Pharmacovigilance: Drug Safety and Regulation
A Qualitative Study of the Canadian & Taiwanese Healthcare Systems

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This report is an investigation of pharmacovigilance (PV) in the societies of Canada and Taiwan. Being a major topic of discussion in the World Health Organization, PV stands to be complex matter at hand. It is influenced by both the policies and regulatory framework of a healthcare system, and additionally by the societal values the populations possess. Through an investigation of the four phases of clinical trials and CHSP-conducted visits to healthcare centres, it is found that constant developments to healthcare policy are made for better PV. The idea of increased patient-physician consultation time decreases erroneous judgment, and the idea of electronic systems advancing drug regulation has brought a deeper understanding to PV in our modern society. Overall, these developments aim to educate the general public regarding the issue of drug safety and serve as encouragements of active participation in one’s health.
INTRODUCTION

The rapid advancement of healthcare in the twenty-first century has brought about efficacious and very much individualized medical care in developed countries. Among the issues faced by the development of effective public healthcare systems lies the problem of drug safety or “pharmacovigilance” (PV). Defined as “the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem” (WHO), PV is a crucial responsibility for healthcare systems to undertake.

In hindsight, the worldwide incidence of Thalidomide in the 1960s (Thalidomide Victims Association of Canada) clearly reflects the inadequacy of a drug regulatory system to prevent the aforementioned “adverse effects,” and serves well to illustrate the paramount importance of the practice of PV. The topic of drug safety is a pervasive problem. It touches upon the improvement of drugs development research, the four phases of clinical trials, as well as the safety of prescribed medication on the market. The interplay between structured research environments and volatile societal contexts prove PV to be an intricate matter of discussion.

Taiwan’s healthcare allows easy access to fast treatment, which vastly differs from our Canadian system; consequently, patient access to drug information and patient-physician relationships vary as well. However, indicators in effective treatment do not necessarily correlate to effective educational PV, as the “Survey of Medication Knowledge and Behaviors Among College Students in Taiwan” (Hsiao et al.) suggests. This report will strive to explore PV in both societies, with an emphasis on context-sensitive observations made in the cities of Kaoshiung, Tainan, and Pingtung in southern Taiwan and Montreal, Canada. The interactions between the system structure and cultural phenomena have led to an interesting, educational development of PV that caters to societal norms in both countries.
**METHODOLOGY**

To delve into the complexity of PV, this report consists of two major parts. In the first, timelines of drug development and research in the four phases of clinical trials in Canada and Taiwan is briefly compared. With the understanding of these major differences, the influence of healthcare systems on the drug evaluation process will be investigated. The latter part comprises the distribution of prescription drugs to the two populations and the analysis of interaction between patient and physician.

**RESULTS & DISCUSSION**

I. THE PHASES OF CLINICAL TRIALS

The World Health Organization has set international standards for the clinical testing of new drugs. It consists of a four-phase procedure followed by both the Canadian and Taiwanese systems for clinical trials.

<table>
<thead>
<tr>
<th>Phase</th>
<th>Biomedical clinical trials of experimental drug, treatment, device or behavioral intervention may proceed through four phases:</th>
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<tbody>
<tr>
<td>I.</td>
<td>Clinical trials test a new biomedical intervention in a small group of people (e.g., 20-80) for the first time to evaluate safety (e.g., to determine a safe dosage range and to identify side effects)</td>
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<tr>
<td>II.</td>
<td>Clinical trials study the biomedical or behavioral intervention in a larger group of people (several hundred) to determine efficacy and to further evaluate its safety.</td>
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<td>III.</td>
<td>Studies investigate the efficacy of the biomedical or behavioral intervention in large groups of human subjects (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions as well as to monitor adverse effects, and to collect information that will allow the intervention to be used safely.</td>
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<tr>
<td>IV.</td>
<td>Studies are conducted after the intervention has been marketed. These studies are designed to monitor effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use.</td>
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Figure 1. Description of the four phases of clinical trials (WHO)
These standards, however, are only general guidelines. The protocols for each phase are still dependent upon the experimental design of the trial and country regulations.

