Personal Pharmacogenetic Testing Enhances Pharmacy Student Knowledge and

Attitude Towards Precision Medicine

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ABSTRACT

Objective: To evaluate if pharmacy students' participation in personal pharmacogenetic

testing enhances their knowledge and attitude towards precision medicine (PM).

Methods: First-year pharmacy students were offered personalized pharmacogenetic

testing as a supplement to a required curricular pharmacogenomics course. Ninety-

eight of 122 (80%) students completed pre- and post-course surveys assessing

knowledge and attitudes regarding PM; 73 students also volunteered for personal

pharmacogenetic testing of the following drug metabolizing enzymes (*CYP2C19*,

CYP2D6, *UGT1A1*) and pharmacodynamics-relevant proteins (interleukin (IL)-28B &

human lymphocyte antigen HLAB*5701).

Results: An online Likert-based survey was distributed to 1st-year PharmD students.

Using a linear mixed effects model, we observed significant improvements in 100% of

knowledge and 70% of attitude-related questions for students who decided to undergo

pharmacogenetic testing.

Conclusion: Personal pharmacogenetic testing significantly enhances knowledge of

and attitude toward pharmacogenomics among PharmD trainees. This study

demonstrates the feasibility and importance of educating future pharmacists by

incorporating pharmacogenetic testing into professional school curricula.

Keywords: pharmacogenomics, genotyping, pharmacy curriculum, pharmacogenetics,

personal pharmacogenetics

INTRODUCTION

The Human Genome Project laid the groundwork in 2003 for an innovative approach in medicine that we today call Precision Medicine.[1] This new era of medicine is centered around combating human diseases through prevention and treatment, based on lifestyle, environment and genetics, serving as the basis for President Obama's Precision Medicine Initiative in 2015.[2] The idea of tailoring patient care to an individual based on his/her lifestyle is not novel, but the incorporation of large quantities of genetic, environmental, and personal tracking data into the patient profile allows clinicians to make much more efficacious, safe, and cost-effective health care decisions.

The impact of precision medicine in the clinical setting today can be observed through the lens of pharmacogenetics. This term was used as early as 1959, when inter-individual drug response was attributed to genetic variation[3] and is particularly apparent today in the setting of clinical oncology.[4] For example, specific cell surface receptors (e.g., Her2) on tumors, mutated intracellular proteins (e.g., Ras), or unique chimeric proteins (e.g., Bcr-Abl) are novel gene-specific targets[4] that have been markedly successful at providing more targeted therapies and improved patient outcomes. Similarly, widespread HLA-B*1502 testing has dramatically reduced the rate of Stevens-Johnsons syndrome in susceptible populations.[5] Moreover, incorporation of pharmacogenetics information into drug development represents an opportunity to improve the drug candidate pipeline.[6]

Traditional genetic testing for educational purposes is often accompanied by ethical concerns with regards to individuals learning about their potential risks for developing various genetic diseases; this type of testing should be supplemented by

well-planned multi-disciplinary support efforts for students, and a means for them to

access genetic counselors regarding their genetic data.[7-9] We wanted to avoid these

controversial issues by focusing solely on pharmacogenetics, which does not carry the

ethical concerns regarding disease risk. Our study was approved by the University of

California, San Francisco (UCSF) Committee on Human Research.

Pharmacists, physicians and other health care professionals must be adequately

trained to understand and appropriately communicate personal genetic data with other

clinicians and patients in order to clinically incorporate the benefits of our rapidly

expanding understanding of pharmacogenetics. Professional organizations such as the

National Coalition for Health and Professional Education in Genetics, the Association of

American Colleges Contemporary Issues in Medicine, the American College of

Physicians, the American Nurses Association, and the American Association of

Colleges of Pharmacy have defined core competencies relating to pharmacogenomics

for inclusion in their respective professional school curricula.[10-12] Due to the recognition

from these large professional organizations on the importance of educating our future

health care professional, efforts to consistently incorporate pharmacogenomics

education into medical and pharmacy school curricula have been attempted at various

institutions,[3,11,13-16] but further research is necessary to determine the most appropriate

structure to systematize the approach.[7,8]

Investing in the early education of future health professionals is critical in order

for clinicians to keep up with technological and genomic advances. Pharmacists are

essential in helping to usher in this new era of medicine, as they are the recognized

drug experts[17] who specialize in a number of areas: pharmacokinetics,

pharmacodynamics, patient care, managed care, and pharmacogenomics.[18]

Pharmacists are the ideal clinicians to spearhead this movement, and the healthcare

system is beginning to accept this paradigm shift as legislation is passing in numerous

states (California, Montana, and Washington among others) to expand the role that

pharmacists will play in the changing landscape of medicine created by the Affordable

Care Act. The American Society of Health-System Pharmacists (ASHP) and an

increasing number of physicians recognize the importance of pharmacists' role in

evaluating pharmacogenetic tests to guide and improve patient outcomes.[18] ASHP

"believes that pharmacists have a responsibility to take a prominent role in the clinical

application of pharmacogenomics" and recommends that "this emerging science be

spearheaded…by pharmacists to promote safe, effective and cost-efficient medication

practices."[19] With the natural fit of pharmacogenomics under the purview of

pharmacists, it was inevitable for us to empirically determine the impact of personal

pharmacogenetic testing on PharmD students' knowledge and attitude towards

precision medicine at a large, public school of pharmacy.

