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 (Pgx) 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: Using a linear mixed effects model, we observed statistically significant improvements in 100% of knowledge and 70% of attitude-related questions for students who decided to undergo personal pharmacogenetic testing.

Conclusion: Personal pharmacogenetic testing significantly enhances knowledge of and attitude related to precision medicine 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 to 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 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.[4–6]

In order for this new era of "precision medicine" to become accepted into clinical practice, we must start by educating our future healthcare providers and clinicians. In our current landscape there have been a number of studies[3,7–14] with promising outcomes regarding the impact of including some form of pharmacogenomics-related education in graduate school curricula. Unfortunately, the uptake into U.S. pharmacy programs still remains minimal. This is evident by a report in 2010 that surveyed the number of hours U.S. pharmacy schools were dedicating to pharmacogenomics-related education. Only 14.5% of schools surveyed spent between 31-60 hours on pharmacogenomics-related topics, and a majority of respondents described the present state of pharmacogenomics instruction at most schools of pharmacy as "poor."[15]

Efforts at using genotyping as a teaching supplement have been described,[7,8,11–14] catalyzing the movement towards the adoption of pharmacogenomics into graduate school curricula. Our study aims to add to this body of knowledge by providing personal pharmacogenetic testing to first year pharmacy students as an adjunct to a curricular

pharmacogenomics course to gauge the impact on knowledge and attitude. This project is innovative as it emphasizes several key themes: 1. students have the autonomy to choose the most relevant gene to have genotyped based on their race or personal desire; 2. the project is the result of a student-led initiative; 3. the project focuses solely on pharmacogenetic variants, avoiding potential controversy that some direct-to-consumer tests faced when providing disease risk assessments; 4. the implementation is feasible; and 5. the findings are very robust.

METHODS

Background

Prior to our current assessment, a smaller pilot study was conducted among first-year PharmD students at UCSF. Biopharmaceutical Sciences (BPS) 115 ("Genetics and Pharmacogenetics") is a required (curricular) pharmacogenomics course in the School of Pharmacy. Objectives for BPS 115 are broadly based and derived from components of genetic competencies put forth by the Accreditation Council for Pharmacy Education.[16] Twenty-two students enrolled in the spring 2013 BPS 115 course volunteered to have their DNA isolated from blood samples and genotyped for variants in *CYP2C19*, a common drug metabolizing enzyme that is important in metabolizing several therapeutic agents including clopidogrel, a widely used anti-platelet agent. The course directors chose to genotype *CYP2C19* because variants in this gene are known to vary by race, and aside from the ability to metabolize certain drugs, the variants are not known to convey disease risk. This circumvents potential ethical issues that may arise when disclosing disease risk. Some universities offering genomic testing for

genetic diseases were criticized for failing to provide genetic counseling or conducting testing in a non-CLIA-certified laboratory.[17]

The BPS 115 course directors held a lecture session to disclose the results of the students' genotypes. During this session, course directors reviewed the clinical implication in terms of drug metabolism of different variants of *CYP2C19*. Following the session, students organized a focus group to ask faculty more questions and create a space for students to continue sharing their learnings and genotypic information with other interested classmates. Students provided a substantial amount of feedback, which was recorded and used to develop a formal study protocol. They unanimously expressed the value of the testing and use of the results as teaching material for the course. Students discussed why it was compelling and crucial to their future as pharmacists and the future of their profession. A sample of representative, unsolicited student comments regarding their experience include:

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

Based on the pilot study's overwhelmingly positive feedback, personal pharmacogenetic testing was incorporated into BPS 115 the following year on a volunteer basis. BPS 115 is part of the core curriculum at the UCSF School of Pharmacy. However, voluntary personal pharmacogenetic testing was temporarily added into the course during the spring 2014 term. One month before the start of the term, an online Likert survey was administered to 122 first-year UCSF School of Pharmacy (SOP) students enrolled in BPS 115.

