



Factors that Lead to Stagnation in Direct Patient Reporting of Adverse Drug Reactions: An Opinion Survey of the General Public and Physicians in Japan

Aki Kitabayashi¹ · Yusuke Inoue²

Received: 15 December 2021 / Accepted: 14 March 2022 / Published online: 27 March 2022
© The Drug Information Association, Inc 2022

Abstract

Objective Data collection from patients regarding adverse drug reactions (ADRs) in Japan have greatly stagnated. To examine the factors underlying this stagnation, we investigated the awareness of and opinions about the direct ADR reporting system among the general public and physicians.

Methods We conducted questionnaire surveys of general citizens and physicians throughout Japan and included the following topics: (1) awareness of the direct patient ADR reporting system, (2) attitude toward this system, (3) reasons for negative opinions of this system, (4) awareness of the physician ADR reporting system, and (5) respondent demographics.

Results Responses were received from 845 citizens and 300 physicians. Most citizens (83.7%) were unaware of the direct patient ADR reporting system. While many citizens supported the idea of the system, 26.7% expressed negative/hesitant opinions. Prominent reasons for negative/hesitant opinions included the patient burden for reporting their own ADRs and expectations that physicians would make reports. Among the general public, the physician reporting system was better known (43.6%). In contrast, many physicians were aware of the direct patient ADR reporting system (65.0%). However, only 46.7% of physicians had supported this system; prominent reasons for disapproval included skepticism toward patients' judgment and the regulatory authorities' assessment.

Conclusion Our survey suggests that stagnation in the reporting system is affected by the attitudes of the general public and physicians. In addition to government measures to improve awareness and eliminate reporting hurdles, the involvement of medical staff in patient reporting needs to be improved.

Keywords Direct patient reporting · Adverse drug reactions · Physician–patient relationship · Patient and public involvement · Questionnaire survey

Introduction

Prior to the approval of pharmaceutical agents, information such as adverse drug reactions (ADRs) is generally limited. Therefore, for the early discovery of ADRs and appropriate use of pharmaceutical agents, post-marketing surveillance is absolutely essential. In the past, this information was obtained from pharmaceutical companies and health-care professionals. These conventional sources of information have recently been supplemented by the introduction of systems in which information on ADRs is gathered directly from the patients and general citizens who experience them. Information collected directly from patients has some drawbacks, such as limitations of details and quality [1]. However, gathering information directly from patients has the great advantage of collecting more information faster and

✉ Yusuke Inoue
yinoue@g.ecc.u-tokyo.ac.jp

Aki Kitabayashi
2243514481@edu.k.u-tokyo.ac.jp

¹ Department of Computational Biology and Medical Sciences, Graduate School of Frontier Sciences, The University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639, Japan

² Department of Public Policy, The Institute of Medical Science, The University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639, Japan

providing new information and perspectives about ADRs in a way otherwise unavailable (e.g., information about the severity and impact of ADRs on daily life) [1]. In the European Union, a 2012 legal revision led to the formulation of a system for gathering information on ADRs from patients and the general public in member states [2, 3]. Regulatory authorities receive more than 100,000 reports of ADRs annually, and relevant information is utilized for the safe use of pharmaceutical agents [4]. In the USA, a system for patients to directly report ADRs to regulatory authorities was established in 1993 [5] and continues until today [6].

However, unlike the situation in Europe and the USA (which are members of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, along with Japan), similar efforts have been only partially successful in Japan and other Asian countries. In Japan, in addition to conventional reports from pharmaceutical companies and healthcare professionals (doctors and pharmacists, etc.), direct patient reports of ADRs were first formally received in March 2019 [7] (direct ADR reporting was initiated on a trial basis in 2012 [8]) based on the systems used in Europe and the USA. The information collected in the reports is processed and analyzed by the pharmacovigilance unit of the regulatory authority and the causal relationship between ADRs and medications is evaluated. Any relevant information is utilized for improving the safety of pharmaceutical agent use. However, only about 100 such patient-filed reports are received annually [8]. Compared to the number of reports filed in the EU (European Union) as an example, this is far behind that of the EU (Table 1), even if we take into account the difference in the population sizes (the EU has approximately 4 times as many citizens as Japan) [9]. In South Korea, of the approximately 1.6 million total ADR reports made from 1989 to 2018, only about 8% were

filed by consumers [10]. In Malaysia and the Philippines, although the receipt of direct reports from patients began in the 2000s [11], detailed statistics regarding these reporting systems are unknown. Overall, there are few reports on this topic in Asian nations where this type of stagnation in patient ADR reports is highly likely.