Based on previous literature demonstrating the benefit of interactive learning in

education,[13,16,17,20] we hypothesized that personal pharmacogenetic testing would

enhance PharmD students' knowledge and attitudes regarding precision medicine.

METHODS

Background

Prior to our current assessment, a smaller pilot study was conducted among first-

year PharmD students at UCSF in the spring of 2013. Twenty-two students enrolled in a

117 required pharmacogenomics course (Biopharmaceutical Sciences (BPS) 115 "Genetics

118 and Pharmacogenetics") volunteered to have their DNA isolated from blood samples

119 and genotyped for variants in *CYP2C19*, a common drug metabolizing enzyme that is

120 important in metabolizing several therapeutic agents including clopidogrel, a widely

121 used anti-platelet agent. The course directors chose to genotype *CYP2C19* because

122 mutations in this gene are known to vary by race, and aside from the ability to

123 metabolize certain drugs, the mutations are not known to convey disease risk. This

124 circumvents potential ethical issues that may arise when disclosing disease risk. Some

125 Universities offering genomic testing for genetic diseases were criticized for failing to

126 provide genetic counseling or conducting testing in a non-CLIA-certified laboratory.[21]

127  The BPS 115 course directors held a lecture session to disclose the results of the

128 students' genotypes. During this session, course directors reviewed the clinical

129 implication in terms of drug metabolism of different variants of *CYP2C19*. Following the

130 session, students organized a focus group to ask faculty more questions and create a

131 space for students to continue sharing their learnings and genotypic information with

132 other interested classmates. Students provided a substantial amount of feedback, which

133 was recorded and used to develop a formal study protocol. They unanimously

134 expressed the value of the testing and use of the results as teaching material for the

135 course. Students discussed why it was compelling and crucial to their future as

136 pharmacists and the future of their profession. A sample of representative, unsolicited

137 student comments regarding their experience include:

139  •  *"I see personal pharmacogenetic testing in the future of pharmacy. It can be time saving.*

140   *It is going to be dependent on factors like whether MDs are willing to order genotyping*

tests instead of starting empirical therapy and dosing, and if we will begin educating our

future clinicians. Implementation will require a new generation of MDs/pharmacists to

lead this movement."

• *"Information outside of academia regarding pharmacogenomics is limited. Many people*

in the public are not aware that testing is even available. As leaders/graduates from this

university, we have to communicate our knowledge to outside communities and the rest

of the world. Having a diverse group of people communicating this information will

spread the word about needing research in more ethnically diverse populations.

Pharmacists will be the most easily accessible group of healthcare practitioners, so

questions about testing will go to us before many in the hospital."

• *"I genuinely enjoyed the class, and I learned a lot. This information inspires me to want*

to look further into why certain populations are fast metabolizers, or slow metabolizer or

do not respond well to certain medications. I would like to personally be involved in

pharmacogenomics in the future during my career."

Survey assessment

Based on the pilot study's overwhelmingly positive feedback, personal

pharmacogenetic testing was incorporated into BPS 115 the following year on a

volunteer basis. One month before the start of the spring 2014 term, a survey was

administered to 122 first-year UCSF School of Pharmacy (SOP) students enrolled in

BPS 115. Selected demographic characteristics of the students are summarized in

Table 1. The survey was designed to assess students' attitudes and knowledge towards

precision medicine and was re-administered to the same students following completion

of the 10-week course. In addition to knowledge- and attitude-assessment questions in

the post-course survey, we also reflection questions, allowing us to assess students'

opinions about participating in pharmacogenetic testing. The knowledge, attitude, and

process measure questions are listed in Supplemental Table 1.

Survey design

The voluntary pre- and post-course survey and pharmacogenetic testing were

approved by the UCSF Committee on Human Research. Written consent and email

addresses were collected from all students who were interested in participating in the

survey. Email addresses were entered into UCSF's Research Electronic Data Capture

(REDCap) system, a secure online utility for conducting surveys. Once a student logged

on to REDCap to take their survey, REDCap would automatically generate and assign

an anonymized, unique identifier linked to the subject's email address. The same

identifier was associated with all surveys that the subject completed.

While the survey asked for basic personal information, REDCap only exported

the assigned identifier with the survey data. To ensure that participation was voluntary,

the names and email addresses associated with the survey results remained restricted

from both primary researchers and course faculty members. Only the primary

researchers were authorized to access the full REDCap data (the course directors were

not involved in the survey-based assessment).

Pharmacogenetic testing

During the course, students had the opportunity to volunteer to have their own

DNA genotyped for several drug metabolizing enzymes as a "hands-on" personal

pharmacogenetic learning experience. This information was used as a teaching

supplement to the course. Participation in the survey and testing was blinded to the

course directors and had no impact on students' grades or performance in the course.

Several days were coordinated to collect de-identified saliva samples from students.

The samples were analyzed in a CLIA-certified laboratory. Students were given the

option to have genotyped either a gene for a drug metabolizing enzyme (*CYP2C19*,

CYP2D6, or *UGT1A1*) or a pharmacodynamics-relevant protein (*IL28B* or *HLAB*5701*).