Survey development was informed by the focus group conducted among the 22 students from the spring 2013 BPS 115 class. We used students' responses to identify themes to guide development of questions designed to assess students' attitudes and knowledge towards precision medicine. A draft of the survey was then piloted among a sample of second-year pharmacy students; these results were used to fine-tune the survey. First-year students were excluded from the design process to avoid influencing them during the actual assessment. We chose a Likert-based response format because

its common use lends itself to easy understanding by respondents, and their answers can easily be quantified and used in statistical tests. Survey questions are summarized in Supplementary Table 1.

The survey was re-administered to the same first-year students following completion of the 10-week course. In addition to knowledge- and attitude-assessment questions in the post-course survey, we also asked separate reflection questions, allowing us to assess students' opinions about participating in pharmacogenetic testing. The knowledge, attitude, and reflection questions are listed in Supplemental Table 1.

Expected outcomes included the following three objectives: (1) increasing understanding of pharmacogenetic concepts in relation to clinical applications, (2) changing attitude toward precision medicine and clinical integration of pharmacogenetics, and (3) enhancing classroom learning of the subject matter (pharmacogenomics).

Survey Assessment

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 login information. The same identifier was

associated with all surveys that the subject completed ensuring no surveys were lost due to individuals forgetting their own self-assigned survey numbers.

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 de-identified 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 as a supplement to the curricular course (BPS 115). Several days were coordinated to collect de-identified saliva samples from students. The samples were analyzed in a UCSF-affiliated CLIA-certified laboratory at San Francisco General Hospital at the rate of $50 per genotype. For the 73 students who participated in genotyping, the total cost was $3,650, which excludes the time the laboratory donated to analyze the samples. Genotyping costs were generously covered by the UCSF School of Pharmacy. Since genotyping was not performed through a commercial supplier, the results were ready much sooner than the 3-6 week turnaround time often seen with direct to consumer genetic testing companies. The total time for participant consent and recruitment, DNA collection, genotyping, and presentation of the data was approximately 150 person-hours. 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 1).

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 variants, clinical significance, and how this information might be incorporated into clinical practice illustrated through clinical cases. At the end of this discussion, the pharmacogeneticist displayed each of the possible genes via PowerPoint slides and revealed each of the possible variants. Next to each variant was a list of anonymized identifiers so that students were able to privately determine their individual genotype status. 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 discuss the cases presented by the pharmacogeneticist among each other, and then initiate an open discussion about how different variants may affect pharmacologic or medical management. During the open discussion, students engaged in an active question and answer session with each other and the pharmacogeneticist; discussions were centered around the presented pharmacogenetic information and clinical cases. Students based

many of their questions and comments on their personal pharmacogenomic data as they discussed potential pharmacologic alternatives and pharmacologic interventions (e.g., dose reductions, discontinuation of meds, drug-drug interactions) to account for potential variants. Additionally, students 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 attending the course lectures and completing assigned readings[18–20] throughout the course (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. We used a linear mixed effect approach to account for unmeasured time-dependent variables. For example, the passage of time

between the pre- and post-course surveys could have influenced knowledge and attitude independently of the curriculum and our study. In addition, this approach also allows us to estimate the effect of the curriculum after accounting for sex and race, unlike a bivariate statistic (e.g., T-test). 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[21] in the R statistical programming language (R Core Team, 2015).[22]

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. Selected demographic characteristics of the students are summarized in Table 2. The genotyped group had significantly more females than the non-genotyped group but the two groups did not significantly differ by race/ethnicity. Attitudinal and knowledge assessment was performed via an electronic online survey using a Likert scale response format. 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.

The results for change in knowledge and attitude are stratified by genotyping status and summarized in Figures 1 and 2, respectively. 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). This was set as an arbitrary cut-off, and we concluded that any positive change in the Likert scale that is at least 0.25 points and 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 statistically significant improvement between pre- and post-survey assessments, regardless of whether students participated in genotyping. The smallest increase in estimates was 0.64, which is more than double our minimum effect size cut-off of 0.25. 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 statistically significant improvement in the pre- and post-Likert scores. In the non-genotyped group, however, only forty percent of the attitudinal questions showed significant improvement. 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 and re-titled “Interpreting Pgx tests in Figure 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, and shown in Figure 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). The 95% confidence interval for this question, however, was much narrower and more robust for the genotyped group as illustrated in Figure 2.

