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ORIGINAL PAPER

Motivation and Knowledge of Portuguese Community Pharmacists Towards the Reporting of Suspected Adverse Reactions to Medicines: A Cross-Sectional Survey

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Abstract

The close contact between patients and community pharmacists, along with the extensive geographical distribution of pharmacies in Portugal, offer exceptional conditions to detect and report adverse drug reactions (ADR). This study aimed to evaluate the motivation and knowledge of spontaneous reporting of ADR by community pharmacists of Porto, Portugal. Secondly, we aimed to generate real-world evidence on the main factors determining ADR report and at raising potential alternatives to the current reporting procedure in community pharmacy. We performed a descriptive, cross-sectional, observational, anonymous web survey-based study. Between April and July 2021, a web survey was implemented, targeting community pharmacists in the Porto district, Portugal. We validated 217 surveys from pharmacists. Regular notifiers seem to be more familiarised than non-regular notifiers with the Portuguese Pharmacovigilance System (PPS), with the *Portal RAM* for reporting suspected ADR, and with the update of the concept of ADR. Moreover, regular notifiers seem to be more proactive with their care in questioning patients about ADR and have more self-knowledge to identify suspected ADR. Conversely, non-regular notifiers, seem to be more reluctant to be judged by their ADR reporting activities. Respondents suggested to simplify and optimise the reporting process (31% of the suggestions), or to integrate a reporting platform into the pharmacy's software (27%). This study identified opportunities to promote the ADR reporting process by community pharmacists, namely receiving feedback from the PPS on the reported case and its regulatory implications, implementing training programs in pharmacovigilance, and creating solutions to simplify the reporting process.

Keywords Adverse drug reaction reporting systems · Health knowledge · Attitudes · Practice · Pharmacist · Community Pharmacist · Pharmacovigilance · Drug monitoring

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Introduction

Adverse drug reactions (ADR) are a public health problem related to noxious or unintended responses to a medicinal product [1]. Indeed, ADR differs from adverse events since ADR denotes a possible causal relationship between the occurrence and the medicinal product [1–3]. ADR contributes to the morbidity and mortality of human populations, responsible for a greater demand for healthcare services and higher health costs [3–8].

Pharmacovigilance is a fundamental science in the drug life cycle and comprises a set of activities focused on medicine-related problems [2, 4, 7, 9, 10]. The World Health Organization (WHO) defines pharmacovigilance as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any

other possible drug-related problems" [11]. Thus, pharmacovigilance plays a consequential role in the surveillance of ADR, although it is a real challenge for physicians, healthcare providers, the WHO and pharmaceutical industries since. Despite the growth of pharmacovigilance structures worldwide, several studies have estimated reporting rates of around 10%, supporting the already identified problem of underreporting [3, 8, 12–17].

Community pharmacists play an important role in drug safety. Given the straight contact between drug consumers and community pharmacists and the extensive geographical distribution of community pharmacies in Portugal, they represent an exceptional place to detect and report ADR. However, there is also evidence of underreporting among pharmacists [4, 8, 18–21] and, in particular, among community pharmacists [4, 18–20].

Some authors have studied the underlying reasons for underreporting among healthcare professionals (HCP), namely among pharmacists [9]. The main contributing factors among HCP seem to be lack of time, uncertainty on drug-event causality, lack of interest, the distance between HCP and patient, and lack of report forms [9, 17]. Other barriers were also identified, such as unawareness of the ADR reporting process and non user-friendly ADR reporting form [22]. Knowledge about pharmacovigilance and the ADR reporting process among HCP still seems to be a very significant barrier, although less among pharmacists compared to physicians and nurses (73.5%, 18.7% and 13.8%, respectively) [23]. Other studies also report that community pharmacists, like general practitioners, have basic knowledge about ADR, although they are unfamiliar with the ADR report guidelines [24, 25]. Despite this, it is also known that both the wrong and the deficient report of ADR can lead to the loss of relevant clinical information, with consequences of different levels, such as health costs [7].

The primary aim of this study was to evaluate the motivation and knowledge of spontaneous reporting of ADR by community pharmacists of Porto, Portugal. Secondly, we aimed to generate real-world evidence on the main factors determining ADR report and at raising potential alternatives to the current reporting procedure in community pharmacy.

Methods

Study Design

We performed a descriptive, cross-sectional, observational, anonymous web survey-based study. Between April and July 2021, a web survey was implemented, targeting community pharmacists in the Porto district, Portugal (see "*study population*" section). The GoogleTM® Forms platform was used, since it is an easy-to-use, free and open-source online survey application that enables users to develop and publish online surveys and collect responses without doing any programming. More details are available on the completed Checklist for Reporting Results in Internet E-Surveys (CHERRIES) (Table 1) [26].

The survey was sent by the Portuguese Pharmaceutical Society to the email of each pharmacist, with a reminder every three weeks, totalling eight emails received per pharmacist. Other channels for disseminating the study were also activated, namely medical dissemination platforms that are standard tools for consultation by community pharmacists. Each participant only had the opportunity to answer a single questionnaire during the period considered for data collection.

