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ORIGINAL RESEARCH

The Efficacy of a Didactic and Case-Based Pharmacogenomics Education Program on Improving the Knowledge and Confidence of Alberta Pharmacists

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Background: Pharmacogenomics (PGx) is the study of how genetic variations for functional proteins, such as metabolizing enzymes and drug receptors, impact drug pharmacokinetics and pharmacodynamics. In theory, pharmacists are well suited to utilize PGx in tailoring medications to patient genetics when providing medication therapy management services. However, PGx education needs to reach pharmacists prior to implementation. The aim of this study is to develop and evaluate a PGx course for pharmacists.

Methods: A PGx education program was created and offered synchronously (virtual) and asynchronously (self-study) to pharmacists in Alberta, Canada. Lectures were delivered by experts live (virtual) with a question-and-answer period for synchronous sessions. These sessions were recorded for asynchronous delivery. Six case studies were discussed in large and small groups ("breakout rooms") in synchronous sessions, and provided for self-study in the asynchronous subgroup. Topics included genetic and PGx concepts; therapeutic applications; ethical, legal, and social considerations; and practical implementation. Pre- and post-course surveys measured self-rated knowledge using a 5-point Likert Scale and tested objective knowledge with a graded quiz.

Results: Thirty-six pharmacists completed the course and both surveys. Participants reported backgrounds in community (88.9%) and hospital (38.9%) practice. Prior education in PGx was reported by 44.4% from degree programs and 27.8% from continuing education. Overall responses to statements about confidence in PGx moved from a median of "Disagree" at baseline to "Agree" after receiving PGx education (2-point difference [1,2] on 5-point Likert Scale; $p < 0.001$), indicating an increase in self-assessed competency in PGx. Likewise, mean participant grades on the knowledge quiz improved (20.8±21.9% pre-course vs 70.2±19.1% post-course, $p < 0.001$). There was no difference in these results between synchronous and asynchronous groups.

Conclusion: A didactic and case-based PGx education program was effective at increasing pharmacist knowledge and confidence in PGx in both synchronous and asynchronous environments. Knowledge gained can be utilized in delivery of patient-centered, personalized medication therapy management in the pharmacy setting.

Keywords: pharmacy practice, pharmacy, pharmacogenetics, virtual learning, medical education, precision medicine, pharmacogenomics

Introduction

Pharmacogenomics (PGx) is a field of medicine and pharmacy that stands to reduce hospitalizations,[1,2] improve drug efficacy and safety,[3–5] and through these measures ultimately reduce patient morbidity and mortality. PGx accomplishes this by tailoring drug therapy to individual patient DNA sequences encoding for drug metabolizing enzymes, transporters, receptors, and other functional proteins.[6,7] Published guidelines are available through the Clinical Pharmacogenetics Implementation Consortium (CPIC), the Dutch Pharmacogenetics Working Group (DPWG), the Canadian Pharmacogenomics Network for Drug Safety (CPNDS), and the French National Network of Pharmacogenetics (RNPGx). A compilation of these guidelines,

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along with dosing labels by the United States Food and Drug Administration (FDA) website, are available through the Pharmacogenomics Knowledge Base (PharmGKB) for the interpretation and application of PGx information.[8,9] Furthermore, PGx information is now incorporated into the drug information available within commonly used online medication resources, such as Lexicomp and Micromedex.[10] PGx reports typically provide phenotype interpretation from genotype to metabolizing enzymes, transporters, receptors, and other functional proteins, occasionally aided by the health-care provider's assessment for phenoconversion. When used in conjunction with other factors such as organ function, laboratory test results, clinical symptoms, concomitant medications, and environment/lifestyle factors,[11] health-care providers are able to tailor a drug therapy plan for the patient in what is known as precision medicine.[12,13] While pharmacists are nominated and acknowledged to be the best-suited health-care provider to interpret PGx test results, and subsequently recommend appropriate drug therapy,[14,15] few pharmacists have the training, knowledge, or confidence to do so currently (Table 1). Within the results of a recent scoping review on the implementation of pharmacogenomics in pharmacy practice,[16] it was identified that settings with well-described pharmacist PGX education programs prior to providing such services saw greater prescriber acceptance of recommendations, compared to studies without pharmacist education. This demonstrates the improved ability of PGx-educated pharmacists to assess drug–gene interactions (DGIs) and communicate the appropriate management of these interactions to other health-care providers. Therefore, it is critical pharmacists are equipped with sufficient knowledge and understanding of pharmacogenomics in order to safely, effectively, and confidently assess medications with pharmacogenetic implications. Albeit the gap in pharmacogenomics education has improved in the last decade,[17–19] currently practicing pharmacists and recent graduates alike will need to be provided with updated information in this rapidly evolving field through continuing education programs. By supplementing pharmacists' established competencies in medication therapy management (MTM) and patient education,[11,20] we can ensure the effective implementation of PGx within the pharmacy patient care process, to the betterment of patient drug therapy outcomes.

There are important considerations in developing a PGx program for practicing pharmacists. One is that effectively studied and validated teaching methods should be utilized. Case-based learning has been shown to be highly effective in the education of pharmacists[21–23] and pharmacy students[24,25] in pharmacogenomics, and has demonstrated its utility in other therapeutic topics as well.[26] While there are a few PGx education programs available for continuing education in Canada, only one of these has been evaluated to date.[21] Teaching methods from these studies and other research in pharmacy education[26–29] can be adopted, there is a need to develop and validate a new program for Alberta pharmacists specifically. In this province, practice is wider in scope compared to other Canadian provinces and to other countries, as it includes the additional authorization to independently prescribe.[30] Other research in Alberta supports the benefit to patients that can be realized with pharmacist prescribing in chronic disease management. In another Alberta-based study, patients with hypertension managed directly by pharmacists (utilizing prescribing when required to titrate or change medications) experienced a 18.3±1.2mmHg reduction in systolic blood pressure, compared to the reduction of 11.8±1.9mmHg observed in a control group receiving standard education without pharmacist prescribing.[31] This ability to ensure patients receive optimal pharmacotherapy can potentially extend into PGx services, as pharmacists can incorporate PGx test results into their medication therapy plan.