**Canada**

The federal government of Canada utilizes the system of clinical trial applications (CTA) from trial sponsors to regulate experiments conducted under the first three phases (Health Canada). A 2008 article in the Canadian Medical Association Journal criticizes the Canadian system for its lack of “data on participants, many of whom are recruited by family physicians.” This jeopardizes the voluntary participants’ safety, depriving the movement toward active PV of its core values. Since then, a Public Clinical Trials Database has been established, making the system more transparent to the population.

![Drug approval system in Canada](Health Canada)

Phase IV trials in Canada, however, are very limited. In a 2011 report, Health Canada was described as “having [a] limited regulatory authority to require label changes that address new safety information or to require manufacturers to undertake additional post-market studies” (Office of the Auditor General of Canada). Submissions of CTAs and information on these trials to Health Canada’s Therapeutic Products Directorate (TPD) are not required (Health Canada). Bill C-17, an amendment to the Foods & Drugs Act proposed in December 2013, strives to increase Health Canada’s regulatory role in phase IV trials. It advances activities of PV in Canada by encouraging the federal authority to more closely monitor the situation of medication on the
market; powers of intervention will be exercised when the safety of patients are at risk (Health Canada). Currently, the bill is still in discussion.

Taiwan

The process of drug evaluation in Taiwan follows a similar structure to the one in Canada. Additionally, “the Department of Health (DOH) founded the ‘Center for Drug Evaluation (CDE)’ as a non-governmental and non-profit organization” (Chen). As a separate organization, the goal of the CDE is to enhance PV activities in Taiwan through regulatory work.

![Function of CDE](image)

**Figure 3. The function of Taiwan’s Centre of Drug Evaluation (Chen)**

Although patients with serious adverse drug reactions are obligated to report their circumstances (Kimura et al.), post-market drug regulation in Taiwan almost echo the situation in Canada (Chen). The 2012 Taiwan Public Health Report indicates that steps have been taken in the education of safe drug use and the regulation of traditional Chinese medicine toward better PV in the system.
II. THE DISTRIBUTION OF PRESCRIPTION DRUGS

The attitude of patients toward – and consequently their usage of – medication are deeply influenced by external social factors. Particularly in light of PV, their relationship with their physician plays a substantial role in this phenomenon (Dugdale, Epstein and Pantilat). The focus on the distribution of prescription drugs from a contextual standpoint is therefore valuable to understanding the social factors that drive patient expectations and decisions.

Canada

One of the main differences between the Canadian and Taiwanese healthcare from the patient’s perspective is the amount of time spent with their physician during their visit. The average consultation time with a general practitioner in Quebec is 17.6 minutes (Lussier and Richard) – whereas Taiwan is notable for its “three-minute visits” (Cheng). Upon the visit to McGill’s Student Clinic, Dr. Pierre-Paul Tellier, a family physician and the director of McGill Student Health Services, illustrated the importance of the patient-physician relationship. He had kept samples of medication such as birth control pills in the clinic cabinets; within the timeframe of his appointments, he was able to educate his patients on the administration of such medication to avoid misuse. Studies have shown that a decrease in patient-physician interaction time leads to the increase in rates of drug prescriptions and erroneous diagnoses (Dugdale, Epstein and Pantilat).
Prescribing Practices

Two studies have found an association between shorter visits and increased rates of medication prescriptions. Davidson et al. found that family practitioners in New Brunswick, Canada, with a rate of prescriptions for elderly persons that was above the average also had a higher visit rate per day (27 vs 22), and a higher number of work days per year (225 vs 186).

Grol et al., in a survey of general practitioners in the Netherlands, found that physicians who expressed feeling a lack of time in their medical practices had higher rates of writing prescriptions than physicians who did not feel a lack of time.

