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Impact of adverse drug reactions on the coding of a hospital stay in Quebec: exploratory descriptive study by simulation

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ABSTRACT

The discharge summary sheet's coding allows calculation of the severity index (SI), mortality index (MI), and resource intensity weight (RIW). These indicators help to describe the burden of care for individual cases and could potentially influence patient-based funding. This study was undertaken to simulate the impact of different adverse drug reactions (ADRs) on the hospital length of stay, thus allowing calculation of the effect of ADRs on the SI, MI, and RIW. This exploratory descriptive study was based on computer simulations. We created, by simulation, seven patient profiles of various complexities representative of our patients. Fifteen types of combination of drug and ADR manifestation comprising 15 ADR caused by eight different drug classes were identified based on the most frequently coded ADR in fiscal years 2016–2017 and 2017–2018. Those 15 combinations were applied to the patient profile to simulate the impact on the SI, MI, and RIW in eight scenarios. From these data, we measured the impact

of the ADRs on these indicators. A total of 1,571 simulations were run. In general, the addition of a couple of drug and ADR manifestation contributed to increases in all three of the indicators. More specifically, the SI and RIW both increased in 30.7% (n = 482), whereas the MI increased in 14.6% (n = 229). For a same scenario, the impact on the three indicators could vary depending on the patient profile to which it was applied. This study has presented simulation data on the impact of the coding of ADRs on the hospital stay of a patient in Quebec.

Keywords: *pharmacovigilance; medical coding; mortality index; severity index; resource intensity weight*

According to regulations associated with recent legislative changes in Canada, health facilities will be required, starting in 2020, to report all serious adverse drug reactions (ADRs) within 30 days of their occurrence.[1] At the same time, funding reform for Quebec health facilities is under consideration by the government. The aim of this reform would be to fund health facilities, at least in part, on the basis of their clinical activity, as indicated by the codes associated with hospital stays.[2] The majority of ADRs are inevitable,[3] and product monographs detail the range of ADRs that can be expected with drug products.[4] In addition, the costs of managing ADRs, as documented in the literature, can be high.[5] The legislative and regulatory changes mentioned above highlight the importance of ensuring adequate coding of ADRs that occur before and during each hospital stay. Appropriate coding is likely to describe resource utilization per hospital stay and to identify measures that could be taken to avoid ADRs.

After a patient has been discharged, the patient's file is read and analyzed by a medical archivist, who validates the quantitative and qualitative data from the hospital stay and then codes the diagnoses (primary and secondary) according to the World Health Organization's International Statistical Classification of Diseases and Related Health Problems.[6] The archivist also codes interventions according to the Canadian Classification of Health Interventions.[7–9] These data are then entered into a software specific to the province of Quebec that produces quantitative indicators concerning the hospital stay, which reflects the burden of care associated with individual cases: the mortality index (MI) (from 1 to 4), the severity index (SI) (from 1 to 4), and the resource intensity weight (RIW) (from 0.0000 to 99.9999). The SI reflects the presence of comorbidities and complications influencing the intensity of the services that the patient needed during the hospital stay. The MI reflects the patient's probability of death during hospitalization. RIW is an "estimate of the importance and the relative volume of the resources used, the diagnostic, therapeutic or maintenance interventions, during the hospitalization."[10] A value of 1 for relative resource use corresponds to the average cost of a typical hospitalization in Quebec.[11] These indicators are derived from many patient-related characteristics, including the major diagnostic category according to ICD-10 (MDC) and the case mix group (CMG). According to the Canadian Institute for Health Information (CIHI), CMG and RIW are two indicators that are common to Quebec and the rest of Canada. However, MDC and SI are indicators specific to Quebec and would be the equivalent of major clinical categories (MCC) and resource intensity level (RIL), respectively. No equivalent indicator is available in the rest of Canada for the MI.[12] Any ADRs experienced by the patient are coded according to the drug class or classes involved in the reaction and the corresponding diagnostic codes. The presence of ADRs is likely to influence the burden of

care associated with each hospital admission (i.e., indicators).

To our knowledge, there are no Canadian data on the impact of ADR on the burden of care associated with hospital admission. We examined the impact of ADR coding on indicators that reflect the provision of inpatient care and services. The objective of this study was to simulate the impact of various ADRs on aspects of the hospital stay and to calculate the effect of ADR coding on the SI, MI, and the RIW.

METHODS

This exploratory descriptive study was based on computer simulation.