The aims of this study were to 1) establish an up-to-date, validated PGx webinar course that covered the competencies established by Roederer et al (Figure 1),[32] key therapeutics identified in scoping the literature available on PGx in pharmacy practice,[16] and insights shared by international PGx experts; 2) evaluate the impact of this course on the knowledge and confidence of Alberta pharmacists in PGx; 3) explore the baseline understanding of PGx among study participants; 4) develop a validated continuing education and course curriculum that can be shared with other Alberta pharmacists asynchronously for wider future implementation of PGx in Alberta.[33]

Methods

General Design

This was a longitudinal survey-based observational study measuring the impact of a training program on pharmacists' knowledge, confidence, and opinions of PGX delivered as either a live two-day webinar, or as a self-study course derived from recordings and written materials included in the live sessions. Participants served as their own control, answering

Table 1 Recent Survey Assessments of Pharmacist Knowledge, Confidence, and Training in Pharmacogenomics. While There Have Been Very Few Studies in Canada Analyzing This Data, Studies Globally Reflect the Current Landscape of Pharmacist Competence in Pharmacogenomics

Reference	Country	Pharmacist Population	Mean Knowledge Score	Self-Rated Confidence/ Understanding Moderate to High	Prior Training or Exposure in PGx	Desiring More PGx Education[d]	Other Findings
Brown et al. (2021)[53]	USA	Pediatric institutional pharmacists at mostly urban academic settings	N/A	N/A	78.6%	50%	Low-use sites cited more barriers in knowledge, support, and ELSI; both high-use and low-use indicate cost and technology barriers
Tsuji et al. (2021)[48]	Japan	Pharmacists in mostly hospital settings (81.3%)	43%	12.5%	25.7%	72.4%	93.6% felt PGx was/could be useful for care, 30.8% could identify 5 or more drugs with PGx indications.
Jarrar et al. (2021)[54]	Palestine (West Bank)	Pharmacists in mostly community or outpatient settings (75%)	N/A	30%	16.8%	N/A	Most pharmacists agree they should know more about (94%) and use (~80%) PGx in patient care.
Edris et al. (2021)[55]	Belgium	Pharmacists (community and hospital)	37%	23%	42%	N/A	Most pharmacists (and physicians) surveyed were unfamiliar with PGx resources (89% of pharmacists were unfamiliar with PharmGKB, 92% with CPIC, 80% with DPWG, and 70% with FDA PGx labels.
Rahma et al. (2020)[56]	United Arab Emirates	Registered pharmacists	56.7%	29.7%	41.5%	57.8%	91.9% of all survey respondents (HCPs including RPhs) support PGx testing. Other barriers identified include cost (62%) and insurance coverage (57.2%). Only 9% of all respondents agree that pharmacists should perform PGx services.
McMurdo et al. (2020)[57]	Canada (Alberta)	Registered pharmacists	N/A	25%	52%	N/A	80% of pharmacists agreed that PGx testing is beneficial and it is important to comprehend test results.
Petit et al. (2020)[47]	Canada (Quebec)	Pharmacists (community, hospital, and other settings)	63.2%	37.7%	72.6%	90.3%	While the proportion of participants with prior training in PGx is high, 66.7% identify this training cumulates to less than 5h of exposure total.
Crown et al (2020)	Canada (Ontario)	Community and primary care clinic pharmacists	56%[a]	Low[b]	57%	High[c]	

(*Continued*)

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Table 1 (Continued).

Reference	Country	Pharmacist Population	Mean Knowledge Score	Self-Rated Confidence/ Understanding Moderate to High	Prior Training or Exposure in PGx	Desiring More PGx Education[d]	Other Findings
Nagy et al. (2020)[46]	Egypt	Pharmacists at the Children's Cancer Hospital	41.7%	13%	9.6%	64%	An 80% survey response rate and overall, mostly agree/strongly agree responses in the opinion surveys of PGx indicate positive opinions on PGx testing among pharmacists and physicians.
Hundertmark et al. (2020)[49]	USA	Hospital pharmacists	N/A	37.4%	24%	88%	58% of pharmacists agree that pharmacists are the best provider to implement PGx testing. Those with residency training are more likely to rate their knowledge higher than those without (p=0.03).
Karuna et al. (2020)[58]	Thailand	Hospital pharmacists	43%	N/A	18.7%	13%	Barriers identified include test reimbursement and ELSI concerns
Algahani (2020)[44]	Saudi Arabia	Hospital pharmacists	59.8%	32.5%	30%	83%	76% agreed pharmacogenomics should be used in practice.
Meloche et al (2020)	Canada (Quebec)	Pharmacists (community and hospital)	N/A	14%	31%	91%	100% of pharmacists agree PGx testing will be able to support medication selection and dosing to some degree. 94% of pharmacists have at least some concerns about genetic discrimination.

Notes: [a]Pre-course scores in an education study. [b]Mean pre-program rated confidence in using PGx 1.6 on a 5-point Likert Scale. [c]143 applicants for 25 seats in the program; color coding: red = poorly rated, orange = moderately rated, yellow = highly rated, [d]Reverse coding used.

Abbreviations: CPIC, clinical pharmacogenomics implementation consortium; DPWG, Dutch Pharmacogenetic Working Group; ELSI, ethical, legal, and social implications; FDA, [United States] Food and Drug Administration; HCP, healthcare provider; PGx, pharmacogenomics; RPh, pharmacist.

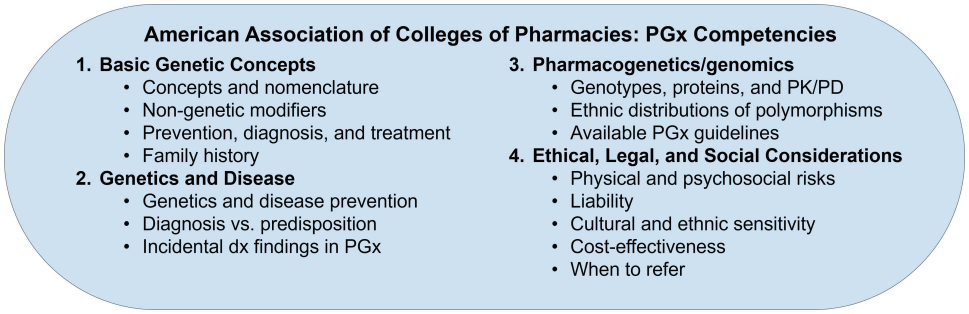

Figure 1 Pharmacogenomic competency domains, adapted from Roederer et al.[32]

the same survey prior to and after the education program. Instructors were invited from Canada, USA, Egypt and Qatar to facilitate incorporation of global perspectives in PGx.

Participants

Recruitment

Practicing pharmacists in the province of Alberta, Canada, were recruited through email correspondence with pharmacy managers, general social media posts, and word-of-mouth referrals for either synchronous, asynchronous, or mixed attendance. After expressing interest from a potential participant, a formal recruitment email was sent to the potential participant with details regarding both the research study and PGx course. The recruitment email contained a link to the implied consent form and pre-course survey. Recruitment commenced March 2021. Synchronous and mixed participants were accepted until the night before course commencement on June 12, 2021, and asynchronous participants were eligible for inclusion in primary outcome data analysis if pre-course and post-course surveys were completed prior to 23:59 September 20, 2021.

Inclusion Criteria

Any pharmacist with an active pharmacy practice Alberta license was eligible for inclusion, and there was no specific exclusion criteria. Pre-course surveys without a matched post-course survey were still eligible for inclusion in the secondary outcome analysis of baseline knowledge and confidence among practicing pharmacists.

