Under-reporting of Adverse Drug Reactions: The Need for an Automated Reporting System

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Résumé :

(traduction)

Bien que plus de 32 000 réactions indésirables aux médicaments soient déclarées annuellement à Santé Canada, cela ne représente qu'environ 5% des cas vécus par les Canadiens chaque année. Cet affichage frappant de sous-déclaration aboutit non seulement à des résultats non représentatifs en ce qui concerne les effets indésirables des médicaments, mais jette également le discrédit sur les bases de données utilisées par les professionnels de la santé, ce qui, à son tour, présente un danger pour la santé et la sécurité des Canadiens. Les principales causes de la sous-déclaration que l'on trouve dans la littérature sont l'ignorance, la méfiance et la léthargie de la part des professionnels de la santé. Bien que Santé Canada se fie à ces professionnels pour signaler volontairement les effets indésirables, il existe le potentiel d'un système de déclaration automatisé pour éliminer les causes de sous-déclaration. L'intégration d'un tel système avec des technologies de l'informatique de la santé actuelles, tels que le dossier de santé électronique et l'utilisation des technologies de communication existantes dans le cadre du système de santé, permettra aux professionnels de la santé d'utiliser des données représentatives sur les réactions indésirables aux médicaments au Canada, ce qui, à son tour, les aidera à mieux servir leurs patients.

Mots-clés :

Réactions indésirables médicamenteuses, Bulletin Canadien des Effets Indésirables, BCEI, e-sante, dossier médical électronique, informatique de la sante, systèmes de sante, pharmacovigilance, déclaration, déclaration volontaire

Abstract:

Although upwards of 32,000 adverse drug reactions are reported to Health Canada annually, this represents only approximately 5% of cases experienced by Canadians every year. This gross display of underreporting not only results in unrepresentative data in regards to adverse drug reactions, but further discredits databases used by healthcare professionals and in turn compromises the health and safety of Canadians. Major causes of underreporting seen in the literature are ignorance, diffidence and lethargy displayed by healthcare professionals. While Health Canada relies on these professionals to voluntarily report adverse drug reactions, the potential exists for an automated reporting system to remove causes of underreporting. Through integrating such a system with current health informatics technologies such as the electronic health record and utilizing existing health system communication technologies, healthcare professionals will be provided with representative data of adverse drug reactions in Canada and in turn be able to better serve their patients.

Keywords:

Adverse drug reactions, Canadian Adverse Reaction Newsletter, CARN, e-Health, electronic patient record, health informatics, health systems, pharmacovigilance, reporting, voluntary reporting

Introduction

Adverse drug reactions (ADRs) are undesirable effects to health products including drugs, medical devices and natural health products (Health Canada, 2012). While an overdose can be seen as an adverse drug reaction, such reactions are typically observed and reported at standard dosage. Over 32,500 adverse drug reaction reports were received by Health Canada in 2010 (Health Canada, 2011a), however this may be an underrepresentation of the true number of cases. Currently, ADRs are reported on a voluntary basis by health care professionals, manufacturers and consumers via www.medeffect.ca. This Health Canada website gives consumers, health care professionals and the industry opportunities to report adverse drug reactions that are either witnessed or experienced personally. Methods of submission include an online reporting option, a printable form that can be faxed and/or mailed and lastly a telephone number allowing reporting over the phone. Regional offices of Health Canada receive these reports before they are processed and sent to the national office. All reports are recorded in Health Canada's Canada Vigilance Database, from where the public is able to search them online. This not only provides physicians with a database to compare adverse reactions they witness, but also provides consumers with a research tool for health products that themselves, friends or family members may have been prescribed. Furthermore, frequent health product appearances and serious cases are published in the *Canadian Adverse Reaction Newsletter* (CARN). This publication is distributed to a mailing list of over 20,000 subscribers (Health Canada, 2014).

Operational Challenge

While the current operational model of adverse drug reaction reporting provides useful tools to Canadians such as the CARN and Canada Vigilance Database, it relies completely on physicians and consumers alike to voluntarily report ADRs. This leads one to speculate about whether 32,500 adverse drug reaction reports is representative of cases experienced in Canada. Furthermore, it raises questions of under-reporting.

In a systematic review conducted by Hazell and Shakir (2006), determinants of under-reporting were examined. Factors associated with under-reporting included ignorance (95%), diffidence (72%) and lethargy (77%). In cases in which lethargy was listed as a reason, physicians displayed a lack of interest in finding a reporting form or stated other excuses (Hazell & Shakir, 2006). This shows that physician's beliefs and attitudes greatly affect the outcome of adverse drug reaction reporting. Furthermore, a voluntary system that relies on these physicians leaves room for error due to personal biases.