It is important to understand the reasons underlying this situation and to identify factors that can bring about improvement. The level of awareness and the opinion of the general public about the direct patient ADR reporting system are important aspects in this regard. In addition, it is imperative to assess the awareness levels and the attitude of physicians who treat the patients as well. This is because of the following reasons: first, patients' attitudes are potentially affected by physician–patient relationships. Patients may believe that publicly reporting problems with pharmaceutical drugs may be detrimental to the physician–patient relationship. In fact, as a number of studies have indicated, patients may hesitate to report ADRs to regulatory authorities because they worry about how their physician may react [1, 5, 12]. Particularly in East Asia, there is little history of separation of dispensaries from medical practice; physicians are deeply involved in the adoption or non-adoption of pharmaceuticals administered during treatment. In such cases, patients may hesitate to report their ADRs and may expect their physicians to report their ADRs to the government.

Second, the attitude of healthcare professionals and specifically the manner in which physicians receive patients' self-reporting of ADRs to the government may affect patients' knowledge and behavior. For example, physicians often advise patients on problems that occur during the treatment process. According to a European study, when prescribing highly novel pharmaceuticals, prescribers and pharmacists are expected to play a strong role in educating patients regarding the ADRs and their role in reporting any ADRs [13]. Conversely, if physicians are ignorant of this type of reporting system or view it unfavorably, patients may lose the opportunity to learn about this type of reporting or may not report ADRs despite knowing about the system. Thus, it is necessary to assess whether healthcare professionals encourage or discourage reporting of ADRs by patients. The attitudes of not only the patients but also the physicians need to be examined in this regard.

In this study, we aimed to identify issues and areas needing improvement in direct patient reporting of ADRs using questionnaire-based surveys of the general public and physicians. The surveys in the present study reflect the state of Japan just before the COVID-19 pandemic; the results may be valuable for considering the attitudes of physicians and the general public regarding reporting of ADRs following ongoing COVID-19 vaccinations.

Table 1 Japan–Europe comparison of the number of adverse drug reaction reports from patients

Year	Number of reports ^a	
	Japan	EU
2015	186	48,782
2016	50	47,238
2017	84	90,385
2018	73	172,762
2019	159	159,860

^aFigures for Japan are for the fiscal year, and figures for Europe are from January to December. Figures in “EU” represent the number of adverse drug reactions (ADRs) reported to EudraVigilance. Note that following the launch of the new EudraVigilance system in November 2017, the figures in 2017, 2018, and 2019 include reports of non-serious suspected adverse drug reactions. See Kitabayashi et al. for further details [9]

Materials and Methods

Study Design and Participants

Citizens and physicians were surveyed as follows. Responses from citizens were obtained via self-administered questionnaires sent by mail. The survey period lasted from March 12 to April 2, 2020. For the participants, we used monitors from Nippon Research Center, Ltd., a major Japanese general survey company with a long-track record in public surveys. This company monitors 70,000 registered individuals, who were publicly recruited through general media and other outreach. Among them, a total of 1400 men and women aged 20–79 years were selected at random to match the general Japanese demographics.

For physician surveys, responses were obtained from self-administered questionnaires hosted on a website. The survey period lasted for seven days, from February 13 to 19, 2020. The survey targeted physicians specializing in internal medicine and surgery from among the 83,000 physicians registered with PLAMEDplus. PLAMEDplus is a private service that provides safety information about drugs to Japanese clinicians. The participating physicians were divided into three approximately similar-sized groups based on age (20–39 years, 40–59 years, ≥ 60 years). Questionnaires were distributed to a total of 1,039 physicians (595 in internal medicine and 444 in surgery).