Study Population

All pharmacists who met the following eligibility criteria were invited to participate in the study: (i) valid enrolment in the Portuguese Pharmaceutical Society and (ii) active professional practice in community pharmacy in the Porto district, Portugal. These eligibility criteria included both community pharmacists who graduated with a 5-year curriculum, resulting in an Integrated Master's degree on Pharmaceutical Sciences and pre-Bologna community pharmacists, who graduated with a 6-year curriculum, resulting in a Graduate's degree in Pharmaceutical Sciences. Exclusion criteria were not considered. The first two survey questions aimed to ensure that pharmacists who did not meet all inclusion criteria were not admitted to the study.

According to the Portuguese Pharmaceutical Society, the district of Porto (in the Northern region of Portugal) had 1908 community pharmacists with professional activity in this area at the time of data collection for this study.

Development of the Survey Tool

The survey consisted of a questionnaire to assess sociodemographic data, motivation associated with spontaneous reporting of ADR, and knowledge about the Portuguese Pharmacovigilance System (PPS). The following question structure was considered: two questions to ensure compliance with the eligibility criteria; five sociodemographic questions to characterise the population (gender, age, educational level, title of community pharmacy specialist and the number of years of professional experience); four questions about previous habits in spontaneous reporting of ADR; thirty-five Likert scale questions on an agreement of statements about knowledge and motivations (ranged from 1 ["completely disagree"] to 5 ["completely agree"]); eleven Likert scale about measures that may increase spontaneous reporting of ADR (ranged from 1 ["completely disagree"] to 5 ["completely agree"]); and an open-ended question ("If you had

Table 1 The data collection is reported on the Checklist for Reporting Results in Internet E-Surveys (CHERRIES)

Item Category	Explanation	
Design	Descriptive, cross-sectional, observational, anonymous web survey-based study. Eligibility criteria included community pharmacists working in the Porto district with valid enrollment in the Portuguese Pharmaceutical Society. The study involved a convenience sample	
IRB (Institutional Review Board) approval and informed consent process	Approval	The study has been approved by the ethics committee of the *Centro Hospitalar e Universitário de São João,* Porto, Portugal
	Informed consent	Electronic informed consent was obtained from the participants to be included in the study
	Data protection	No information that allows for personal identification was collected
Development and pre-testing	A multidisciplinary team composed by pharmacists and physicians developed the questionnaire. The pre-testing was made within a group of 10 community pharmacists. All decisions were made in a consensus meeting by all elements of the research team, with ultimate responsibility for the principal investigator	
Recruitment process	Survey type	The web survey was collected on an online platform
	Contact mode	The survey was sent by email to each pharmacist by the Portuguese Pharmaceutical Society
	Advertising the survey	Every three weeks, a reminder was made, and other channels like medical dissemination platforms were used
Survey administration	Web/E-mail	The survey was made on GoogleTM® Forms, a free and open-source online platform. It was collected automatically when the participants answered the survey
	Context	The survey was disseminated using the mailing lists of the Portuguese Pharmaceutical Society and through official pages of Pharmaceutical or Medical interest, and on social media
	Mandatory/voluntary	The questionnaire was voluntary
	Incentives	None
	Time/date	Between April and July 2021
	Randomization of items or questionnaire	N/A
	Adaptive questioning	The questionnaire was designed only to let participants who met the eligibility criteria proceed in their responses
	Number of items	58 questions (includes two eligibility questions)
	Number of screens	10 screens
	Completeness check	A survey with 56 questions was implemented, of which 46 were on a Likert scale. All items with only one possible answer were mandatory, except for the last open-ended question, which was optional
	Review step	It was possible to go back to the questionnaire and change the answers

Table 1 (continued)

Item Category	Explanation	
Response rates	Unique site visitor	N/A
	View rate	N/A
	Participation rate	N/A
	Completion rate	N/A
Preventing multiple entries	Cookies used	Not used
	IP check	Not used
	Log file analysis	Not used
	Registration	Not used
Analysis	Handling of incomplete surveys	Only the surveys that filled the eligibility criteria were accepted
	Questionnaires submitted with an atypical timestamp	N/A
	Statistical correction	N/A

the opportunity to make a change to the ADR suspect report process, what would you do?").

The preliminary survey was developed by a team of pharmacists and physicians based on previous literature on this topic and the team's experience from the Porto Pharmacovigilance Centre, INFARMED, I.P.. The preliminary survey was pre-tested in ten community pharmacists outside the Porto district, with different geographic locations, age, gender, academic studies (pos- and pre-Bologna pharmacists), community pharmacy specialist and years of professional experience (Fig. 1). This pre-test allowed for identifying and correcting any critical issues in the drafting, spelling errors, ordering and structure of the survey. All decisions were made in a consensus meeting by all elements of the research team, with ultimate responsibility for the principal investigator.

Statistical Analysis

For the descriptive analysis, categorical variables were described with frequency and percentage, while the continuous variable was described with mean and standard deviation (SD).

Questions 8 ("*Has ever reported an ADR?*") and 9 ("*Usually reports ADR*?") were used to stratify users by familiarity on notifying ADR in three levels: "*1. Never notified*" (Q8 = No), "2. *Doesn't usually notify*" (Q8 = Yes, Q9 = No), "3. *Usually notifies*" (Q8 = Yes, Q9 = Yes). Analysis to questions 1 to 35 was stratified according to these previously described levels, while questions 36 to 46 were analysed without stratification.