The study was conducted at CHU Sainte-Justine, a 500-bed mother–child university hospital in the province of Quebec. The study included data from three fiscal years (2016–2017 to 2018–2019).

The simulation was based on the identification of typical patient profiles and application of most frequently coded couples of drug and ADR manifestation to these patient profiles in different scenarios with different variations of variables. The researchers consisted of two medical archivists (DN, ID), a research assistant (PR), and study collaborators (AD, DL, JFB). The protocol was approved by the Institutional Research Ethics Board (#2951).

Identification of Typical Patients

As a first step, we used Med-GPS® software (Logibec, Montréal, Canada) to generate seven standardized patients among those seen over the defined study period. The standardized patients, designated as patients A through G, were characterized by the association of an MDC and its main CMGs.[13] We first selected the MDCs most frequently encountered in our establishment. MDCs considered to be unrepresentative of the population at risk for ADRs (e.g., MDC15, newborns) were excluded, where other MDCs (e.g., MDC17, lymphatic tumor, hematology, chemotherapy, radiotherapy) were favored. The CMGs most frequently connected to these MDCs were chosen as the main CMGs of interest for our simulation study. In addition, to limit the complexity of simulations, certain patient profiles with frequently encountered MDCs could not be considered for inclusion (e.g., MDC3, diseases/troubles related to ear, nose, mouth, throat, craniofacial). From these seven standardized patients, variations were made to apply the scenarios (e.g., age, sex, and multiple secondary diagnoses to vary the SI, MI, and/or RIW).

Identification of Drug-Manifestation Combinations Associated with ADRs

As a second step, we identified 15 drug-manifestation combinations associated with ADRs, of different severity and representing the most frequently coded ADRs during fiscal years 2016–2017 and 2017–2018. We then created a spreadsheet listing the total number of ADRs and the total number of severe ADRs induced by each drug class. In this spreadsheet, eight codes corresponding to drug classes of the ICD-10 were selected for the high frequency of total ADRs and/or the high frequency of severe ADRs, as well as for overall diversity. Then, the clinical manifestations associated with drugs in the eight drug classes were sought. For each drug class, two clinical manifestations were chosen: one more serious and the other less severe (except for one class of drug which was associated with only one serious clinical manifestation).

Identification and Application of Scenarios

As the third step, we created eight scenarios to test the impact on the three indicators of interest of adding the ADR-associated drug-manifestation combinations to the typical patient profiles. The scenarios were designed to investigate the following effects: (1) the effect of adding a single ADR to the seven standardized patients; (2) the effect of adding one ADR when complementary

diagnoses were added to the standardized patients; (3) the effect of multiple ADRs on a single standardized patient profile; (4) the effect of ADRs when the age of the standardized patients was varied; (5) the effect of ADRs when the sex of the standardized patients was varied; (6) the effect of ADRs when the SI of the standardized patients was varied; (7) the effect of ADRs when the MI of the standardized patients was varied; and (8) the effect of ADRs when the RIW associated with the standardized patients was varied.

The eight scenarios were tested using Med-Echo-Plus® software (Logibec, Montréal, Canada) by adding the ADR-associated drug-manifestation combinations to the standardized patient profiles. Taking into account available resources, we tried to make the most simulations.

Analysis Plan

The values of SI, MI, and RIW before and after each simulation were recorded in a spreadsheet (Excel^{MD}, Microsoft, Seattle, Washington, Etats-Unis). Only descriptive statistics were calculated. For each scenario, the 75th percentile (min, max) of variation in the three indicators were calculated, along with the proportion of simulations with a change in each indicator. Snapshots of the simulations were retained because the simulated data could not be saved and extracted from the software.

RESULTS

A total of 1,571 different simulations were run from January 1 to February 15, 2019: 486 simulations for scenario 1, 336 simulations for scenario 2, 57 simulations for scenario 3, 330 simulations for each of scenarios 4 and 5, 12 simulations for each of scenarios 6 and 7, and 8 simulations for scenario 8. The number of simulations for each scenario took into account the feasibility to perform the scenario and availability of the data.

Table 1 presents the profile of each standardized patient before the addition of ADRs, including the MDC and the main CMG.

Table 2 presents the profile of the 15 ADR-associated drug-manifestation combinations, including the drug class code and diagnosis code.

Table 3 summarizes the eight scenarios used for testing the impact of adding the ADR-associated drug-manifestation combinations on the SI, MI, and RIW.

