European Review for Medical and Pharmacological Sciences 2022; 26: 1196-1214

Measuring pharmacovigilance knowledge and attitudes among healthcare sciences students: development and validation of a universal questionnaire

D. ŽIVANOVIĆ[1], V. MIJATOVIĆ JOVIN[2], J. JAVORAC[1,3,4], S. KVRGIĆ[5,6], A. RAŠKOVIĆ[2], S. STOJKOV[1,7], S. KAŠIKOVIĆ LEČIĆ[3,4], N. SAVIĆ[8], M. KRALJ[9], A. MILENKOVIĆ[3]

[1]Department of Biomedical Sciences, College of Vocational Studies for the Education of Preschool Teachers and Sports Trainers, Subotica, Serbia
[2]Department of Pharmacology, Toxicology and Clinical Pharmacology, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia
[3]Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica, Serbia
[4]Department of Internal Medicine, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia
[5]Institute for Public Health of Vojvodina, Novi Sad, Serbia
[6]Department of Social Medicine, Medical Statistics and Informatics, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia
[7]Faculty of Pharmacy, University of Business Academy, Novi Sad, Serbia
[8]Department of Health Studies, Faculty of Health and Business Studies, Singidunum University, Valjevo, Serbia
[9]Syneos Health, Belgrade, Serbia

Abstract. – OBJECTIVE: Pharmacovigilance education and reporting of adverse drug reactions (ADRs) are important competencies that healthcare sciences students should develop before completing their studies and entering clinical practice. Since students frequently lack adequate knowledge in this area and fail to recognize the importance of ADRs monitoring and reporting, the aim of this study was to develop and validate a unique and reliable instrument for assessing health sciences students' knowledge and attitudes toward pharmacovigilance and ADRs reporting.

SUBJECTS AND METHODS: A cross-sectional observational study was conducted from February to July 2021 to examine students' knowledge and attitudes toward pharmacovigilance activities. Students of medicine, dentistry, pharmacy, and nursing science of three faculties in the Autonomous Province of Vojvodina, Serbia were examined. A total of 211 of them completed the specially designed, three-section questionnaire (Demographic data section, Pharmacovigilance Knowledge test, PVKT, and Pharmacovigilance Attitude Questionnaire, PVAQ). The questionnaire was posted on the Google Forms platform, and the link was distributed to respondents via the official websites and social networks of all three faculties.

RESULTS: Findings demonstrated good psychometric properties and reliability of the questionnaire. Six questions were removed from the PVKT after item analyses. After excluding these items, the calculated ordinal alpha of the final version of the PVKT, which included 14 items, was good (αord = 0.83), as were other statistical indicators. PVAQ reliability testing also revealed great performance of this questionnaire-calculated ordinal alpha for two PVAQ subscales was excellent (αord = 0.91, for both scales).

CONCLUSIONS: This questionnaire has favorable validity and reliability in assessing healthcare sciences students' knowledge and attitudes toward pharmacovigilance and ADRs reporting.

Key Words:
Pharmacovigilance, Adverse drug reactions reporting, Healthcare sciences students, Knowledge and attitudes, Questionnaire.

Introduction

There is no drug that can be declared completely safe[1,2]. The application of any medicine carries the potential risk of adverse drug reactions (ADRs) – all those effects that may occur during the therapeutic application of any pharmaceutical formulation, but do not have a therapeutic purpose. Drug safety is now one of the

Corresponding Author: Dejan B. Živanović, MSc; e-mail: dejanzivanovic@vsovsu.rs

most important public health issues worldwide. At any given time, nearly one-fifth of the world's adult population uses one or more drugs[3]. ADRs are the immediate cause of approximately 5% of hospitalizations, one of the top ten leading causes of death, and a significant contributor to additional healthcare costs globally. Considering this, an effective local and global pharmacovigilance system is a necessary precondition for safer use of drugs and medical devices in a modern integrated health care system[4-8]. The World Health Organization (WHO) defines pharmacovigilance (PV) as "the science and activities related to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem"[9]. By making ADR information available to public, pharmacovigilance activities also achieve their most important goal of protecting and improving public health[2,5].

All healthcare professionals involved in the prescription, preparation, administration, or distribution of drugs within primary, secondary, or tertiary health care services (physicians, dentists, nurses, and pharmacists, in particular) have an ethical, professional, and legally mandated obligation to report adverse drug reactions. Even so, under-reporting of ADRs by healthcare professionals is a worldwide problem[10,11]. According to recent research, healthcare practitioners in many countries around the world are inconsistent in reporting observed ADRs, which may explain why some countries are still unable to meet the WHO criterion for an effective pharmacovigilance system[12-14]. Despite the fact that healthcare providers have the greatest opportunity for early detection, identification, and reporting of ADRs, studies[15-17] show that healthcare professionals' attitudes toward ADRs reporting are influenced by a variety of factors. These include a lack of understanding of the importance of pharmacovigilance and how to report ADRs, being preoccupied with daily professional activities, burdensome administrative procedures, failing to inform patients about the possibility of spontaneous reporting of ADRs and instructions on how to do so, and focusing solely on ADRs registered during hospitalization. Some personal factors, such as feeling uncomfortable and/or afraid of being accused of reporting ADRs that could have been avoided, feelings of shame and/or guilt as a result of the professional mistake, and a lack of motivation for this type of professional activity, can all contribute to ADRs under-reporting. In an effort to improve the efficiency of global pharmacovigilance, many authors[18-21] nowadays emphasize the importance of acquiring the necessary knowledge and developing positive attitudes toward ADRs reporting while studying medicine, dentistry, nursing science, pharmacy and other related sciences. Pharmacovigilance education and ADRs reporting are important competencies that health science students should develop before finishing their studies and entering clinical practice. However, previous findings indicate that students frequently lack adequate knowledge in this area and fail to recognize the significance of post-marketing ADRs monitoring and reporting. Considering this, the aim of this study was to create and validate a universal and reliable instrument for assessing health sciences students' knowledge and attitudes toward pharmacovigilance and ADRs reporting.

Subjects and Methods

Study Settings

From February to July 2021, a cross-sectional observational study was conducted to examine the knowledge and attitudes toward pharmacovigilance activities among students of medicine, dentistry, pharmacy, and nursing science in the Autonomous Province of Vojvodina, Serbia. Students from three higher education medical institutions in this province participated in the study: the Faculty of Medicine, University of Novi Sad, Serbia (integrated studies of medicine, dentistry and pharmacy, first degree academic and vocational studies of nursing science), the Faculty of Pharmacy Novi Sad (integrated studies of pharmacy and vocational studies of nursing science), and the Faculty of Dentistry Pančevo (integrated studies of dentistry), the latter two within the University of Business Academy Novi Sad, Serbia. The Ministry of Education, Science, and Technological Development of the Republic of Serbia has accredited all three faculties for study programs in the field of health sciences.

Study Participants

The study sample consisted of students from accredited study programs of the above-mentioned higher education institutions in Vojvodina. Those faculties educate four profiles of healthcare professionals who are directly or indirectly involved in the application of drugs and medical devices in professional practice (Medicine, Dentistry, Pharmacy, and Nursing). The criterion for inclusion in this study was passing at least one

of the exams related to students' knowledge and attitudes toward pharmacovigilance. Respondents who did not pass the exam in at least one relevant subject, as well as those whose answers revealed a discrepancy between the information about passing the exam in a specific subject and a year of study, were excluded. Depending on the study program and faculty, respondents could potentially attend at least one of the following subjects: general pharmacology, special pharmacology, pharmacotherapy, pharmacology with toxicology, clinical pharmacology, pharmacology and toxicology, fundamentals of pharmacotherapy, clinical pharmacy, neuropharmacology, drug interactions and adverse reactions. Based on the expected effect of medium size (f = 0.25), the calculated minimum sample size for one-way analysis of variance with four groups of respondents was n = 180. The representation of respondents from included faculties and study programs in the total sample was proportional to the number of students at each included faculty.

Instruments and Data Collection

In consultation with experts in the fields of pharmacology, social medicine, and applied statistics, we developed a structured questionnaire for this study based on surveys used in previous studies and curricula from the pharmacology group of subjects. The questions in the first section of the questionnaire referred to respondents' socio-demographic and general information, which may be relevant to their acquired knowledge and attitudes toward reporting ADRs. The second and third parts of the questionnaire were made up of two newly developed instruments, the Pharmacovigilance Knowledge Test, PVKT, and the Pharmacovigilance Attitudes Questionnaire, PVAQ.

