Clinical pharmacogenetics: A feasibility study of pharmacy students using a clinical decision support system during their didactic training

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Abstract
Background: Pharmacogenetic testing in clinical practice is feasible and cost-effective, and positively impacts healthcare quality and costs. Integrating pharmacogenetics into the pharmacy setting has shown promise in improving medication safety, effectiveness, and efficiency. Implementation across health care settings, however, continues to be limited. Pharmacy students' ability to utilize pharmacogenetic information in their decision-making processes may be enhanced with a software-based clinical decision support system (CDSS).
Aims: To evaluate the feasibility of incorporating a pharmacogenetic CDSS into pharmacy student education. To evaluate the impact of a CDSS compared with usual decision-making methods (UDM) on appropriateness of medication selection and efficiency of pharmacy students' medication decision-making.
Methods: A cross-sectional study design was employed, including a controlled crossover trial with two intervention arms, CDSS and UDM, and a nested qualitative study to explore student perceptions. Fifty-one third-year pharmacy students were recruited and participated in two clinical scenarios, alternating between CDSS and UDM methods. Performance outcomes were assessed based on the appropriateness of therapeutic recommendations and the efficiency of therapeutic decision making. An online survey was conducted to gather students' feedback on using the CDSS.
Results: In Scenario 1 (antiplatelet therapy), 89% of students in the CDSS group selected the optimal drug (ticagrelor) compared to 39% in the UDM group ($p<0.001$). In Scenario 2 (behavioral health therapy), 50% of students in the CDSS group chose the optimal drug versus 41% in the UDM group, and students in the CDSS group chose fewer drugs (4 drugs) than students in the UDM group (10 drugs). For both scenarios, students in the CDSS group used only the CDSS as a resource, while the UDM group used multiple resources. The survey revealed high student satisfaction, with 94% of the students finding the CDSS useful.
Conclusions: The study demonstrates that, compared to UDM, a CDSS improves the appropriateness and efficiency of pharmacy students' therapeutic recommendations. Integrating a CDSS into pharmacy education can enhance students' competency in utilizing pharmacogenetic information, advancing personalized medicine and optimizing patient care.

Keywords: pharmacogenetics, pharmacogenomics, clinical decision support system, pharmacy education, personalized medicine, therapeutic recommendations, pharmacy students

Background

Pharmacogenetic testing, a key component of precision medicine, examines genetic-based variation in pharmacokinetics and pharmacodynamics to identify how individuals may respond to specific medications.[1] Using pharmacogenetic testing in clinical practice is feasible and cost-effective, and has a positive effect on healthcare quality and costs.[2–4]

For pharmacists, incorporating pharmacogenetic information into medication reviews is a logical and increasingly necessary advancement in practice.

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The clinical utility of pharmacogenetic-guided treatment was evaluated in two urban community pharmacies in 2021.[5]

In this study, involving 213 patients diagnosed with major depressive disorder and/or generalized anxiety disorder, participants receiving pharmacogenetically informed treatment showed significantly greater improvements in depression, anxiety, and functional disability over six months compared to the control group. Specifically, the intervention group achieved a 36% reduction in PHQ-9 scores versus 18% in the control group, GAD-7 scores improved by 41% versus 23%, and Sheehan Disability Scale (SDS) scores improved by 44% versus 18%. Pharmacists in this study identified appropriate patients, facilitated pharmacogenetic testing, interpreted the results, and collaborated with prescribers to optimize therapy, and these interventions led to clinically and statistically significant improvements. Other studies point to positive relationships between pharmacogenetics and patient outcomes. [6–8] Nevertheless, despite growing evidence of clinical benefit, pharmacogenetic information remains underutilized in routine pharmacy practice. Barriers include limited integration of pharmacogenomic data into standard medication reviews and a lack of accessible, user-friendly tools that synthesize this information alongside other clinical data. [9]

The quality of pharmacogenetic implementation is closely related to the quality of education delivered to future pharmacy professionals.[10] Educators play a critical role in preparing pharmacy students to interpret and apply complex clinical data, including pharmacogenetic test results, in a real-world context. Clinical decision support systems (CDSS) are valuable tools that can assist in this process. By integrating current evidence with patient-specific data, a CDSS can facilitate shared decision-making between patients and clinicians.[11] For pharmacy students, the introduction of pharmacogenetic data adds another layer of complexity to medication therapy decision-making, highlighting the importance of structured educational interventions and decision support tools that aid in the application of this information during training.