We also asked students to reflect on their experiences being a part of this pilot project. We categorized these reflections as “genotyped group” versus “non-genotyped group.” Students were more likely to have favorable impressions of precision medicine if they were in the genotyped group versus those in the non-genotyped group. 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, 77% 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 3).

For the non-genotyped group, 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 (Table 3).

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 study. This finding provides strong support that an interactive hands-on approach to educating future pharmacists about pharmacogenetics is a fundamental curricular change that would benefit professional doctorate programs. 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.

Efforts at pharmacogenetics education have been made in the past. A genotyping exercise was piloted in 2009 by Knoell et al. at The Ohio State University[13] where authors collected DNA samples from 10 PharmD student volunteers to genotype the Angiotensin Converting Enzyme (ACE) gene. Results were presented and

discussed in a classroom setting in the context of a patient-counseling workshop. Their Likert-based survey results demonstrated that 85% of students either agreed or strongly agreed that "the genotyping exercise was beneficial in terms of helping them better connect to course content."[13] Nearly one-third of those students also stated that they would have liked to see more relevant genes being tested. This observation underscores why our study emphasized students' autonomy regarding which gene they chose to be genotyped for.

A 2009 study conducted at Temple University School of Pharmacy took a laboratory based 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.[8] 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] Similarly, a pilot study by Kisor et al. explored a curricular based laboratory course in which PharmD students used their own DNA (buccal swab) to genotype cytochrome P450 2C19 using PCR and gel electrophoresis. These results were successfully used to arrive at a "clinical decision" based on a dosing algorithm relative to the use of clopidogrel.[11]

Another innovative study in 2013 by Salari and colleagues conducted at Stanford University's School of Medicine included personalized pharmacogenetic testing as an interactive supplement to an elective course for medical students. That study found a statistically significant impact on enhancing medical student knowledge and attitudes towards personal genome testing and precision medicine.[7] In 2014 at Ohio Northern

University, Bova et al. implemented a web-blog based introduction to pharmacogenetics and precision medicine as an elective course in the PharmD curriculum. Although students did not undergo personal pharmacogenetic testing, results of a pre- and post-course survey demonstrated a statistically significant improvement in a majority of questions relating to students' knowledge of pharmacogenetics and precision medicine.[12]

Most recently in 2016, Adams et al. published promising results from the University of Pittsburgh demonstrating significant improvements in PharmD students' knowledge and attitude after participating in personal pharmacogenetic testing. Students were genotyped using commercial genetic testing supplied by 23andMe,[14] which raised some questions about the potential to discover undesired information about genetic disease risk. Efforts were made to mitigate this risk by focusing on pharmacogenetics genes, but the raw data provided by 23andMe to each consumer includes data about other non-pharmacogenetic genes. The ethics of uncovering genetic disease risk is a serious consideration when choosing how to provide personal pharmacogenetic testing to students. In our study, we desired to eliminate the chance of conveying any sort of disease risk by focusing on a selected number of genes that were solely pharmacogenetically relevant.

The results presented in our innovative curricular approach to increasing knowledge and improving attitudes towards pharmacogenetic testing and precision medicine are encouraging. 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 and our

curriculum. Based on our experience, implementing personal pharmacogenetic testing across all US pharmacy school curricula would not be extremely arduous. Student participation was very high in the absence of incentives; the time and effort dedicated toward collection and processing of DNA was fairly minimal; performing genotyping in-house was orders of magnitude less expensive than commercially available tests; and the 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 a worthwhile investment if we wish to adequately incorporate pharmacogenetics into medical practice.

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

391 educating our providers who do not wish to undergo pharmacogenetic testing
392 themselves. Although the impact was less for the non-genotyped group, specifically in
393 terms of attitudinal assessment, this information is still important when considering
394 curricular redesign as it allows various interventions or combinations of them to be
395 utilized to achieve maximal learning outcomes. Sixty percent of the non-genotyped
396 students also mentioned that they regretted their decision not to volunteer for personal
397 pharmacogenetic genotyping, which illustrates how the idea of Pgx is still new and will
398 require some more research and time to become commonplace. It is evident that the
399 experience is a shared and interactive one that not only stems from one's own personal
400 pharmacogenetic information, but also from that of his/her peers.

