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25 **ABSTRACT**

26 **Objective:** To evaluate if pharmacy students' participation in personal pharmacogenetic
27 testing enhances their knowledge and attitude towards precision medicine (PM).

28 **Methods:** First-year pharmacy students were offered personalized pharmacogenetic
29 testing as a supplement to a required curricular pharmacogenomics course. Ninety-
30 eight of 122 (80%) students completed pre- and post-course surveys assessing
31 knowledge and attitudes regarding PM; 73 students also volunteered for personal
32 pharmacogenetic testing of the following drug metabolizing enzymes (*CYP2C19*,
33 *CYP2D6*, *UGT1A1*) and pharmacodynamics-relevant proteins (interleukin (IL)-28B &
34 human lymphocyte antigen HLAB*5701).

35 **Results:** An online Likert-based survey was distributed to 1st-year PharmD students.
36 Using a linear mixed effects model, we observed significant improvements in 100% of
37 knowledge and 70% of attitude-related questions for students who decided to undergo
38 pharmacogenetic testing.

39 **Conclusion:** Personal pharmacogenetic testing significantly enhances knowledge of
40 and attitude toward pharmacogenomics among PharmD trainees. This study
41 demonstrates the feasibility and importance of educating future pharmacists by
42 incorporating pharmacogenetic testing into professional school curricula.

43

44 **Keywords:** pharmacogenomics, genotyping, pharmacy curriculum, pharmacogenetics,
45 personal pharmacogenetics

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47

48 **INTRODUCTION**

49 The Human Genome Project laid the groundwork in 2003 for an innovative
50 approach in medicine that we today call Precision Medicine.¹ This new era of medicine
51 is centered around combating human diseases through prevention and treatment,
52 based on lifestyle, environment and genetics, serving as the basis for President
53 Obama's Precision Medicine Initiative in 2015.² The idea of tailoring patient care to an
54 individual based on his/her lifestyle is not novel, but the incorporation of large quantities
55 of genetic, environmental, and personal tracking data into the patient profile allows
56 clinicians to make much more efficacious, safe, and cost-effective health care decisions.

57 The impact of precision medicine in the clinical setting today can be observed
58 through the lens of pharmacogenetics. This term was used as early as 1959, when
59 inter-individual drug response was attributed to genetic variation³ and is particularly
60 apparent today in the setting of clinical oncology.⁴ For example, specific cell surface
61 receptors (e.g., Her2) on tumors, mutated intracellular proteins (e.g., Ras), or unique
62 chimeric proteins (e.g., Bcr-Abl) are novel gene-specific targets⁴ that have been
63 markedly successful at providing more targeted therapies and improved patient
64 outcomes. Similarly, widespread HLA-B*1502 testing has dramatically reduced the rate
65 of Stevens-Johnsons syndrome in susceptible populations.⁵ Moreover, incorporation of
66 pharmacogenetics information into drug development represents an opportunity to
67 improve the drug candidate pipeline.⁶

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

71 well-planned multi-disciplinary support efforts for students, and a means for them to
72 access genetic counselors regarding their genetic data.⁷⁻⁹ We wanted to avoid these
73 controversial issues by focusing solely on pharmacogenetics, which does not carry the
74 ethical concerns regarding disease risk. Our study was approved by the University of
75 California, San Francisco (UCSF) Committee on Human Research.

76 Pharmacists, physicians and other health care professionals must be adequately
77 trained to understand and appropriately communicate personal genetic data with other
78 clinicians and patients in order to clinically incorporate the benefits of our rapidly
79 expanding understanding of pharmacogenetics. Professional organizations such as the
80 National Coalition for Health and Professional Education in Genetics, the Association of
81 American Colleges Contemporary Issues in Medicine, the American College of
82 Physicians, the American Nurses Association, and the American Association of
83 Colleges of Pharmacy have defined core competencies relating to pharmacogenomics
84 for inclusion in their respective professional school curricula.¹⁰⁻¹² Due to the recognition
85 from these large professional organizations on the importance of educating our future
86 health care professional, efforts to consistently incorporate pharmacogenomics
87 education into medical and pharmacy school curricula have been attempted at various
88 institutions,^{3,11,13-16} but further research is necessary to determine the most appropriate
89 structure to systematize the approach.^{7,8}