Each of the genes coding these enzymes/proteins has its own unique clinical implication

and varying allele frequency (and therefore varying activity) among ethnic groups (Table

2). Genotyping results for these genes allow clinicians to properly develop an

appropriate medication regimen tailored for individual patients.

Unveiling of pharmacogenetic results

Once genotyping was completed, students were given their personal

pharmacogenetic information during a regularly scheduled class period for BPS 115; the

class session was divided into two sessions. During the first session, a

pharmacogeneticist was invited to review and discuss each of the genes under

evaluation, their mutations, clinical significance, and how this information might be

incorporated into clinical practice. The first part of the session was didactic, while the

teaching methodology used in the second half of the session emphasized an *active*

learning classroom model in which students were given 15 minutes to share and

discuss among each other, and then initiate an open discussion. During the open

discussion, students engaged in an active question and answer session with each other

and the pharmacogeneticist. Students based many of their questions on their personal

pharmacogenomic data, and expressed interest in strategies for pharmacists to play a

more active role in the future of this specialty. This session did not require specific

preparatory work besides completing assigned readings pertaining to the course and

basic concepts of pharmacogenetics.

Statistical analysis

We defined our outcome as change in knowledge or attitude regarding precision

medicine. Specifically, we assigned integer values to the 5-point Likert scale (i.e., 1 =

strongly disagree, 2 = disagree, 3 = neutral, 4 = agree and 5 = strongly agree) and then

examined the change in Likert scores for each knowledge and attitude question by

calculating the difference between pre- and post-survey responses. For example, a pre-

survey response of 3 (neutral) followed by a post-survey response of 4 (agree) to the

same question would be a gain of 1 Likert point. This difference served as our

dependent variable. Our analysis was stratified into two groups: (1) students who

participated in the personal genotyping and the survey (the genotyped group), and (2)

those who participated in the survey but not in personal genotyping (the non-genotyped

group). The effect of the pharmacogenetic testing on knowledge and attitude was

estimated using linear mixed effects analysis. Variables for sex and race were included

as fixed effects, with a random intercept for student. Estimates whose confidence

intervals excluded the null value were considered statistically significant at an alpha

level of 0.05. Survey results were analyzed using the lme4 package[22] in the R statistical

programming language (R Core Team, 2015).[23]

Expected outcomes included the following three objectives: (1) increasing

understanding of pharmacogenetic concepts and clinical applications, (2) changing

attitude toward precision medicine and clinical integration of pharmacogenetics, and (3)

enhancing classroom learning of the subject matter (pharmacogenomics).

RESULTS

In total, 98 (80%) of the 122 students enrolled in the spring 2014 BPS 115 course

voluntarily completed the pre- and post-course surveys. Of these 98, 73 (74.5%)

students also took part in genotyping, leaving 25 students (25.5%) to comprise the

surveyed but not genotyped group. Attitudinal and knowledge assessment was

performed via an electronic online survey using a Likert scale response format. The 6

knowledge and 10 attitude questions (Supplementary Table 1) are listed in order of

appearance on the pre- and post-course surveys. Baseline scores in knowledge and

attitude were similar for both groups. The mean baseline Likert score for knowledge

questions was (3.03) in the genotyped group and (3.14) in the non-genotyped group.

For the attitude questions, the mean baseline score was (3.85) in the genotyped group

and (3.83) in the non-genotyped group.

Results for change in knowledge and attitude are stratified by genotyping status

in Tables 3 and 4, respectively. To keep our results clinically meaningful, we limited our

analysis to results with a minimum effect size of 0.25 Likert points (i.e., a difference in

means between pre- and post-survey results of 0.25 Likert points). Effect estimates

whose confidence intervals excluded the null value (i.e., 0) were determined to be

statistically significant.

One-hundred percent of responses to the knowledge questions showed

significant improvement between pre- and post-survey assessments, regardless of

whether students participated in genotyping. The smallest increase in estimates was

0.64. The mean change in knowledge across all knowledge questions was not

significantly different between the genotyped (0.99) and non-genotyped (1.05) groups (p

= 0.68). Seventy percent of the attitude questions in students who underwent

genotyping showed a considerable improvement in the pre- and post-Likert scores

(Table 4). Forty percent of the attitudinal questions showed significant improvement

among students in the non-genotyped group. While the mean change in attitude was

slightly higher among those who did not participate in genotyping (0.36) versus those

who did (0.30), the difference was not statistically significant (p = 0.31). The correlation

between pre- and post-survey responses was fairly consistent for knowledge (Pearson's

r = 0.63) and attitude (r = 0.62) questions.

In the genotyped group, the knowledge assessment question with the largest

increase (1.32 Likert points, 95% confidence interval [CI]: 1.10-1.53) asked students to

identify with the following statement: "I am aware of the types of knowledge and

resources needed to interpret a pharmacogenetic test" (Knowledge Question 4,

Supplementary Table 1). Among the non-genotyped group, the knowledge assessment

question with the largest increase (1.32, 95% CI: 1.01-1.63) asked students whether

they "…understand how to evaluate the clinical validity and utility of a pharmacogenetic

test" (Knowledge Question 5, Supplementary Table 1). The attitude assessment

question with the largest increase was the same for genotyped (0.52, 95%CI: 0.34-0.70)

and non-genotyped (0.52, 95%CI: 0.20-0.84) students. This question asked students

whether "Pharmacogenetic testing, when applicable, should be integrated into patient

care" (Attitude Question 6, Supplementary Table 1).

