White Paper

Driving adoption of digital tools in post-marketing safety studies: patients and investigators weigh in

Alyssa Palmer, Consultant, Consulting Services, IQVIA, APAC
Shriharsha Sarkar, Senior Principal, Consulting Services, APAC

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Introduction

In-depth interviews provide keys to increasing uptake of user-friendly apps that derive patient outcomes, safety data and market insights

The issue

Biopharma is rapidly introducing mobile digital tools to capture data in clinical and real-world research – including patient-centered outcomes, safety data and adverse event reports. These tools (often smart-

phone apps) promise to streamline data recording from patients and providers, speed data delivery, and review, improve quality, and reduce the number of face-to-face patient-investigator interactions needed (especially critical in the age of COVID-19).

Mobile health (mHealth) developers worldwide are churning out these digital tools to solve the shortcomings of traditional data collection methods. However, these are dependent on patients, investigators and healthcare workers adopting the innovations, as well as regulators accepting them as better than the current, largely manual, processes.

Digital health tool adoption is challenging worldwide; it is especially pertinent in hotbeds of mHealth activity such as China, South Korea and the wider Asia Pacific. With a target population of 4.3 billion and growing number of government-mandated post-marketing surveillance (PMS) requirements, Asia Pacific offers vast opportunities. From identifying the right motivations for patients, investigators and regulators to adopting culturally tailored data collection applications, the focus on patient-reported outcomes (PRO) and safety data digital tools is here to stay.

Furthermore, well-designed apps and survey methods can also give biopharma and device companies insights into market trends and consumer needs, increasing the return-on-investment in PMS and real-world evidence research.

This article explores the key considerations for digital tools uptake by patients and physicians and how Biopharma and clinical research partners can improve the design or selection of direct-to-patient data collection platforms in China, South Korea and other Asia Pacific markets.

Troubles with traditional methods

Post-market surveillance data traditionally has been collected via real-world patient studies or by spontaneous reporting: medical staff collecting information about patient drug use and adverse events through observations and interviews. These interactions may occur while the patient is in hospital, or during routine visits between patients and providers.

In Asia Pacific, five key markets have government-led post-marketing guidelines: Japan's Pharmaceuticals and Medical Devices Agency (PMDA), Republic of Korea's Ministry of Food and Drug Safety (MFDS), China's National Medicinal Products Administration (NMPA, previously known as CFDA), Philippines' Food and Drug Administration (FDA) and India's Central Drugs Standard Control Organisation (CDSCO).

While PMS regulations are well-defined and regulated in Japan and South Korea, the practice is evolving in countries like China and Philippines. In 2017, China's NMPA began increasing post-marketing surveillance oversight, including a stricter review processes and higher standards for timely real-world adverse event reporting, with penalties for non-compliance. This raised the stakes regarding the efficiency and thoroughness of traditional reporting processes.

PHARMACOVIGILANCE

A field dedicated to analyzing and managing the risk posed by healthcare products once they have entered the market. Traditionally, post-marketing safety data or events are collected through spontaneous reporting by healthcare professionals, patients, or other individuals in the healthcare lifecycle. Complementing this process are post-marketing surveillance (PMS) studies mandated by a regulatory authority or proposed by Biopharma, Medical Device or Consumer Health manufacturers as part of their risk management plan.

PHARMACOVIGILANCE GAPS

Despite established guidelines in most countries, including China, there are deep problems in capturing real-world data about product safety. A study of 12 countries conducted by Hazell and Shakir reported that only 6% of adverse drug reactions are captured through the current pharmacovigilance system[1]. This is an alarmingly low percentage, that demonstrates the urgent need for better tools and greater adoption to detect safety signals.