401 Barriers to the acceptance of Pgx are multi-faceted and one method for
402 increasing acceptance is to break inter-professional barriers. Calinski and Kisor provide
403 an example of lessons learned when physician assistant students and pharmacy
404 students discuss cases related to the pharmacogenomics of Plavix (clopidogrel).[10] It is
405 important that health care professionals understand not only their roles and impact in
406 regards to precision medicine and Pgx but also the impact and role of their health care
407 professional counterparts.

408 Potential biases should be considered when reviewing the results of our study.
409 Knowledge and attitude were measured by self-assessment. This method is not as
410 robust as objective data, but given the ubiquitous use of surveys as well as the logistical
411 restraints of adding personal pharmacogenetic testing into an already established
412 curricular course, self-assessments were a viable option. Some unmeasured
413 characteristics of genotyped students (e.g., attitudes toward providing biological

414 samples) may have differed from non-genotyped students such that comparison of pre-
415 /post- results between these two groups would not be valid (i.e., selection bias).
416 However, we found no significant difference in baseline knowledge or attitude between
417 the two groups. Nonetheless, it is possible that participants who elected to be
418 genotyped would be more receptive to pharmacogenetics and thus that their attitudes
419 would improve by a larger share than those who elected not to be genotyped. Although
420 we found that 40% of the attitude questions showed a significant improvement among
421 students who elected not to be genotyped, compared to 70% for those students in the
422 genotyped group, the results for the non-genotyped group may have been
423 underpowered given the smaller number of students who chose to be genotyped (25
424 versus 73). It is also possible that students who volunteer for genotyping may naturally
425 be more inclined to have a positive attitude towards the topic at hand versus those who
426 chose not to be genotyped. Given that the effect estimates for all knowledge and
427 attitude assessment questions were positive, regardless of genotyping status, we feel
428 that the influence of this type of selection bias is minimal. Our analyses were conducted
429 under the assumption that the intervals between Likert values are equal. We felt it
430 reasonable, for example, to assume that “Agree” is halfway between “Neutral” and
431 “Strongly agree;” this is a common assumption practiced in analysis of survey results.[23]
432 It is likely that even students who elected not to be genotyped benefitted from the
433 *active classroom model* in which students were given 15 minutes to share and discuss
434 results with all students, followed by an open discussion revolving around the clinical
435 cases and information presented by the pharmacogeneticist. The gain in knowledge and
436 attitude for both the genotyped and non-genotyped group is interesting and questions

whether our results are attributable to personal pharmacogenetic testing versus traditional didactic coursework. The difference in improvement between groups is greater for the knowledge-related items than for attitude, consistent with the belief that knowledge affects attitude, which in turn affects behavior.[24,25] The genotyped group had tighter confidence intervals and more robust data as we would have expected based on sample size. However, that both groups improved in knowledge and attitude is encouraging, suggesting that once participation in genetic testing surpasses some threshold, non-genotyped students may learn vicariously through experiences and learning environment created by genotyped students. In essence, the rising tide of pharmacogenetic education lifted all boats.

Isolating the impact of genetic testing without overly-disrupting the course structure posed logistical challenges. As with intervention trials, preventing crossover (e.g., non-compliance or contamination) between treatment groups would have been difficult. Ideally, students would have been randomized into testing and non-testing groups prior to the start of the course. The course material for these two groups would then have been presented separately, in effect creating two versions of BPS 115 (one for those randomized to genetic testing and another for those not receiving genetic testing). This approach imposed too many logistical restrictions.

In order to overcome these limitations, a future cluster-based randomized study with several pharmacy school curricula could be implemented. Since self-efficacy—which was not measured in this study—is useful for predicting future behavior, we plan to contact these students for a long-term follow-up to assess 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 U.S. 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. This dynamic allows more room for pharmacy schools to personalize the incorporation of Pgx into their curricula.

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 curricular BPS 115 course, with further goals of permanently incorporating it into this course. 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 innovative and student-led initiative has a significantly positive impact on the next generation of pharmacists, who by law will have an expanding role as the front line providers of healthcare[26] as we transition into an era of precision medicine.

