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## INTEGRATING PHARMACOGENETICS INTO MEDICAL EDUCATION: AN UPDATED SYSTEMATIC REVIEW OF CROSS-SECTIONAL STUDIES

Actuality. The remarkable rise in the consumption of prescription drugs significantly increases the need for monitoring their safety and efficacy. Identifying genomic variations is one of the main factors that may affect individuals' responses to specific medications, advancing professionals towards achieving precision medicine.

**Research purpose.** The presence of various barriers, including insufficient knowledge among physicians, decelerates the global clinical implementation of pharmacogenomics (PGx). This review aims to update the evidence regarding the attitudes and knowledge of medical students and physicians towards the role of genetic information in treating human diseases and perspectives on PGx as a mandatory discipline in medical training programmes.

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Materials and methods. This systematic review was conducted in accordance with the updated guidelines of the PRISMA 2020

Statement. PubMed and Google Scholar databases were utilised as sources for data collection, with an emphasis on recent cross-sectional studies assessing the attitudes and knowledge of healthcare professionals (HCPs) towards PGx. Research results. Despite the poor understanding of PGx among medical students and physicians, a significant number of them recognised its efficacy. Physicians acknowledged the necessity and advantages of point-of-care PGx testing. Fewer than 10% of paediatricians were well-acquainted with PGx, and only 7.2% were aware of the recommendations by the Clinical Pharmacogenetics Interview Constraints. The provide the provide the provide the physicians of the provide the physicians and physicians acknowledged the provide the physicians of the provide the physicians of the physicians acknowledge the physicians of the physicians of the physicians of the physicians acknowledge the physicians acknowledge the physicians acknowledge the physicians of the physicians of the physicians of the physicians acknowledge t Implementation Consortium. Nevertheless, they expressed a willingness to enhance their knowledge of PGx. Although physicians demonstrated a positive attitude towards PGx testing, only 45.1% of respondents were convinced of its availability in their institutional departments. Limited accessibility to PGx content, primarily due to high costs, and patient uncertainty regarding test results were cited as the main barriers to the adoption of PGx.

Conclusion. There is limited awareness regarding PGx and its application in clinical practice among various HCPs. Further analysis of the barriers to the clinical implementation of PGx is crucial.

Key words: pharmacogenetics, pharmacogenomics, personalised medicine, knowledge, attitude, genomic testing.

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## ІНТЕГРАЦІЯ ФАРМАКОГЕНЕТИКИ В МЕДИЧНУ ОСВІТУ: ОНОВЛЕНИЙ СИСТЕМАТИЧНИЙ ОГЛЯД ПЕРЕХРЕСНО-СЕКЦІЙНИХ ДОСЛІДЖЕНЬ

Актуальність. Надмірне зростання споживання рецептурних лікарських засобів значно підвищує потребу в моніторингу їх безпеки та ефективності. Виявлення геномних варіацій є одним з основних факторів, які можуть впливати на реакцію людини на конкретні лікарські засоби, просуваючи фахівців на шляху до досягнення прецизійної (або високоточної) медицини.

**Мета дослідження.** Наявність різних бар'єрів, включаючи недостатній рівень знань серед лікарів, уповільнює глобальне клінічне впровадження фармакогеноміки (PGx). Цей огляд має на меті актуалізувати дані щодо ставлення і знань студентів-медиків і лікарів про роль генетичної інформації в лікуванні захворювань людини, а також перспективи PGx як обов'язкової дисципліни в програмах підготовки медичних працівників.

Матеріали та методи. Цей систематичний огляд було проведено відповідно до оновлених рекомендацій заяви PRISMA 2020. Для збору даних були використані бази даних PubMed і Google Scholar з акцентом на нещодавні перехресні дослідження, які оцінювали ставлення та знання медичних працівників (МП) щодо PGx.

**Результати дослідження.** Незважаючи на недостатнє розуміння PGx серед студентів-медиків та лікарів, значна частина з них визнала його ефективність. Лікарі визнали необхідність та переваги ПЛР-тестування на місці надання медичної допомоги. Менше 10% педіатрів були добре знайомі з PGx і лише 7,2% знали про рекомендації Консорціуму з впровадження клінічної фармакогенетики. Тим не менш, вони висловили бажання поглибити свої знання про PGx. Хоча лікарі продемонстрували позитивне ставлення до PGx-тестування, лише 45,1% респондентів були переконані в його доступності в закладах охорони здоров'я. Обмежений доступ до контенту PGx, насамперед через високу вартість, і невпевненість пацієнтів у результатах тестів були названі основними бар'єрами на шляху до впровадження PGx.