To conduct a comprehensive medication review, pharmacists must evaluate pharmacogenetic results in the broader context of both evidence-based guidelines and a patient's medical history, demographics, comorbidities, concurrent medications, and laboratory data.[12] The intersection of pharmacogenetic and pharmacologic data allows identification of drug-drug-gene interactions, also known as phenoconversion, underscoring the need for advanced decision support tools that incorporate multiple variables. Pharmacists use complex cognitive processes when evaluating therapeutic options in multifaceted cases.[13]

This study was designed to answer two questions:

1. Does the incorporation of a pharmacogenetic CDSS into pharmacy education aid students in selecting an appropriate therapeutic course of action in complex patient cases?
2. Does the CDSS improve the efficiency of therapeutic decision making in pharmacy students?

Objective

While pharmacogenetic-guided treatment improves patient outcomes, it is difficult to implement in the clinical scenario. Incorporating pharmacogenetic test results with other patient characteristics can be time consuming and challenging. Addressing these challenges by teaching students to incorporate these results into their practice could increase uptake of pharmacogenetic testing and utilization. The first step is to assess whether it is feasible to incorporate pharmacogenetic CDSS into student education, and the second step is to evaluate the appropriateness and efficiency of doing so.

Methods

We used a cross-sectional study design that included a randomized-controlled crossover trial with two intervention arms—clinical decision support software (CDSS) and usual decision-making (UDM)—along with a survey to explore student perceptions of using the CDSS (Figure 1). The cross-over design ensured that all students had the same overall experience and equal opportunity to learn about and use the CDSS.

Usual Decision-Making (UDM)

In the United States, the competence of pharmacy students in each therapeutic area is evaluated against educational outcomes and standards established by the Accreditation Council for Pharmacy Education. Manchester students are trained to use drug information resources (specifically Lexicomp® and Micromedex®) and therapeutic guidelines as part of the first-year drug information course and within a case conferences course sequence over the second and third years. In clinical cases/scenarios where drug selection is impacted by patient's genetics or when pharmacogenetics is implemented, students are educated on the use of pertinent resources, such as the Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines, to support selection of most appropriate therapy. A collaboration between the Pharmacogenomics Knowledge Base (PharmGKB, http://www.pharmgkb.org) and the National Institutes of Health (NIH), CPIC was created to provide freely available, evidence-based, peer-reviewed, and updated pharmacogenetic clinical practice guidelines.

Clinical Decision Support Software (CDSS)

The CDSS used in this study (TreatGx 2023; GenXys Health Care Systems, Vancouver, BC) is designed to identify condition-specific medication options that are filtered using patient variables. Disease-specific guidelines are used to create the core list of medications used for that condition. Patient variables, including liver and renal function, medical conditions, current drug therapy, allergies, and pharmacogenetics, are then used to refine the core list, and some drugs are moved to an excluded section, with reasons provided for this exclusion. For those drugs that remain, the system displays dosages and other information, such as dose adjustments for renal function or pharmacogenetics as well as any drug-drug interactions. The software uses proprietary algorithms created from data in the product monographs, other published sources, and an Application Programming Interface (API) to a North American drug-drug interaction database. Additional software capabilities are also available, such as sorting the drugs by side effects. The software is used commercially in North America, Africa, and Europe.

Procedures

Students in the third professional year of Manchester University's 2 + 4 pharmacy program were recruited and rewarded for participation with bonus points for a single course. At Manchester, pharmacogenetics is taught primarily in a first-year, required Pharmacokinetics and Pharmacogenomics course (2 credits). Application of pharmacogenetics to specific drugs is addressed in each of the integrated pharmacotherapy modules during the students' second and third years. The students completed the activity one month prior to starting their advanced pharmacy practice experiences, and therefore had all the relevant curriculum-based didactic knowledge necessary for engaging in the selected patient scenarios.

This activity was administered via two clinical scenarios (Scenarios 1 and 2) to the two groups of pharmacy students (Groups 1 and 2). Students were randomly assigned to groups. For Scenario 1, Group 1 used only UDM, while Group 2 used both the CDSS and UDM. For Scenario 2, Group 1 used the CDSS and UDM, while Group 2 used only UDM (Figure 1).

Prior to the activity, students were given access to a video tutorial regarding the use of the CDSS, and access to the CDSS approximately 72-hours later. The tutorial showed how to log in to the system and use the software; demonstrated how to specify patient characteristics including renal function, liver function, medical conditions, and current medications; and described how to review condition-specific drug options adjusted for these characteristics.

