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ORIGINAL RESEARCH ARTICLE

Comparative Analysis of Information Provided in German Adverse Drug Reaction Reports Sent by Physicians, Pharmacists and Consumers

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Abstract

Introduction Adverse drug reactions (ADRs) can be reported by Health Care Professionals (HCPs; e.g., physicians, pharmacists) and non-Health Care Professionals (non-HCPs; e.g., consumers). Previous studies investigating differences between reports from HCPs and non-HCPs rarely considered the completeness of information provided. In addition, they mostly did not distinguish between physicians and pharmacists or were performed years ago. The aim of our study was to analyse and compare the completeness of information provided in reports from physicians, pharmacists and consumers from Germany in a more recent dataset.

Materials and methods We analysed all spontaneous reports from Germany received between 2018 and 2021 in the ADR database EudraVigilance exclusively reported by physicians (n = 69,976), pharmacists (n = 42,396) or consumers (n = 121,144). Demographical parameters of the patients were analysed descriptively. Completeness of reports was evaluated applying an established score (vigiGrade). Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using logistic regression analysis in order to identify report, patient, drug or ADR-specific information provided more often in reports from physicians, pharmacists or consumers.

Results Within the study period the number of reports per year by physicians and pharmacists decreased steadily, while an opposite trend was observed for consumer reports. The proportion of female patients was higher in reports from pharmacists (64.4%) and consumers (64.8%) compared to those from physicians (55.3%). On average, patients in reports from pharmacists (58.7) were older compared to those from physicians (53.5) and consumers (52.6). As an example for the presence of specific information, the time to onset of the ADR could be calculated more often in consumer compared to physician (OR 1.9 [1.8–1.9]) and pharmacist reports (OR 1.7 [1.6–1.7]). In contrast, pharmacist (OR 0.5 [0.4–0.5]) and consumer (OR 0.5 [0.5–0.5]) reports included the indication of the suspected drug less often than physician reports. Physician reports on average (mean = 0.5) were slightly more complete according to the vigiGrade score compared to reports from consumers (mean = 0.4) and pharmacists (mean = 0.4).

Conclusion The ADR reports from consumers were comparable with regard to the completeness score with those from physicians and pharmacists underlining their value. Differences in completeness of specific information between the reporter types were found, suggesting that a common reporting of interactions between the three reporters may further improve the completeness of ADR reports. Furthermore, stratified analysis of ADR reports per reporter type may be helpful for certain objectives in scientific research.

Extended author information available on the last page of the article

Key Points

Throughout the period analysed, the annual number of reports from physicians and pharmacists steadily decreased, while the respective number of consumer reports increased.

Physicians' reports followed by consumers and pharmacists' reports were more complete with regard to relevant information according to an established score (vigiGrade). In our analysis, physicians reported information regarding the indication of a drug more often, while the time period between the start of the drug therapy and the ADR occurrence (time to onset) could more often be calculated in reports from consumers.

Based on our analysis and existing literature, we suggest how the quality and number of spontaneous reports could be improved, by time-saving and streamlined assistance in the preparation of spontaneous reports by use of appropriate software.

1 Introduction

Spontaneous reports are one valuable tool used in pharmacovigilance practice for the detection of adverse drug reactions (ADRs) after marketing authorisation [1]. Initially, in Germany ADRs were mainly reported by physicians. Non-Health Care Professionals (non-HCPs, in the following "consumers") could also report ADRs, however, few consumer reports were received in in the first years of recording. The first reports from pharmacists were recorded in 1986 [2].

In recent decades, various actions including legislative changes have been taken in the European Union (EU) to facilitate and draw attention to ADR reporting [3–7]. Among these were the possibility to report ADRs online and an appeal to report ADRs to the competent authorities in the package leaflet. Further on, since legislative changes in 2012 pharmaceutical companies are obliged to forward non-serious ADR reports (e.g., from consumers) to the competent authorities. These actions very likely contributed substantially to the enormous increase in the number of reports, especially from consumers [2, 8].

Meanwhile some studies and reviews have been published analysing the content and overall qualitative differences of spontaneous reports with regard to the reporting person's qualifications, most of which were carried out in Denmark, the UK and the Netherlands [9]. The vast majority of them focused on the reported drug(s) and/or ADR(s) and identified differences and found that consumers and healthcare professionals (HCPs)/physicians mentioned different ADRs. Notably, consumer reports complement HCP reports by covering different ADRs and drugs [9–12].

Very few of these studies focused on the quality of documentation and the type of information reported in relation to the reporters' qualification. This limited number of studies included, among others, datasets from France, the USA and the Netherlands [12–14]. Most of these studies used relatively small data sets and suggested additional investigations [9, 15].

The main aim of this study was to investigate and compare the amount and the type of information relevant for pharmacovigilance practice provided in reports from physicians, pharmacists and consumers in spontaneous reports from Germany contained in the European ADR database EudraVigilance. To the best of our knowledge, this represents the first study for Germany in this regard and, so far, only few studies investigated a dataset of this magnitude, comprising almost a quarter of a million reports. Finally, our analysis may provide scientific data which could be helpful for a discussion how the quality and therewith the value of spontaneous reports from various reporters could be improved.

2 Methods

2.1 EudraVigilance

ADRs are defined as noxious and unintended responses to medicinal products which can occur within or outside (e.g., off-label use) the terms of the marketing authorization [16]. Suspected cases of ADRs can be reported by healthcare professionals (HCPs) (e.g., pharmacists, physicians, nursing staff) as well as by non-healthcare professionals (non-HCPs) (e.g., consumers, lawyers) [17, 18]. Physicians and pharmacists, for example, are obliged to report suspected cases of ADRs according to their professional code of conduct [2, 18].

The ADR database EudraVigilance (EV), which is operated by the European Medicines Agency (EMA), contains ADR reports from all member states of the European Economic Area [17]. In EV drugs are coded with the EudraVigilance medicinal product dictionary and ADRs are coded in accordance with the MedDRA® (Medical Dictionary for Regulatory Activities) terminology [17, 19].

MedDRA® is the international medical terminology developed under the auspices of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The MedDRA® trademark is owned by the International

Federation of Pharmaceutical Manufacturers and Associations (IFPMA) on behalf of the ICH.

Our analysis refers to spontaneous reports, these are unsolicited reports spontaneously reported in everyday practice, which are not collected in any organized data collection scheme such as clinical trials. Spontaneously submitted ADR reports have to include certain information to fulfil the minimum criteria (e.g., identifiable reporter and patient, at least one suspected drug and suspected ADR) [4]. Spontaneous ADR reports may contain structured and unstructured (free-text) information [20].

The primary source qualification (in the following "reporter type") describes if the person who reported the ADR was an HCP or a non-HCP together with a more detailed specification (e.g., physician, consumer). Theoretically, one ADR report can contain several reporter types, for example, if information to the same case was reported by a physician and a consumer [4]. In order to analyse if there are differences between different reporter types, we restricted our analysis to those reports listing only one reporter type within the detailed specification. Note that despite that restriction, one ADR report may have been reported by more than one person of the same reporter type. We assume that the reporter type "pharmacists" also covers reports from other pharmacy staff such as pharmaceutical technical assistants (PTA). Further information regarding the reporting channels has been published elsewhere [2].

The designation of reports as "serious" or "non-serious" corresponds to the legal definition of the seriousness of the ADR reports, but not to its clinical severity. Therefore, all reports, including at least one ADR that was life-threatening, conferred lasting or significant disability or incapacity, led to death, required or prolonged hospitalization, led to congenital abnormalities, respectively birth defects, or endangered the patient and required medical or surgical intervention/treatment ("other") are considered as serious [4].