Questionnaires

The questionnaire items included the following topics: (1) awareness of the direct patient reporting system for ADRs, (2) opinions about the direct patient reporting system for ADRs (approve, somewhat approve, somewhat disapprove, disapprove), (3) reasons for negative opinions about the system, (4) awareness of the physician reporting system for ADRs, and (5) basic characteristics of respondents. Multiple responses were permitted in (3). Participants could choose from a list of sample responses or respond in their own words if none of the given responses were applicable. The questionnaire was developed based on comments from experts with deep knowledge of pharmaceutical risk management and pre-tested with the support of collaborators (Acknowledgements).

Data Analysis

Statistical analysis was conducted using the IBM SPSS Statistics v.25 package. Pearson's chi-squared test was used to compare the public and physician groups in terms of awareness of the direct patient reporting system and approval/disapproval

of the system. Additionally, we also compared the responses to these items among the physician specialties (internal medicine and surgery). Statistical significance was set at $p < 0.05$.

Ethical Issues

Our survey falls outside the scope of the Japanese government's Ethical Guidelines for Medical and Health Research Involving Human Subjects, and there are no national guidelines in Japan for social and behavioral research. Therefore, our study was carried out in accordance with the Ethical Principles for Sociological Research of the Japan Sociological Society, which does not require an ethical review. All survey participants gave their consent to participate in the anonymous surveys, and the authors did not obtain any personal information about the participants. The respondents agreed to participate after they were informed about the purpose of the study and their right to quit the survey. They were provided with the option "I don't want to respond" for all questions.

Results

Respondent Characteristics

The characteristics of the respondents are listed in Table 2. A total of 845 members of the general public responded (response rate: 60.4%). The survey was sent to 700 men and 700 women and the completion rates were 55.6% and 65.1%, respectively. Approximately 40% of the general public respondents visited hospitals during the survey period (all reasons included). We received responses from 300 physicians (184 in internal medicine and 116 in surgery; response rate: 28.9%). In addition, among the physicians in internal medicine, 62 physicians reported that their primary area of expertise was psychiatry. Although 90% of the responding physicians were men, this figure roughly reflects the current sex ratio among physicians in Japan (approximately 80% (78.1%) of physicians in Japan are men) [14]. Across Japan, 63.6% of physicians work in hospitals, while 31.7% work in clinics. Compared to these nationwide figures, the present study included a slightly elevated percentage of respondents working in clinics. The ratio of internists to surgeons among respondents was roughly equivalent to the national average (internists:surgeons = 1.6:1).

Awareness of and Opinion About the Direct Patient Reporting System

Awareness of the System (General Public and Physicians)

Approximately 80% of the general public responded that they had never heard of the system (Table 3). Another

Table 2 Demographic characteristics and clinical background of survey respondents

Characteristics	General public (n = 845)		Physicians (n = 300)		
	Number	(%)	Number	(%)	
Sex	Male	389	46.0	270	90.0
	Female	456	54.0	30	10.0
Age, years	20–30	201	23.8	99	33.0
	40–50	316	37.4	103	34.3
	60–	328	38.8	98	32.7
Residential area ^a	Cities (central)	368	43.6	175	58.3
	Cities (peripheral)	382	45.2	106	35.3
	Other areas	87	10.3	16	5.3
Level of education	Middle school or below	37	4.4	0	0.0
	High school graduate	435	51.5	0	0.0
	College or above	364	43.1	300	100.0
Previous hospital visit	Currently visiting	339	40.1	–	–
	Within the past 1 year	250	29.6	–	–
	≥ 1 year ago	249	29.5	–	–
Workplace (physicians only)	General clinic (no beds)	–	–	137	45.7
	Hospital	–	–	161	53.7
	Other	–	–	2	0.7
Specialty (physicians only)	Internal medicine (including psychiatry)	–	–	184	61.3
	(Psychiatry)	–	–	(62)	(20.7)
	Surgery	–	–	116	38.7
Career length (physicians only)	≤ 15 years	–	–	117	39.0
	16–30 years	–	–	107	35.7
	31 years–	–	–	76	25.3
No. of patients received (physicians only)	≤ 100	–	–	73	24.3
	101–300	–	–	90	30.0
	301–	–	–	137	45.7