The PVKT refers to necessary pharmacovigilance knowledge, and the original version of the questionnaire included 20 multiple-choice questions on the fundamentals of ADR monitoring, identification, and reporting, as well as local and global pharmacovigilance legislative. Each question had four possible answers, one of which was correct. The test was graded binary: 1 (one) point for each correct answer, or 0 (zero) for each incorrect answer.

The PVAQ included 20 allegations about respondents' attitudes toward ADRs reporting. The respondents indicated their level of agreement or disagreement with the statement by selecting one of the suggested answers on a five-point Likert scale (1 – *I do not agree at all*, 5 – *I completely agree*). The majority of the PVAQ items were created in such a way that a higher score reflects more negative attitudes toward pharmacovigilance.

The Google Forms platform was used to conduct the survey. The questionnaire link was distributed to respondents *via* the official websites and social networks of all three faculties. Furthermore, the student offices of all three faculties sent an e-mail with a link to all students who took courses in the previously mentioned subjects.

Statistical Analyses

All analyses were performed using the R programming language and statistical computing environment (R Core Team, 2019). The results of statistical analysis were displayed graphically and/or tabularly. The numerical values of the outcomes were showcased in absolute and/or relative values. The analysis included the following descriptive statistics: arithmetic means, standard deviation, standard error of arithmetic mean, trimmed mean, skewness (distribution skew), kurtosis (distribution flattening), median, interquartile range, frequencies, percentage representation. The following statistical tests were used in the analysis:

- to determine the normality of the distribution, the univariate Shapiro-Wilk test was used, consulting values of skewness and kurtosis;
- to determine the dimensionality of tests and questionnaires, exploratory factor analysis on matrices of tetrachoric or polychoric correlations was used, depending on whether the test items were scored binary, or were ordinarily scrambled polytomy items (five-point Likert-type scale);
- to determine the correlation between variables whose distribution deviates from normal, Spearman's rank correlation coefficient was used;
- to determine differences in variables whose distribution deviates from normal, a non-parametric substitution for the analysis of variance was used – the Kruskal-Wallis rank-sum test;
- for post-hoc pairwise comparisons, the Wilcoxon rank-sum test was used with Benjamini & Holm ("fdr") correction for multiple comparisons;
- the ordinal alpha coefficient (α_{ord} – Cronbach's alpha based on matrices of tetrachoric or polychoric correlations), Guttman's Lamb-

da 6 (λ_6) reliability coefficient (based on Guttman's Image theory), as well as the omega coefficient (based on a factor model), were used to determine the reliability of the test;
- in addition to factor analysis, the average inter-item correlation (h1) was used to assess the homogeneity of the instruments.

Ethical Consideration

This research was approved by the Ethics Committee of the Medical Faculty of the University of Novi Sad, Serbia. Based on that decision, the deans of all three faculties involved in this study gave written consent for their students to be included in the study. The questionnaire was completed anonymously and voluntarily. Respondents were given detailed information about the study's objective and methodology in the questionnaire's preamble, and they were given the option to withdraw at any time. By clicking on the provided field in the preamble, each respondent indicated that they were familiar with the research's purpose and conditions, as well as that they voluntarily agreed to complete the questionnaire (informed consent).

Results

Sociodemographic Data

A total of 211 students were included in this study. The average age of the respondents was M = 23.84 years (SD = 3.48, Me = 23), and the age distribution was positively skewed (Figure 1). Females made up the majority of the sample (79.15%), which is usual in studies involving students studying healthcare sciences. The largest number of respondents were attending the Faculty of Medicine of the University of Novi Sad (68.25%), followed by the Faculty of Dentistry of the University of Business Academy in Pančevo (18.48%) and the Faculty of Pharmacy of the University of Business Academy in Novi Sad (13.27%). The study sample included 37% of medical students attending 3rd to 6th year, 27% of dentistry students attending 2nd to 5th year, 19.9% of pharmacy students attending 3rd to 5th year, and 16.1% of nursing students (9% from academic, and 7.1% from vocational study programs), attending 2nd to 4th year. The largest number of respondents (83.41%) had no prior professional experience in healthcare. The respondents' Grade Point Average (GPA) in this study was M = 8.71, ranging from 6 to 10 (SD = 0.64, Me = 8.75), and the distribution was polymodal (Figure 2). In terms of the exams relevant to this study, the most students passed General Pharmacology (almost three-quarters of the total sample) and Special Pharmacology (more than 58%), followed by Pharmacotherapy and Pharmacology with Toxicology (slightly less than a quarter), while other exams were passed by a relatively small number of respondents. Detailed data on the sociodemographic structure and characteristics of the sample are given in Table I.

The Pharmacovigilance Knowledge Test, PVKT

In this section of the questionnaire, we tested students' knowledge about pharmacovigilance activities. Originally, the test consisted of 20 multiple-choice questions, each with only one correct answer. The homogeneity and construct validity of the PVKT were examined using factor analysis. The principal axis method on the matrix of tetrachoric correlations was applied as the extraction method. Several alternative criteria were used to determine the number of factors that should have been retained, but the results were ambiguous. Parallel analysis[22,23] proposed a solution with eight factors, but such a solution was rejected as inadequate due to having too many factors in relation to the number of test items. Since at least three variables (items) are needed for the factor to be defined, determining the required number of factors for the parallel analysis was not possible. The other criteria were also conflicted considering the number of factors that should be retained. The criterion of VSS1 (*Very Simple Structure 1*) recommended two factors, the criterion of VSS2 (*Very Simple Structure 2*) recommended three, while Velicer's MAP (*Minimum Average Partial*) criterion recommended one factor, as well as BIC (*Bayes Information Criterion*) and the Guttman-Kaiser root one criterion[24]. Cattell' scree plot suggested two factors, the first of which explained 2.5 more variances than the second (Figure 3). Despite being lower than the usual criterion, this ratio indicated that the scale was one-dimensional (3:1). Based on this finding, as well as the fact that all three criteria agreed that the instrument was one-dimensional, we decided to isolate one factor and treat the instrument as one-dimensional.

The Kaiser-Meyer-Olkin coefficient (KMO) for the scale was KMO = 0.69 (eligibility limit is 0.60). This result was satisfying because the closer the KMO gets to the upper limit (the upper limit is 1), the more homogeneous the instru-

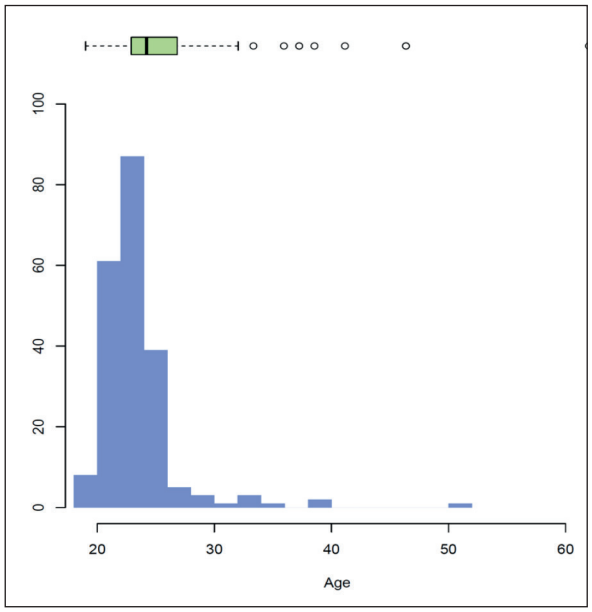

Figure 1. Histogram and box diagram of the age distribution of the respondents.

ment becomes and the likelihood of isolating a smaller number of relevant, interpretable components increases. The Bartlett's Test of Sphericity was statistically significant ($\chi 2$ (190) = 519.5028, $p<0.001$), indicating that the non-diagonal elements in the matrix of item intercorrelations were significantly different from zero value, thus approving use of factor analysis. Table II displays the descriptive indicators for the PVKT items.

