BMC Digital Health

RESEARCH

Open Access

Effectiveness of mobile applications in enhancing adverse drug reaction reporting: a systematic review

Liyanage PH[1], Madhushika MT[1*] and Liyanage PLGC[1]

Abstract

Background Adverse drug reactions (ADRs) have a significant impact on the healthcare system worldwide. Underreporting of ADRs is identified as a main issue in pharmacovigilance. Mobile applications(apps) have been introduced as a solution for the underreporting of ADRs. This systematic review was conducted to assess the efficacy of the mobile applications in enhancing ADR reporting.

Methodology The review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The MEDLINE (via PubMed) and Google Scholar databases were used to retrieve papers published between 1983 – 2023 by using advanced search strategies and keywords in the computerized searches. A total of 1955 articles were found, and six articles that met the inclusion criteria were selected for the study.

Results The six studies comprised in this systematic review showcased six distinct mobile apps designed for reporting ADRs: VigiBIP (France), My eReport France (France), MedWatcher (United States of America), ADR reporting app© (App©-India), the WEB-RADR project containing three separate apps; Yellow Card (UK), LAREB (Netherlands), HALMED (Croatia), and Med Safety (13 African countries, including Ghana, Burkina Faso, Zambia, Nigeria, Uganda, Botswana, Tanzania, Ethiopia, and others). All the apps have helped to increase the rate and magnitude of reporting ADRs. The efficacy was determined using both the quantity and quality of the reports received. The apps; MedWatcher, VigiBIP ($p=0.01$), My eReport France ($p=0.002$), and WEB-RADR apps {Yellow Card ($p<0.01$), LAREB ($p=0.5$), HALMED ($p<0.01$)} revealed better reporting rates among patients compared to conventional methods. The completeness and characteristics of Med Safety App reports (missing information: 0%) were higher when compared with the paper-based ADR reporting forms {(Council for International Organizations of Medical Sciences (CIOMS) form (missing information: -29.6%)}. The average completeness score of the ADR reporting app© (App©) was significantly better than the traditional paper-based system on the Wilcoxon two-sample test ($p<0.001$) and Kolmogorov–Smirnov test ($p<0.001$). Furthermore, MedWatcher indicated a high vigigrade completeness score (averaging 0.80), which was considered 55.9% as well documented. My eReport France demonstrated a high clinical quality score in the ClinDoc tool and was considered 36% as well documented, indicating better quality when compared to their control groups.

Conclusions Mobile apps were implemented to address the issue of underreporting. The quality of reporting was better when ADRs were reported through mobile apps compared to manual methods. However, reporting rates

*Correspondence:
Madhushika MT
thiliniminipura@gmail.com

can benefit from further enhancement. Mobile apps hold the potential to increase ADR reporting, requiring more studies to explore a conclusive assessment of efficacy.

Keywords Drug-Related Side Effects, Adverse Reactions, Mobile Applications, Pharmacovigilance, Underreporting, Adverse Drug Reaction Reporting Systems

Introduction

Adverse Drug Reactions (ADRs) significantly affect the healthcare system, impacting the health and economy worldwide. When preparing medicinal drugs, experiments are conducted thoroughly during the pre-marketing phase to determine the drug's safety. However, it is equally necessary to maintain post-marketing surveillance as well as to evaluate ADRs which are not detected during the drug development process. The activities related to the detection, assessment, understanding, and prevention of ADRs or any other problems related to medicinal products are known as pharmacovigilance [1]. The primary purposes of pharmacovigilance include drug safety surveillance, monitoring drug abuse and adverse effects, and ensuring the safety of new products. Further, drug experiments are performed on a smaller group of people during the drug development process. The trial period is too brief for the detection of ADRs. As a result, certain ADRs may go unreported. Individuals with special healthcare needs, such as children, pregnant mothers, and the elderly with several comorbidities, are often left out from these studies [2]. Hence, after the drugs are introduced to the community, there should be a surveillance system to collect and analyse the ADRs of drugs, which systematically promises drug safety and patient safety. This can be achieved by reporting and monitoring ADRs.

Underreporting of ADRs is identified as a pressing issue in Pharmacovigilance, as it directly affects the patient's safety and healthcare delivery [3]. This issue can cause difficulties in assessing the exact extent of the potential risks and the nature of the reactions. Early detection and accurate reporting are pivotal to minimise the impact. When assessing ADR reporting on a global scale, it is evident that pharmacovigilance in most countries primarily relies on spontaneous reporting systems [4]. Various spontaneous ADR reporting methods have been identified, including manual paper-based reporting methods, web-based mobile applications and specialized reporting mechanisms with technological advancements. One example of a specialized reporting mechanism with technological advancements is the use of artificial intelligence (AI) driven platforms, which analyse large datasets to detect potential ADRs earlier and more efficiently [5, 6]. Furthermore, an advanced, scalable electronic health record (EHR) based system has been developed and implemented that automatically sends electronic adverse drug event (ADE) reports to the Food and Drug Administration (FDA) in real-time [7].

Each of these strategies has its strengths and weaknesses. For example, paper-based manual reporting is considered to be time-consuming and error-prone, yet it continues to find acceptance in some places where technology is poorly developed [2]. Mobile applications(apps) based on the Internet are convenient and fast, allowing medical personnel to document ADRs very easily. However, they do not always address the integration aspect [8]. AI-based solutions provide more accurate and fast reporting at an affordable cost. However, many healthcare settings may not know how to put it into practice. Although the EHR system can be fast and provide instant reporting, this system can be rather costly to develop. Furthermore, it is likely to face the problem of interfacing with the current health information technology (IT) systems [7].

The newly improved methods for reporting ADRs have been identified as comparatively more efficient and accurate. With the advancements in technology, mobile apps are considered as a globally accessible method in both developed and developing countries. However, despite the widespread availability of these mobile apps, limited evidence is available regarding their effectiveness over conventional reporting methods of ADRs. As digital health tools become more widely adopted, it is crucial to evaluate the impact of these technologies to inform future pharmacovigilance strategies and policies. Therefore, this review seeks to answer the following research question: How effective are mobile apps in enhancing the reporting of ADRs compared to conventional methods?

Methodology

Methods

A systematic review was conducted according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [9].