^aFor physicians, the scale of the municipality where their workplace is located

14.0% of the general public responded that they had heard of the system but knew little about it. These results show that awareness of the system and its specifics need to be improved. In contrast, more than 60% of the physicians responded that they were aware of the system. This result indicates differences between physicians and the general public regarding the direct patient reporting system and low awareness of the system among the general public (who are responsible for reporting their own ADRs). Thus, the general public and physicians demonstrated a significant difference in their answers to this question (Table 3(i)). The increased level of awareness was true for physicians in all areas of expertise (data not shown in the tables; 67.9% in internal medicine and 60.3% in surgery responded that they were aware of the system). Notably, the awareness of psychiatrists was particularly low compared to other internal physicians (43.5% in psychiatry responded that they were not aware of the system, $p = 0.017$).

Opinions About the System and Reasons for Opinions (General Public and Physicians)

More than half of the general public supported the direct patient reporting system for ADRs. Approximately 80% of these respondents chose “There are things that only those patients taking the drug would understand” as the reason for a positive opinion (Table 4). This exact reasoning was the basis for establishing the direct patient/public adverse reaction reporting system, suggesting that many people may identify with this policy. There was also a high level of awareness about contributing to others (“I want my experiences to help other people”) and about the incompleteness of the reports by healthcare professionals and pharmaceutical companies. Additionally, about 40% of people were also interested in knowing more about what they had experienced.

In contrast, among all of the general public respondents, roughly 30% disapproved of or were unsure about the idea

Table 3 Awareness and opinion about direct patient reporting of adverse drug reactions (ADRs) (general public and physicians)

(i) Awareness of system for patients to report their own suspected ADRs directly to the government			
	I have heard of it and am familiar with it	I have heard of it but know little about it	I have never heard of it
General public (<i>n</i> = 845)**	20 (2.4%)	118 (14.0%)	707 (83.7%)
Physicians (<i>n</i> = 300)**	60 (20.0%)	135 (45.0%)	105 (35.0%)
(ii) Opinion about the system for patients to report their own suspected ADRs directly to the government			
	Approve/somewhat approve	Unsure	Disapprove/somewhat disapprove
General public (<i>n</i> = 845)**	614 (73.4%)	194 (23.2%)	29 (3.5%)
Physicians (<i>n</i> = 300)**	140 (46.7%)	95 (31.7%)	65 (21.7%)
(iii) Awareness of physicians' obligation to report suspected ADRs to the government			
	I have heard of it and am familiar with it	I have heard of it but know little about it	I have never heard of it
General public (<i>n</i> = 845)**	49 (5.8%)	319 (37.8%)	476 (56.4%)
Physicians (<i>n</i> = 300)**	130 (43.3%)	140 (46.7%)	30 (10.0%)

**A significant difference was found by Pearson's chi-squared test ($p < 0.01$)

Table 4 Reasons for approving the direct patient reporting of adverse drug reactions (ADRs) (for the general public who responded positively when asked whether they approve of the direct ADR reporting system; refer to Table 2(ii))

General public (612)	
“Certain conditions or factors would be understood only by those patients consuming the medicines”	477 (78.0%)
“I want my experiences to help other people”	339 (55.2%)
“Reports by healthcare professionals and companies can be biased”	291 (47.6%)
“I want to know more about what I experienced”	234 (38.2%)
Other	2 (0.3%)

General public: excludes two non-respondents

of the system. Among physicians, an even larger percentage of respondents (more than half) were not in support of the direct patient reporting system. One in five physicians responded that they disapproved of the system. The general public and physicians demonstrated a significant difference in their answers to this question (Table 3(ii)). Differences in specialty did not seem to affect the physicians' responses to this question ($p = 0.859$).

