

Abstract

Title: PGX LEARN – Pharmacogenetic Learning And Educational environments for community pharmacists to be Ready for the Next generation

Background: Pharmacogenomics is an integral component of precision medicine that can help guide drug selection and dosing to improve medication response and decrease rates of adverse events. Historically, private companies have supplied pharmacogenetic tests that required an order by a healthcare provider, but the Food and Drug Administration approved the first direct-to-consumer (DTC) pharmacogenomic test in October 2018, which would make pharmacogenomic testing more widely available. [1] As a result, there is an anticipated increase in need for patient counseling and interpretation of pharmacogenomic results. Pharmacists are distinctly suited to meet this need because of their unique training, high level of trust among the public, and strategic placement in the community setting. [2] However, pharmacists report a lack in self-confidence to interpret pharmacogenetic results, despite agreeing that it is relevant to their clinical practice. [3,4] Since pharmacogenomics has recently been incorporated into pharmacy school curriculums, it is possible that this lack of confidence stems from minimal education in this topic.[6] Regarding education, pharmacists reported that they prefer lecture, printed and active learning methods for building self-confidence in interpreting pharmacogenetic information. [3,4] Being able provide pharmacists with an educational program that is efficient yet comprehensive in delivery is critical to being able to meet the increase in the anticipated need of pharmacogenetic test interpretation due to the busy nature of community pharmacy.

Methods:

Community pharmacists, identified through a University of Southern California (USC) preceptor listserv, were invited to participate in a live continuing-education (CE) event. All participants provided demographic data, completed a knowledge-based pre-test, attended a lecture followed by one of two educational programs (randomly assigned 1:1 to passive or active learning), then completed a matched knowledge-based post-test. Those unable to attend a live event were randomly assigned to the passive or active learning arm and participated in the educational sessions online.

Pharmacists also rated their perceived self-confidence regarding interpreting pharmacogenetic data using a 5-point Likert scale prior to and after completing the educational programs. The two exams featured matched questions assessing pharmacists' comprehension/understanding, interpretation, and application of pharmacogenomic data. Fischer's exact test was used to detect differences in improvements of knowledge scores between active and passive groups in each session and between sessions. Fisher's exact test was used to detect differences in changes of self-confidence ratings between the active and passive groups in each session and between sessions.

Results: Thirty-seven (37) pharmacists participated in the CE events who fulfilled requirements of to complete the CE were included for analysis. For the primary outcome, scores improved significantly more in the online session compared to the live session with no difference in improvement of scores between passive and active groups ($p=0.030$). Confidence was improved overall regardless of online or in-person learning. Subgroup analysis showed that confidence ratings were significantly improved ($p = 0.045$) after the educational events in the active group only. The proportion of participants with improved confidence rating in the active group 92% ($=11/12$) was significantly higher than those in the passive group 50% ($=3/6$).

Conclusion: This online CE session in pharmacogenomics, incorporating either active or passive learning patient cases, improved participants comprehension, interpretation, and application of pharmacogenetic knowledge. When creating a pharmacogenomics CE event, inclusion of an active eCase was well received by community pharmacists and may improve their self-confidence in interpreting pharmacogenetic data.

TITLE: PGX LEARN – Pharmacogenetic Learning And Educational environments for community pharmacists to be Ready for the Next generation

Primary Investigator (Resident): Negin Sazgar

Co-Investigator: Scott Mosley

Residency Preceptor: Richard Dang

BACKGROUND:

Pharmacogenomics is an integral component of precision medicine. Response rates, adverse events and appropriate doses of medications can vary depending on an individual's pharmacogenomic profile. Historically, private companies have been available to test for pharmacogenetic data when ordered by a healthcare provider, but the Food and Drug Administration approved the first direct-to-consumer (DTC) pharmacogenomic test in October 2018, which would make pharmacogenomic testing more widely available.[1] Although the DTC test is not currently being sold, they will soon be stocked on pharmacy shelves and available for purchase online. Pharmacists are uniquely qualified to interpret and explain pharmacogenomic data.[2] Additionally, pharmacists are at the front-line of managing this anticipated increase in pharmacogenomic data as they are one of the most accessible, trusted, and frequently visited members of the healthcare community.