Based on the means of the respondents' item scores, the majority of the PVKT questions were simple to answer. The most difficult question was question 17 (*The use of a registered drug in a manner, in indications and/or in a dose not listed in the Summary of Product Characteristics (SmPC), is marked in pharmacovigilance as:*), to which only 17% of respondents gave the correct answer. Among the more difficult questions were question 16 (*When reporting an adverse drug reaction, the minimum information to be provided about the patient includes:*), to which 34% of re-

Table I. Sociodemographic structure of study respondents.

	n	%
Gender		
Female	167	79.15
Male	44	20.85
Faculty		
Faculty of Medicine, University of Novi Sad	144	68.25
Faculty of Dentistry in Pančevo, University of Business Academy in Novi Sad	39	18.48
Faculty of Pharmacy, University of Business Academy in Novi Sad	28	13.27
Study program		
Integrated academic studies in Medicine	78	37.0
Integrated academic studies in Dentistry	57	27.0
Integrated academic studies in Pharmacy	42	19.9
Basic academic studies in Nursing	19	9.0
Basic vocational studies in Nursing	15	7.1
Previous professional experience in healthcare		
Non	176	83.41
Yes, but currently unemployed	19	9.00
Yes, currently employed	14	6.64
Other	2	0.95
Passed exam in the relevant subject		
General Pharmacology	155	73.46
Special Pharmacology	123	58.29
Pharmacotherapy	52	24.64
Pharmacology with Toxicology	51	24.17
Clinical Pharmacology	32	15.17
Pharmacology and Toxicology	26	12.32
Basics of Pharmacotherapy	26	12.32
Clinical Pharmacy	22	10.43
Neuropharmacology	10	4.74
Drug interaction and Adverse reactions	8	3.79

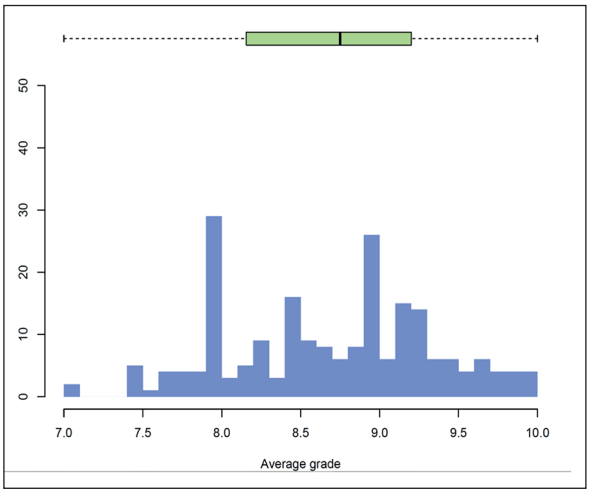

Figure 2. Histogram and box diagram of the Grade Point Average (GPA) of the respondents.

spondents correctly answered, and question 5 (*In practical terms, pharmacovigilance involves the detection and monitoring of adverse drug reactions in:*) to which the correct answer was given by 36% of respondents.

Since these were binary variables and some of them deviated significantly from the normal distribution (skewness and kurtosis outside the range of -2 to 2), we decided to perform exploratory factor analysis on a matrix of tetrachoric correlations. The isolated factor accounted for 22% of the test variance. Six of the twenty items had insufficient load values (> 0.30), so they were removed from the PVKT (Table III). The excluded items (17, 18, 15, 10, 19, and 20) are displayed in Italic style font at the bottom of Table III, with bolded load values.

The items we proposed for elimination were examined using separate component analysis with a single factor. However, no appropriate solution was found because only one item had a satisfactory factor load on a particular factor. Based on this finding, we can conclude that the excluded items did not have a special subject of measurement. After removing the previously mentioned six items, KMO on the remaining set of 14 items increased significantly to KMO = 0.73. Given that KMO is also a measure of a set of items' representativity level for the domain they are intended to measure, it is safe to conclude that PVKT is sufficiently representative. Measures of representativeness for retained items were also satisfactory, ranging from 0.61 to 0.80.

The reliability of the PVKT calculated as ordinal alpha (Cronbach's alpha on the tetrachoric correlation matrix) was good ($\alpha_{ord} = 0.83$). Similarly, the coefficient based on Guttman's image theory was satisfactory ($\lambda_6 = 0.87$). Furthermore, the factor analysis-based reliability coefficient[25] had

Table II. Descriptive indicators for items in the Pharmacovigilance Knowledge Test, PVKT.

Item No.	Mean (M)	Standard Deviation (SD)	Median	Trimmed mean†	Skewness	Kurtosis	Standard error of the mean (SG)
01	0.77	0.42	1	0.84	-1.29	-0.34	0.03
02	0.59	0.49	1	0.61	-0.35	-1.88	0.03
03	0.89	0.32	1	0.98	-2.42	3.85	0.02
04	0.87	0.33	1	0.96	-2.21	2.91	0.02
05	0.36	0.48	0	0.33	0.58	-1.67	0.03
06	0.89	0.32	1	0.98	-2.42	3.85	0,02
07	0.49	0.50	0	0.49	0.03	-2.01	0.03
08	0.56	0.50	1	0.57	-0.24	-1.95	0.03
09	0.84	0.36	1	0.93	-1.88	1.54	0.03
10	0.61	0.49	1	0.64	-0.45	-1.80	0.03
11	0.36	0.48	0	0.32	0.60	-1.65	0.03
12	0.84	0.36	1	0.93	-1.88	1.54	0.03
13	0.66	0.47	1	0.70	-0.69	-1.54	0.03
14	0.68	0.47	1	0.72	-0.76	-1.44	0.03
15	0.72	0.45	1	0.78	-0.98	-1.05	0.03
16	0.34	0.47	0	0.30	0.69	-1.54	0.03
17	0.14	0.35	0	0.05	2.03	2.15	0.02
18	0.50	0.50	1	0.50	-0.01	-2.01	0.03
19	0.53	0.50	1	0.54	-0.12	-1.99	0.03
20	0.47	0.50	0	0.47	0.10	-2.00	0.03

†The mean when 2.5% of the highest and 2.5% of the lowest results are removed.

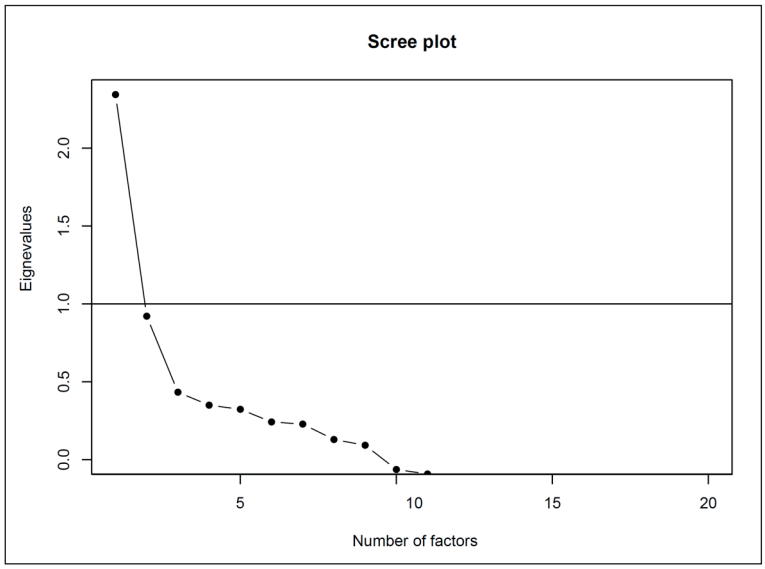

Figure 3. Scree plot on the Pharmacovigilance Knowledge Test, PVKT.

a satisfactory value, ω = 0.74. The average item discrimination calculated by Fisher's Z-transformation was 0.5, with item discrimination ranging from 0.3 to 0.8. These outcomes are within the acceptable ranges for item discrimination. The average interitem correlation was h1 = 0.26, which is within the recommended range (0.2-0.5). Because this measure is often used as an indicator of homogeneity, this finding supports the hypothesis that PVKT is fundamentally one-dimensional.

The PVKT had a possible score range of 0 to 14. The respondents' average score on this test was M = 9.14 (SD = 2.65, Me = 10). There was a significant and low correlation between the scores on PKT and the GPA of respondents [ρ (211) = 0.22, $p<0.05$]. Because the PVKT had a score range from 0 to 14, a score of 7 could be used to represent the approximate average difficulty of this test. A nonparametric substitute for the t-test, the one-sample Wilcoxon signed rank test, was used to determine whether the average achieved score was higher than that value. The calculated difference was statistically significant (V = 17478, $p<0.001$), indicating that the respondents correctly answered more than 50% of the correct answers (score 7).

The Pharmacovigilance Attitudes Questionnaire, PVAQ

This instrument included 20 items and a five-point agreement Likert scale to assess respondents' agreement with various statements about pharmacovigilance and ADRs reporting. The agreement scale was divided into five categories, with 1 indicated "*I do not agree at all*", and 5 indicated "*I completely agree*" with the given statement. The majority of questionnaire items were reflected in such a way that a higher score on the item indicated more negative attitudes toward pharmacovigilance. Negatively reflected items were item 4 and all items from 8 to 20, with the exception of item 18. Descriptive indicators for PVAQ items are displayed in Table IV.