Outcomes

The primary outcome of this research study was the change in median Likert Scale scores for opinion/confidence questions, as well as the change in mean knowledge quiz scores, in paired data analyses of pre-course and post-course surveys. The secondary outcomes of interest were the baseline demographic, individual opinion/confidence answers, and knowledge quiz scores in the pre-course survey only. The secondary outcomes were compared among subgroups of pharmacists based on prior training in pharmacy, years of practice, age, gender, and prior exposure to pharmacogenomics.

Survey Design

A survey was created to collect demographic and pharmacy education/experience pre-course and measure subjective and objective competency in pharmacogenomics both pre- and post-course. Education and experience questions focused on practice environment as well as prior exposure to PGx information. There were 11 questions on pharmacist opinions and confidence on pharmacogenomics, each to be rated on a Likert Scale, with possible answers consisting of "Strongly Agree," "Agree," "Neutral," Disagree," and "Strongly Disagree." The survey closed with 7 exam-style questions testing pharmacogenomics knowledge, with varied question types that included single choice and multiple checkbox answers to total a maximum potential mark out of 14. Questions for both Likert Scale and knowledge quiz were created utilizing a review of similar research and consultation with experts. The topics addressed in these were considered of high importance for pharmacist PGx competencies according to the American Association of Colleges of Pharmacy.[32] Survey questions underwent face validation by pharmacy educators and practicing pharmacists to ensure clarity of questions. The surveys took approximately 10 minutes for participants to complete. The full survey is available in Supplementary Materials 1.

Pharmacogenomics Education Course Content

The training program consisted of 11 lectures (Supplementary Materials 2, Table S2.1) by various experts covering the competences and therapeutics identified in Figure 1[32] and the scoping review,[16] respectively, and 6 case studies developed by the research team (Supplementary Materials 2, Table S2.2). Speakers were invited by the research team based on their expertise in the field of PGx in pharmacy, with an aim to recruit experts from different countries to incorporate an international PGx approach. The therapeutic areas of focus for this course were selected based on a scoping review on the use of pharmacogenomics in pharmacy practices.[16,28] Particularly, the applications of PGx in cardiovascular, psychiatric, and pain indications, which all have guidelines available from organizations such as the CPIC, were found in the literature to be feasible and clinically useful in the pharmacy setting.[16] The AACP PGx Competency statement[32] also informed the education sessions on basic genetic and pharmacogenetic knowledge, as well as the ethical, legal, social, and practical implications of use of PGx in pharmacy practice. The pharmacist patient care process[11,34] was utilized within a dedicated session as well as throughout course and case-study design to emphasize the role of PGx information in concert with other patient characteristics and the larger clinical picture.

The preliminary design of this research study and course was a completely synchronous program to take place over two days, ideally in a live conference setting. However, due to the circumstances of the COVID-19 pandemic, the decision was made to utilize virtual venues in concordance with public health guidelines at the time. Participants were provided with the option to attend both days live (synchronous, virtually), self-study (asynchronous, online), or a combination of these options suitable to their schedule and commitments (mixed).

Synchronous Course

For participants able to attend some or all the content live, a virtual course was held over Zoom (Zoom Video Communications, Inc., San Jose, California) on June 12–13, 2021, for 5 hours each day. Handouts were provided the night prior to each day, containing lecture slides and case studies without answer keys. Within each major topic, case studies would be provided for participants to work through with the facilitators in between didactic sessions. Breakout rooms were included in half of the cases to allow participants to interact with one another and solve problems posed within the cases together with a course facilitator (a research team member and the invited speaker). Each didactic lecture included a question-and-answer period with the speaker, with questions from the chat-box read out by a moderator. The use of a chat-box was to ensure participant confidentiality in recordings of sessions in alignment with research ethics, as these recordings were used in the asynchronous course described below. The breakout rooms where discussions occurred between facilitators and speakers were not recorded. Live didactic sessions ran for 15–45 minutes per session (including the Q&A), and 15–30 minutes were spent on each of the case studies.

Asynchronous Course

For participants requiring self-study for some or all the course content, the live sessions were recorded and organized into individual modules. Case studies were provided with answer keys and instructions on the suggested timing to complete the case within the order of the video content. Mixed participants unable to attend the first day live were provided the session recordings, handouts, and case studies by email, with sufficient time to complete these before the second day sessions. Completely asynchronous participants were given access as "viewers" of a Google Drive folder (Google LLC, Mountain View, California) after completing the pre-course survey. The course folder contained instructions for completing the course, each individual session video with slide handout, case studies with answer keys, and supplementary materials such as additional readings and resources referenced in the course. Asynchronous participants were advised of a deadline of September 13, 2021, to complete the post-course survey.

Data Collection

Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Alberta.[35,36] REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies. Pharmacists who expressed interest in participating were sent a pre-course survey from REDCap prior to attending the live course or receiving access to the course materials depending on synchronous or

asynchronous participation, respectively. After participants completed either synchronous or asynchronous learning, they received the post-course survey by email. Synchronous participants were given time before closing remarks to complete the post-course survey, and asynchronous participants were provided direction to complete the post-course survey as soon as reasonably possible after viewing all videos and completing all case studies. Participants were not provided with their answers to either survey after completion.

Statistical Analysis

Participant demographic data was summarized as mean ± standard deviation (SD), or n (%) for normally distributed numerical variables and categorical variables, respectively. The Central Limit Theorem (CLT) was applied to non-normal data with an $n \geq 30$, while non-normal data with an $n < 30$ was summarized as median (interquartile range; IQR). Likert scale responses were coded as follows: Strongly Disagree (1), Disagree (2), Neutral (3), Agree (4), and Strongly Agree (5), with a higher number reflecting more positive opinions/greater self-confidence. Answers to these questions were analyzed for the primary outcome by paired Wilcoxon Rank Sum analysis for the Likert scales used, and the knowledge-based quiz was graded by the research team and compared pre- and post-education as mean ± SD in a paired Student's *t*-test if distribution was normal or CLT could be applied. If these assumptions were not met, Wilcoxon Rank Sum was used for analysis. In the secondary analysis, individual responses to Likert scale and knowledge test questions were summarized as n (%). Subgroup comparisons of Likert-scale responses and non-normal knowledge test data were compared using Wilcoxon Rank Sum or Kruskal–Wallis test depending on the number of groups. If significance was found with Kruskal–Wallis, the Dunn test was used for multiple comparisons and adjusted p-values were manually calculated for the number of comparisons. A forward selection linear regression was built for knowledge test scores for all pre-course surveys received using demographic and education history data and mean value of confidence rated on the Likert-scale questions. A similar regression was built for mean confidence scores using demographic and education history data and knowledge test scores pre-course. The mean values were used in the linear regression on confidence scoring rather than median for higher sensitivity. Lastly, to validate the subjective survey administered, mean Likert responses were compared to mean test grades for participants in a linear analysis for all pre-course surveys, all post-course surveys, and the calculated difference in these values from pre-course to post-course. All statistical analyses were performed using STATA version 17 (StataCorp, College Station, Texas, USA), and a $p < 0.05$ was considered statistically significant.