90 Investing in the early education of future health professionals is critical in order
91 for clinicians to keep up with technological and genomic advances. Pharmacists are
92 essential in helping to usher in this new era of medicine, as they are the recognized
93 drug experts¹⁷ who specialize in a number of areas: pharmacokinetics,

94 pharmacodynamics, patient care, managed care, and pharmacogenomics.¹⁸
95 Pharmacists are the ideal clinicians to spearhead this movement, and the healthcare
96 system is beginning to accept this paradigm shift as legislation is passing in numerous
97 states (California, Montana, and Washington among others) to expand the role that
98 pharmacists will play in the changing landscape of medicine created by the Affordable
99 Care Act. The American Society of Health-System Pharmacists (ASHP) and an
100 increasing number of physicians recognize the importance of pharmacists' role in
101 evaluating pharmacogenetic tests to guide and improve patient outcomes.¹⁸ ASHP
102 "believes that pharmacists have a responsibility to take a prominent role in the clinical
103 application of pharmacogenomics" and recommends that "this emerging science be
104 spearheaded...by pharmacists to promote safe, effective and cost-efficient medication
105 practices."¹⁹ With the natural fit of pharmacogenomics under the purview of
106 pharmacists, it was inevitable for us to empirically determine the impact of personal
107 pharmacogenetic testing on PharmD students' knowledge and attitude towards
108 precision medicine at a large, public school of pharmacy.

109 Based on previous literature demonstrating the benefit of interactive learning in
110 education,^{13,16,17,20} we hypothesized that personal pharmacogenetic testing would
111 enhance PharmD students' knowledge and attitudes regarding precision medicine.

112

113 **METHODS**

114 **Background**

115 Prior to our current assessment, a smaller pilot study was conducted among first-
116 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:

- 138
- 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*

141 *tests instead of starting empirical therapy and dosing, and if we will begin educating our*
142 *future clinicians. Implementation will require a new generation of MDs/pharmacists to*
143 *lead this movement.”*

144
145 • *“Information outside of academia regarding pharmacogenomics is limited. Many people*
146 *in the public are not aware that testing is even available. As leaders/graduates from this*
147 *university, we have to communicate our knowledge to outside communities and the rest*
148 *of the world. Having a diverse group of people communicating this information will*
149 *spread the word about needing research in more ethnically diverse populations.*
150 *Pharmacists will be the most easily accessible group of healthcare practitioners, so*
151 *questions about testing will go to us before many in the hospital.”*

152
153 • *“I genuinely enjoyed the class, and I learned a lot. This information inspires me to want*
154 *to look further into why certain populations are fast metabolizers, or slow metabolizer or*
155 *do not respond well to certain medications. I would like to personally be involved in*
156 *pharmacogenomics in the future during my career.”*

157

158 **Survey assessment**

159 Based on the pilot study’s overwhelmingly positive feedback, personal
160 pharmacogenetic testing was incorporated into BPS 115 the following year on a
161 volunteer basis. One month before the start of the spring 2014 term, a survey was
162 administered to 122 first-year UCSF School of Pharmacy (SOP) students enrolled in
163 BPS 115. Selected demographic characteristics of the students are summarized in
164 Table 1. The survey was designed to assess students’ attitudes and knowledge towards
165 precision medicine and was re-administered to the same students following completion

166 of the 10-week course. In addition to knowledge- and attitude-assessment questions in
167 the post-course survey, we also reflection questions, allowing us to assess students'
168 opinions about participating in pharmacogenetic testing. The knowledge, attitude, and
169 process measure questions are listed in Supplemental Table 1.

170

171 **Survey design**

172 The voluntary pre- and post-course survey and pharmacogenetic testing were
173 approved by the UCSF Committee on Human Research. Written consent and email
174 addresses were collected from all students who were interested in participating in the
175 survey. Email addresses were entered into UCSF's Research Electronic Data Capture
176 (REDCap) system, a secure online utility for conducting surveys. Once a student logged
177 on to REDCap to take their survey, REDCap would automatically generate and assign
178 an anonymized, unique identifier linked to the subject's email address. The same
179 identifier was associated with all surveys that the subject completed.

180 While the survey asked for basic personal information, REDCap only exported
181 the assigned identifier with the survey data. To ensure that participation was voluntary,
182 the names and email addresses associated with the survey results remained restricted
183 from both primary researchers and course faculty members. Only the primary
184 researchers were authorized to access the full REDCap data (the course directors were
185 not involved in the survey-based assessment).