More recently, Tamblyn et al. studied the appropriateness of prescriptions of anti-inflammatory drugs for hip pain and assessment of their complications in a cohort of family medicine and internal medicine physicians in Montreal, Canada. They concluded that shorter visits, especially those less than 15 minutes, were a risk factor for inappropriate prescribing and management of gastrointestinal side effects.

Figure 4. The relationship between time spent with physician and medication prescription (Dugdale, Epstein and Pantilat)

Dr. Frederique Van den Eynde at the Douglas Mental Health Institute expressed the possibility for variability in physician practice in Montreal as well as the rest of Canada. He believes “we jump too quickly to medication” as a solution to illness; ultimately, it is the physician’s responsibility to appropriately administer medication as he or she sees fit.

The patient has the responsibility of retrieving the medication at a pharmacy once it is prescribed. In special environments such as long-term care institutions, patients are administered drugs by nurses. One of the nurses from the CHSP visit at the Jewish Eldercare Centre drew out a length of packets: two weeks’ worth of a patient’s medication. The centre has the drugs dispensed through an electronic system to avoid errors in dosage. Although the nurse mentioned any drugs lost – such as when dropped accidentally – is unrecoverable, any missed medication can be easily monitored. This system adopted for large institutions is highly efficient and increases the safety of patients by reducing human error in the process.
Taiwan

An established primary care system verses the lack thereof in Taiwan redefines a physician’s role from the patient’s perspective. The health professionals from the CHSP visits frequently referred to their system as being a “free-market.” This indicates several social and cultural values the Taiwanese have toward healthcare. The term itself suggests competition – specifically competition between clinics (Bennett, Hung and Lauderdale). Efficiency, low wait times, effective prescriptions became the factors that attract patients.

The majority of Taiwanese patients have a high expectation of the physician to relieve their illness as quickly as possible; naturally, this turns into a cultural phenomenon where the “patient’s main objective is to obtain medicine [from the doctor]” (Bennett, Hung and Lauderdale). Interestingly, the Dr. Li-Shen Xu from the Health Centre of Lujhu mentioned that the National Health Insurance (NHI) of Taiwan covered drug costs, encouraging this expectation. One of the only restrictions on prescription medicine is on antibiotics. However, if self-paid, the patient can access the drug all the same. Though through the NHI, the prescription for drugs can be controlled, the free-market reality of the Taiwanese healthcare system does not necessarily achieve the results of PV the NHI is trying to establish.

Nevertheless, hospitals and clinics still embark upon activities of PV. The health promotion work at the Buddhist Da Lin Tzu Chi General Hospital focuses on preventative health in Taiwan. Near the counter for claiming medication stands a Patient Drug Information Inquiry System. The electronic system allows patients to scan the barcode on their prescription form and learn about their medication. There is also an information desk dedicated to the same purpose. Though the Taiwanese may not spend as much time as Canadians with their physicians (Lussier and Richard; Cheng), these other adopted ways encourage the idea of PV.
One of the more unique aspects of Taiwanese healthcare is the prevalent use of electronic medical records. Personal NHI cards are used to record drugs physicians prescribe, and the information can be accessed throughout the system (Taiwan NHI Administration, Ministry of Health and Welfare). This system contributes to avoiding any adverse drug reactions that may occur.

CONCLUSION

As seen through the regulatory frameworks of clinical trials, both the Canadian and Taiwanese systems have yet to achieve the ideal in terms of PV activities. The CHSP-conducted visits, however, show that each system has its own interpretation of PV that is context-sensitive. Whether it be the patient-physician relationship or the Patient Drug Information Inquiry System, the two healthcare systems strive to educate their respective populations. When it comes down to
the complex issue of PV, of the intricacies that link the abiotic with the biotic, one cannot solely depend upon institutional regulatory work to prevent adverse events from happening. The increased education of the public, and the healthcare system’s active role in this education, is the key to the international goal of pharmacovigilance.

REFERENCES