Firstly, we applied an analysis of variance combined with principal component analysis (ANOVA–PCA) to evaluate how different these three groups are regarding their answers to the survey. We start by performing a dimensionality reduction with Principal Components Analysis (PCA) and, from here, we perform an Analysis of Variance (ANOVA) to evaluate the differences among the groups. PCA was applied to questions 1 to 35, and ANOVA was applied to the resulting first three principal components, which accounted for 35.7% of the variance of the sample. Assuming only the first three components, ANOVA showed that there were statistically significant differences among the three groups defined initially ($p < 0.001$) but that the responses between groups "1. Never notified" and "2. Doesn't usually notify" were similar ($p = 0.683$) and each different from responses from group "3. Usually notifies" ($p < 0.001$ in both cases). This suggests that the group of usual notifiers has a different perception of ADR reports than that of none or infrequent notifiers. Based on this, we assumed that it was meaningless to discriminate between groups 1 and 2, and those were then treated as a single group (non-regular notifiers).

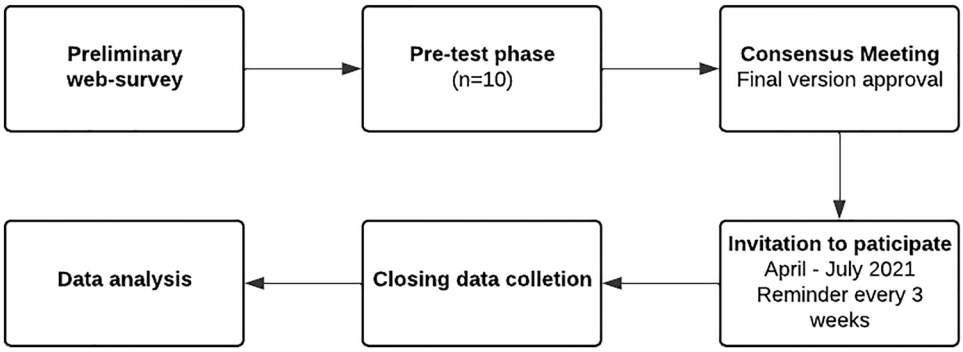

Fig. 1 Flowchart of the web-survey implementation process from the pre-validation phase to the final version of data analysis

For all 35 questions, the median values were presented as a measure of central tendency and the respective interquartile range (IQR) since it was observed that the data did not follow a normal distribution. We compared the response to each question between both groups using the Mann–Whitney U test. The Bonferroni adjustment for multiple comparisons was used for post hoc analysis; $p < 0.05$ indicated significant differences. The statistical analysis was performed using R version 4.1.0, with package 'Likert' version 1.3.5.

Qualitative Analysis

After the analysis of the suggestions for the open question, some key sentences were elaborated in order to be able to group similar suggestions. These sentences were read and grouped independently by two reviewers (R.FdS. and J.M.) and, by final consensus, key sentences were established. All authors reviewed and agreed with all sentences.

Results

Sample Characteristics

From April to July 2021, there were 461 attempts to respond to the survey, but only 220 met the eligibility criteria. Of the 220 surveys collected, only 217 were considered for stratification, given that three respondents did not fit any stratum, as answers to those questions were either missing or set as "*Don't know*" (Q8 and Q9), hence being removed in the stratified analysis to subsequent questions.

Considering the population base of this study (n = 1908), the response rate was 11.5%. Of the 220 surveys from pharmacists included, 118 (85.5%) were female and 32 (14.5%) were male, with a mean age of 38.2 ± 9.55 years, as seen in Table 2. Regarding the academic degree, about half of the pharmacists presented an Integrated Master's degree in Pharmaceutical Sciences (n = 115; 52.3%), and the others presented a Bachelor's degree in Pharmaceutical Sciences (n = 105; 47.7%). 130 (59%) pharmacists presented a professional experience of 11 years or more, and only 13 (5.91%) of the respondents had less than one year of professional experience. Most respondents were not specialists in community pharmacy (n = 189; 85.9%) to the Portuguese Pharmaceutical Society.

As for reporting suspected ADR, 101 (45.9%) respondents have already reported some, while 117 (53.2%) did not. Regarding the habit of ADR reporting by community pharmacists, 42 (41.6%) said they usually report ADR, against 58 (57.4%) who never reported ADR. Considering the difficulties in reporting suspected ADR, 65 (64.4%) of the inquired consider that they have no difficulties in doing so.

Knowledge and Motivations of Pharmacists

Table 3 shows the degree of agreement for the questions regarding knowledge and motivations of the participants between each group (non-regular notifiers [n = 175] and regular notifiers [n = 42]). All participants in both groups responded to all 35 questions. As can be seen, regular notifiers seem to be more familiar with the PPS (QO1), with the Portal RAM (Q03) as an instrument for reporting suspected ADR, and with the update of the concept of ADR (QO5) than non-regular notifiers. In addition, regular notifiers seem to be more proactive with the care in questioning patients about ADR (Q13) and have more self-knowledge to identify suspected ADR (Q14). Non-regular notifiers, compared to regular notifiers, seem to be more reluctant to be judged by the report of a suspected ADR (Q23).