Throughout the activity, the groups were isolated in different rooms, each with a faculty facilitator. Students were instructed to work individually and not to discuss therapeutic recommendations, but discussions pertinent to technical issues or use of the software were permitted among study participants and between participants and faculty. All students were permitted to access their "usual" resources, described below.

After both scenarios were completed, students took an online survey regarding their perceptions of the CDSS.

Scenarios and questions

The two scenarios, with related questions, were slightly modified from cases in the repository of the American Association of Colleges of Pharmacy (AACP) Pharmacogenomics Special Interest Group (AACP Pharmacogenomics SIG Case Library).

Scenario 1 was related to antiplatelet therapy. The scenario described the demographics, past medical history, social history, family history, allergies, current medications, and laboratory results (including pharmacogenetic results) of a 76-year-old patient (BT) referred to the pharmacist by a primary care prescriber who wished to change the patient from prasugrel to clopidogrel. The students were expected to account for all information, including that the patient had just undergone percutaneous coronary intervention with coronary artery stent placement and been placed on dual-antiplatelet therapy (aspirin and prasugrel), and for the pharmacogenetic variants that relate to anti-platelet therapy metabolism, when answering two questions:

a. What is your recommendation for BT regarding antiplatelet therapy?
b. What would be the expected starting dose for the antiplatelet medication of choice in this case?

Scenario 2 described the demographics, past medical history, social history, family history, allergies, current medications, and laboratory results (including pharmacogenetic results) of a 45-year-old patient (AM) referred to the pharmacist by psychiatry to determine the most appropriate antidepressant therapy. The students were expected to account for all information, including that the patient had pharmacogenetic variants that could impact metabolism of some SSRIs, and had been diagnosed with major depressive disorder and generalized anxiety disorder and tried sertraline and fluoxetine but did not find them helpful (adequate dose and duration for each medication trial), when answering two questions:

a. What is your recommendation for AM regarding antidepressant therapy?
b. What would be the expected starting dose for the antidepressant medication of choice in this case?

Analysis

Three categories were used to assess the appropriateness of drugs selected by students:

- Optimal: drug adjusted appropriately for all patient variables.
- Sub-optimal: for example, a drug-drug interaction that leads to reduced serum levels of one of the drugs. This categorization was also used when the patient in the scenario had already received an adequate dose and duration of the selected medication.
- Inappropriate: for example, a drug-drug interaction that results in a high risk of bleeding.

Differences between proportions of students by choice of medication were calculated using the "N-1" chi-squared test as recommended by Campbell (2007) and Richardson (2011). This variant of the chi-squared test used for analyzing two-by-two tables is especially appropriate when sample sizes are small, and is used to assess the relationship between educational methods and learning outcomes[14] .

Performance outcomes were assessed based on the appropriateness of medication choices and the efficiency of problem-solving techniques employed by students in both groups. Appropriateness was evaluated by comparing the students' solutions to established pharmacogenetic principles and guidelines (Tables 1 & 3). Efficiency was assessed by how many resources the students accessed to fulfill the assignment and by the number of drugs selected for a given case. The use of fewer resources indicated that the student was being more efficient with their time, i.e., getting to the answer more quickly. The study was considered exempt by Manchester University IRB.

Results

All 64 third-year pharmacy students were invited to participate. A total of 51 students participated in the study, with 33 assigned to the control group (UDM) and 18 assigned to the intervention group (CDSS) for Scenario 1. For Scenario 2, seven students dropped out due to issues with scheduling the sessions, leaving 26 students in the intervention group and 18 in the control group.