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Table 1: Drug Metabolizing Enzymes, Function, and Variant Allele Frequencies

Enzyme (reference)	Function	Variant Allele Frequency (decreased function) by Race
CYP2D6[27–29]	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[28–30]	Affects cardiovascular drugs including clopidogrel and proton pump inhibitors and some antidepressant medications	Black: 5% Caucasian: 2-5% Asian: 19%
UGT1A1[31]	Affects some anticancer drugs and is responsible for hyperbilirubinemia induced by Gilbert's syndrome.	Black: 19% Caucasian: 8% Asian: 2%
HLAB*5701[32]	When present can cause Stevens Johnson Syndrome and delayed hypersensitivity mostly among Asians.	Black: 1% Caucasian: 6-7% Asian: up to 20%
IL28b[33]	C/C Alleles predicts drug efficacy towards chronic hepatitis C infections	Black: 24-50% Caucasian: 8-13% Asian: 0-1%

Table 2: 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%)
***: P-value < 0.05**		

Table 3: Reflections of Genotyped and Non-Genotyped Group

Genotyped Group N = 73			
Question	**Disagree + Strongly Disagree, N (%)**	**Neutral, N (%)**	**Agree + Strongly Agree, N (%)**
Glad to have participated in Pgx testing	3.00%	8.00%	89.0%
I believe I have a better understanding of Pgx principles	1.40%	13.60%	85.0%
Felt more engaged because I had undergone Pgx testing	4.00%	19.0%	77.0%
My participation reinforced concepts taught in BPS 115	2.70%	13.8%	83.5%
Non-Genotyped Group N = 25			
Question	**Disagree + Strongly Disagree, N (%)**	**Neutral, N (%)**	**Agree + Strongly Agree, N (%)**
I regret not participating in Pgx	20%	20%	60%
Classmates Pgx results reinforced concepts	4.0%	28%	68%
I am interested in participating in more comprehensive genetic tests	4.0%	28%	68%
If offered again, I would undergo Pgx testing	8.0%	32%	60%