**Висновок.** Поінформованість щодо PGx та його застосування в клінічній практиці серед різних спеціалістів охорони здоров'я є обмеженою. Подальший аналіз бар'єрів на шляху клінічного впровадження PGx має вирішальне значення.

**Ключові слова:** фармакогенетика, фармакогеноміка, персоналізована медицина, знання медичних працівників, геномне тестування.

Actuality. Medication therapy is one of the essential interventions to prevent and manage diseases. The rate of medication prescriptions has increased by 42.6% per 100,000 persons from 2004 to 2019 in the United Kingdom (UK) (Naser, 2022; Royal College of Physicians and British Pharmacological Society, 2022). The total number of prescription drugs rose to approximately 6.3 billion in the United States (US) in 2020 (IQVIA Institute for Human Data Science, 2025; Ho, 2023). This remarkable rise in the consumption of prescription drugs has significantly increased the demand for monitoring their safety and efficacy. Pharmacogenetics (PGx) and personalised medicine are promising strategies to optimise the benefits of treatments while reducing their adverse effects (Royal College of Physicians and British Pharmacological Society, 2022). The close correlation between pharmacotherapy and genetics was a milestone in coining the term "Pharmacogenetics" in 1959 by Professor Friedrich Vogel (Müller, 2020; Auwerx, 2022). Identifying genomic variations (patients' individual characteristics) is one of the main factors that may affect an individual's response to certain medications. This advancement moves professionals towards achieving precision medicine (also known as personalised or customised medicine), aiming to prevent diseases and provide targeted, safer, and cost-effective therapies (Barbarino, 2018; Gajare, 2021). Of note, despite the historical perspective of PGx, the presence of many barriers, including insufficient knowledge among physicians, continues to slow its global clinical implementation (Hansen, 2022; Virelli, 2021). Health care professionals, as key stakeholders, play an essential role in the organisation and administration of PGx in practice. While ordering tests, interpreting results, and informing patients about the aim and process of the procedure, they collaborate with other members of the team who contribute to designing the process (Kabbani, 2023: 1189976).

The decision at the 3rd Annual Meeting of the International Society of Pharmacogenomics (ISP) in Santorini, Greece (held on 2 October 2004), led to recommendations for including PGx teaching programmes in medical, pharmaceutical, and health school curricula worldwide (Gurwitz, 2005: 221-225). Despite progress in PGx education globally since these recommendations were established, challenges remain in providing uniform PGx education and integrating PGx knowledge into routine practice (Pisanu, 2014; Karas, 2019). Observations of the educational frameworks in various medical schools in Canada and the US reveal either the inaccessibility or the brief duration of PGx courses (Virelli, 2021: 509). The Position Statement of The Royal College of Pathologists of Australasia, reviewed in July 2022, documented that most Australian physicians remain unaware of recent advancements in PGx and their clinical applications (The Royal College of Pathologists of Australalia, 2018). Similarly, a recent study revealed that most healthcare workers in the United Arab Emirates (UAE) did not receive specific PGx education during their training (Rahma, 2020: 216).

**Research purpose.** This review aims to update the evidence relating to the attitudes and knowledge of medical students and physicians regarding the role of genetic

information in drug management and the treatment of human diseases. Furthermore, the perspectives on PGx as a mandatory discipline in medical training programmes are discussed. It is worth noting that various authors use the terms pharmacogenetics and pharmacogenomics interchangeably (Hansen, 2022: 3230–3238). Both terms describe the role of genetic information in patient drug response (Dere, 2009: 13–16). Therefore, in this study, the acronym PGx is used to reference both concepts.

**Materials and methods.** This systematic review was conducted in accordance with the updated guidelines of the PRISMA 2020 statement checklist (Page, 2021: 71).