Search strategy

A search for bibliographic references was followed through MEDLINE (via PubMed) and Google Scholar to explore scientific literature on the effectiveness of using mobile apps in ADR reporting among healthcare professionals published between 1983 and 2023. An advanced

Table 1 The combination of keywords used in the search strategy

Search #	Keywords
1	**(Mobile Applications)** OR (**Smartphone Applications)** OR (**Mobile Apps)** OR (**Smartphone Apps)** OR (**Portable Software Apps)** OR (**Portable Software Applications)** OR (**Portable Electronic Apps)** OR (**Portable Electronic Applications)** OR (**Mobile Technology)** OR (**Web Applications)** OR (**Web Platforms)** OR (**Mobile Health Applications)**
2	**(Pharmacovigilance)** OR (**Adverse Event Reporting)** OR (**Drug Monitoring)** OR (**Drug Safety Monitoring)** OR (**Drug Surveillance)** OR (**Drug Safety Reporting)** OR (**Drug Monitoring)** OR (**Medication monitoring)** OR (**Drug Safety Assessment)** OR (**Drug Evaluation)** OR (**Medication Side Effects)** OR (**ADRs Investigation)** OR (**ADRs Management)** OR (**ADRs Response)** OR (**Drug-Related Side Effects and Adverse Reactions)** OR (**Drug Side Effects)** OR (**Adverse Drug Reactions)** OR (**Adverse Drug Events)** OR (**Side Effects of Drugs)**
3	(**#1**) AND (**#2**)

search strategy was used by combining the keywords according to Table 1. EndNote 21 was used to remove the duplications of the retrieved articles. Furthermore, the citations were re-evaluated to identify additional studies.

Study selection

The titles and abstracts in all the retrieved scientific papers were initially screened by the primary author based on the selection criteria. The full-text articles of the remaining studies were independently reviewed by the primary author to conclude the eligibility. All included articles were then independently reviewed by a second author to ensure that they met the inclusion criteria. The third author reviewed the article in case of any disagreement and made the final decision.

Inclusion and exclusion criteria

The inclusion criteria for the review were as follows: articles published in the English language between 1983 and 2023, focusing on human studies, with a clinical trial study design. Articles that did not meet these criteria were excluded. Particularly, ongoing research articles, narrative reviews, books and documents, and non-English publications were excluded to maintain a focus on completed clinical trials and ensure the consistency and relevance of the data.

Data extraction

The data extracted consists of the first author's name, publication year, journal reference, study population, year of the study, reported challenges to program implementation, proposed solutions to the challenges, study limitations and quality.

Quality assessment

The quality of the selected articles was assessed according to the Jadad score [10]. This grading system focuses on the three main key areas: randomization, blinding, and long-term patient follow-up. The highest attainable score is 5; with a breakdown of 2 points for the randomized section, 2 points for the blinding section, and 1 point for the patient follow-up section. A score exceeding 3 points classifies the study as good quality. The quality assessment of the selected article was initially reviewed by the primary author and subsequently re-evaluated by the second author. As a further quality assessment, the mHealth evidence reporting and assessment (mERA) checklist was used alongside the Jadad score [41]. The checklist was used to assess the mobile apps used in this review. As described by Agarwal et al. (2016), the mERA checklist is designed to assist authors in reporting the effectiveness of mHealth interventions and to support peer reviewers and editors in evaluating such studies [41].

Ethics approval

Since the systematic review contains full anonymized data, no ethics approval was required.

Results

By using advanced search strategies and keywords in the computerized searches, books and documents were initially excluded from the Medline search engine (via PubMed) and Google Scholar. Through the search strategy and cross-referencing, 1955 unduplicated articles were found. From it, 1,926 articles were excluded after a thorough screening of their title and abstracts. After, we retained 29 articles for more comprehensive full-text reading. Of them, 23 articles were excluded based on the full-text review, either for not meeting the selection criteria or being irrelevant to the scope of this review. Hence, six articles met the selection criteria and were included in the final analysis. Following the evaluation using the Jadad Score, it was determined that the articles related to the ADR reporting app© (App©), My eReport France, WEB-RADR apps, and Med Safety were of good quality. However, articles related to the MedWatcher and VigiBIP were found to be of lower quality. The mERA checklist revealed strengths in platform accessibility (iOS/Android), national pharmacovigilance integration, and user-centred design tailored to local healthcare contexts. Each app supported real-time ADR reporting and data submission. However, they varied in scalability due to region-specific interoperability, regulatory standards, and

infrastructure constraints, particularly in low-resource settings.

Below, Fig. 1 represents a flow chart of the article selection process and the various mobile apps currently available for ADR reporting and their features are listed in Table 2.

The six (6) eligible studies included in this systematic review were published between 2010 – 2023 with diverse study designs (Table 3). Overall, all studies had a common objective to evaluate the effectiveness of ADR reporting through mobile apps. After going through six studies on mobile apps for detecting ADRs, four (4) studies showed that they were effective in increasing the rate of ADR reporting among patients, and four (4) studies concluded app reports were better in quality. Articles have stressed the significance of introducing apps for ADR reporting, highlighting the continuous improvement of technology in society. The efficacy was concluded with both the quantity; of the ADR reporting rates, and the quality; completeness, accuracy, reliability, and average time needed for report submission.

The web and mobile app MedWatcher were developed by Epidemico, which is a Boston-based health informatics company, the USA, in partnership with the FDA Centre for Devices and Radiologic Health (CDRH) [17]. This app was launched in September 2012 to the US public for reporting ADE to the FDA along with a Facebook patient group, particularly for submitting reports involving a hysteroscopic sterilization device with the brand name Essure. The study assessed the potential for participatory epidemiology in post-marketing medical device surveillance, encouraging the submission of individual case safety reports (ICSRs) through online tools. Over the 132 months of post-marketing authorization, CDRH received 943 reports for Essure devices [18] in the FDA's specialized database developed for reporting ADRs related to medical devices: Manufacturer and User Facility Device Experience (MAUDE) [19].

In comparison, during the 19-month study period, 1349 reports were received via the MedWatcher app, averaging 103 per month (ratio 14.7:1). On average, 15 times more reports have been submitted per month via the app with patient community support compared to traditional pharmacovigilance portals. It stated that the reporting time has decreased from 40 min via traditional routes to 11.4 min via the MedWatcher app, facilitating more ADR submissions. VigiGrade completeness scores, developed by the Uppsala Monitoring Centre of the World Health Organization (WHO-UMC), have been used to determine the completeness of the submitted reports. The app received an average completeness score of 0.8 (± 0.15) and the reports in VigiBase submitted via traditional routes received a score of 0.45. App reports were considered "well documented" 55.9% of the time, while the international average was 13% [20]. This suggests that the reports received via the app were more complete on average and were considered more well-documented than reports received by regulatory agencies worldwide [11].