Figure 1: Change in Likert Score for Knowledge

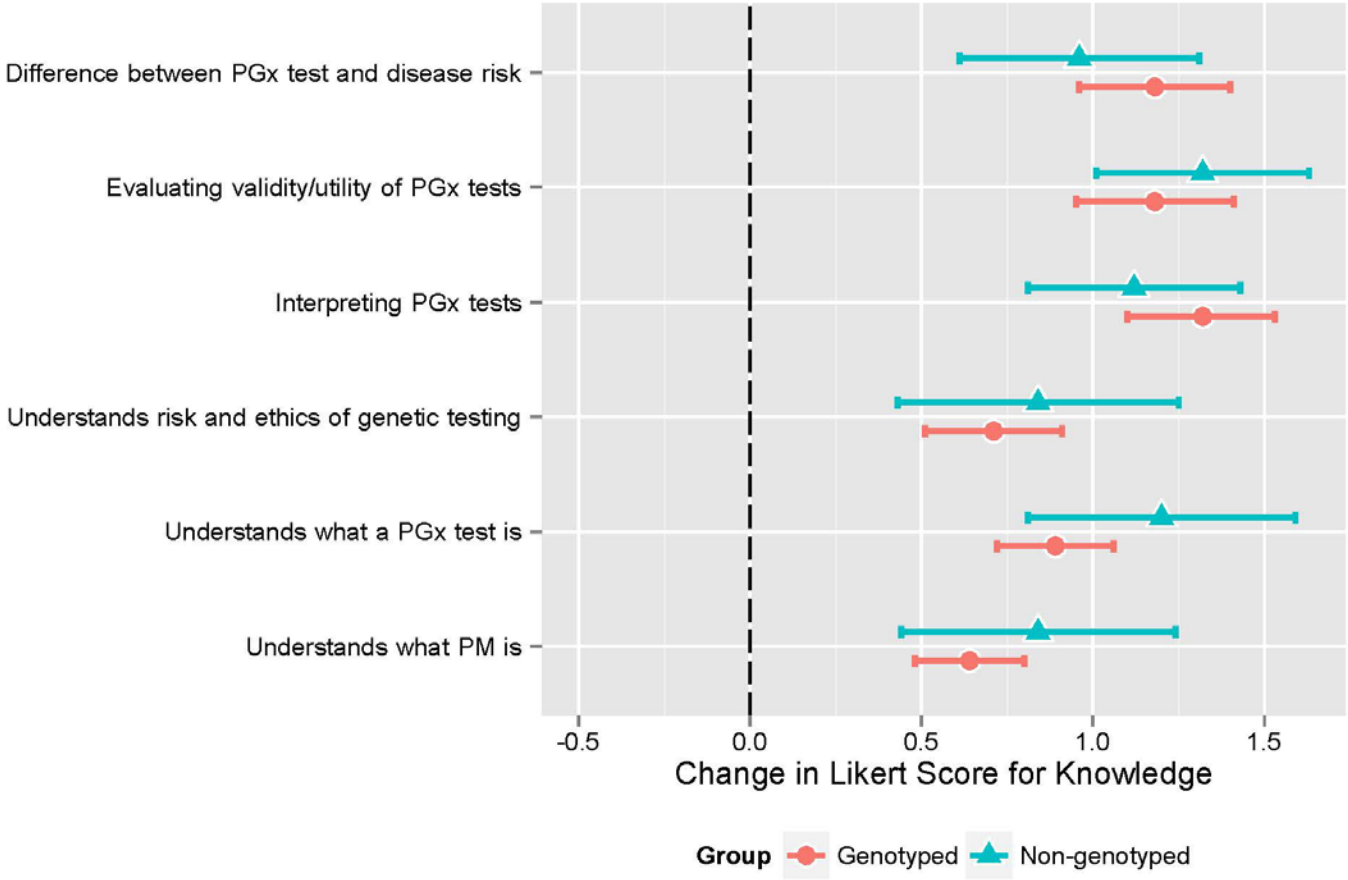
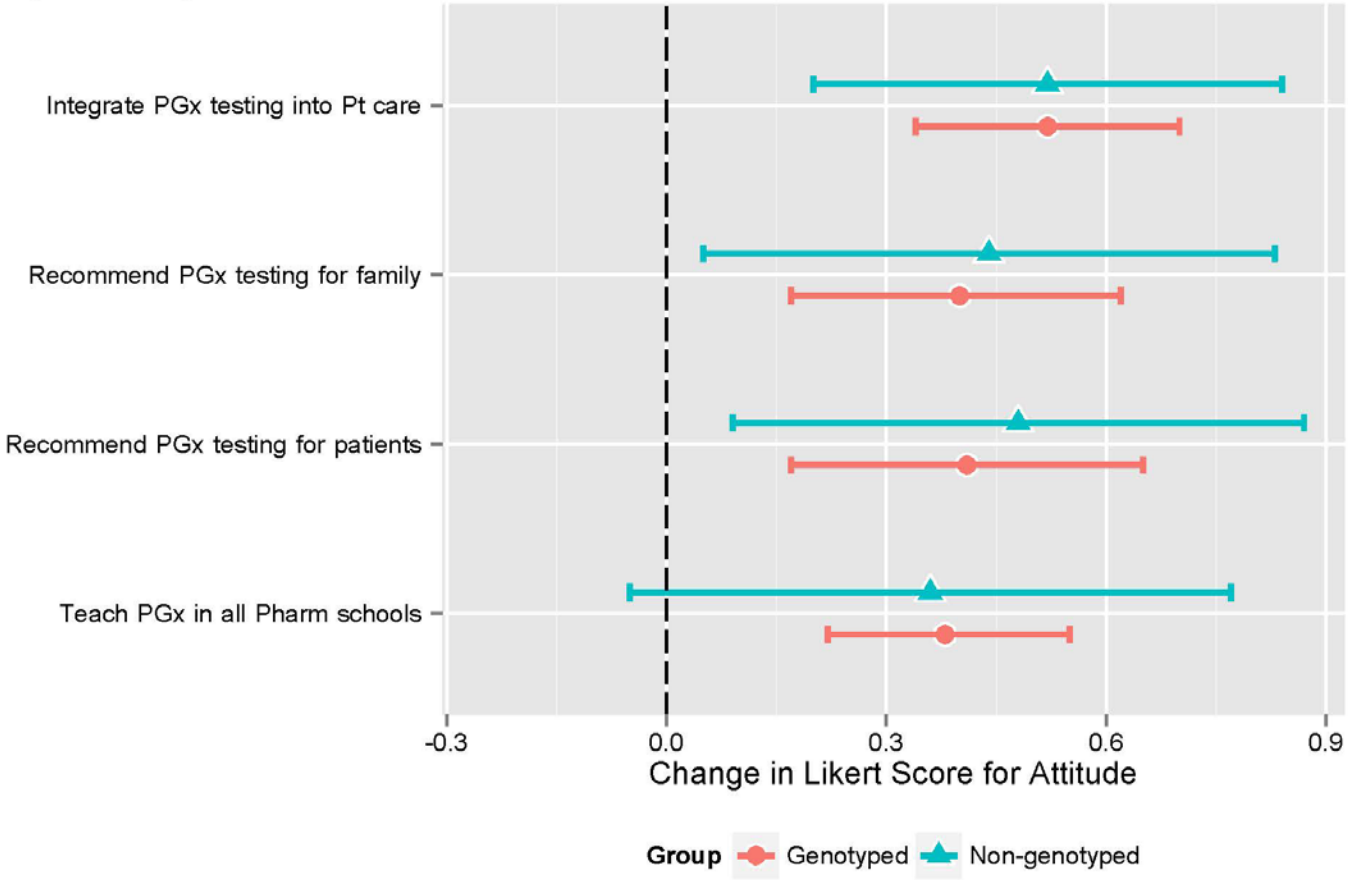


