

## Review

# Barriers to adverse drug reaction reporting in Malaysia: a narrative review based on theoretical domains framework

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Received December 10, 2020; Accepted April 20, 2021.

## Abstract

### Objectives

This review aims to determine the common barriers to adverse drug reaction (ADR) reporting in Malaysia based on theoretical domains framework (TDF).

### Methods

Three online databases, PubMed (Medline), Scopus and Web of Science, were searched from 2000 to 2020 to identify related quantitative and qualitative studies.

### Key findings

Eleven articles were reviewed – nine quantitative and two qualitative studies. Three domains from TDF were identified as the most common: (1) knowledge, (2) skills and (3) environmental context and resources. Lack of awareness of an ADR reporting system, lack of clinical and ADR knowledge and lack of time were identified as the main barriers. Additionally, assumption of healthcare professionals (HCPs) of ADR to be too insignificant or too well known and unavailability of the ADR form were also reported as barriers for reporting an ADR.

### Conclusions

The findings from this narrative review could be useful for the policymakers in planning strategies at the national level to improve the reporting rate of ADR in Malaysia. It is necessary to promote and publicize pharmacovigilance activities and to enhance communication and engagement between the Malaysian ADR Advisory Committee and the HCPs and consumers. There is also a need to increase training and continuous education related to ADR and pharmacovigilance system and making ADR reporting compulsory for all HCPs.

**Keywords:** adverse drug reactions; under-reporting; barriers

## Introduction

According to the World Health Organization (WHO), an adverse drug reaction (ADR) is defined as ‘a response to a drug that is noxious and unintended and occurs at doses normally used in humans

for the prophylaxis, diagnosis, or therapy of disease, or modification of any physiological function’.<sup>[1]</sup> Whereas a serious adverse reaction is defined by the Food and Drug Administration (FDA)<sup>[2]</sup> as ‘the patient outcome that leads to death, life-threatening (real risk of

dying), hospitalisation (initial or prolonged), disability (significant, persistent, or permanent), congenital anomaly, or required intervention to prevent permanent impairment or damage'.

ADRs are ranked as the fourth to sixth leading causes of death with fatal ADRs being as high as 0.32% cases.<sup>[3]</sup> Hospital admission leads to massive economic burden on society and especially on patients.<sup>[4]</sup> A study reported that 5% of hospital admissions in the United States are due to an ADR.<sup>[5]</sup> In Sweden, ADR was found to have caused 12% of admission to an internal medicine clinic.<sup>[6]</sup> On top of that, 10–20% of the inpatients may experience at least one ADR during their hospital stay.<sup>[7, 8]</sup> Some patients may experience only minor symptoms due to ADRs; however, ADRs can cause death in as many as 0.1–0.3% of the hospitalized patients.<sup>[9, 10]</sup>

WHO-initiated program called the International Program for Adverse Drug Reaction Monitoring plays a vital role in global drug safety monitoring.<sup>[11]</sup> FDA and European Medicines Agency collaborate with WHO to improve pharmacovigilance by ensuring sharing of information among these health authorities to increase advance regulatory in protecting global community.<sup>[12]</sup> One of the initiatives is the spontaneous reporting system that plays an essential role in identifying ADR.

The Malaysian healthcare system comprises government-led, subsidized public services and privately funded services which provide healthcare services for all Malaysian populations. The Malaysian Adverse Drug Reactions Advisory Committee (MADRAC) was established under the Drug Control Authority and is responsible for performing activities of pharmacovigilance on medicinal products registered in Malaysia.<sup>[13]</sup> The pharmacovigilance system was established in 1987, while Malaysia became a member of the WHO Program for International Drug Monitoring in 1990.<sup>[13, 14]</sup> Pharmacovigilance incorporates the detection, assessment, understanding and prevention of ADRs. Hence, this system compiles drug-related injuries and provides warning or withdrawal recommendations of pharmaceutical agents.<sup>[15]</sup> ADR reporting is an essential responsibility of healthcare professionals (HCPs) to protect patients from harm during the post-marketing surveillance period.<sup>[16]</sup> HCPs are encouraged to report all suspected ADRs.<sup>[14]</sup> Detecting and reporting a rare or delayed ADR could contribute to the advancement of patient care.<sup>[17]</sup> In 2017, consumer ADR reporting procedure was first launched in Malaysia. However, consumers' awareness of ADR reporting has been identified as a challenge.<sup>[18]</sup>

