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PGx Implementation Research Programs at Vanderbilt

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5/2/17

The vision

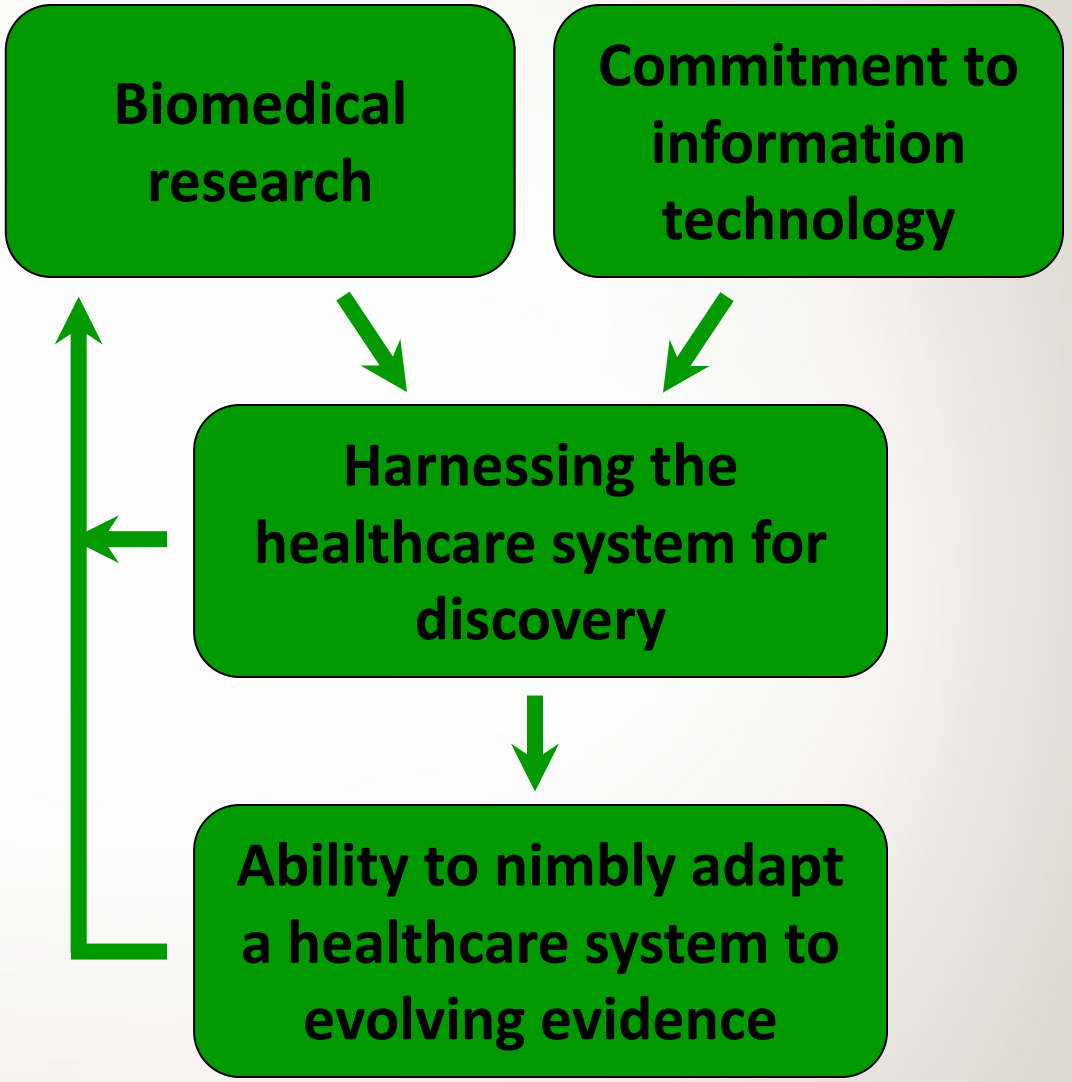
"Here's my sequence..."

New Yorker, 2000

How will this vision actually start to be tested and become reality?

"Here's my sequence..."

New Yorker, 2000



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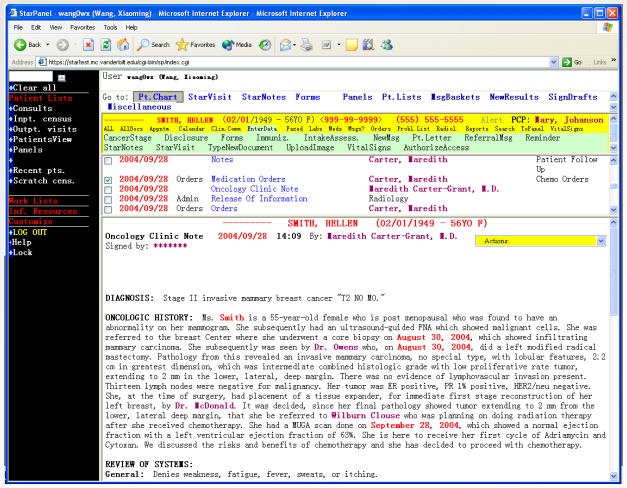

EHR feeds both discovery and implementation

Discovery

Implementation

VanderbiltBioVU

De-identified DNA repository

>235k samples

PREDICT, IGNITE, (eMERGE)

- CLIA genomics lab
- Integrated decision support for genomics
- Genomic databases
- Track outcomes

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Discovery: Resources for EMR-based research at Vanderbilt

The Synthetic Derivative

A de-identified and continuously-updated image of the EMR: ~2.5 million subjects

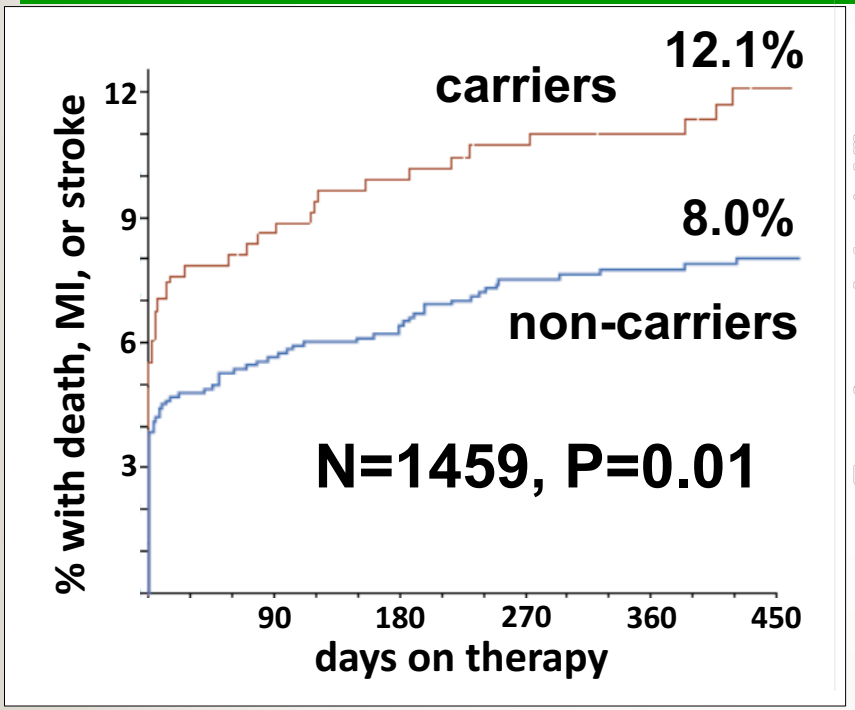
BioVU

Subjects with DNA: ~235k

EHRs for drug response:

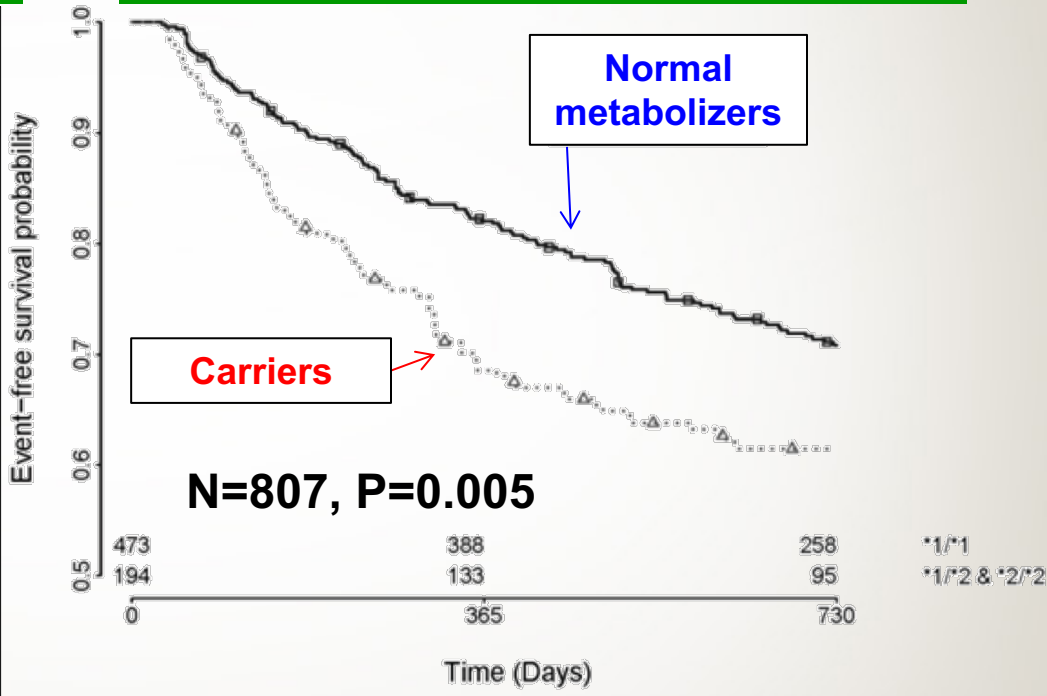
Clopidogrel adverse events associated with *CYP2C19* status

From clinical trials



Mega et al., 2009

From the EHR



Delaney et al. *Clin Pharm Ther.* 2012

How do we routinize PGx implementation?

PREDICT: Pharmacogenomic Resource for Enhanced Decisions In Care and Treatment

"Here's my sequence..."

New Yorker, 2000

...the right drug, the first time.

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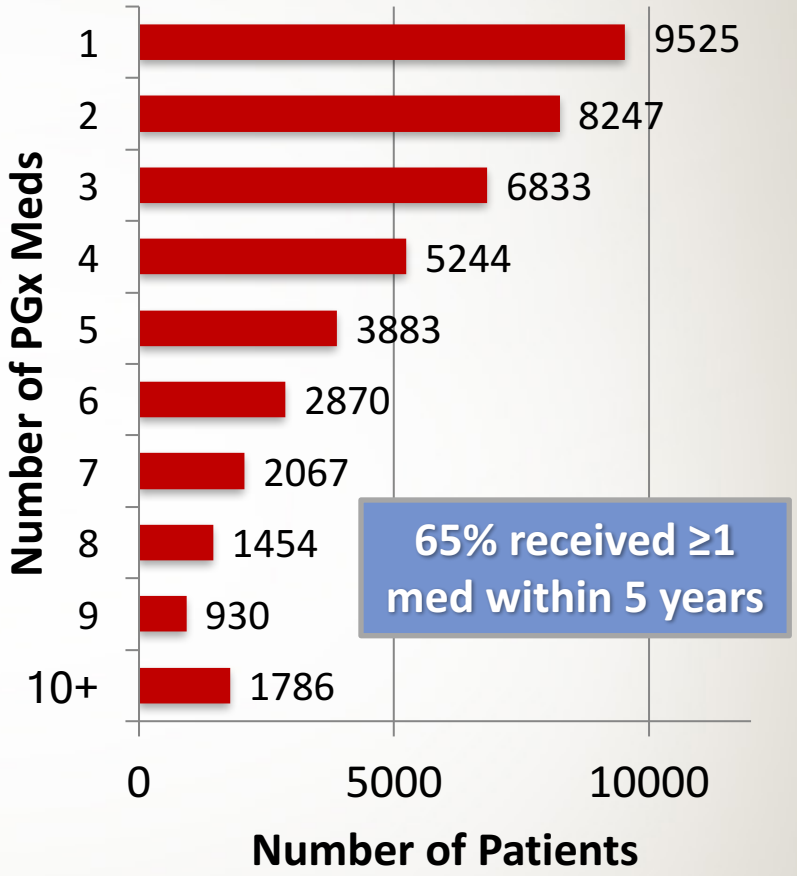
A Case for Prospective Genotyping:

identifying a high risk group

52,942 Vanderbilt "Medical Home" patients followed for up to 5 years….

How many patients received drug(s) that have a recognized pharmacogenetic story?



Estimated number of severe adverse events mitigated : 383
(~12-18 events for the average PCP over 5 years)