Figure 2: Change in Likert Score for Attitude



Supplementary Table 1. Knowledge and Attitude Assessment Questions from Pre and Post Survey

	Genotyped (N=73) Effect Size; 95% CI	Non-Genotyped (N=25) Effect Size; 95% CI
Knowledge		
1. I understand what precision medicine is.	0.64; 0.48-0.80	0.84; 0.44-1.24
2. I understand what a pharmacogenetic test is.	0.89; 0.72-1.06	1.20; 0.81-1.59
3. I understand how a pharmacogenetic test differs from a genetic test for disease risk.	1.18; 0.96-1.40	0.96; 0.61-1.31
4. I am aware of the types of knowledge and resources needed to interpret a pharmacogenetic test result.	1.32; 1.10-1.53	1.12; 0.81-1.43
5. I understand how to evaluate the clinical validity and utility of a pharmacogenetic test.	1.18; 0.95-1.41	1.32; 1.01-1.63
6. I understand the risks, benefits, and ethical considerations of personal genetic testing.	0.71; 0.51-0.91	0.84; 0.43-1.25
Attitude		
1. The use of personal genetic information in health care is beneficial to patients.	0.33; 0.16-0.50	0.20; -0.16-0.56
2. 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
3. In addition to factors like age, race, and drug interactions, genetic information is an important consideration during routine clinical practice.	0.26; 0.04-0.48	0.28; -0.03-0.59
4. I would recommend pharmacogenetic testing for a patient.	0.41; 0.17-0.65	0.48; 0.09-0.87
5. I would recommend pharmacogenetic testing for a family member.	0.40; 0.17-0.62	0.44; 0.05-0.83
6. Pharmacogenetic testing, when applicable, should be integrated into patient care.	0.52; 0.34-0.70	0.52; 0.20-0.84

7. Pharmacists should be trained to interpret and apply pharmacogenetic test results.	0.30; 0.13-0.48	0.44; 0.16-0.72
8. Pharmacogenetics should be integrated into the curricula at all pharmacy schools.	0.38; 0.22-0.55	0.36; -0.05-0.77
9. Pharmacogenetics will likely play an important role in my future career.	0.10; -0.10-0.29	0.28; -0.07-0.63
10. Pharmacists play a crucial role in the future of precision medicine.	0.22; 0.06-0.38	0.24; -0.09-0.57
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.		