2.2 Identification of Reports from Physicians, Pharmacists or Consumers

All spontaneous ADR reports from Germany received between 1 January 2018 and 31 December 2021 were extracted (n = 548,347) (see Fig. 1) from EV. In order to exclude the influence of reports referring to vaccines, all reports listing any vaccine as suspected/interacting drug were excluded (n = 276,353). As one example, COVID19 vaccines could have been subject to an overstimulated reporting, because they were subject to intense public debates [21]. Besides that, we excluded all reports containing hyposensitising solutions as suspected/interacting drugs (n = 4579) as well as duplicates, identified via equal case report identifiers (n = 154).

Only reports whose reporter type was exclusively specified as "physician" or "pharmacist" or "consumer" were further investigated (n = 233,516). Within these, 69,976 reports (30.0%) referred to physicians', 42,396 (18.2%) to pharmacists', and 121,144 (51.9%) to consumers.

2.3 Descriptive Analysis

All reports identified for physicians, pharmacists or consumers were analysed descriptively regarding their superordinate classification of seriousness (serious yes/no), year of receipt, and distribution of sex and age of the patients. Means, together with standard deviations (± sd), and medians including their interquartile ranges (IQRs) were calculated for patients' age and the quality of documentation (see below). For all other results, frequencies and percentages were calculated.

2.4 Quality of Documentation

An overall estimation of the quality of documentation was performed by applying a computer-based algorithm according to a published score (vigiGrade) [22]. This score, ranging from 0.07 to 1, was originally created to assess the provided information in the structured format of ADR reports in the global ADR database of the World Health Organization (WHO)—VigiBase [23]. According to the original publication, a report with a vigiScore > 0.8 is defined as "well documented". For the assessment of the ADR reports in EV, the score was slightly adapted.

2.5 Consideration of Relevant Information

All sub-datasets were screened for the presence of certain information in the structured format of each ADR report. Please note that the quality of the information provided was not assessed.

The information provided was assigned to four categories: (1) report-related information, (2) patient-related information, (3) drug-related information, and (4) ADR-related information.

Sub-analyses of serious and non-serious ADR reports were performed.

2.6 Report-Related Information

The country of origin, report type, seriousness, and the narrative were categorized as report-related information. The country of origin (Germany), the report type (spontaneous report), and if the report was classified as serious (yes or no) was provided in each ADR report. In the narrative, the reporter has the option of supplying further information regarding the ADR in an unstructured free text format. In

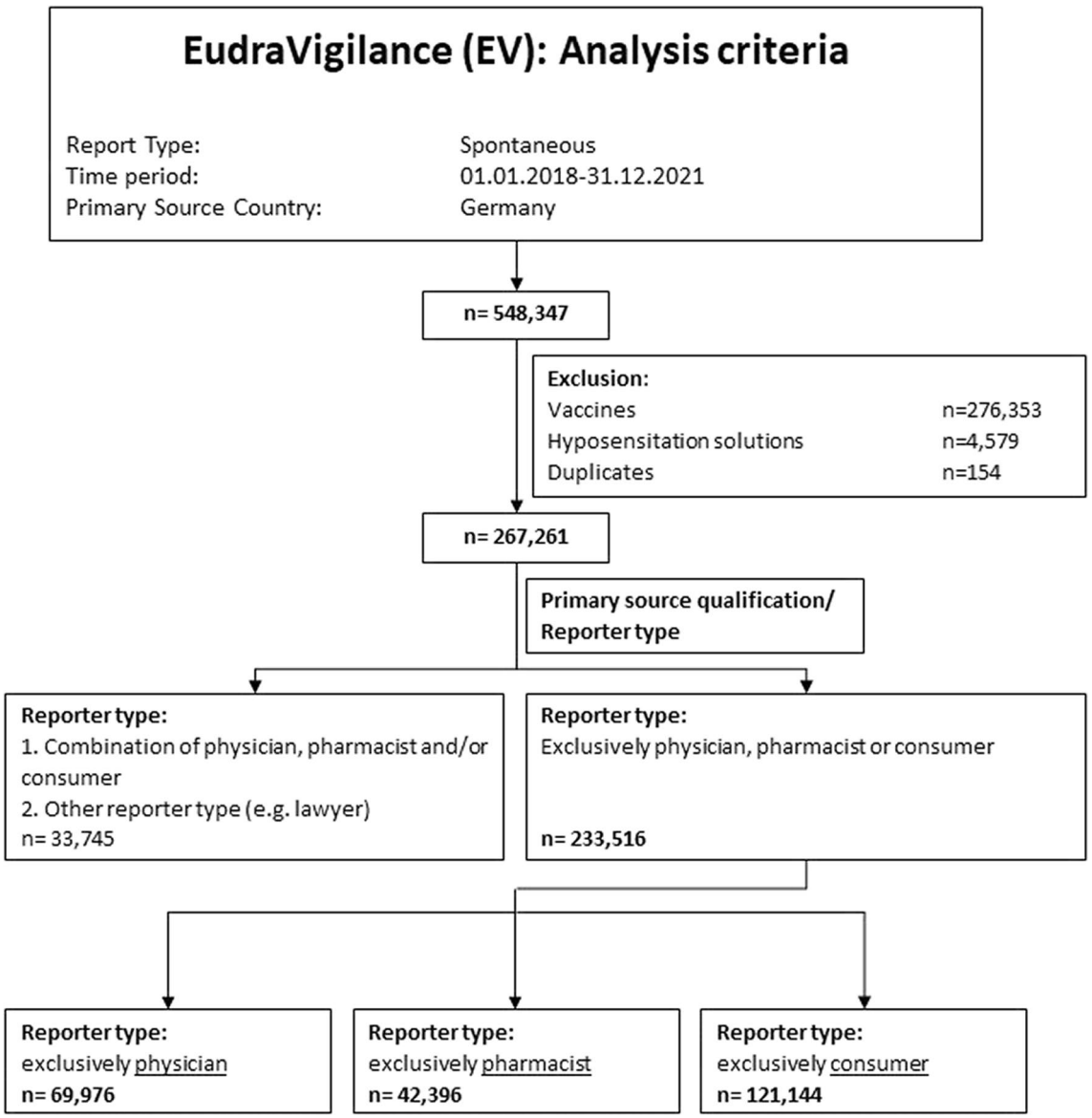

Fig. 1 Flowchart. Identification of adverse drug reaction (ADR) reports exclusively reported by physicians, pharmacists or consumers as reporter type in EudraVigilance (EV)

this case, we analysed if the respective reporter provided any further information as free text.

2.7 Patient-Related Information

Sex, age, height, weight and medical histories of the patients were categorized as patient-related information. Sex can be coded as female, male and not specified. Age, height and weight are numerical values or reported as not available. The medical history contains co-morbidities and previous conditions of the patients or is stated as not available. In this case, "not available" does not necessarily mean that the patient has no co-morbidities or previous conditions, it can also indicate that the information was not reported. In our analyses, not specified in case of sex or not available in case of age, height, weight and medical history were considered as information not provided.

2.8 Drug-Related Information

Drugs reported as suspected/interacting, action taken with the drug, applied dose of the drug, indication of the drug, reporting of suspected/interacting drugs classified as black triangle drugs and concomitant drugs were categorized as drug-related information. In accordance with the minimum criteria of ADR reports, at least one drug has to be reported

as suspected/interacting. Among others, action taken with the drug can be reported as withdrawn, continued, dose reduced, or information not available. The applied dose of the drug can be supplied as a numerical value with its unit name (e.g., milligram), as the number of applied dosage forms (e.g., one dose administered) or set to "not available". The indication describes the underlying disease or condition for which the drug was taken by the patient or is reported as "not available". The drugs classified as concomitant were not considered to be causative for the described ADR(s) by the reporter. In this category, all drugs taken concomitantly can be reported or set to "not available". In this case, our data did not allow distinguishing whether the patient did not receive any concomitant medication or if the medication was not mentioned in the report.