Among the questions that showed statistically significant differences between the two groups with different reporting habits, we sought to understand the influence of other variables on the knowledge and attitudes of community pharmacists. To a significance level of 0.05, we observed that there is a statistically significant association between the years of professional experience and the answers to Q05 ("I am familiar with the update of the concept of ADR") ($p = 0.008$, $\chi 2 = 32.888$). Community pharmacists between 4 and 10 years old of professional experience and between 11 and 20 years old of professional experience present lower scores of knowledge about the evolution of the ADR concept than the other three professional experience ranges (27.77%

Table 2 Summary of the characteristics of the population included in this study

	Total (N = 220)
Gender	
Female	188 (85.5%)
Male	32 (14.5%)
Age	
Mean (SD)	38.2 (9.55)
Academic Studies	
Pharmacist (5-year curriculum, resulting in a Master's degree in Pharmaceutical Sciences)	115 (52.3%)
Pre-Bologna Pharmacist (6-year curriculum, resulting in a Graduate's degree in Pharmaceutical Sciences)	105 (47.7%)
Professional Experience	
< 1 year	13 (5.91%)
1–3 years	23 (10.5%)
4–10 years	54 (24.5%)
11–20 years	78 (35.5%)
> 20 years	52 (23.6%)
Specialist in Community Pharmacy	
Yes	22 (10.0%)
No	189 (85.9%)
Don't know/Don't answer	9 (4.09%)
Reported a suspected ADR	
Yes	101 (45.9%)
No	117 (53.2%)
Don't know/Don't answer	2 (0.909%)
Usually reports suspected ADR	
Yes	42 (41.6%)
No	58 (57.4%)
Don't know/Don't answer	1 (0.990%)
Difficulties in reporting suspected ADR	
Yes	30 (29.7%)
No	65 (64.4%)
Don't know/Don't answer	6 (5.94%)

N (%) except for age (mean (SD))

and 27.27% negative answers, respectively, compared to 16.67–21,57% in the remaining professional experience ranges) (Table 4).

Measures that Can Increase the Reporting of Suspected ADR

Figure 2 presents the results related to the questions intended to identify strategies that could encourage or improve the ADR reporting process by community pharmacists. Notably, most pharmacists do not defend the act of reporting as payable to the reporter (Q36). On the other hand, they would be more willing to report ADR if they got feedback from the PPS regarding the assessment of the reported case (Q38) or implications of the ADR and actions taken by regulatory authorities (Q39). The relevance of implementing awareness campaigns for both community pharmacists (Q41) and patients (Q42), as well as training actions by the Portuguese Pharmaceutical Society (Q44), was a point of agreement among the answers. The existence of a mobile/tablet application for ADR reporting (Q40) and the implementation of a tool in the software of community pharmacies for the automatic reporting of ADR to the PPS (Q45) was also a convergence point. Finally, community pharmacists strongly agree with an internal dynamic within pharmacy teams for a more organised reporting of ADR (Q46).

The questionnaire featured an open-ended question which aimed to understand what community pharmacists would change about the process of reporting suspected ADR. The results are shown in Table 5. The most prevalent suggestions were related to simplifying and optimising the reporting process (31% of the suggestions), followed by integrating a spontaneous reporting platform into community pharmacy software (27%). Also, 11% of the suggestions fall on a more

Table 3 Statements relating to knowledge and motivations of pharmacists about reporting suspected ADR