There are more than 60 000 registered doctors and 12 000 pharmacists in Malaysia.<sup>[19, 20]</sup> In 2018, the number of reported ADRs was about 26 000, with 16 000 reports from pharmacists.<sup>[21]</sup> Like many other pharmacovigilance systems around the world, the ADR report by HCPs is considered low.<sup>[14, 22]</sup> Findings from previous studies have documented negative attitudes and inadequate knowledge among physicians, pharmacists and consumers as the most common reasons for ADR under-reporting.<sup>[23–28]</sup> However, data on these reasons are still scarce.<sup>[14]</sup> ADR reporting is through voluntary basis and HCPs or consumers do not get any remuneration or benefits for reporting an ADR in Malaysia.

In order to develop strategies to address under-reporting of ADRs, it is important to understand the barriers to ADR reporting. A theory can be used to better understand these phenomena. Theoretical domains framework (TDF) is a psychological theory that has been extensively used to identify barriers to changes in health care to develop interventions.<sup>[29, 30]</sup> It consists of 12 domains covering the main factors influencing behaviour and barriers to behavioural change which include: (1) knowledge; (2) skills; (3) social/professional role and identity; (4) beliefs about capabilities; (5)

beliefs about consequences; (6) motivation and goals; (7) memory, attention and decision processes; (8) environmental context and resources; (9) social influences (norms); (10) emotion; (11) behavioural regulation and (12) nature of the behaviours.<sup>[29]</sup>

The aim of this narrative review is to establish an evidence-based understanding of the barriers associated with ADR reporting among HCPs and consumers in Malaysia by integrating TDF. The findings from this study can be used to understand the common barriers associated with ADR reporting and eventually help in planning and designing personalized interventions to improve the situation.

## Methods

This narrative review is based on SANRA (scale for the quality assessment of narrative review articles) to guide synthesis of this information into a quality narrative review.<sup>[31]</sup>

A literature search was performed in May 2020. Three online databases, that is, PubMed (Medline), Scopus and Web of Science, were searched to identify relevant articles from 2000 to 2020. The following keywords were used: 'challenges', 'adverse drug reaction reporting' and 'Malaysia' using Boolean connectors 'OR' and 'AND', field tags, parentheses and query sets. The synonyms of 'challenges' chosen in the advanced search findings are 'barriers' OR 'predictors' OR 'limitations' OR 'weaknesses', while 'adverse drug reaction reporting' as 'pharmacovigilance'.

Quantitative and qualitative studies were included if they were primary research investigating factors affecting ADR reporting and published in English. As this study is an exploratory study, all identified studies were included but were rigorously and critically appraised by both authors to identify methodological limitations and potential biases. However, review articles, letters to the editor and case reports were excluded.

## Results

Eleven articles were identified. The characteristics of each study are described in Table 1. Nine studies were quantitative study,<sup>[22, 24, 25, 27, 28, 31–35]</sup> that is, cross-sectional design study, whereas two studies were qualitative.<sup>[23, 36]</sup> Four studies were conducted among community pharmacists (CPs),<sup>[23, 25, 27, 36]</sup> three among the public,<sup>[24, 34, 35]</sup> three among other physicians or general practitioners<sup>[22, 32, 33]</sup> and one among hospital pharmacists.<sup>[28]</sup>

Based on the TDF, a total of five domains were identified to be relevant to the barriers of ADR reporting. These domains include (1) knowledge; (2) skills; (3) beliefs about capabilities; (4) motivation and goals and (5) environment context and resources. The constructs of each domain are presented in Table 2. The selection of domains was deliberated by both authors until consensus was reached. Most of the published articles were in the domain 'knowledge' ( $n=9$ ), followed by 'skills' ( $n=7$ ) and 'environmental context and resources' ( $n=5$ ) (Figure 1). These top 3 domains will be discussed further.