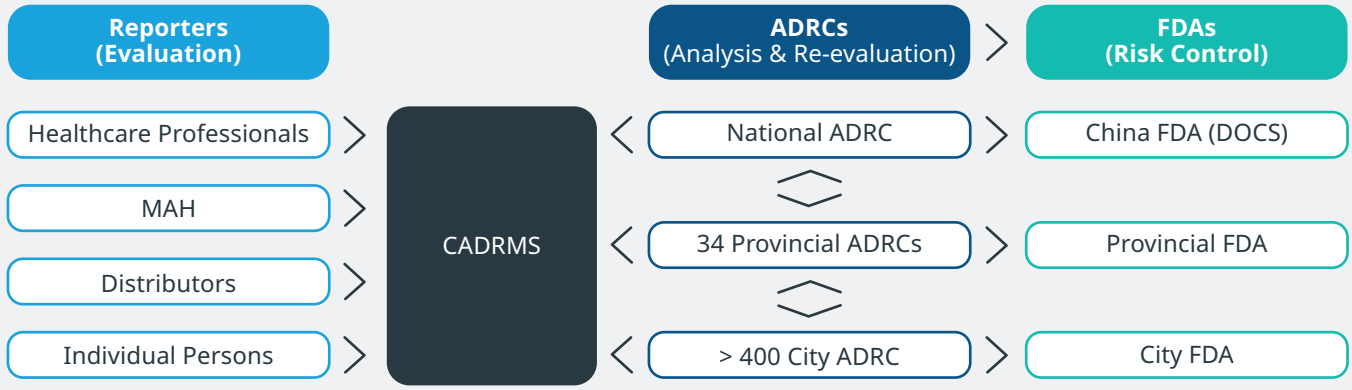
POST-MARKETING SURVEILLANCE STUDIES IN BRIEF

PMS studies or safety studies monitor the safety, efficacy and quality of approved products in the real-world setting [3, 4]. Safety is measured in the form of serious/ non-serious adverse drug reactions (ADRs) or risks associated with the exposure of the product, while efficacy is determined based on long-term clinical outcome.

DRUG INTENSIVE MONITORING STUDIES

As of 2011, NMPA introduced a preliminary guideline for drug intensive monitoring (DIM) to observe safety effects of new drugs entering the China market[5]. The primary focus of PMS studies, otherwise known as DIM studies in China, are to monitor the safety, efficacy and quality of approved products in the real-world/ routine clinical setting.

Figure 1: Overview of Pharmacovigilance in China



Source: Pharmacovigilance in China: Current Situation, Successes and Challenges, Li Zhang et.all.

A major drawback with the PMS studies is that physicians and patients have little incentive to participate: data collection is time consuming and tedious with little financial, medical or personal benefit in return. In addition, because most data is collected during infrequent patient visits, relevant information about symptoms, co-morbidities, self-medication, and changes in condition may not be accurately recorded into the health information systems.

Though digital solutions exist in the market, a bottleneck in adoption is an industry-wide reluctance to view patient-reported data as being objective. While there has been significant progress in psychometric validation of patient reported outcomes/ questionnaires, which are well accepted in estimating quality of life in clinical trials, there is a lack of inclusivity in the post-marketing space for evaluating long term safety and effectiveness of drugs.

The result: an unclear picture of patient safety trends, potential risk of not receiving license renewal and misinformation about product safety. Many events are missed entirely because patients neglect to report them or deem them irrelevant. Even if reported, the pharmacovigilance process used in some countries and the internal processes of Biopharma requires multiple manual steps that deter interest and acceptance.

A direct-to-patient app for PRO and symptom reporting, complimented with a physician portal for reviewing the data in real time, has the potential to bridge the gap in several ways:

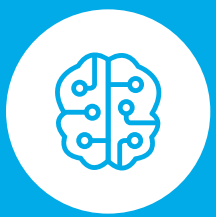
1. Increase compliance in reporting adverse drug reactions.
2. Pique patient interest in observational trial participation, especially when patient engagement with the physician is low.
3. Provide an opportunity for increased patient education on disease and symptom management from a trusted source (their physicians).
4. Create a secure and easy-to-use channel to track ad-hoc and on-call discussions.
5. Instill confidence in patients that their disease is being tracked and prioritized by healthcare providers.

Design thinking in mHealth development or selection

Too often companies create apps and platforms in isolation, making assumptions about what users will want. The result? A solution that may look exciting but does not meet user needs. Such costly mistakes can be avoided by engaging end users in development or having a thorough due diligence process while selecting a solution. This is much more likely to result in a tool that is user-friendly, reliable, robust and delivers value.

Design thinking is a customer-centric approach to problem-solving, where teams engage with customers, to understand their needs and the obstacles they face in dealing with a product or process. This helps the teams develop empathy with their audience and can new solutions or feature to make a product more valuable and engaging for customers.