If more than one drug was reported as suspected/interacting per ADR report, information regarding action taken with the drug, applied dose, and indication of the drug can be reported for each drug. Here, information was classified as available if action taken with drug, applied dose, or indication was reported for at least one drug.

Further on, we determined the number of drugs reported as suspected/interacting and reported as concomitant per ADR report.

In order to identify reports with at least one black triangle drug reported as suspected/interacting, the "list of medicinal products under additional monitoring" was used [24]. All active ingredients with a date of inclusion in 2022 were removed. Drugs labelled with a black triangle in the package leaflet or product information leaflet are subject to additional surveillance (e.g., new active ingredients, biologicals or drugs with conditional approvals).

2.9 Adverse Drug Reaction (ADR)-Related Information

The reported ADR(s), the outcome of the ADR(s), the time to onset of the ADR(s), as well as if the ADR is known or designated as a medically important event are categorized as ADR-related information. In accordance with the minimum criteria of ADR reports, at least one ADR has to be reported. The outcome describes, among others, if the ADR is r*ecovered/resolved, fatal* or *not recovered/not resolved* or *unknown*. The time to onset describes the time between the first intake of a drug and the occurrence of the ADR. It can be calculated based on the start date of the drug reported as suspected/interacting and the start date of the ADR. If multiple ADRs per report were mentioned, an outcome and a time to onset could be reported or calculated for each ADR. Information was counted as available if at least one outcome apart from unknown was reported, respectively, one time to onset could be calculated for one ADR. If the calculated time to onset was negative, the time to onset was classified as not available (caused by, e.g., coding errors or if the suspected/interacting drug was taken after the ADR occurred).

The number of reported ADRs per ADR report was analysed.

All reports were analysed to determine if at least one ADR contained in the "designated medical event list" was reported. The list of designated medical events describes drug-related serious events defined by the EMA and is publicly available on the EMA's website [25].

We determined whether at least one of the reported drug-ADR combinations per ADR report was already listed as known in SIDER. SIDER lists more than 140,000 known drug-ADR combinations based, for example, on information from package inserts. Further information on the content, data collection, and structure of SIDER can be found elsewhere [26, 27].

2.9.1 Logistic Regression Analyses

Logistic regression analyses were performed for the comparisons of physician versus consumer reports, physician versus pharmacist reports, pharmacist versus consumer reports, and serious versus non-serious reports of all reporter types. To this end, the reporter type, respectively, the classification serious/non-serious, was set as the outcome variable and all other variables, which were analysed in the consideration of relevant information as covariates. Country of origin, report type, and seriousness were not included as variables in the logistic regression models since all reports contained information on these three aspects. The results of the logistic regression analyses are presented as odds ratios (ORs) with 95% confidence intervals (CI) in square brackets [lower CI–upper CI].

All results of the logistic regression analyses are presented by mentioning the reference group last (e.g., in case of "physicians versus pharmacists", pharmacists are considered as reference). Concerning the analyses of non-serious and serious reports within each reporter type, serious reports were always considered as the reference.

2.9.2 Reports per Physician, Pharmacist and Consumer

The number of reports from physicians and pharmacists was considered in relation to the number of practising physicians respectively pharmacists per year in Germany. For this purpose, the numbers of practising physicians in outpatient and hospital settings for each year were extracted from the "Ärztestatistik zum 31. Dezember 2021" provided by the *Bundesärztekammer* [28]. The numbers of practising pharmacists represents the number of pharmacists, pharmacists in internship (PhiP), pharmaceutical technical assistants (PTAs), pharmacy technicians and pharmacist assistants in

public pharmacies, and pharmacists working in hospital pharmacies, which were extracted for each year from "Die Apotheke - Zahlen Daten Fakten 2021/2022" published by the *Bundesvereinigung deutscher Apothekerverbände* [29, 30]. In order to consider the number of reports from consumers in relation to the number of potentially drug-exposed inhabitants in Germany, we extracted the number of German inhabitants from statista "Bevölkerung—Einwohnerzahl von Deutschland 1990–2021" and subtracted the number of practising pharmacists and practicing physicians, as reports from these professionals were to be included in the respective categories [31]. The resulting number was multiplied with the proportion of Germans expected to take any medication according to a German survey [32].

Note that this is only an approximation since one pharmacist or physician or consumer can have submitted more than one ADR report and one ADR report can be reported by more than one pharmacist or physician.

3 Results

3.1 Descriptive Analysis

3.1.1 Report-Related Information

In total 233,516 reports were identified exclusively listing a physician, pharmacist or consumer as reporter type. The largest proportion of reports extracted referred to consumers (51.9%/n = 121,144), followed by physicians (30.0%/n = 69,976) and pharmacists (18.2%/n = 42,396) (Table 1).

Regarding the whole dataset, the lowest number of reports was received in 2021, whereas the number of reports between 2018 and 2020 was fairly similar. While the number of reports from physicians and pharmacists steadily decreased from 2018 to 2021 (physicians n = 20,633 to 12,759; pharmacists n = 14,036 to n = 7129), the number of reports from consumers increased steadily from 2018 to 2020 (n = 26,208 to n = 36,325) and decreased in 2021 (n = 27,753) compared to 2020.

Table 1 Descriptive analyses of adverse drug reaction (ADR) reports per reporter type of the total dataset and the sub-datasets (physician, pharmacist, consumer) with regard to the classification serious/non-serious, the receive year, and the demographical parameters (sex, age) of the patients

	Total (% total)	Physicians' reports (% of total/% of physicians' reports)	Pharmacists' reports (% of total/% of pharmacists' reports)	Consumer reports (% of total/% of consumers' reports)
Number of reports				
Number of reports per primary source qualification	233,516 (100%)	69,976 (30.0%/100%)	42,396 (18.2%/100%)	121,144 (51.9%/100%)
Number of reports classified as serious[a]				
Yes	55,758 (23.9%)	32,039 (57.5%/45.8%)	7558 (13.6%/17.8%)	16,161 (29.0%/13.3%)
No	177,758 (76.1%)	37,937 (21.3%/54.2%)	34,838 (19.6%/82.2%)	104,983 (59.1%/86.7%)
Number of reports received per year				
2018	60,877 (26.1%)	20,633 (33.9%/29.5%)	14,036 (23.1%/33.1%)	26,208 (43.1%/21.6%)
2019	63,619 (27.2%)	20,289 (31.9%/29.0%)	12,472 (19.6%/29.4%)	30,858 (48.5%/25.5%)
2020	61,379 (26.3%)	16,295 (26.5%/23.3%)	8759 (14.3%/20.7%)	36,325 (59.2%/30.0%)
2021	47,641 (20.4%)	12,759 (26.8%/18.2%)	7129 (15.0%/16.8%)	27,753 (58.3%/22.9%)
Number of reports per sex				
Female	144,535 (61.9%)	38,706 (26.8%/55.3%)	27,320 (18.9%/64.4%)	78,509 (54.3%/64.8%)
Male	81,145 (34.7%)	28,049 (34.6%/40.1%)	13,687 (16.9%/32.3%)	39,409 (48.6%/32.5%)
Not specified	7836 (3.4%)	3221 (41.1%/4.6%)	1389 (17.7%/3.3%)	3226 (41.2%/2.7%)
	Total	Physician	Pharmacist	Consumer
Age distribution				
Mean (Sd) age	54.1 (± 21.4)	53.5 (± 21.8)	58.7 (± 20.5)	52.6 (± 21.2)
Median [IQR] age	57 [38–71]	56 [38–71]	62 [47–75]	54 [36–70]
Not specified	97,564	23,490	17,173	56,901

Sd standard deviation, *IQR* interquartile range

[a]Each ADR report is classified as either serious or non-serious

Reports from physicians were more often classified as serious (45.8%/*n* = 32,039), i.e., comprising ADRs leading to hospitalization or prolongation thereof (19.6%/*n* = 13,706) or death (2.8%/*n* = 1967), compared to reports from pharmacists (serious: 17.8%/*n* = 7558; hospitalisation: 10.7%/*n* = 4523; death: 0.4%/*n* = 189) and consumers (serious: 13.3%/*n* = 16,161; hospitalisation: 2.9%/*n* = 3457; death: 0.3%/*n* = 419) (Table Appendix 1/Table Appendix 4; appendices are provided as Online Supplementary Material).