# 1. Eligibility Criteria

Cross-sectional studies assessing PGx attitudes and knowledge of medical students, general practitioners (GPs) and medical specialists through validated questionnaires; comparative studies presenting data related to attitudes and knowledge of multiple professional categories if results were presented for each group separately, such as medical vs pharmacy students (with priority for medical data) or US vs Japanese paediatricians (emphasising paediatricians' data independent of country), were the main eligibility criteria for inclusion. Reviews, intervention studies, case reports, letters to editors and abstracts were defined as exclusion criteria.

## 2. Information Sources

Relevant English-language studies on the topic, published on PubMed and Google Scholar databases, were referred to as sources of data collection.

### 3. Search Strategy and Search Terms

Manual searches by the independent reviewers were performed by combining the search terms "knowledge and attitude", "medical students", "medical practitioners", "medical specialists", "pharmacogenetics" and "pharmacogenomics". Studies published from 2020 till present were selected as recent advances in the field. To support results discussion, older scientific studies and reviews were considered.

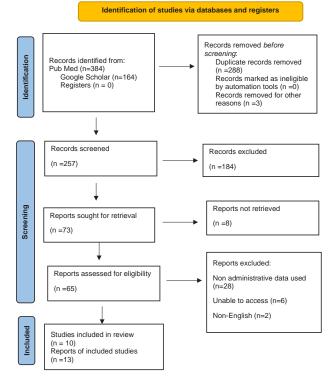
### 4. Data Items, Outcome Assessment

Attitudes and knowledge of medical students, GPs and medical specialists were assessed, evaluating the basic knowledge of PGx and its importance in practice, knowledge of the influence of genetics (patients' genotype and phenotype) on drug therapy, considered factors before prescription, PGx education preferences, knowledge of FDA (US Food and Drug Administration) drug labels, training and practical experience in PGx, confidence in ordering PGx testing, attitudes towards PGx in routine clinical practice, interest in learning PGx, perceived PGx innovative characteristics, and barriers to applying PGx testing.

#### 5. Study Risk of Bias Assessment

In order to reduce the risk of bias of the present review, the following variables were considered when reviewing the methodology section of every single included report: sampling strategies, items which would lead to inaccuracy in cross-sectional studies (techniques of collecting data), and applied statistical techniques to prevent confounding. Inevitable heterogeneity in the targeted sample population, applying self-administered questionnaires and absence of pilot testing (e.g., the study by Jessel et al.) would increase the risk of bias in cross-sectional studies (fig). Moreover, potential common biases such as nonresponse bias, recall bias and interviewer bias were anticipated (Wang, 2020; Jager, 2020).

6. Study Selection



# Fig. PRISMA flow diagram for included studies

### 7. Study Characteristics

All research used validated questionnaires composed of various questions to evaluate the knowledge and attitudes of participants towards PGx content and barriers to applying PGx testing in clinical practice, as well as to gather data on the demographic characteristics (age, gender, etc.) of respondents. The details related to the characteristics of included studies are summarised in table.

8. Results of individual studies and Discussion

The findings of studies evaluating the knowledge and attitudes of medical students, general practitioners (GPs), and medical specialists towards PGx are dis-