## Discussion

### Knowledge

The leading cause of under-reporting of ADRs in Malaysia is the ignorance of the existence of an ADR reporting system, its function and its importance. For instance, 9 of the 11 published papers identified that being unaware of the national ADR reporting system as one of the main barriers of under-reporting among HCPs

**Table 1** Characteristics of articles from the literature search strategy ( $n=11$ )

No.	Author	Objectives	Study design	Population	Findings
1.	Zin <i>et al.</i> <sup>[27]</sup>	To assess the knowledge, attitudes and practice of adverse drug reaction reporting, as well as barriers and facilitators of adverse drug reaction reporting, among community pharmacists in Malaysia	Self-administered questionnaire	219 community pharmacists	Lack of information from the patient Insufficient clinical knowledge makes it difficult to ascertain an adverse drug reaction incident Uncertain of the association between the observed adverse reaction and the drug consumed Not having easy access to an adverse drug reaction reporting form Lack of time to complete an adverse drug reaction form It was not necessary to report well-recognized adverse drug reactions
2.	Elkalmi <i>et al.</i> <sup>[25]</sup>	To explore awareness and attitudes of community pharmacists towards the national adverse drug reaction reporting system activities in the northern states of Malaysia	Self-administered questionnaire	470 community pharmacists	Lack of knowledge on adverse drug reaction reporting Unavailability of the reporting form Do not know the address where the reporting form should be sent
3.	Elkalmi <i>et al.</i> <sup>[23]</sup>	To ascertain the perception of practising community pharmacists towards adverse drug reactions reporting and to identify the problems with the current system in place for adverse drug reaction reporting in Malaysia	A qualitative study utilizing face-to-face interviews	16 community pharmacists	Majority of the pharmacists were not aware that the pharmacovigilance system was already in place in Malaysia Lack of knowledge about adverse drug reaction reporting processes
4.	Ting <i>et al.</i> <sup>[36]</sup>	To investigate community pharmacists' knowledge, attitudes and views on adverse drug reaction reporting	A qualitative study utilizing face-to-face interviews	7 community pharmacists	Lack of awareness on adverse drug reaction reporting Patient's limited knowledge about their medications
5.	Hadi <i>et al.</i> <sup>[28]</sup>	To evaluate knowledge, facilitators and barriers towards adverse drug reaction reporting among hospital pharmacists in Malaysia	Self-administered questionnaire	Registered hospital pharmacists from 10 randomly chosen public hospitals	Insufficient information from the patient Reaction assumed to be already well known Too busy to report Forgot to report
6.	Mohamed <i>et al.</i> <sup>[32]</sup>	To determine the practice, knowledge, attitude and perception of general practitioners in Malaysia towards adverse drug reaction reporting	Self-administered questionnaire	21 private general practitioners	Not aware of the adverse drug reaction reporting scheme Lack of information on how to report adverse drug reactions
7.	Agarwal <i>et al.</i> <sup>[33]</sup>	To determine current status of knowledge, practices and attitudes towards adverse drug reaction reporting among private practitioners in the Klang region of Malaysia	Self-administered questionnaire	238 private practitioners	Uncertainty about the type of adverse drug reaction to be reported Are willing to report only if they are confident that it is an adverse drug reaction A significant number agrees that it is nearly impossible to determine if it is an adverse drug reaction Inadequate knowledge about the purpose of adverse drug reaction reporting and other unsatisfactory practices
8.	Aziz <i>et al.</i> <sup>[22]</sup>	To identify factors, which would predict physicians' failure to send adverse drug reaction reports	Face-to-face interview using a structured questionnaire	Physicians	Adverse drug reaction considered to be too trivial or too well known to be reported Low educational level decreases the confidence to report adverse drug reaction Ease of completing adverse drug reaction form

**Table 1** Continued

No.	Author	Objectives	Study design	Population	Findings
9.	Mohammad <i>et al.</i> <sup>[34]</sup>	To assess the knowledge and attitudes of consumers towards adverse drug reactions and to determine the common barriers towards reporting an adverse drug reaction in Malaysia	Self-administered questionnaire	400 public	Inadequate knowledge Unaware of the adverse drug reaction reporting centre in Malaysia Not aware of the adverse drug reaction reporting procedure Inadequate knowledge regarding the drugs Unawareness of the reporting procedure Lack of an online process to report an adverse drug reaction Lack of time, incentives, proper advertisement, motivation Uncertainty of an adverse drug reaction Lack of awareness of the adverse drug reaction monitoring system
10	Hariraj and Aziz <sup>[35]</sup>	To examine public awareness about adverse drug reaction reporting in Malaysia and patients' confidence in reporting adverse drug reactions	Face-to-face interview with a structured questionnaire	860 public	
11.	Elkalmi <i>et al.</i> <sup>[24]</sup>	To explore the knowledge of the general population towards adverse drug reaction and their reporting system	Self-administered questionnaire	334 public	Unawareness about the existence of adverse drug reaction centre set up by the Ministry of Health