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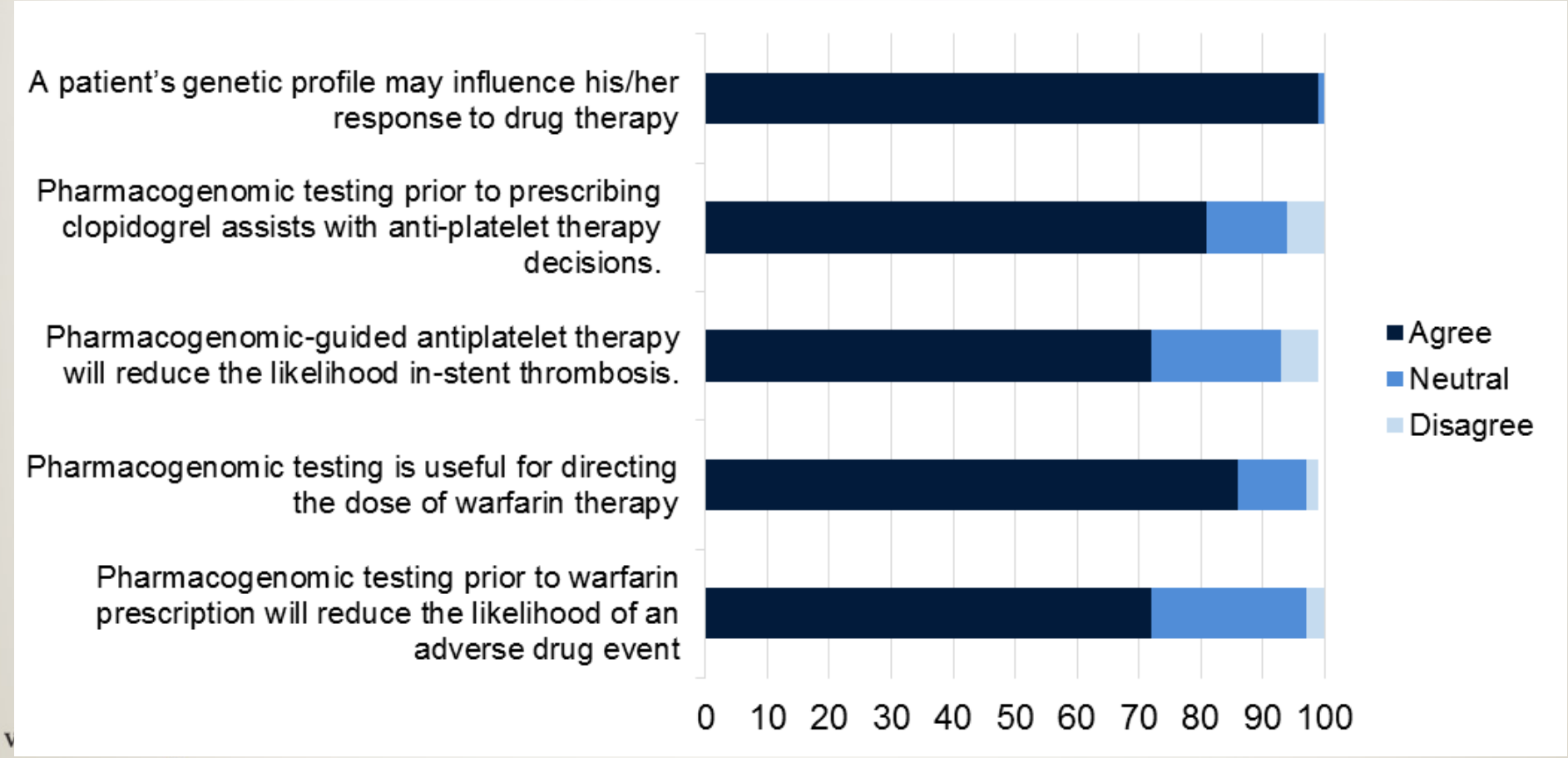
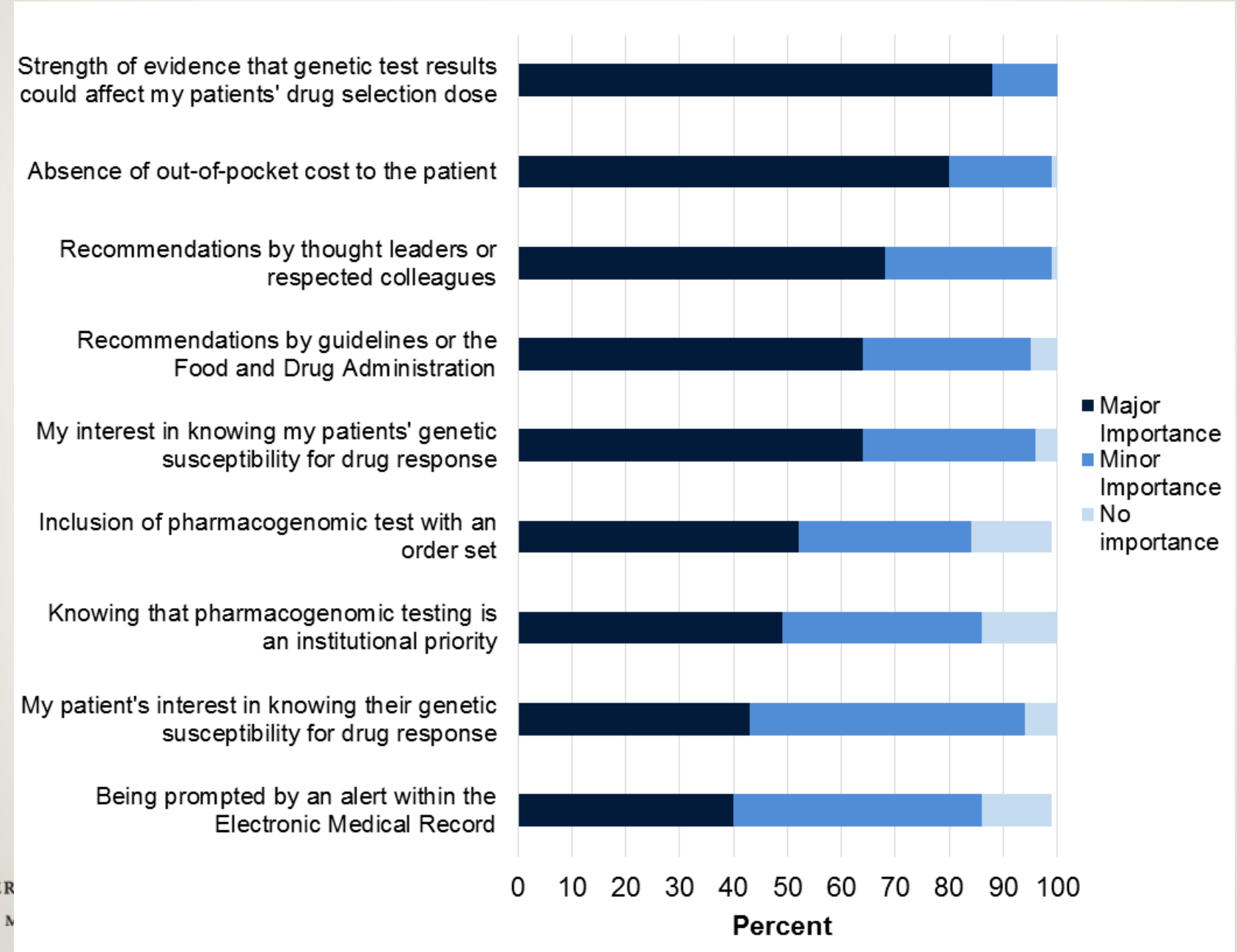
Schildcrout et al, CPT 2012

Provider Opinions

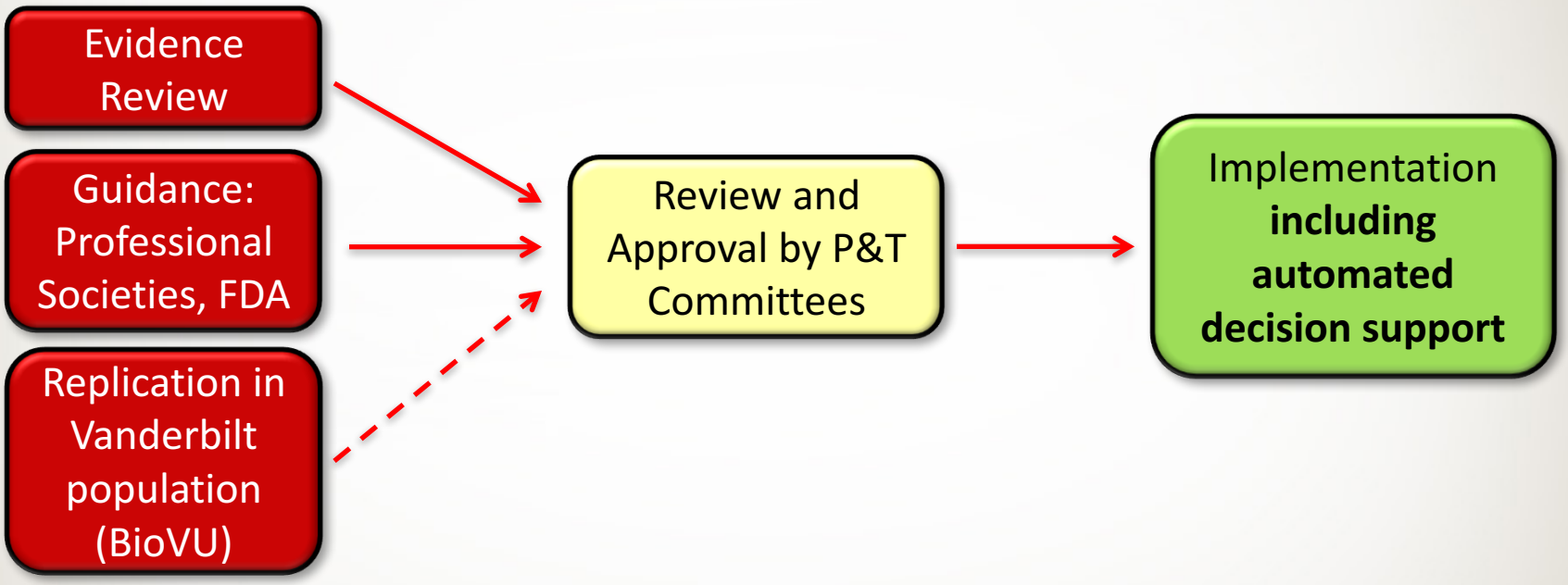
Surveyed 121 VU providers encountering PGx prescribing; 80 responded (66% response rate)