Ethics Approval

Informed implied consent form was included on the cover page of both the pre-course and post-course surveys. Electronic Consent was implied by completion of the surveys, documented in the de-identified participant record by the completed status on the REDCap database. Written (wet ink) consent was not sought out due to the virtual nature of participation for live course participants from a broad geographical region, and due to the asynchronous nature of participation for self-study course participants. Within this study design, participants never met in person with the research team. However, the study procedures were explained to each participant through the invitation email approved through ethics, with a member of the research team responding to any potential participant queries in a timely manner. The study team's contact information was provided to all participants within the implied consent form, which participants were advised to print for their records. This study and consent procedure was approved by the University of Alberta Research Ethics Board (Pro 0108818).

Results

Participants

At least 2000 pharmacists were reached through social media, email, and word of mouth referrals (Figure 2). While there is no method to determine the true number of potential participants reached by social media, interested pharmacists reached out through email and social media for more information, and were subsequently sent an email invitation to participate in the study. There were 69 Alberta pharmacists invited to complete the initial pre-course survey. A total of 36 pharmacists were included in the primary outcome analysis: 10 attended all live Zoom sessions synchronously, 9

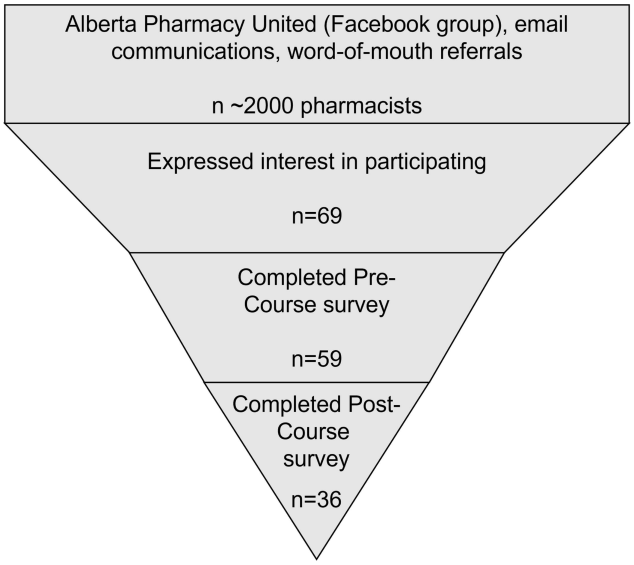

Figure 2 Pharmacists were recruited to participate through a variety of measures that resulted in 69 official study invitations. Of these, 85.5% completed the initial survey, and 52.2% completed both surveys.

participated through a combination of synchronous and asynchronous methods, and 17 completed the course asynchronously only. An additional 23 pre-course surveys without a matched post-course survey were included in the secondary analyses. Pharmacist demographics are summarized in Table 2. Most pharmacists who completed both surveys for primary analysis had community experience (88.9%) and over a third had worked in hospital settings. In the primary analysis, only 11 (30.6%) had no prior education or exposure to pharmacogenomics.

Knowledge, Confidence, and Opinions

Survey Validation

In addition to face validation, simple linear regression analyses were performed to determine correlation between subjectively rated knowledge (mean Likert scale responses) and objectively tested knowledge (mean scoring on quiz portion of survey). Moderate, statistically significant relationships between subjective and objective knowledge was observed (pre-course $r = 0.476$, $p < 0.001$; post-course $r = 0.401$; $p = 0.015$). This indicated that a participant's subjectively rated knowledge was proportional to their objectively tested knowledge, with this relationship slightly stronger prior to education.

Subjective Self-Rated Confidence

Impact of Pharmacogenomics Course on Confidence

As noted in the statistical analysis, Likert Scale responses were coded 1 = "Strongly Disagree" to 5 = "Strongly Agree". Pharmacist responses to Likert Scale statements changed from a median of "Disagree" (2 [2,3]) to "Agree" (4 [4,4]) after pharmacogenomics education ($p < 0.001$) in the 36 participants included in the primary analysis, indicating an overall improvement in participant self-rated knowledge. The improvement in mean subjectively rated knowledge (Likert scales) was determined to have a positive linear relationship with improvements in objective knowledge test grades with pharmacogenomics education (Figure 3), meaning those who experienced greater improvement in their own self-assessed competency, had also experienced greater improvement in their objectively tested knowledge. Statistically significant improvements in subjective responses were observed consistently among each individual question (Figure 4), showing global improvement among all PGx domains. There was no significant difference in the change in subjective knowledge or the final subjective knowledge as rated on the Likert scale based on course participation method, all methods demonstrated improvement in PGx

Table 2 Demographics, Education, and Pharmacogenomics Exposure for Participating Pharmacists

Characteristic	Completed Course (n=36) Mean ± SD or n (%)		Pre-Course Survey Only (n=23) Mean ± SD or n (%)	
Gender				
Male	13[a]	(36.1)	8	(34.8)
Female	22[a]	(61.1)	15	(65.2)
Age (years)	37.3 ± 8.3[a]		39.3 ± 9.0	
Years of Practice				
Less than 2 years	4	(11.1)	5	(21.7)
2–5 years	4	(11.1)	–	–
6–10 years	11	(30.6)	3	(13.0)
More than 10 years	17	(47.2)	15	(65.2)
Country of Entry-to-Practice Degree[a]				
Canada	25	(69.4)	18	(78.3)
Egypt	4	(11.1)	1	(4.4)
India	2	(5.6)	1	(4.4)
Other	4[b]	(11.1)	3[f]	(13.0)
Highest Degree Obtained				
Bachelor's	27	(75.0)	13	(56.5)
Pharm D	5	(13.9)	4	(17.4)
Master's	1	(2.8)	2	(8.7)
PhD	3	(8.3)	2	(8.7)
Additional Training or Certifications[c]				
Additional Prescribing Authorization	22	(61.1)	17	(73.9)
Certification to Administer Injections	31	(86.1)	18	(78.3)
Certified Diabetes Educator	3	(8.3)	2	(8.7)
Accredited Canadian Pharmacy Resident	4	(11.1)	2	(8.7)
Other	6[d]	(16.7)	–	–
Settings of Pharmacy Practice in Career[c]				
Community Pharmacy	32	(88.9)	21	(91.3)
Hospital	14	(38.9)	7	(30.4)
Primary Care Network	–	–	1	(4.4)
Research/Academics	3	(8.3)	1	(4.4)
Industry	2	(5.6)	–	–
Other	3[e]	(8.3)	2[g]	(8.7)
Prior Pharmacogenomics Exposure				
Education on PGx in Degree Program	16	(44.4)	7	(30.4)
Education on PGx in Post-Graduate or Continuing Education	10	(27.8)	4	(17.4)
Prior Experience with PGx Testing	1	(2.8)	4	(17.4)

Notes: [a]Denotes one missing value; [b]n=1 each of Nigeria, Philippines, South Africa, and United Kingdom; [c]Participants could select more than one choice; [d]n=1 each of Board Certified Ambulatory Care Pharmacist, Board Certified Psychiatric Pharmacist, Certified Respiratory Educator, Hepatitis C Prescriber, Certified Tobacco Educator; [e]n=1 each of Government Drug Program, Military, and Corporate. [f]n=1 each of Libya, Nepal, and United Kingdom; [g]n=1 each of Military and Corporate.