The reasons for the negative responses were as follows (Table 5). Among the general public, the most common reason (chosen by more than half of respondents) was, “I don't think patients can suitably assess their own ADRs.” The next most common reason was “It's a major burden for patients to make their own reports,” followed by, “I think reports should be made by physicians and medical staff.” The percentage of the general public who felt that “Reports should be made by physicians and medical staff” increased with the age of the respondents (data not shown in table; 48.2% of respondents aged ≥ 60 years chose this answer). As a reason for the negative assessment of the direct patient reporting system among physicians, 70% of respondents chose “I don't think patients can suitably assess their own ADRs.” Other reasons included “I don't think regulatory authorities can suitably assess patient reports,” “I don't think regulatory authorities can suitably

assess treatment,” and “I think reports by medical staff are sufficient.”

Awareness of and Attitudes Toward Physicians' Obligation to Report ADRs

About 90% of physicians were aware of their legal obligation to report ADRs (Table 3(iii)). Differences in specialty did not seem to affect the physicians' responses to this question ($p = 0.785$). The general public was more aware of the physician reporting system for ADRs (approximately 40%) than of the direct patient reporting system. The percentage of the general public who disapproved of the direct patient reporting system did not differ greatly between those who were aware of the physician reporting system (unsure: 22.2%, opposed: 2.7%) and those who were not aware of it (unsure: 23.7%, opposed: 4.1%).

In contrast, among physicians who disapproved of direct patient reporting, a difference was observed in attitudes between physicians who were aware of the physician reporting system (unsure: 30.0%, opposed: 21.9%) and those who were not aware of it (unsure: 50.0%, opposed: 20.0%). Thus, physicians with little interest in their own reporting system were more inclined to disapprove of the direct patient reporting system.

Table 5 Reasons for disapproving the direct patient reporting of adverse drug reactions (ADRs) (for the general public and physicians who responded negatively to a question about whether they approved of the direct ADR reporting system; refer to Table 2(ii))

Physicians (160)		General public (218)	
“I don’t think that the patients can suitably assess their own ADRs”	112 (70.0%)	“I don’t think patients can suitably assess their own ADRs”	125 (57.3%)
“I don’t think that the regulatory authorities can suitably assess patients’ reports”	46 (28.8%)	“It’s a major burden for patients to make their own reports”	86 (39.4%)
“I don’t think that the regulatory authorities can suitably assess treatment”	32 (20.0%)	“I think reports should be made by physicians and medical staff”	74 (33.9%)
“I think reports by medical staff are sufficient”	22 (13.8%)	“I think the system has little recognition and is ineffective”	49 (22.5%)
“I don’t think patients can make reports on their own”	15 (9.4%)	“I don’t think patients gain any benefit from making their own reports”	36 (16.6%)
		“I think reports should be made by the pharmaceutical company who manufactured the drug”	
		“I don’t think regulatory authorities can suitably assess patient’s ADR reports”	
Other	10 (0.6%)	Other	20 (9.2%)

General public: excludes five non-respondents

Discussion

In Japan, the number of direct patient reports of ADRs has stagnated. In the present study, we examined the acceptance of this reporting system among the general public and physicians. Our results showed that awareness of the system is low, particularly among the general public. Although many members of the general public supported the concept of this system, some were skeptical about the utility of this system. Knowledge of the direct patient reporting system for ADRs was more common among physicians than among the general public; however, more than half of the physicians took a skeptical stance toward this system.

Based on these results, we report the following findings. Awareness of the direct patient reporting system for ADRs was extremely low among both the general public and physicians, implying that increasing awareness of the system may be beneficial for improving ADR report rates. The percentage of respondents who approved of the direct patient reporting system was high among the general public; therefore, being aware of the system may lead to a change in behavior, which may in turn lead to increased reporting of ADRs.