**Table 2** Domains and its constructs

Domains	Constructs [study]
Knowledge	Awareness about ADR reporting system, procedure and what should be reported <sup>[23, 25, 27, 32, 33, 36]</sup>
Skills	Insufficient knowledge to report ADR/uncertain about the type of ADR to report Unsure of the association between drug and reaction Do not know how to report ADR form difficult <sup>[22, 25, 27, 28, 32, 34]</sup>
Beliefs about capabilities (self-efficacy)	No confidence to report <sup>[25, 30]</sup>
Motivation and goals (intention)	Lack of incentives <sup>[34]</sup>
Memory, attention and decision processes	Forgot to report <sup>[28]</sup>
Environmental context and resources (environmental constraints)	Insufficient information from patients Time constraint Lack of access to an ADR form <sup>[25, 27, 28, 34, 36]</sup>

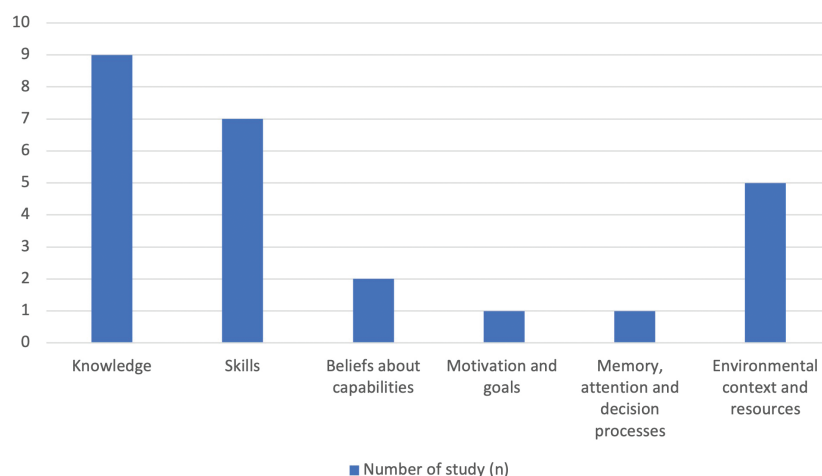
(physicians and pharmacists) and consumers.<sup>[23, 25, 27, 32, 33, 36]</sup> Among the general public or consumers, about 66–92% were not aware of the ADR reporting system in Malaysia,<sup>[24, 34, 35]</sup> whereas 40% of the physicians<sup>[22]</sup> and 75% of the CPs<sup>[25]</sup> who responded to questionnaires were not aware of the system. However, among the 25% of CPs who were aware of the system, only two claimed that they have sent an ADR report.<sup>[25]</sup>

Elkalmi *et al.*<sup>[25]</sup> in 2014 reported that 44.6% of the CPs were not sure of the postal address to send their ADR reports. However, ADR reports can also be submitted through online<sup>[13]</sup> and more than half ( $n = 71$ ; 68.3%) of the CPs were unaware of the existence of this service which is available at the MADRAC website.<sup>[25]</sup>

Although the pharmacovigilance system is well established around the world, many countries, especially Asian countries, still face under-reporting of ADRs. The lack of awareness of pharmacovigilance among public and physicians is also reported in other Asian countries.<sup>[14]</sup> This shows that it is crucial to promote and

increase the publicity of pharmacovigilance activities. Aziz *et al.* in 2007<sup>[22]</sup> suggested that the MADRAC should promote its activities aggressively. Although some efforts have been made, for example, the MADRAC bulletin which is published three times per year<sup>[37]</sup> and easily accessible via the online or mailing list, the awareness is still considered low.

