Taking a Novel Approach: Update on Innovations in Pharmacogenetics Education

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Weitzel et al. *Am J Pharm Ed*. 2016;80(7):122.

Disclosure

- I declare no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.

- The University of Florida College of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

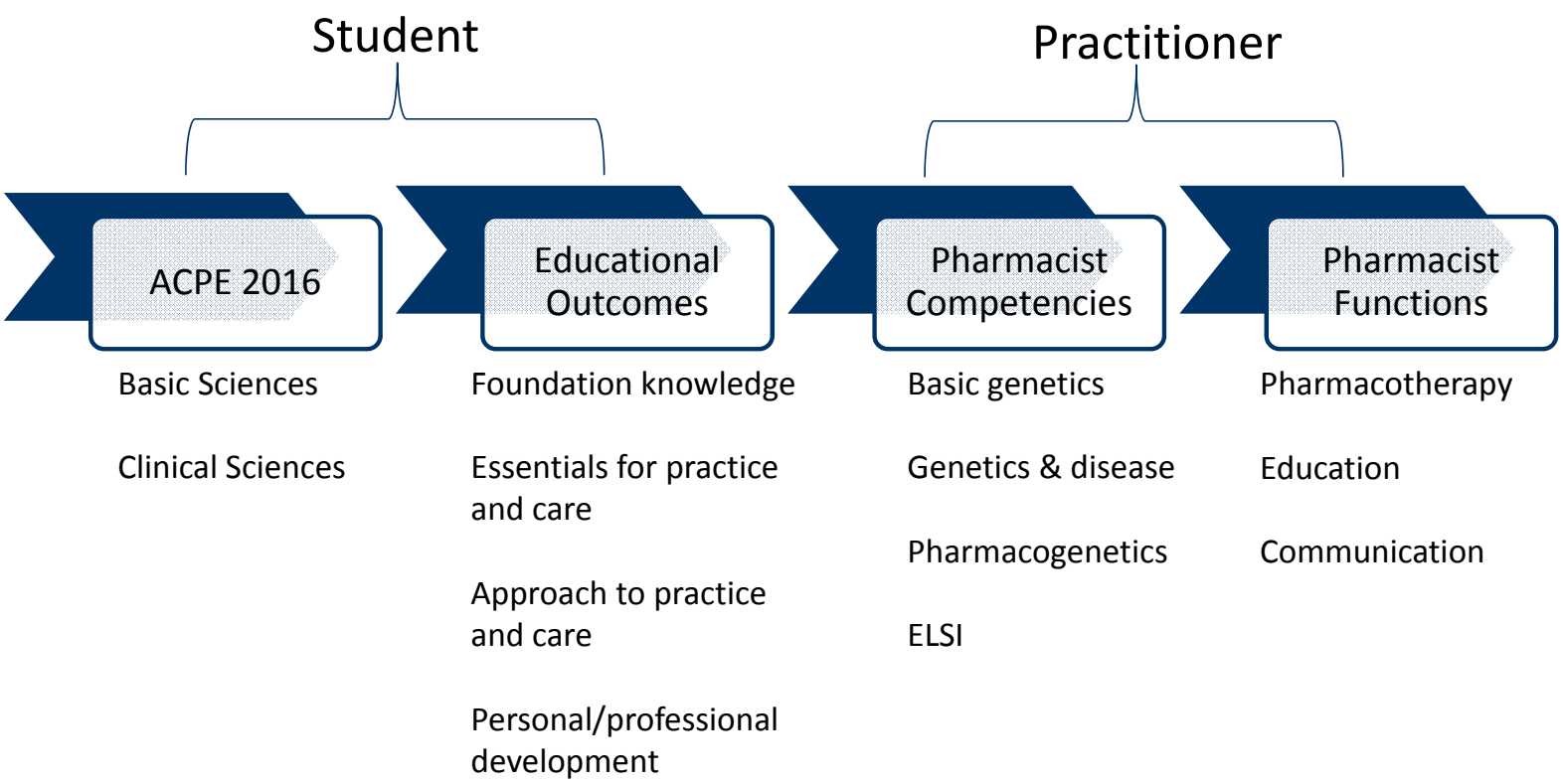
Objectives

1. Define the need for patient-centered teaching approaches in pharmacogenetics
2. Summarize recent innovations in pharmacogenetics teaching and learning strategies
3. Identify examples of novel teaching methods and resources for patient-centered teaching in clinical pharmacogenetics

Which of the following type of learners do you primarily teach/train in your practice setting?

- A. Pharmacy students
- B. Pharmacy Residents
- C. Pharmacists
- D. Other health professional students/trainees
- E. Other health professionals

Education to Practice



Why is pharmacogenetics different?

Pharmacogenomics Coverage in Medical and Pharmacy Schools

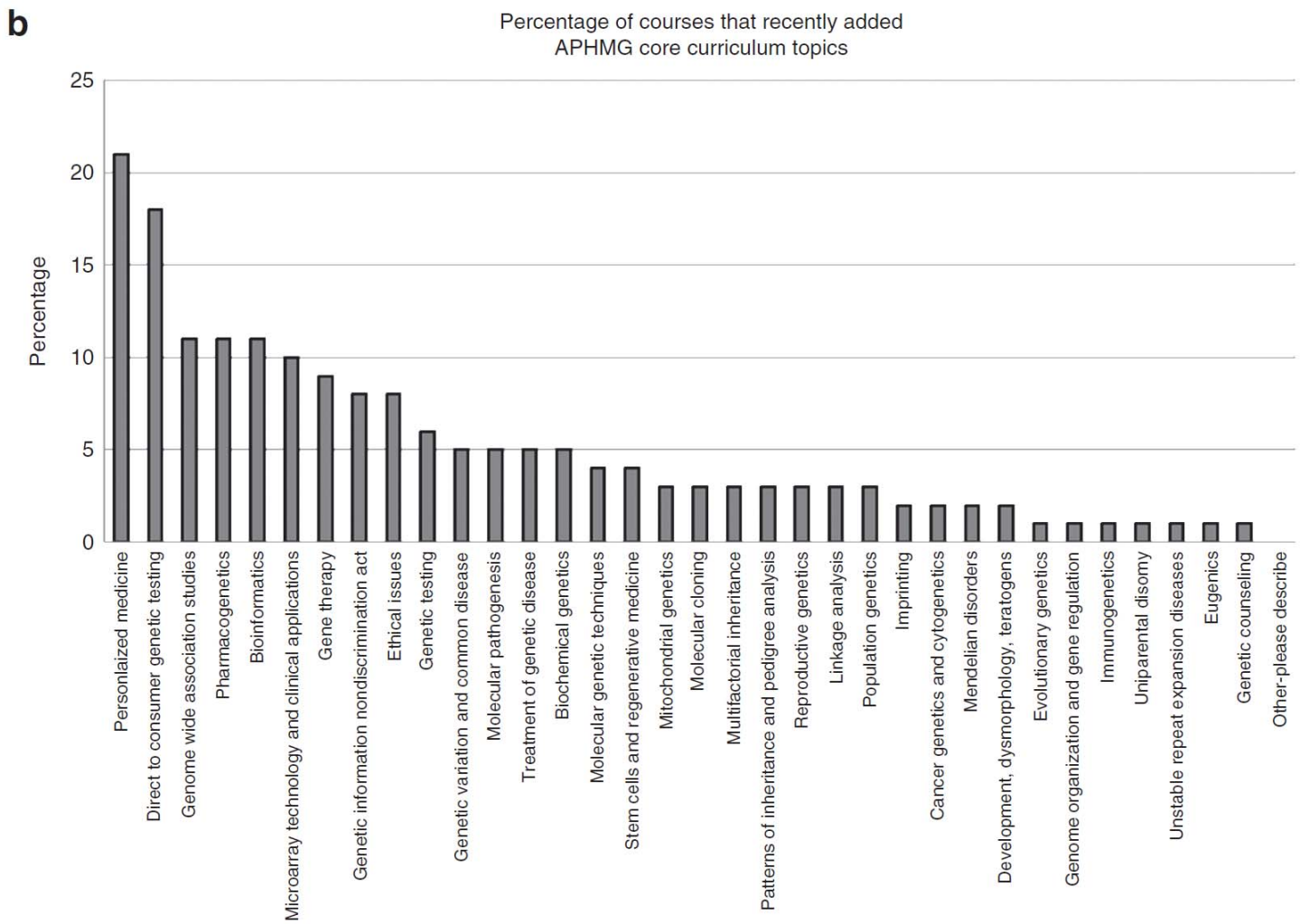
- Pharmacy schools
  - 89% provide instruction in pharmacogenomics
  - Number of hours provided
    - 40.6% - less than 10 hours
    - 42.0% - 10 to 30 hours
- Medical schools
  - 82% of medical schools incorporate pharmacogenomics
  - Only 28% had more than 4 hours of coursework
  - 76% considered pharmacogenomics instruction ‘poor’ or ‘not at all adequate’

Green JS et al. Pharmacogenomics. 2010;11:1331-40.
Murphy JE et al. Am J Pharm Ed. 2010. 74(1):7.