3.1.2 Patient-Related Information

Almost two-thirds of all consumer (64.8%) and pharmacists' (64.4%) reports referred to females, compared to slightly more than half of the physicians' reports (55.3%) (Table 1).

A substantial proportion of reports did not contain any information regarding the patients' age (total: 41.8%/*n* = 97,564; physician: 33.6%/*n* = 23,490; pharmacist: 40.5%/*n* = 17,173; consumer: 47.0%/*n* = 56,901). The mean and median age of the patients from all reports containing respective information were almost similar in reports from consumers (mean 52.6 (± 21.2); median 54 [36–70]) and physicians (mean 53.5 (± 21.8); median 56 [38–71]), while patients in the pharmacists' reports were slightly older (mean 58.7 (± 20.5); median 62 [47–75]).

3.2 Quality of Documentation According to the vigiGrade Completeness Score

Overall, physicians' reports scored the highest vigiGrade score on average (mean 0.5 (± 0.3); median 0.4 [0.2–0.6]), followed by consumer (mean 0.4 (± 0.3); median 0.4 [0.2–0.6]) and pharmacists' reports (mean 0.4 (± 0.3); median 0.3 [0.2–0.5]) (Fig. 2/Table Appendix 2). The scores for reports from physicians and consumers were more widely dispersed and were more often greater than 0.5 than scores from pharmacists' reports.

No considerable differences regarding the quality of documentation for serious and non-serious reports for the three reporter types were observed (Table Appendix 2).

3.3 Analyses of Information Provided

3.3.1 Report-Related Iformation

The vast majority of the reports from all three reporter types contained a narrative, which was more often provided in consumer than in physicians' (OR 1.8 [1.7–1.9]) and pharmacists' (OR 1.9 [1.8–2.0]) reports, and less often provided in pharmacist versus physicians' reports' (OR 0.8 [0.8–0.9]) (Table 2; Fig. 4; Figure 4 is provided as Online Supplementary Material). Additionally, a narrative was less often present in reports classified as non-serious versus serious for all three reporter types (physicians: OR 0.2 [0.2–0.2]; pharmacist: OR 0.1 [0.1–0.2]; consumer OR 0.1 [0.1–0.2]) (Table Appendix 3/Table Appendix 4).

3.3.2 Patient-Related Information

Almost all reports contained information about the sex of the patient (Table 2/Fig. 3). It was more often reported in consumers' compared to physicians' (OR 2.2 [2.1–2.3]) and pharmacists' reports (OR 1.2 [1.1–1.3]) (Table 2/Fig. 4).

Two-thirds of reports from physicians contained information regarding the patient's age (66.4%). Age was similarly often provided in reports from pharmacists (OR 1.0 [0.9–1.0]) and less often reported by consumers (OR 0.6 [0.6–0.6]) compared to physicians. Concerning all three reporter types, the age of the patient was less often included in non-serious versus serious reports (physician: OR 0.7

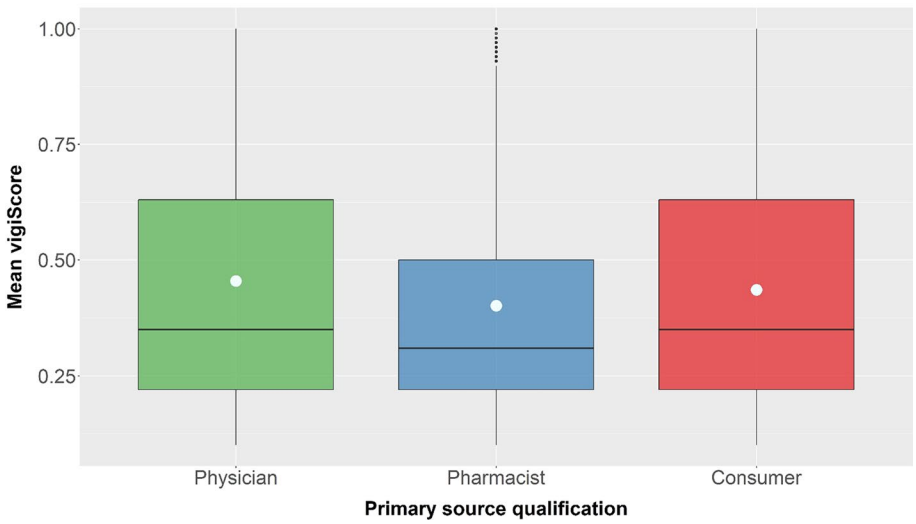

Fig. 2 Boxplots of VigiGrade completeness scores per adverse drug reaction (ADR) report from physicians, pharmacists and consumers. Medians are visualized by the bar and means by the white dot within the boxplot. The lower and upper borders of the boxplot indicate the first (25%) and third quartile (75%) of the scores, respectively. The whiskers indicate the minimum and maximum of the scores. Black dots indicate outliers

Table 2 Number of reports with report, patient, drug and adverse drug reaction (ADR)-related information

Observation	Number of reports with information			Logistic regression analysis		
	Physicians reports (n = 69,976)	Pharmacists reports (n = 42,396)	Consumer reports (n = 121,144)	OR [± 95.0% CI], p value consumer versus physician (reference)	OR [± 95.0% CI], p value pharmacist versus physician (reference)	OR [± 95.0% CI], p value consumer versus pharmacist (reference)
Report-related factors						
Report type[a]	69,976 [100%]	42,396 [100%]	121,144 [100%]	–	–	–
Seriousness[b]	69,976 [100%]	42,396 [100%]	121,144 [100%]	–	–	–
Country[a]	69,976 [100%]	42,396 [100%]	121,144 [100%]	–	–	–
Narrative	66,534 [95.1%]	40,356 [95.2%]	117,958 [97.4%]	1.8 [1.7–1.9]***	0.8 [0.8–0.9]***	1.9 [1.8–2.0]***
Patient-related factors						
Sex	66,755 [95.4%]	41,007 [96.7%]	117,918 [97.3%]	2.2 [2.1–2.3]***	1.8 [1.7–1.9]***	1.2 [1.1–1.3]***
Age	46,486 [66.4%]	25,223 [59.5%]	64,243 [53.0%]	0.6 [0.6–0.6]***	1.0 [0.9–1.0]**	0.6 [0.6–0.6]***
Height	20,854 [29.8%]	9390 [22.1%]	37,851 [31.2%]	1.5 [1.4–1.6]***	2.0 [1.9–2.2]***	0.6 [0.6–0.7]***
Weight	22,188 [31.7%]	9294 [21.9%]	38,510 [31.8%]	0.6 [0.6–0.6]***	0.4 [0.4–0.5]***	1.8 [1.6–1.9]***
Medical history	40,269 [57.5%]	14,927 [35.2%]	61,545 [50.8%]	1.0 [1.0–1.0]	0.5 [0.5–0.6]***	1.9 [1.8–1.9]***
Drug-related factors						
Action taken with drug	40,365 [57.7%]	20,948 [49.4%]	52,469 [43.3%]	0.6 [0.6–0.6]***	0.9 [0.9–1.0]***	0.6 [0.6–0.6]***
Dose	38,320 [54.8%]	18,052 [42.6%]	66,747 [55.1%]	1.2 [1.2–1.2]***	0.8 [0.8–0.8]***	1.5 [1.4–1.5]***
Indication	49,178 [70.3%]	19,353 [45.6%]	61,211 [50.5%]	0.5 [0.5–0.5]***	0.5 [0.4–0.5]***	1.1 [1.1–1.1]***
Concomitant drugs	19,678 [28.1%]	11,153 [26.3%]	24,059 [19.9%]	0.7 [0.7–0.7]***	1.1 [1.1–1.2]***	0.6 [0.6–0.6]***
ADR-related factors						
Outcome	38,890 [55.6%]	19,925 [47.0%]	66,332 [54.8%]	1.2 [1.2–1.3]***	1.1 [1.1–1.1]***	1.2 [1.2–1.2]***
Time to onset	25,832 [36.9%]	13,033 [30.7%]	56,224 [46.4%]	1.9 [1.8–1.9]***	1.2 [1.2–1.3]***	1.7 [1.6–1.7]***