Misconception regarding ADR reporting still exists as there are insufficient information and explanation concerning ADR reporting.<sup>[19]</sup> Physicians are still unaware of the definition of pharmacovigilance: how, where and when to report an ADR.<sup>[19]</sup> About 44% of the CPs did not report an ADR because they do not know how to report.<sup>[25]</sup> Thus, regular and more significant communication between HCPs and MADRAC is essential. Another strategy is for the MADRAC to provide regular feedback following the submission of ADR reports by HCPs, as suggested by Biriell and Edwards.<sup>[38]</sup> This is because evidence shows that personal encouragement and regular feedback encourage continuous reporting.<sup>[39]</sup>



**Figure 1** Number of studies according to the domains in TDF.

A majority of the articles reviewed stated that lack of knowledge as another main barrier for reporting ADRs in Malaysia. Periodic or continuous education and training related to ADR or pharmacovigilance by the MADRAC could benefit HCPs<sup>[22, 27, 28]</sup> and equip them with necessary knowledge and skills for ADR reporting.

### Skills

Uncertainty of which ADR to report was correlated with HCPs' and consumers' lack of knowledge about ADR. Consumers who hold a diploma or higher degree were more aware of the reporting system than those with lower education levels. The odds of being confident in reporting an ADR were 2.5 times more in highly educated consumers than those with primary or no education at all.<sup>[35]</sup>

The study by Aziz *et al.*<sup>[22]</sup> showed that consultants were more likely to report ADRs compared with medical officers and housemen. As expected, consultants are more knowledgeable and have vast working experiences compared with their subordinates. Hence, consultants are more likely to diagnose an ADR compared with their subordinates.

However, this is not the case with CPs. CPs stated that they did not have sufficient clinical knowledge to detect ADRs.<sup>[25, 27]</sup> However, no relationship was found between the length of practice, type of practice, the average number of prescriptions and the reporting practices of CPs.<sup>[25]</sup> Although clinical expertise provides confidence in identifying possible ADRs, spontaneous ADR reporting is needless of such expertise. Any clinical signs or symptoms should be reported knowing that the reports will later be assessed to establish the validity. Thus, it is always recommended to report even if there is a feeling of uncertainty.

One of the strongest predictors of under-reporting of ADR was physicians considering ADRs to be too insignificant or too well known.<sup>[22]</sup> Physicians who presumed an ADR being too well known and too insignificant were 28 times more likely not to suspect an ADR compared with those who assumed otherwise. Besides, physicians who were unsure if a drug caused an ADR were eight times more likely to report an ADR than those who were confident with the drug-ADR association.<sup>[22]</sup> Consistently, Aziz *et al.*<sup>[22]</sup> also reported that the physicians who were unaware of the function and purpose of ADRs monitoring were foreseen to be five times more likely not to send an ADR report compared with those who were aware of the monitoring system. There is a misunderstanding among physicians regarding the types of reactions to be reported. Almost

all physicians who responded to a survey stated that it is necessary to report only severe ADRs which lead to (i) hospitalization ( $n=95$ , 91.3%), (ii) life-threatening situations ( $n=100$ , 96.1%), (iii) congenital disorders ( $n=100$ , 96.1%) and (iv) persistent disability ( $n=101$ , 97.1%). In contrast, the MADRAC requires all types of ADRs to be reported so that newly discovered reactions can be recognized.<sup>[22, 37]</sup>

One of the suggested strategies is for education and training in ADR reporting. This strategy has shown to increase reporting rates.<sup>[40]</sup> The MADRAC can train fellow HCPs in the government and private practice to ensure that they have sufficient knowledge in managing ADR. Another suggestion is for the MADRAC to develop an educational package in collaboration with universities which offer medical<sup>[22]</sup> and allied health sciences courses such as pharmacy and nursing.

### Environmental context and resources

The most common drug information source in Malaysia is the Malaysian Monthly Index of Medical Specialties (MIMS). In Malaysia, to facilitate HCPs report ADRs, an ADR form is readily attached at the back of the MIMS book.<sup>[25]</sup> Despite this, the most significant barrier that prevents CPs and consumers from reporting an ADR was the unavailability of a reporting form.<sup>[25, 34]</sup> About 52% of the CPs stated that the forms were not readily available at their community pharmacies<sup>[25]</sup> and agreed that readily available and accessible reporting form is essential to ensure that they report an ADR.<sup>[27]</sup> On top of that, 80.8% of the CPs indicated that they would report an ADR if there was a toll-free number provided by the relevant authorities.<sup>[25]</sup> Additionally, utilization of proper documentation tools and greater access to information technology (IT) will likely increase ADR reporting among HCPs and consumers.<sup>[27]</sup>

Out of the 184 CPs surveyed by Zin *et al.*,<sup>[27]</sup> 84% state that lack of information from patients hinders them from submitting an ADR form. This is similar to the previous findings in Malaysia.<sup>[41, 42]</sup> Sometimes, it is difficult to substantiate an ADR if the information received from patients is incomplete or inaccurate.