Pharmacy School Coverage of Applications-Based Content

Concept	Coverage
Basic assessment and evaluation strategies to assess pharmacy-related services directed toward the provision of pharmacogenetic/pharmacogenomic services and education either for the individual patient or public at large	13.0%
One's professional role in the referral to genetics services, or provision, follow-up, and quality review of pharmacogenetic tests	17.4%
Public policy issues, including regulatory statements and issues, aimed at pharmacogenetic/pharmacogenomic services and interventions	29%
The ethical, legal and social issues related to pharmacogenetic/genetic testing and recording of genetic information (eg, privacy, the potential for genetic discrimination in health insurance and employment)	53.6%

Murphy JE et al. Am J Pharm Ed. 2010. 74(1):7.



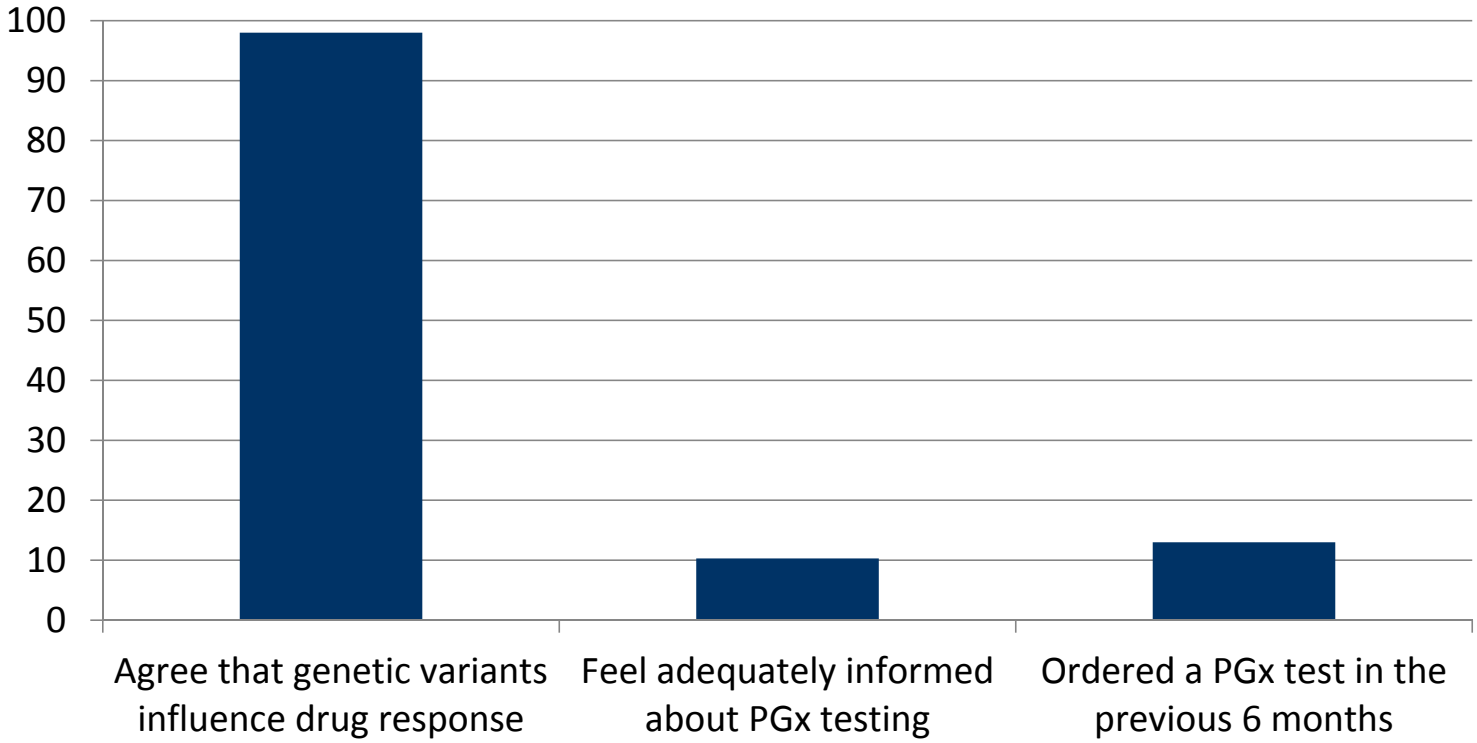
Plunkett-Rondeau J et al. Genet Med. 2015;17(11):927-34.

Practitioner Knowledge and Comfort Level

- Schwartz et al:
  - 72% of hospital pharmacists (n = 660) favor implementing PGx
  - Only 25% confident in abilities to interpret pharmacogenomic test results
- Roederer et al:
  - 83% of pharmacists rated their knowledge of pharmacogenomics as 'poor' or 'fair'
- McCullough et al:
  - 85% of pharmacists agreed that pharmacists should be required to be knowledgeable about pharmacogenomics
  - 63% felt they could not accurately apply pharmacogenomics test results to drug therapy, selection, and monitoring

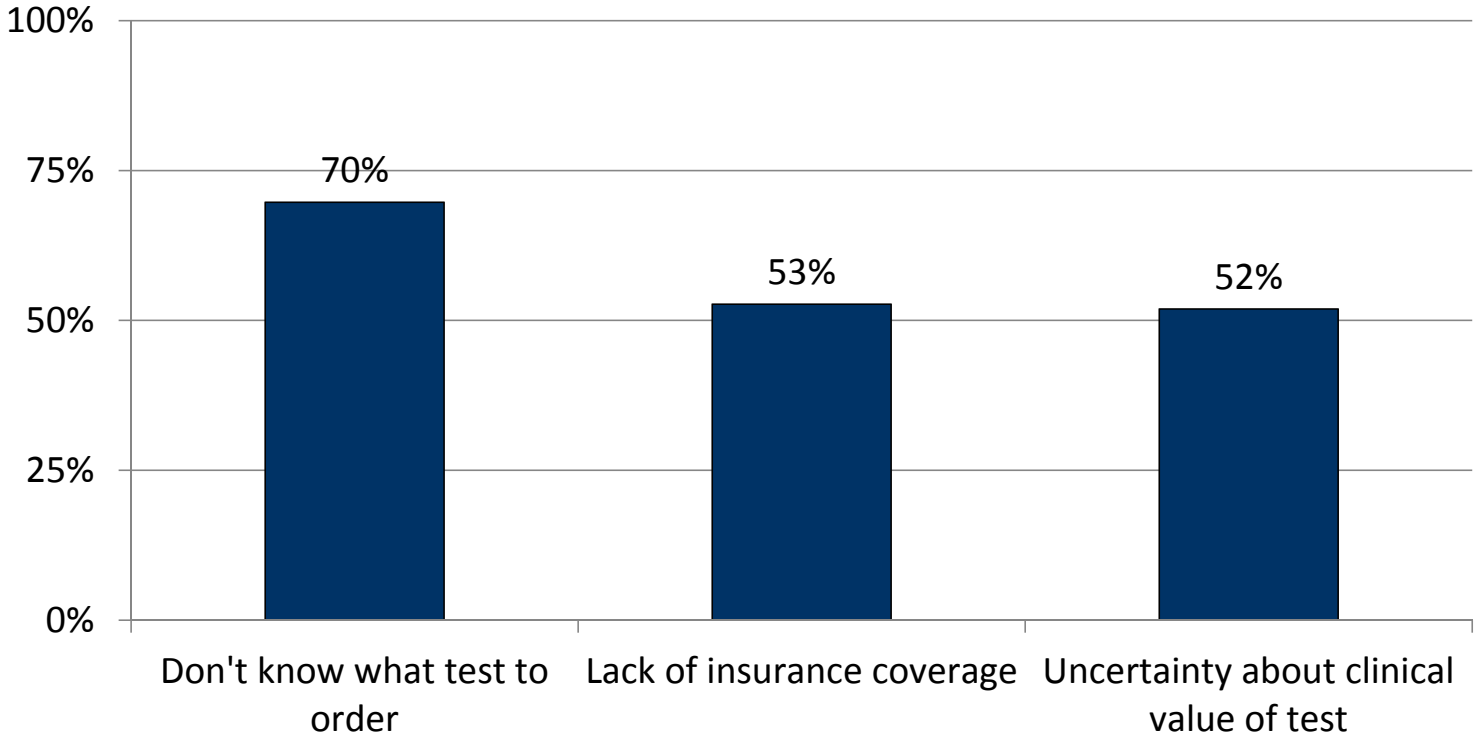
Schwartz EJ et al. Personal Med. 2017;14(1):27-35.
Roederer M et al. Personal Med. 2012;9:19-27.
McCullough et al. Am J Pharm Ed. 2011;75:51.