It is noteworthy that awareness of the system for patients was far lower among the general public (16.4%) than that for healthcare professionals (43.6%). One highly likely explanation is that government efforts to publicize the system have been ineffective, although the general public may also be responsible for the low level of interest in this issue. Some citizens may feel that ADRs and other aspects of healthcare are best left to healthcare professionals. In particular, the proportion of the general public who felt that “Reports should be made by physicians and medical staff” and the skepticism regarding the direct reporting system increased

with age. Therefore, as per these findings, increasing awareness of the system alone may not lead to more widespread reporting.

Many physicians professed a negative opinion toward the reporting system. As this result shows, many physicians with a negative attitude toward the system had little confidence in patients’ assessments of ADRs. This view is consistent with the above-mentioned tendency of patients and the general public to depend on physicians. However, this may also imply that patients’, as well as the general public, experiences with pharmaceutical drugs may be restricted to discussions with their physicians, and may not be shared with others.

It is concerning that even physicians did not show sufficient interest in their role in reporting ADRs associated with pharmaceutical agents. This result has also been reported in previous studies. A 1990s Japanese literature report indicated that physicians had little interest in the Adverse Drug Reaction Monitoring System (hereafter, “the Monitoring System”), the forerunner to the physician reporting system for ADRs [15]. In this case, even if problems with pharmaceutical drugs are suspected during a patient’s treatment, not only will the physicians not suggest to the patient that they report the problems, the physicians themselves may not report the problems.

Prospects

Merely transplanting the direct patient reporting system developed in the West to countries in other regions does not ensure that the system will be established smoothly. In Japan, a certain amount of time and considerable government effort may be necessary for a culture to take root in

which patients make their own voices heard. Solutions for dealing with this issue are not currently being discussed in Japan, and further policy developments are unclear.

We propose that improving awareness of the direct patient reporting system and eliminating hurdles in reporting by consumers and patients are necessary measures to resolve this issue. Currently, the reporting of ADRs associated with pharmaceutical drugs requires the provision of detailed information regarding the patients themselves and the treating physicians; this may be an obstacle to reporting. Analyzing ADR patterns requires the collection of a significant amount of data. Data collection on that scale will likely require a re-evaluation of the procedure for submitting information and revamping this procedure to make it user-friendly for the members of the general public and patients.

As discussed earlier, the current system for reporting ADRs may be ineffective and limited by the physician–patient relationship. Physicians are responsible for the treatment of patients in their charge. Separate from these responsibilities, however, physicians should also shoulder roles with regard to pharmaceutical drug-associated ADRs. These roles include alerting other patients and society as well as supporting the use of the patient direct reporting system. These social roles of physicians likely need to be enforced and publicized anew. In fact, in Japan, ADR reporting and/or pharmacovigilance are treated in a very limited manner in the Core Curriculum for Medical Education and on the National Medical Examination. Therefore, we need to place more emphasis on pharmacovigilance in medical school education so that physicians are more interested in reporting ADRs.

In addition to the support of physicians, the involvement of other stakeholders in spreading awareness about this system may be of great significance. For example, a closer relationship between patients and other medical staff such as pharmacists would greatly facilitate the sharing of information on therapeutic drugs during treatment. In general, physicians play a significant role in both patient treatment as well as medicine disbursement in East Asia. For example, similar to the situation in Japan, the separation of dispensaries from medical practice was not an easy task in Korea and Taiwan; in these countries, physicians traditionally handle prescribing as well as dispensing medicines [16]. In a 1990s Japanese literature report, interest in and awareness of the monitoring system was higher among pharmacists than among physicians [15]. In addition, of all ADR reports filed with the authorities by healthcare professionals in 2017, approximately 70% were filed by pharmacists; physicians filed less than 20% of the ADR reports [17]. Therefore, support by pharmacists (such as by increasing awareness of the direct reporting system among the general public) may be effective for enabling the general public to report their own ADRs.

In addition to medical staff, the government needs to make efforts to improve the system. The overall responses of the general public and physicians in the present study indicate that the significance and value of assembling patients' experiences are not shared by the society. The government must clarify the values and aims behind its policies to the society and make efforts to increase awareness of the system among the general public and physicians, such as by publicizing the system through patient groups and placing more emphasis on pharmacovigilance in medical school education; this will then prompt the public to use the direct ADR reporting system.

