

# Designing a Surveillance System in Canada to Detect Adverse Interactions Between Traditional Chinese Medicine and Western Medicine: Issues and Considerations

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**Abstract.** The use of Chinese medicinal materials (CMM) in the context of Traditional Chinese Medicine (TCM) is increasingly prevalent in Canada and worldwide. Self-medication with CMM and concurrent usage with Western medicine are also common. While taking CMM carries recognized risk of adverse effects on their own, their interactions with Western medicine can further generate additional adverse effects but are largely underestimated and undetected due to under-reporting. This is especially true in Canada and other Western countries where CMM is regulated as natural products. Currently worldwide, surveillance of CMM is variable and primarily through spontaneous and voluntary reporting systems. Current approaches in the Western world, including Canada, are by-and-large ineffective in detecting CMM-Western medicine adverse interactions. We propose the development of a Canadian surveillance system for CMM usage that involves both health professionals and patients so as to increase detection of potential adverse reactions and improve safety. As a first step, we will carry out surveys and focus groups with the stakeholder groups to identify desirable features of such a surveillance system as important ground work.

**Keywords.** Traditional Chinese medicine, electronic surveillance system, Adverse Drug Reaction

## 1. Introduction

The motivation of this review and our project is to create an electronic surveillance system to be used by health professionals and patients in Canada to monitor concurrent use of Chinese and Western medicine to detect potential adverse interactions. This article has three components: 1. review the literature regarding the prevalence of Chinese medicine usage worldwide and in Canada, and the associated challenges in minimizing risks; 2. identify the current surveillance approaches to detect potential adverse interactions between Chinese and Western medicine usage and areas needing improvement; 3. propose a study to engage key stakeholders to identify desirable features of a monitoring approach, so as to guide our future efforts to optimally create an electronic surveillance system to detect potential side effects associated with Chinese medicine with or without concurrent Western medicine.

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## 2. Traditional Chinese Medicine: Usage and Associated Risks

Traditional Chinese medicine (TCM) has been a large part of Chinese culture and the primary medical management system in China for more than 3000 years [1]. TCM is built on a holistic view of health and involves different modalities, including acupuncture, massage, cupping, and the use of Chinese medicinal materials (CMM) [2].

CMM is often referred to as Chinese herbal medicine or TCM in medical literature. In China, more than 10,000 natural substances are used as CMM, 86.8% of which are herbs, 12.5% animal products, and 0.7% minerals [1]. Only about 500 CMMs are commonly used outside of China [3].

Traditionally, CMM is consumed as decoction; based on the patients' conditions, TCM doctors prescribe dry CMM ingredients, and patients prepare the decoction by themselves at home. Nowadays, pharmaceutical companies prepare formulations into pills, powder, ointment, granules, oral liquids, capsules, tablets, and injections for convenient consumption [4]. These new formulations are made available over the counter (OTC). In this article, the traditional individualized decoction will be called **prescription-CMM** and the modern pre-made formulations will be called **OTC-CMM**.

### 2.1. Increasing Prevalence of CMM Usage Worldwide and in Canada

In China, the number of CMM users exceeds 0.7 billion as of 2014, and CMM is accessible in over 170 countries and regions around the world [5]. In the western world, CMM becomes increasingly prevalent in many countries, including Australia, European countries, USA and Canada [1]. CMM is especially popular among Chinese immigrants in western countries, with 80-100% prevalence found in recent studies. The use of prescription-CMM and OTC-CMM are roughly equal [2, 6].

In Canada, the use of CMM is rapidly expanding with increasing Chinese emigration [7]. In a WHO report in 2014, the estimated prevalence of complementary and alternative medicine usage in Canada is 70%, and TCM represents a significant portion [8]. In different provinces across Canada, CMM can be easily found and accessible for use in hospitals, TCM clinics, herbalists, and grocery stores [9].

### 2.2. Improper CMM Use and Failure to Report CMM Use

Studies suggest that self-medication with CMM is very common and widespread in China mainland, Taiwan, Hong Kong, and Western world [1, 10]. In a recent study among Chinese immigrants in US, a striking 93% of CMM users acknowledged self-medication with herbal products [6]. Another US study revealed that patients got CMM information from friends (54.4%) and family (31.8%) much more often than from TCM practitioners (27.7%) [2]. Self-medication and obtaining CMM information from unreliable sources expose patients to risks of CMM-related adverse reactions.