The dimensionality and construct validity of PVAQ were assessed using exploratory factor analysis. The criteria for determining the number of factors that should be retained were also conflicted here, as they were in PVKT. Parallel analysis suggested four factors, BIC and Velicer's MAP criteria three, while Guttman-Kaiser root one criterion test, Cattel's scree plot (Figure 4), VSS1 and VSS2 suggested two factors. The calculated KMO value for PVAQ was KMO = 0.88, which is considered as a good value, on the border of being excellent. The Bartlett's Test of Sphericity was statistically significant (χ^2 (190) = 1906.461, $p<0.001$), indicating that the intercorrelations of PVAQ items are significantly different from zero value, and that the use of factor analysis is appropriate. The main axis method on the matrix of polychoric correlations was applied, and two isolated factors were placed in the oblimin position (Table V). Together, these two factors explained 52% of the total variance of scores on PVAQ items (the first factor 29.3%, and the second 22.7%). The first factor accounted for 56.4% of the common

Table III. Factor load values of PVKT items in a one-factor solution.

Item No.	Question	Load values
06	In legal terms, the term "adverse drug reaction" includes any harmful and unintentionally provoked reaction to a drug that has occurred during the application of:	0.894
03	The National Regulatory Body for monitoring adverse drug reactions in the Republic of Serbia is:	0.780
04	Reporting a suspected adverse drug reaction is a professional obligation of:	0.715
09	Death, imminent threat to the patient's life, permanent or severe health damage resulting from the use of the drug should be reported as:	0.638
07	If there is an inverted black triangle symbol on the packaging of a medicine, it means that:	0.578
13	Spontaneous reporting means the voluntary reporting of adverse reactions to medicines on the market, by:	0.530
11	In case of a newly discovered serious adverse drug reaction, emergency safety measures DO NOT include:	0.476
01	The main purpose of pharmacovigilance is:	0.419
14	In addition to adverse drug reactions, the following events may be reported to the National Pharmacovigilance Center:	0.411
16	In the context of pharmacovigilance, the term "new drug" is a drug that:	0.374
12	According to the current legislation in the Republic of Serbia, a serious adverse drug reaction should be reported to the regulatory authority within:	0.369
08	According to the National Pharmacovigilance Regulations document, an "unexpected adverse reaction" is a reaction to a drug:	0.357
02	The ultimate goal of pharmacovigilance is:	0.353
05	In practical terms, pharmacovigilance involves the detection and monitoring of adverse drug reactions in:	0.352
20	*The name of the unique, global electronic database of adverse drug reactions established by the World Health Organization (WHO) is:*	**0.286**
19	*Mandatory reporting of adverse drug reactions includes:*	**0.270**
10	*In accordance with the regulatory principles of the European Union, the status of additional monitoring in the Republic of Serbia is always granted to the following categories of drugs:*	**0.208**
15	*A healthcare professional may report an adverse drug reaction via:*	**0.193**
18	*When reporting an adverse drug reaction, the minimum information to be provided about the patient includes:*	**0.061**
17	*The use of a registered drug in a manner, in indications and/or in a dose not listed in the Summary of Product Characteristics (SmPC), is marked in pharmacovigilance as:*	**-0.012**

variance, while the second accounted for 43.6%.

The first factor was identified as a Negative attitude toward ADRs reporting and includes 13 PVAQ items. It is characterized by an unwillingness to report ADRs as this may jeopardize a healthcare professional's career and reputation (items 12, 13, 16, 11, 8, 10, 14, 19, 9, 15, 17, 4 and 20). This is also a behavioral component of the attitude toward pharmacovigilance. The second isolated factor was identified as a Positive atti-

Table IV. Descriptive indicators for items in the Pharmacovigilance Attitude Questionnaire, PVAQ.

Item No.	Mean (M)	Standard Deviation (SD)	Median	Trimmed mean‡	Skewness	Kurtosis	Standard error of the mean
01	4.57	0.70	5	4.70	-1.99	5.43	0.05
02	4.72	0.65	5	4.87	-2.84	9.83	0.04
03	4.64	0.71	5	4.79	-2.44	7.12	0.05
04†	2.96 (3.04)	1.03	3	2.93 (3.07)	0.16 (-0.16)	-0.51	0.07
05	4.65	0.77	5	4.85	-2.61	7.21	0.05
06	4.82	0.57	5	4.98	-4.12	19.83	0.04
07	4.70	0.66	5	4.86	-2.72	8.92	0.05
08†	1.94 (4.06)	1.26	1 (5)	1.71 (4.29)	1.20 (-1.2)	0.30	0.09
09†	2.71 (3.29)	1.48	3	2.63 (3.37)	0.20 (-0.2)	-1.37	0.10
10†	2.75 (3.25)	1.31	3	2.69 (3.31)	0.18 (-0.18)	-1.09	0.09
11†	2.86 (3.14)	1.37	3	2.82 (3.18)	0.05 (-0.05)	-1.23	0.09
12†	2.53 (3.47)	1.36	3	2.41 (3.59)	0.38 (-0.38)	-1.04	0.09
13†	2.31 (3.69)	1.23	2 (4)	2.17 (3.83)	0.66 (-0.66)	-0.50	0.08
14†	2.63 (3.37)	1.19	3	2.55 (3.45)	0.23 (-0.23)	-0.65	0.08
15†	2.65 (3.35)	1.23	3	2.59 (3.41)	0.28 (-0.28)	-0.95	0.08
16†	2.29 (3.71)	1.26	2 (4)	2.14 (3.86)	0.67 (-0.67)	-0.56	0.09
17†	3.11 (2.89)	1.17	3	3.14 (2.86)	-0.15 (0.15)	-0.72	0.08
18	3.87	1.03	4	3.98	-0.69	-0.03	0.07
19†	2.60 (3.4)	1.19	3	2.53 (3.47)	0.25 (-0.25)	-0.74	0.08
20†	3.46 (2.54)	1.45	4 (2)	3.57 (2.43)	-0.43 (0.43)	-1.19	0.10

†Negatively reflected items during the formation of summation scores; In parentheses are given the values after reflection (recoding). ‡The mean when 2.5% of the highest and 2.5% of the lowest results are removed.

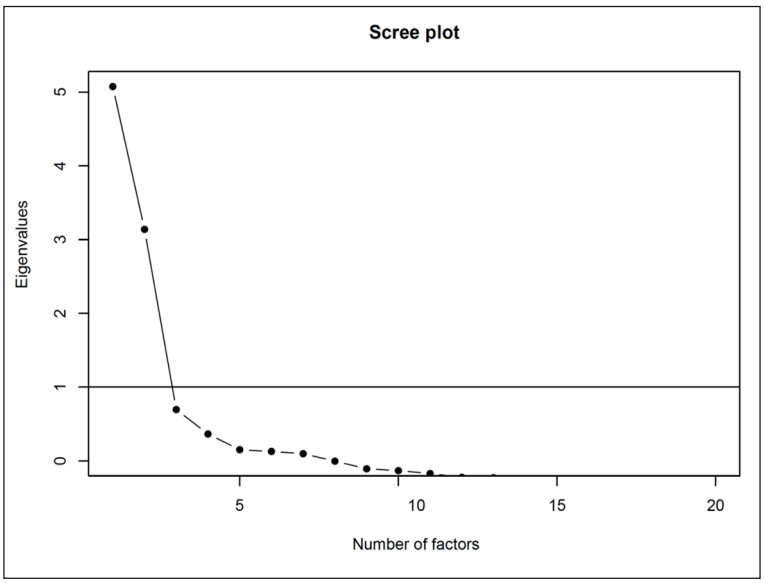

Figure 4. Scree plot on the Pharmacovigilance Attitude Questionnaire, PVAQ.

tude toward pharmacovigilance and includes a total of seven items in the PVAQ. This factor is characterized by positive attitudes toward the importance of pharmacovigilance in the promotion and preservation of public health, which are not necessarily related to personal willingness to act in accordance with them. At the same time, this reflects a cognitive component of pharmacovigilance attitudes.

Given that the first factor is made up of negatively reflected items, it is reasonable to assume that these are artifacts, implying that the isolat-

Table V. Matrix of the set of PVAQ items in a two-factor solution and oblimin position.