The recent COVID-19 situation may be a good opportunity for many people to consider the personal relevance of risks of pharmaceutical drugs. In Japan, although COVID-19 vaccinations have been implemented, ADRs have been reported on a scale and with a frequency that was unforeseen in clinical trial results [18, 19]. For example, the frequency of fever (38 °C or higher) and headache (in clinical trials vs. post-marketing) is 40.1% vs. 61.9% for fever and 47.6% vs. 67.6% for headache, respectively [18, 19]. This re-confirms the significance of post-market surveillance. The current situation has served as an opportunity for the general public to consider the risks of pharmaceutical therapeutic agents. However, there are still a lack of support mechanisms for gathering pertinent patient data on ADRs and sufficient involvement of the government and experts who will utilize the information gathered in this process.

The present study has several limitations. This study was conducted considering factors, such as the clinical expertise of physicians, age groups, and sex. However, the sample size was small. Additionally, a more detailed study that considers the diversity of individual participants is likely necessary. For example, the target population for this study was limited to those who were 20 years old or older, which is the legal age of adulthood for Japanese people, so we have not fully investigated ADR reporting by minors. Even so, this study enabled us to identify fundamental differences in awareness about the direct ADR reporting system between the physicians and the general public. Furthermore, it was surprising that there was a particularly low level of awareness among psychiatrists about the direct patient reporting system. It is difficult at this point to give a definitive view on this; however, it is suspected that many psychiatrists may feel that there are many symptoms for which there are no effective medications, and they may find it difficult to draw a line between the person's subjective symptoms and the effects of medications. As the risk of ADRs can be a troubling problem in psychiatry, more detailed studies are needed in the future.

Conclusion

We examined Japan as a case study for evaluating the decrease in direct patient reporting of ADRs. We found that the traditional physician–patient relationship may be a causative factor for the lower awareness and poor utilization of the reporting system. In addition to improving awareness of the system and attitudes toward it among the general public and physicians, reporting hurdles need to be removed and the roles of government authorities, and medical staff, including the involvement of other healthcare professionals in addition to physicians, needs to be improved.

Acknowledgements

We would like to thank Dr. Hiroaki Yanagawa of Tokushima University, Mr. Jugo Hanai of Yaku-Hi-Ren, Dr. Sachiko Juman of Mukogawa Women's University, and members of the Department of Public Policy, The Institute of Medical Science, The University of Tokyo, for their help in preparing and evaluating this questionnaire. We would like to express our sincere gratitude for their kind assistance.

Author Contributions

Both AK and YI conceptualized the original study and prepared the article draft; both authors approved the final version of the manuscript.

Funding

This work was supported by a grant from the Ministry of Health, Labour and Welfare Research Project for Research on Policy Planning and Evaluation [20HA2011]. The sponsors played no role in the study design, collection, analysis, and interpretation of data, writing the report, or in the decision to submit the article for publication.

Declarations

Conflict of interest

The authors have nothing to disclose.