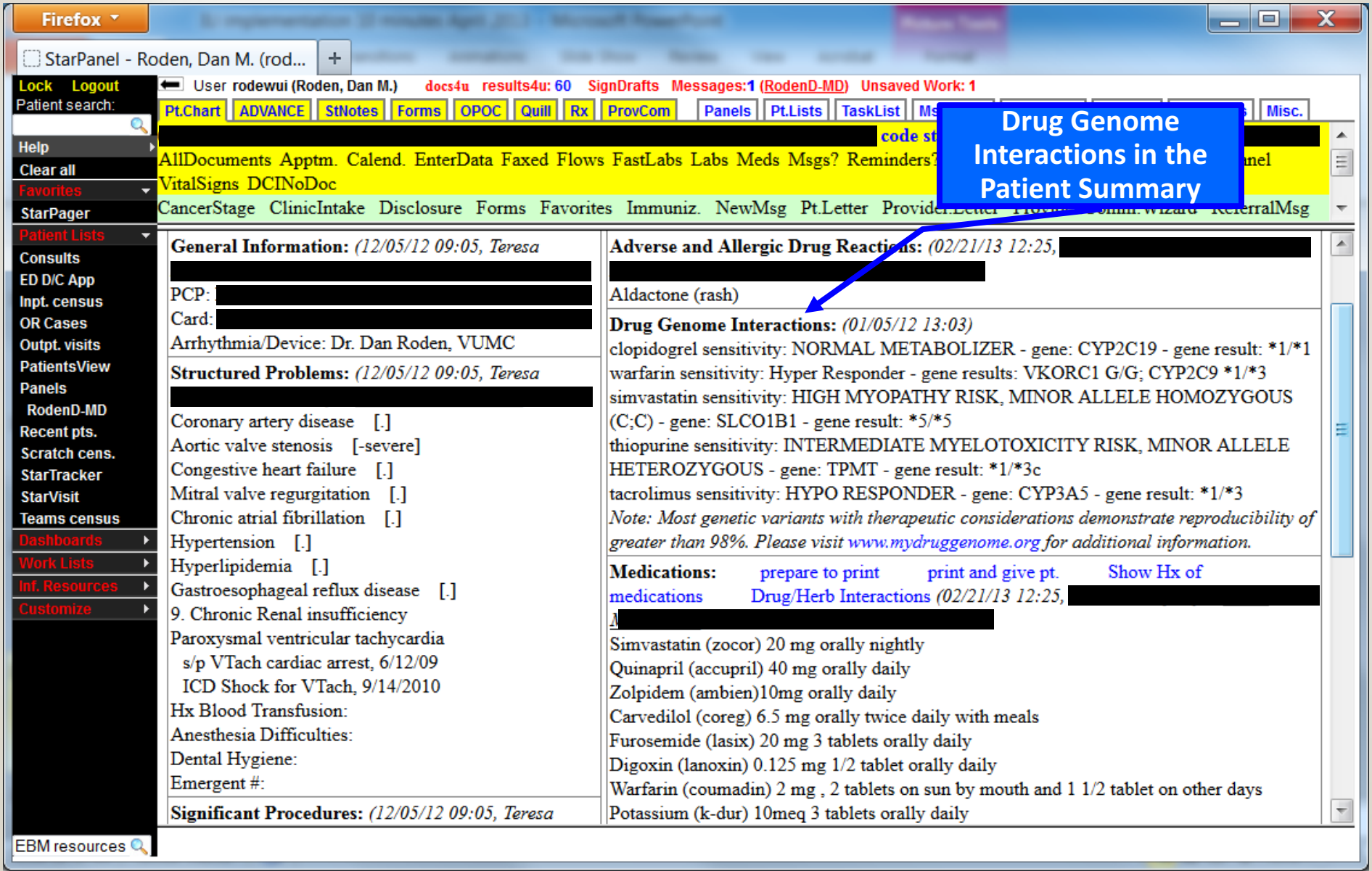
Factors influencing ordering of PGx tests



Selection of PREDICT Drug-Gene Interactions



Genetic results visible passively in EHR



Clinical Decision Support within E-Prescribing

Drug-Genome Advisor

Intermediate Metabolizer - clopidogrel (Plavix) - Rare Risk Allele

Substitution recommended due to increased cardiovascular risks

If not otherwise contraindicated:

- ☐ Prescribe prasugrel (Effient) 10 mg daily

  Prasugrel should not be given to patients:

  - history of stroke or transient ischemic attack
  - >= 75 years of age [Current patient age: 51]
  - with body weight < 60 kg [Current patient weight: 59.0 kg as of 10/12/2012]

- ☐ Prescribe ticagrelor (Brilinta) 90 mg twice daily

  Ticagrelor should not be given to patients:

  - history of severe hepatic impairment
  - intracranial bleed

- ☑ Continue with clopidogrel (Plavix) prescription

  Primary override reason:

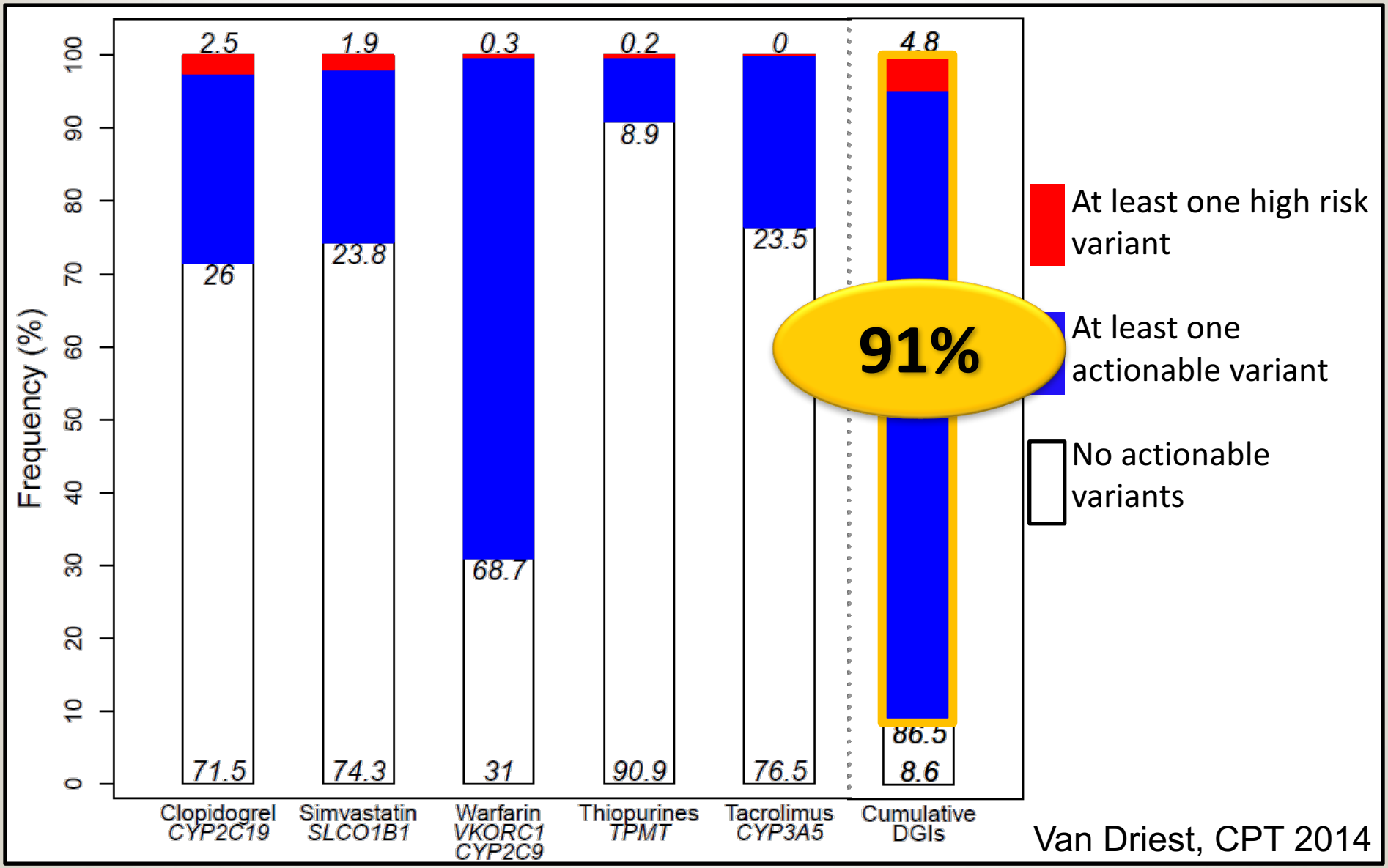
  - ☐ Contraindicated for prasugrel or ticagrelor
  - ☐ Potential side effects
  - ☐ Provider/Patient opts for clopidogrel
  - ☐ Cost

Evidence Link

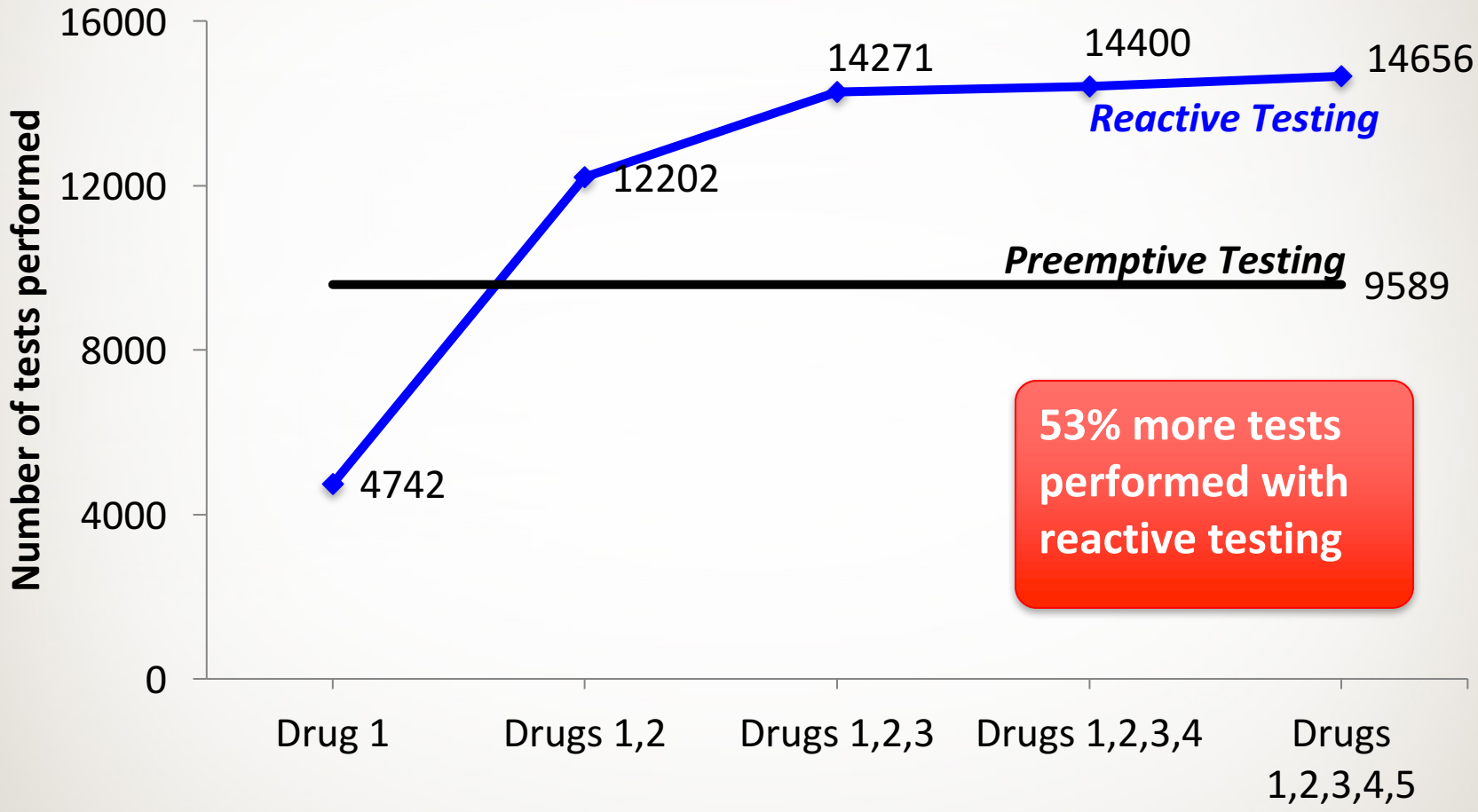
This patient has been tested for CYP2C19 variants which has identified the presence of one copy of a rare risk allele which is associated with intermediate metabolism of clopidogrel. Intermediate metabolizers treated with clopidogrel at normal doses are associated with higher rates of stent thrombosis and other cardiovascular events. The Vanderbilt P&T Committee recommends that prasugrel or ticagelor replace clopidogrel for poor metabolizers unless contraindicated. If not feasible, maintain standard dose of clopidogrel. The guidelines above were developed based on the outcome studies of patients who received a drug-eluting stent into a coronary artery. However, there is not a national consensus on drug/dose guidance particularly associated with the population possessing extremely rare genetic variants.