Number of reports and the proportion of reports with information of the categories investigated grouped into report-, patient-, drug- and ADR-related information. In addition, logistic regression analyses were performed for physician versus consumer reports, physician versus pharmacist reports and pharmacist versus consumer reports including patient, drug- and ADR-related information as covariables. Note that if the upper CI was lesser than 1, we assumed that the observation was more frequently reported for physicians (consumers vs. physicians, pharmacists vs. physicians) and pharmacists (consumers vs. pharmacists). If the lower CI was greater than 1 we assumed that the observation was more frequently reported for consumers (consumers vs. physicians, consumers vs. pharmacists) and pharmacists (pharmacists vs. physicians)

OR odds ratio, *CI* confidence interval

p values coded as: 0 '***'; 0.001 '**'; 0.01 '*'; 0.05 '.'; 0.1 ' ' 1

[a]Category was part of the filter criteria

[b]Automatically assigned to all reports

[0.7–0.7]; pharmacist: OR 0.4 [0.4–0.4]; consumer: OR 0.4 [0.4–0.4]) (Table Appendix 3/Table Appendix 4).

Consumers (0.6 [0.6–0.7]) and physicians (pharmacist vs. physician OR 2.0 [1.9–2.2]) less likely provided information about patients' height compared to pharmacists (height: 22.1%, weight: 21.9%), whereas the opposite applies to the weight (consumer versus pharmacist OR 1.8 [1.6–1.9]; pharmacist versus physician OR 0.4 [0.4–0.5]) (Table 2/Fig. 3).

The medical history of the patients was clearly less often reported in pharmacists' (35.2%) compared to physicians' (OR 0.5 [0.5–0.6]) and consumer reports (consumer vs. pharmacist OR 1.9 [1.8–1.9]) (Table 2/Fig. 4). Across all three reporter types, reports classified as serious more frequently included a medical history compared to non-serious reports (Table Appendix 3/Table Appendix 4). Physicians (25.0%) and consumers (16.6%) also more often provided more than two medical histories compared to pharmacists (8.6%) (Table 3).

3.3.3 Drug-Related Information

Physicians (20.9%) more often reported more than one suspected/interacting drug than pharmacists (10.7%) and consumers (11.8%) (Table 4).

Information regarding the action taken with at least one of the suspected/interacting drugs was less frequently reported by pharmacists (OR 0.9 [0.9–1.0]) and consumers (OR 0.6 [0.6–0.6]) compared to physicians (57.7%) (Table 2; Figs. 3 and 4). Slight differences between non-serious and serious reports concerning the proportion of reports with this

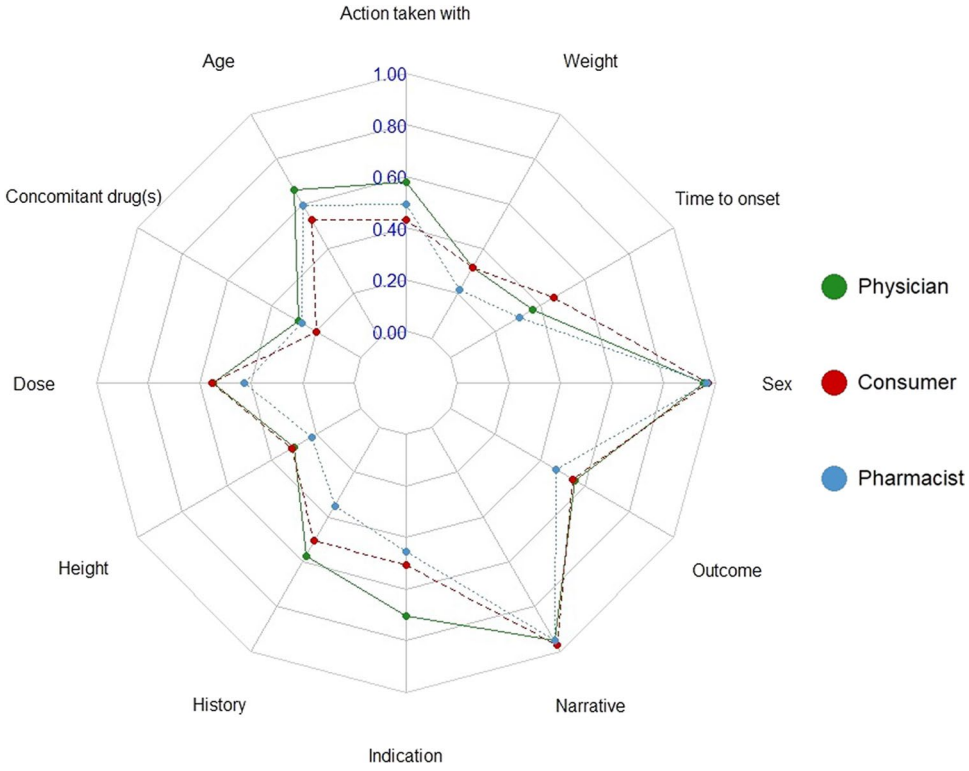

Fig. 3 Radar chart of the proportion of reports with information on the categories investigated per reporter type. Categories analysed are listed anti-clockwise in alphabetical order. The more distant the dot is from the centre of the radar chart, the higher the number of reports that included information on the respective category

Table 3 Number of reported medical histories per adverse drug reaction (ADR) report and their percentage share in reports from physicians, pharmacists and consumer

Count medical history	Number of reported medical histories					
	Physicians reports (n = 69,976)		Pharmacist reports (n = 42,396)		Consumer reports (n = 121,144)	
	Number of reports [%]	Sum of reports with ≥ count of medical histories [%]	Number of reports [%]	Sum of reports with ≥ count of medical histories [%]	Number of reports [%]	Sum of reports with ≥ count of medical histories [%]
No medical history	29,707 [42.5%]	69,976 [100%]	27,469 [64.8%]	42,396 [100%]	59,599 [49.2%]	121,144 [100%]
1	15,213 [21.7%]	40,269 [57.6%]	8329 [19.6%]	14,927 [35.2%]	28,411 [23.5%]	61,545 [50.9%]
2	7645 [10.9%]	25,056 [35.9%]	2988 [7.0%]	6598 [15.6%]	13,047 [10.8%]	33,134 [27.4%]
3	5475 [7.8%]	17,411 [25.0%]	1473 [3.5%]	3610 [8.6%]	7676 [6.3%]	20,087 [16.6%]
4	3584 [5.1%]	11,936 [17.2%]	808 [1.9%]	2137 [5.1%]	4645 [3.8%]	12,411 [10.3%]
5	2351 [3.4%]	8352 [12.1%]	453 [1.1%]	1329 [3.2%]	2764 [2.3%]	7766 [6.5%]
> 5	6001 [8.7%]	6001 [8.7%]	876 [2.1%]	876 [2.1%]	5002 [4.2%]	5002 [4.2%]

information from the three reporter types were observed (Table Appendix 3/Table Appendix 4).