Practitioner Knowledge and Comfort Level

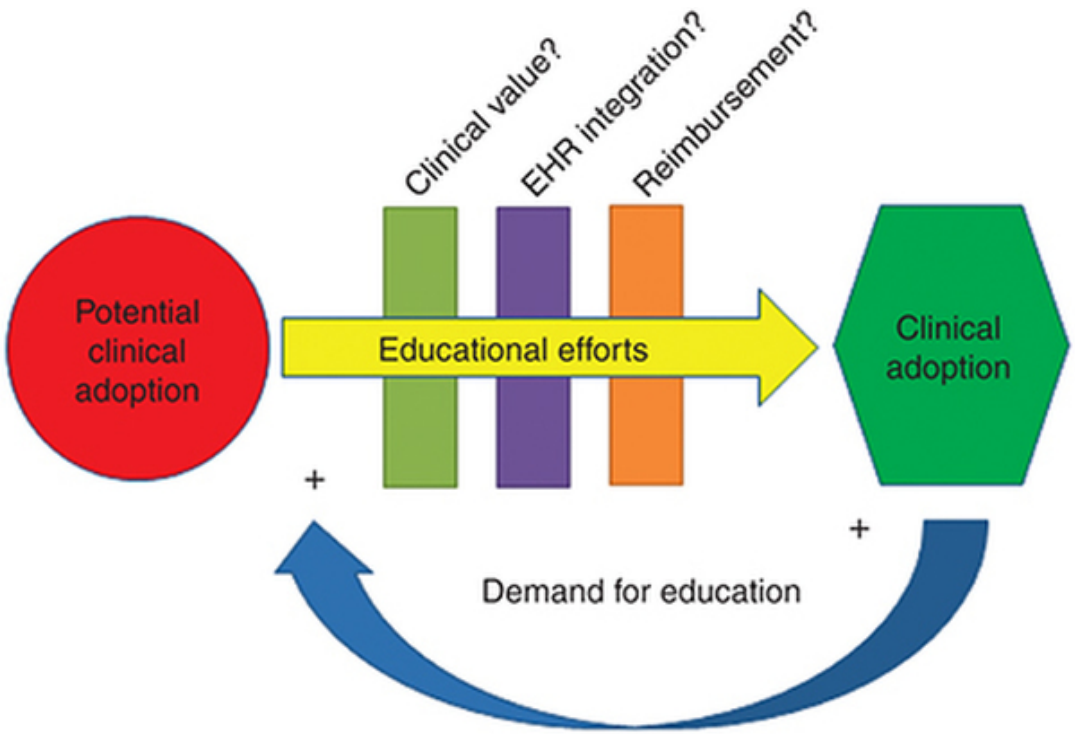


Stanek EJ et al. Clin Pharmacol Ther. 2012;91:450-7.

Reasons a pharmacogenomic test was not ordered



Johansan Taber K et al. *Pharmacogenomics Personalized Med*. 2014;7:145-62.



Feero WG et al. Translational research is a key to nongeneticist physicians' genomics education. *Genetics in Medicine*. 2014;16(12):871.

Why is pharmacogenetics different?

- Lack of appropriate training in school and continuing education
  - Lag time between rate of evidence and technology development and their integration into education and practice

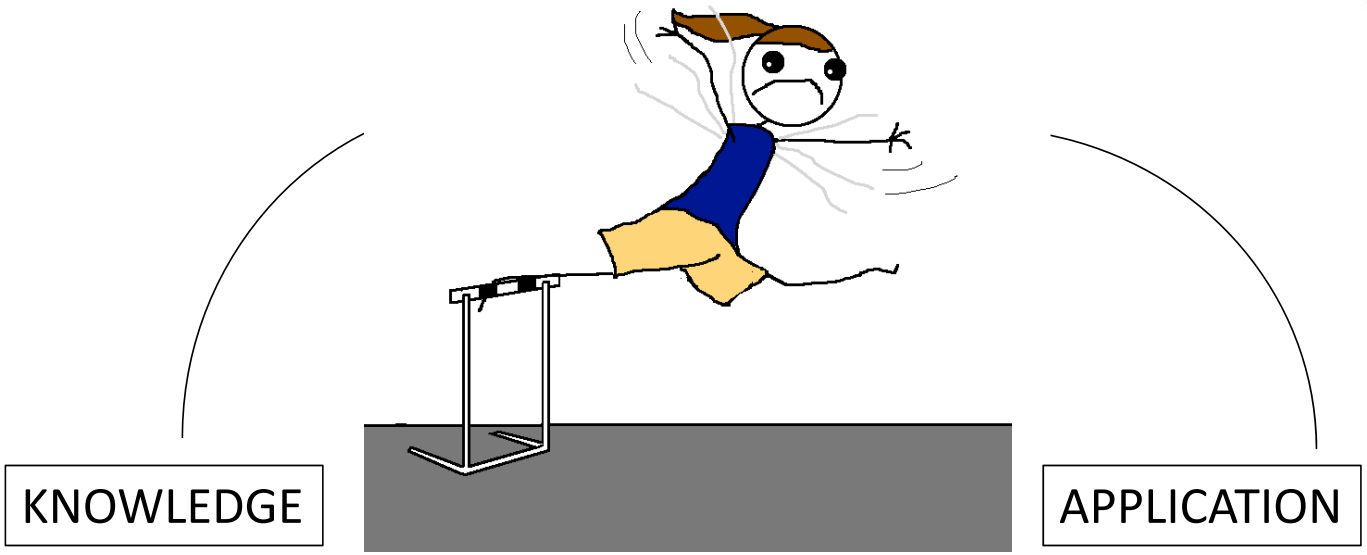
- Lack of clinical experience with pharmacogenomics activities and tools
  - Underrepresented in clinical training
  - How to find, interpret, and apply evidence
  - How to understand and compare different pharmacogenomics tests

Plunkett-Rondeau. Genet Med. 2015;17:927-34.

What do you think is the most challenging aspect of pharmacogenomics to teach/learn?

- A. Complexity of underpinning science
- B. Diversity/breadth of drugs/disease states affected by genomic variability
- C. How to change a specific patient's drug therapy based on pharmacogenetic variability
- D. How to navigate practical issues – reimbursement, lab testing, etc.

How do we get over the hurdle?

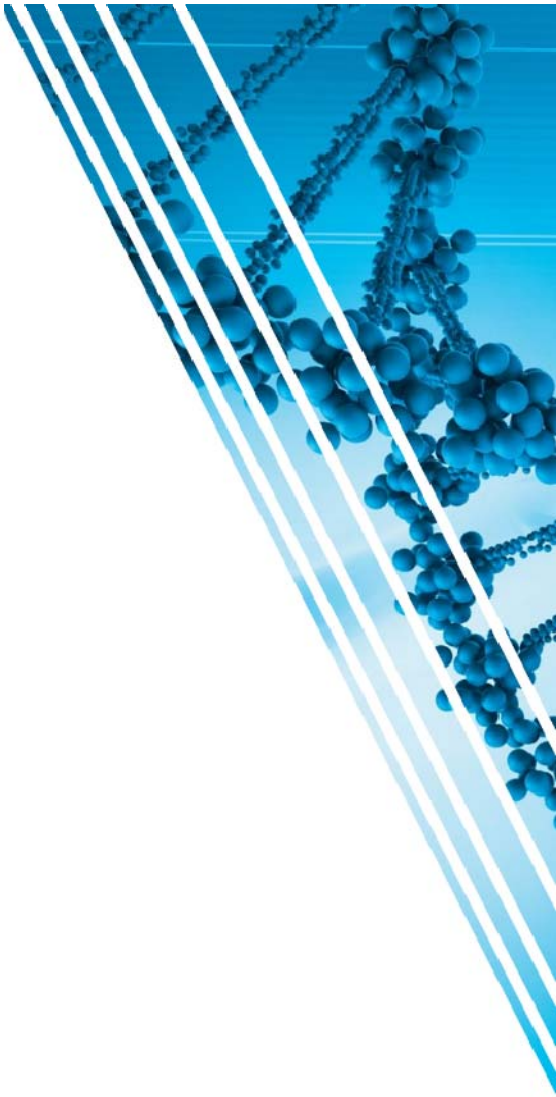


Creating Teachable Moments in Pharmacogenomics

...unplanned opportunities that arise when educators have an ideal chance to offer insight and learners have an ideal chance to apply knowledge.

Creating teachable moments in pharmacogenomics education and training programs

- Focus on what learners need to know and what their motivation is
- Provide knowledge and skills that are useful in practice today
- Engage learners in pharmacogenomics content



What learners need to know

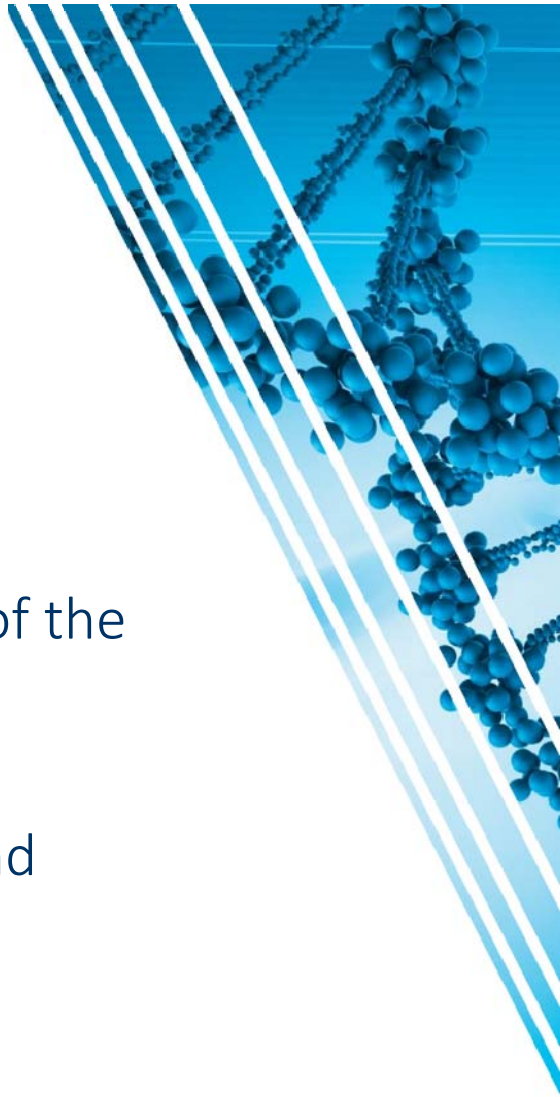
Drivers ≠ Mechanics

Focus on behaviors you want to change

- Identify patients who may benefit from pharmacogenomics testing?
- Know which pharmacogenomics test to order?
- Interpret pharmacogenomics laboratory reports?
- Recommend/implement drug therapy changes?
- Begin a new clinical service?