Continue Cancel

Frequency of actionable genotypes in the first 10,000 PREDICT patients



Multiplexed Genetics Testing can save money too



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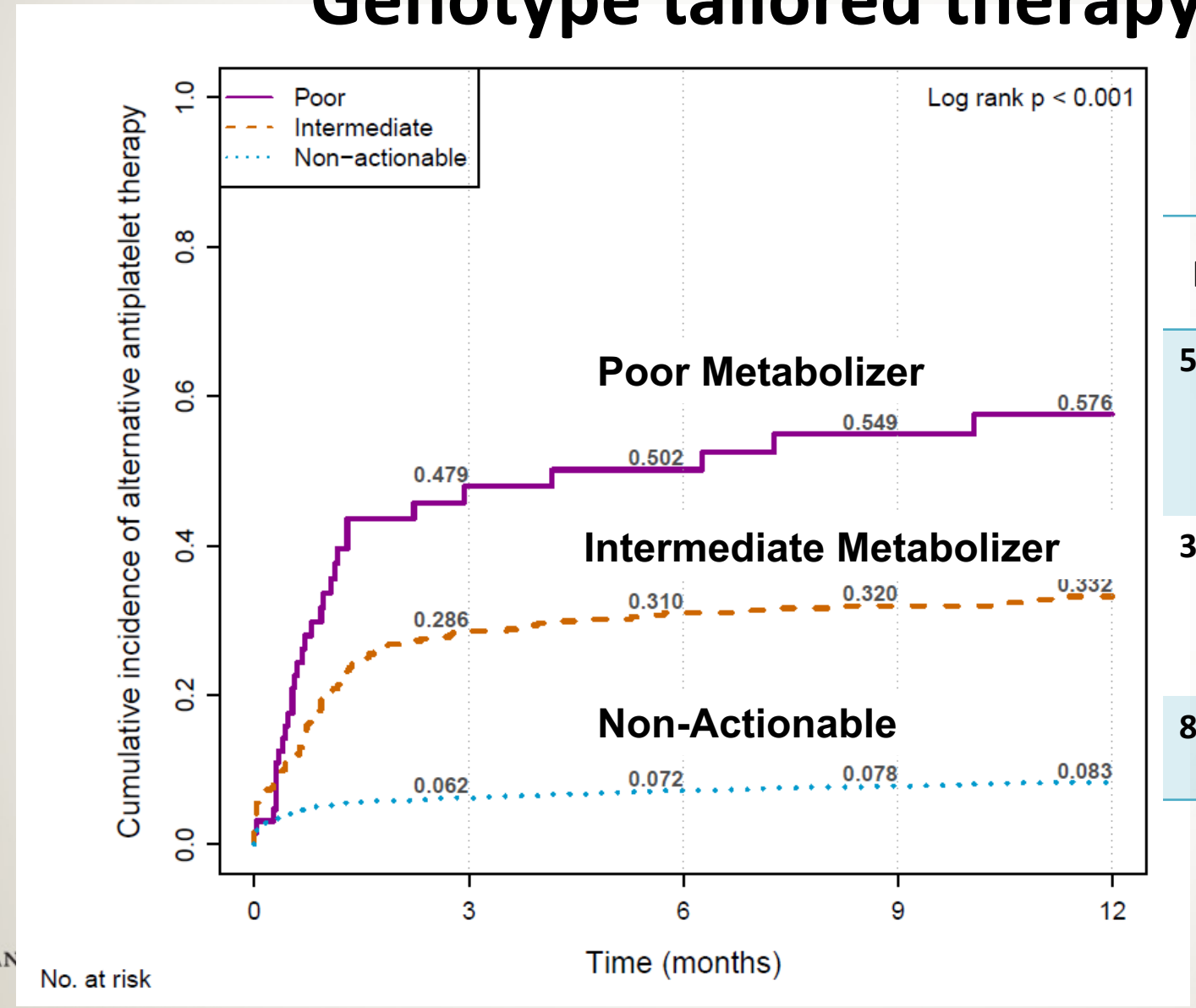
Van Driest et al, Clin Pharmacol Therap. 2014

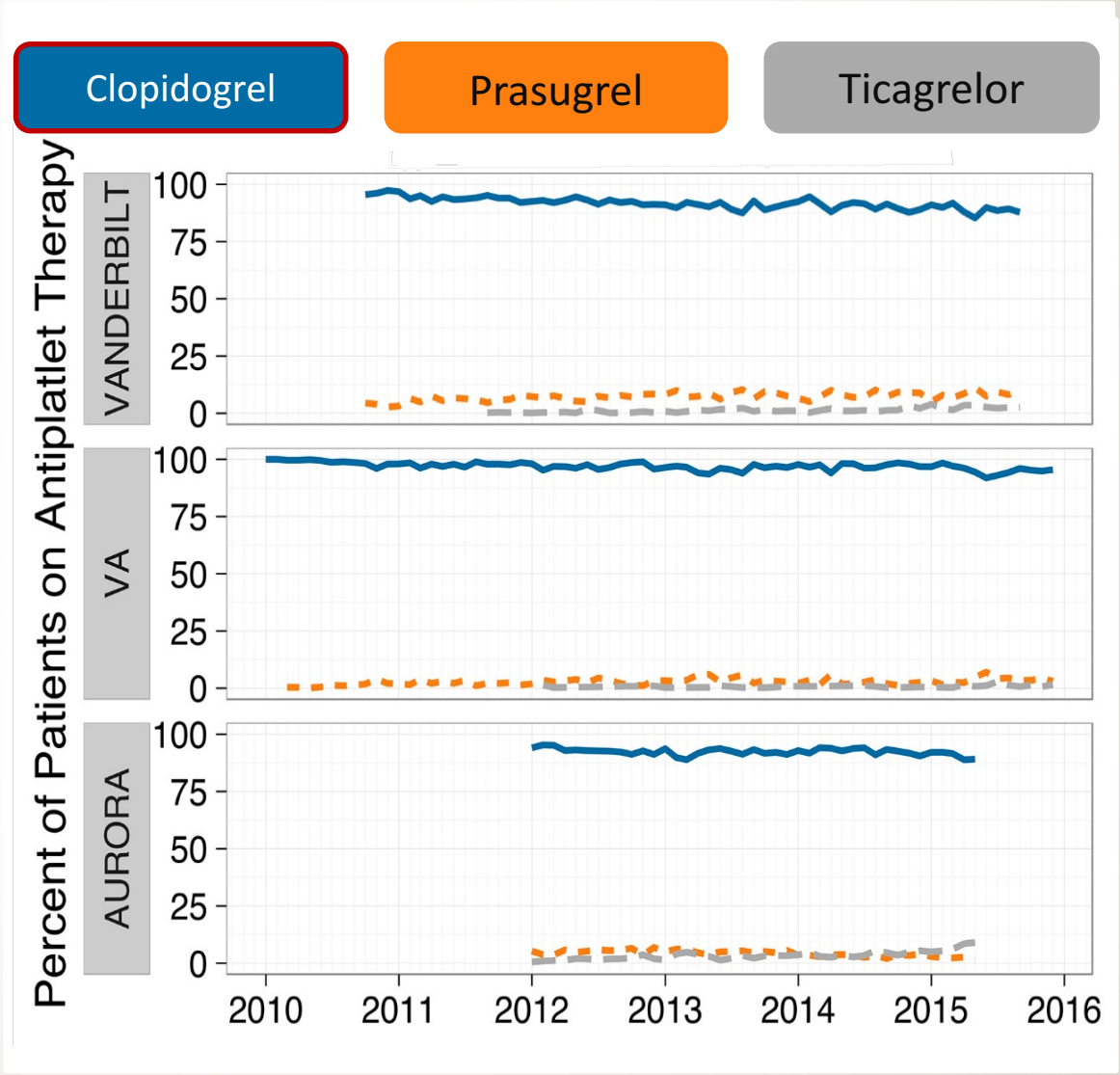
Do providers follow recommendations? Genotype tailored therapy



