Consumer reporting of adverse drug reactions

Systems that allow patients to report side effects of the drugs they are taking have yielded valuable information for improving drugs safety and health care

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Any new medication or therapy that has been approved for market authorization after extensive tests and trials is supposed to be efficient and, more importantly, safe. Yet, drug safety is not guaranteed: Many medications can still cause unexpected side effects that only come to light after approval. One of the worst examples is thalidomide, which caused severe birth defects and malformations in babies born to mothers who had taken the drug as a sedative against morning sickness and nausea in the late 1950s and 1960s.

The thalidomide scandal was not only a wake-up call to improve drug testing and increase the requirements for safety, but it also made clear that a system for monitoring post-market drug safety was required. Many countries established reporting systems for adverse drug reactions to inform authorities about unexpected side effects. Today, spontaneous post-market reporting is the principle means for registering side effects and other problems with medical products on the market and it helps authorities to quickly react to any problems. Nonetheless, there is still much room for improvement given that adverse drug reactions are one of the leading causes of morbidity and mortality in health care.

The first reporting systems for adverse drug effects introduced in the 1960s were usually reserved for healthcare professionals and provided no venue for patients to report safety issues. Consumers in only a few countries, including the USA, Canada, and New Zealand, were able to directly submit information on adverse effects to their national authorities. In Europe, this has only changed during the past decade when the Netherlands, Denmark, the UK, and Sweden opened their reporting systems to consumers. In 2012, the EU passed legislation that requires all member states to introduce so-called consumer reporting systems. Experts in the field think that this is a major step in the right direction to improve drug safety. “It had been known for some time that suspected adverse drug reactions were underreported, meaning that including consumer reports was inevitable in order to monitor the post-market safety of medicines”, commented Andreas Vilhelmssoon, researcher at the Division of Social Medicine and Global Health Department at Lund University in Sweden.

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Indeed, there was initial reluctance in Europe to open their system to non-experts [1]. Would reports by consumers be at all useful without verifying the symptoms described? Would consumer reports just swamp the system with useless information? “There was quite a bit of debate amongst professionals about whether this was the way to go—whether patients would know how to report, whether they would be reporting the right thing, or whether they would be swayed by the media so you get masses of reports of one particular event because it came up as an issue on TV”, said Tony Avery, professor of Primary Health Care at the University of Nottingham, UK.

But there were also good reasons to move ahead; underreporting was a well-recognized issue. Healthcare professionals often lack the time to examine their patients thoroughly and sometimes even fail to inform the authorities of serious adverse drug reactions. Tapping into patients’ experience directly was seen as a means to increase the rate of reporting and to improve signal detection [1]. Other reasons to open reporting systems to consumers include a general tendency in health care to take patients’ experience and reports more seriously, and to value their views. “There was a societal move towards getting consumers and patients more involved in their care and towards a feeling that they had a perspective to play”, Avery explained.

The Netherlands and Denmark opened their reporting systems to consumers in 2003, and the Dutch pharmacovigilance center Lareb set out a pilot study. “Our aim was to see if we could work with patient reports at all and whether they contained enough medical information to use them in pharmacovigilance”, explained Florence van Hunsel, who coordinates the signal detection process at Lareb. The results were overwhelmingly positive and removed all doubts. “After the pilot study, our whole center thought this is something we need to do. We need to involve the public in adverse
drug reaction reporting, so let’s go for it”, van Hunsel said.

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In the UK, the “Yellow Card System”, through which doctors report adverse drug reactions to the Medicines and Healthcare products Regulatory Agency (MHRA), was opened to consumer reports in 2005. Swedish patients have been able to submit reports to the Medical Products Agency (MPA) since 2008. Even before that, a Swedish non-profit organization named KILEN collected reports from consumers who wished to share their experiences with medical products. Both the reports from the UK Yellow Card System and from KILEN have been thoroughly analyzed quantitatively and qualitatively, and the conclusions were very similar to those of the Dutch group: Consumer reports are a valuable addition to reports from healthcare professionals [2-4].