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Author/ Total Publication Targeted Country Study setting number of Main evaluated indices year of the group respondents article Rahawi et al. US and Japan AMA, Mount Sinai 282 Paediatricians 1.Familiarity with PGx 2020 Hospital, 2. Attitude on PGx Nemours Children's 3. PGx education preferences Health System Alzoubi et al. JUST, YU, KAUH, 424 Jordan Senior medical 1. Knowledge of PGx students, 2021 hospitals of MOH, 2. Attitude towards PGx 3. Future expectations and practice of RMS. NGOs interns. residents. PGx GP, specialist 4. Perceived barriers to apply PGx doctors testing in Jordan Muflih et al. KAUH 1. Knowledge of PGx (role of genetic Jordan 200 Physicians, variations in patient's drug response, 2021 residents. fellows, FDA drugs labels) 2. Attitude to POC-PGx testing, PGx medical innovative characteristics (compatibility, specialists complexity, trialability, ...) University of Jordan and the JUST Zawiah et al. 852 1. Knowledge of PGx Jordan Doctor of Attitude towards PGx
Preparedness to apply PGx 2021 Pharmacy (Pharm-D) and medical 4. Factors influencing knowledge, attitudes, and preparedness students NA 154 Albitar & Physicians and 1. Familiarity with the terms "genetics Syria Alchamat pharmacists and PGx", 2021 2. Knowledge of PGx, PGX testing and its impact on prescribing medications, patient's genotype and phenotype roles in medication 2.Attitude towards PGx Guo et al. China "Wenjuanxing" 422 1. Awareness of PGx Physicians, pharmacists. 2021 (<u>www.wjx.cn</u>) survey 2. Factors interfere with PGx clinical platform available in researchers implementation different institutions 3. Factors promoting the implementation and hospitals of PGx 4. Current status of implementing of PGx testing Agrawal et al. 2021 Pt JNM Medical 138 1. Knowledge of PGx 0India Secondyear MBBS 2. Relevance of knowledge of PGx College students 1. Perceived knowledge of PGx testing Jia et al. China Online medical 366 Physicians platforms for chronic of differing and knowledge related to resources of 2022 disease management specialties PGx testing and health service: 2. Confidence in personal capacity to order PGx testing MEDLINKER and 3. Attitudes towards the use of PGx "Dazhuanjia" testing in routine clinical practices 4.Practical experience of ordering PGx testing 5.Perceived obstacles to increasing the uptake of PGx testing and preferred sources to learn about PGx testing 1. Experience with PGx testing Alberta Health Jessel et al. Canada 20 Paediatric psychiatrists, 2. Indications for PGx testing 2022 Services, Foothills Medical 3. Barriers and Facilitators of PGx paediatricians Centre testing 4. Ethical, legal and social implications for PGx testing 5. Education preferences Thiagarajan et UniSZA 95 1. Interest in learning PGx Malavsia Pharmacv 2. Knowledge of PGx al. 2023 and final year medical students

### **Characteristics of included studies**

Table

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9. Support Unfunded. 10. Competing interests Reported.

11. Availability of data and other materials

Studies included in review are all peer-reviewed and available in literature.

Abbreviations: UniSZA: University Sultan Zainal Abidin, JUST: Jordan University of Science and Technology, YU: Yarmouk University, KAUH: King Abdullah University Hospital, MOH: Ministry of Health, RMS: Royal Medical Services, NGOs: Non-Governmental Organizations, GP: General Practitioners, PGx: Pharmacogenetics (Pharmacogenomics), AMA: American Medical Association, NA: Not Available, FDA: Food and Drug Administration, POC: Point-of-Care

Results and discussion. In their descriptive, cross-sectional study involving 59 pharmacy and 36 final-year medical students, Thiagarajan et al. (Thiagarajan, 2023: 723-731) examined the knowledge of participants about PGx. A higher mean knowledge score was observed among pharmacy students (15.58) compared to medical students (14.56). However, 83.3% (n = 30) of the final-year medical student population provided the correct answer to the question, "The use of patient-specific information and biomarkers to make more informed choices regarding the optimal therapeutic treatment regimen for a given patient," determining the base knowledge level of respondents about the concept of personalised medicine. Despite pharmacy students demonstrating a higher level of knowledge in PGx compared to medical students, 22.2% of final-year medical students expressed greater interest in learning PGx compared to pharmacy students (18.8%, r = -0.127, p < 0.05).

Likewise, a descriptive, cross-sectional study involving 127 fourth-year medical students and above, 44 interns, 110 residents, 34 general practitioners, and 109 specialist doctors, was performed by Alzoubi and colleagues (Alzoubi, 2021, p. e13658). Despite poor insight among respondents towards PGx (5.42  $\pm$  1.51 out of 10), a large number of medical students and physicians  $(21.18 \pm 2.58 \text{ out of } 24)$  believed in the efficacy and utility of PGx in patient medication, as well as its application in their future practice  $(10.44 \pm 1.64 \text{ out of } 12)$ . Furthermore, limited accessibility to PGx content was identified as one of the main barriers to using PGx testing, as expressed by 86.8% of the physicians surveyed. Another survey was conducted by Muflih et al. in Jordan (Muflih, 2021, pp.655-665). Encouragingly, the majority of participants had received guidance in genetics through various sources. Among the questions provided to evaluate physicians' knowledge of PGx testing, the highest percentage of correct answers (73.5%) was related to "*identifying the possible relationship between the intensity of adverse events for some medications and individuals' genotypes.*" This was followed by 69.5%, which related to "*belief in the role of genetic variability in medication responses.*" Regarding characteristics of PGx that influence physicians' perceptions and attitudes, the highest scores were associated with agreement on the requirement for (4.28  $\pm$  0.8) and advantages of point-of-care (POC) PGx testing (4.22  $\pm$  0.84), which may help to diminish adverse drug effects. Compatibility with practice (3.68  $\pm$ 1.1) was also highly rated, representing a favourable attitude among respondents towards POC-PGx testing.