Expected Skills of all Practicing Pharmacists: ASHP Position Statement

- Design patient-specific pharmacotherapy regimens to optimize patient outcomes based on the patient's pharmacogenomic profile that also consider:
  - Pharmacokinetic and pharmacodynamic properties of the drug;
  - And pertinent patient-specific factors such as comorbidities, other drug therapy, demographics, and laboratory data.



Expected Skills of all Practicing Pharmacists: ASHP Position Statement

- Educate patients, pharmacists, and other health care professionals about pharmacogenomic principles and appropriate indications for clinical pharmacogenomic testing, including the cost-effective use of pharmacogenomic testing.

- Communicate pharmacogenomic-specific drug therapy recommendations to the health care team, including documentation of interpretation of results in the patient's health record.

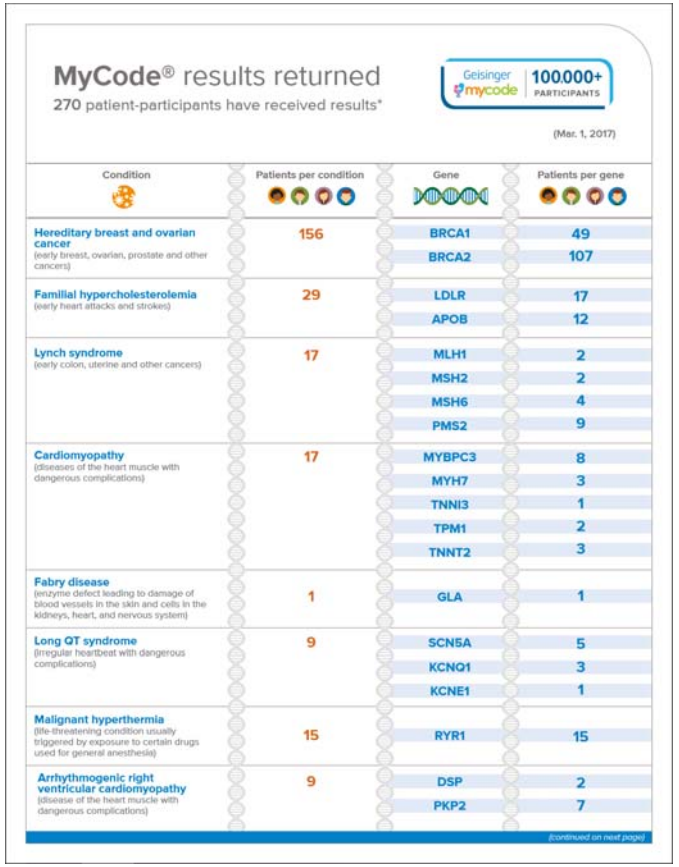
Provide knowledge and skills that are useful today

- What do learners need to know/do to be able to reach their goal?

Provide knowledge and skills that are useful today

- Case conferences that continue AFTER implementation
  - Example: UF Health PMP-Pediatric Psychiatry
  - Ongoing post-implementation discussions with psychiatry residents/fellows

- Discussions that incorporate existing genomic- or pharmacogenomics-decision making processes within an institution
  - Example: GenomeFIRST Case Conference Series from Geisinger Health
    - Discussion of incidental findings in research cases
    - Aimed at a broad audience of non-experts



MyCode® results returned

270 patient-participants have received results*

Geisinger mycode 100,000+ PARTICIPANTS

(Mar. 1, 2017)

Condition	Patients per condition	Gene	Patients per gene
Hereditary breast and ovarian cancer (early breast, ovarian, prostate and other cancers)	156	BRCA1	49
		BRCA2	107
Familial hypercholesterolemia (early heart attacks and strokes)	29	LDLR	17
		APOB	12
Lynch syndrome (early colon, uterine and other cancers)	17	MLH1	2
		MSH2	2
		MSH6	4
		PMS2	9
Cardiomyopathy (diseases of the heart muscle with dangerous complications)	17	MYBPC3	8
		MYH7	3
		TNNI3	1
		TPM1	2
		TNNT2	3
Fabry disease (enzyme defect leading to damage of blood vessels in the skin and cells in the kidneys, heart, and nervous system)	1	GLA	1
Long QT syndrome (irregular heartbeat with dangerous complications)	9	SCN5A	5
		KCNQ1	3
		KCNE1	1
Malignant hyperthermia (life-threatening condition usually triggered by exposure to certain drugs used for general anesthesia)	15	RYR1	15
Arrhythmogenic right ventricular cardiomyopathy (disease of the heart muscle with dangerous complications)	9	DSP	2
		PKP2	7

(continued on next page)

go.geisinger.org/results

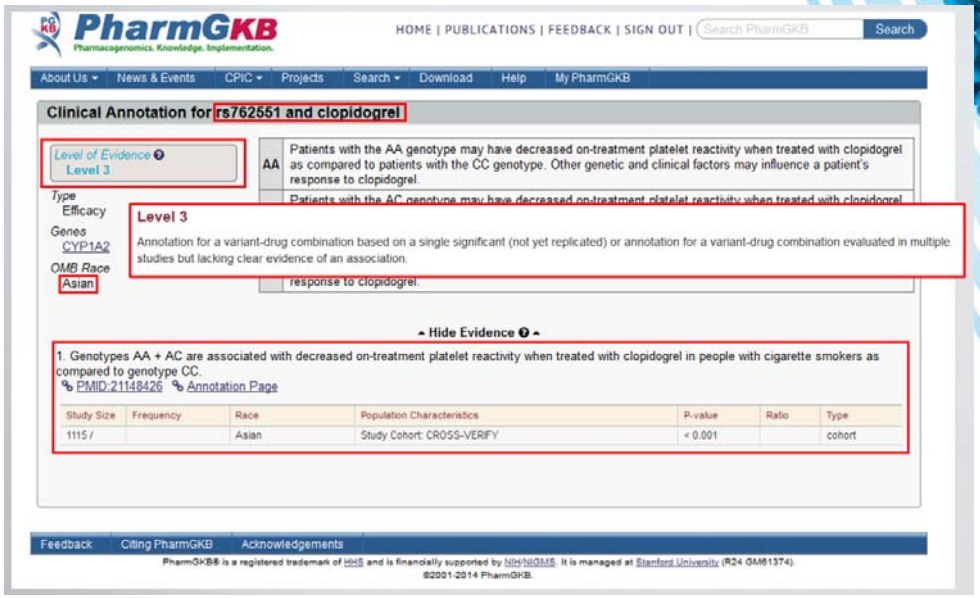
Provide knowledge and skills that are useful today

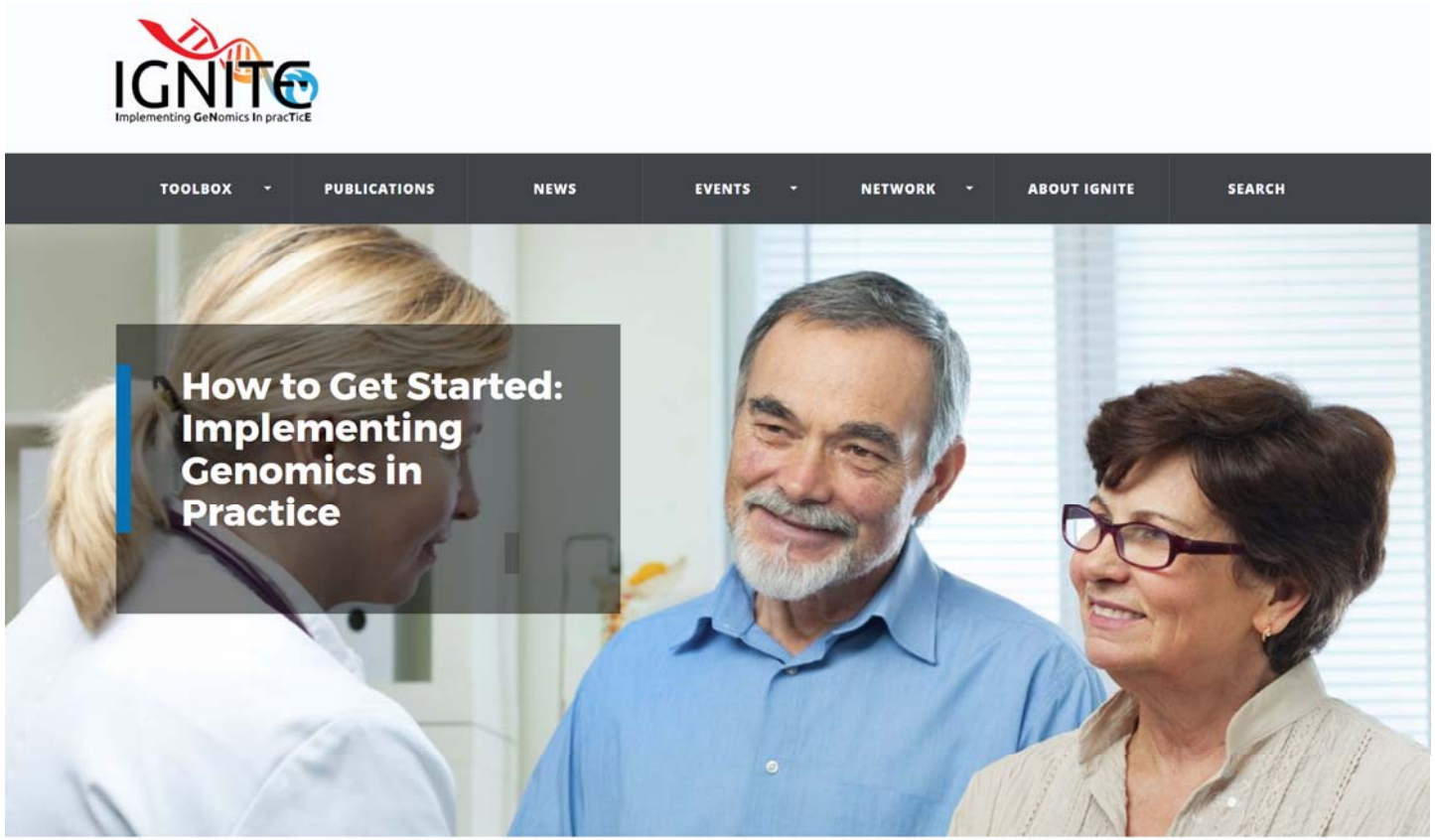
- Hands-On Learning and Activities
  - Patient-centered
  - Allow participants to practice needed real-world skills
  - Are associated with feedback from stakeholders
  - Example: Skills-driven assignments using real-world information (e.g., PharmGKB, pharmacogenomics databases, drug information resources)