Abbreviations: PGx, pharmacogenomics; SD, standard deviation.

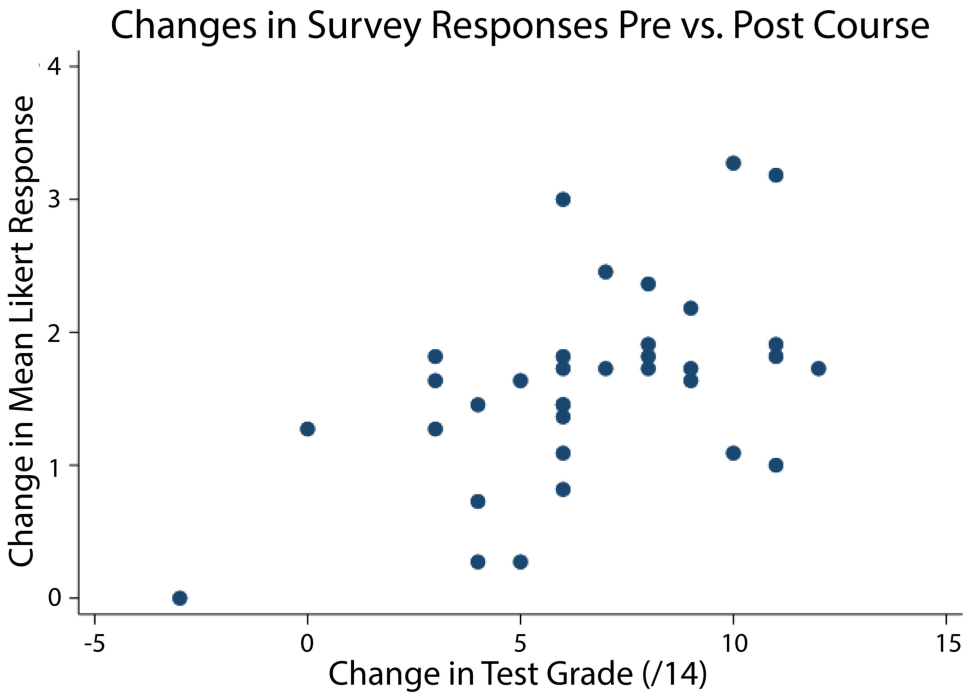

Figure 3 Mean Likert responses in agreeance with confidence in pharmacogenomics increased by 0.12±0.20 points for every correct answer gained on the knowledge test after education (r = 0.516; p = 0.002; n = 34).

subjective and objective knowledge. Furthermore, there were no identified participant characteristics such as experience, years of practice, or prior use of PGx that indicated a difference in final post-course confidence.

Baseline Confidence Assessment

Among the 59 pre-course surveys received, median responses for nearly all questions were "Disagree" (2) at baseline. Only the two opinion-based statements, "Pharmacogenomics can enhance the provision of medication-related services (eg, dispensing, care-planning)" and "Pharmacogenomics testing is cost-effective" received median responses greater than 2 (these were 4 and 3, respectively). There was a significant difference in baseline median confidence/opinions between pharmacists with prior PGx training in their degree program vs those without (2 [2,3] vs 2 [1.5,2]; p = 0.003); and in internationally educated pharmacists vs Canadian graduates (3 [2,4] vs 2 [2,2]; p = 0.005).

When a forward selection linear regression was built with the mean Likert responses, higher objective knowledge test scores (p = 0.001), international education (p = 0.006), prior experience with PGx testing (p = 0.137, included due to plausible effect), and prior PGx education in degree program (p = 0.002) and in continuing education (p = 0.021) were all found to fit a model that explained 53.1% of the variation in mean Likert responses agreeing with positive opinions and subjective knowledge in PGx pre-course (p < 0.001). Objective knowledge test scores alone appeared to account for 22.6% of the variation in Likert responses on its own in pre-course analysis. This relationship was slightly less strong post-course, with only 16.1% of variation in Likert responses explained by objective knowledge.

Objective Tested Knowledge

Impact of Pharmacogenomics Course on Knowledge

Mean participant grades in the knowledge test portion of the survey improved significantly pre-course vs post-course (20.8±21.9% vs 70.2±19.1%, p < 0.001; Figure 5). Each question saw significant improvement in correct responses post-course (Table 3). There was no difference between course participation methods and the quantitative test grade improvement of participants (synchronous, asynchronous, mixed; 64.3% [42.9, 78.6], 42.9% [42.9,57.1], 42.9% [35.7, 50.0]; p = 0.199), albeit synchronous participation had numerically greater test grade improvement than asynchronous and mixed methods. In comparing standalone post-course grades, there was only a significant difference in median grades