The Netherlands, Sweden, UK, and Denmark have pioneered consumer reporting, but the process has been a bit slower in other European countries. Italy allows consumers to report adverse effects since 2004, but the response from the public, at least in the first few years, was negligible—possibly because reports had to be sent by post. Other European countries opened their systems to consumer reporting in the 2000s, including Croatia, the Czech Republic, Malta, and Switzerland; Norway followed in 2010 and France in 2011. In some countries (Belgium, Denmark, Italy), consumer organizations were involved in the development. In Belgium, for example, the consumer organization Test-Aankoop has been collecting reports since 2006 and has been transferring information to the national Federal Agency for Medicines and Health Products since 2007. Most countries, however, only implemented consumer reporting in 2012 or 2013 after the European pharmacovigilance legislation was adopted.

The percentage of adverse drug reaction reports coming from consumers varies considerably between countries: Those that have established consumer reporting systems earlier generally have higher reporting rates [5]. Today, a considerable proportion of all reports in the Netherlands, the UK, Sweden, and the USA come from patients, and consumers are playing an increasingly important role in detecting new adverse drug reactions. “In almost all signals, patients were contributing considerably. It’s a mix of health care professionals and patients”, said van Hunsel, referring to the situation in the Netherlands. “Not the messenger is important, but the message”, she added.

Consumer reports played a substantial role in detecting an association between the Pandemrix influenza H1N1 vaccine and narcolepsy after the Swedish MPA had received numerous reports from both healthcare professionals and consumers. In another case, consumer reports helped Lareb uncover that patients may not recover normal sexual functioning for months or even years after they stopped taking serotonin reuptake inhibitors to treat depression [1]. Sexual dysfunction was known as a side effect of these drugs, but it was assumed that the problems would vanish with time. As many patients are probably quite reluctant to speak to their physicians about their sexual life, the anonymity of consumer reporting may have helped them to report and thus to uncover the long-term effects of these drugs.

In the Netherlands, patients also played an important role in discovering a connection between pathological gambling and the use of the dopamine agonist pergolide for treating Parkinson’s disease [1]. Another example are reports of “electric shock sensations” in association with serotonin reuptake inhibitors by both patients and healthcare professionals in the Netherlands and the UK, “but the patients really showed us how severe the reaction could be”, van Hunsel said. The same reaction was later found to be associated with one of the newer drugs on the market, duloxetine, a combined serotonin and norepinephrine reuptake inhibitor. “For duloxetine, we had a signal mainly based on patient reports. We found that signal a lot earlier because patients were involved”, van Hunsel said. It again demonstrated the value of consumer reports as physicians might reject such peculiar reactions that are difficult to comprehend as an outsider. “Physicians, when being told about electric shock sensations, might just dismiss it as being a strange thing the patients are talking about and not put in a report”, Avery explained.

There is similarity and overlap in reports by patients and healthcare professionals [6], but there are also notable differences. Consumer reports can, for instance, include detailed descriptions that are usually not found in reports by healthcare professionals, and this is exactly why they are valuable [4,7]. Healthcare professionals and patients may have different motivations for reporting. Physicians mainly report novel potential side effects, side effects of newly marketed drugs, and serious or severe adverse reactions [7]. “[I]n addition to altruistic motives, non-recovery and the severity of the reaction is the main reason for reporting”, van Hunsel said about the reasons why patients show interest in reporting their symptoms. “Not having recovered is a constant reminder to the patient”.

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Even if patients report well-known drug reactions, their reports are nonetheless informative. By way of example, van Hunsel quoted muscle problems that can arise as an adverse reaction to statins. “Many health care professionals would not report that anymore because it is in the drug label. But the patients’ reports we received really gave some insight into how severe these muscle problems can become. We learned what kind of impact these symptoms can have on the quality of life and daily activities. This information is very relevant to us even though it is about a well-established adverse drug reaction”, she said.

Moreover, patients’ reports often contain more details compared to reports by professionals. This is already reflected in the length of the reports—according to a study that analyzed reports received by the UK Yellow Card System between October 2005 and September 2007, patients used an average of 58 words to describe the suspected reaction, whereas healthcare professionals used 16 [4]. In one report, for example, a patient goes into detail of describing how a hypoglycemic reaction at night got her to the accidents and emergency department, that a
doctor was called out to her house twice, how the reaction did not wake her up, and how dangerous that might have been, had family members not been with her. A physician on the same reaction to the same drug reads: “Erratic diabetic control” [4].