Item No.	Item	F1	F2
12	If I report adverse drug reactions too often, it could negatively affect my future professional reputation.	0.795	
13	I believe that reporting moderate and/or rare ADRs is unnecessary, as it can lead to an unnecessary withdrawal of a product from the market.	0.777	
16	The occurrence of ADRs to drugs from unreputable manufacturers should be given special attention, because I believe that in most circumstances, the drug's brand is also a guarantee of its safety.	0.740	
11	Certain ADRs should be reported carefully, since they could be attributed to my professional incompetence or negligent work.	0.721	
08	In some cases, reporting ADRs is not recommended.	0.716	
10	If I report all ADRs unconditionally, I'm worried that I'll have a variety of problems in my future work, or even get punished.	0.684	
14	The majority of RARE ADRs are the result of insufficient healthcare professional observation or manipulation by competing pharmaceutical corporations.	0.678	
19	I am aversive towards reporting ADRs because I believe the existing procedure for their reporting in the Republic of Serbia is overly burdensome administratively.	0.659	
09	I am convinced that my future decisions on reporting ADRs will be greatly influenced by the business policy of the institution where I will be employed and/or the opinions and attitudes of those who will be my superiors.	0.627	
15	The reporting of ADRs should be mainly focused on new drugs, as I believe that the effects of drugs that have been used for a long time have already been investigated thoroughly.	0.598	
17	I don't feel confident in identifying and reporting ADRs that are not already described in the Summary of Product Characteristics (SmPC).	0.554	
04	I am skeptical of information derived from so-called spontaneous reporting of ADRs by patients, and I believe it should always be considered carefully.	0.522	
20	I am dissatisfied because of the lack of financial incentive for healthcare professionals who monitor and report ADRs, as I believe this activity requires additional effort and time.	0.424	
06	Healthcare professionals who monitor and report ADRs make an important contribution to the effectiveness of the national pharmacovigilance system.		0.921
07	As much as possible, I am willing to monitor and report ADRs for medications that I will use in future clinical practice.		0.904
02	I believe that having access to ADRs information is very important to the quality of my future professional work.		0.863
03	Safe use of drugs is possible only if health professionals continuously enrich the existing knowledge about ADRs.		0.794
05	All health professionals involved in the application of medications should be responsible for ADRs monitoring and reporting.		0.784
01	Pharmacovigilance is an important aspect of maintaining public health and I believe it should be studied in more detail during studies.		0.741
18	Based on my experience from studies so far, I believe that healthcare professionals generally do not have enough time for ADRs monitoring and reporting.	0.382	0.420

Note: For clarity, insignificant factor loads (<0.3) are not shown; F1 – factor loading for factor identified as Negative attitude toward reporting ADRs; F2 – factor loading for factor identified as Positive attitude toward pharmacovigilance

ed factors are actually factors of methods that evolved as a result of different item orientation. The correlation of regression factor scores of these two dimensions was r = -0.17. Although the direction of this correlation was anticipated, the degree of correlation discovered was relatively low; it was expected that if the respondents have a positive attitude toward pharmacovigilance (high score on the second factor), they should be willing to report ADRs at the same time (high score on the first factor). Given the relatively low correlation between factor scores on the two dimensions, treating them as separate subscales of this questionnaire would be completely rational. However, this unexpectedly low correlation between the two isolated factors indicates that these are not method factors (if they were method factors, the correlation would be significantly higher). Therefore, we decided to treat the two isolated factors as independent subscales.

The first subscale (*Positive attitudes toward ADRs reporting*, PAADR) was found to have an excellent reliability, calculated as ordinal alpha, $\alpha_{ord} = 0.91$. Guttman's reliability coefficient was $\lambda_6 = 0.92$, and the reliability coefficient based on factor analysis was $\omega = 0.91$. All items have satisfactory discriminativity, ranging from 0.37 to 0.75, with an average discriminant value of 0.63. The calculated average interitem correlation of this subscale was h1 = 0.42, indicating its homogeneity (one-dimensionality). The PAADR subscale consists of 13 items and a possible score range of 13 to 65. The average score on our sample of respondents was 43.12 (SD = 10.63, Me = 45). The distribution of scores was slightly negative (Sk = -0.78). The average answer score on items was 3.32, which is higher than the middle category. This average score was also significantly higher than the theoretical mean score (summation 39, average item score 3). Wilcoxon's (one-way) equivalent pair test was used to determine whether the average score on this scale differed significantly from this value, and it confirmed the existence of a statistically significant difference (V = 14380, $p<0.001$).

The second subscale (*Positive attitudes toward pharmacovigilance*, PAPV) contains seven items (6, 7, 2, 3, 5, 1, and 18). After statistical testing, this subscale was found to have excellent reliability. Ordinal alpha was $\alpha_{ord} = 0.91$, Guttman's reliability coefficient was $\lambda_6 = 0.92$, while the determined reliability coefficient based on factor analysis was $\omega = 0.89$. The average discrimination of items in the second subscale was 0.76, ranging from 0.32 to 0.87. Despite the fact that two items (Item 6 - *Healthcare professionals who monitor and report ADRs make an important contribution to the effectiveness of the national pharmacovigilance system* and item 7 - *As much as possible, I am willing to monitor and report ADRs for medications that I will use in future clinical practice*) had discriminating coefficients that are higher than the recommended upper limit (0.8), the content analysis determined that they are not redundant, thus they were not deleted from this subscale. The average interitem correlation of this scale was h1 = 0.58. Although this value is slightly higher than the recommended upper limit, it can be considered acceptable and has not been the result of the existence of redundant items.

This subscale has a minimum summation score of 7 and a maximum summation score of 35. The average score obtained on this sample of respondents was 31.98 (SD = 3.68, Me = 33). The distribution was noticeably negative (Sk = -3.21), indicating that respondents expressed very positive attitudes toward pharmacovigilance (corresponds to an average choice response to items of 4.57). Since the Shapiro-Wilk test revealed that the summation scores on both subscales deviated significantly from the normal distribution ($W_{PAADR} = 0.95119$, $W_{PAPV} = 0.69555$, $p<0.001$ in both cases), the Wilcoxson Signed Rank test, a nonparametric substitute for the *t*-test for repeated measurements, was used to examine this difference. The scores were converted to average item scores by dividing the total score on each of the subscales by the number of items it contains, since the scales do not have the same range of scores. The result of the Wilcoxson test was statistically significant (V = 590, $p<0.001$), indicating that the respondents had significantly more positive attitudes toward pharmacovigilance than they did toward their own involvement in the ADRs monitoring and reporting. In order to investigate the convergent validity of the PVKT, correlations (Spearman's correlation rank – ρ) were calculated with the student's grades in the exams they passed. Table VI shows the statistically significant correlations that were discovered.

Positive attitudes toward ADRs reporting, positive attitudes toward pharmacovigilance, and the Grade Point Average (GPA) during studies all had positive correlations, as expected, but they were low. The direction of correlations confirmed PVKT's construct (convergent) validity, but the magnitude of correlations was lowered due to the unreliability of correlates (this especially refers to the grades given by respondents; the correlation toward them

Table VI. Spearman's correlation rank of PVKT and other measures.

Measure	ρ	ρc	*p*	n
PAADR	0.27	0.31	0.00	211
PAPV	0.18	0.21	0.01	211
Final grade in Pharmacology and Toxicology	0.47	0.52	0.02	25
Grade Point Average (GPA) during studies	0.22	0.24	0.00	211

Note: ρc denotes correlation with attenuation correction (unreliability of measures); for correlations with grades, the correlation was corrected for instrument unreliability.

Table VII. Spearman's correlation rank of the PAADR subscale and other measures.

Measure	ρ	ρc	*p*	n
The grade from Clinical Pharmacology	0.37	0.39	0.04	31
The grade from Pharmacotherapy	0.30	0.32	0.03	50
The grade from Pharmacology with Toxicology	0.34	0.36	0.02	46
Grade Point Average (GPA) during studies	0.20	0.21	0.00	211

Note: ρc denotes correlation with attenuation correction (unreliability of measures); for correlations with grades, the correlation was corrected for instrument unreliability.

Table VIII. Spearman's correlation rank of the PAPV subscale and other variables.

Variable	ρ	ρc	*p*	n
The grade from Special Pharmacology	0.23	0.24	0.01	120
The grade from Clinical Pharmacology	0.39	0.43	0.03	31
Grade Point Average (GPA) during studies	0.23	0.25	0.00	211

Note: ρc denotes correlation with attenuation correction (unreliability of measures); for correlations with grades, the correlation was corrected for instrument unreliability.

could not be corrected, because their reliability is unknown). PVKT mostly correlated with the grade from the subject Pharmacology and Toxicology, at a moderate level. However, it should be noted that this correlation was obtained on a separate sample of 25 subjects. Correlations with grades from other relevant subjects were not statistically significant. Table VII displays statistically significant rank correlations between PAADR scale scores and grades from relevant subjects during studies.