Although pharmacists are distinctively suited to interpret pharmacogenomic information and strategically placed to offer patient counseling and recommendations to prescribers, many pharmacists do not feel confident in their ability to do so.[3, 4] Hospital-based and community-based pharmacists agree that they should be able to interpret pharmacogenetic testing and provide recommendations on therapy based on pharmacogenomic testing.[3] However, despite agreeing they should be involved in precision medicine, many pharmacists lack the self-confidence to make clinical decisions regarding pharmacogenetic data. Only 14% of this group of inpatient and outpatient pharmacists agreed that they felt comfortable applying the results of a pharmacogenomics test to drug therapy, selection, dosing or monitoring. Additionally, only 25% of this group agreed they would be able to identify medications that require pharmacogenomic testing. These data did not vary across pharmacists with various years of experience. However, respondents with 5 or fewer years of experience were more likely to agree that pharmacogenomics was an integral part of their pharmacy curriculum.[3]

With pharmacogenetics advancing in practice and included as a key element for accreditation of pharmacy school (PharmD) curriculums, it is apparent that pharmacists support pharmacogenetic education and training.[6,7] Sixty-seven percent (67%) of pharmacists surveyed agreed that pharmacogenomics should be a focal part of pharmacy school education, but only 10% agreed that this education was an integral part to their curriculum/education.[3] In 2019, Berenbrok *et al*, published a qualitative analysis identifying the educational needs for implementing clinical pharmacogenomic services in the community setting. A recurring message shared during interviews with 11 pharmacists, was that they “know the basics, but that’s about it” regarding pharmacogenomics. Participants in their study described that active learning was preferred in building their confidence in interpreting pharmacogenomic data. Additionally, they emphasized the utility of a guideline for pharmacogenomics. Interestingly, none of the surveyed pharmacists mentioned Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines as a possible resource.[4] This lack of awareness that guidelines for pharmacogenomics exist was similar to what McCullough *et al* reported in 2011, in which only 20% of pharmacists agreed that they could identify reliable sources of information regarding pharmacogenomics for health care providers.

Regarding proper training or education, pharmacists reported that lecture-based format (live or web-archived)[3], printed reading material[3] and active learning avenues would help to build confidence for interpreting pharmacogenetic data.[4] An assessment of education provided to outpatient, inpatient, and administration-based pharmacists has been conducted featuring pre- and post-testing of pharmacogenomic

knowledge. Between tests, pharmacists were provided with 1-hour live or web-archived lectures regarding pharmacogenetic testing. Post-educational testing was conducted after two months. On average, pharmacists improved their correct response rate from 46% or 53%, with the greatest improvement seen in pharmacists with the least bedside time performed. Additionally, with increasing years of experience, pharmacists showed poorer scores on both surveys, but overall, all groups showed similar improvement in survey performance.

The American Society of Health-System Pharmacists endorses that pharmacists have the responsibility to clinical application of pharmacogenomics.[2] Additionally, given that there will be easier access to obtain pharmacogenomic information through direct-to-consumer tests, pharmacists, especially those in the community setting, will need to properly interpret results. However, pharmacists can be busy with many tasks in the community setting. Thus, being able provide pharmacists with an education program that is efficient yet comprehensive in delivery is critical to being able to meet the increase in the anticipated need of pharmacogenetic test interpretation. The objective of this study is to determine if lecture-based or a role-playing case-based educational program improve understanding, interpretation, and application of pharmacogenetic data for pharmacists in the community setting.

METHODS:

Research Design: Retrospective trial

Study Subjects

This study was designated as “exempt” by the University of Southern California Institutional Review Board. Community pharmacists were eligible to partake in the study and were invited through a USC preceptor listserv. A live CE event was hosted at a venue in the Los Angeles metropolitan area for a duration of 1 hour. Participants completed a knowledge-based pre-test prior to the session, attended a lecture followed by one of two educational programs (traditional didactic, or active learning), then completed a matched knowledge-based post-test. Each test will be approximately 5 minutes in length. Questions used in the pre and post-tests are available in **Appendix 1**. The CE platform administered the knowledge-based pre-test and post-test as well as common CE assessment questions and confidence ratings. Responses were collected on the CE platform. Participants were also asked to provide feedback regarding the CE session and answered common assessment questions regarding the quality of the session. Those unable to attend a live event were randomly assigned to the traditional or active learning arm and participated in the educational sessions online.