The Toulouse University Pharmacovigilance Centre (TUPVC) has developed VigiBIP, a free smartphone app available on both Android and Apple stores for reporting ADRs and requesting safety information. This mobile phone app VigiBIP, launched in January 2015 in France, was one of the first pharmacovigilance apps in Europe. The trial compared the main characteristics between spontaneous ADR reports received through VigiBIP with classical methods such as phone, e-mail, fax, letter and website within a 25-month trial period (10 January, 2015 and 1 February, 2017). A total of 4,102 reports were received by TUPVC, with 193 (4.7%) submitted via the VigiBIP app and 3,909 (95.3%) through other methods. The VigiBIP app predominantly received reports from patients and practitioners working outside of hospitals, whereas hospital-based practitioners primarily submitted reports through traditional methods. The detailed analysis highlights the distribution of reports obtained via the VigiBIP app and traditional methods. From hospital reporters {112 (58.0%), vs. 2648 (67.8%)} with a p value of 0.005, from patient reporters {13 (6.7%), vs. 133 (3.4%)} with a p value of 0.01, and from extra-Hospital Reporters {68 (35.2%), vs. 1126 (28.8%)} a p value of 0.06 was received respectively. The results concluded that proportionally, more reports were received from patients using VigiBIP than with the classical methods [12].

Another Android based mobile ADR reporting app (App©) was developed by Sachin Kumar Kuchya et al., in 2015. A comprehensive comparison between the traditional paper-based and App-based methods of submitting suspected ADRs (sADRs) data has been evaluated. The ADR Monitoring Centre (AMC) at the Department of Pharmacology at Netaji Subhash Chandra Bose Medical College (NSCB MC) Jabalpur received 403 sADR data in total, which were chosen for evaluation. Upon screening, a validation rate of 96.2% (257/267) via paper-based submissions and a perfect 100% (136/136) via App© has been identified. The app-based submissions exhibited an average completeness score of 34.7 (± 2.4) with a significant difference of 29.2 (± 2.4) with paper-based submissions ($p < 0.001$). This scoring system was done according to the appropriate algorithms and scaling of the Wilcoxon two-sample test and Kolmogorov Smirnov test. The completeness score data conclusively demonstrates that the ADR reporting app was the better method for submitting high-quality reports when compared with traditional paper systems. Both methods contain the same form,

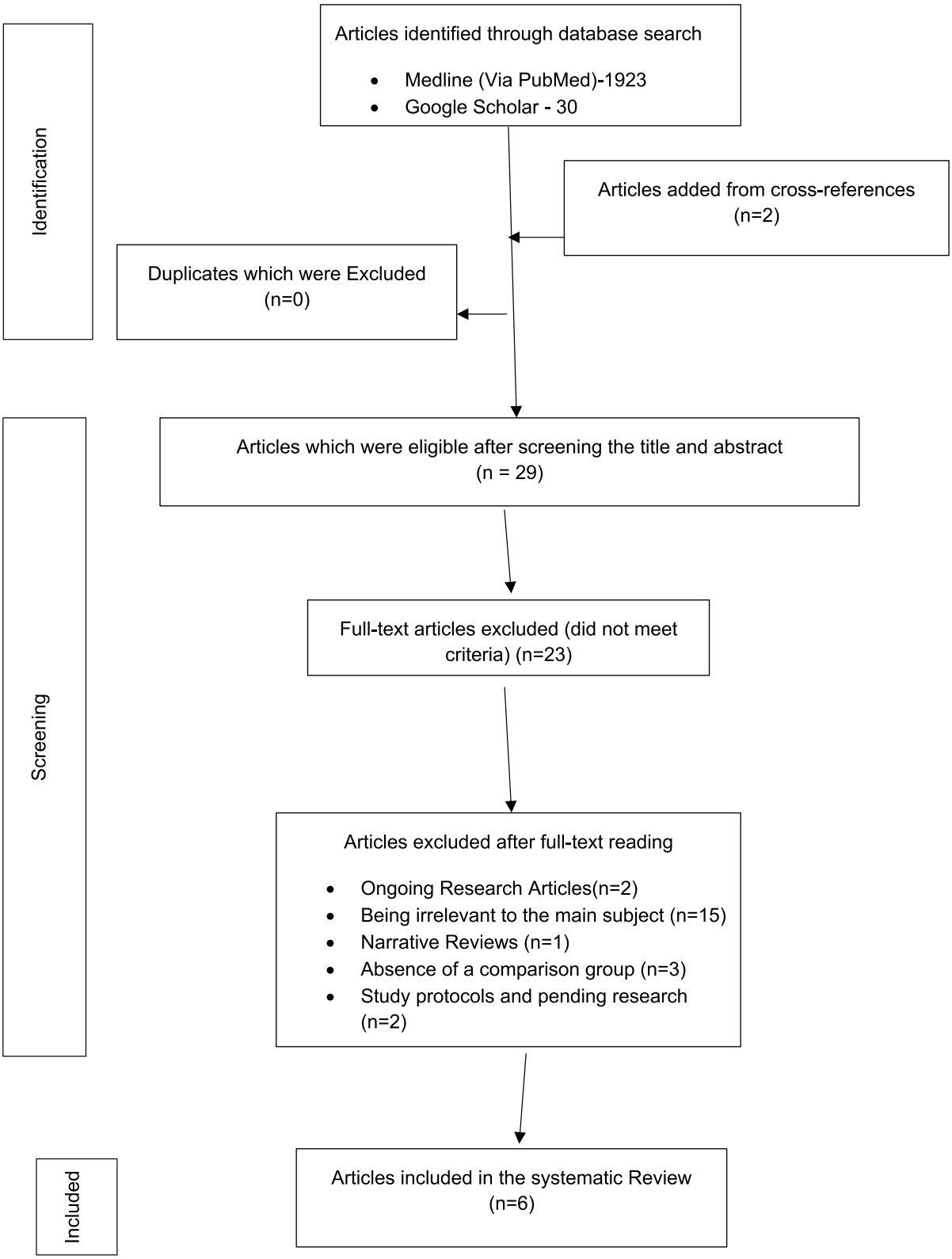

Fig. 1 Flow chart of the literature selection process according to the PRISMA guideline

Table 2 Mobile Apps Available for ADRs Reporting

Name of the app	Country of implementation	Date of implementation	Operating system (iOS, Android, or both)	Author and year (References)	Features of the app
MedWatcher	United States of America	2012	Both	Chi Y. Bahk, et al. 2019 [11]	Images can be uploaded Customizable Two-way communication channel An average of 11.4 min is needed to conclude a report
VigiBIP	France	2015	Both	Franç ois Montastruc, et al. 2017 [12]	Images can be uploaded Customizable Two-way communication channel
ADR reporting app© (App©)	India	2015	Android mobile app	Sachin Kumar Kuchya, et al. 2017 [13]	Bilateral standardization Auto save reporter data Mandatory Data Validation User friendly interface
My eReport France	France	2015	Both	Gilles Defer, et al. 2020 [14]	Images can be uploaded User-friendly interface European standards compatibility (ICH-E2B format)
WEB-RADR apps	UK (Yellow Card) Netherlands (LAREB) Croatia (HALMED)	2015 2016 2016	Both	Ingrid Oosterhuis, et al. 2018 [15]	Allows more free text Images can be uploaded Functions offline Customizable Interface of the app adapts to the device Designed for multiregional use Two-way communication channel
Med Safety	13 African countries, including Ghana, Burkina Faso, Zambia, Nigeria, Uganda, Botswana, Tanzania, Ethiopia, and others	2019	Both	Seth Kwaku Seaneke, et al. 2023 [16]	Two-way communication channel Designed for multi-region use Language Contains "News" and "Watch List User friendly layout

although the only difference is that in the paper-based method, the data is filled in after downloading the PDF version and filling them out, and in app based method, the data is entered into the form via App© [13].