As expected, the PAADR subscale showed positive correlations with the grades in the relevant subjects. The direction and level of correlations confirmed the construct (convergent) validity of the PAADR subscale. When compared to PVKT, identified correlations of the PAADR subscale with grades were higher. All correlations, except for the correlation with the average success during studies, were of a moderate degree. The grades from the subjects Pharmacology and Pharmacology with Toxicology had the highest level of correlation, followed by a slightly lower correlation with the grade from Pharmacotherapy, and the lowest correlation was with the GPA during the studies. Correlations with grades from other relevant subjects were not statistically significant. In addition, the correlations of the PAPV subscale with the grades from the relevant subjects and the GPA during studies were also examined (Table VIII).

The PAPV scale significantly correlated only with the grades from the subjects Special Pharmacology (low positive correlation), Clinical Pharmacology (moderate positive correlation) and the GPA during the studies (low positive correlation). Other correlations of the PAADR subscale with grades from relevant subjects were not statistically significant. Finally, based on the results of statistical analyses, it was confirmed that PVKT and PAADR correlated the most with the grade from the subject Pharmacology and Toxicology.

The final, validated versions of the Pharmacovigilance Knowledge Test, PVKT, and Pharmacovigilance Attitude Questionnaire, PVAQ, are given in Tables IX and X.

Discussion

The knowledge-attitude questionnaires are widely used in medical education, healthcare and management[26]. Knowledge and attitude assessment is a quantitative research method (predefined questions formatted in standardized questionnaires) that provides access to quantitative and qualitative information on the characteristics of the investigated population[27]. There is a limited number of studies in the literature that investigated knowledge and attitudes toward pharmacovigilance among students from various health sciences study programs. The majority of studies available focused on pharmacy students, with a smaller number including students of medicine, dentistry, and, in particular, nursing science[19]. Despite the fact that nurses are objectively a significant source of information on ADRs due to their direct participation in the drug administration process, medical doctors and pharmacists are designated as the health professionals who report ADRs the most frequently[12,13,28,29]. In addition, there is data in the literature on prejudices regarding the role of nurses in reporting ADRs, and pharmacovigilance systems of some countries still do not recognize this profile of health professionals as ADRs reporters[30,31].

The first study on students' knowledge and attitudes toward pharmacovigilance (KAPV) was published in 2011[19]. However, only a few valid measuring instruments are currently available to enable a methodologically correct KAPV evaluation in the student population. Knowledge tests are frequently heterogeneous in content because they examine knowledge from various subdomains, even though they have a single subject of measurement – knowledge from the field for which they are intended[32]. Taking this into account, we intended to create and validate a universal, understandable, and representative questionnaire to assess health sciences students' knowledge and attitudes toward pharmacovigilance and ADRs reporting. We included students from all three faculties that educate future healthcare professionals in the Autonomous Province of Vojvodina, Serbia, to increase the sample's representativeness. A total of 242 students completed the questionnaire, with 211 (87.19%) meeting the criteria for inclusion in the study.

Originally, the questionnaire we designed included 20 questions about fundamental pharmacovigilance knowledge and 20 statements representing attitudes toward ADRs reporting practices. The knowledge test questions were based on the pharmacological group of subjects' curriculums and only included pharmacovigilance knowledge that should be adopted by students of all health sciences, regardless of their study program. In order to increase the representativeness of the set of items for the measuring domain, six questions were excluded from the knowledge test after statistical testing. The final, validated version of the *Pharmacovigilance Knowledge Test*, PVKT in our questionnaire contains 14 questions to measure fundamental knowledge of pharmacovigilance, which is similar to the number of questions in previous studies that included predominantly pharmacy students[19].

Lack of knowledge and skills in pharmacovigilance has been identified in the literature as one of the three most common reasons for not reporting ADRs[31]. However, after analyzing the responses obtained in our study, it was found that respondents in the observed sample demonstrated a high level of knowledge in the field of pharmacovigilance, in contrast to the majority of available studies in which students' scores were generally and/or significantly lower than the possible maximum score[33-36]. On our PVKT, the possible scores ranged from 0 to 14, with respondents achieving an average score of M = 9.14 (SD = 2.65, Me = 10). Students from the University of Novi Sad's Medical Faculty (MFUNS) performed best on the knowledge test, followed by students from the University of Business Academy in Novi Sad's Faculty of Pharmacy (FPUBANS) and students from the University of Business Academy in Novi Sad's Faculty of Dentistry Pančevo (FDPUBANS), respectively.

Considering the differences between study programs, students from integrated academic studies of medicine performed the best on the PVKT, followed by students from integrated academic studies of pharmacy and first-degree academic studies of nursing science. Students pursuing integrated academic studies in dentistry and first-degree vocational studies in nursing achieved the lowest and nearly equal scores. Unlike the findings of our study, which revealed the highest level of knowledge among students of medicine, the small number of previous studies including students from various study programs showed superior knowledge on pharmacovigilance and ADRs reporting among pharmacy students[37-39].

To assess respondents' attitudes toward pharmacovigilance and ADRs reporting, The Pharmacovigilance Attitude Questionnaire, PVAQ was

Table IX. Validated version of Pharmacovigilance Knowledge Test, *PVKT.*

Item No.	Item
01	**The main purpose of pharmacovigilance is:** • determining the prevalence of adverse drug reactions • *detecting, understanding, and preventing adverse drug reactions* • limiting new drug over-registration • an analysis of the rationale for the use of specific drugs in national medical and pharmaceutical practice
02	**The ultimate goal of pharmacovigilance is:** • enabling safe self-medication of patients • protection of drug manufacturers' legal interests • *protection of public health* • protection of healthcare professionals from criminal liability
03	**The National Regulatory Body for monitoring adverse drug reactions in the Republic of Serbia is:** • National Institute for Medical Research • *National Agency for Medicines and Medical Devices* • Health Council of Serbia • National Council for Research in Medicine and Pharmacy
04	**Reporting a suspected adverse drug reaction is a professional obligation of:** • medication-administering physicians, dentists, and nurses • the pharmacist who dispensed the patient's medication at the pharmacy • the prescribing physician or dentist only • *all health professionals involved in drug administration*
05	**In practical terms, pharmacovigilance involves the detection and monitoring of adverse drug reactions in:** • preclinical phase of drug development • clinical phase of drug development • *post-registration (post-marketing) phase of drug development* • preclinical, clinical and post-registration phase of drug development
06	**In legal terms, the term "adverse drug reaction" includes any harmful and unintentionally provoked reaction to a drug that has occurred during the application of:** • higher doses of drug than the recommended therapeutic range • lowest recommended therapeutic doses of drugs *doses of the drug recommended for humans (for treatment, disease prevention, diagnosis) or when using any dose of the drug during a clinical trial* • submaximal therapeutic doses of drugs
07	**If there is an inverted black triangle symbol on the packaging of a medicine, it means that:** • only adults and children over the age of 13 can use the drug safely • the drug strongly affects the patient's psychophysical abilities • the drug is not registered in the Republic of Serbia • *the drug is monitored more intensively than other drugs (it is extremely important to report any suspicion of adverse reactions to this drug)*
08	**According to the National Pharmacovigilance Regulations document, an "unexpected adverse reaction" is a reaction to a drug:** • which can cause immediate life-threatening to the patient • *whose nature, severity or outcome are not described in the Summary of Product Characteristics (SmPC)* • which the healthcare provider had no prior clinical experience with • which had not previously been manifested by the treated organ or organ system
09	**Death, imminent threat to the patient's life, permanent or severe health damage resulting from the use of the drug should be reported as:** • *serious adverse drug reaction* • unexpected adverse drug reaction • adverse drug reaction • adverse drug experience
10	**In the context of pharmacovigilance, the term "new drug" is a drug that:** • is used for over five years, but with a new indication and/or method of application • *is less than five years in use* • has not previously been available on the domestic market and/or had been in use for less than three years • the first two answers are correct

Table continued

Table IX. ***(Continued).*** Validated version of Pharmacovigilance Knowledge Test, *PVKT.*

Item No.	Item
11	**In case of a newly discovered serious adverse drug reaction, emergency safety measures DO NOT include:** • the drug's withdrawal from the market • corrections to information in the summary of the Summary of Product Characteristics (SmPC) • informing health authorities and the general public about the discovered risk • *investigating potential liabilities and sanctioning drug manufacturers*
12	**According to the current legislation in the Republic of Serbia, a serious adverse drug reaction should be reported to the regulatory authority within:** • *immediately* • within 7 days • within 10 days • within 14 days
13	**Spontaneous reporting means the voluntary reporting of adverse reactions to medicines on the market, by:** • healthcare professionals and healthcare institutions • patients who used the drug • *the first two answers are correct* • independent expert bodies
14	**In addition to adverse drug reactions, the following events may be reported to the National Pharmacovigilance Center:** • adverse reactions caused by the use of medical devices • suspect in medical mistakes and drug overdosing • suspect in drug abuse and unauthorized use of drugs • *all of the previous answers are correct*