- Practice-based tools that help learners achieve program goals

Hands-On Learning and Activities

- You are a clinical pharmacist in a hospital
- Cardiologist approaches you to ask:
  - Whether he should perform *CYP2C19* testing for his clopidogrel patients?
  - If so, who should he test?





SPARK Toolbox

www.ignite-genomics.org

IGNITE
Implementing GeNomics In pracTicE

TOOLBOX | PUBLICATIONS | NEWS | EVENTS | NETWORK | ABOUT IGNITE | SEARCH

Clinicians

ALL / CLINICIANS / EDUCATORS / RESEARCHERS /

Browse resources intended to help clinicians implement genomics in patient care, or SEARCH BY KEYWORD.

How to Get Started: Implementing Genomic Medicine

Just getting started? The tools below provide background information, benefits of adoption of genomic medicine in patient care, and summarize key challenges and stakeholders to consider for your implementation.

Ready to begin implementing? See specific resources below for common pharmacogenomic and genomic medicine implementations.

+ Clinical Implementation of Genomic Medicine and Pharmacogenomics

+ CYP2C19 - Clopidogrel

+ CYP2C19 - Clopidogrel

+ CYP2D6-Opioids

+ CYP2D6 and CYP2C19-SSRIs

+ TPMT-Thiopurines

+ Family History

+ APOL1

− CYP2C19 - Clopidogrel

+ Evidence Overview: CYP2C19 – Clopidogrel
+ Clinical Implementation Publications: CYP2C19-Clopidogrel
+ Clinical Pharmacogenetics Implementation Consortium Guideline Resources: CYP2C19-Clopidogrel
+ PharmGKB Resources: CYP2C19
+ Genotyping Resources: CYP2C19
+ Implementation Workflow Examples: CYP2C19-Clopidogrel
+ Clinical Decision Support: CYP2C19-Clopidogrel
+ Data Collection and Implementation Metrics: CYP2C19-Clopidogrel
+ Resources for Patients and Providers: CYP2C19-Clopidogrel

+ **Clinical Pharmacogenetics Implementation Consortium Guideline Resources: CYP2C19-Clopidogrel**

+ **PharmGKB Resources: CYP2C19**

+ **Genotyping Resources: CYP2C19**

+ **Implementation Workflow Examples: CYP2C19-Clopidogrel**

+ **Clinical Decision Support: CYP2C19-Clopidogrel**

+ **Data Collection and Implementation Metrics: CYP2C19-Clopidogrel**

− **Resources for Patients and Providers: CYP2C19-Clopidogrel**

- Information on Genetic Testing for Clopidogrel (Plavix)
  Source: University of Florida Health Personalized Medicine Program
- Video: CYP2C19 and Clopidogrel (Plavix) Response NEW
  Source: Coriell Personalized Medicine Collaborative
- Patient Education Brochure for Clopidogrel NEW
  Source: Icahn School of Medicine at Mount Sinai
- CYP2C19 Summary for Patients and Their Families NEW
  Source: St. Jude Children's Research Hospital
- CYP2C19-Clopidogrel Pharmacogenomic Lab Test Summary
  Source: Mayo Clinic Center for Individualized Medicine
- Guide for Patient Consultation about Pharmacogenomics
  Source: Indiana University
- Medical Genetics Summary: Clopidogrel Therapy and CYP2C19 Genotype NEW
  Source: NIH National Center for Biotechnology Information
- CYP2C19 Information Page NEW
  Source: St. Jude Children's Research Hospital
- PMP Clopidogrel Handout
  Source: University of Florida Health Personalized Medicine Program
- Education Handouts NEW
  Source: Cincinnati Children's Hospital

Practice-Based Tools

GEC•KO
Genetics Education Canada · Knowledge Organization
on the run

PHARMACOGENOMICS: CODEINE AND BREASTFEEDING

Codeine's analgesic properties are the result of its metabolism by the enzyme cytochrome P450 2D6 (CYP 2D6), which is coded by a highly variable (polymorphic) gene with over 80 variant alleles that contribute to enzyme activity. A functional gene duplication results in an ultra-rapid metabolizer (UM) phenotype and consequently higher plasma concentrations of the active metabolite, morphine. Two alleles with no activity result in a poor metabolizer (PM) phenotype and these individuals receive little to no therapeutic benefit from codeine.

Women who are UMs of codeine will have significantly higher than normal levels of morphine in breast milk and thus potentially problematic or lethal levels in their newborn. Central nervous system (CNS) depression in the infant appears to worsen after 4 days, likely because of the accumulation of morphine with continued breastfeeding. **Analgesics other than codeine (e.g. non-steroidal anti-inflammatory drugs (NSAIDs)) are recommended for use by nursing mothers. If codeine is necessary, it should not be used for longer than 4 days[1].** While maternal genotyping could be considered before codeine is prescribed, education about the signs of CNS depression in the infant might be an equally important preventiv

http://geneticseducation.ca/

PGx Recommendations by CYP2D6 Genotype

SSRI	Gene	Phenotype	Implication	Therapeutic Recommendation
Citalopram	CYP2C19	Ultra-rapid metabolizer	Increase probability of drug failure due to lower plasma levels	Select alternative drug not predominantly metabolized by CYP2C19
		Normal metabolizer	Normal metabolism	Initiate therapy with recommended starting dose
		Intermediate metabolizer	Reduced metabolism compared to normal metabolizers	Initiate therapy with recommended starting dose
		Poor metabolizer	Increase the probability of side effects due to higher plasma levels	Consider a 50% reduction of recommended starting dose or select alternative drug not predominantly metabolized by CYP2C19
Fluoxetine	N/A	N/A	The evidence surrounding pharmacogenomic factors in fluoxetine use is considered preliminary at this point	
Fluvoxamine	CYP2D6	Ultra-rapid metabolizer	No data available for fluvoxamine	No recommendation for fluvoxamine due to lack of evidence
		Normal metabolizer	Normal metabolism	Initiate therapy with recommended starting dose
		Intermediate metabolizer	Higher plasma concentrations may increase the probability of side effects	Initiate therapy with recommended starting dose
		Poor metabolizer	Increase the probability of side effects due to higher plasma levels	Select alternative drug not predominantly metabolized by CYP2D6, if use is warranted consider a 50% reduction of initial dose
		Ultra-rapid	Increase probability of drug failure due to r plasma levels	Select alternative drug not predominantly metabolized by CYP2D6
			nal metabolism	Initiate therapy with recommended starting dose
			na concentrations may probability of side effects	Initiate therapy with recommended starting dose
			probability of side effects igher plasma levels	Select alternative drug not predominantly metabolized by CYP2D6, if use is warranted consider a 50% reduction of initial dose

UF Health PMP
Provider "Cheat Sheet"

JAX Home > Education & Learning > Clinicians

PRECISION MEDICINE FOR YOUR PRACTICE

CME and CNE modules on the clinical applications of genetic testing

How can genetics be used in clinic with *my* patients? Can genetic information really improve outcomes? Genetic testing is constantly changing. How can I keep up?