Pharmacists rated their perceived self-confidence regarding interpreting pharmacogenetic data using a 5-point Likert scale prior to beginning and after completing the educational programs. Confidence rating options included: “not confident at all”, “slightly confident”, “somewhat confident”, “fairly confident” and “completely confident”.

Pre-tests and post-test exams were approximately 5 minutes in length. The two exams featured matched questions assessing pharmacists’ comprehension/understanding, interpretation, and application of pharmacogenomic data.

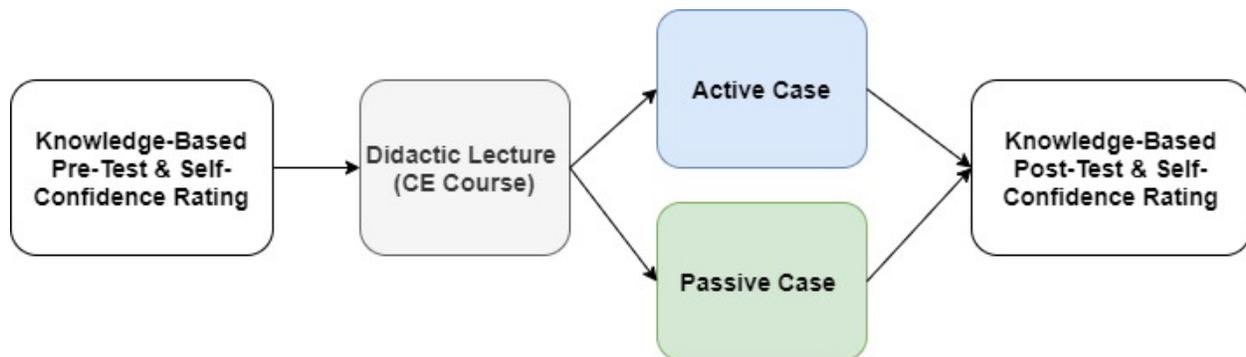
Pharmacists who did not complete the pre-test, post-test, pre-confidence rating or post-confidence rating were excluded from the data analyses.

Trial Design:

Pharmacists attended a 30-minute lecture regarding the interpretation of pharmacogenetic results. After completion of this lecture, pharmacists were randomly assigned to one of two educational arms prior to the start of continuing session. The first group were assigned the “Traditional Didactic Learning” arm. This group attended a second lecture during which a case was explained and reviewed. The second group

of pharmacists were assigned to the “Active Learning” arm. This group completed an active role-playing, case-based game featuring pharmacogenomic patient cases (“eCases”). These eCases were created using Twine software with the help of pharmacy-student-led programmers and content provided by pharmacists. eCases allow users to explore the narrative of a patient presentation within a specific practice setting, gather additional information, and select a treatment plan. eCases are an interactive, web-based patient case using decision tree algorithms to allow participants to explore different pathways throughout the pharmacists' patient care process. This allows learners to role-play with a case to apply knowledge learned and receive immediate feedback to enhance opportunities for learning.

The live course, passive case and active case debrief sessions were recorded to be used for individuals who choose to participate in the online CE course.



Outcome Measures:

Primary: To determine whether a lecture-based or a role-playing case-based educational program improves comprehension, interpretation, and application of pharmacogenetic data for pharmacists in the community setting. To determine if there is a difference in the level of comprehension, interpretation, and application of pharmacogenetic data with live or online education sessions.

Secondary: To determine whether an educational program improves perceived self-confidence of pharmacists in identifying, interpreting and applying pharmacogenetic data. To determine if there is a difference in the perceived self-confidence of pharmacists in identifying, interpreting and applying pharmacogenetic data with live or online education sessions.

Statistical Analysis:

Fischer's exact test was used to detect differences within baseline characteristics. Scores were calculated as the sum of correct number of responses for each individual (out of six total questions). Score improvements were calculated as the difference between pre- and post-test scores. Fischer's exact test was used to detect differences between improvement in assessment scores between passive and active groups in the live session and in the online session and to detect differences between the online and live groups. Confidence rating improvements were calculated as the difference between pre- and post-test confidence ratings. Fisher's exact test was used to detect improvements in confidence ratings between the active and passive groups in the live session and in the online session and to detect for improvements between online and live sessions.