Rate	Adjusted HR
58%	**8.1** (5.4,12.1)
33%	**5.0** (4.0,6.3)
8%	**Ref**

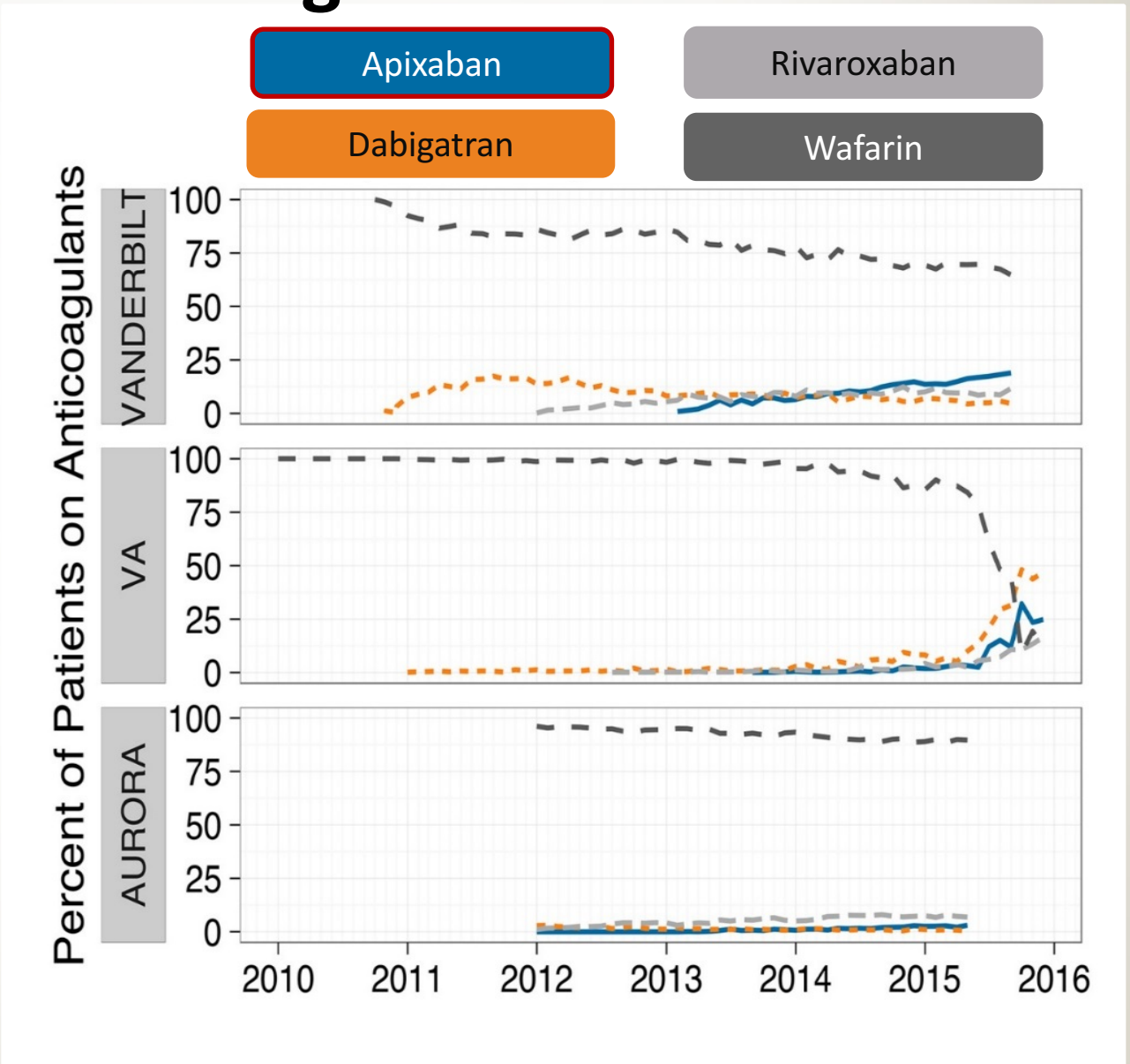
IGNITE CPIC Prescribing Study: Antiplatelet drugs

Clopidogrel remains the most commonly prescribed antiplatelet drug



IGNITE CPIC Prescribing Study: Anticoagulants

Warfarin still most frequent anticoagulant except at VA



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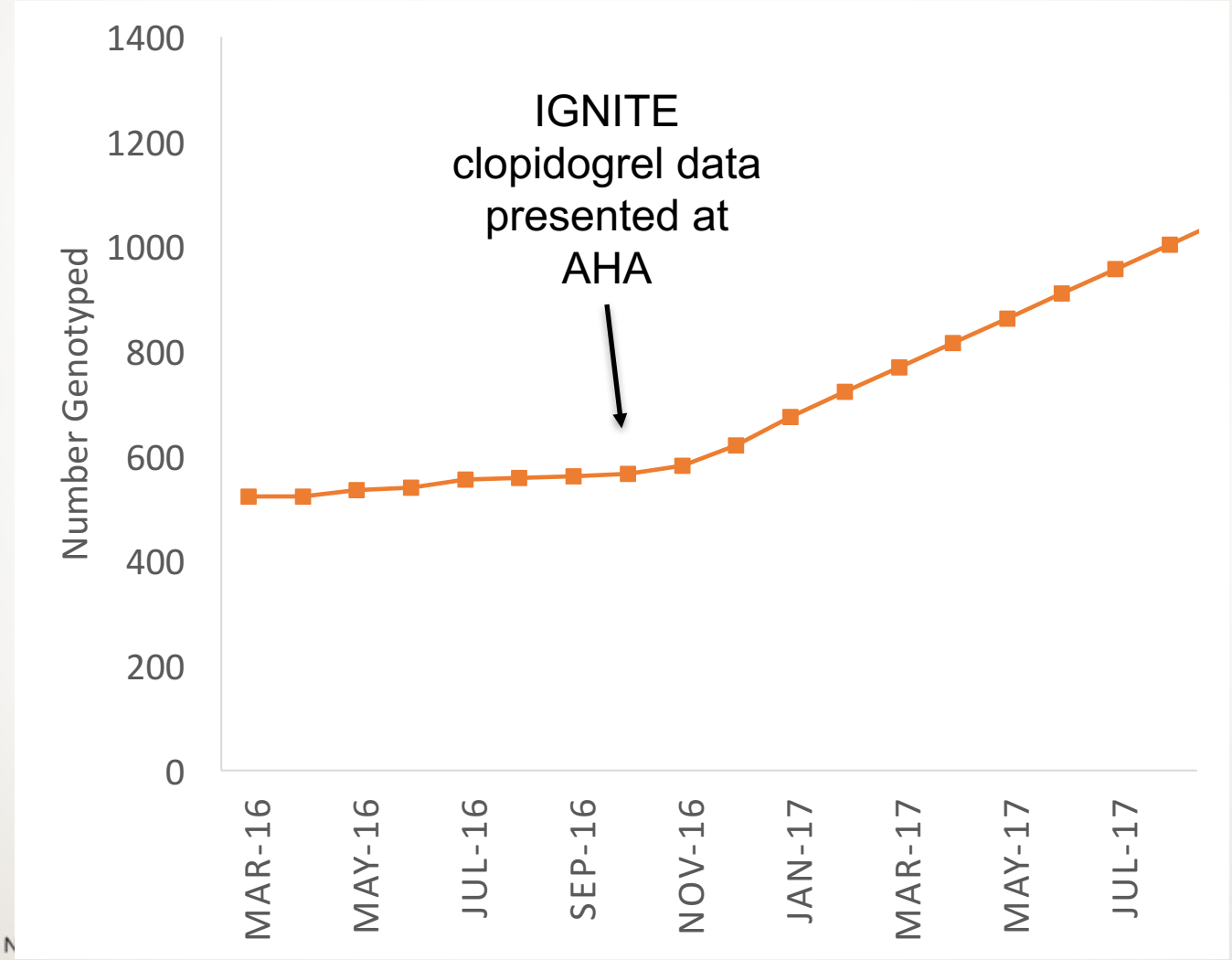
Increasing Adoption at Sanford Health (part of our IGNITE site)