Precision Medicine for Your Practice is an educational program being developed by Scripps Translational Science Institute (Scripps), the American Medical Association (AMA), and The Jackson Laboratory (JAX) to help clinicians answer these questions. In each module, you will have the opportunity to:

- Practice applying genetic information to realistic cases
- Assess the utility of genetic information
- Learn about benefits and limitations of new genetic tests

https://www.jax.org/education-and-learning

Engage Learners in Pharmacogenomics Content

Using participatory genomic testing with learners can create a "push" teachable moment

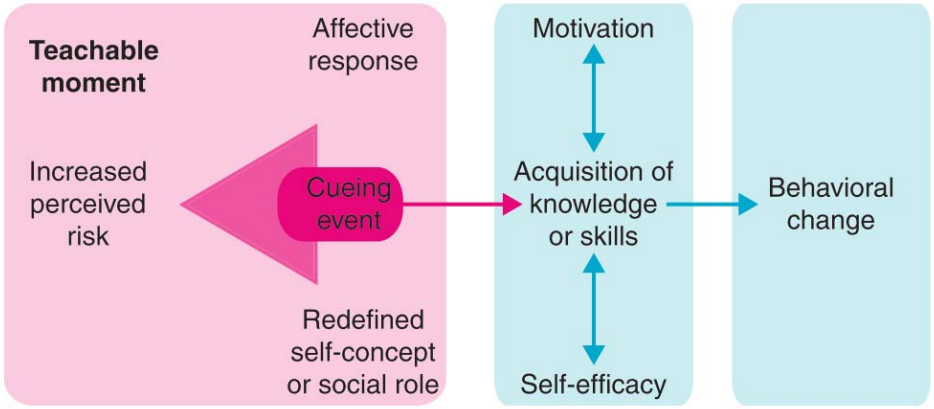


Figure 1. Teachable moments are distinguished by a cueing event (also called a triggering or sentinel event) that increases perception of risk, elicits an emotional response, and/or represents a life experience that changes an individual's self-concept or one of their social roles [10]. In the case of the Stanford GENE 210 curriculum, the cueing event was the experience of personal genotyping. The students who were surveyed overwhelmingly felt that having their personal data motivated them to acquire new knowledge (the course material) and skills

Boguski MS et al. Genome Med. 2013;5:22.

Participatory genomic testing in the classroom

- N = 31 medical and graduate students
  - 23 students underwent personal genome testing
  - 8 students used a de-identified dataset
- Students' reflections
  - 83% of tested students stated they were pleased with their decision versus 12.5% of non-tested student
- Students' knowledge
  - 70% of tested students self-reported a better understanding on the basis of testing
  - Tested students demonstrated a mean 31% increase in pre- to post-test scores on knowledge questions (significantly higher than those not tested)

Salari K et al. *PLOS One*. 2013;8:e68853.

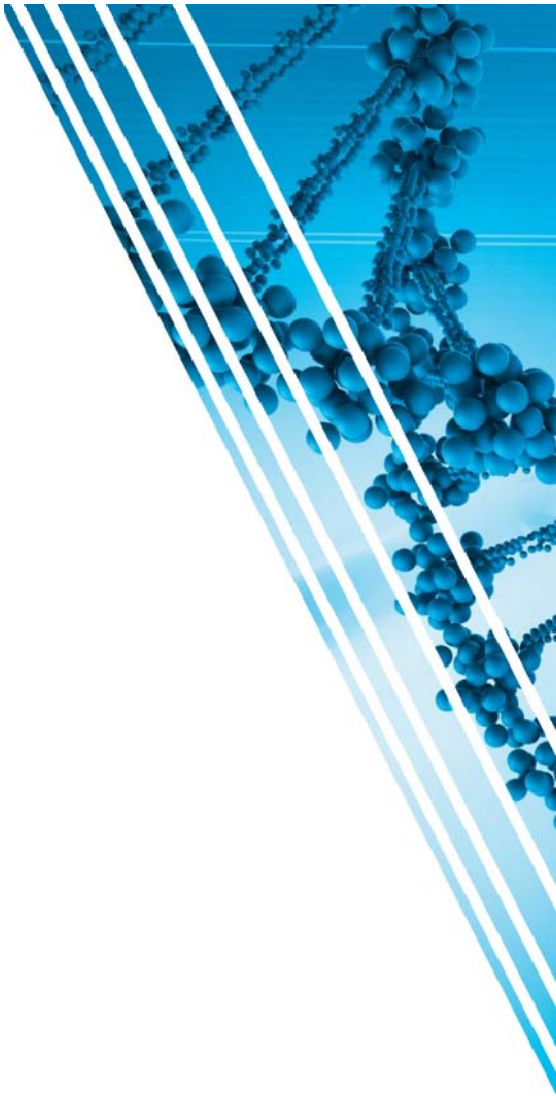
Effect of Participatory Genotype Testing on Knowledge, Attitudes and Beliefs

	Krynetskiy et al (2009)	Adams et al (2016)	Weitzel et al (2016)	Frick et al (2016)	Surofchy et al (2017)	Remsberg et al (2017)
Student Genotyping	Single SNP analysis (rs1801280) within *NAT2*	Commercial laboratory testing (23andMe)	Panel-based testing in research laboratory for relevant clinical SNPs	Commercial laboratory testing (23andMe)	Single gene encoding drug metabolizing enzyme or pharmacodynamics-relevant protein in research lab	Single gene testing of *TAS2R38* with phenotype testing
Effect on Knowledge	N/A	82.9% (14.1) vs 90.5% (9.0) correct on the presurvey vs postsurvey, respectively; $p<0.001$	45% on questions related to knowledge of PGx vs. 80% after completing the course; $p<0.01$	Increased knowledge of PGx resources pre- vs. post (17.9% vs. 56.4%, $p<0.0001$); upheld in both genotyped and non-genotyped students	Increased knowledge pre- vs. post, but not significantly different in genotyped vs. non-genotyped students	Achievement of competency
Effect on Attitudes and Beliefs	Increased understanding of PGx analysis Highlighted importance of this topic to future practice	Greater increase in confidence Improved student's self-perceived ability to empathize	Improved self-reported understanding Increased comfort level and confidence	Greater increase in confidence Improved students' reflections and attitudes toward PGx	Increase in mean attitude pre- vs. post, but not significantly different in genotyped vs. non-genotyped students	Perceptions of and confidence in their abilities in pharmacogenomics patient care skills areas improved

Krynetskiy et al. Am J Pharm Ed. 2009;73(4):71.
Weitzel et al. *Am J Pharm Ed*. 2016;80(7):122.
Surofchy et al. *Innovations Pharm*. 2017;8(1):2.
Adams et al. *Am J Pharm Ed*. 2016; 80(1):3.
Frick et al. *Front Pharmacol. 2016;7:241*.
Remsberg et al. *Am J Pharm Ed*. 2017;81(1):11.

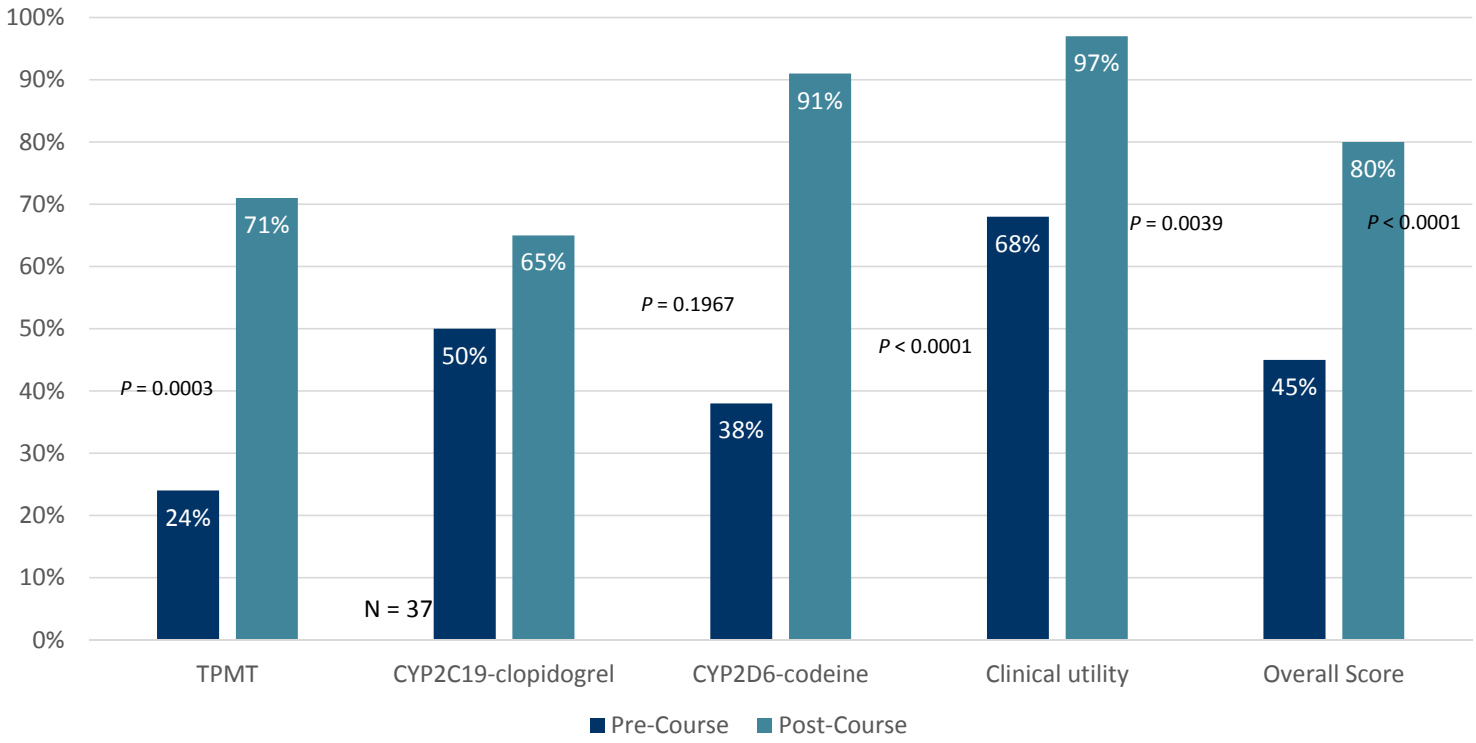
Personal Genotyping in the Classroom

- Pharmacogenomics course
  - N = 37
    - All students underwent personal genotyping
- Genomic Medicine Course
  - N = 21 students
- Both courses
  - N = 16 students completed both courses in sequence and completed pre- and post-course surveys in both courses



Weitzel et al. *Am J Pharm Ed*. 2016;80(7):122.