RESULTS:

Baseline characteristics are shown in **Table 1**. Of twenty-six (26) participants who agreed to participate in the live CE session, 22 participants attended the live CE talk and completed a pre-test. Of the 22 participants attending the live session, 7 participants were pre-assigned to attend the passive case and 15 were pre-assigned to the active cases. Two participants in the passive group and two participants in the active group did not complete the post-test and were excluded from the final result. Of the 40 participants who signed-up for the online session, only 19 participants completed the pre-test and post-test surveys to be completed in the study. Of the total 37 participants in the study, 18 participants and 19 participants took part in the live and online sessions, respectively. Of the total number of participants, 17 participants were assigned to the passive group and 20 participants were assigned to the active group. Seventeen out of 19 participants in the online session were female (89%, Fischer's exact test $p = 0.029$). Eleven out of 18 participants in the live session have practiced for >10 years (61%, $p = 0.024$). Additionally, 11 out of 19 participants in the online session were new practitioners (58%, $p = 0.024$).

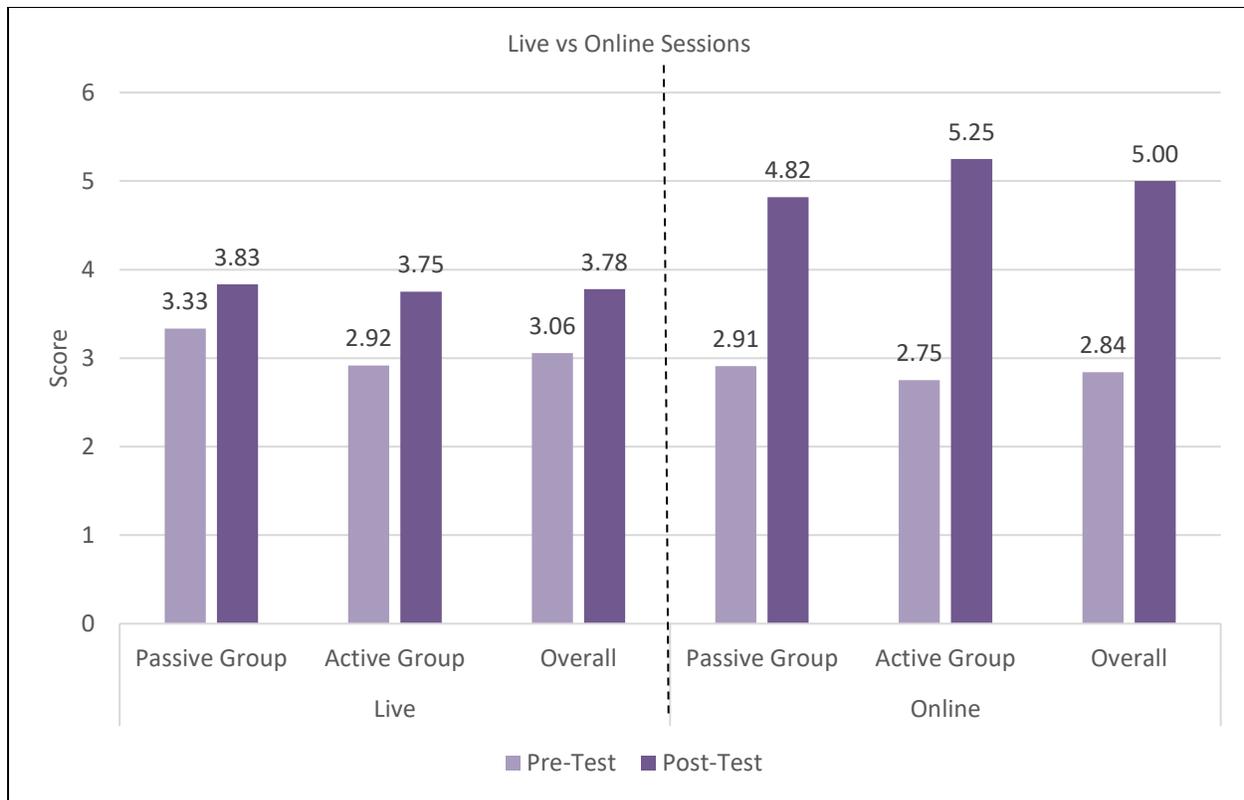
Table 1:

Baseline Characteristics			
	Overall (n = 37)	Passive Group (n = 17)	Active Group (n = 20)
Female (%)	27 (72%)	11 (65%)	16 (80%)
Years of Practice			
1-3 years (%)	14 (38%)	8 (47%)	6 (30%)
4-6 years (%)	3 (8%)	3 (18%)	0 (0%)
7-10 years (%)	5 (13%)	2 (11%)	3 (15%)
>10 years (%)	15 (41%)	4 (24%)	11 (55%)
Live vs Online			
	Live (n = 18)	Online (n = 19)	
Female (%)	10 (55%)	17 (89%)	
Years of Practice			
1-3 years (%)	3 (17%)	11 (58%)	
4-6 years (%)	1 (5%)	2 (11%)	
7-10 years (%)	3 (17%)	2 (11%)	
>10 years (%)	11 (61%)	4 (20%)	

Primary Outcome:

There were no differences in baseline pre-test scores between any groups. The average baseline pre-test score of participants was approximately 3 correct answers, regardless of group or session. In the live session, there was no difference in score improvement for passive or active groups. Passive and active groups showed an average increase in scores by one additional question being correctly answered after the education session. In the online session, there was a greater improvement in post-test scores overall, with nearly 3 additional questions being answered correctly after the education session. Online sessions showed a greater improvement in assessment scores compared to the live session ($p = 0.030$). Eighty-two percent (82%) of online participants improved their scores compared to 50% of participants in the live session. Like the live session, there were no differences in score improvement within the online session between passive and active groups. (**Figure 1**)

Figure 1: Assessment Scores for Pre- and Post-Education Test Scores



Secondary Outcome:

In the live session, 17 of 18 participants in the live session and 17 of 19 participants in the online session reported a confidence level of “somewhat confident” or less (Figures 2 & 3). After the education session, confidence in participants in both sessions improved overall. Fourteen (14) of 18 participants in the live session reported being “somewhat confident” or better. (Figure 4) In the online group, all participants reported being “fairly confident” or higher. (Figure 5)

In subgroup analysis, confidence ratings were significantly improved ($p = 0.044$) after the educational events in the active group greater than in passive group in the live session only. The proportion of pharmacists who reported an improvement in their confidence ratings was significantly greater in the active group 92% (=11/12) than those in the passive group 50% (=3/6) who reported no change or a decrease in their confidence after the activity. None of the participants in the active group reported “not confident at all” versus two participants in the passive case group after the activity was completed.

Figure 2: Pre-Test Confidence Ratings in the Passive and Active Live Session Groups

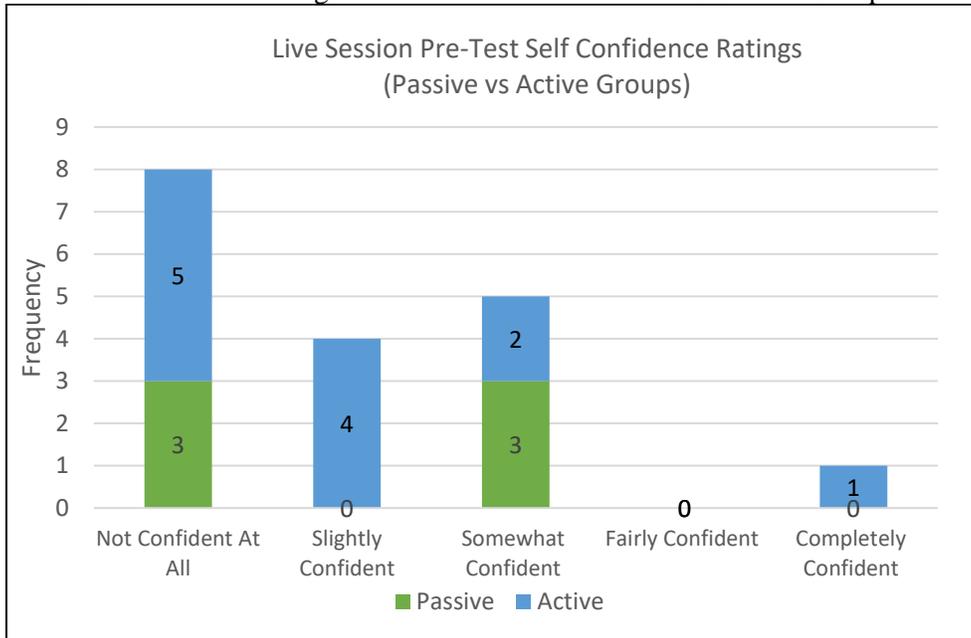


Figure 3: Pre-Test Confidence Ratings in the Passive and Active Online Session Groups