Furthermore, many CMM users do not disclose to their physicians about their CMM usage [11]. A recent US study revealed that only 36% of CMM users inform their physicians. Of the 64% users who did not report, only half was willing to discuss their CMM usage with their physicians [2]. Main reasons for patients' non-disclosure include: not thinking physicians need to know; worrying about negative responses from their physicians; not being asked by their physicians about CMM use or disclosure [12].

From Western health professionals' perspectives, unfamiliarity with TCM and CMM is identified as a major barrier in patient care. A survey among pharmacists in

Alberta showed that 20% pharmacists disapproved of CMM use while 64% felt unprepared to counsel patients regarding CMM [13]. These reasons contribute to the inadequate communication between patients and healthcare providers on CMM usage, as suggested by a study in US which found that only 5% of participants report that their physicians had ever asked about their CMM usage [6].

### 3. Adverse Drug Reactions Surveillance in TCM

While CMM are medications and can cause adverse reactions as all drugs do, they are regulated as dietary supplements in US, as natural health products in Canada, and as therapeutics goods in Australia [14]. Thus, adverse reactions of CMM are not strictly tracked similar to Western medicine in these countries and can easily go undetected.

Some adverse drug reactions (ADRs) of CMM are caused by inappropriate usage [15]: 1. Oversimplified information about contraindications and special warnings in prescribing leaflets of OTC-CMM; 2. inappropriate dosing and timing of CMM; 3. incorrect preparation of prescription-CMM by patients; 4. adverse interactions between different CMM; 5. adverse interactions between CMM and Western medicine.

Even with adherent CMM usage by patients, there are additional risks of ADRs due to [15, 16]: inaccurate species identification (e.g. “ginseng” can refer to four different plants), growth condition of herbs, environmental contamination, manufacture handling, intrinsic toxicities of some ingredients, and inactive ingredients in formulas (e.g. alcohol, oil and honey are common inactive ingredients which can introduce unwanted side effects). All these risks expose CMM users to a wide range of ADRs.

In China, CMM is considered medicine and is monitored accordingly in the national ADR monitoring system. A national study in 2013 recorded more than 223,000 reported cases of CMM-associated ADRs (17.3% of all ADR reports), the vast majority of which was due to OTC-CMM [17].

In countries where CMM is regulated as natural products, CMM-related ADRs are largely under-reported [18]. Reports suggested that: the US surveillance system could only detect 1% of all herb-related ADRs [19]; in UK, only 0.5% of the ADR reports were herbal medicine related [16].

#### 3.1. Current CMM Surveillance Systems and Associated Challenges

Pharmacovigilance of CMM is operated under the general pharmacovigilance system with Western medication. Currently, pharmacovigilance depends on spontaneous reporting system (SRS), which relies on voluntary rather than obligated reporting of suspected ADRs by healthcare providers, pharmaceutical companies, and patients [20].

The SRS system in China receives more than one million reports per year [17], and the national centre posts “ADR information bulletin” and “Pharmacovigilance News” to disseminate information on the safety of medications and current pharmaceutical concerns in China [15, 17]. SRS is similarly used in other Asian countries including Singapore [19] and India [21], and also in western countries [14, 18].

One main challenge of SRS is that it relies significantly on health professionals to carry out the reporting, as the general public would usually not report due to a lack of awareness of its existence and mechanisms of reporting. As a result, information from patients may be largely missed in SRS. A recent study in China showed that patients only contribute to 0.6% of the reports to the pharmacovigilance system [17].

A proposed solution to improve patient reporting is to build an active post-marketing risk identification and analysis system. In 2008, US launched Sentinel Initiative to build and implement such a national active surveillance system with the ability to track information of all patients [22]. Such active reporting systems would be beneficial to pharmacovigilance of CMM and can largely complement the current SRS.

Other surveillance methods in addition to SRS are also used worldwide. Prescription Event Monitoring is developed in UK to monitor new prescription drugs, including herbal medicine. In this method, herbalists were sent a questionnaire that requests adverse event that the patients experienced when treated with a specific herbal medicine [23]. Poison Control Centres also play a key role in pharmacovigilance on herbal medicines. In US, Poison Control Centres receive reports of ADRs related to dietary supplements and are essential for detecting ADRs of herbal medicines [24].