Pharmacogenomics Knowledge



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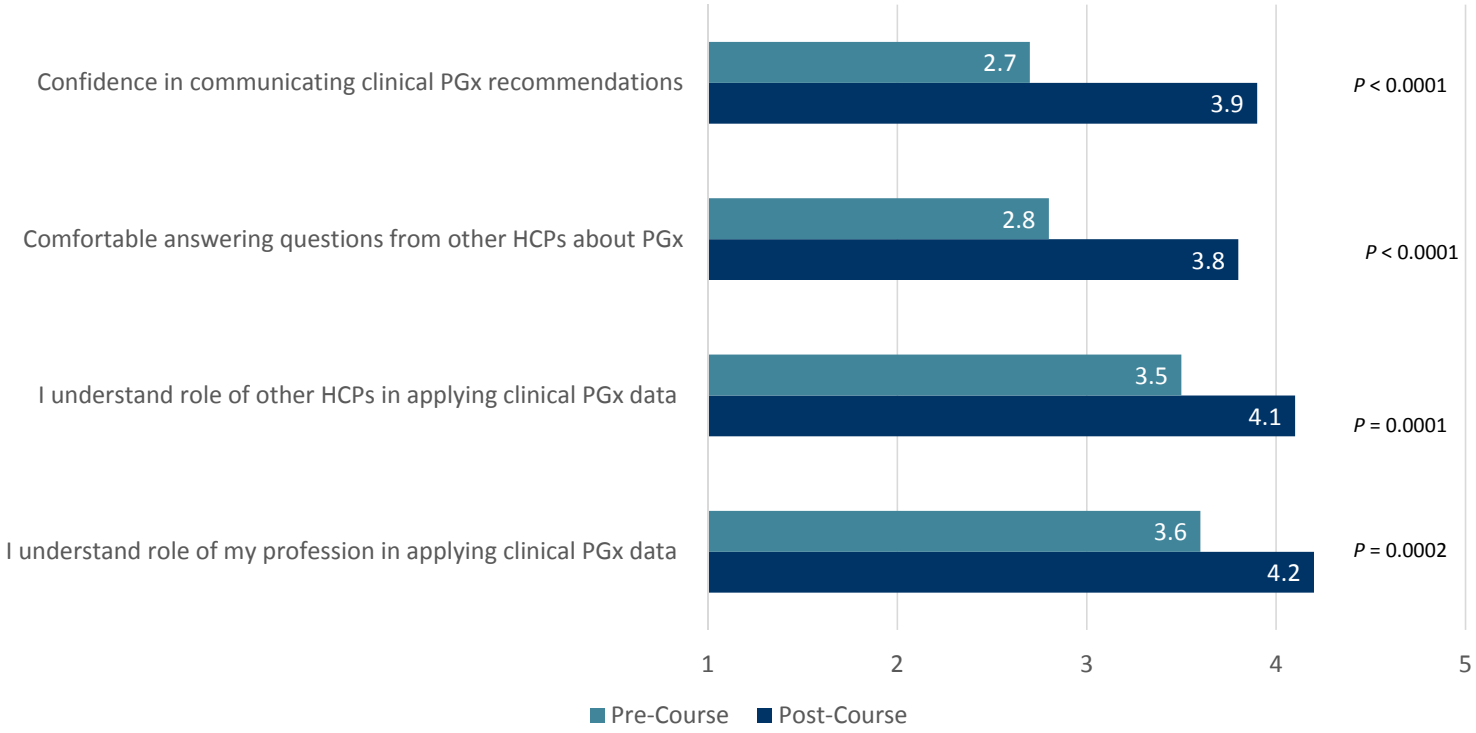
Attitudes/Beliefs: Health Care Professionals



N = 37; Responses to questions based on Likert scale (1=strongly disagree and 5=strongly agree)

Weitzel et al. *Am J Pharm Ed*. 2016;80(7):122.

Box 1. Ethical Issues Regarding Educational Use of PGT

- Anonymity
- Confidentiality
- Coercion
- Ability to make informed decision about PGT
- Need for genetic counseling and psychological support
- Impact of test results on students and their families
- Conflicts of interest among faculty with ties to genomic testing companies
- Financial considerations

Garber KB et al. Trends Genet. 2016;32(6):317-20.

Effects of Personal Genotyping on Student Knowledge and Self-Efficacy

Control

Enrolled in Required Pharmacogenetics Course

Intervention

Enrolled in Required Pharmacogenetics Course

Enrolled in Elective Clinical Pharmacogenetics Course

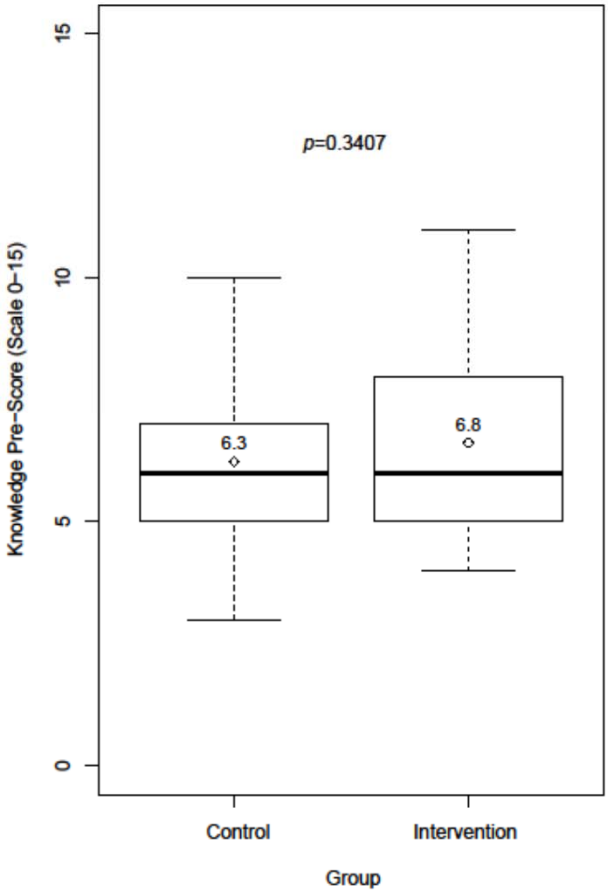
Option to undergo panel-based genotyping and used genetic data in patient cases

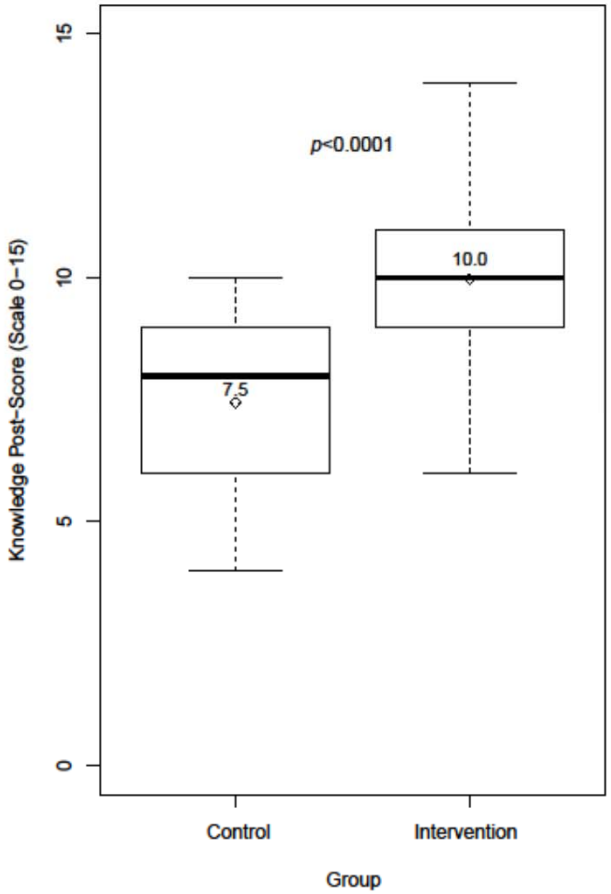
Arwood et al. Data accepted for presentation. Translational Science Meeting:Washington DC; April 2016.