Question	Non-regular notifiers (median[1], [IQR]) n = 175[2]	Regular notifiers (median[1], [IQR]) n = 42[2]	Mann–Whitney U test (Bonferroni adjustment)
Q01. I am familiar with the Portuguese Pharmacovigilance System	3 [3, 4]	4 [3, 5]	**0.022**[3]
Q02. I am familiar with the existence of the Porto Pharmacovigilance Centre	3 [3, 5]	4 [3, 5]	1.000
Q03. I am familiar with the Portal RAM for reporting suspected ADR	3 [2.5, 4]	4 [3, 5]	**0.007**[3]
Q04. I am familiar with the different means for reporting suspected ADR	3 [2, 4]	4 [3, 4]	0.095
Q05. I am familiar with the update of the concept of ADR	3 [2, 4]	4 [3, 5]	**0.010**[3]
Q06. I am aware that users can report suspected ADR directly to the Portuguese Pharmacovigilance System	4 [3, 5]	5 [4, 5]	1.000
Q07. Pharmacovigilance is an important activity in the drug life cycle	5 [5]	5 [5]	1.000
Q08. Pharmacovigilance is a minor activity in the care practice universe of the Community Pharmacist	1 [1]	1 [1, 2]	1.000
Q09. Reporting a suspected ADR is a simple and intuitive process	3 [3, 4]	4 [3, 4]	0.410
Q10. Reporting a suspected ADR is a fast process	3 [2, 4]	3 [3, 4]	1.000
Q11. I have a habit of reading the pharmacovigilance bulletin edited by INFARMED	3 [2, 4]	3 [3, 4]	1.000
Q12. I am familiar with my deontological and ethical obligations to report suspected ADR	4 [4, 5]	5 [4.25, 5]	0.082
Q13. I am careful to question the patient about ADR in my professional activity, assuming a proactive position in this issue	4 [3, 4]	4 [4, 5]	**< 0.001**[3]
Q14. As a health professional, I have enough knowledge to identify a suspected ADR	4 [3, 4]	5 [4, 5]	**0.002**[3]
Q15. In my daily practice of interaction with the patient, I can easily detect suspected ADR	3 [3, 4]	4 [3, 4]	1.000
Q16. I believe that the report suspected ADR to the Porto Pharmacovigilance System may impact the patient's quality of life at the personal, social, and/or economic level	4 [3, 5]	5 [4, 5]	0.573
Q17. I fear that the reporter`s confidentiality may be broken during the ADR report process	1 [1, 2]	1 [1, 2]	1.000
Q18. I fear that the patient´s anonymity may be broken during the ADR report process	1 [1, 2]	1.5 [1, 2]	1.000
Q19. I fear that the adverse reaction may not be due to the suspected drug	3 [3, 4]	3 [3, 4]	1.000
Q20. I only report an ADR if I am certain that it is related to the use of a particular drug	4 [3, 5]	3 [2, 4.75]	0.064
Q21. It is almost impossible to determine if a drug is responsible for a certain ADR	2 [2, 3]	2 [1, 3]	1.000
Q22. When I know that a new drug has been introduced in the market, I am careful to read the SmPC on information about ADR or undesirable effects	4 [3, 5]	4 [3, 5]	1.000
Q23. I am reluctant to be judged by the report of a suspected ADR	2 [1, 3]	1 [1, 2]	**0.037**[3]
Q24. I am reluctant to admit that it may have contributed to the occurrence of ADR in the patient	2 [1, 3]	1 [1, 3]	1.000
Q25. The report of a single case is relevant to the knowledge of the safety profile of that drug	4 [3, 5]	4 [3, 5]	1.000
Q26. When it comes to an ADR described in the SmPC, I find it important to report	3 [2, 4]	4 [3, 5]	1.000
Q27. I find it important to report when it comes to an unexpected ADR (not described in the SmPC)	5 [5]	5 [5]	1.000
Q28. When it comes to a frequent ADR, I find it important to report	4 [2, 5]	4 [3, 5]	1.000
Q29. When it comes to a non – severe ADR, I find it important to report	4 [3, 5]	5 [4, 5]	1.000
Q30. I report suspected ADR for the clinical impact that this information has on other users taking that drug	4 [3, 5]	5 [4, 5]	1.000
Q31. I believe that the spontaneous report of suspected ADR has regulatory consequences on the use of that drug	4 [3, 5]	5 [4, 5]	0.139
Q32. I report suspected ADR for the need to share experiences of my professional practice	3 [2, 4]	3 [3, 5]	0.665
Q33. When it comes to a recent marketing authorization drug (< 2 years), I have additional concerns in the report of suspected ADR	4 [3, 5]	5 [4, 5]	0.203
Q34. The time taken to report is the determining factor not to report, or not report as much as I wish, the suspected ADR that I know	3 [3, 4]	3 [1.25, 4]	1.000
Q35. In view of a suspected ADR, I contact the pharmaceutical industry (e.g. Medical Sales Representatives)	3 [2, 4]	3 [2, 4]	1.000

[1]Likert scale: 1 = Strongly disagree, 2 = Disagree, 3 = Neither, 4 = Agree, 5 = Strongly Agree

[2]All participants from each group responded to all 35 questions.

[3]Statistically significant differences ($p < 0.05$)

IQR Interquartile range

Table 4 Influence of surveyed academic degree, years of professional experience and specialisation in community pharmacy in the knowledge and motivations of pharmacists about reporting suspected ADR

Question	Academic Degree[1]	Professional Experience[1]	Specialization in Community Pharmacy[1]
Q01. I am familiar with the Portuguese Pharmacovigilance System	0.141	0.089	0.068
Q03. I am familiar with the Portal RAM for reporting suspected ADR	0.891	0.551	0.146
Q05. I am familiar with the update of the concept of ADR	0.106	**0.008**[2]	0.076
Q13. I am careful to question the patient about ADR in my professional activity, assuming a proactive position in this issue	0.992	0.826	0.546
Q14. As a health professional, I have enough knowledge to identify a suspected ADR	0.399	0.215	0.500
Q23. I am reluctant to be judged by the report of a suspected ADR	0.547	0.532	0.265

[1]P-values for Pearson's Chi-squared test

[2]Statistically significant ($p < 0.05$)