Another study, carried out by Lopez-Gonzalez, Herdeiro, & Figueiras (2009), estimated the extent of ADR underreporting. Across 12 countries, adverse drug reactions were under-reported at a median rate of 94%. When further examined between standard reactions and those deemed serious, the rate of under-reporting was still significant at a median of 85% (Lopez-Gonzalez, Herdeiro, & Figueiras, 2009). This indicates that a gross portion of adverse drug reactions are being left unreported and raises concern for the representativeness of ADRs experienced by Canadians in the current databases.

To date, no legislation or regulations exist that require health professionals to report adverse drug reactions. However regulations are in place for market authorization holders (MAHs), otherwise known as industry stakeholders, making reporting mandatory in the event of an incident regarding one of their own marketed products (Health Canada, 2011b). While regulations such as these may be difficult and time-consuming to impose on health professionals, a gap is left to be filled by a health informatics solution.

Proposed Informatics Application

Throughout the current literature regarding underreporting of ADRs, it can be seen that a strictly voluntary model provides fundamental information through reports, but also hinders the quantity and accuracy of information that is being provided to Canadians.

Currently, adverse reaction reports come from three sources– consumers, health care professionals and MAHs. The latter of the three sources is regulated by government legislation, and is thus required to report cases to Health Canada. Consumers and health care professionals however, are not required to report reactions

Based on this knowledge, the most effective means of increasing adverse reaction reporting lies in the field of the health care professional. This includes but is not limited to health clinics, hospitals and pharmacies. It is clear that

while a voluntary reporting system is effective for the needs of market authorization holders and consumers, it is not adequate to ensure representative reporting in health care settings.

When proposing a solution for such a case, one must take into consideration determinants that lead to under-reporting in physicians. As discussed previously, ignorance, diffidence and lethargy were all factors affecting physicians reporting habits (Hazell & Shakir, 2006). While a voluntary system requires physicians to manually input adverse reactions into the reporting means provided, an automated reporting system eliminates the need for health professional participation. This in turn, would leave no room for these three determinants of under-reporting to skew data.

As we shift towards steady integration of technology into healthcare administration and practice (Coiera, 2003), adverse drug reaction reporting and monitoring systems are being developed and implemented around the world. The Health Evaluation through Logical Processing (HELP) system currently in place at the Latter Day Saints (LDS) Hospital in Salt Lake City, USA, is an early front-runner of such technology. This system, however, does not completely eradicate the role of the doctor in ADR reporting. First, it gathers information from the laboratory, radiology department and the hospital pharmacy. Then, using predetermined parameters, the system signals to a healthcare professional that an adverse drug reaction has occurred. It is up to the doctor's discretion at this point to either confirm or reject the adverse drug reaction (Thürmann, 2001).

However in a study by Dormann et al. (2000), a similar automated system was compared to standard manual reporting. In this case, thirty-four adverse drug reactions were detected by the automated system, however physicians only reported seventeen. Thus, the automated system was associated with a 100% increase in ARs captured.

In Brent, United Kingdom, a team of health informaticians developed a method of information extraction in order to trend adverse drug reactions. General practices under examination used a Clinical Information Management System (CIMS) to code details of patient treatment and prescribing using the Read classification system. These Read