An examination of students' attitudes (n = 98) revealed that students were more

likely to have favorable impressions of precision medicine among those who had

volunteered for personal genotyping versus those who did not get genotyped. Among

the 73 students who were genotyped, 89% said that they were glad to have

participated, and 85% stated that they had a better understanding of the principles of

pharmacogenetics. Furthermore, 76.7% of the genotyped group said they felt more

engaged during BPS 115, and 83.5% agreed that their participation in genotyping

reinforced the concepts taught in the course (Table 5).

For students who did not volunteer to be genotyped, 60% regretted their decision

and the same 60% stated that they would choose to undergo pharmacogenetic testing if

it was offered to them again. Sixty-eight percent of students in the non-genotyped group

stated that concepts taught in the course were reinforced after seeing their classmates

receive their genetic results. Lastly, 68% of students in the non-genotyped group said

they would be interested in participating in more comprehensive genetic testing to learn

about other traits.

DISCUSSION

We found that incorporating genetic testing as an adjunct to School of Pharmacy

PharmD curriculum significantly enhanced students' knowledge and attitudes of

precision medicine. In both the genotyped and non-genotyped groups, there was an

increase in all of the knowledge assessment questions before and after the course. The

significance of this finding is extraordinary as it demonstrates that an interactive hands-

on approach to educating future pharmacists about pharmacogenetics is a fundamental

curricular change that should become commonplace across all professional doctorate

programs in the country. As pharmacogenomics becomes increasingly fundamental for

pharmacists in our health system, knowledge and acceptance of this new era of

precision medicine is required for pharmacists to begin designing and developing

personalized pharmacotherapy.

There were 132 AACP (American Association of College of Pharmacy)

recognized and accredited schools of pharmacy in 2015.[20,24] In 2008-2009, 75 of 109

accredited schools of pharmacy surveyed revealed that 69 (92%) included

pharmacogenomics in their curriculum and 67 (89.3% of total) taught the material at a

PharmD level,[20] but the depth of inclusion was limited. Among these 69 schools

surveyed, the most time spent on the topic of pharmacogenomics was between 31-60

hours, which was observed for only 10 (14.5%) of the schools. Topic coverage was less

than 10 hours in 28 (40.6%), and between 11-30 hours for 29 (42%) of the schools (2

schools did not respond to this question).[20] Based on these numbers, it is evident that

there is much room for pharmacogenomics to be incorporated into pharmacy school

curricula, particularly since the degree of inclusion is still quite low and the majority of

the colleges surveyed did not "have plans for faculty development in the area of

pharmacogenomics content expertise."[20]

In 2009, a study conducted at Temple University School of Pharmacy took a

different approach to increase pharmacy student understanding of pharmacogenomics.

The study involved 70 second-year PharmD students and an analysis of single

nucleotide polymorphisms of the *NAT2* gene based on DNA extracted from their

saliva.[16] The study concluded that a laboratory session in pharmacogenomics was

beneficial in helping students understand the relevance of pharmacogenomic analysis in

designing/creating a patient medication regimen.[8]

Another study by Salari and colleagues conducted at Stanford University's

School of Medicine aimed to increase the depth of pharmacogenomics understanding

by including personalized pharmacogenetic testing as an interactive supplement to an

elective course. That study found a statistically significant impact on enhancing medical

student knowledge and attitudes towards personal genome testing and precision

medicine.[13] It is important to attempt to replicate these results in other graduate

programs across the country, and in the current study we showed that the benefits of

pharmacogenetics testing are applicable to PharmD programs.

Physicians are often unable to address pharmacotherapy based on a patient's

genetics due to time constraints,[25] further justifying the importance of pharmacists in this

new area of precision medicine. Given that pharmacists are the most extensively trained

drug experts[17] in the health care system, the ability to interpret and understand this type

of information falls directly under the purview of their pharmaceutical training. The role

of pharmacists in the healthcare system is expanding, as reflected by recent legislation.

More than 30 states have proposed provider status legislation[26] and two federal bills

H.R. 592 and S. 314 have been introduced to Congress to amend the Social Security

Act to cover pharmacist services under the Medicare program. These types of

legislative initiatives are steps in the right direction to ultimately increase patient access

to care through expansion of pharmacy services.

The results presented in this innovative curricular approach to increasing

knowledge and improving attitudes towards pharmacogenetic testing and precision

medicine are promising. The overwhelming majority (80%) of students completed pre-

and post-course surveys, and 75% of them took part in personal pharmacogenetic

testing, which is significant considering the novelty of this idea to students. In our

experience, the feasibility of implementing personal pharmacogenetic testing across all

US pharmacy school curricula would not be arduous. Student participation was very

high in the absence of incentives; the effort dedicated toward collection and processing

of DNA was fairly minimal; and discussion of genotyping results was limited to only one

class session. Instructors could limit their selection of genetic tests to inexpensive ones

to optimize widespread dissemination of an educational session of this type. Educating

our future providers and providing them with tools to adequately adapt and provide for

their patients in an ever-changing healthcare landscape is an investment that will have

major implications in the future health of our nation.