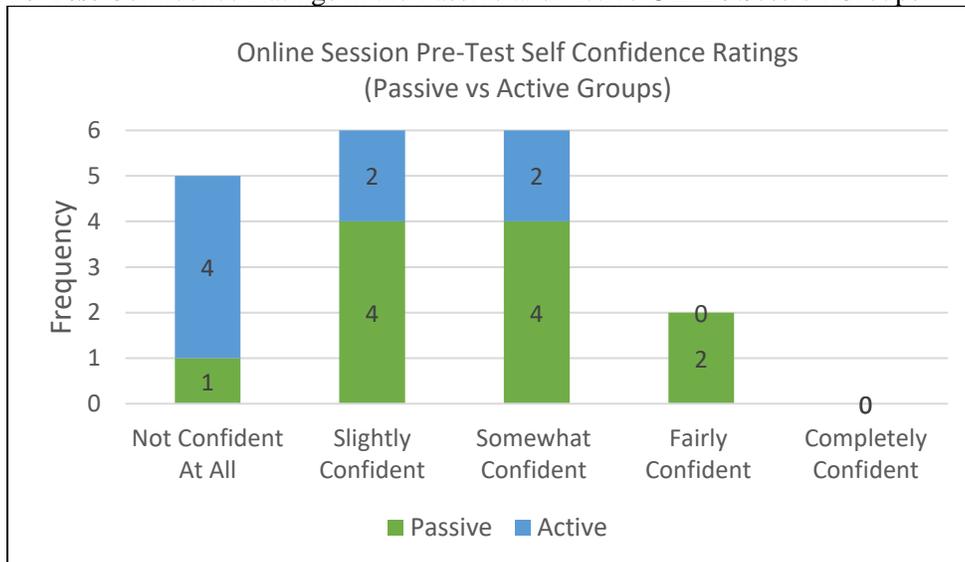


Figure 4: Post-Test Confidence Ratings in the Passive and Active **Live Session Groups**