Furthermore, an app named My eReport France was developed by the eVeDrug® company to increase ADR reporting by persons with multiple sclerosis receiving a first-line disease-modifying drug (DMD). The study protocol VigipSEP, has been previously published [21]. Here, the objective of this study was to determine if the ADR reporting by persons with multiple sclerosis receiving first-line DMD with the use of the app, compared to traditional reporting. Therefore, an open, multi-centric, cluster-randomized controlled trial was conducted. Clusters were randomly assigned in a 1:1 ratio using the two arms; the experimental arm by utilizing the My eReport France App, and the controlled arm, by employing traditional reporting methods [10]. Persons with multiple sclerosis initiating or switching to a first-line disease-modifying drug between the period 18 April, 2017 and 24 April, 2019 were included. The primary outcomes were determined initially by measuring the mean number of ADR reports per patient using the centre-level analysis and then by the number of ADR reports per patient for the individual-level analysis using the hierarchical Poisson regression model [21]. Particularly, a total of 24 centres were randomized including 159 patients; 91 in the experimental arm, and 68 in the control arm. Among the 91 patients in the experimental arm, there were 64 ADRs in 43 reports (1.49 reactions by report, range 1–12) with a clinical quality score, median [50–64] 57%, 23 (36%) were well documented, 40 (62%) were moderately documented, and 1 (2%) was poorly documented. Among the 68 participants in the control arm, 3 ADRs were documented across 2 reports (range: 1–2), with a median clinical quality score of 79% [range: 71–79]. Two

Table 3 Study characteristics

Author and year	Study population and setting (T/C)	Name of the Mobile App	Study Period	Intervention (T)	Control (C)	*P* Value
Chi Y. Bahk, et al. 2019 [11]	Patients and Physicians App is primarily intended for the patients using the app reside in the USA	MedWatcher	11 May, 2013 to 7 December, 2014	Through the MedWatcher app (19 month duration) 1349 reports (an average 103 per month) with (ratio 14.7:1) 11.4 min (±10) was spent to complete a Essure AE report Average VigiGrade completeness scores were high, averaging 0.80 (±0.15) Considered "well documented" 55.9% of the time compared with an international Average of 13% for all medical products 24% of reports from physicians are considered well documented	Through conventional methods (132 months post- marketing authorization duration) 943 reports (an average of seven per month) 40 min was spent to complete a voluntary AE report Average VigiGrade completeness score is 0.45 for the 7.0 million reports	-
François Montastruc, et al. 2017 [12]	healthcare professionals general public	VigiBIP	10 January, 2015 to 1 February, 2017	Through the VigiBIP app Reports received—193 (4.7%) Hospital Reporters- 112 (58.0%) Patient Reporters- 13 (6.7%) Extra-Hospital Reporters- 68 (35.2%)	Through conventional methods (phone, e-mail, fax, letter, website) Reports received −3909 (95.3%) Hospital Reporters- 2648 (67.8%) Patient Reporters- 133 (3.4%) Extra-Hospital Reporters- 1126 (28.8%)	Hospital Reporters ($p=0.005$) Patient Reporters ($p=0.01$) Extra-Hospital Reporters- ($p=0.06$)
Sachin Kumar Kuchya, et al. 2017 [13]	Healthcare professionals	ADR reporting app© (App©)	1 March, 2015 to 31 January 2016	Through the ADR reporting app© (App©) Valid Submissions 100% (136/136) Average completeness score- 34.7 (±2.4)	Through conventional methods (paper based ADRs form) Valid Submissions 96.2% (257/267) Average completeness score- 29.2 (±2.4)	($p<0.001$)

Table 3 (continued)

Author and year	Study population and setting (T/C)	Name of the Mobile App	Study Period	Intervention (T)	Control (C)	*P* Value
Gilles Defer, et al. 2020 [14]	Persons with relapsing remitting multiple sclerosis The median age of patients was 38 years sclerosis academic expert centers and general hospitals, and by private practice neurologists	My eReport France App	18 April, 2017 to 24 April, 2019	Through the My eReport France App Mean number of ADRs reports per patient- 0.47 64 ADRs in 43 reports from 91 patients Clinical quality score of the 64 ADRs reported Median (57%), 23 (36%) were well documented 40 (62%) were moderately documented 1 (2%) was poorly documented	Through conventional methods Mean number of ADRs reports per patient- 0.03 3 ADRs in 2 reports 68 patients Clinical quality score of the 3 ADRs reported Median [71–79] (79%) 2 excellently documented one was well documented	($p = 0.002$)
Ingrid Oosterhuis, et al. 2018 [15]	Physicians Pharmacists Other health professionals Patients	WEB-RADR apps	launch date of the app in each country to 1 September, 2016	Through the WEB-RADR apps **UK- 144 (28%)** Physicians-[19–29]% Pharmacists- [29–37]% Other health professionals-[0–10]% Patients-(28%) **Netherlands- 106 (60%)** Physicians- [19–29]% Pharmacists- [0–10]% Other health professionals-[0–10]% Patients-(60%) **Croatia- 37 (32%)** Physicians-[0–10]% Pharmacists- [60]% Other health professionals-[0–10]% Patients- (32%) Moderate quality of app: 78–85% for all countries	Through conventional methods (paper forms and electronic forms) **UK- 22,582 (18%)** Physicians- [29–37]% Pharmacists- [19]% Other health professionals-[19–29]% Patients-(28%) **Netherlands- 5779 (57%)** Physicians-[19–29]% Pharmacists-[9–19]% Other health professionals-[0–10]% Patients-(57%) **Croatia- 307 (7%)** Physicians-[40–50]% Pharmacists- [40–50]% Other health professionals-[0–10]% Patients-(7%) Moderate quality of reference: 78–98% for all countries	UK ($p < 0.01$) Netherlands ($p = 0.5$) Croatian ($p < 0.01$)

Table 3 (continued)