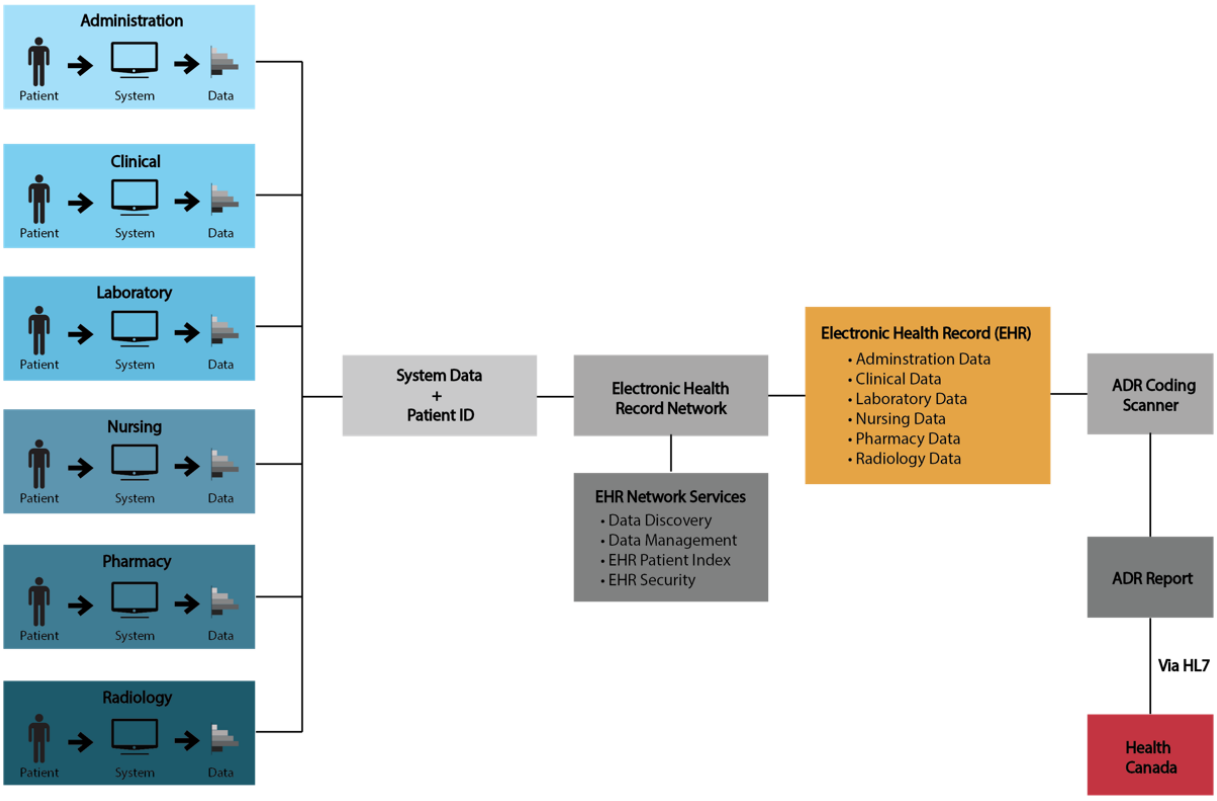

Figure 1

Electronic Health Record and automated ADR reporting system interoperation. This model illustrates the potential interactions of a proposed informatics system (adapted from lecture on Electronic Health Record, 30 September, 2011).

codes could then be analyzed by an informatics system in order to recognize adverse drug reactions and further trend them based upon age, ethnicity and sex (Tsang, Majeed, Banarsee, Gnani, & Aylin, 2010).

While the system observed in Brent was not specifically used for adverse drug reaction reporting to a government authority, it was able to use procedural codes and classifications in order to recognize adverse reactions in an electronic information setting. A system such as this, once refined, could potentially act as a solution to under-reporting of ADRs.

The Electronic Health Record (EHR) provides an opportunity for the implementation of an automated adverse drug reaction reporting system. Defined by the Government of Canada as "secure and private lifetime record that describe[s] a person's health history and care," their implementation is currently a pan-Canadian initiative, with all provinces having established at least one core EHR system (Office of the Auditor General of Canada, 2010).

Through the usage of standardized vocabularies, clinical systems such as an automated reporting system and an EHR are able to interoperate in a meaningful way. The Systemized Nomenclature of Medicine Clinical Terms (SNOMED-CT) is currently used as a standard for clinical terminology, and is seen as a first choice due to its comprehensive clinical terminology system (Héja, Surján, & Varga, 2008). Another medical classification currently used in Canada is the ICD-10-CA, a coding system that permits coding of signs, symptoms, abnormal finds, causes of disease and most importantly under our circumstances – adverse effects of drugs in therapeutic use (Canadian Institute for Health Information, 2009). The use and implementation of vocabularies such as these, would allow ease of automated reporting across multiple systems.

Figure 1 demonstrates a model of the proposed automated adverse drug reaction reporting system. It can clearly be seen through the model that this system works very closely with the EHR. Once information is compiled from all regions of a healthcare setting as seen on the left of the model, an electronic health record is created. This allows simplified access by health care professionals to the most current and widespread patient clinical data. Furthermore, this data is coded using terminology from standard nomenclature or structured vocabulary including, but not limited to, SNOMED-CT and ICD-10-CA.

In order to classify an adverse drug reaction, SNOMED-CT uses the term "adverse reaction to drug (disorder)," and labels it with the Concept ID: 62014003 and SNOMEDID: DF-10010. Under this grouping, adverse drug effect, adverse drug reaction and ADR are also classified (International Health Terminology Standards Development Organization, 2008).