CPs reported that ADR reporting is time-consuming and that they lack time to fill up the forms.<sup>[25, 27]</sup> The study by Mohammad *et al.*<sup>[34]</sup> also shows that consumers did not report ADRs due to lack of time. This finding is similar to studies conducted in Western countries such as France, Sweden,<sup>[6]</sup> Germany<sup>[43]</sup> and the Netherlands.<sup>[44]</sup>

In contrast, Aziz *et al.* reported that time is not a barrier for physician to report an ADR. This was supported by a study in Wuhan, China.<sup>[45]</sup> In these studies, the reasons for under-reporting highlighted were the voluntary reporting procedure and lack of basic knowledge about ADRs. However, lack of time is not a valid reason for reporting ADRs that might be detrimental for patients as with any other equivalent health outcomes.

One of the suggestions given to increase ADR reporting is to make reporting an ADR mandatory for all. This is in response to the findings by Elkalmi *et al.*,<sup>[25]</sup> in which more than half of the CPs claimed that they will only report if it was made compulsory. In Malaysia, as stipulated in the Sales of Drug Act 1952: Control of Drugs and Cosmetics Regulations 1984, it is compulsory for Marketing Authorization Holders (MAHs) to report an ADR of a product.<sup>[46]</sup> However, HCPs are encouraged to report all suspected ADRs.<sup>[14]</sup> Currently, ADR reporting has also been included in the provisional registered pharmacist's (PRP) training module. The number of ADR reports is slowly increasing in trend, as the greatest number of reported ADR cases came from the pharmacists.<sup>[47]</sup> Another suggestion was to provide incentives for HCPs who submit the ADR reports.<sup>[34]</sup> However, CPs stated that financial reimbursement was not crucial in making the decision to report an ADR.<sup>[27]</sup>

### Future direction

In line with the Industrial Revolution 4.0, the MADRAC should consider developing digital platforms such as smart gadgets applications (apps). These apps should be free and easily downloaded from the Apple store and Android Google Playstore to ensure that it is accessible to all. Other than ADR forms, these apps should also contain relevant information related to ADR to educate HCPs and consumers. However, the standard hardcopy form should be maintained as well. ADR reporting can also be incorporated into the Pharmacy Information System (PhIS).<sup>[48]</sup> PhIS provides a better and more efficient pharmacy system for patients in the government hospital and health clinics as the number of patients and medical prescriptions increases 4% yearly.<sup>[49]</sup> It involves online services on patient information, drug prescription and dispensary. With PhIS, more pharmacists and other HCPs can easily report ADRs.

### Limitations

Five of the studies reviewed were done in single centres or state, and some were undertaken with specific groups. Hence, the findings from this study should be carefully interpreted and may have limited generalizability. It may not represent a population of the CPs, physicians or consumers or represent the population of Malaysia in terms of social status and education level. Results of studies performed in Malaysia may not be relevant to other countries.

### Conclusion

This review has determined the main barriers to reporting an ADR in Malaysia. Barriers were mainly categorized in the domains 'knowledge', 'skills' and 'environmental context and resources' based on TDF. Lack of awareness of an ADR reporting system and the possible contributing factors to report ADR such as lack of clinical and ADR knowledge and lack of time are among the prominent barriers. Additionally, assumption of HCPs of an ADR being too insignificant or too well known and unavailability of the ADR forms are also some of the commonly reported barriers.

Strategies to improve ADR reporting such as promotion and publicity of pharmacovigilance improve communication and engagement of MADRAC, and the HCPs and consumers are warranted. Training and continuous education related to ADR and pharmacovigilance system and making ADR reporting compulsory for all HCPs could also be considered. Lastly, the ADR form should be made accessible for all. All these strategies could further improve the involvement of physicians, pharmacists and consumers in reporting ADRs and eventually ensure patient safety.

### Conflict of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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