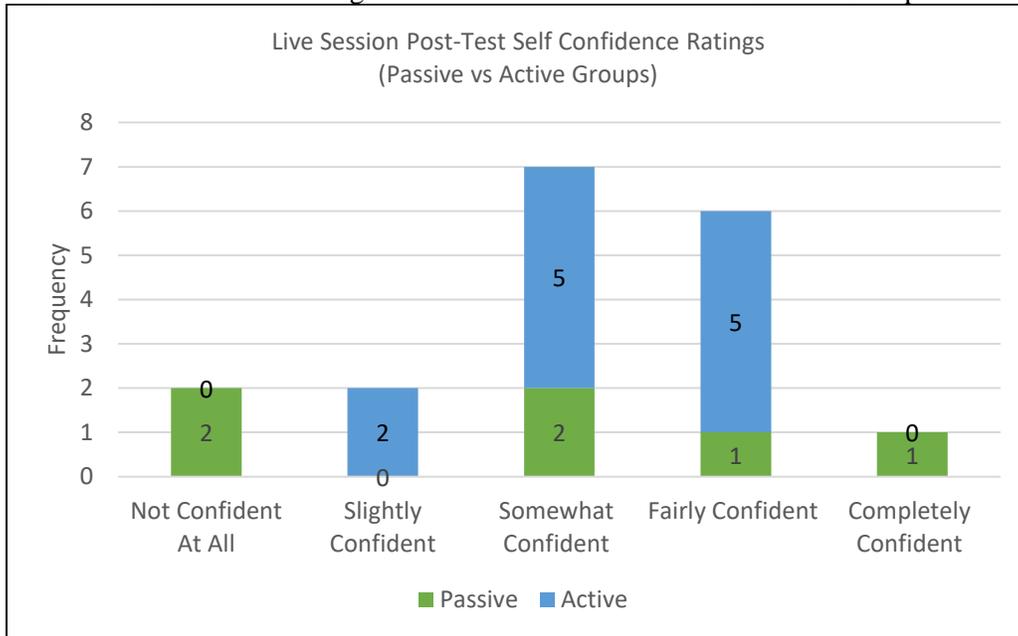
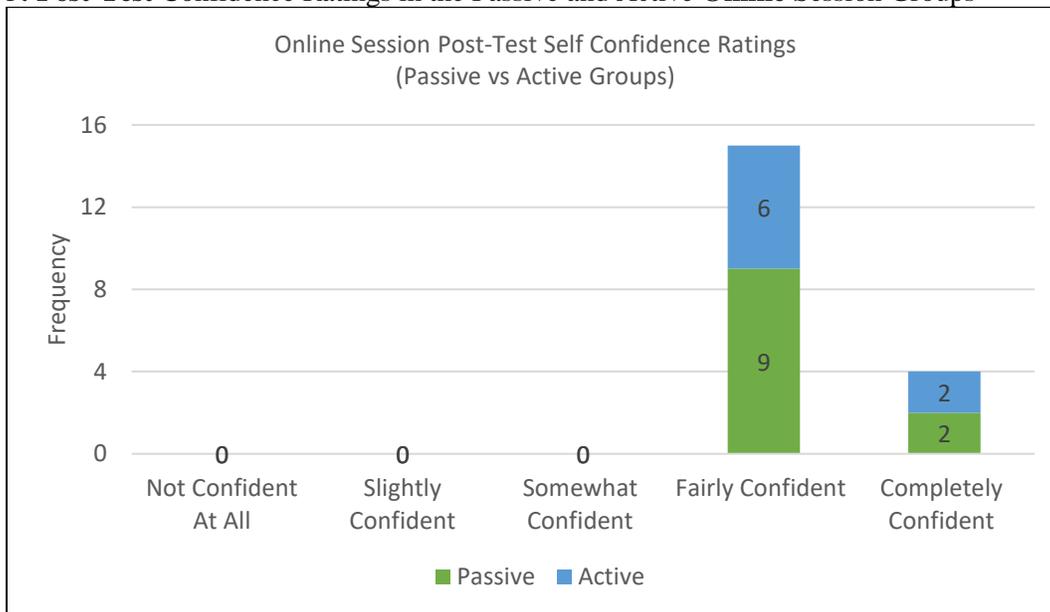


Figure 5: Post-Test Confidence Ratings in the Passive and Active **Online Session Groups**



Additional Comments:

Based on participant feedback, the active case was enjoyed by many participants, citing the active eCase was “fun”, “interactive” “amazing, so cool”. The passive case was described as “simplified” and “informative”.

DISCUSSION:

Due to the anticipated need of pharmacists to interpret pharmacogenetic tests, a comprehensive yet efficient and enjoyable education program is necessary to improve pharmacist knowledge and confidence. In our study, we found that educational interventions, whether live or online, improves confidence as shown by improvements in confidence in both online and live session participants.

Overall in the online session, knowledge scores improved from 50% to 83% in the online group and from 50% to 66% in the live session. The live session score improvement is similar to a previous study in which pharmacists improved their correct response rate from 46% to 53%. In this study, pharmacists attended online or live education sessions and differences between the delivery methods were not described. In our study, we see a dramatic difference in improvement scores in online learning group versus the in-person group. [5]A possible explanation for the differences in improvement previously reported, as well as differences between the live and online platform in our study, may be that the pre and post-tests were not monitored, nor were learners instructed to refrain from utilizing resources to assist in answering questions.

Overall, most participants reported low confidence scores before completing the CE in live and online sessions. Mirroring data seen in previous studies [3, 5], many pharmacists in our study felt “not confident at all” to “somewhat confident” regarding their ability to interpret and make recommendations based on pharmacogenetic tests. In our study, we found that confidence ratings improved after the 1-hour live CE section, suggesting that a CE course would be helpful in improving pharmacist knowledge and confidence in interpreting this anticipated increase in patient-specific pharmacogenomic results. Additionally, confidence ratings were improved by a greater proportion of participants in the active group vs the passive group (92% vs 50%) in the live session. This result may suggest that the interactive, role-playing scenario resembles actual patient encounters than what can be demonstrated in a traditional, didactic case as commonly used in CE programs and lecture-style courses. Additionally, eCases provide immediate feedback to facilitate learning. Although the interactive eCase may have improved confidence in participants, this did not translate into improved knowledge as seen by similar improvements in assessment scores within the live session or online session, regardless of being in the passive or active group.