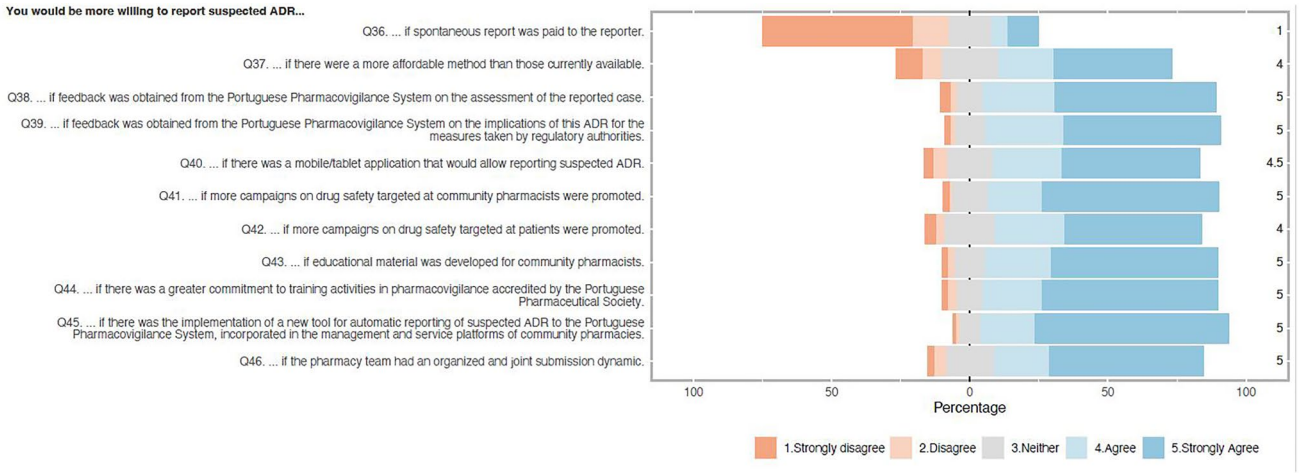

Fig. 2 Pharmacists' perspectives on measures that can increase the reporting of suspected ADR (N = 220)

Table 5 Pharmacists' suggestions on changes needed to increase reporting of suspected ADR

Suggestion	n (%)
Simplify and streamline the reporting process	32 (31)
Integrate the spontaneous reporting form into the pharmacy fulfillment software	28 (27)
Invest in pharmacovigilance training for community pharmacists	11 (11)
Provide feedback on the reported case to the reporter	10 (10)
Valuing the spontaneous reporting of ADR as a fundamental pharmaceutical act	5 (5)
Promote greater patient awareness of ADR self-report	4 (4)
Involve different agents in the health field (pharmacist, doctor, nurse, patient, industry) in the management and follow-up of ADR	3 (3)
Automatic communication of the spontaneous report made by the pharmacist to the clinical system used by the physician	2 (2)
Informatization	1 (1)
Development of a hotline to report suspected ADR	1 (1)
Promote awareness with the Technical Directorates of community pharmacy	1 (1)
Pay for the act of spontaneous report	1 (1)
No opinion	3 (3)

significant investment in training in pharmacovigilance and providing feedback to the pharmacist regarding the reported case (10%). The suggestions given by 5% or fewer participants, although not less important, were related to valuing the spontaneous act of ADR reporting as a pharmaceutical act (5%), promoting patient awareness for self-reporting of ADR (4%), promoting multidisciplinarity among the different health professionals (pharmacists, physicians, nurses), users, and the pharmaceutical industry itself in ADR management and follow-up (3%). The informatisation (1%), the development of a hotline for ADR reporting (1%), the payment of the spontaneous report act (1%), and the awareness of the topic among the technical directions of community pharmacies (1%) were other suggestions left by community pharmacists.

Discussion

Our study showed that community pharmacists from Porto, Portugal, are quite active in reporting ADR although there are still some that are not so familiar with the process. Importantly, our study identified pharmacists-raised potential improvements to the current reporting procedure, which can be used to counteract the underreporting seen in the routine activity of our pharmacovigilance centre.

Community pharmacies are the healthcare network with the most significant coverage in Portugal, assuming a central position in managing medication and patients' illnesses. In line with this, community pharmacists are close to patients and are present in their treatment plans since the drug is dispensed and during monitoring [9, 10, 27]. In the United Kingdom, community pharmacists are the second most reporting ADR (19%) after hospital pharmacists (65%), despite 13% of reports did not identify the origin of the pharmaceutical activity [28]. Also, pharmacists have an inherent responsibility to detect and monitor ADR [27], since their wide-ranging education includes areas like clinical pharmacy, pharmacology, pharmacotherapy and toxicology. But, although a retrospective analysis of 20 years of activity of the Porto Pharmacovigilance Centre showed that pharmacists are the seconds that most report among HCP (n = 2,790; 28.7%) [29], underreporting is evident among Portuguese community pharmacists, for whom the number of annual reports per pharmacist is lower than 1% versus 43% in the case of Dutch [30]. In fact, the prevalence of ADR reports from pharmacists is among the highest in Portugal [31, 32]. For that reason, we wanted to characterise the motivation and knowledge of spontaneous reporting of ADR by community pharmacists of Porto, Portugal. Surprisingly, it was clear that community pharmacists from Porto demonstrated a positive attitude towards ADR reporting. Indeed, our results show that about 46% of the community pharmacists surveyed have reported a suspected ADR at least once, and about 42% usually do so. Still, most respondents have never reported suspected ADR (58%), which might contribute to the low reporting rates of ADR described in the literature (around 10%) [3, 8, 12–17]. These low ADR reporting rates (14–44%) are consistent among studies conducted across Europe, Asia and Africa [33–38]. Spontaneous reporting is a suitable method for early detection of safety problems, providing regulatory authorities with real-world evidence [3–5, 7–9]. However, the spontaneous nature of this reporting method contributes to underreporting precisely because it is a method that depends on the proactivity of the notifier [39].