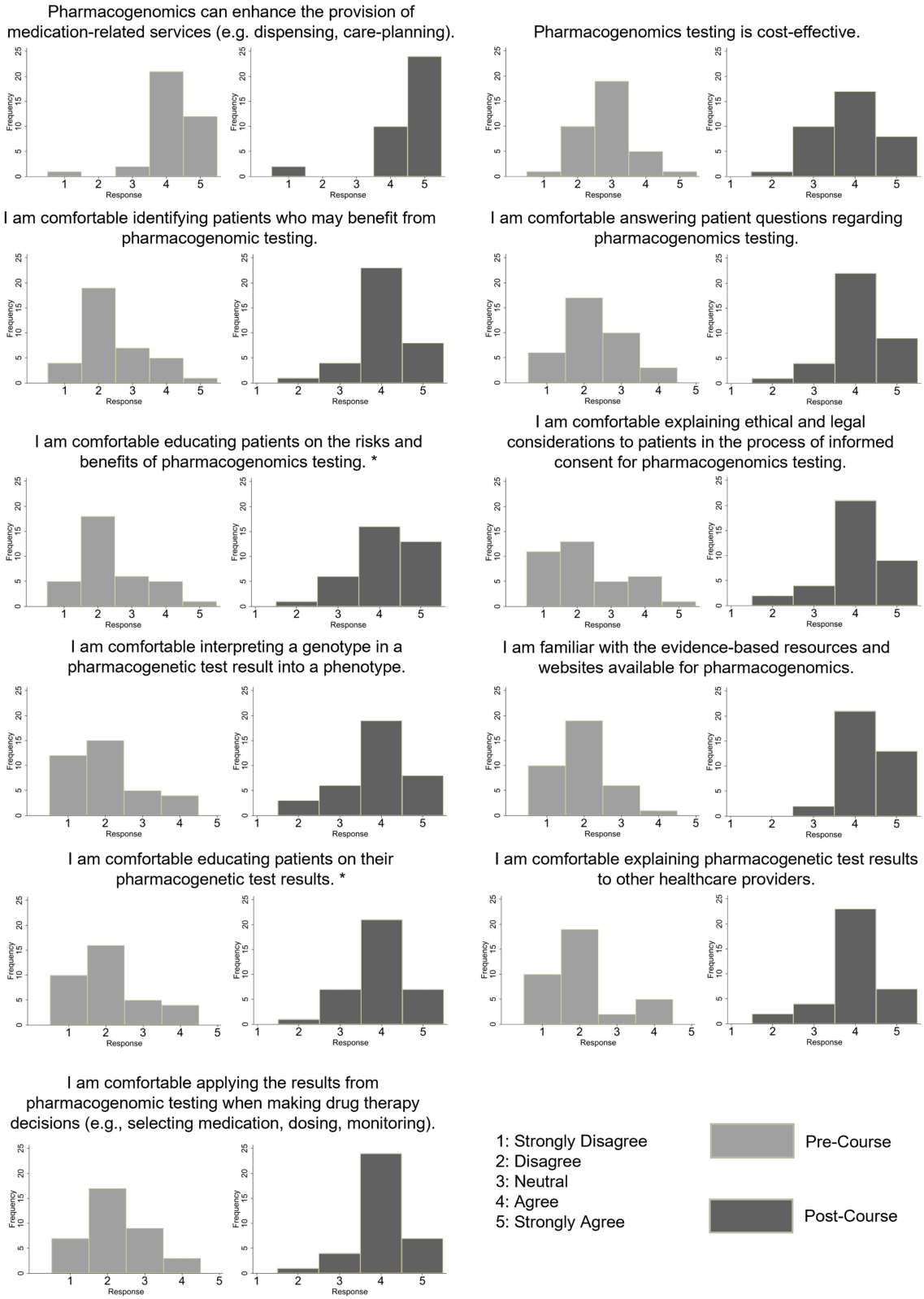

Figure 4 Frequencies of responses to 11 Likert scale (1–5) questions by participants (n = 36) before and after pharmacogenomics education. *One missing value in pre-course survey.

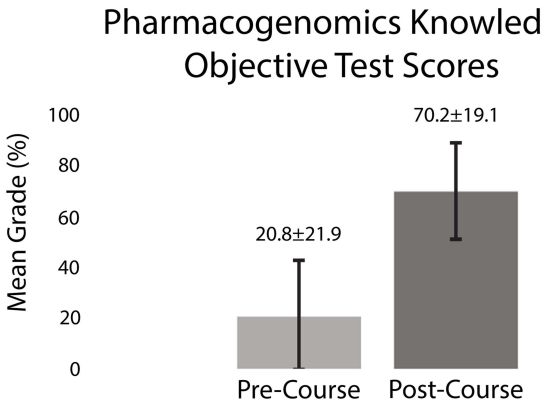

Figure 5 Pharmacists (n = 36) completed a knowledge test before and after pharmacogenomics education.

between the synchronous and mixed groups (78.6% [78.6, 92.9] vs 64.3% [42.9, 78.6]; adj-p=0.014), while the difference in synchronous vs asynchronous (78.6 [57.1, 78.6]) approached significance (adj-p=0.091). The only demographic/exposure factor found to impact post-course grades was that hospital experience resulted in better post course grades (64.0±21.3% without hospital experience vs 80.1±8.5% with hospital experience; p = 0.003).

Baseline Knowledge Assessment

In a forward selection linear regression analysis, practice experience less than 10 years (p = 0.034), hospital practice (p = 0.005), foreign pharmacy education (p = 0.209), and higher subjective self-assessments (p = 0.012) all predicted higher pre-course tested knowledge, accounting for 38.2% of variation in pre-course knowledge test scores (p < 0.001). While country of pharmacy education was not significant, it was included in the multivariate model due to its effect on other covariates (without interaction), and impact on r^2. As noted in the subjective Likert response results, higher post-course subjective confidence/opinions predicted better post-test grades.

Discussion

Pharmacogenomics in clinical practice involves testing genes for certain metabolizing enzymes, receptors, and other functional proteins that are involved in drug disposition and/or effect.[6,7] This information is used alongside other patient factors such as signs, symptoms, lab values, and preferences, to select optimal drug therapy.[12,13] Other components of PGx include the education the HCP must provide the patient before and after testing, and the communication of PGx information with other health-care providers. Such clinical PGx use in pharmacy practice has increased dramatically over the last decade.[16] This study resulted in the development of a two-day webinar-style course in PGX for practicing pharmacists to support future clinical implementation. This course was further adapted as a self-study program, and both methods of learning showed significant improvement in self-rated (subjective) knowledge as well as proportional improvement in tested (objective) knowledge. Interest in this course was relatively high considering the COVID-19 pandemic, wherein pharmacists' priorities were already stretched in delivering vaccinations, asymptomatic testing, managing drug shortages exacerbated by the crisis, and patient education, all in addition to pre-existing clinical and distributive roles.[37] In social-media and email communications, there were 69 pharmacists that reached out with interest in this research study, and of these, 85.5% completed the initial survey and 52.2% completed both pre- and post-course surveys. Anecdotally, many potential participants indicated that the flexibility provided by the self-study option suited their current practice and educational needs as they could complete the material between these competing priorities. While online learning has been present for much of the history of the internet, the recent COVID-19 pandemic has appeared to enhance learners' ability to utilize this platform for education,[38] and this benefit lends itself to this course in many ways. Due to the online nature, speakers were able to be recruited worldwide and as far away as USA, Egypt and Qatar. This allowed the facilitation of a global perspective on the emerging field of PGx, which truly has been an international effort over the last decade. It also brought in a diverse population of Alberta pharmacists within both the synchronous and asynchronous platforms. Participants varied in practice experience, education, and prior knowledge in PGx. Despite these differences, only hospital practice experience

Table 3 Breakdown of Participant (n = 36) Responses to Knowledge Test Questions (in Bold Text) Pre Vs Post Course

