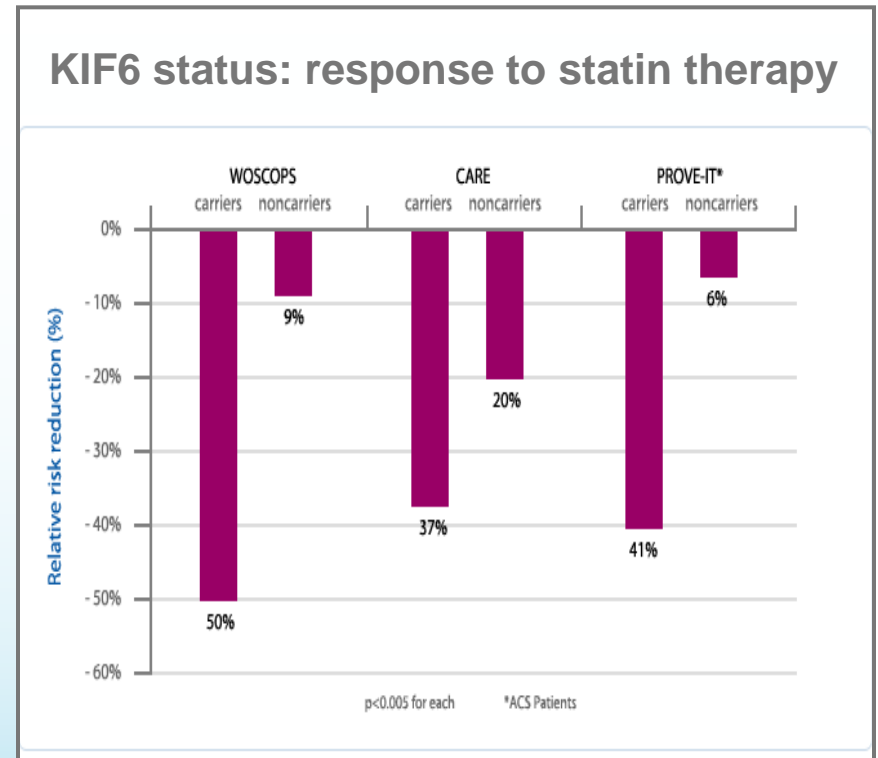
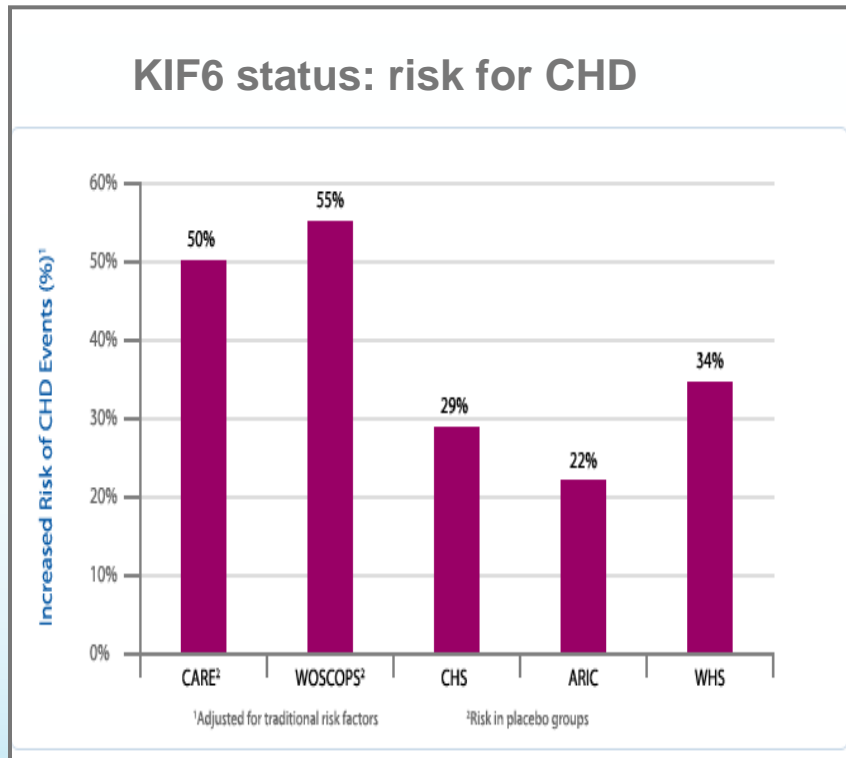
Conclusions

In a selected sample of subjects who completed follow-up after undergoing consumer genomewide testing, such testing did not result in any measurable short-term changes in psychological health, diet or exercise behavior, or use of screening tests.

Potential effects of this type of genetic testing on the population at large are not known.

What if there is a direct connection between the information and the consumer's medical need?

KIF6 is an important enzyme implicated in CHD



Adherence to Statin Therapy

CELERA AND MEDCO ENTER RESEARCH COLLABORATION TO EVALUATE THE EFFECT OF *KIF6* TESTING ON COMPLIANCE WITH STATIN THERAPY IN PATIENTS WITH CARDIOVASCULAR DISEASE

ALAMEDA, CA, and FRANKLIN LAKES, N.J. – Celera Corporation (NASDAQ:CRA) and Medco Health Solutions, Inc. (NYSE:MHF), today announced that they have entered into a research collaboration to evaluate whether testing for a gene variant called *KIF6* increases patient compliance with statin therapy. Current studies have suggested that only about 50% of the patients who receive a prescription for a lipid-lowering drug are on their medication after six months¹. This level of adherence falls to 30 to 40 percent in patients with coronary artery disease².

“A study of this nature has the potential to show that understanding your genetic risk can improve patient compliance,” said Medco Vice President of Personalized Medicine Development Dr. Felix Frueh. “Medco’s research partnership with Celera will provide more evidence that personalized medicine can improve patient compliance.”

Enrollment completed, results Q3 2011

...what if ...

30 million patients take a statin per year

12 month adherence increases from 40 to 45 percent

12 month survival increases 1 percent

\$200 cost for genetic test

\$1,258 savings per adherent patient (incl. pharmacy)

→ 300,000 lives saved at expense of \$13,500 per live

→ OR: 300,000 lives saved and \$1.9 billion saved if
genetic information already available

Concluding thoughts

- Payers overall enthusiasm is high for this field
- Biomarker development strategies should include
 - > Commercial biomarker distribution strategy
 - > Consideration of clinical utility studies
 - > Involvement of payer perspectives earlier than mid-Phase III
 - > Potential health economic evaluations