References

- Inácio P, Cavaco A, Airaksinen M. The value of patient reporting to the pharmacovigilance system: a systematic review. *Br J Clin Pharmacol*. 2017;83:227–46.
- Health Action International. Direct patient reporting in the European Union - A snapshot of reporting systems in seven member states. <https://digicollections.net/medicinedocs/documents/s22088en/s22088en.pdf>. Accessed 8 Dec 2021.
- Borg J-J, Aislaitner G, Pirozynski M, et al. Strengthening and rationalizing pharmacovigilance in the EU: where is Europe heading to? A review of the new EU legislation on pharmacovigilance. *Drug Saf*. 2011;34:187–97.
- European Medicines Agency. Annual Report 2019. https://www.ema.europa.eu/en/documents/annual-report/2019-annual-report-european-medicines-agency_en.pdf. Accessed 8 Dec 2021.
- Yamamoto M, Nakayama T. Drug information for the patients in Western countries: patient reporting of adverse drug reactions [in Japanese]. *Pharmac Lib Bull*. 2008;53:190–202.
- Food and Drug Administration. FDA Adverse Event Reporting System (FAERS) Public Dashboard. <https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard>. Accessed 8 Dec 2021.
- Ministry of Health, Labour and Welfare, Pharmaceutical Safety and Environmental Health Bureau. Patient adverse drug reaction reporting [in Japanese]. Ministry of Health, Labour and Welfare, Pharmaceutical Safety and Environmental Health Bureau (ed). Safety Information for Pharmaceuticals and Medical Devices No. 363, 2019:3–5.
- Pharmaceuticals and Medical Devices Agency. Patient adverse drug reaction reporting: Summary of trials and future developments [in Japanese]. <https://www.pmda.go.jp/files/000228628.pdf>. Accessed 8 Dec 2021.
- Kitabayashi A, Inoue Y. Current status and challenges of the system for adverse drug reaction reporting from patients and consumers in japan: a comparison with the situation in Europe [in Japanese]. *Jpn J Clin Pharmacol Ther*. 2021;52:117–25.
- Kim S, Yu YM, You M, et al. A cross-sectional survey of knowledge, attitude, and willingness to engage in spontaneous reporting of adverse drug reactions by Korean consumers. *BMC Public Health*. 2020;20:1527.
- Leán R. Patient participation in pharmacovigilance. Dissertation, University of Groningen, 2018.
- Yamamoto M, Kubota K, Okazaki M, et al. Patients views and experiences in online reporting adverse drug reactions: findings of a national pilot study in Japan. *Patient Prefer Adherence*. 2015;9:173–84.
- Januskiene J, Segec A, Slattery J, et al. What are the patients' and health care professionals' understanding and behaviors towards adverse drug reaction reporting and additional monitoring? *Pharmacoepidemiol Drug Saf*. 2020;30:334–41.
- Ministry of Health, Labour and Welfare. Statistics of Physicians, Dentists and Pharmacists 2018. [in Japanese]. <https://www.mhlw.go.jp/toukei/saikin/hw/ishi/18/dl/kekka-1.pdf>. Accessed 8 Dec 2021.
- Takahashi R, Tsukada T, Tomonaga F. Results of a survey on the attitudes of physicians and pharmacists regarding the Adverse Drug Reaction Monitoring System. *Jpn J Clin Pharmacol Ther*. 1990;21:279–80.
- Jeong H-S. Pharmaceutical reforms: implications through comparisons of Korea and Japan. *Health Policy*. 2009;93:165–71.
- Agawa H. Let's actively cooperate! -Safety information reporting from healthcare professionals to PMDA. Presented at the 20th Annual Meeting of the Japanese Society of Drug Informatics Minato-ku, Tokyo, 8–9 July 2017. <https://www.pmda.go.jp/files/000219085.pdf>. Accessed 8 Dec 2021.
- Juntendo University COVID-19 vaccine Research Office. Materials 2; Focused research conducted in the early phase after the initiation of COVID-19 vaccination (cohort study), the interim report of aggregated data of health observation diary (No. 11). Presented at the 66th Annual Health Sciences Council Vaccination Committee Adverse Drug Reaction Study Group, 2021 15th Pharmaceutical Affairs and Food Sanitation Council Pharmaceutical Affairs Committee Pharmaceuticals Safety Measures Department Safety Measures Investigation Committee (Jointly hosted) Chiyoda-ku, Tokyo, 4 August 2021. https://www.mhlw.go.jp/stf/shingi2/0000208910_00028.html. Accessed 8 December 2021. Conference minutes (August 4). https://www.mhlw.go.jp/stf/newpage_20348.html. Accessed 8 Dec 2021.

19. Takeda Pharmaceutical Company Limited, Package Inserts of “COVID-19 Vaccine Moderna Intramuscular Injection”. (7th Ed. Nov, 2021) https://www.pmda.go.jp/PmdaSearch/iyakuDetail/ResultDataSetPDF/400256_631341EA1020_1_07. Accessed 8 Dec 2021.