186

187 **Pharmacogenetic testing**

188 During the course, students had the opportunity to volunteer to have their own
189 DNA genotyped for several drug metabolizing enzymes as a “hands-on” personal
190 pharmacogenetic learning experience. This information was used as a teaching
191 supplement to the course. Participation in the survey and testing was blinded to the
192 course directors and had no impact on students’ grades or performance in the course.
193 Several days were coordinated to collect de-identified saliva samples from students.
194 The samples were analyzed in a CLIA-certified laboratory. Students were given the
195 option to have genotyped either a gene for a drug metabolizing enzyme (*CYP2C19*,
196 *CYP2D6*, or *UGT1A1*) or a pharmacodynamics-relevant protein (*IL28B* or *HLAB*5701*).
197 Each of the genes coding these enzymes/proteins has its own unique clinical implication
198 and varying allele frequency (and therefore varying activity) among ethnic groups (Table
199 2). Genotyping results for these genes allow clinicians to properly develop an
200 appropriate medication regimen tailored for individual patients.

201

202 **Unveiling of pharmacogenetic results**

203 Once genotyping was completed, students were given their personal
204 pharmacogenetic information during a regularly scheduled class period for BPS 115; the
205 class session was divided into two sessions. During the first session, a
206 pharmacogeneticist was invited to review and discuss each of the genes under
207 evaluation, their mutations, clinical significance, and how this information might be
208 incorporated into clinical practice. The first part of the session was didactic, while the
209 teaching methodology used in the second half of the session emphasized an *active*
210 *learning classroom model* in which students were given 15 minutes to share and

211 discuss among each other, and then initiate an open discussion. During the open
212 discussion, students engaged in an active question and answer session with each other
213 and the pharmacogeneticist. Students based many of their questions on their personal
214 pharmacogenomic data, and expressed interest in strategies for pharmacists to play a
215 more active role in the future of this specialty. This session did not require specific
216 preparatory work besides completing assigned readings pertaining to the course and
217 basic concepts of pharmacogenetics.

218

219 **Statistical analysis**

220 We defined our outcome as change in knowledge or attitude regarding precision
221 medicine. Specifically, we assigned integer values to the 5-point Likert scale (i.e., 1 =
222 strongly disagree, 2 = disagree, 3 = neutral, 4 = agree and 5 = strongly agree) and then
223 examined the change in Likert scores for each knowledge and attitude question by
224 calculating the difference between pre- and post-survey responses. For example, a pre-
225 survey response of 3 (neutral) followed by a post-survey response of 4 (agree) to the
226 same question would be a gain of 1 Likert point. This difference served as our
227 dependent variable. Our analysis was stratified into two groups: (1) students who
228 participated in the personal genotyping and the survey (the genotyped group), and (2)
229 those who participated in the survey but not in personal genotyping (the non-genotyped
230 group). The effect of the pharmacogenetic testing on knowledge and attitude was
231 estimated using linear mixed effects analysis. Variables for sex and race were included
232 as fixed effects, with a random intercept for student. Estimates whose confidence
233 intervals excluded the null value were considered statistically significant at an alpha

234 level of 0.05. Survey results were analyzed using the lme4 package²² in the R statistical
235 programming language (R Core Team, 2015).²³

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

240

241 **RESULTS**

242 In total, 98 (80%) of the 122 students enrolled in the spring 2014 BPS 115 course
243 voluntarily completed the pre- and post-course surveys. Of these 98, 73 (74.5%)
244 students also took part in genotyping, leaving 25 students (25.5%) to comprise the
245 surveyed but not genotyped group. Attitudinal and knowledge assessment was
246 performed via an electronic online survey using a Likert scale response format. The 6
247 knowledge and 10 attitude questions (Supplementary Table 1) are listed in order of
248 appearance on the pre- and post-course surveys. Baseline scores in knowledge and
249 attitude were similar for both groups. The mean baseline Likert score for knowledge
250 questions was (3.03) in the genotyped group and (3.14) in the non-genotyped group.
251 For the attitude questions, the mean baseline score was (3.85) in the genotyped group
252 and (3.83) in the non-genotyped group.