Results from the survey conducted by Albitar and Alchamat (Albitar, 2021), involving 51 physicians and 74 pharmacists, demonstrated that a lower percentage of physicians (45%) were familiar with the term PGx compared to pharmacists (71.6%). Similarly, the percentage of respondents declaring good knowledge of PGx was significantly higher among pharmacists (10 pharmacists vs 1 physician). Regarding knowledge of PGx testing, only 4 physicians out of 29 respondents declared familiarity (p = 0.001). Furthermore, physicians displayed a poor understanding of the impact of patient genotype on drug response, as evaluated by the Percentage Knowledge Assessment Score (PKS;  $41.2\% \pm 10.8\%$ ) compared to pharmacists ( $48.9\% \pm 15.3\%$ ). Although 76% of respondents believed in the role of patient phenotype in selecting proper medication, pharmacists were significantly more knowledgeable (p = 0.003). Additionally, 33% of physicians (37 out of 112 total respondents) were interested in ordering PGx prior to drug administration compared to 47.3% of pharmacists (53 out of 112 respondents), representing their attitude towards PGx.

A survey conducted by Rahawi et al. (Rahawi, 2020: 437-444) included 210 paediatricians from the US and 72 from Japan. Fewer than 10% of participants reported being well-acquainted with PGx, and only 7.2% were aware of Clinical Pharmacogenetics Implementation Consortium (CPIC) recommendations, which served as a criterion for assessing general PGx knowledge. While 45.9% (96 of 209) of US paediatricians were relatively familiar with PGx, 36.1% (25 of 72) of Japanese paediatricians were not. Nevertheless, over 80% of respondents (81.7%, 219 of 268) exhibited a positive attitude towards the use of PGx testing to optimise drug administration efficacy, and 84.0% (225 of 268) believed it could manage adverse reactions. Although 33% of Japanese paediatricians compared to 8.2% of US paediatricians described PGx as a challenging subject, they agreed to enhance their knowledge of PGx through preferred sources such as seminars or lectures (64.8%, 149 of 230), grand rounds (53.9%, 124 of 230), and Continuing Medical Education (CME/CE) courses (55.7%, 128 of 230).

Guo et al. (Guo, 2021: 682020) surveyed 117 physicians, 132 pharmacists, and 173 researchers to compare their understanding of PGx. The findings revealed that physicians had the lowest awareness level of PGx, with agreement rates below 50% on items assessing basic PGx knowledge. Among factors impeding the application of PGx, "lack of sector standards for PGx's clinical applications" was the most cited (20%). Although more than 70% of participants supported the formulation of relevant regulations and standardisation of PGx DNA detection to promote PGx implementation, physicians expressed the least agreement (56.4%), whereas researchers displayed the highest agreement (65.3%).

In their survey in China, Jia and co-authors (Jia, 2022, p.2021) found that 61.5% of participants rated their perceived knowledge as "fair." Participants generally exhibited inadequate knowledge, with fewer than 10% aware of internal PGx guidelines and fewer than 50% informed about CPIC guidelines, Clinical Genomic Resources (ClinGen), and the Pharmacogenomics Knowledge Base (PharmGKB). Physicians self-assessed their capabilities regarding PGx testing, with the highest mean score  $(3.42 \pm 0.08)$  relating to "recognition [of] which drugs require PGx testing", followed by (3.40±0.09) which showed "belief in precision medicine based on PGx results". More than half recognised the benefits of PGx testing, such as "improvement of safety and efficacy of drugs", "refining medication regimen", and "providing cost-effectiveness pharmacotherapy", reflecting their favourable attitudes towards PGx testing, particularly in the era of targeted cancer therapy (78.95  $\pm$  1.26). Despite this, only 45.1% were convinced of the availability of PGx testing in their institutional departments. While 60.4% indicated "lack of PGx knowledge" as a barrier to utilising PGx testing in clinical settings, more than half preferred academic conferences to enhance their PGx knowledge.