Which pharmacogene is most relevant to antiplatelet selection?				
Response	Pre-Course n(%)		Post-Course n(%)	
CYP1A2	–	–	–	–
CYP2C9	3	(8.3)	5	(13.9)
CYP2C19 *	14	(38.9)	30	(83.3)
CYP2D6	2	(5.6)	0	–
COMT	1	(2.8)	0	–
I don't know	16	(44.4)	1	(2.8)
If a patient provides you with a result for a CYP2D6 test, and is asking you to provide their physician with a recommendation for treatment of depression, which online resource would you find most useful in interpreting their phenotype (metabolism status)?				
Response	Pre-Course n(%)		Pre-Course n(%)	
Lexicomp	3	(8.3)	1	(2.8)
eCPS	1	(2.8)	–	–
PharmGKB.org *	3	(8.3)	32	(88.9)
PharmacyGenes.org	2	(5.6)	1	(2.8)
I don't know	27	(75.0)	2	(5.6)
Which of the following would be considered the MOST correct definition of incidental findings in the context of pharmacogenomic testing?				
Response	Pre-Course n(%)		Pre-Course n(%)	
Coincidental identification of a drug-gene interaction that was not the focus of the test ordered (e.g. CYP2C19 testing for antiplatelet selection that also shows patient is at higher risk of side effects from their current antidepressant)	8	(22.2)	14	(38.9)
Identification of polymorphisms that indicate a different risk of an inheritable disease (e.g. CACNA1S testing to determine the risk of malignant hyperthermia with volatile anesthetics and succinylcholine that also reveals genetic risk for the development of hypokalemic periodic paralysis, an inheritable and sometimes debilitating disease) *	1	(2.8)	18	(50.0)
Finding a drug-gene interaction for which there is no current drug-related problem (e.g. panel testing shows ultrarapid metabolism of PPIs via CYP2C19, however the patient feels GERD is well controlled at current low dosage)	6	(16.7)	1	(2.8)
I don't know	21	(58.3)	3	(8.3)
Pharmacogenetic testing for VKORC1 looks at a change in drug effect at the level of:				
Response	Pre-Course n(%)		Pre-Course n(%)	
Pharmacokinetics	3	(8.3)	10	(27.8)
Pharmacodynamics*	3	(8.3)	22	(61.1)
Off-Target effect	1	(2.8)	2	(5.6)
I don't know	29	(80.6)	2	(5.6)

(*Continued*)

Table 3 (Continued).

HLA-B genotyping in patients with Chinese ancestry is suggested in the FDA guidelines for which antiepileptic drugs? (check all that apply)				
Response	Pre-Course n(%)		Pre-Course n(%)	
Phenytoin *	7	(19.4)	17	(47.2)
Valproic acid	2	(5.6)	2	(5.6)
Lamotrigine	5	(13.9)	5	(13.9)
Carbamazepine *	9	(25.0)	30	(83.3)
I don't know	22	(61.1)	3	(8.3)
Which medications have known drug-gene interactions, with therapy modification recommendations available through a clinical guideline? (check all that apply)				
Response	Pre-Course n(%)		Pre-Course n(%)	
Sertraline *	7	(19.4)	32	(88.9)
Bupropion *	3	(8.3)	12	(33.3)
Hydromorphone	7	(19.4)	13	(36.1)
Metoprolol *	3	(8.3)	23	(63.9)
Pravastatin	7	(19.4)	6	(16.7)
I don't know	21	(58.3)	1	(2.8)
Which of the following cannot be done without the patient's consent regarding the sharing of pharmacogenetic test results? **i) Sharing results with a patient's physician** **ii) Sharing results with an insurance company** **iii) Sharing results with a related patient who may carry the same gene** **iv) Documenting results on the patients' pharmacy care record**				
Response	Pre-Course n(%)		Pre-Course n(%)	
i, ii, and iv	–	–	–	–
i and iv	1	(2.8)	1	(2.8)
only i	1	(2.8)	1	(2.8)
only iv	2	(5.6)	3	(8.3)
i, ii, iii, and iv *	18	(50.0)	29	(80.6)
I don't know	14	(38.9)	2	(5.6)

Note: Correct answers are shaded in yellow and indicated by *.

appeared to lead to the greatest retained PGx knowledge indicated by testing, and no participant characteristics affected the level of confidence experienced post-course.

The results of this study suggest a positive effect of this pharmacogenomics course on both subjective and objective short-term knowledge of pharmacists in pharmacogenomics. Pharmacists transitioned from a median of "Disagree" with competency statements pre-course, to a median "Agree" post-course, indicating positive opinions of their own abilities to manage, interpret, and communicate pharmacogenomic information after receiving education, ie, a greater level of confidence. Tested knowledge also improved by more than 3-fold, with participants answering on average 6.9±3.2 more questions correct (out of a total possible score of 14) in post-course surveys compared to pre-course. Furthermore, there

is strong correlation (r = 0.516; p = 0.002) between improvements in pharmacists' tested and self-rated knowledge assessments. This observation indicates two things: 1) improved knowledge was observed by participants themselves, therefore supporting pharmacists confidently applying PGx in practice; and 2) that high self-rated confidence after learning was not simply hubris. This correlation, in addition to moderately strong linear relationships between pre and post course subjective and objective knowledge measures validates pharmacists' ability to recognize and accurately rate their own knowledge in pharmacogenomics using the survey in this study. Thus, they felt more confident in their knowledge and appear able to actualize this potential with the correct use of knowledge gained.

The course provided to study participants included a blend of didactic and case-based learning similar to those used by Zembles et al.,[23] Kisor et al[39] and Crown et al.[21] The results of this research were congruent with the latter two studies in both subjective and objective measures.[21,39] While Zembles did not report knowledge results, their study did reveal high satisfaction with this method of training congruent with findings of Crown.[21,23] The mixture of learning methods in the presented study had also supported learning by providing the immediate opportunity within case studies to practice knowledge and skills gained in the lectures. Another study by Kisor et al indicated the critical need for experiential education in PGx training.[40] While Kisor et al did see pharmacist knowledge improve in all domains of the AACP pharmacogenomics competencies without case-based learning,[32,40] other research, including the results of this study, supports the use of case studies in long-term retention of knowledge gained. One study on pharmacist education in weight management saw the best subjective and objective knowledge four weeks after learning in the small-group discussions, closely followed by large-group discussions, compared to lecture-only groups, indicating better knowledge retention with peer-based learning.[28] The size of the group discussions in the presented study was of similar size to the small-groups in Sarayani et al, with even smaller groups in the three break-out room portions of the live course. Other studies have proved the merits of peer discussion in pharmacist and pharmacy student education in pharmacogenomics,[28,41] with particular interest in the "flipped classroom" concept, wherein lectures are delivered asynchronously while classroom time is entirely devoted to utilize critical thinking and application of knowledge gained from lectures.[42] One such study on pharmacy students found that specific pharmacogenomic items with flipped content had significant improvement in correct responses on test questions compared to traditional didactic methods.[43] Such a method could be adopted for future pharmacogenomics courses such as this, to allow more time for participant interaction, questions, and practice within cases while shortening the overall time required for live attendance. While asynchronous participants did not receive the benefit of a formal group discussion, the case studies were presented in a scripted format, allowing the participant to read the questions as if they were being asked by a facilitator. They would be asked to solve the question posed before turning to the answer key, then proceed with the next question, thus accomplishing the experiential component. One case study is provided, for example, in Supplementary Materials 3. This design of asynchronous case study appears to be effective in providing similar quality of education to live group discussion, as post-course knowledge and confidence did not appear to differ between synchronous and asynchronous participation methods. The difference in post-course grades seen between synchronous and mixed methods (78.6% [78.6, 92.9] vs 64.3% [42.9, 78.6]; adj-p=0.014), may be explained by the gap that many participants had between day 1 of live participation, and final course completion indicated by the date of the post-course survey (approximately 3 months). This suggests that future iterations of this course forgo the blended live/self-study route, opting for either a full synchronous or full asynchronous learning only.