Author and year	Study population and setting (T/C)	Name of the Mobile App	Study Period	Intervention (T)	Control (C)	*P* Value
Seth Kwaku Seaneke, et al. 2023 [16]	Healthcare Professionals	Med Safety App	14 December, 2020 to 15 January, 2021	Trough the Med Safety App (Total *n* = 122) Physicians- 15 (12.3%) Nurses- 0 (0%) Pharmacists-72 (59.0%) Disease Control Officers- 0 (0.0%) Other Healthcare Professionals- 12 (9.8%) Consumers and lawyers- 23 (18.9%) Not stated/missing- 0 (0.0%)	Through conventional methods (FDA's paper-based CIOMS 1 form) (Total *n* = 6825) Physicians- 324 (4.7%) Nurses- 1104 (16.2%) Pharmacists- 1104 (15.6%) Disease Control Officers- 1278 (18.7) Other Healthcare Professionals- 868 (12.7%) Consumers and lawyers- 171 (2.5%) Not stated/missing- 2018 (29.6)	-

were excellently documented, and one was well documented [12]. The clinical quality was assessed according to the ClinDoc tool. Furthermore, the mean number of reports per patients was significantly higher in centres that used the app: 0.47 vs. 0.03 by traditional methods in control centres ($p=0.002$). Hence, Apps were suggested to increase ADR reporting by patients and improve the emergence of new safety information for pharmacovigilance [22]. There were no ADR reports submitted by any healthcare professionals including neurologists. Here, this result was consistent with the 94% underreporting of ADRs by healthcare professionals in real-world practice fields [23].

The Web-Recognising Adverse Drug Reactions (WEB-RADR) project was first introduced in European countries- the UK, Netherlands and Croatia. Subsequently, the project, in collaboration with the WHO-UMC and the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA), developed a generic version known as the Med Safety app. This app was designed to facilitate ADR reporting in low and middle-income countries, as well as other non-EU nations. The countries are Burkina Faso, Zambia, Armenia, Ghana, Ethiopia, Botswana, Ivory Coast, Uganda, the Democratic Republic of the Congo, Nigeria, Pakistan and Kyrgyzstan [24]. The WEB-RADR app was developed for the spontaneous reporting of ADRs. The app was launched in the UK (Yellow Card) on 14 July 2015, in the Netherlands (LAREB) on 29 January 2016, and in Croatia (HALMED) on 18 May 2016. The study period spanned from the launch date of each app in its respective country until September 1, 2016.The objective of this study was to assess the characteristics and contribution to signals of the reports submitted via the WEB-RADR app. The two arms of the study were the reference sample reports (paper forms and electronic forms) and WEB-RADR app reports. Although physicians, pharmacists and other health professionals have participated in submitting reports, a higher proportion of app reports were submitted by patients. In the UK, a total of 144 app reports were submitted, with contributions from physicians [19–29]%, pharmacists [29–37]%, other health professionals [0–10]%, and patients (28%). In contrast, 22,582 reference sample reports were recorded, comprising physicians [29–37]%, pharmacists [19]%, other health professionals [19–29]%, and patients [28%]. Similarly, in the Netherlands, 106 app reports were submitted, with contributions from physicians [19–29]%, pharmacists [0–10]%, other health professionals [0–10]%, and patients (60%). This is compared to 5,779 reference sample reports, which included physicians [19–29]%, pharmacists [9–19]%, other health professionals [0–10]%, and patients (57%). In Croatia, a total of 37 app reports were documented, with contributions from physicians [0–10]%, pharmacists [60]%, other health professionals [0–10]%, and patients (32%). This contrasts with 307 reference sample reports, which included physicians [40–50]%, pharmacists [40–50]%, other health professionals [0–10]%, and patients (7%). Both the UK and Croatia showcase a significant disparity ($p<0.01$) between the two reporting methods, but it's insignificant ($p=0.5$) in the Netherlands. According to the vigiPoint feature, there was a significant difference in the proportions of app reports and reference reports in the following. The app sample has a higher proportion of reports submitted by the pharmacists in the UK, and the patients in Croatia. In contrast, the proportion in the reference sample has a higher proportion of physicians in Croatia and other health professionals in the UK. Dual quality measurements, using vigiGrade for technical completeness of the reports and ClinDoc for clinical quality is a special characteristic of the study [15].

As mentioned above, the WHO, in partnership with the MHRA, and the UMC has supported low- and middle-income countries (LMICs) to roll out the ADR reporting app, the Med Safety App. In June 2018, Ghana launched the Med Safety App following a successful pilot program in Burkina Faso and Zambia [25]. Throughout the study period, the ADRs reports received through the Med Safety App ($n=122$), and as the comparison group, the FDA's paper-based Council for International Organizations of Medical Sciences (CIOMS) 1 form ($n=6825$) were recorded and analysed. The completeness and characteristics of Med Safety App reports (missing information 0%) were higher when compared with paper-based CIOMS 1 forms (missing information 29.6%). As of the end of February 2021, 21 months after the launch, there were 996 downloads, with 120 safety reports received through the Med Safety App. Among these reports, 99 (82.5%) were submitted by healthcare professionals, and the remaining 21 (17.5%) were from patients. And 121 of 350 participants provided answers to the questionnaire sent as a Google form, representing a response rate of 34.6%. In further analysis concerning the profession, Med Safety App n (%) and CIOMS 1 paper form n (%): {15 (12.3), vs. 324 (4.7)} from physicians, {0 (0.0), vs. 1104 (16.2)} from nurses, {72 (59.0), vs. 1062 (15.6)} from pharmacists, {0 (0.0), vs. 1278 (18.7)} from Disease Control Officers, {12 (9.8), vs. 868 (12.7)} from other healthcare professionals, {23 (18.9), vs. 171 (2.5)} from consumers and lawyers and {0 (0.0), vs. 2018 (29.6)} either not stated or missing were reported respectively. And of them, 81 (66.94%) were males with the rest being females. Most participants were satisfied with the features of the app. However, given that only one-third of participants used the app suggests a potential necessity for public awareness regarding the app's uses and efficacy [16].