The dose of at least one drug classified as suspected/interacting was more often present in physician (pharmacist vs. physician OR 0.8 [0.8–0.8]) and consumer (1.5 [1.4–1.5]) reports compared to pharmacists' reports (42.6%) (Table 2; Figs. 3 and 4).

Consumers (OR 0.5 [0.5–0.5]) and pharmacists (OR 0.5 [0.4–0.5]) clearly less often specified an indication for at least one drug reported as suspected/interacting than physicians (70.3%).

The proportion of reports with at least one black triangle drug reported as suspected/interacting was higher in physicians' (21.5%) than in reports from pharmacists (10.6%) and consumers (9.9%) (Table 4).

Concomitant drugs were reported less often in consumers' reports (19.9%) compared to physicians' (OR 0.7 [0.7–0.7]) and pharmacists' (0.6 [0.6–0.6]) reports

Table 4 The number of suspected/interacting and concomitant drugs per adverse drug reaction (ADR) report and the number of reports with at least one black triangle drug listed as suspected/interacting drug with their percentage share in reports from physicians, pharmacists and consumers

Drug-related information						
Observation	Physicians reports (n = 69,976)		Pharmacists reports (n = 42,396)		Consumer reports (n = 121,144)	
Number of reported suspected/interacting drugs						
Count of suspected/interacting drugs	Number of reports [%]	Sum of reports with ≥ count of suspected/interacting drugs [%]	Number of reports [%]	Sum of reports with ≥ count of suspected/interacting drugs [%]	Number of reports [%]	Sum of reports with ≥ count of suspected/interacting drugs [%]
1	55,367 [79.1%]	69,976 [100%]	37,864 [89.3%]	42,396 [100%]	106,719 [88.1%]	121,144 [100%]
2	9215 [13.2%]	14,609 [20.9%]	3282 [7.7%]	4532 [10.7%]	10,758 [8.9%]	14,425 [11.8%]
3	2859 [4.1%]	5394 [7.7%]	731 [1.7%]	1250 [3.0%]	2237 [1.8%]	3667 [2.9%]
4	1236 [1.8%]	2535 [3.6%]	277 [0.7%]	519 [1.3%]	761 [0.6%]	1430 [1.1%]
5	540 [0.8%]	1299 [1.8%]	113 [0.3%]	242 [0.6%]	271 [0.2%]	669 [0.5%]
>5	759 [1.0%]	759 [1.0%]	129 [0.3%]	129 [0.3%]	398 [0.3%]	398 [0.3%]
Reports with black triangle drug in suspected/interacting drug						
Black triangle drug in suspected/interacting drug	Physicians reports (n = 69,976) Number of reports [%]		Pharmacists reports (n = 42,396) Number of reports [%]		Consumer reports (n = 121,144) Number of reports [%]	
At least one	15,067 [21.5%]		4482 [10.6%]		11,976 [9.9%]	
None	54,909 [78.5%]		37,914 [89.4%]		109,168 [90.1%]	
Number of reported concomitant drugs						
Count of reported concomitant drugs	Number of reports [%]	Sum of reports with ≥ count of concomitant drugs [%]	Number of reports [%]	Sum of reports with ≥ count of concomitant drugs [%]	Number of reports [%]	Sum of reports with ≥ count of concomitant drugs [%]
0	50,298 [71.9%]	69,976 [100%]	31,243 [73.7%]	42,396 [100%]	97,085 [80.1%]	121,144 [100%]
1	5909 [8.4%]	19,678 [28.0%]	3048 [7.2%]	11,153 [26.2%]	10,841 [8.9%]	24,059 [19.7%]
2	3585 [5.1%]	13,769 [19.6%]	1878 [4.4%]	8105 [19.0%]	5232 [4.3%]	13,218 [10.8%]
3	2531 [3.6%]	10,184 [14.5%]	1443 [3.4%]	6227 [14.6%]	2986 [2.5%]	7986 [6.5%]
4	1888 [2.7%]	7653 [10.9%]	1179 [2.8%]	4784 [11.2%]	1716 [1.4%]	5000 [4.0%]
5	1334 [1.9%]	5765 [8.2%]	893 [2.1%]	3605 [8.4%]	1114 [0.9%]	3284 [2.6%]
>5	4431 [6.3%]	4431 [6.3%]	2712 [6.3%]	2712 [6.3%]	2170 [1.7%]	2170 [1.7%]

(Table 2; Fig. 3). According to the logistic regression analyses concomitant drugs were more likely reported from pharmacists than physicians (OR 1.1 [1.1–1.2]) (Table 2; Fig. 4). For all three reporter types, concomitant drugs were less often included in non-serious versus serious reports (pharmacists: 0.2 [0.2–0.2]; physicians: 0.4 [0.4–0.5]; consumer: 0.2 [0.2–0.2]) (Table Appendix 3/Table Appendix 4). Regarding the number of concomitant drugs per ADR report, physicians (28.0%) and pharmacists (26.2%) more frequently reported more than one concomitant drug compared to consumers (19.7%) (Table 4).

3.3.4 ADR-Related Information

A higher proportion of reports from physicians (44.7%) contained only one ADR compared to reports from pharmacists (36.4%) and consumers (36.6%) (Table 5).

At least one outcome per ADR report was more often provided in physicians' (55.6%) and consumers' (54.8%) than in pharmacists' (47.0%) reports (Table 2; Fig. 3). However, logistic regression analyses showed that the information was more often included in consumer (OR 1.2 [1.2–1.3]) and pharmacist (OR 1.1 [1.1–1.1]) compared to physicians' reports (Table 2; Fig. 4).

Table 5 Number of reported adverse drug reactions (ADRs) per ADR report, the number of reports describing an ADR from the designated medical events list and containing at least one known ADR-drug combination contained in SIDER with their percentage share in reports from physicians, pharmacists and consumers

ADR-related information						
Observation	Physicians reports (n = 69,976)		Pharmacists reports (n = 42,396)		Consumer reports (n = 121,144)	
Number of reported ADR						
Count of reported ADR	Number of reports [%]	Sum of reports with ≥ count of reported ADR [%]	Number of reports [%]	Sum of reports with ≥ count of reported ADR[%]	Number of reports [%]	Sum of reports with ≥ count of reported ADR [%]
1	31,279 [44.7%]	69,976 [100%]	15,419 [36.4%]	42,396 [100%]	44,329 [36.6%]	69,976 [100%]
2	17,293 [24.7%]	38,697 [55.3%]	12,488 [29.5%]	26,977 [63.7%]	29,718 [24.5%]	38,697 [63.5%]
3	9443 [13.5%]	21,404 [30.6%]	7101 [16.7%]	14,489 [34.2%]	18,740 [15.5%]	21,404 [39.0%]
4	5037 [7.2%]	11,961 [17.1%]	3501 [8.3%]	7388 [17.5%]	10,666 [8.8%]	11,961 [23.5%]
5	2752 [3.9%]	6924 [9.9%]	1737 [4.1%]	3887 [9.2%]	6188 [5.1%]	6924 [14.7%]
>5	4172 [6.0%]	4172 [6.0%]	2150 [5.1%]	2150 [5.1%]	4172 [9.6%]	4172 [9.6%]
Reports listing a designated medical event as ADR						
	Physicians reports (n = 69,976)		Pharmacists reports (n = 42,396)		Consumer reports (n = 121,144)	
	Number of reports [%]		Number of reports [%]		Number of reports [%]	
At least one	3380 [4.8%]		484 [1.1%]		874 [0.7%]	
None	66,596 [95.2%]		41,912 [98.9%]		120,270 [99.3%]	
Reports containing at least one known ADR-drug combination (SIDER)						
	Physicians reports (n = 69,976)		Pharmacists reports (n = 42,396)		Consumer reports (n = 121,144)	
	Number of reports [%]		Number of reports [%]		Number of reports [%]	
At least one	14,376 [20.5%]		7217 [17.0%]		21,219 [17.5%]	
None	55,600 [79.5%]		35,179 [83.0%]		99,925 [82.5%]	

The time to onset based on the information of the start date of drug therapy and the ADR occurrence could be calculated more often in reports from consumers (46.4%) compared to reports from physicians (OR 1.9 [1.8–1.9]) and pharmacists (OR 1.7 [1.6–1.7]) (Table 2; Figs. 3 and 4).