One of our most noteworthy findings was in regard to Knowledge Question #4

(Supplementary Table 1): "I am aware of the types of knowledge and resources needed

to interpret a pharmacogenetic test." The effect size was fairly large among genotyped

students, (1.32, 95%CI: 1.10-1.53), demonstrating that students felt confident utilizing

their resources to interpret a pharmacogenetic test. This observation suggests that a

curriculum designed to include similar personal pharmacogenetic testing will prepare

students to keep up with the precision medicine revolution and ensure that patients are

being treated by a confident and knowledgeable health care professional.

Sixty-eight percent of non-genotyped students reported that their classmates'

participation in genotyping positively impacted their learning in the course, as described

in the evaluation and assessment section above. This underscores the impact that the

shared experience of personal pharmacogenetic testing had and the potential it has in

educating our providers who do not wish to undergo pharmacogenetic testing

themselves. This information is important when considering curricular redesign as it

allows various interventions or combinations of them to be utilized to achieve maximal

learning outcomes. Sixty percent of the non-genotyped students also mentioned that

they regretted their decision not to volunteer for personal pharmacogenetic genotyping.

It is evident that the experience is a shared and interactive one that not only stems from

one's own personal pharmacogenetic information, but also from that of his/her peers.

Potential biases should be considered when reviewing the results of our study.

Some unmeasured characteristics of genotyped students (e.g., attitudes toward

providing biological samples) may have differed from non-genotyped students such that

comparison of pre-/post- results between these two groups would not be valid (i.e.,

selection bias). However, we found no significant difference in baseline knowledge or

attitude between the two groups. Nonetheless, it is possible that participants who

elected to be genotyped would be more receptive to pharmacogenetics and thus that

their attitudes would improve by a larger share than those who elected not to be

genotyped. Although we found that 40% of the attitude questions showed a significant

improvement among students who elected not to be genotyped, compared to 70% for

those students in the genotyped group, the results for the non-genotyped group may

have been underpowered given the smaller number of students who chose to be

genotyped (25 versus 73). Given that the effect estimates for all knowledge and attitude

assessment questions were positive, regardless of genotyping status, we feel that the

influence of this type of selection bias is minimal. Our analyses were conducted under

the assumption that the intervals between Likert values are equal. We felt it reasonable,

for example, to assume that "Agree" is halfway between "Neutral" and "Strongly agree;"

this is a common assumption practiced in analysis of survey results.[27]

Our study did not show significant differences between the genotyped and non-

genotyped groups with respect to attitudes or knowledge of pharmacogenetics testing.

This may have been due to the relatively few number of students who elected not to be

genotyped (n = 25), which reduced statistical power to detect a difference. In addition, it

is likely that even students who elected not to be genotyped benefitted from the

exercise of discussing the results of their classmates and also from the *active

classroom model* in which genotyped students were given 15 minutes to share and

discuss results with all students, followed by an open discussion. Our results appear to

be consistent with a recent report, which described the incorporation of cadaver exome

sequencing into first-year medical student curriculum as a form of active learning. It was

demonstrated that this active and team based type learning was a potentially powerful

educational innovation which helps to improve their genetic knowledge base.[28] In that

report, students benefitted from a discussion of genetics made relevant to them without

being genotyped directly. Thus, it is possible that pharmacogenetics testing of a subset

of students had benefits on the entire classroom.

In order to overcome these limitations, a future cluster-based randomized study

with several pharmacy school curricula could be implemented. In addition, long-term

follow-up with these students would allow study of the lasting effects that personal

pharmacogenetic testing has had on their personal and professional lives. Furthermore,

we hope that this study serves as a means to further accelerate the dissemination of

personal pharmacogenetic testing into US pharmacy school curricula.

SUMMARY

Pharmacy students in their first year of the PharmD curriculum showed

significant enhancements in their knowledge and attitudes towards precision medicine

after participating in personalized pharmacogenetic testing. Even students who were

enrolled in the course but did not partake in personalized pharmacogenetic testing had

an enhancement in knowledge and attitude about precision medicine, likely as a result

of engagement with their classmates and faculty regarding the results.

Incorporation of personal pharmacogenetic testing into pharmacy school

curricula is a simple and efficacious method of educating our future health care

professionals. Personal pharmacogenetic testing continues at UCSF through the School

of Pharmacy's BPS 115 course with further goals of incorporating it into the core

curriculum. We believe that the new era of Precision Medicine ushered in by President

Obama's Precision Medicine Initiative will only be successful if coupled with education

of a new generation of health care providers. Herein, we have demonstrated that this

novel educational approach has a profoundly positive impact on the next generation of

pharmacists, who by law will have an expanding role as the front line providers of

healthcare.

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REFERENCES

1. Bahcall O. Precision medicine. *Nature*. 2015;526(7573):335.
    doi:10.1038/526335a.

2. NIH framework points the way forward for building national, large-scale research
    cohort, a key component of the President's Precision Medicine Initiative | National
    Institutes of Health (NIH). http://www.nih.gov/news-events/news-releases/nih-
    framework-points-way-forward-building-national-large-scale-research-cohort-key-
    component-presidents-precision-medicine-initiative. Accessed January 4, 2016.

3. Brazeau D a., Brazeau G a. A required course in human genomics,
    pharmacogenomics, and bioinformatics. *Am J Pharm Educ*. 2006;70(6):1-6.
    doi:10.5688/aj7006125.