Table 4 Strengths and Limitations of the Selected Study Articles

Name of the app	Strengths	Limitations
MedWatcher	● Two-way communication channel ● Direct patient involvement ● User-friendly web and mobile app ● Increase efficiency ● Utilization of the VigiGrade completeness scores to evaluate the quality of the data ● Anonymized versions were available for privacy and safety ● Images can be submitted ● More complete reports	● The app is primarily intended for the patients using the app reside in the USA ● Available only in English
VigiBIP	● Ease of patient reporting (Data and Photographs of ADRs) ● Better clinical characteristics documentation of ADRs for causality assessment ● Two-way communication channel	● Non-presentiveness of users ● Potential lack of medical information
ADR reporting app© (App©)	● Ensures mandatory data has been entered leading to valid and complete reports ● The reporter information is saved, reducing the need to repetitive data entry ● Bilateral standardization has been introduced for the communication gap between input operator and output analyzer ● Built-in algorithm for Causality assessment enhances the reporter's knowledge, objectivity ● User friendly interface	● Signatures cannot be placed in App© submissions ● Only available in Android platforms lacking versions for iOS, Lumia and desktop ● Follow up on previous cases need to filled afresh
My eReport France	● New opportunities for Real-world Data Collection ● Early detection of ADRs ● Pictures can be uploaded ● Directly report submission to the Regional Center of Pharmacovigilance,	● Due to the international diversity of pharmacology systems results may not be directly replicable in other countries with similar ADR reporting mechanisms ● Persons with multiple sclerosis, chronic condition with an evolving therapeutic regimen were only included ● User experience and app design were not considered
WEB-RADR apps Contains 3 Apps (Yellow Card, LAREB, HALMED)	● Dual Quality Measurements, vigiGrade (technical completeness of the reports) and ClinDoc (clinical quality)	● Potential biases in app user preferences
Med Safety	● Designed to support low- and middle-income countries (LMICs) use ● Use of this app in low-resource settings ● Two-way risk communication ● Designed for multi-region use Language ● Security of the app ● Source of safety information provided through the app	● There is currently no study that documents challenges and facilitators for the use of a mobile app for reporting ADRs in LMICs ● Concerned about the privacy and security of personal information

There were several strengths and limitations noted in the studies we referred (Table 4). Increasing direct patient involvement, two-way risk communication, and a user-friendly interface were some of the most important strengths highlighted with the app implementation. The limitation faced by the majority was language diversity. In countries where multiple languages are spoken, users have different native languages. However, most of the apps were designed using English as the native language, which might have raised linguistic limitations with the potential users.

Discussion

This systematic review delves into the horizons of exploring the efficacy of utilizing mobile apps for ADR reporting. When choosing studies for this systematic review factors such as reporting rates, availability of comparison group, accuracy and completeness score, response time, timeliness of reporting and uses satisfaction were taken into consideration. Hence, we identified studies where mobile apps have been efficiently compared to other ADR reporting methods [11–16]. In the selected studies, several experiments have been conducted to examine the efficacy of mobile apps. Four out of the six selected studies forefront the idea that mobile apps were an effective method of ADR reporting rates among patients with statistically supported results (MedWatcher, VigiBIP, My

eReport, WEB-RADR in the Netherlands and Croatia). Four of the studies concluded that app reports were better in quality and completeness (MedWatcher, VigiBIP, ADR Reporting App©, Med Safety). When skimming through articles, a consistent trend emerged showcasing mobile apps as a potential tool in increasing the rate and magnitude of ADR reporting. The reports received by patients have been noted to be rapidly increasing. Meanwhile, the quality of ADR reports from healthcare professionals is much higher. Mobile applications have significantly improved ADR reporting by enabling real-time data submission, which reduces the risk of errors and missing information. completeness is enhanced through features like free-text descriptions and photo uploads, resulting in higher-quality reports. The ability to submit reports immediately helps manage time efficiently by bypassing delays associated with conventional methods, facilitating faster detection of potential drug safety issues. Additionally, apps include features such as automated alerts and reminders, which encourage timely follow-ups and further enhance the overall quality of reporting. A study stated that spontaneous reporting by healthcare professionals was identified as the greatest source of drug safety data in post-marketing settings [26]. The majority of the population favours mobile applications and has recommended it to others as well [16, 27]. Despite all the efforts that have been made to enhance the spontaneous notification mechanisms, underreporting of suspected ADRs remains a persistent concern [28].

The vast technological advancements in the 21st Century have created a new era of user-friendly platforms for both patients and healthcare professionals for ADR awareness. Caller Tunes (the message or sound the caller hears before the receiver answers the call) is a more specialised mobile application that has been developed to disseminate information on ADRs in low and middle-income countries [29]. This was initialised in Accra, Ghana and has shown a significant increase in direct ADR awareness in the society. Furthermore, according to the study [7], the use of electronic reporting tools was demonstrated as a promising leap for ADR reporting. Here, a widely applicable scalable system within electronic health records (EHR) to send EHR-based system to automatically send electronic ADE reports to the FDA in real-time has also been introduced. This strategy captures electronic health records in triggering ADR reports when clinicians discontinue medications due to ADRs. This is an extremely successful strategy for achieving a modest increase (1.45 to 5.4-fold) in ADR reporting rates. Moreover, several studies have been initiated to show the efficacy of combining new technologies to facilitate safety signals. A study showed that there is a broad scope of social media conversations, such as those on Twitter by spreading awareness posts of health-related topics with integrating drug safety signals from the USA FDA Adverse Event Reporting Systems [30]. Through distinct mobile applications, these advancements represent a broader shift towards utilizing technology for enhanced ADR reporting. This underscores the exciting potential for further advancements beyond mobile applications in the context of identifying ADRs and strengthening pharmacovigilance efforts. By exploring diverse technological innovations, we can develop an understanding of ADRs, ultimately leading to safer and more effective health practices.

Patients feel the need to explain their ADRs in their own words with accurate explanations, and some have poor knowledge of medical terms, which makes understanding difficult [31]. With consideration of these factors, an option to include free written text when describing ADRs has been introduced as a solution in apps. A recent academic review confirmed that patient reports include more detailed and descriptive new ADR information due to this feature [32]. Moreover, spontaneous patient ADR reporting has complemented healthcare professional reporting as well by including reports with similar relevance to clinical information and additional information on the impact of ADRs on daily life. Further, mobile applications enable patients to report ADRs in real time, increasing the timeliness and volume of ADR data collected. Some studies are illustrating how patient-reported ADRs, through apps, improve pharmacovigilance by capturing new, detailed, and patient centred data that healthcare professionals might not always observe. This includes reports on the personal impact of ADRs on daily life and aids in creating a more comprehensive safety profile of medications. Additionally, patient reports have proven valuable in identifying rare ADRs that may go unreported in traditional healthcare settings, ultimately enhancing drug safety monitoring [26, 33–35].

Another study shows that apps have taken measurements to improve the status of reporting through simplicity and quality [25]. Features like saving the users' previous login data have created a user-friendly platform for follow-up report submissions [13]. Moreover, mobile apps have been introduced in both developed countries (WEB-RADR apps) and low and middle-income developing countries (Med safety apps). To minimise underreporting in African countries, implementations such as access to free internet hotspot, and free SMS alerts in selected healthcare facilities have been introduced [33]. To optimize user engagement, visually attractive interfaces have been designed. Most of the apps were designed using English as the native language. Therefore, new advanced features for the user to select their preferred language have been developed [22]. In every

instance, steps have been taken to secure the privacy and the anonymity of the user. This is a very important feature within apps that help maintain patient rights along the way. Mobile apps, such as the WEB-RADR and Med Safety apps, adhere to stringent data protection regulations, such as GDPR (General Data Protection Regulation) in the European Union and similar privacy laws in other regions, ensuring that users' personal information is safeguarded [33, 36]. Data encryption techniques are commonly employed to protect user data during transmission and storage [36]. Additionally, secure login methods, including two-factor authentication, are often incorporated to enhance security [13]. User reports are frequently anonymized or de-identified to maintain anonymity before being processed or shared with relevant authorities [36]. These features help mitigate concerns regarding the confidentiality of patient data while maintaining trust and encouraging active participation in ADR reporting.