253 Results for change in knowledge and attitude are stratified by genotyping status
254 in Tables 3 and 4, respectively. To keep our results clinically meaningful, we limited our
255 analysis to results with a minimum effect size of 0.25 Likert points (i.e., a difference in
256 means between pre- and post-survey results of 0.25 Likert points). Effect estimates

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

259 One-hundred percent of responses to the knowledge questions showed
260 significant improvement between pre- and post-survey assessments, regardless of
261 whether students participated in genotyping. The smallest increase in estimates was
262 0.64. The mean change in knowledge across all knowledge questions was not
263 significantly different between the genotyped (0.99) and non-genotyped (1.05) groups (p
264 = 0.68). Seventy percent of the attitude questions in students who underwent
265 genotyping showed a considerable improvement in the pre- and post-Likert scores
266 (Table 4). Forty percent of the attitudinal questions showed significant improvement
267 among students in the non-genotyped group. While the mean change in attitude was
268 slightly higher among those who did not participate in genotyping (0.36) versus those
269 who did (0.30), the difference was not statistically significant ($p = 0.31$). The correlation
270 between pre- and post-survey responses was fairly consistent for knowledge (Pearson's
271 $r = 0.63$) and attitude ($r = 0.62$) questions.

272 In the genotyped group, the knowledge assessment question with the largest
273 increase (1.32 Likert points, 95% confidence interval [CI]: 1.10-1.53) asked students to
274 identify with the following statement: "I am aware of the types of knowledge and
275 resources needed to interpret a pharmacogenetic test" (Knowledge Question 4,
276 Supplementary Table 1). Among the non-genotyped group, the knowledge assessment
277 question with the largest increase (1.32, 95% CI: 1.01-1.63) asked students whether
278 they "...understand how to evaluate the clinical validity and utility of a pharmacogenetic
279 test" (Knowledge Question 5, Supplementary Table 1). The attitude assessment

280 question with the largest increase was the same for genotyped (0.52, 95%CI: 0.34-0.70)
281 and non-genotyped (0.52, 95%CI: 0.20-0.84) students. This question asked students
282 whether “Pharmacogenetic testing, when applicable, should be integrated into patient
283 care” (Attitude Question 6, Supplementary Table 1).

284 An examination of students’ attitudes (n = 98) revealed that students were more
285 likely to have favorable impressions of precision medicine among those who had
286 volunteered for personal genotyping versus those who did not get genotyped. Among
287 the 73 students who were genotyped, 89% said that they were glad to have
288 participated, and 85% stated that they had a better understanding of the principles of
289 pharmacogenetics. Furthermore, 76.7% of the genotyped group said they felt more
290 engaged during BPS 115, and 83.5% agreed that their participation in genotyping
291 reinforced the concepts taught in the course (Table 5).

292 For students who did not volunteer to be genotyped, 60% regretted their decision
293 and the same 60% stated that they would choose to undergo pharmacogenetic testing if
294 it was offered to them again. Sixty-eight percent of students in the non-genotyped group
295 stated that concepts taught in the course were reinforced after seeing their classmates
296 receive their genetic results. Lastly, 68% of students in the non-genotyped group said
297 they would be interested in participating in more comprehensive genetic testing to learn
298 about other traits.

299

300 **DISCUSSION**

301 We found that incorporating genetic testing as an adjunct to School of Pharmacy
302 PharmD curriculum significantly enhanced students’ knowledge and attitudes of

303 precision medicine. In both the genotyped and non-genotyped groups, there was an
304 increase in all of the knowledge assessment questions before and after the course. The
305 significance of this finding is extraordinary as it demonstrates that an interactive hands-
306 on approach to educating future pharmacists about pharmacogenetics is a fundamental
307 curricular change that should become commonplace across all professional doctorate
308 programs in the country. As pharmacogenomics becomes increasingly fundamental for
309 pharmacists in our health system, knowledge and acceptance of this new era of
310 precision medicine is required for pharmacists to begin designing and developing
311 personalized pharmacotherapy.