Figure 1. Study Flow

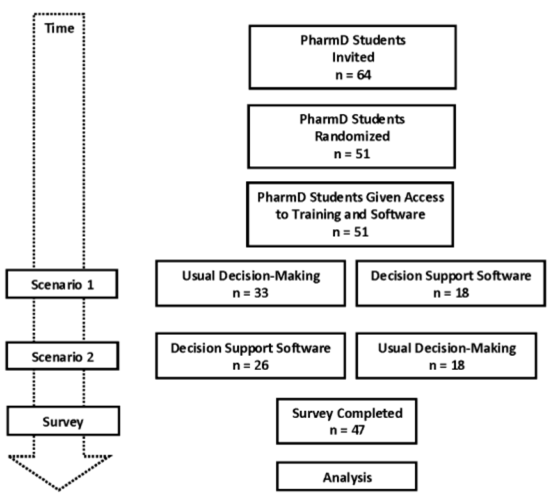

Table 1. Student Drug Selection for Scenario 1

Drug Selected	Classification*	Usual Decision-Making n (%) n = 33	Clinical Decision Support Software n (%) n = 18	Chi² (p value)
Ticagrelor	Optimal	13 (39)	16 (89)	11.2 (p<0.001)
Prasugrel	Sub-optimal	18 (55)	1 (6)	12.9 (p<0.001)
Clopidogrel	Sub-optimal	1 (3)	0	
Aspirin alone	Inappropriate	0	1 (6)	0.26 (0.6)
Ticlopidine	Inappropriate	1 (3)	0	

* Optimal: drug adjusted appropriately for all patient variables. Sub-optimal: for example, a drug-drug interaction that leads to reduced serum levels of one of the drugs. Inappropriate: for example, a drug-drug interaction that results in a high risk of bleeding.

Table 2. Resources Used by Students for Scenario 1

Source Used*	Usual Decision-Making n = 33	Clinical Decision Support Software n = 18
Treat Gx	0	18
CPIC Guidelines#	9	1
Lexicomp	12	0
Micromedex	6	1
Primary Literature	15	0

*Some students used and cited more than one source.
Clinical Pharmacogenetics Implementation Consortium guidelines [15]

In Scenario 2, 13 (50%) students in the CDSS group chose an optimal drug versus 7 (41%) students in the UDM group. Sub-optimal drugs were selected by 50% of both groups. No students in the CDSS group selected a drug considered inappropriate or sub-optimal by CPIC, compared to 3 (17%) students in the UDM group. There was a larger number of potential drugs for this scenario than for the first one . Students using UDM selected a larger number of these potential drugs (10) compared with students using the CDSS (4).

Table 3. Student Drug Selection for Scenario 2

Drug Selected	Classification*	Usual Decision-Making n (%) n = 18	Clinical Decision Support Software n (%) n = 26	Chi^2 (P Value)
Bupropion	Optimal	1 (6)	0	
Desvenlafaxine	Optimal	1 (6)	0	
Duloxetine	Optimal	3 (17)	13 (50)	
Fluvoxamine	Optimal	1 (6)	0	
Paroxetine	Optimal	1 (6)	0	
Combined	**Optimal**	**7 (38.8%)**	**13 (50%)**	**0.526 (0.46)**
Amitriptyline	Sub-optimal (CYP2D6 reduce dose by 25%)	3 (17)	0	
Citalopram	Sub-optimal	0	1 (4)	
Fluoxetine	Sub-optimal (Previous Trial)	4 (22)	11 (42)	
Nortriptyline	Sub-optimal (Reduce dose by 25% CPIC)	1 (6)	0	
Sertraline	Sub-optimal (Previous Trial)	1 (6)	1 (4)	
Combined	**Sub-optimal**	**9 (50%)**	**13 (50%)**	**NS#**
Venlafaxine	Inappropriate (CYP2D6)	2 (11)	0	NS#

* Optimal: drug adjusted appropriately for all patient variables. Sub-optimal: for example, a drug-drug interaction that leads to reduced serum levels of one of the drugs [16]. Inappropriate: for example, a drug-drug interaction that results in a high risk of adverse drug event.
#NS Not statistically significant

Table 4. Resources Used by Students for Scenario 2

Source Used*	Usual Decision-Making n = 18	Clinical Decision Support Software n = 26
Treat Gx	0	26
CPIC Guidelines#	8	0
Lexicomp	4	0
Pharmacotherapy: A Pathophysiologic Approach	3	0
Primary Literature	1	0
Source Not Listed	4	0

*Some students used and cited more than one source.
Clinical Pharmacogenetics Implementation Consortium guidelines. [17]

Four resources were used by the UDM group in Scenario 1 (Table 2) and five in Scenario 2 (Table 4). The 51 students using UDM only accessed resources 62 times (Tables 2 and 4). Of the 44 students in the CDSS arm, 1 used an additional resource.

The online survey was completed by 47 students (Figure 2). Forty-four students (94%), strongly or somewhat agreed that "Overall, I found TreatGx to be useful as a clinical decision support tool," two students were neutral, and one somewhat disagreed.