Note: The correct answers are displayed in Italic style font.

used in the third section of our questionnaire. It was divided into two subscales: Positive attitudes toward ADRs reporting, PAADR (13 items), and Positive attitudes toward pharmacovigilance, PAPV (7 items). The PVAQ items were created by combining statements from the literature about the most common causes of ADRs non-reporting and negative attitudes toward pharmacovigilance[15-17,31]. For the purpose of statistical processing of the obtained data, all items in the questionnaire were reflected so that the higher score on the items indicated more positive attitudes toward pharmacovigilance, which should be kept in mind when interpreting the meaning of scores on these items. The calculated average score on the PAADR scale (43.12; SD = 10.63, Me = 45) clearly indicates that the respondents slightly tend to have more positive attitudes toward ADRs reporting. The average score obtained on the PAPV subscale (31.98; SD = 3.68, Me = 33) indicates very positive attitudes of the students toward pharmacovigilance. Despite the usually observed lack of knowledge about the importance and manner of ADRs reporting, generally positive attitudes toward pharmacovigilance among health sciences students have been also found in several previous studies[33,40,41]. The majority of our respondents (94.7% in total) agreed with the statement that healthcare professionals contribute significantly to the effectiveness of the national pharmacovigilance system by reporting ADRs and expressed willingness to monitor and report ADRs as much as possible in future practice (92.6% in total). The majority also agreed that monitoring and reporting of ADRs should be a professional obligation of all healthcare professionals involved in the drug administration process (90% in total). It is worth noting that 62.4% of respondents in our sample agreed with the statement that healthcare professionals do not have enough time in their daily practice to report ADRs (31.8% agreed, and 30.6% strongly agreed on this statement), which is consistent with the findings of previous studies[17,19]. Furthermore, response analysis revealed that more than half of study participants are dissatisfied because there are no financial incentives for healthcare providers who report ADRs (17.4% of respondents agreed, and 33.5% strongly agreed with this statement). More than a third of respondents do not feel confident identifying and reporting of ADRs that are not already described in the summary of product characteristics, *SmPC* (35.9% in total). Nearly the same number of respondents agreed with the statement that certain

Table X. Validated version of Pharmacovigilance Attitude Questionnaire, *PVAQ*.

Item No.	Item
01	Pharmacovigilance is an important aspect of maintaining public health and I believe it should be studied in more detail during studies.
02	I believe that having access to ADRs information is very important to the quality of my future professional work.
03	Safe use of drugs is possible only if health professionals continuously enrich the existing knowledge about ADRs.
04	I am skeptical of information derived from so-called spontaneous reporting of ADRs by patients, and I believe it should always be considered carefully.
05	All health professionals involved in the application of medications should be responsible for ADRs monitoring and reporting.
06	Healthcare professionals who monitor and report ADRs make an important contribution to the effectiveness of the national pharmacovigilance system.
07	As much as possible, I am willing to monitor and report ADRs for medications that I will use in future clinical practice.
08	In some cases, reporting ADRs is not recommended.
09	I am convinced that my future decisions on reporting ADRs will be greatly influenced by the business policy of the institution where I will be employed and/or the opinions and attitudes of those who will be my superiors.
10	If I report all ADRs unconditionally, I'm worried that I'll have a variety of problems in my future work, or even get punished.
11	Certain ADRs should be reported carefully, since they could be attributed to my professional incompetence or negligent work.
12	If I report adverse drug reactions too often, it could negatively affect my future professional reputation.
13	I believe that reporting moderate and/or rare ADRs is unnecessary, as it can lead to an unnecessary withdrawal of a product from the market.
14	The majority of RARE ADRs are the result of insufficient healthcare professional observation or manipulation by competing pharmaceutical corporations.
15	The reporting of ADRs should be mainly focused on new drugs, as I believe that the effects of drugs that have been used for a long time have already been investigated thoroughly.
16	The occurrence of ADRs to drugs from unreputable manufacturers should be given special attention, because I believe that in most circumstances, the drug's brand is also a guarantee of its safety.
17	I don't feel confident in identifying and reporting ADRs that are not already described in the Summary of Product Characteristics (S*m*PC).
18	Based on my experience from studies so far, I believe that healthcare professionals generally do not have enough time for ADRs monitoring and reporting.
19	I am aversive towards reporting ADRs because I believe the existing procedure for their reporting in the Republic of Serbia is overly burdensome administratively.
20	I am dissatisfied because of the lack of financial incentive for healthcare professionals who monitor and report ADRs, as I believe this activity requires additional effort and time.

Note: On a five-point Likert scale, the respondent should select one of the following answers for each statement: 1. strongly disagree. 2. disagree. 3. neither agree nor disagree. 4. agree 5. strongly agree.

ADRs should be reported carefully because they could be attributed to professional incompetence or negligent work (34.7% in total). As many as 29.8% of respondents are concerned about experiencing inconvenience or punishment as a result of unconditional reporting of all observed ADRs in the future. 32.6% of them are convinced that their future decisions on reporting ADRs will be greatly influenced by the business policy of the institution where they will be employed, as well as the opinions and attitudes of their superiors. In general, with a significantly lower standard deviation on the PAPV subscale compared to the PAADR subscale, the findings of our study clearly indicate that subjects in the observed sample have significantly more positive attitudes toward pharmacovigilance than willingness to report ADRs ($p<0.001$), which is an unusual finding compared to other similar studies[39,42-45].

Limitation of the Study

Similar to surveys used in other studies, it was not possible to avoid questions regarding local pharmacovigilance legislation when developing *Pharmacovigilance Knowledge Test* (PVKT). However, the number of these items has been kept to a bare minimum, and answers can be easily replaced to meet the needs of researchers from other countries. Unequal representation of respondents from different study programs in the total sample may have influenced the values of the achieved average scores in both sections of the questionnaire used in this study. Furthermore, the issue of respondent honesty and the desire to answer in a socially acceptable and/or desirable manner is a limiting factor in any psychometric study, including this one.

Conclusions

We developed a questionnaire with favorable validity and reliability for assessing healthcare sciences students' knowledge and attitudes toward pharmacovigilance and ADRs reporting. The results of this study can help identify the current need for additional pharmacovigilance education and training in the student population, as well as improve existing curriculums of relevant subjects in study programs in medicine, dentistry, pharmacy, and nursing science. With minor modifications to the section for collecting sociodemographic data, this questionnaire can also be used to assess the need for Continuing Medical Education (CME) in the population of graduate health professionals.

Acknowledgements

The Ministry of Education and Science of the Republic of Serbia (grants numbered 41012 and 172050) and Provincial Secretariat for Higher Education and Scientific Research of the Autonomous Province of Vojvodina (grant numbered 142-451-3176/2020-02) supported this research work.

Conflict of Interest

The authors declare that they have no conflict of interests.

References

1) Moore N, Berdaï D, Blin P, Droz C. Pharmacovigilance - The next chapter. Therapie 2019; 74: 557-567.
2) Fornasier G, Francescon S, Leone R, Baldo P. An historical overview over pharmacovigilance. Int J Clin Pharm 2018; 40: 744-747.
3) Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, Farrar K, Park BK, Breckenridge AM. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. BMJ 2004; 329: 15-19.
4) Al Hamid A, Ghaleb M, Aljadhey H, Aslanpour Z. A systematic review of hospitalization resulting from medicine-related problems in adult patients. Br J Clin Pharmacol 2014; 78: 202-217.
5) Giardina C, Cutroneo PM, Mocciaro E, Russo GT, Mandraffino G, Basile G, Rapisarda F, Ferrara R, Spina E, Arcoraci V. Adverse Drug Reactions in Hospitalized Patients: Results of the FORWARD (Facilitation of Reporting in Hospital Ward) Study. Front Pharmacol 2018; 9: 350.
6) Potlog Shchory M, Goldstein LH, Arcavi L, Shihmanter R, Berkovitch M, Levy A. Increasing adverse drug reaction reporting - How can we do better? PLoS One 2020; 15: e0235591.
7) Khamisy-Farah R, Damiani G, Kong JD, Wu JH, Bragazzi NL. Safety profile of Dupilumab during pregnancy: a data mining and disproportionality analysis of over 37,000 reports from the WHO individual case safety reporting database (VigiBase™). Eur Rev Med Pharmacol Sci 2021; 25: 5448-5451.
8) Campbell JE, Gossell-Williams M, Lee MG. A Review of pharmacovigilance. West Indian Med J 2014; 63: 771-774.
9) Bepari A, Niazi SK, Rahman I, Dervesh AM. The comparative evaluation of knowledge, attitude, and practice of different health-care profession-

als about the pharmacovigilance system of India. J Adv Pharm Technol Res 2019; 10: 68-74.