### *3.2. Necessity of a Surveillance System for CMM Use in Canada*

Since CMM is regulated as natural health products in Canada, no medication-like surveillance and reporting system is in place to detect CMM-related ADRs. Meanwhile, the dual use of CMM and Western medicine is common among Chinese in the Western world [10]; for example, a recent study in Greater Vancouver, B.C., Canada uncovered that 28% of Chinese patients used CMM in addition to Western medicine, and 2 in 3 patients did not report this concomitant usage to their family doctors [25]. Therefore, health professionals need to be highly vigilant of potential concomitant CMM and Western medicine use by their patients. Also, patients need to be educated about potential ADRs related to CMM use and diligent in watching for and reporting them to their health professionals. Conceivably, setting up a Canadian surveillance system, with joint participation of health professionals and patients, would be ideal to transparently document CMM usage and detect potential CMM-Western medicine ADRs.

Designing a new and effective surveillance system needs to be done carefully not only to address historical challenges, but also ensure expanded and improved contribution of detections by health professionals and patients. This tool needs to have a just-in-time education function for the users to obtain more information about CMM-Western medicine ADRs. This tool should also promote collaboration between Western Medicine and TCM practitioners, thereby improving communication, mutual knowledge exchange, and cooperation, which may in turn encourage the patients to be more willingly to disclose concomitant CMM and Western medicine usage to their health professionals. This new system will hopefully lower the threshold of reporting and raise mutual understanding amongst these stakeholders, leading to a continuously improving tool to raise detection of CMM-Western medicine ADRs. This is why we are motivated to engage health professionals and patients to identify desirable features as a first step of designing such a surveillance system.

## **4. Identifying the Desirable Features of stakeholders: First Step in Developing a Canadian Electronic Surveillance System**

The proliferation of modern information and communication technologies such as mobile phones and tablets have greatly helped users to easily acquire knowledge, share information and participate in surveillance activities [26]. This leads to the rise of co-creation between producers of knowledge, systems designers, and consumers to

improve electronic products. For example, Tripadvisor involves the participating hotels, restaurants, airlines, and customers to work with this highly popular and successful electronic platform for crowdsourcing to help select best restaurants, hotels, and other travel related activities [27]. Amazon, Airbnb, and Uber are similar electronic platforms that thrive based on same principles [28]. How can we emulate these electronic platforms to establish one for surveillance of CMM in order to document all medication-related symptoms and flag unique or recurring symptoms for deeper scrutiny? How can we engage all stakeholders to actively contribute to it?

Before constructing this electronic platform, we need to gain an understanding of four stakeholder groups that will conceivably contribute to and benefit from this platform: patients, Western medical doctors, TCM doctors, and pharmacists. Specifically, we will identify: 1. the attitudes of each of these groups in the usage of CMM, and the concomitant use of CMM and Western medicine in disease management; 2. the perception of the patients in terms of safety of CMM use and their interest in reporting to their health professionals of this use; 3. the interest of health professionals in wanting to know of concomitant CMM and Western medicine use; 4. how would each group report CMM use, and what features they would like to see in this electronic surveillance system that would be attractive to them?

To achieve our goals, we will carry out four activities, the first two of which will be done at this stage:

1. We will conduct a general survey in all four stakeholder groups. The surveys, including both closed-ended and open-ended questions, will capture participants' demographic information, their historical experiences with CMM, and their interest in tracking of CMM use to potentially uncover ADRs.

2. We will conduct open-ended and semi-structured focus groups for each of the 4 groups of stakeholders. Participants will be asked to share their experience and specific ideas in response to the following topics: CMM usage and their experience of CMM side effects/CMM-prescription medication interaction; their ideas on the necessity of a surveillance/communication system and their input on preferred communication, and educational features of a CMM surveillance system.

Based on our findings from 1 & 2, our roadmap will tackle the next two steps:

3. We will incorporate the stakeholders' suggestions to design a surveillance system with an electronic database linked to a web-based portal and an app to facilitate desktop and mobile data input, data analysis and visualization, and data storage. Throughout this design phase, we will engage stakeholders in usability testing.

4. With the electronic platform prototype completed, we will run a clinical trial and test its effectiveness. Further changes will be made on the app according to users' feedback and informed by evidence uncovered in the trial.

## 5. Summary

At the ITC 2017 conference, we will report our findings and discuss the preliminary design of this new electronic surveillance system. We anticipate that this system will help to bridge the communication between TCM doctors, western health professionals and patients in the following ways: 1. raise the public awareness of CMM-Western medicine interactions; 2. understand the frequency of CMM-Western medicine usage; 3. screen suspected cases of CMM-related adverse events for fuller exploration; 4. educating patients and healthcare providers about potential risks related to CMM usage.

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