312 There were 132 AACP (American Association of College of Pharmacy)
313 recognized and accredited schools of pharmacy in 2015.^{20,24} In 2008-2009, 75 of 109
314 accredited schools of pharmacy surveyed revealed that 69 (92%) included
315 pharmacogenomics in their curriculum and 67 (89.3% of total) taught the material at a
316 PharmD level,²⁰ but the depth of inclusion was limited. Among these 69 schools
317 surveyed, the most time spent on the topic of pharmacogenomics was between 31-60
318 hours, which was observed for only 10 (14.5%) of the schools. Topic coverage was less
319 than 10 hours in 28 (40.6%), and between 11-30 hours for 29 (42%) of the schools (2
320 schools did not respond to this question).²⁰ Based on these numbers, it is evident that
321 there is much room for pharmacogenomics to be incorporated into pharmacy school
322 curricula, particularly since the degree of inclusion is still quite low and the majority of
323 the colleges surveyed did not “have plans for faculty development in the area of
324 pharmacogenomics content expertise.”²⁰

325 In 2009, a study conducted at Temple University School of Pharmacy took a
326 different approach to increase pharmacy student understanding of pharmacogenomics.
327 The study involved 70 second-year PharmD students and an analysis of single
328 nucleotide polymorphisms of the *NAT2* gene based on DNA extracted from their
329 saliva.¹⁶ The study concluded that a laboratory session in pharmacogenomics was
330 beneficial in helping students understand the relevance of pharmacogenomic analysis in
331 designing/creating a patient medication regimen.⁸

332 Another study by Salari and colleagues conducted at Stanford University's
333 School of Medicine aimed to increase the depth of pharmacogenomics understanding
334 by including personalized pharmacogenetic testing as an interactive supplement to an
335 elective course. That study found a statistically significant impact on enhancing medical
336 student knowledge and attitudes towards personal genome testing and precision
337 medicine.¹³ It is important to attempt to replicate these results in other graduate
338 programs across the country, and in the current study we showed that the benefits of
339 pharmacogenetics testing are applicable to PharmD programs.

340 Physicians are often unable to address pharmacotherapy based on a patient's
341 genetics due to time constraints,²⁵ further justifying the importance of pharmacists in this
342 new area of precision medicine. Given that pharmacists are the most extensively trained
343 drug experts¹⁷ in the health care system, the ability to interpret and understand this type
344 of information falls directly under the purview of their pharmaceutical training. The role
345 of pharmacists in the healthcare system is expanding, as reflected by recent legislation.
346 More than 30 states have proposed provider status legislation²⁶ and two federal bills
347 H.R. 592 and S. 314 have been introduced to Congress to amend the Social Security

348 Act to cover pharmacist services under the Medicare program. These types of
349 legislative initiatives are steps in the right direction to ultimately increase patient access
350 to care through expansion of pharmacy services.

351 The results presented in this innovative curricular approach to increasing
352 knowledge and improving attitudes towards pharmacogenetic testing and precision
353 medicine are promising. The overwhelming majority (80%) of students completed pre-
354 and post-course surveys, and 75% of them took part in personal pharmacogenetic
355 testing, which is significant considering the novelty of this idea to students. In our
356 experience, the feasibility of implementing personal pharmacogenetic testing across all
357 US pharmacy school curricula would not be arduous. Student participation was very
358 high in the absence of incentives; the effort dedicated toward collection and processing
359 of DNA was fairly minimal; and discussion of genotyping results was limited to only one
360 class session. Instructors could limit their selection of genetic tests to inexpensive ones
361 to optimize widespread dissemination of an educational session of this type. Educating
362 our future providers and providing them with tools to adequately adapt and provide for
363 their patients in an ever-changing healthcare landscape is an investment that will have
364 major implications in the future health of our nation.

365 One of our most noteworthy findings was in regard to Knowledge Question #4
366 (Supplementary Table 1): “I am aware of the types of knowledge and resources needed
367 to interpret a pharmacogenetic test.” The effect size was fairly large among genotyped
368 students, (1.32, 95%CI: 1.10-1.53), demonstrating that students felt confident utilizing
369 their resources to interpret a pharmacogenetic test. This observation suggests that a
370 curriculum designed to include similar personal pharmacogenetic testing will prepare

371 students to keep up with the precision medicine revolution and ensure that patients are
372 being treated by a confident and knowledgeable health care professional.

373 Sixty-eight percent of non-genotyped students reported that their classmates'
374 participation in genotyping positively impacted their learning in the course, as described
375 in the evaluation and assessment section above. This underscores the impact that the
376 shared experience of personal pharmacogenetic testing had and the potential it has in
377 educating our providers who do not wish to undergo pharmacogenetic testing
378 themselves. This information is important when considering curricular redesign as it
379 allows various interventions or combinations of them to be utilized to achieve maximal
380 learning outcomes. Sixty percent of the non-genotyped students also mentioned that
381 they regretted their decision not to volunteer for personal pharmacogenetic genotyping.
382 It is evident that the experience is a shared and interactive one that not only stems from
383 one's own personal pharmacogenetic information, but also from that of his/her peers.