The key to design thinking, (or human centered design) is observing customers in their own environments to see how they perform tasks, and to talk to them about their pain points and what they'd like to change. That feedback is used to brainstorm relevant solutions, and to iterate on those ideas through continued feedback loops, until a fully formed product emerges.



One study conducted by IBM on the economic impact of design thinking found that teams who employ design thinking in product design achieve faster project execution, develop products that better meet users' needs, and are able to accelerate time-to-market, all of which translates into significant financial returns. The study also found that these projects see lower rates of failure resulting from teams that make assumptions about what customers want without incorporating their feedback in the process.[2]

IQVIA pharmacovigilance case study

At IQVIA, we tested a prototype patient symptom reporting app in conjunction with a prototype physician review portal, using WeChat as an entry point, to gather feedback on the uptake of this digital tool in PMS studies in China. The IQVIA project teams then conducted in-depth interviews using a formal interview guide to gauge user responses and identify opportunities to improve the models.

The interviews generated compelling insights into the behaviors, attitude, and digital experiences of patients and physicians, which informed iterations in the platform and app designs, and provided insights into how the tools could be used by biopharma and device companies to improve marketing and engagement strategies across Asia Pacific.

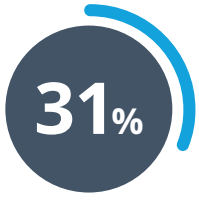
#1 DIGITALLY SAVVY PATIENTS & PHYSICIANS SEEK CONVENIENCE AND ACTIONABLE INSIGHTS

Patients interviewed ranged in age from 35 to 60, had participated in medical research or observational studies in the past five years, and were living with a chronic illness of diabetes, asthma and rheumatoid arthritis. All of them used digital tools on a regular basis, suggesting a level of comfort with technology that is consistent with data about the broader consumer population in China.

used WeChat (social messaging and lifestyle platform)

used apps daily, including Didi, Hungry, taxi services (food and transport)

used email



used hospital apps

They were also apprehensive about drug safety and side effects related to being a part of clinical research. Most said they trusted their doctors and Biopharma companies to keep them safe, and believed that the benefits of feeling better, losing weight and/or free medication outweighed any concerns.

Physicians, on the other hand, are facing technology fatigue with an overload of applications associated with medical products and disease management. To better manage time and patient information, they prefer having a one-stop solution for each study, rather than having to deal with multiple non-interoperable applications.

Dashboards that are well-designed, customizable and insight-generating were viewed as an important way to digest the influx of patient data during the study conduct. A key concern for safety data collection is the reporting of serious adverse events within a strict timeline of 24 hours from the point of identification. When asked, the investigators shared that daily review of dashboards that flagged serious adverse events (SAE) in a timely and appropriate manner is not a challenge; which was otherwise presumed by Biopharma as a burden to physicians and hospital staff.

#2 POOR GUIDANCE LEADS TO UNDER-REPORTING WHICH LIMITS INSIGHTS

Providing patients with an easy real-time solution to encourage an increase in consistency and prompt questionnaire and symptom reporting was a primary goal. The interviews underscored that need:

- Patients consistently showed confusion about when and what to report
- Investigators were frustrated by the inconsistency in reporting process and structure
- A common misconception for adopting a patient-centered reporting model by Biopharma is the over-reporting of symptoms or potential adverse events that might undermine the product prematurely.

Contrary to the belief by Biopharma about over-reporting, nearly 60% of the 16 investigators interviewed said that under-reporting is a problem in their clinical research vs. 33% who had concerns

about over-reporting. They said that patients often forgot adverse events by the patient visit, and are frequently uncertain about the timing, severity and frequency of these events.

Patients said that lack of clarity about what they were expected to report and to whom contributed to under-reporting. Many said that if the symptom was mild, for example discomfort from low blood sugar or a minor cold, they would deal with it on their own and not mention it to their physicians.

They were more likely to report significant or surprising symptoms, such as leg numbness or blisters around injection sites, as soon as they occurred or at the physician visit. They were also more likely to report symptoms that their physicians specifically discussed. As one 60-year-old patients with rheumatoid arthritis said: "If I am told by the doctor about the side effects of the medication and experience a symptom he mentioned, I will go back to this doctor. If I experience other symptoms that he did not mention, I will go to other doctors for the other symptoms."