The reasons for underreporting are known, but local and national needs are highly conditioned by the characteristics of the pharmacovigilance system implemented and the dynamics established throughout the process. Since 2000 the PPS has been decentralised, reaching the milestone of ten regional units in 2021, which are responsible for all processes associated with the management of ADR reports [9]. PPS is mainly based on spontaneous ADR reports performed by HCP or consumers. In 1976, Inman [40] first proposed a list of "seven deadly sins" as the potential reason of ADR underreporting. However, although later studies were dedicated to the analysis of these relationships [41–45], most studies failed to identify associations or, when identified, only one or two attitudes were associated with underreporting [45–47].

Our study is a pioneer since we performed a stratified analysis based on previous habits of reporting suspected ADR, in order to look for differences on subpopulations that could guide future interventions to fight underreporting. Although all respondents recognise the importance of pharmacovigilance and are familiar with the reporting process, pharmacists who have reporting habits are more familiar with the PPS and the *Portal RAM*, and with the evolution of the RAM concept. In addition, they seem to be more proactive in questioning patients about potential ADR, and refer to have more self-knowledge to identify suspected ADR, probably supporting the data showing that they are less reluctant to be judged by the report of a suspected ADR. Interestingly, these issues were not influenced by either the academic degree, the duration of professional experience, or the title of specialist in community pharmacy, except the familiarity with the update of the concept of ADR, for which recent graduates (less than 4 years of practise) and older pharmacists (more than 20 years of experience) showed higher scores than others. This suggests that continuous education on pharmacovigilance is a valuable tool to improve scientific and technical skills on reporting ADR [35]. In line with this view, it was interesting to note that community pharmacists of our study ranked in third that training in pharmacovigilance would be helpful to promote

ADR reporting. This formative strategy also finds support in published literature, with final-year pharmacy students having insufficient knowledge about pharmacovigilance [48, 49] that extends over the years of work, leading to the finding that postgraduate pharmacists show almost the same knowledge of expert pharmacists [9]. A study by Tucklu et al., [36] found that only 17% of the community pharmacists defined the concept of "pharmacovigilance" correctly, and only 26% defined the concept of "ADR" correctly. This might be associated with the undergraduate education curriculum since only about 37% of pharmacy students consider themselves prepared to report ADR in their future professional practice [48], a finding reported in other studies [50]. The association between awareness, knowledge and underreporting may well indicate that providing education and training in pharmacovigilance is essential to improve ADR reporting rate[32]. Published data also report that when faced with an ADR, professionals show several uncertainties about the type of information they should report and how and to whom they should report [8, 51]. According to Vessal et al. [37], the main reason for non-reporting in a group of community pharmacists who have never reported is the uncertainty of the association of ADR with certain drugs. Thus, the difficulty of detecting ADR could be overcome with new educational approaches such as hands-on involvement with real cases, to place ADR reporting closer to the day-to-day reality of work in community pharmacies.

In the systematic review of Hazell et al., [52], common reasons for not reporting among HCP included lack of time, different care priorities, uncertainty about the drug causing ADR, difficulty accessing forms, lack of awareness of requirements for reporting and lack of understanding of the purpose of spontaneous reporting systems. Some studies reported lack of time as an important reason for failure to report among the pharmacists [21, 53]. Even so, Cavaco et al., [54] concluded that lack of time was not a primary barrier, although it is a variable of a particularly subjective nature because the perception of time is very variable. In our study, participants also referred lack of time as an obstacle to reporting, despite not being a primary barrier, with no statistically significant differences between regular and non-regular notifiers. Moreover, our study showed that both groups have similar attitudes concerning the identification of the drug causing the putative ADR, although non-regular notifiers tend to have a more cautious approach. In addition, the process's simplicity is widely described in the literature as one of the main factors to report by pharmacists [10, 19].

Community pharmacists in Porto city are, therefore, not different in terms of issues such as time pressure and difficulties in identifying causative drugs [4, 55, 56]. Most pharmacists' respondents agreed that they would only report ADR if they were sure on the association with a medical drug and that serious ADR are already well described before a drug is put on the market. This evidence has been previously reported in the literature [4, 8, 19]. According to Suyagh et al., [35], only 6% of the pharmacists report serious ADR and prefer to contact the physician or forward the patient to an emergency department. In our study, community pharmacists find it essential to report ADR described in the SmPC, unexpected ADR not described in the SmPC, frequent ADR and non-severe ADR. As such, they find it important to report the severity or frequency of ADR.

The pharmacists in our study state that they frequently report to the medical sales representatives who visit them in pharmacies, agreeing with Toklu et al., [36], in which 46,2% of the respondents inform the medical sales representatives or the drug company verbally. Also, 13% of community pharmacists believed that ADR reporting was primarily the prescriber's responsibility and directed the patient to the prescriber.

In our study, judgment was not a genuine concern among the community pharmacists, mostly among regular notifiers, and participants knew they had deontological and ethical obligations to report suspected ADR. These results are in line with some studies [30, 37] but in opposition with others that undercover the fear of legal liability when reporting ADR [10] or the idea that pharmacists do not have this responsibility [38], which is quite worrying.