The ICD-10-CA classification system, like SNOMED-CT, also uses codes in order to establish a classification. "Drugs, medicaments and biological substances causing adverse effects in therapeutic use" are classified under the codes Y40-Y59 (Canadian Institute for Health Information, 2009, p. XX-89). Furthermore, the code T88.7 classifies "unspecified adverse effect[s] of drug[s] or medicament[s]" (p. XIX-130).

While cross mapping exists between SNOMED-CT and ICD-10-CM, it does not yet exist for ICD-10-CA (Canada Health Infoway, 2013b). Thus, the proposed automated reporting system would be required to scan the electronic health record for both SNOMED-CT and ICD-10-CA codes related to adverse drug reactions.

Once the aforementioned scan is completed by the automated system, it would either flag an electronic health record as being ADR-positive or ADR-negative. ADR-positive results, results containing one or more adverse drug reactions, would then be flagged for conversion of relevant information into an ADR report. A copy of the current Health Canada adverse reaction reporting form can be found at http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/medeff/report-declaration/ar-ei_cons_form-eng.pdf . Reports include information such as age, sex, health outcomes, drug prescriptions and treatment – all of which can be found in an electronic health record. Procedure codes such as ICD-10-CA and SNOMED-CT would be used to scan and extract this information into meaningful and complete reports.

Upon creation, these reports would be automatically sent to Health Canada using Health Level 7 (HL7). This international set of open standards allows automatic communication between health systems developed independently (Coeira, 2003). In our case the systems communicating would be the Electronic Health Record based adverse reaction report and the adverse reaction database in place at Health Canada, which would be receiving the reports. Through the implementation of Health Level 7 based intersystem communication, labor and time involved negotiat-

ing application-to-application interfaces would be reduced, along with the elimination of the need for custom developed programming and interface maintenance (Canada Health Infoway, 2013a). With infrastructure already in place at Health Canada to deal with incoming ADR reports, there is no need for any additional elements to the system. This proposed solution is not only simple in concept, but is able to deliver results in harmony with existing medical information technologies.

Since EHRs are not in place across all health care facilities in Canada, it must be understood that this system cannot be implemented throughout the country immediately. As EHR utilization across the country develops, so would the proposed automated adverse reaction reporting system. The first step is to implement the system into current EHR -based set ups such as Alberta Netcare, in order to serve as a model for other provinces (Graham et al., 2008). This implementation would then serve as pilot study for further expansion and development.

While the use of electronic health records is limited under privacy laws, precedent already exists in which they have been used for research purposes (Hodge, Gostin, & Jacobson, 1999). The Electronic Primary Care Research Network, being an example, enables healthcare institutions to safely transfer information such as EHRs (University of Minnesota, 2010). Furthermore, EHRs contain a unique patient identifier that is unidentifiable outside the organization in which it serves, thus alleviating ethical issues such as privacy of information.

As mentioned previously, Health Canada currently provides feedback regarding ADRs to healthcare professionals through the Canadian Adverse Reaction Newsletter, eNotices and the Canada Vigilance Database. Feedback from regulatory agencies plays a crucial role in the reduction of adverse reactions, especially in those related to concomitant drug use and serious adverse reactions (Brewer & Colditz, 1999). A study in Germany conducted by *Pharmacoepidemiology and Drug Safety* found that adverse drug reactions resulted in direct costs of over 740 million dollars, assuming that ADRs were responsible for 5.8% of hospital admissions. With 30% of ADRs deemed to be preventable through mechanisms such as monitoring, reporting and feedback systems, potential savings of just fewer than 250 million dollars are displayed (Rottenkobler et al., 2011). While the entirety of these savings cannot be attributed to an automated reporting system, it goes to show the potential for economic savings after the implementation of such a system.

Conclusion

While a voluntary adverse drug reaction reporting system, such as that currently in place in Canada, is cost-efficient, it is not effective and does not accurately represent ADRs experienced by Canadians consumers, health professionals and market authorization holders alike. Under-reporting of ADRs due to voluntary systems has been exhibited in Canada, as well as other countries across the globe.

The implementation of an automated adverse drug reaction reporting system would not only provide Health Canada with more representative data, but brings with it increased health and safety to Canadians and vast economic benefits. Unlike campaigns focused on change in habits of the physician to eradicate ignorance, diffidence and lethargy, this system achieves a solution without new legislation or behavioral change.

Although an automated reporting system will not be introduced and deemed effective overnight, its development and gradual implementation is a step towards an informatics solution. Once integrated with widespread electronic medical records, it will provide health administrators and regulators a powerful tool leading to a healthier future for Canadians.

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