Among the subgroup analyses, an interesting finding of this study was the high level of agreement among pharmacists with the statements "Pharmacogenomics can enhance the provision of medication-related services (eg, dispensing, care-planning)" and "Pharmacogenomics testing is cost-effective." Many studies before this also show a high degree of support by pharmacists in the clinical utility and feasibility of pharmacogenomics even with low rated or tested knowledge.[44,45,47–49] As with this study, other research has shown that subjective (self-rated) knowledge is greater in those with prior PGx training.[49] However, this study conflicts with other findings that objective (tested) knowledge is also higher in those with prior PGx training,[47] as this study did not find a difference in pre-course test scores between those with PGx education in degree, in continuing education, or prior use of PGx, compared to those with no prior exposure. Some potential explanations for this observation include the rapid changes occurring and quickly advancing technology in PGx, and/or possibly due to knowledge decay in unused information. Other medical skills, such as resuscitation,

follow a trend wherein the skills learned in a course are lost after 12 months if not frequently used, whereas knowledge is retained better when it is utilized more frequently in practice.[50]

In 2015, the United States Accreditation Council for Pharmacy Education addressed the knowledge gap in pharmacists by adding pharmacogenomics to the required curricula of entry-level Doctor of Pharmacy programs.[17] Although Canada has no formal requirement for PGx education in pharmacy schools at present, adoption of PGx has occurred across most of the country's University pharmacy degree curricula. Therefore, incoming pharmacy graduates within North America are likely to have an acceptable base-level of knowledge of PGx applications.[18,19] It should be noted, however, that pharmacogenomics is still a relatively new field, and as such, guidelines have been known to change as new evidence becomes available. One example of such is the CPIC guidelines for clopidogrel dosing in percutaneous coronary intervention (PCI) patients, which did not provide a phenotype for *CYP2C19* *2/*17 in 2011, and therefore recommended clopidogrel therapy in these patients.[51] In 2013, these guidelines were updated to interpret an "intermediate metabolizer" phenotype from this particular genotype based on more current evidence, thus changing the medication selection advice in these patients to an alternative antiplatelet therapy such as ticagrelor or prasugrel.[52] It is due to frequent changes in evidence, such as this example, that even those with prior education in PGx will need ongoing updates to their knowledge through courses such as this.

While pharmacy curriculums are teaching pharmacogenomics to incoming pharmacists,[19] Alberta currently has a limited ability to utilize this in practice. Green Shield, a Canadian pharmacy benefit manager, has only recently added PGx testing to their services while Alberta's largest benefit manager, Alberta Blue Cross, has yet to provide these services to its beneficiaries. In part, this is due to the limited evidence available to support cost-efficacy to date, as one review found that within pharmacy practice, no research to date has followed real-world economic outcomes.[16] With most patients required to pay for this out of pocket ($200–$1000), the demand for pharmacogenomics testing is currently limited. Furthermore, it is reasonable to assume that if the pharmacist population, as shown in this study, is not confident in their ability to manage, interpret, and educate patients and providers on PGx information, they likely will not recommend PGx testing in the first place. Therefore, in addition to recurring education to manage knowledge decay and the changes in information available, pharmacists must also have the opportunity to utilize learned PGx skills in practice, to the benefit of both their ability to provide care, and importantly, to the benefit that PGx can have on patient outcomes.

Limitations & Strengths

While this study demonstrates the effectiveness of a PGx course on pharmacist competency in this subject, the study and the course itself are not without limitations. A previously validated survey measuring the specific competencies identified by AACP[32] and the therapeutics supported in the literature[16] was not available, and thus had to be created for this study. In addition to undergoing face validation, the observation of congruency between self-reported competence (Likert Scales) and objective knowledge (quiz grades) in baseline, final, and changes between assessments indicates construct validity of the tool used in this study. Further to assessment of survey results, although instructions indicated these were to be completed to the best of the participant's ability, there is no way to confirm that participants did not check resources or notes while completing the quiz. However, a strength of the quiz portion was the inclusion of an option for "I don't know" with each question to minimize correct guesses that falsely overestimate knowledge. Another noted limitation of this study was its inability to measure long-term knowledge retention post-course. Despite longitudinal evaluation was not the focus of the research presented, where only short-term efficacy is reported in this study. Another future study within the same funding grant proposal will be recruiting those participants and their pharmacies to test and educate eligible patients about their PGX and drug gene possible interactions. They will also be responsible to point out possible interventions in their patients' current therapy. This practical component in the upcoming study will test and reflect the long-term knowledge retention.

Another strength of this study was the utilization of current guidelines and resources in the generation of course content. These guidelines are subject to frequent updates and changes given the growing body of evidence in this relatively new field. Additionally, the AACP competencies[32] themselves are likely to be updated in the near future. Thus, it is imperative that these clinical and competency updates reach all pharmacists in an accessible format to ensure that

PGx practices remain current. This applies to all pharmacists regardless of prior education in pharmacogenomics, as evident by the lack of difference in pre-course objectively measured knowledge between pharmacists with prior PGx education and those without. Therefore, this study highlights the need for recurring PGx education for pharmacists regardless of PGx knowledge background. Another strength of this paper is the comparison between synchronous and asynchronous learning, something that has not been evaluated to date in the available literature of pharmacogenomics education in pharmacists. This study showed no difference in these different learning methods, which may support more accessible PGx education in the future.

Conclusions

A PGx course for pharmacists was developed using evidence-based resources and collaboration with field experts, utilizing a blend of didactic lectures with case studies for experiential education. This course was delivered to Alberta pharmacists in live and self-study formats and was found to significantly improve subjectively rated and objectively tested knowledge in PGx regardless of participation format among pharmacists with varying practice experience, education, and prior exposure to PGx information. Knowledge gained can be utilized in delivery of patient-centered, personalized medication therapy management in the pharmacy setting, and this course can be adopted for broader education of pharmacists regardless of current practice in both synchronous and asynchronous learning environments.

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Author Contributions

MH: MSc. student, methodology, data acquisition, statistical analysis, writing – original draft, writing- reviewing and revising; SHM: grant co-PI, conceptualization, methodology and study design, funding acquisition, statistical analysis, writing- reviewing and revising; DAH: grant PI and setting research study idea and design, conceptualization, main curricula setting and nominating speakers, methodology and study design, funding acquisition, writing- reviewing and revising. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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