10) Terblanche A, Meyer JC, Godman B, Summers RS. Impact of a pharmacist-driven pharmacovigilance system in a secondary hospital in the Gauteng Province of South Africa. Hosp Pract (1995). 2018; 46: 221-228.
11) Yang J, Zheng L, Yu WG, Gu YC. Clinical pharmacist interventions in managing Key Monitoring Drugs in China. Eur Rev Med Pharmacol Sci 2021; 25: 1006-1015.
12) Zimmermann A, Flis A, Gaworska-Krzemińska A, Cohen MN. Drug-safety reporting in Polish nursing practice - Cross sectional surveys. PLoS One 2020; 15: e0241377.
13) Griffith R. Nurses must report adverse drug reactions. Br J Nurs 2013; 22: 484-485.
14) Klein E, Bourdette D. Postmarketing adverse drug reactions: A duty to report? Neurol Clin Pract 2013; 3: 288-294.
15) Jeetu G, Anusha G. Pharmacovigilance: a worldwide master key for drug safety monitoring. J Young Pharm 2010; 2: 315-320.
16) Pal SN, Duncombe C, Falzon D, Olsson S. WHO strategy for collecting safety data in public health programmes: complementing spontaneous reporting systems. Drug Saf 2013; 36: 75-81.
17) Gahr M, Eller J, Connemann BJ, Schönfeldt-Lecuona C. Subjective reasons for non-reporting of adverse drug reactions in a sample of physicians in outpatient care. Pharmacopsychiatry 2016; 49: 57-61.
18) Salehi T, Seyedfatemi N, Mirzaee MS, Maleki M, Mardani A. Nurses' knowledge, attitudes, and practice in relation to pharmacovigilance and adverse drug reaction reporting: A systematic review. Biomed Res Int 2021; 2021: 6630404.
19) Alwhaibi M, Al Aloola NA. Healthcare students' knowledge, attitude and perception of pharmacovigilance: A systematic review. PLoS One 2020; 15: e0233393.
20) Chhabra KG, Sharma A, Chhabra C, Reddy JJ, Deolia SG, Mittal Y. Knowledge, attitude, and practices regarding pharmacovigilance and adverse drug reaction reporting among dental students in a teaching hospital, Jodhpur, India: A Cross-sectional Study. J Contemp Dent Pract 2017; 18: 964-969.
21) Güner MD, Ekmekci PE. Healthcare professionals' pharmacovigilance knowledge and adverse drug reaction reporting behavior and factors determining the reporting rates. J Drug Assess 2019; 8: 13-20.
22) Achim A. Determining the number of factors using parallel analysis and its recent variants: Comment on Lim and Jahng (2019). Psychol Methods 2021; 26: 69-73.
23) Horn JL. A rationale and test for the number of factors in factor analysis. Psychometrika 1965; 30: 179-185.
24) Wilson P, Cooper C. Finding the magic number: Investigating methods used to extract the number of factors in a factor analysis. Psychologist 2008; 21: 866-867.
25) Zinbarg RE, Revelle W, Yovel I, Li W. Cronbach's α, Revelle's β, and Mcdonald's ωH: Their relations with each other and two alternative conceptualizations of reliability. Psychometrika 2005; 70: 123–133.
26) Peng S, He J, Huang J, Tan J, Liu M, Liu X, Wu Y. A chronic kidney disease patient awareness questionnaire: Development and validation. PLoS One 2019; 14: e0216391.
27) Andrade C, Menon V, Ameen S, Kumar Praharaj S. Designing and conducting knowledge, attitude, and practice surveys in psychiatry: Practical guidance. Indian J Psychol Med 2020; 42: 478-481.
28) Hussain R, Hassali MA, Ur Rehman A, Muneswarao J, Atif M, Babar ZU. A qualitative evaluation of adverse drug reaction reporting system in Pakistan: Findings from the nurses' perspective. Int J Environ Res Public Health 2020; 17: 3039.
29) Renzi E, Di Simone E, Di Muzio M. Measuring knowledge, attitudes and behavior of nurses in medication management: cross-cultural comparisons in Italy and Malta. Eur Rev Med Pharmacol Sci 2020; 24: 5167-5175.
30) Ekman E, Bäckström M. Attitudes among hospital physicians to the reporting of adverse drug reactions in Sweden. Eur J Clin Pharmacol 2009; 65: 43-46.
31) Varallo FR, Guimarães Sde O, Abjaude SA, Mastroianni Pde C. Causes for the underreporting of adverse drug events by health professionals: a systematic review. Rev Esc Enferm USP 2014; 48: 739-747.
32) Schmidt FL. Statistical significance testing and cumulative knowledge in psychology: Implications for training of researchers. Psychol Methods 1996; 1: 115-129.
33) Meher BR, Joshua N, Asha B, Mukherji D. A questionnaire based study to assess knowledge, attitude and practice of pharmacovigilance among undergraduate medical students in a Tertiary Care Teaching Hospital of South India. Perspect Clin Res 2015; 6: 217-221.
34) Palaian S, Ibrahim MIM, Mishra P, Shankar PR. Assessment of a Pharmacovigilance Module: An interventional study on knowledge, attitude, and practice of pharmacy students. J Pharm Bioallied Sci 2021; 13: 248-255.
35) Upadhyaya HB, Vora MB, Nagar JG, Patel PB. Knowledge, attitude and practices toward pharmacovigilance and adverse drug reactions in postgraduate students of Tertiary Care Hospital in Gujarat. J Adv Pharm Technol Res 2015; 6: 29-34.
36) Abubakar AR, Ismail S, Rahman NI, Haque M. Comparative study on drug safety surveillance between medical students of Malaysia and Nigeria. Ther Clin Risk Manag 2015; 11: 1015-1025.

37) Alwhaibi M, Alhindi G, Alshamrani M, Essa MB, A Al Aloola N, Alhawassi TM. Pharmacovigilance in healthcare education: students' knowledge, attitude and perception: a cross-sectional study in Saudi Arabia. BMC Med Educ 2020; 20: 210.

38) Seselja Perisin A, Bukic J, Rusic D, Leskur D, Bozic J, Mihanovic A, Vilovic M, Cohadzic T, Modun D. Teaching Pharmacovigilance to Healthcare Students: Identifying Gaps and Opportunities for Improvement. Pharmacy (Basel) 2021; 9: 147.

39) Umair Khan M, Ahmad A, Ejaz A, Ata Rizvi S, Sardar A, Hussain K, Zaffar T, Q Jamshed S. Comparison of the knowledge, attitudes, and perception of barriers regarding adverse drug reaction reporting between pharmacy and medical students in Pakistan. J Educ Eval Health Prof 2015; 12: 28.

40) Schutte T, Tichelaar J, Reumerman MO, van Eekeren R, Rissmann R, Kramers C, Richir MC, van Puijenbroek EP, van Agtmael MA; Education Committee/Working Group Research in Education of the Dutch Society of Clinical Pharmacology and Biopharmacy (NVKF&B), Utrecht, The Netherlands. Pharmacovigilance Skills, Knowledge and Attitudes in our Future Doctors - A Nationwide Study in the Netherlands. Basic Clin Pharmacol Toxicol 2017; 120: 475-481.

41) Schutte T, Tichelaar J, Reumerman MO, van Eekeren R, Rolfes L, van Puijenbroek EP, Richir MC, van Agtmael MA. Feasibility and Educational Value of a Student-Run Pharmacovigilance Programme: A Prospective Cohort Study. Drug Saf 2017;40: 409-418.

42) Marko S. A study of knowledge, attitude, and practice of pharmacovigilance among medical students at a tertiary care teaching hospital in Madhya Pradesh, India. Natl J Physiol Pharm Pharmacol 2019; 9: 851–855.

43) Yu YM, Kim S, Choi KH, Jeong KH, Lee E. Impact of knowledge, attitude and preceptor behaviour in pharmacovigilance education. Basic Clin Pharmacol Toxicol 2019; 124: 591-599.

44) Katyal J, Arora E, Gupta YK. Impact of increased focus on pharmacovigilance on knowledge and attitude towards adverse drug reaction reporting among medical students in India. Int J Risk Saf Med 2020; 31: 15-24.

45) Chhabra KG, Sharma A, Chhabra C, Reddy JJ, Deolia SG, Mittal Y. Knowledge, attitude, and practices regarding pharmacovigilance and adverse drug reaction reporting among dental students in a Teaching Hospital, Jodhpur, India: a cross-sectional Study. J Contemp Dent Pract 2017; 18: 964-969.