Despite the effectiveness of mobile apps, it is important to focus on the drawbacks as well. Various strategies have been introduced to improve the loopholes faced while using mobile apps. For instance, drop-down menus were introduced as a strategy to save reporting time [34], although the study shows that people prefer to explain ADRs in their own words instead of having to choose them from a drop-down menu [22]. Some users might be hesitant to report because of the Privacy and security concerns. Most of the time, language barriers have been accounted in multi-cultural countries. In order to report through apps, devices should be available with the required storage and space capacities. However, in low-income countries, the limitation of devices has become a potential challenge [25]. These shortcomings highly affect the reporting rates. Thus, the issue of underreporting remains a challenge in pharmacovigilance, regardless of the geographical location.

However, the observation that conventional methods generated more ADRs compared to mobile applications is significant and reflects several potential factors. Knowledge and awareness regarding mobile applications may be limited among healthcare professionals and patients, which explains why conventional methods are more familiar among them. Further, many healthcare settings in resource limited areas face infrastructure challenges like the availability of smartphones and internet access [37]. On some occasions, concerns over data privacy and security, complex app designs and regular updates of the app also discourage users from using these mobile applications [32].

In terms of study limitations in this systematic review, the search was limited to two databases. Therefore, there's a chance for some relevant studies to be missed. The search was based on studies published in English or where an English translation was available. The overall risk of bias across the studies indicates notable concerns, particularly in terms of performance and selection biases. The high risk of performance bias due to lack of blinding is a consistent issue that may affect the reliability of the findings. The unclear randomization and allocation methods further suggest that the results should be interpreted with caution. Efforts to improve study designs by incorporating proper blinding and randomization techniques are essential for enhancing the validity and reliability of future ADR research. Further, studies included in this review were limited to certain countries and did not have global coverage. More apps such as ADR PVPI, Bijwerking etc., have been introduced and are used to report ADRs. However, currently, there aren't any studies that have been conducted to qualify the inclusion criteria of this systematic review [25, 35, 38]. Moreover, some apps have been introduced, but the relevant researchers contain ongoing data with study protocols to be done in the future [14, 39]. Some do not contain a comparison group to clarify the efficacy accurately [33, 35, 40]. Therefore, those studies have been excluded from the studies included in the systematic review. Some of the studies included have a limited selected study population, but ADRs can always differ depending on the geographical location and the ethnicity of the people.

The findings of this systematic review indicate that mobile applications are a promising tool for enhancing both the quantity and quality of ADR reporting. This review underscores their potential to streamline pharmacovigilance by enabling real-time data submission, improving completeness, and increasing user engagement through patient-centred features. This has significant implications for strengthening drug safety monitoring, especially in resource-limited settings where traditional reporting methods face barriers like limited access to infrastructure. The integration of mobile apps not only supports timelier ADR detection but also enables more detailed and patient-oriented data collection, which can be critical for identifying rare and severe ADRs. While the review also highlights ongoing challenges such as underreporting, data privacy concerns, and language barriers, the overall potential of mobile apps to transform pharmacovigilance is evident, suggesting that expanding their use beyond current levels could enhance global healthcare safety practices.

Conclusion

New mobile apps have been introduced as a complementary route to promote spontaneous reporting of ADRs. These apps offer a user-friendly platform, empowering both patients and healthcare professionals to report

first-hand experiences directly to pharmacological databases. The reports submitted through apps featured better quality while resulting in more timely submissions. Although the overall quality of app submissions was better, reporting rates could benefit from further enhancement. More studies are needed to explore the problems encountered with mobile apps for ADR reporting. Hence, qualitative studies with in-depth interviews are needed to identify problems and facilitate fine-tuning mobile apps for much more efficient reporting.

Acknowledgements
Special thanks to the publisher of the mERA checklist. It was reproduced from Guidelines for reporting of health interventions using mobile phones: mobile health (mHealth) evidence reporting and assessment (mERA) checklist, by Smisha Agarwal, Amnesty E LeFevre, Jaime Lee, Kelly L'Engle, Garrett Mehl, Chaitali Sinha, Alain Labrique, BMJ 2016;352:i1174, 21 Jan 2025] with permission from BMJ Publishing Group Ltd

Authors' contributions
Author contributions P.H.L. wrote the first and subsequent drafts. P.H.L. and M.T.M. reviewed the articles, extracted the data and validated them. P.L.G.C.L developed the ideas, supervised, reviewed and edited. All the authors read and approved the final article.

Funding
No funds or grants were received.

Data availability
The datasets generated and analysed during the current study are available in the Google Drive repository. (https://drive.google.com/drive/folders/1Boo8zdty4i9_bMFUnXeaMGLrf5LwwL3z?usp=drive_link) These datasets contain the minimal information required to interpret, replicate, and build upon the findings presented in this article. Access to the data is unrestricted, supporting transparency and reproducibility in research.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Pharmacology, Faculty of Medicine, University of Ruhuna, Galle, Sri Lanka.