Pharmacists additionally reported enjoying the active session, while participants in the passive session reported it to be more “informative”. This also corresponds with previous studies found that live courses with active learning components were preferred by pharmacists [3, 4]. Additionally, it seems that new practitioners seem to prefer online learning as demonstrated by baseline demographic information collected.

Limitations to this study includes our small sample size within a small network of community pharmacists who identify as USC student pharmacist preceptors, which can be expanded upon in future studies. These data support the utility of CE programs to improve comprehension, interpretation, and application of pharmacogenetic data. The online format, which requires less resources and more flexibility, may be a better avenue for delivery. Additionally, when designing a CE program for pharmacists regarding pharmacogenetics (and other topics), inclusion of an active learning eCase can be incorporated into didactic lecture based material to improve self-confidence of participants.

References

1. Food and Drug Administration (FDA). FDA News Release: FDA authorizes first direct-to-consumer test for detecting genetic variants that may be associated with medication metabolism. <https://www.fda.gov/news-events/press-announcements/fda-authorizes-first-direct-consumer-test-detecting-genetic-variants-may-be-associated-medication>. Published October 31, 2018. Accessed August 30, 2019.
2. Haider CY, Hoffman JM, Johnson, S. ASHP statement on the pharmacist's role in clinical pharmacogenomics. *Am J Health Syst Pharm*. 2015;72(7);579-81. doi: 10.2146/sp150003.
3. McCullough KB, Formea CM, Berg KD, et al. Assessment of pharmacogenomics educational needs of pharmacists. *Amer J of Pharm Educ*. 2011; 75(3); 1-6. doi.org/10.5688/ajpe75351.
4. Berenbrok LA, Hart KM, Harriman S, et al. Community pharmacists' educational needs for implementing clinical pharmacogenomic services. *J Am Pharm Assoc*. 2019; 59(40):539-544. DOI: <https://doi.org/10.1016/j.japh.2019.03.005>
5. Formea CM, Nicolson WT, McCullough KB. Development and evaluation of pharmacogenomic educational program for pharmacists. *Am J Pharm Ed*. 2013; 77(1).
6. Latif DA, McKay AB. Pharmacogenetics and pharmacogenomics instruction in colleges and schools of pharmacy in the United States. *Am J of Pharm Educ*. 2005; 69(2): 152-156.
7. Accreditation Council for Pharmacy Education. (2015). Accreditation standards and key elements for the professional program in pharmacy leading to the Doctor of Pharmacy Degree. *ACPE*, 39.

Appendix 1:

- 1) Which of the following drug/adverse event pairs have known pharmacogenetic associations?
 - a) Abacavir / neutropenia
 - b) Mercaptopurine / myelosuppression**
 - c) Atorvastatin / myopathy
- 2) Warfarin metabolism is affected by genetic variants in which gene? (LO #2)
 - a) CYP2C9**
 - b) CYP3A4
 - c) CYP2D6
 - d) CYP1A2
- 3) A CYP2C19 *2/*2, *2/*3 or *3/*3 genotype would correspond to which metabolic phenotype?
 - a) Ultra-rapid metabolizer
 - b) Extensive metabolizer
 - c) Intermediate metabolizer
 - d) Poor metabolizer**
- 4) Which CYP2D6 phenotype would be at risk of insufficient analgesia with codeine?
 - a) Ultra-rapid metabolizer
 - b) Extensive metabolizer
 - c) Poor metabolizer**
- 5) You have a patient who comes to your pharmacy and has been on a therapeutic dose of paroxetine for 2 months. She states that she has experienced many side effects from the medication and would like to have a pharmacogenetic test to help guide her therapy. Which CYP enzyme metabolic phenotype would warrant switching to an alternative therapy?
 - a) CYP2D6 Ultra-rapid metabolizer**
 - b) CYP2D6 Extensive metabolizer
 - c) CYP2D6 Intermediate metabolizer
- 6) You have a patient who was started on simvastatin 10 mg. He reports dark urine and muscle pain. Which gene is associated with increased risk of myopathy with simvastatin?
 - a) EGFR
 - b) HLA-B
 - c) VKORC1
 - d) SLCO1B1**