4. Rao US, Rao PS. Pharmacogenomics Strategies for implementation of an
    effective pharmacogenomics program in pharmacy education. *Am J Pha*.
    2015;16:905-911.

5. Chen P, Lin J-J, Lu C-S, et al. Carbamazepine-induced toxic effects and HLA-
    B*1502 screening in Taiwan. *N Engl J Med*. 2011;364(12):1126-1133.
    doi:10.1056/NEJMoa1009717.

6. Harper AR, Topol EJ. Pharmacogenomics in clinical practice and drug
    development. *Nat Biotechnol*. 2012;30(11):1117-1124. doi:10.1038/nbt.2424.

7. Vernez SL, Salari K, Ormond KE, Lee SS-J. Personal genome testing in medical
    education: student experiences with genotyping in the classroom. *Genome Med*.
    2013;5(3):24. doi:10.1186/gm428.

8. Walt DR, Kuhlik A, Epstein SK, et al. Lessons learned from the introduction of

personalized genotyping into a medical school curriculum. *Genet Med*.

2011;13(1):63-66. doi:10.1097/GIM.0b013e3181f872ac.

9.   Taylor ATS, Rogers JC. The ethical implications of genetic testing in the

classroom. *Biochem Mol Biol Educ*. 2011;39(4):253-260. doi:10.1002/bmb.20521.

10. Lee KC, Hudmon S, Joseph D. Pharmacogenomics Evaluation of a shared

pharmacogenomics. *Futur Sci Gr*. 2015;16:315-322.

11. Nickola TJ, Munson AM. Pharmacogenomics primer course for first professional

year pharmacy students. *Pharmacogenomics*. 2014;15(1):39-48.

doi:10.2217/pgs.13.197.

12. Accreditation Council for Pharmacy Education. Accreditation Standards and Key

Elements for the Professional Program in Pharmacy Leading to the Doctor of

Pharmacy Degree. 2015:39. https://www.acpe-

accredit.org/pdf/Standards2016FINAL.pdf.

13. Salari K, Karczewski KJ, Hudgins L, Ormond KE. Evidence That Personal

Genome Testing Enhances Student Learning in a Course on Genomics and

Personalized Medicine. *PLoS One*. 2013;8(7):1-8.

doi:10.1371/journal.pone.0068853.

14. Springer J a., Iannotti N V., Kane MD, Haynes K, Sprague JE.

Pharmacogenomics training using an instructional software system. *Am J Pharm*

Educ. 2011;75(2):32. doi:10.5688/ajpe75232.

15. Lee K, Ma J, Hudmon KS, Kuo GM. A train-the-trainer approach to a shared

pharmacogenomics curriculum for US colleges and schools of pharmacy. *Am J*

Pharm Educ. 2012;76(10):193. doi:10.5688/ajpe7610193.

16.   Krynetskiy E, Lee Calligaro I. Introducing pharmacy students to

pharmacogenomic analysis. *Am J Pharm Educ.* 2009;73(4):71.

http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2720367&tool=pmcentr

ez&rendertype=abstract.

17.   McCullough KB, Formea CM, Berg KD, et al. Assessment of the

pharmacogenomics educational needs of pharmacists. *Am J Pharm Educ.*

2011;75(3):51. doi:10.5688/ajpe75351.

18.   Zeevaart JG, Wang L, Thakur V V, et al. Emerging Roles for Pharmacists in

Clinical Implementation of Pharmacogenomics. *NIH Public Access.*

2009;130(29):9492-9499. doi:10.1021/ja8019214.Optimization.

19.   Haidar C-E, Hoffman JM, Johnson SG, Relling M V, Crews KR. ASHP Statement

on the Pharmacist's Role in Clinical Pharmacogenomics. *Am J Heal Pharm.*

2015;72(7):579-581. doi:10.2146/sp150003.

20.   Murphy JE, Green JS, Adams LA, Squire RB, Kuo GM, McKay A.

Pharmacogenomics in the curricula of colleges and schools of pharmacy in the

United States. *Am J Pharm Educ.* 2010;74(1):7. doi:10.5688/aj690223.

21.   Callier SL. Swabbing students: should universities be allowed to facilitate

educational DNA testing? *Am J Bioeth.* 2012;12(4):32-40.

doi:10.1080/15265161.2012.656803.

22.   Bates D, Maechler M, Bolker B, Walker S. Fitting Linear Mixed-Effects Models

Using {lme4}. 2015:1-48. doi:10.18637/jss.v067.i01.

23.   Team RC. R: A Language and Environment for Statistical Computing. 2015.

http://www.r-project.org/.

24. AACP. AACP - Academic Pharmacy's Vital Statistics.

http://www.aacp.org/about/pages/vitalstats.aspx. Accessed February 1, 2016.

25. Brock TP, Faulkner CM, Williams DM, Smith SR. Continuing-education programs

in pharmacogenomics for pharmacists. *Am J Health Syst Pharm*. 2002;59(8):722-

725. http://www.ncbi.nlm.nih.gov/pubmed/11977857.

26. APHA. More states address pharmacists' provider status recognition | American

Pharmacists Association. *Am Pharm Assoc*. https://www.pharmacist.com/more-

states-address-pharmacists-provider-status-recognition. Accessed January 26,

2016.