Received: 28 June 2024 Accepted: 18 March 2025
Published online: 13 May 2025

References

1. Organization WH. Safety of medicines: a guide to detecting and reporting adverse drug reactions: why health professionals need to take action. Geneva: World Health Organization. 2002.
2. Madhushika M, et al. Evolution of adverse drug reactions reporting systems: paper based to software based. Eur J Clin Pharmacol. 2022;78(9):1385–90.
3. Montastruc F, et al. Adverse drug reaction reports received through the mobile app, VigiBIP®: a comparison with classical methods of reporting. Drug Saf. 2018;41:511–4.
4. Defer G, et al. Société Francophone de la Sclérose en Plaques (SFSEP). Adverse drug reaction reporting using a mobile device application by persons with multiple sclerosis: a cluster randomized controlled trial. Drug Saf. 2021;44(2):223–33.
5. Tomašev N, et al. A clinically applicable approach to continuous prediction of future acute kidney injury. Nature. 2019;572(7767):116–9.
6. Danysz K, et al. Artificial intelligence and the future of the drug safety professional. Drug Saf. 2019;42:491–7.
7. Linder JA, Haas JS, Iyer A, Labuzetta MA, Ibara M, Celeste M, Getty G, Bates DW. Secondary use of electronic health record data: spontaneous triggered adverse drug event reporting. Pharmacoepidemiol Drug Saf. 2010;19(12):1211–5. https://doi.org/10.1002/pds.2027.
8. Hazell L, Shakir SA. Under-reporting of adverse drug reactions. Drug Saf. 2006;29(5):385–96.
9. Page MJ, et al. Updating guidance for reporting systematic reviews: development of the PRISMA 2020 statement. J Clin Epidemiol. 2021;134:103–12.
10. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials. 1996;17(1):1–12. https://doi.org/10.1016/0197-2456(95)00134-4. PMID: 8721797.
11. Bahk CY, et al. Increasing patient engagement in pharmacovigilance through online community outreach and mobile reporting applications: an analysis of adverse event reporting for the essure device in the US. Pharmaceut Med. 2015;29(6):331–40.
12. Montastruc F, et al. Adverse Drug Reaction Reports Received Through the Mobile App, VigiBIP(®): A Comparison with Classical Methods of Reporting. Drug Saf. 2018;41(5):511–4.
13. Kuchya SK, Shrivastava SJIJBCP. Comparison of methods of submission of suspected adverse drug reactions to the ADR monitoring centers in India. 2017;6:2032–7.
14. Defer G, et al. Adverse drug reaction reporting using a mobile device application by persons with multiple sclerosis: a cluster randomized controlled trial. 2021;44:223–33.
15. Oosterhuis I, et al. Characteristics, quality and contribution to signal detection of spontaneous reports of adverse drug reactions via the WEB-RADR mobile application: a descriptive cross-sectional study. 2018;41:969–78.
16. Seaneke SK, et al. First results from the lessons learnt from the deployment of the Med Safety App for reporting adverse drug reactions in Ghana. Digit Health. 2023;9:20552076231211276.
17. Bahk CY, et al. Increasing patient engagement in pharmacovigilance through online community outreach and mobile reporting applications: an analysis of adverse event reporting for the Essure device in the US. Pharm Med. 2015;29:331–40.
18. Franchini M, et al. Essure permanent birth control, effectiveness and safety: an Italian 11-year survey. J Minim Invasive Gynecol. 2017;24(4):640–5.
19. Lalani C, et al. Reporting of death in US food and drug administration medical device adverse event reports in categories other than death. JAMA Intern Med. 2021;181(9):1217–23.
20. Bergvall T, Norén GN, Lindquist M. vigiGrade: a tool to identify well-documented individual case reports and highlight systematic data quality issues. Drug Saf. 2014;37(1):65–77.
21. Defer G, et al. Dedicated mobile application for drug adverse reaction reporting by patients with relapsing remitting multiple sclerosis (Vigip-SEP study): study protocol for a randomized controlled trial. Trials. 2018;19(1):174.
22. de Vries ST, et al. Factors influencing the use of a mobile app for reporting adverse drug reactions and receiving safety information: a qualitative study. Drug Saf. 2017;40(5):443–55.
23. Hazell L, Shakir SA. Under-reporting of adverse drug reactions : a systematic review. Drug Saf. 2006;29(5):385–96.
24. Med safety app: an international mobile tool for drug safety. Uppsala reports 2020 17 March 2020; Available from: https://www.uppsalareports.org/articles/med-safety-app-an-international-mobile-tool-for-drug-safety. Cited 1996.
25. Fukushima A, et al. Smartphone-based mobile applications for adverse drug reactions reporting: global status and country experience. BMC Med Inform Decis Mak. 2022;22(1):118.

26. van Hunsel F, de Waal S, Härmark L. The contribution of direct patient reported ADRs to drug safety signals in the Netherlands from 2010 to 2015. Pharmacoepidemiol Drug Saf. 2017;26(8):977–83.
27. Wilson K, et al. An evaluation of the feasibility and usability of a proof of concept mobile app for adverse event reporting post influenza vaccination. Hum Vaccin Immunother. 2016;12(7):1738–48.
28. Parracha ER, et al. Mobile apps for quick adverse drug reaction report: A scoping review. Pharmacoepidemiol Drug Saf. 2023;32(1):19–27.
29. Appiah B, et al. Factors that influence the intention to use mobile phone caller tunes for patient reporting of adverse drug reactions: a qualitative study. Ther Adv Drug Saf. 2019;10:2042098619871190.
30. Li Y, Jimeno Yepes A, Xiao C. Combining social media and FDA adverse event reporting system to detect adverse drug reactions. Drug Safety. 2020;43:893–903.
31. de Vries ST, et al. Interest in a mobile app for two-way risk communication: a survey study among European healthcare professionals and patients. Drug Saf. 2018;41(7):697–712.
32. Inácio P, Cavaco A, Airaksinen M. The value of patient reporting to the pharmacovigilance system: a systematic review. Br J Clin Pharmacol. 2017;83(2):227–46.
33. Kiguba R, et al. Facilitators and barriers to uptake of the med safety mobile app for adverse drug reaction reporting by health workers in uganda: a qualitative study. Drug Saf. 2023;46(6):565–74.
34. de Vries ST, et al. Use of a patient-friendly terms list in the adverse drug reaction report form: a database study. Drug Saf. 2019;42(7):881–6.
35. Prakash J, et al. "ADR PvPI" Android mobile app: report adverse drug reaction at any time anywhere in India. Indian J Pharmacol. 2019;51(4):236–42.
36. de Vries ST, et al. Factors influencing the use of a mobile app for reporting adverse drug reactions and receiving safety information: a qualitative study. Drug Saf. 2017;40:443–55.
37. Seaneke SK, et al. First results from the lessons learnt from the deployment of the Med Safety App for reporting adverse drug reactions in Ghana. Digital Health. 2023;9:20552076231211276.
38. Labh R, Gupta S, Gupta R. Advances in pharmacovigilance in India: role of mobile application. Indian J Med Spec. 2020;11(3):124–6.
39. Kiguba R, et al. Effectiveness of the Med Safety mobile application in improving adverse drug reaction reporting by healthcare professionals in Uganda: a protocol for a pragmatic cluster-randomised controlled trial. BMJ Open. 2022;12(7): e061725.
40. Pierce CE, et al. Recommendations on the Use of Mobile Applications for the Collection and Communication of Pharmaceutical Product Safety Information: Lessons from IMI WEB-RADR. Drug Saf. 2019;42(4):477–89.
41. Agarwal S, LeFevre AE, Lee J, L'engle K, Mehl G, Sinha C, Labrique A. Guidelines for reporting of health interventions using mobile phones: mobile health (mHealth) evidence reporting and assessment (mERA) checklist. bmj. 2016;352:i1174.

Publisher's Note