We also aimed at raising potential alternatives to the current reporting procedure in community pharmacy. One of the measures to increase reporting seems to be the payment of ADR reporting, although not supported by most respondents. This measure had already been evaluated previously by Herdeiro et al., [4] and Hughes et al., [28], with results agreeing with ours. This was also highlighted during the structured face-to-face interview study[18] with United Kingdom community pharmacists in the late 1990s, with 37% of respondents believing a fee would increase reporting rates. Although the reasons that led many pharmacists to want to be paid have not been studied, this may reflect their point of view based on the time they spend and the work involved with this task [28]. From a deontological point of view, it can be questionable since Portuguese law states that health professionals communicate "*as quickly as possible (…) the ADR and serious or unexpected ADR suspicions of which they are aware resulting from the use of medicines*" [57].

Porto community pharmacists showed more willingness to report ADR if there were more campaigns related to medicines safety aimed at both HCP and users and the development of educational material for pharmacies and training accredited by the Portuguese Pharmaceutical Society. According to Tocklu et al., [36], pharmacists enrolled on a pharmacovigilance course had more knowledge about this theme. Granas et al., [51] evaluated the impact that educational programmes in pharmacovigilance had on a group of

community pharmacists. It was possible to see that it positively impacted their adopted position after the training. So, this could be an option to increase the community pharmacists' knowledge and enrol them in this subject.

Some of the suggested measures are consistent with the evidence published in several studies [9, 58–60]. Perhaps it makes sense to think of joint solutions between the PPS and the technology supply companies of pharmacies, developing new digital tools to report directly through the pharmacy's internal software. Developing an app for ADR reporting is also not an innovative idea [61], as is the example of VigiBIP® developed by the Toulouse University Pharmacovigilance Centre [62]. VigiBIP® is a free smartphone app available on Android and Apple stores to report ADR and request drug safety information. Also, an app developed for two-way risk communication—may reduce the time between experiencing and reporting an ADR and lead to more informed patients and HCP. The Web-RADR project [63] is an example of this and aims to improve traditional pharmacovigilance activities by using new tools to identify potential new ADR earlier and improve drug safety communication (mobile app).

HCP such as physicians, nurses and pharmacists should be considered players in improving the outcome of the pharmacologic therapeutic plans. The professionals who have pharmacotherapeutic and pharmacology knowledge are essential to obtaining ADR reports of higher quality [36]. Pharmacists must be more involved in the reporting process, and regulatory authorities need to encourage pharmacists to be an active part of the system. This idea was emphasised in the answers in the sense that pharmacists consider that there should be feedback from the PPS regarding the assessment of the reported case and the implications and measures taken by the regulatory authorities themselves. While PPS feedback on reported cases has been a reality for many years, there is an identified need to make the reporter's response more targeted and personalised. However, the *Portal RAM* back office is not yet fully user-friendly in automatically generating feedback based on case data. Lastly, community pharmacy teams should have well-established ADR reporting dynamics, which is only achieved after proper training of employees and optimisation of the process.

In line with the "Knowledge-Attitude-Practice (KAP) model" as the theoretical underpinning for developing the hypothesised relationships [64] and previous studies, we suggest that modifying some attitudes and knowledge should improve the participation of community pharmacists in the spontaneous reporting system.

Weaknesses and Strengths

Compared with other studies, one strength of our study is its comprehensiveness in relating global scope and the topics covered. Moreover, our study includes a set of suggestions to reverse underreporting, constituting a strong contribution to the implementation of new national policies supported by the Portuguese Pharmaceutical Society. Finally, it is a pioneer in analysing subgroups based on the reporting habits of suspected ADR. No study was identified in the literature that performed this analysis based on this variable.

However, this study also has some limitations. The methodology used for disseminating the survey focused on intercepting the target audience (i.e., those who meet the eligibility criteria), but many surveys were eliminated for not meeting the eligibility criteria (n = 240). This might have resulted from a "snowball" phenomenon generated by forwarding the invitation to participate among pharmacists outside the target population. The identification and consequent exclusion of some of these surveys of respondents outside the target population will have minimised the impact of this bias. Also, the fact that the survey was done online did not allow the researchers to confirm the veracity of the answers, namely the eligibility criteria. Although we are dealing with an instructed population, and the answers to this survey do not impact their personal or professional activity, the response bias associated with self-report must be considered when interpreting the results. Finally, the low response rate (11.5%) may limit the representativeness of the population and, consequently, the results obtained. However, this response rate is similar among surveys of pharmacists regarding ADR [37, 55, 65], and the sample included active community pharmacists with different sociodemographic characteristics, thus presenting very different points of view.

Conclusion

This study identified some opportunities to promote the ADR reporting process by community pharmacists, namely receiving feedback from the PPS on the reported case and its putative regulatory implications, implementing training programs in pharmacovigilance, and creating solutions to simplify the reporting process.

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Data Availability Not applicable.

Code Availability Not applicable.

Declarations

Competing interests The authors declare that they have no conflicts of interest.

Ethical Approval All procedures followed the ethical standards of the ethics committee of the *Centro Hospitalar e Universitário de São João* and the Helsinki Declaration of 1964 and its later amendments. This ethics committee approved the study (CE-82-21).

Consent to Participate Informed consent was obtained from the participants for being included in the study.

Consent for Publication Informed consent was obtained from the participants to publish data in an aggregated form under scientific publication.

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