27. Garson GD. Testing Statistical Assumptions. *Blue B Ser*. 2012:1-52.

http://www.statisticalassociates.com/assumptions.pdf.

28. Gerhard GS, Paynton B, Popoff SN. Integrating Cadaver Exome Sequencing Into

a First-Year Medical Student Curriculum. *JAMA*. January 2016:1-2.

doi:10.1001/jama.2015.19465.

29. Bernard S, Neville KA, Nguyen AT, Flockhart A. Interethnic Differences in Genetic

Polymorphisms of CYP2D6 in the U.S. Population: Clinical Implications.

Oncologist. 2006:126-135.

30. Mizutani T. PM frequencies of major CYPs in Asians and Caucasians. *Drug

Metab Rev*. 2003;35(2-3):99-106. doi:10.1081/DMR-120023681.

31. Zhou S-F, Liu J-P, Chowbay B. Polymorphism of human cytochrome P450

enzymes and its clinical impact. *Drug Metab Rev*. 2009;41(2):89-295.

doi:10.1080/03602530902843483.

32. Desta Z, Zhao X, Shin J-G, Flockhart D a. Clinical significance of the cytochrome

538 P450 2C19 genetic polymorphism. *Clin Pharmacokinet*. 2002;41(12):913-958.

539 doi:10.2165/00003088-200241120-00002.

540 33. Burchell B, Hume R. Molecular genetic basis of Gilbert's syndrome. *J*

541 *Gastroenterol Hepatol*. 1999;14(10):960-966. doi:10.1046/j.1440-

542 1746.1999.01984.x.

543 34. Martin M a, Hoffman JM, Freimuth RR, et al. Clinical Pharmacogenetics

544 Implementation Consortium Guidelines for HLA-B Genotype and Abacavir Dosing:

545 2014 update. *Clin Pharmacol Ther*. 2014;95(5):499-500.

546 doi:10.1038/clpt.2014.38.

547 35. Lexicomp. IL28B in Pharmacogenomics. Lexicomp. *Wolter Kluwer*. 2016.

548 http://www.crlonline.com.ucsf.idm.oclc.org/lco/action/doc/retrieve/docid/genom_f/3

549 583763. Accessed January 16, 2016.

Table 1: Gender and Race/Ethnicity of Participants and Nonparticipants		
Characteristic	**Genotyped Group N = 73**	**Non-Genotyped Group N = 25**
Percent female	71.2	60.0
Race/Ethnicity	N (%)	N (%)
Hispanic	0 (0.0%)	1 (4.0%)
Black	1 (1.40%)	1 (4.`0%)
White	15 (20.5%)	4 (16.0%)
Asian	41 (56.2%)	17 (68.0%)
Other*	14 (19.2%)	2 (8.00%)
Pacific Islander	2 (2.70%)	0 (0.00%)

Table 2: Drug Metabolizing Enzymes, Function, and Mutation Frequencies		
Enzyme (reference)	**Function**	**Decreased Function Mutation Frequency by Race**
CYP2D6[29–31]	Affects large numbers of drugs, notably analgesics, tamoxifen, and antidepressants and medications for attention deficit disorder.	Black:0-5% Caucasian: 5-14% Asian: 0-1%
CYP2C19[30–32]	Affects cardiovascular drugs including clopidogrel and proton pump inhibitors and some antidepressant medications	Black: 5% Caucasian: 2-5% Asian: 19%
UGT1A1[33]	Affects some anticancer drugs and is responsible for hyperbilirubinemia induced by Gilbert's syndrome.	Black: 19% Caucasian: 8% Asian: 2%
HLAB*5701[34]	When present can cause Stevens Johnson Syndrome and delayed hypersensitivity mostly among Asians.	Black: 1% Caucasian: 6-7% Asian: up to 20%
IL28b[35]	C/C Alleles predicts drug efficacy towards chronic hepatitis C infections	Black: 24-50% Caucasian: 8-13% Asian: 0-1%

Table 3: Knowledge Assessment in Participants and Non Participants [a]				
	Genotyped Group N = 73		**Non-Genotyped Group N = 25**	
Question	**Estimate Change**	**95% CI**	**Estimate**	**95% CI**
I am aware of the types of knowledge and resources needed to interpret a pharmacogenetic test result.	1.32[a]	1.10 – 1.53 [a]	1.12 [a]	0.81 – 1.43 [a]
I understand how to evaluate the clinical validity and utility of a pharmacogenetic test.	1.18 [a]	0.95 – 1.41 [a]	1.32 [a]	1.01 – 1.63 [a]
I understand how a pharmacogenetic test differs from a genetic test for disease risk.	1.18 [a]	0.96 – 1.40 [a]	0.96 [a]	0.61 – 1.31 [a]
I understand what a pharmacogenetic test is.	0.89 [a]	0.72 – 1.06 [a]	1.20 [a]	0.81 – 1.59 [a]
I understand the risks, benefits, and ethical considerations of personal genetic testing.	0.71 [a]	0.51 – 0.91 [a]	0.84 [a]	0.43 – 1.25 [a]
I understand what precision medicine is.	0.64 [a]	0.48 – 0.80 [a]	0.84 [a]	0.44 – 1.24 [a]
[a]Statistically significant, clinically meaningful effect sizes				