Designated medical important events were mentioned in only a few reports and in proportion were more often contained in physician (4.8%) than in pharmacist (1.1%) and consumer (0.7%) reports (Table 5).

In total about 10% of the drugs reported in our dataset were included in SIDER. For these drugs a slightly greater proportion of reports from physicians (20.5%) included drug-ADR combinations already known in SIDER compared to reports of pharmacists (17.0%) and consumers (17.5%).

3.4 Number of Reports per Physicians, Pharmacists and Drug-Exposed Inhabitants in Germany

Despite the increase of the number of practicing physicians and pharmacists between 2018 and 2021, the number of ADR reports from both decreased (Table 6). Thus, the calculated numbers of reports per 100 practicing physicians and pharmacists decreased, too. Without consideration that one physician/pharmacist could have reported more than one ADR per year, six per 100 practicing physicians and 11 per 100 practicing pharmacists reported an ADR in 2018 compared to three per 100 practicing physicians and six per 100 practicing pharmacists in 2021. The number of reports from consumers per 10,000 potentially drug-exposed inhabitants increased continuously from 2018 to 2020 and slightly decreased in 2021.

4 Discussion

Our analysis revealed several differences among reports from the three reporter types. Among others, the time to onset could be calculated more often in consumer reports and, details about the patients' medical history and the indications of the suspected drugs were more likely to be found

Table 6 Number of reports per 100 practicing physicians/pharmacists and 10,000 potentially drug-exposed inhabitants in Germany

Year	Physician reports (n = 69,976)			Pharmacist reports (n = 42,396)			Consumer reports (n = 121,144)		
	Reports per year	Practicing physicians per year[a]	Reports per 100 practicing physicians	Reports per year	Pharmacists (pharmaceutical staff) per year[b]	Reports per 100 pharmacists (pharmaceutical staff)	Reports per year	Potentially drug exposed inhabitants per year[c]	Reports per 10,000 potentially drug exposed inhabitants
2018	20,633	359,099	5.7	14,036	128,309	10.9	26,208	45,310,393	5.8
2019	20,289	367,100	5.5	12,472	130,308	9.6	30,858	45,387,253	6.8
2020	16,295	373,304	4.4	8759	130,755	6.7	36,325	45,378,112	8.0
2021	12,759	378,650	3.4	7129	130,463	5.5	27,753	45,419,257	6.1

[a]Corresponds to the total number of physicians in outpatient and hospital settings from "Ärztestatistik zum 31. Dezember 2021" provided by the *Bundesärztekammer* [28]

[b]Corresponds to the total number of pharmacists, pharmacists in internship (PhiP), pharmaceutical technical assistants (PTAs), pharmacy technician in public pharmacies, pharmacist assistants and pharmacists working in hospital pharmacies from "Die Apotheke - Zahlen Daten Fakten 2021/2022" published by the *Bundesvereinigung deutscher Apothekerverbände* [29, 30]

[c]Corresponds to the share of potentially drug-exposed inhabitants in Germany according to a German survey. The number of German inhabitants was taken from statista "Bevölkerung—Einwohnerzahl von Deutschland 1990–2021" [31]. The percentual share of potentially drug-exposed inhabitants was taken from "Prütz, Franziska, et al. "Inanspruchnahme ambulanter medizinischer Leistungen in Deutschland–Ergebnisse der Studie GEDA 2019/2020-EHIS." (2021)" [32]

in physicians' reports compared to the other reporter types, respectively. According to the vigiGrade score, physicians' reports scored marginally better than those from pharmacists and consumers.

4.1 Descriptive Analysis

Further explanations for the increasing numbers of consumer reports besides the already mentioned legislative changes in forwarding non-serious reports by marketing authorization holders, are an increased awareness of ADR reporting systems, how to report ADRs and facilitation of reporting. In contrast, the decline of reports from physicians and pharmacist in general might be associated with the increased reporting of consumers themselves. Further on, the decline of ADR reports from physicians in 2020 and 2021 might correlate with the fact that patients consulted physicians less frequently during the first year of the COVID-19-pandemic [33]. Similarly, pharmacist-consumer contacts might have been reduced as well.

In summary, reports from the three reporter types appear to represent different populations of patients and thereby complement each other. A study covering ADR reports from the European Economic Area performed in EudraVigilance showed that patients in consumer reports were on average younger compared to those in HCP reports (physicians and pharmacists combined), too [8]. Possibly, consumers more often report their ADRs online and this approach might be used more often by younger than older consumers. In addition, older adults in general consult physicians more often than younger adults, probably also regarding drug-related problems. Additionally, serious ADRs requiring medical contact might occur more often in older compared to younger adults [2, 34, 35]. Pharmacies in Germany offer low-threshold services regarding medication analyses. This might be an important point of contact to recognize ADRs especially in older polymedicated patients [36].

The higher proportion of reports referring to females from all three reporter types, which was also described in other studies, could generally reflect that females consult physicians more often, suffer from ADRs more often, report ADRs more frequently, and, especially, in case of younger females, take more drugs compared to males [8, 9, 35, 37, 38].

4.2 Completeness Score (vigiGrade)

In a previous study (2007–2012) performed in VigiBase, the VigiGrade completeness score differed, dependent on the country of origin, between the three reporter types [22]. Concerning the analysed reports from Germany, the reports from physicians were clearly more often classified as "well documented" than those from pharmacist and consumers in this study. However, these results may no longer reflect the current situation. As in our study, a current study from South Africa showed only minor differences between all reporter types, suggesting that physicians' reports were slightly more complete [39].

4.3 Information Provided in Reports from Physicians, Pharmacists and Consumers

Our analysis revealed that information on patients' age, weight, height and medical history were not available in a

large number of the reports. However, the age of the patient is a highly relevant information regarding the analyses of ADR reports, since ADRs might differ between younger (e.g., children) and older patients. Information regarding the weight and height of the patient may not only be relevant for correct dosing in children, but also give a hint regarding the body composition, which may impact on pharmacokinetics and pharmacodynamics of specific drugs. Thus, these information may be important to identify specific patients with a higher risk to develop certain ADRs [40]. The same applies to the medical history of the patient, since certain comorbidities have been shown to be a decisive (co-)factor in the occurrence of specific ADRs [41].

Information regarding the dose, action taken with the drug and the indication of drug therapy were partially missing in more than 50% of the reports. In addition, the number of reports with sufficient information to calculate a time to onset was also low for all three reporter types (< 50%). However, the latter could be calculated more often in reports from consumers than from physicians and pharmacists. As already seen in a US study, consumers may know the exact start date of their drug therapy and date of the ADR more accurately than physicians and pharmacists [13]. In summary, information concerning drug therapy, as well as the start date of the ADR are highly relevant for the assessment of the causal relationship between the intake of a drug and the occurrence of an ADR as well as the further course of the ADR.