Agrawal et al. (Agrawal, 2021: 19-24) analysed PGx knowledge and its relevance in practice among 138 second-year MBBS students. Ninety-five per cent were aware of the definition of PGx, 90% knew the aim of PGx, and 80% answered correctly to the question, "Whether the genetic variations influence the hemolytic anemia in Glucose-6-Phosphate Dehydrogenase (G6PD) deficient people". Of the respondents, 93% believed PGx should be part of diagnosis and treatment, and 84% stated that PGx is relevant to their profession. Additionally, 84% supported linking pharmacovigilance and PGx for better drug safety, and 82% believed PGx education should be included in the MBBS curriculum. However, only 46% answered correctly to the question, "Is the knowledge of PGX likely to decrease the number of adverse drug reactions (ADRs)?". Although the survey results demonstrated good basic knowledge of PGx and its relevance to medical practice, they revealed imperfect understanding of genetic variations in drug targets, metabolising enzymes, transporters, PGx's impact on drug development costs, and the availability of PGx testing in India.

Jessel et al. (Jessel, 2022: 18-27) assessed PGx knowledge and attitudes among paediatric psychiatrists and paediatricians. Forty-five percent (9 of 20) of respondents reported low familiarity with PGx, and 20% (4 of 20) had applied PGx testing. Fourteen participants believed PGx testing could reduce adverse drug events (mean = 6.3, 95% CI = 5.2-7.6). However, respondents highlighted lack of knowledge and low self-efficacy in interpreting PGx testing results (mean = 2.5, 95% CI = 1.6–3.4) and identifying results (mean = 3.7, 95% CI = 2.7-4.7). Despite concerns about barriers to PGx utilisation, such as high costs, 95% (19 of 20) expressed willingness to improve their knowledge of PGx testing interpretation and guidelines for clinical decisions through online medical education courses (75%, 15 of 20), grand rounds (70%, 14 of 20), and seminars or lectures (55%, 11 of 20).

A paper-based cross-sectional survey was conducted by Zawiah and colleagues (Zawiah, 2021, pp. 125-32). Regarding knowledge assessment, the overall students' mean (SD) Percentage Knowledge Score (PKS) across all respondents was poor, with only a few participants (6.9%, n = 59; 95% CI, 5.40–8.84) having a good understanding of PGx concepts. A significant proportion of Pharm-D (66.2%) and medical students (70.9%) could not correctly define the PGx concept. However, 90.6% of respondents believed that PGx testing could help reduce the rate of adverse events due to drug therapy. A high percentage also agreed that PGx testing could optimize drug dosing and improve drug efficacy. Despite showing a positive attitude towards PGx, both groups did not feel adequately prepared to apply it in practice. Several barriers, such as the lack of accessible PGx testing, limited sources of knowledge, lack of insurance coverage, patient uncertainty regarding test results, as well as cultural and religious beliefs, were mentioned as limiting factors for the adoption of PGx in Jordanian healthcare settings (Alzoubi, 2021; AlEjielat, 2016). Overall, it appears that pharmacists have slightly greater PGx knowledge compared to medical practitioners and specialists. Despite limited knowledge, there was a positive attitude toward improving PGx understanding and its application in practice. The most common barrier to its implementation was the poor availability of genomic testing.

*A. Further perspectives on integrating pharmacogenetics into medical practice* 

A PGx course is presented as an elective in postgraduate studies in China [Guo, 2021, p. 682020]. In Jordan, there is a lack of obligatory PGx courses in the curriculum for Pharm-D students and a poor PGx education program for medical students at universities (Zawiah, 2021; Al-Eitan, 2014). In 2005, the International Society of PGx (ISP) recommended incorporating 4–8 academic educational hours for teaching PGx in the curriculum. However, only a few