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There are also differences in regard to what is considered as a severe adverse reaction. “Health care professionals and regulatory authorities have their own definitions, like having a kidney or liver failure or being hospitalized”, Avery said. For patients, it is also important how drug reactions affect their daily life, their social interactions, and their job performance. These effects can have quite an impact, even if the reaction would not classify as “serious”, according to the criteria of the Council for International Organizations of Medical Sciences (CIOMS).

“I can’t make any plans as I used to”, wrote one patient; “I have been unable to work for over 18 months and started part time again”, another reported, and a third patient described herself as “harming myself, my pets and husband…” [4]. “Consumer reports can be of significant importance since they describe the burden of adverse drug reactions for individuals, which is a major health component that is missing from public health estimates of disease burden in a population”, Vilhelmsson commented. What matters in the end is what matters to the patient. “When you go through the filter of the health care professionals, you will lose important information. Physicians will make their own judgement whether they think this is important enough to report. Putting it into the hands of the patients allows for a new avenue of identifying potential problems”, Avery said.

Just how much this filter applies becomes evident from a study of doctor–patient interactions when patients experience side effects from taking statins [8]. A total of 650 adults with self-reported adverse drug reactions took part in the study. Among those who met literature criteria for adverse drug reactions [8], most reported that their physicians denied a possible connection between symptoms and medication. For example, in 51% of the cases where patients talked to a physician about neuropathy symptoms, the physician dismissed the potential link to statins. If physicians do not even acknowledge known side effects, it is even more likely that they will fail to detect and report unexpected ADRs. In the most benign scenario, a physician may just want their patients to continue taking their medicine. However, “we need to move away from this paternal approach. If a patient complains about muscle ache after taking statins, for example, it is easy to downplay that”, Avery commented.

The value of the patient perspective in pharmacovigilance is now broadly acknowledged. The challenge now is to improve the system to get the maximum out of patient data. A key aspect of improving the reporting system is raising public awareness. Approximately 17% of the population in the Netherlands and 8.5% of the population in the UK know that consumers can report adverse drug reactions, and in other countries, the numbers are even lower [1]. “They need to know that we take them seriously. And we need to aid them in reporting”, van Hunsel commented. To this end, pharmacovigilance centers could, for example, form partnerships with patient organizations [1]. To maintain the efforts and encourage patients also means providing feedback about how the information in their reports will be used. “It is important to make sure that they don’t have unrealistic expectations. Some may be astounded that they reported a side effect and the drug is still being used. They may not realize that it takes many reports to even get to a level where a side effect makes it into a patient leaflet or a warning letter to doctors”, Avery said.

In addition, even if patient reports are a complement to professional reports in detecting new signals, their value goes beyond just the quantitative aspect. The detailed descriptions of their daily experience with medical products are a resource that could add a new quality to health research. “We feel that this is one of the main aspects that patients can bring to pharmacovigilance”, van Hunsel said. Patient reports can thereby yield useful insights for the healthcare community. “Depending on exactly how the questionnaire is structured, consumer reports can contain valuable information on how and why they are prescribed a medical treatment, if it is off-label use or for the wrong reasons or maybe in violation with the guidelines”, Vilhelmsson explained.

“Since these reports also include how the medicine is affecting the user in his or her daily life, they also contain valuable information regarding adherence to medicines and how treatment procedures may be optimized. Consumer reporting may be one vital way to safeguard public health by collecting as many views and experiences as possible to get a more comprehensive picture of pharmaceutical treatment”. In addition, the detailed information in consumer reports could also be important for other patients experiencing similar adverse drug reactions. “As a pharmacovigilance community we have to think about how to use this information and how to make it available to the public”, van Hunsel said.

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Taking the perspective and experiences of patients more seriously has been a general trend both in medical practice and in clinical research for many years now. “It is now considered very important to have patient and public involvement in research. It is acknowledged that it does add value because you are more likely to be focusing on the things that matter to patients”, Avery commented. Expanding consumer reporting in health care both geographically and in terms of harvesting information from these reports is not just part of this general trend but could help to improve drug safety and health care through active involvement of the end users. Ultimately, medical treatments are for the benefit of the patients, and listening to what they have to say seems an obvious thing to do.

References
learnt from the Dutch and Swedish systems.

Drug Saf 38: 337–347