Discussion

As precision medicine becomes more integrated into healthcare, the incorporation of pharmacogenetics into pharmacy practice is essential.[18] Clinical decision support systems have demonstrated benefits in reducing medication errors in hospital settings,[19] but their broader applications—particularly those integrating pharmacogenetic data with other patient-specific variables such as renal and liver function, comorbidities, and drug-drug interactions—remain underexplored, especially in educational settings.

This study aimed to evaluate the effectiveness of a CDSS in improving the appropriateness of medication recommendations made by pharmacy students, while also examining the efficiency of the decision-making process in terms of the number of information resources used. Compared to usual decision-making (UDM), which involves traditional resources such as pharmacogenetic guidelines and electronic drug databases, students using the CDSS made more accurate therapeutic choices while using fewer reference materials.

In the first scenario, involving antiplatelet therapy, CDSS use was associated with a substantial improvement in appropriate drug selection: 89% of students in the CDSS group selected ticagrelor, the optimal choice, compared to only 39% in the UDM group. This outcome suggests that the CDSS effectively supports complex clinical reasoning by integrating multiple variables—including drug-gene interactions—into a clear recommendation, leading to safer and more appropriate prescribing. In contrast, a majority (57%) of students in the UDM group selected suboptimal therapies, underscoring the difficulty of synthesizing multiple pieces of clinical information without decision support.

In the second scenario, focused on behavioral health pharmacotherapy, there was a narrower margin between the two groups—with optimal drug selection at 50% in the CDSS groups versus 41% in the UDM group. This may reflect the inherent complexity and ambiguity in mental health prescribing, where therapeutic decisions often depend on nuanced clinical judgment and where guidelines are less prescriptive.[20] Nonetheless, use of the CDSS still showed a positive impact.

An unexpected finding was the reduced variation in drug choices among CDSS users. Students in the UDM group chose a wider range of therapies, which, while reflective of exploratory thinking, may also increase the risk of inappropriate prescribing. This aligns with the literature, which indicates that variation in prescribing [21] and polypharmacy [22] is associated with poorer adherence to best practices and with increased patient risk. Efforts to standardize prescribing through tools such as formularies and essential medicine lists—Sweden's "Wise List," for example, or the UK's local formularies [23]—aim to address this risk. Using a CDSS may serve a similar role in educational settings by promoting more appropriate, evidence-based decisions.

The study also demonstrated greater efficiency in the decision-making process in the CDSS group, where students used significantly fewer additional resources. While reliance on fewer sources can introduce selection bias, especially in training settings, this streamlined process more closely reflects real-world clinical environments, where time constraints limit the ability to consult multiple references. Use of a CDSS can thus bridge the gap between thorough academic training and the realities of practice by efficiently providing focused, evidence-based recommendations.

Importantly, students reported high satisfaction with the CDSS: 94% found it useful in supporting clinical decisions. This level of endorsement suggests that a CDSS not only enhances cognitive performance but is well accepted as a learning tool. Furthermore, identifying the differences in medication and dosing choices between the UDM and CDSS groups creates a valuable opportunity for educators to engage students in critical reflection and pharmacotherapy reconciliation—activities that strengthen clinical reasoning skills.

Despite these encouraging results, the study had limitations. Attrition between scenarios reduced the sample size, potentially limiting statistical power. The study also focused exclusively on third-year students, which may restrict generalizability to other levels of pharmacy training or to practicing clinicians. Additionally, while the CDSS supported medication selection, the study did not incorporate shared decision-making elements, such as patient preferences and values—an important aspect of real-world practice.

Future research should evaluate the long-term impact of CDSS exposure on clinical decision-making during advanced practice experiences and early professional practice. Studies that assess its impact on patient outcomes, as well as its cost-effectiveness in pharmacy education, would further inform its broader implementation.

Conclusion

This study demonstrates that a CDSS designed to incorporate pharmacogenetics and other key clinical variables can significantly improve both the appropriateness of therapeutic recommendations and the efficiency of decision making for pharmacy students. By reducing variability in prescribing, supporting evidence-based decisions, and enhancing user satisfaction, CDSS holds promise as a valuable tool in pharmacy education and a means to better prepare students for the evolving demands of personalized medicine.

Conflicts of Interest: Martin Dawes and Diana Dawes are affiliated with GenXys Health Care Systems Inc., the company that developed the clinical decision support software used in this study. The pharmacogenetic cases used in this study were developed independently by the American Association of Colleges of Pharmacy Pharmacogenomics Special Interest Group.
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Figure 2. Survey Results (n = 47)