British medical schools implemented these recommendations (Higgs, 2008: 101-105). In India, despite discussing PGx and personalised medicine as components of general pharmacology, only about half could define these terms correctly (Satyavardhan, 2021: 21193-21205). The shortage in PGx education has reflected knowledge gaps among healthcare staff. The integration of PGx tests into routine practice depends on both physicians' decisions and patients' engagement (Frigon, 2019, pp.589-598). Highlighting this in medical curricula, as well as continuous education and updating knowledge through online courses, web booklets, webinars, and the presentation of regulatory guidelines for primary and specialty care providers, seems essential (Luzum, 2021: 649-661). In their survey, Adesta et al. (Adesta, 2021, p. 684907) presented training modules (TM) consisting of both fundamental (offline TM1) and extensive (online TM2) concepts of PGx to healthcare professionals, targeting family physicians and specialists across different areas of medical expertise (93.4% of participants in TM1 and 61.8% in TM2); only 27.9% had accessed PGx education before the survey. Authors observed a significant improvement in perception (acceptance of PGx's importance and application in clinics), self-efficacy (competency in incorporating PGx knowledge into appropriate treatment, and apprising patients), and knowledge (ability to manage patients as case scenarios using PGx information) among respondents by 84.8%, 64.2%, and 53% respectively after TM1. These indices were further enhanced by 88.1%, 70.6%, and 64.5% after TM2, respectively, indicating the adequacy of information provided through hybrid TM. It is also worth noting that follow-up evaluation activities are mandatory (Lee, 2023: 100007). Knowledgeable healthcare providers are essential to inform one of the main stakeholders (the patient) involved in the PGx implementation process. Aware patients about PGx testing can significantly impact physicians' decision-making to identify effective treatment (Luzum, 2021: 649-661). Moreover, providing PGx technologies may foster enthusiasm among physicians towards the application of personalized medicine (Abdela, 2017: 279-285). The persistent increase in research in the field of PGx over the past two decades reflects a heightened interest in PGx (Müller, 2020: 155–161). Interestingly, despite this growing interest, many recent articles report a need for adequate awareness among healthcare providers and unavailability of PGx courses as potential limitations in the application of PGx in primary care globally (Alzoubi, 2021; Virelli, 2021; Giri, 2021).

Therefore, including comprehensive pharmacogenetic content in medical college curricula and offering clinical clerkship experience focusing on medical students are necessary to prepare future medical practitioners for geno-type-based therapy. Similarly, a relevant program has been provided by the warfarin pharmacogenetics service of the University of Illinois at Chicago Colleges of Pharmacy and Medicine for pharmacy students, residents, and fellows, as articulated by Drozda and colleagues (Drozda, 2013: 175). Emphasising PGx education for pharmacists, physicians, and nurses would support high-quality patient care (Giri, 2021: 752–755). Overall, it is believed that the state of PGx education worldwide (Europe, Asia, Africa, North America, South America, Australia, and Oceania) has considerably improved since 2005 (Karas, 2019: 643–657).

B. Study limitations and suggested future investigations This study has three obvious potential limitations. First, only English-language articles were included in this review. Second, the relationship between the sociodemographic characteristics of participants, such as age, gender, profession, duration of practice, etc., and the level of PGx knowledge and attitude among providers has not been explored. Therefore, conducting a systematic review that reflects the relationship between the sociodemographic characteristics of physicians and their level of knowledge and attitude would be required for a more comprehensive analysis in the future. Third, we did not include a separate evaluation of medical students, practitioners, and specialists, followed by a comparison, which appears interesting. A global statistical comparison of PGx knowledge and attitudes among physicians at different levels could provide valuable insights, helping to identify countries with limited access to PGx resources and/or its clinical application.

### Conclusions

Applying biological information in clinical settings may improve drug therapy outcomes while minimising adverse reactions. Despite numerous studies and published articles in the field, several barriers have been highlighted in the literature regarding the adoption of PGx testing in clinical practice. The findings of this review revealed a limited awareness of the term PGx and its application in clinical practice among various healthcare professionals. Hence, analysing the barriers to the clinical implementation of PGx and developing strategies to train a wellprepared workforce is crucial going forward.

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Parchami Ghazaee S. - suggesting topic of the article, collecting sources of article, writing the article; Tymchenko I.M. - literary editing, data collection;

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Marchenko-Tolsta K.S. – conclusions, proofreading of the text and analysis of literary sources; Novykova L.H. – correction and literary editing;

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