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Table 4: Attitude Assessment in Participants and Non Participants [a]				
	Genotyped Group N = 73		**Non-Genotyped Group N = 25**	
Question	**Estimate Change**	**95% CI**	**Estimate**	**95% CI**
Pharmacogenetic testing, when applicable, should be integrated into patient care.	0.52 [a]	0.34 – 0.70 [a]	0.52 [a]	0.20 – 0.84 [a]
I would recommend pharmacogenetic testing for a patient.	0.41 [a]	0.17 – 0.65 [a]	0.48 [a]	0.09 – 0.87 [a]
I would recommend pharmacogenetic testing for a family member.	0.40 [a]	0.17 – 0.62 [a]	0.44 [a]	0.05 – 0.83 [a]
Pharmacogenetics should be integrated into the curricula at all pharmacy schools.	0.38 [a]	0.22 – 0.55 [a]	0.36	-0.05 – 0.77
The use of personal genetic information in health care is beneficial to patients.	0.33 [a]	0.16 – 0.50 [a]	0.20	-0.16 – 0.56
Pharmacists should be trained to interpret and apply pharmacogenetic test results.	0.30 [a]	0.13 – 0.48 [a]	0.44 [a]	0.16 – 0.72 [a]
In addition to factors like age, race, and drug interactions, genetic information is an important consideration during routine clinical practice.	0.26 [a]	0.04 – 0.48 [a]	0.28	-0.03 – 0.59
Pharmacists play a crucial role in the future of precision medicine.	0.22	0.06–0.38	0.24	-0.09 – 0.57
Pharmacogenetics will likely play an important role in my future career.	0.10	-0.10 – 0.29	0.28	-0.07 – 0.63
The use of personal genetic information in health care may cause unnecessary harm to patients.	0.03	-0.26 – 0.31	0.32	-0.21 – 0.85
[a]Statistically significant, clinically meaningful effect sizes				

Question	Genotyped Group N = 73			Non-Genotyped Group N = 25		
	Disagree + Strongly Disagree, N (%)	Neutral, N (%)	Agree + Strongly Agree, N (%)	Disagree + Strongly Disagree, N (%)	Neutral, N (%)	Agree + Strongly Agree, N (%)
I am glad that I participated in the pharmacogenetic testing.	2 (3%)	6 (8%)	65 (89%)	na	na	na
I believe that I have a better understanding of the principles of pharmacogenetics on the basis of having undergone personal pharmacogenetic testing	1 (1.4%)	10 (13.6%)	62 (85%)	na	na	na
I felt more personally engaged during BPS115 because I had undergone the pharmacogenetic testing.	3 (4%)	14 (19%)	56 (77%)	na	na	na
My participation in the pharmacogenetic testing reinforced the concepts taught in BPS115	2 (2.7%)	10 (13.8%)	61 (83.5%)	na	na	na
I regret that I did not participate in the pharmacogenetic testing.	na	na	na	5 (20%)	5 (20%)	15 (60%)
Seeing my classmates' genetic results reinforced the concepts taught in BPS115	na	na	na	1 (4%)	7 (28%)	17 (68%)
I would be interested in participating in more comprehensive genetic testing to learn about other traits.	na	na	na	1 (4%)	7 (28%)	17 (68%)
If offered to me again, I would choose to undergo pharmacogenetic testing.	na	na	na	2 (8%)	8 (32%)	15 (60%)

Table 5: Reflections of Participants and Non Participants

Supplementary Table 1. Knowledge and Attitude Assessment Questions from Pre and Post Survey
Knowledge
1. I understand what precision medicine is.
2. I understand what a pharmacogenetic test is.
3. I understand how a pharmacogenetic test differs from a genetic test for disease risk.
4. I am aware of the types of knowledge and resources needed to interpret a pharmacogenetic test result.
5. I understand how to evaluate the clinical validity and utility of a pharmacogenetic test.
6. I understand the risks, benefits, and ethical considerations of personal genetic testing.
Attitude
1. The use of personal genetic information in health care is beneficial to patients.
2. The use of personal genetic information in health care may cause unnecessary harm to patients.
3. In addition to factors like age, race, and drug interactions, genetic information is an important consideration during routine clinical practice.
4. I would recommend pharmacogenetic testing for a patient.
5. I would recommend pharmacogenetic testing for a family member.
6. Pharmacogenetic testing, when applicable, should be integrated into patient care.
7. Pharmacists should be trained to interpret and apply pharmacogenetic test results.
8. Pharmacogenetics should be integrated into the curricula at all pharmacy schools.
9. Pharmacogenetics will likely play an important role in my future career.
10. Pharmacists play a crucial role in the future of precision medicine.
Reflection
1. I am glad that I participated in the pharmacogenetic testing.
2. I believe that I have a better understanding of the principles of pharmacogenetics on the basis of having undergone personal pharmacogenetic testing
3. I felt more personally engaged during BPS115 because I had undergone the pharmacogenetic testing.
4. My participation in the pharmacogenetic testing reinforced the concepts taught in BPS115
5. I regret that I did not participate in the pharmacogenetic testing.
6. Seeing my classmates' genetic results reinforced the concepts taught in BPS115
7. I would be interested in participating in more comprehensive genetic testing to learn about other traits.
8. If offered to me again, I would choose to undergo pharmacogenetic testing.