The absence of the aforementioned information in approximately every second ADR report is a relevant important finding in terms of pharmacovigilance. It should encourage further studies to elucidate the underlying reasons since it bears the potential to significantly increase the relevance and impact of submitted ADR reports.

As in an Italian and a US Study, a higher proportion of reports from physicians (and pharmacists) listed at least one concomitant drug compared to consumers. In our study, this could be attributed to the older average age of the patient's in the reports from physicians and pharmacists, possibly associated with more drugs taken in these age groups compared to those of consumers [35]. However, the proportions of reports with concomitant drugs were rather low for all three reporter types in our analysis (< 30%). This could reflect patients not taking any co-medications, reporters not distinguishing between concomitant and suspected/interacting drugs or information not being provided.

Nearly twice as many reports from physicians than from consumers and pharmacists listed at least one black triangle drug as suspected/interacting. Possibly, physicians and pharmacists are more aware about the additional monitoring processes and the meaning of the black triangle symbol than patients [41, 42]. In fact, according to a Finish study physicians were more likely to report ADRs if they were aware of the additional monitoring process [41]. Furthermore, in a German study, physicians more often reported ADRs to newly authorised drugs which may be more frequently labelled with a black triangle than older ones. Additionally the Finish study indicated that pharmacists did not see their relevance in the process of additional monitoring, which might also apply to our results [41].

In contrast to other studies, we could not confirm that consumers more likely reported known ADRs compared to physicians and pharmacists [8, 43]. However, we only considered one database, namely SIDER, for the detection of known ADRs and only about 10% of the drugs reported in our dataset were included in SIDER clearly limiting the value of our results. Given that SIDER is based on drug labels, especially new ADRs not yet included therein could not be covered in this analysis.

ADRs listed as designated medical events were more often provided in reports from physicians (and pharmacists) compared to consumers which is in line with another study. The lower proportions of reports with designated medical events found in our study (< 5%) compared to the aforementioned study (40–50%), might be caused by the fact that in that study the "MedDRA® list of serious events" was additionally considered. Further, the higher proportion of non-serious reports in our analysis may have contributed to the lower proportion of reports with designated medical events.

4.4 Suggestions

The results of our analysis could serve as a basis for further initiatives aiming to improve the quality and therewith the value of spontaneous reports from each reporter type.

In order to maintain the positive trend of increasing numbers of consumer reports further campaigns to inform consumers about the possibility and the importance to report ADRs could be helpful [11]. In this regard it could also be highlighted which information is particularly relevant (e.g., the time to onset) and why they should be provided. Thereby, the quality of documentation and the value of their reports could be increased [43]. Meanwhile, physicians and pharmacists should be reminded of the possibility and importance of spontaneous reporting, for example, via appeals in their professional journals to encourage ADR reporting [44, 45].

In order to distinguish between patients without any medical histories/co-medications and reports in which a respective medical history/co-medication is not provided, the introduction of additional coding, i.e., "the patient has no medical history/concomintant drug", could be helpful. In this respect, online reporting tools could be designed to precisely query these situations with drop-down menus allowing to select the appropriate answer "yes/no/unknown"[44].

Minimising the amount of time spent on reporting could possibly counteract the decreasing number of reports and may

improve the completeness of information provided by physicians and pharmacists [43, 45, 46]. Among other factors, the entry of information to a web based or printout reporting format requires a considerable amount of time. Therefore, spontaneous reporting systems allowing simple creations of reports via interfacing with practice/pharmacy software applications thereby sharing personal data already stored in one system albeit still meeting data protection requirements could be valuable tools. In this respect, automatic transfer of relevant data to an optional ADR reporting file would only require a final check before electronic submission [43, 44, 47].

A more interactive exchange between all three reporter types may further increase the quality of documentation of their reports [44, 48]. As already suggested by Hadi et al., granting pharmacists access to certain patient data could be useful in order to enhance the value of the pharmacists' reports [49]. However, in the EU and Germany, strict data protection regulations have to be considered which could complicate the implementation of such applications.

5 Strengths and Limitations

Our analysis provides the current status of the quality of ADR reports from different reporter types especially after the changes in legal requirements.

However, the inherent limitations to analyses performed in spontaneous reporting systems have to be taken into account. One of the major limitations is the unknown amount of under-reporting that may differ, among others, between the analysed reporter types, as well as for serious and non-serious ADR reports.

Furthermore, we only considered if specific information were provided. The quality or relevance of the information provided for pharmacovigilance was not assessed. However, this would be difficult to quantify as a basis for a comparison.

In addition, we could not distinguish between initial reports and reports with follow-ups that might be submitted on request, and thus, may have influenced the completeness of the respective reports. Consumer reports in particular, if submitted via a pharmaceutical company, could contain additional information as a result of explicit inquiries by specifically trained employees. Additionally, possibly at the time of analysis not all follow-up reports, especially those from 2021 may have been received.

Please note that the calculations of reporting rates per 100 physicians/pharmacists and 10,000 potentially drug-exposed inhabitants are estimations since one physician or pharmacist may also have reported more than one ADR.

Our analysis only covers ADR reports related to drugs, thus, the results may not be transferrable to vaccines. We only considered reports coded with one primary source qualification. It may be possible that some of these reports were reported by more than one reporter type but not encoded as such. However, we assume that this would only apply to a small number of our reports and, therefore, should not affect our results substantially. In addition, the number of reports coded with more than one reporter type was rather low (7.7%, 20,473/267,261 reports of total dataset) and should not substantially affect our observations.

6 Conclusion

In terms of the overall completeness, the ADR reports from consumers were comparable with regard to the information provided to those from physicians and pharmacists highlighting their value to gain further information on ADRs. Besides further campaigns to continuously increase the awareness towards ADR reporting systems, a more intense interacting among all three reporter types may further improve the completeness of ADR reports.

Finally, since reports from consumers, physicians and pharmacist may differ in terms of presence of certain information, the population of patients covered, and the reported drugs/ADRs, stratified analysis of ADR reports per reporter type dependent on the research question are recommended [2, 9–12].

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40264-023-01355-8.

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Declarations

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Conflict of interest MS and DD were supported by the ANKA project, which is funded by own resources of the German Federal Institute for Drugs and Medical Devices (BfArM) and own resources of the Institute for Medical Biometry, Informatics and Epidemiology (IMBIE) at the University Hospital of Bonn (V-2020.2/68502/2020-2024). The analyses and results presented in this manuscript constitute a subproject within the ANKA project. The remaining authors have no other conflicts of interest that are directly relevant to the content of this manuscript.

Data availability statement The pseudonymised ADR reports from EudraVigilance are not publicly accessible due to data protection requirements. Distinct levels of access are provided for various stakeholders (https://www.ema.europa.eu/en/human-regulatory/research-development/pharmacovigilance/eudravigilance/access-eudravigilance-data). Being one of the competent authorities in Germany, the highest level of access is granted to the Federal Institute for Drugs and Medical Devices (BfArM). Nevertheless, even with the lowest access level, researchers can perform the same analysis in EudraVigilance (EV) with aggregated data (public access: www.adrreports.eu/en/index.html). For further information regarding the processing of personal data in the context of the operation of EudraVigilance Human we refer to the European Medicines Agency's Data Protection Notice for EudraVigilance Human.

Ethics approval The presented study is a retrospective analysis of pseudonymised reports of adverse drug reactions. According to the local ethics committee of the Medical Faculty of Bonn no ethics approval is needed for this study (file no. 100/21).

Consent for publication Not applicable.

Consent to participate Not applicable.

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