384 Potential biases should be considered when reviewing the results of our study.
385 Some unmeasured characteristics of genotyped students (e.g., attitudes toward
386 providing biological samples) may have differed from non-genotyped students such that
387 comparison of pre-/post- results between these two groups would not be valid (i.e.,
388 selection bias). However, we found no significant difference in baseline knowledge or
389 attitude between the two groups. Nonetheless, it is possible that participants who
390 elected to be genotyped would be more receptive to pharmacogenetics and thus that
391 their attitudes would improve by a larger share than those who elected not to be
392 genotyped. Although we found that 40% of the attitude questions showed a significant
393 improvement among students who elected not to be genotyped, compared to 70% for

394 those students in the genotyped group, the results for the non-genotyped group may
395 have been underpowered given the smaller number of students who chose to be
396 genotyped (25 versus 73). Given that the effect estimates for all knowledge and attitude
397 assessment questions were positive, regardless of genotyping status, we feel that the
398 influence of this type of selection bias is minimal. Our analyses were conducted under
399 the assumption that the intervals between Likert values are equal. We felt it reasonable,
400 for example, to assume that “Agree” is halfway between “Neutral” and “Strongly agree,”
401 this is a common assumption practiced in analysis of survey results.²⁷

402 Our study did not show significant differences between the genotyped and non-
403 genotyped groups with respect to attitudes or knowledge of pharmacogenetics testing.
404 This may have been due to the relatively few number of students who elected not to be
405 genotyped (n = 25), which reduced statistical power to detect a difference. In addition, it
406 is likely that even students who elected not to be genotyped benefitted from the
407 exercise of discussing the results of their classmates and also from the *active*
408 *classroom model* in which genotyped students were given 15 minutes to share and
409 discuss results with all students, followed by an open discussion. Our results appear to
410 be consistent with a recent report, which described the incorporation of cadaver exome
411 sequencing into first-year medical student curriculum as a form of active learning. It was
412 demonstrated that this active and team based type learning was a potentially powerful
413 educational innovation which helps to improve their genetic knowledge base.²⁸ In that
414 report, students benefitted from a discussion of genetics made relevant to them without
415 being genotyped directly. Thus, it is possible that pharmacogenetics testing of a subset
416 of students had benefits on the entire classroom.

417 In order to overcome these limitations, a future cluster-based randomized study
418 with several pharmacy school curricula could be implemented. In addition, long-term
419 follow-up with these students would allow study of the lasting effects that personal
420 pharmacogenetic testing has had on their personal and professional lives. Furthermore,
421 we hope that this study serves as a means to further accelerate the dissemination of
422 personal pharmacogenetic testing into US pharmacy school curricula.

423

424 **SUMMARY**

425 Pharmacy students in their first year of the PharmD curriculum showed
426 significant enhancements in their knowledge and attitudes towards precision medicine
427 after participating in personalized pharmacogenetic testing. Even students who were
428 enrolled in the course but did not partake in personalized pharmacogenetic testing had
429 an enhancement in knowledge and attitude about precision medicine, likely as a result
430 of engagement with their classmates and faculty regarding the results.

431 Incorporation of personal pharmacogenetic testing into pharmacy school
432 curricula is a simple and efficacious method of educating our future health care
433 professionals. Personal pharmacogenetic testing continues at UCSF through the School
434 of Pharmacy's BPS 115 course with further goals of incorporating it into the core
435 curriculum. We believe that the new era of Precision Medicine ushered in by President
436 Obama's Precision Medicine Initiative will only be successful if coupled with education
437 of a new generation of health care providers. Herein, we have demonstrated that this
438 novel educational approach has a profoundly positive impact on the next generation of

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

441

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445

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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%)

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%
HLA-B*57:01 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				
Question	Genotyped Group N = 73		Non-Genotyped Group N = 25	
	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

^aStatistically significant, clinically meaningful effect sizes

Table 4: Attitude Assessment in Participants and Non Participants ^a				
Question	Genotyped Group N = 73		Non-Genotyped Group N = 25	
	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

^aStatistically significant, clinically meaningful effect sizes

Table 5: Reflections of Participants and Non Participants

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%)

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.