Effects of Personal Genotyping and on Student Knowledge and Self-Efficacy

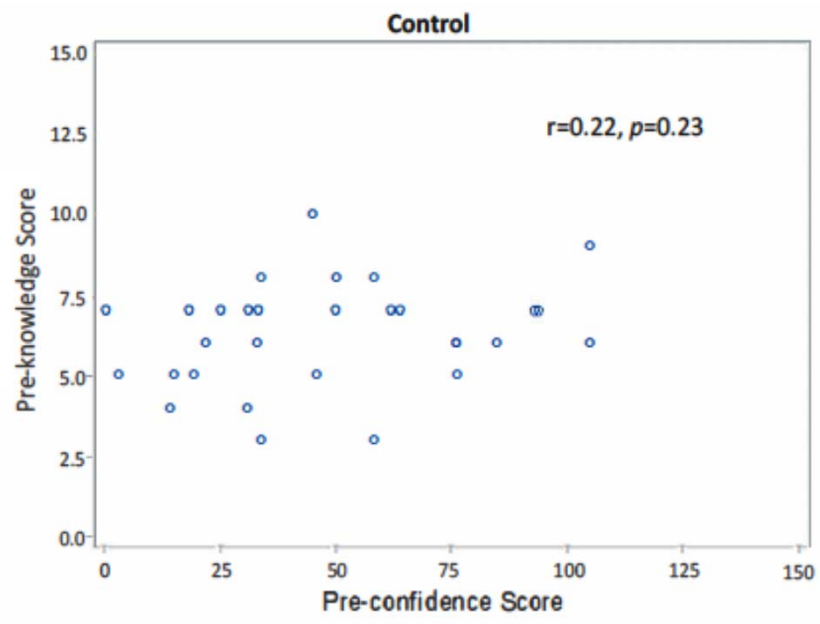
Metrics of student preparedness	Comparison
Knowledge	• Pre knowledge tests scores for intervention vs. control • Post knowledge tests scores for intervention vs. control • 15 case-based questions in "Knowledge of Pharmacogenomics" section (1 per lecture/topic)
Self-efficacy to perform pharmacist's roles in clinical PGx	• Pre vs. Post within each group and intervention vs. control • Questions related to statements from the ASHP Statement on the Pharmacist's Role in Pharmacogenomics
Correlation of confidence with knowledge (i.e., do students actually know what they think they know?)	• Pre- vs. Post correlation of student confidence with knowledge within each group and intervention vs. control • Confidence level with each question in the "Knowledge of Pharmacogenomics" section

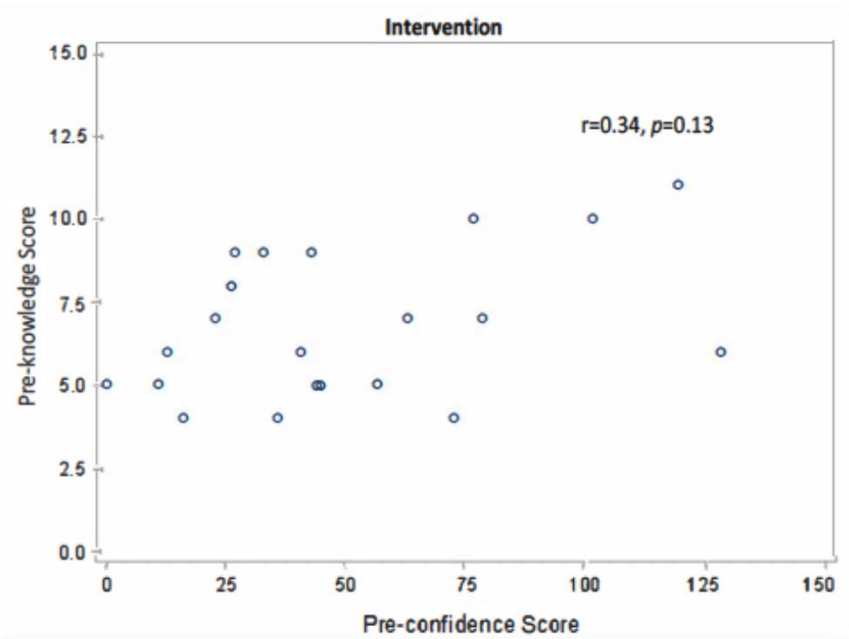
Knowledge Results



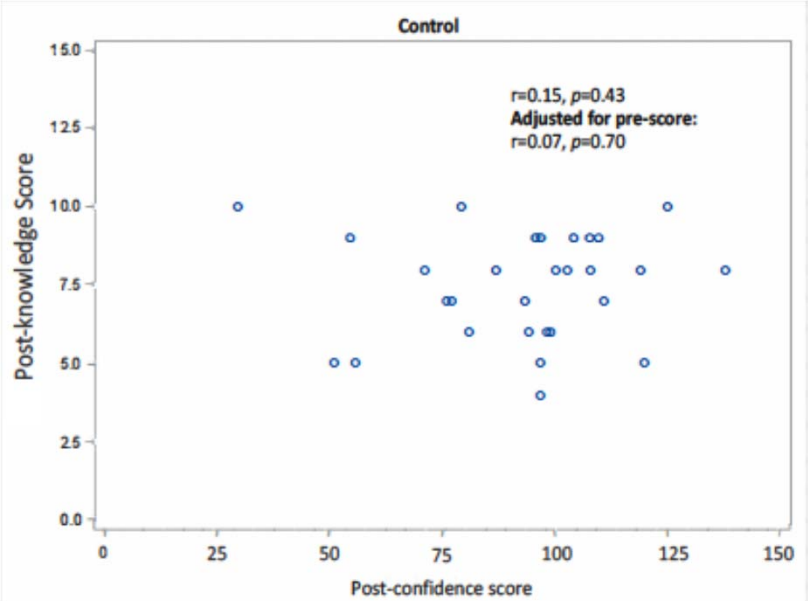


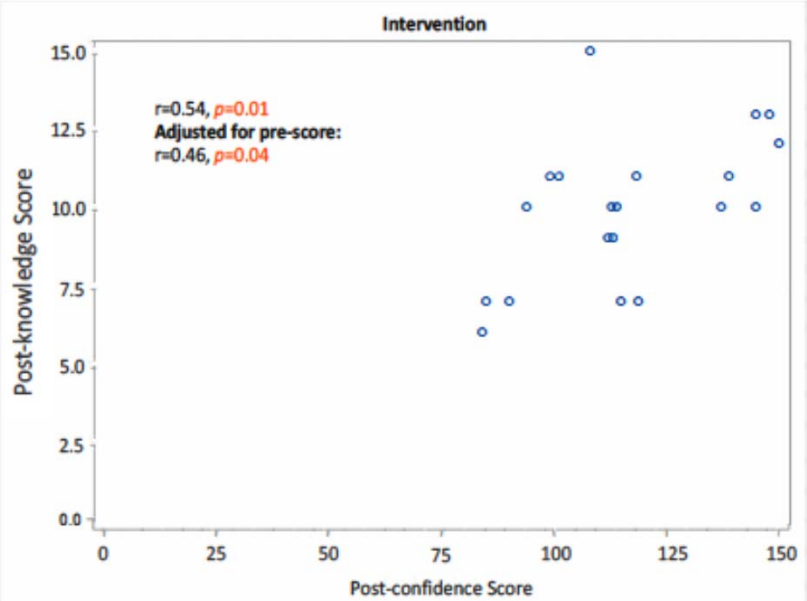
Results of correlation of confidence with knowledge: Pre-survey





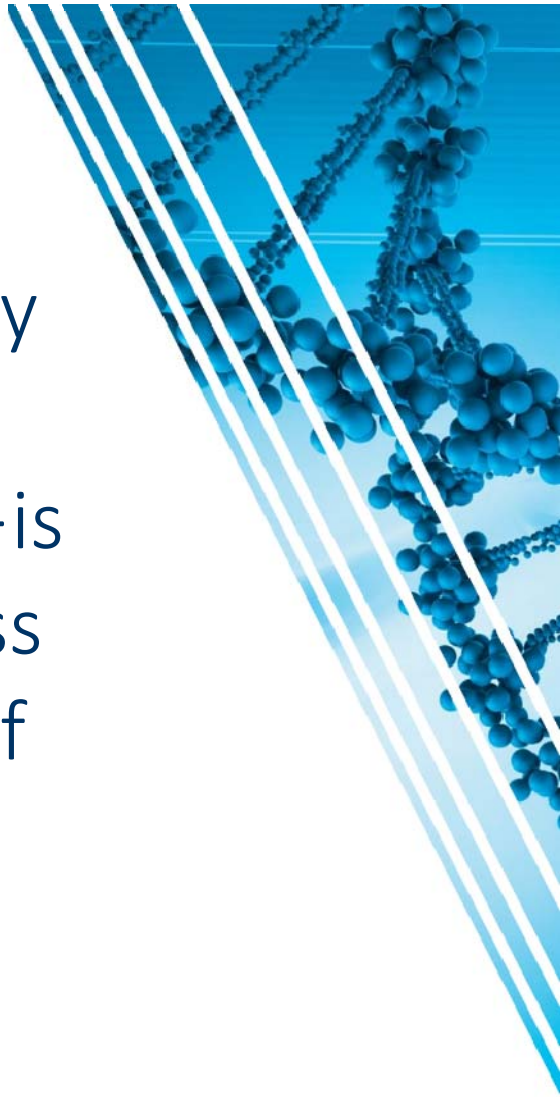
Results of correlation of confidence with knowledge: Post-survey





Why is pharmacogenetics different?

“Humankind will not be well served by this elegant science unless the final step—*provider and public education*—is pursued with the intensity and success that have marked the past 20 years of genomic research.”



Passamani E. Clin Pharmacol Ther. 2013;94:192-5.