Preliminary results - Evaluating cost effectiveness

PGx Scenario	Incremental cost effectiveness ratio of genotyping
Clopidogrel – CYP2C19	$36,618
Simvastatin – SLC01B1	$1,405,163
Warfarin – CYP2C9/VKORC1	$371,649

right

RATIONAL INTEGRATION OF GENOMIC HEALTHCARE TESTING

beta site:
https://rightsim.org/RIGHT/

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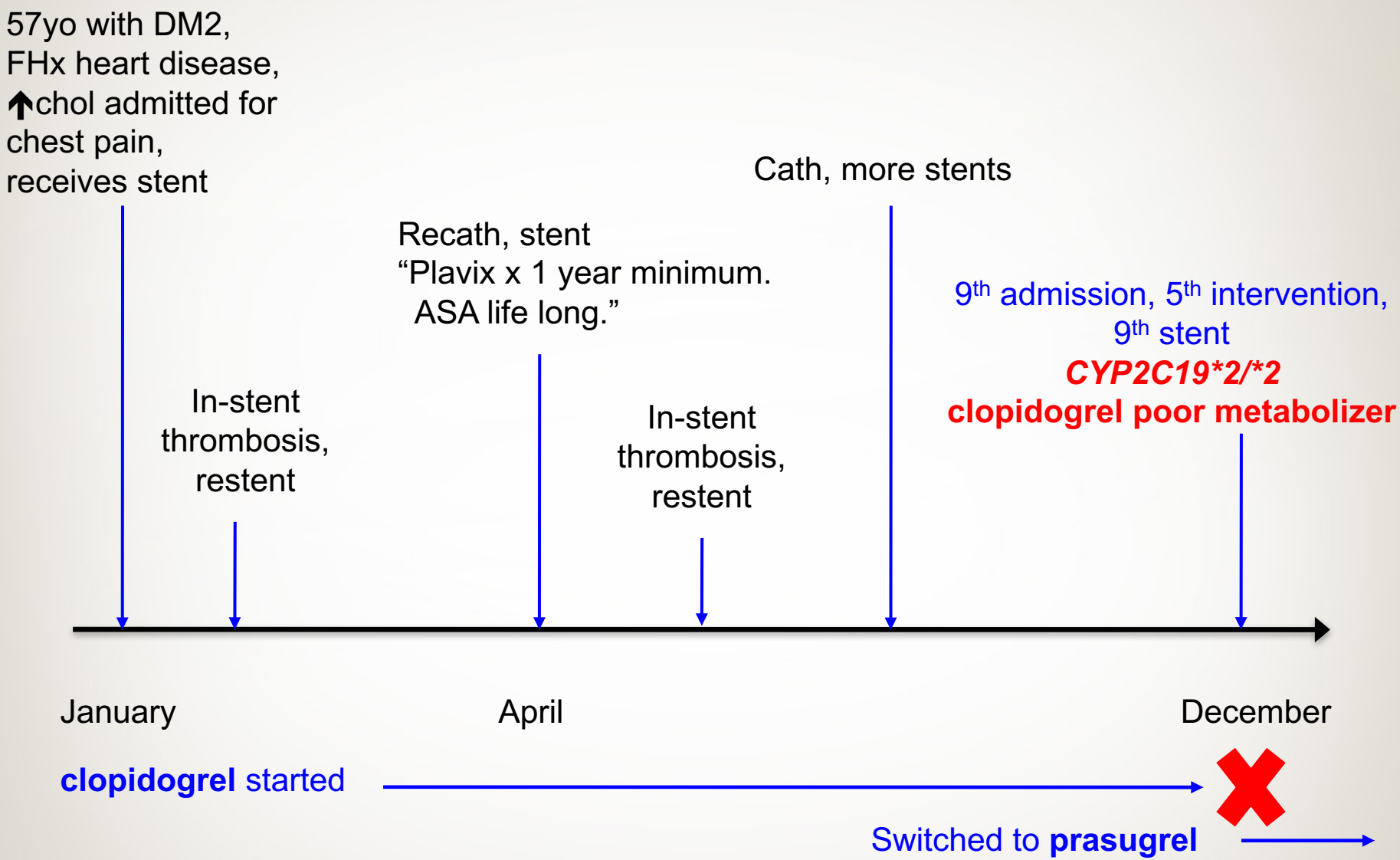
A few of the lessons learned

- Implementation is about the lab, process, EHR, and people
  - PGx is a “bleeding edge” of lab tests
  - MU-mediated EHR upheaval
  - Each EHR implementation has been different
- Local provider buy-in driven by 1) belief in clinical efficacy, 2) ease of use (e.g., CDS), 3) familiarity
- Advice changes frequently and opportunities to (re)use data accrue over time
  - Need for surveillance

What personalizing medicine really means



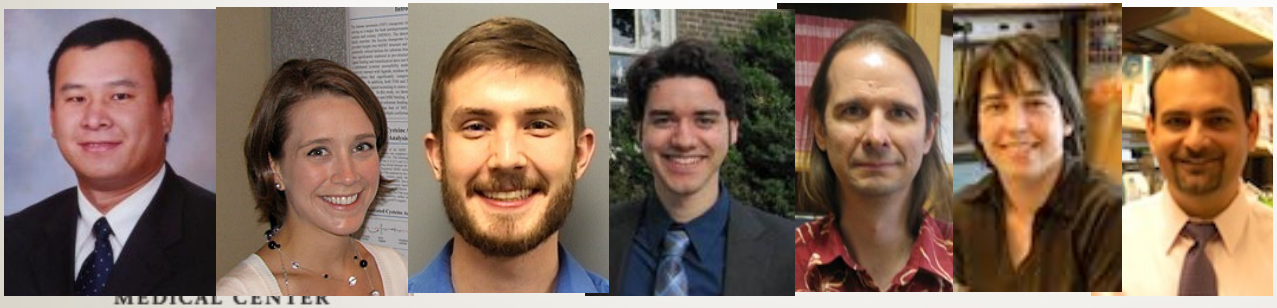
A sampling of the team

All of Us
THE FUTURE OF HEALTH BEGINS WITH YOU
The Precision Medicine Initiative

The eMERGE Network
electronic Medical Records & Genomics
A consortium of biorepositories linked to electronic medical records data for conducting genomic studies

PGRN
Pharmacogenomics Research Network

IGNITE
Implementing GeNomics In practicE



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