This inconsistency in what and when symptoms are reported underscores the need for a more structured real-time digital reporting solution. An app that can be accessed around-the-clock would make it easier for patients to report symptoms in real-time and could provide clarity about what to report and what details to include through educational features or pop-up guidance tools.

It could also reduce patients' concerns about overburdening the physician with their complaints. Several patients reported reticence to report minor symptoms, including one who said: "The doctor is so busy, when do they have time (to respond to me)?"

#3 EXCITEMENT AND CONCERNS OF DIGITAL ADOPTION TO BE ADDRESSED

Both patients and investigators had a positive response to the idea of using a digital solution. 94% of patients and 85% of physicians said they would be interested in using an app and platform like the one demonstrated for symptom reporting in a study. Though both groups also reported some concerns.

60% of the 16 investigators interviewed said that under-reporting is a problem in their clinical research vs. 33% who had concerns about over-reporting

Patients: The patients interviewed currently use a combination of apps, diaries, and face-to-face meetings to communicate their symptoms to their physicians. Most (88%) believe the current reporting process is convenient, but they saw potential benefits from an all-digital approach. These included:

- *Speed of communication "like chatting"*
- *with the physician*
- *Convenience of capturing relevant information outside of the clinical setting*
- *Reassurance that someone will see the message*

While patients largely understood the goals of the tool, they also shared the feedback that after going through the entire process, if they didn't get a prompt response they would be disappointed. Other concerns included:

- *Lack of clarity on what to report and how to phrase things*
- *Uncertainty about who will read the feedback*
- *Uncertainty about who will respond and how quickly*
- *Preference to shut off phones outside of work*

To mitigate some of these issues, they suggested including a phone-in or voice-to-text option offering opportunities to connect directly with their physicians via the app; and providing disease information that is highly specific to their condition.

Investigators: Most of the investigators surveyed had either seen or expect to see uptake of digital solutions in other aspects of clinical research, and thought it was a viable solution to address issues related to adverse event reporting. As one investigator said: "Now is the tech era, and eventually everyone will use digital solutions."

However, some investigators felt that not all indications would be suitable for digital reporting. They were concerned that older patient groups may be less likely to adopt technology as part of their healthcare routine. They also worried that lack of confidence with technology, lack of education, and medical conditions such as poor eyesight and limited digital mobility could be barriers preventing patients from using these tools correctly. In these cases, a hybrid approach was thought to be a viable alternative, giving patients multiple ways to engage with the app (i.e. voice, voice-to-text), and/or multiple channels (app, phone, face-to-face) to report these events.

Some of their suggested additions to the solution included:

- *Automated reminders to report symptoms*
- *Opportunities to provide more detail and images to explain symptoms*
- *Automatic language translation*

New iterations: forging ahead

There is a positive trend to re-focus on post-marketed drug surveillance, possibly linked to a key change in country regulatory authorities accepting international data for medical product registration[6]. However, as the safety profile of the product might not be specific to the local population, it would increase the need to collect more safety data through PMS studies or improved spontaneous reporting methods. This calls for a change in the safety reporting framework; patient centered outcomes and patient enabled safety reporting by leveraging on the growing mHealth industry.

All the insights discussed above are critical in designing and/or validating digital tools to consider value-driven features that directly respond to the needs of the end-users. They highlight patients' and physicians' general familiarity and comfort with using apps, and the potential for including mhealth technology in traditional safety data collection and pharmacovigilance models.

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About the authors

LAKSHMI SAMEERA DUMPALA
Regional Strategy Senior Manager, Observational Clinical Project Manager, IQVIA, APAC

As a Regional Strategy Senior Manager in the Real World research team, Lakshmi leads discussions around data gaps and evidence generation needed for product launch, safety management, market access and marketing with top pharmaceutical clients in key markets like China and South Korea. With over 6 years at IQVIA she acquired a background in pricing, proposals, budget negotiation, contracting and partnerships management. Lakshmi has since initiated many internal projects to keep IQVIA's competitive edge in meeting the unique needs of the Asia Pacific market.

Lakshmi is currently pursuing her MSc in Public Health and holds a BSc in Biomedical Engineering from National University of Singapore.

CONTACT US
79 Anson Road #19-01
Singapore 079906
iqvia.com