TABLE 1. Profile of Each Standardized Patient before the Addition of ADRs, Including the MDC and the Main CMG

Standardized Patient Profiles	MDC		CMG		Values of the Indicators		
	Codes	Description	Codes	Description	SI	MI	RIW
A	1	Diseases and disorders of the nervous system	53	Convulsions	2	1–3	0.6885
B			58	Other disorders of the nervous system	1–3	1–2	0.8694–1.8314
C	6	Diseases and disorders of the digestive system	254	Other disorders of the digestive tract	1	1	0.3782
D	16	Diseases and disorders of the blood, hematopoietic organs, or the immune system	661	Platelet coagulation disorders	1–3	1	1.4285–1.9632

TABLE 1. (Continued) Profile of Each Standardized Patient before the Addition of ADRs, Including the MDC and the Main CMG

Standardized Patient Profiles	MDC		CMG		Values of the Indicators		
	Codes	Description	Codes	Description	SI	MI	RIW
E	17	Lymphatic, tumor, hematology, chemotherapy, and radiotherapy	690	Acute leukemia	1–3	1–2	1.8575–5.8278
F			691	Lymphoma or chronic leukemia	2	1	1.7855
G			3	Bone marrow transplantation	2	1	7.2894

CMG, case mix group; MDC, major diagnostic category; MI, mortality index; RIW, resource intensity weight; SI, severity index.

TABLE 2. Profile of 15 ADR-Associated Drug-Manifestation Combinations Including Drug Class Code and Diagnosis Code

ADRs Couples	Drug Class		Diagnostic	
	Code	Description	Code	Description
ADR1	Y43.1	Antitumor antimetabolites causing adverse effects during their therapeutic use	K12.3	Oral mucositis (ulcerative)
ADR2			D61.1	Medicated aplastic anemia (medullary aplasia)
ADR3	Y40.8	Other systemic antibiotics that cause induced adverse reactions during therapeutic use	L27.0	Generalized rashes due to medication
ADR4			T88.6	Anaphylactic shock due to adverse effects of an appropriate drug substance and properly administered
ADR5	Y46.6	Antiepileptic drugs, other and unspecified, causing adverse effects during their therapeutic use	E87.2	Metabolic acidosis
ADR6			R06.8	Breathing abnormalities, other and unspecified
ADR7	Y47.1	Benzodiazepines causing adverse effects during their therapeutic use	G25.3	Myoclonus
ADR8			R26.0	Ataxic approach
ADR9	Y59.3	Induced immunoglobulin causing adverse effects during their therapeutic use	I95.2	Drug hypotension
ADR10			T80.9	Transfusional reaction
ADR11	Y42.0	Glucocorticoids and synthetic analogues that have caused adverse effects during their therapeutic use	R73.9	Hyperglycemia, unspecified
ADR12			E27.3	Adrenocortical insufficiency
ADR13	Y45.0	Opioids and related analgesics	K59.0	Constipation
ADR14			R09.2	Respiratory stop
ADR15	Y43.3	Other antitumor medicines that have caused adverse effects during their therapeutic use	K85.3	Acute pancreatitis induced by drugs

ADR, adverse drug reaction.

TABLE 3. Profile of the Eight Scenarios Used for Testing the Impact of Adding the ADR-Associated Drug-Manifestation Combinations on the Severity Index, the Mortality Index, and the Resource Intensity Weight

Scenarios with Variations of Variables		Total	Profile of Observed Impacts on the SI, MI, and RIW Specifically Related to the Studied Variable	SI	MI	RIW
				75th Percentile [Min–Max]% Simulation with Variation		
1	An ADR	486	The impact of an EIM is different depending on the basic patient profile. Examples: - Patient C (SI = 1, MI = 1, RIW = 0.3782) + ADR5 => ↑ SI = 2 + ↑ MI = 2 + ↑ RIW = 0.6886 - Patient E (SI = 3, MI = 2, RIW = 5.8278) + ADR5 => ↑ SI = 4 + ↑ RIW = 10.0429	2 [0–2]	3 [0–3]	3.9703 [0–42,151]
				88.3%	41.4%	88.3%
2	MDC	336	No impact is observed on the simulations performed	0 [0–0]	0 [0–0]	0 [0–0]
				0%	0%	0%
3	Multiple ADRs	57	There is a cumulative effect on the SI and RIW in associations of multiple ADRs. Examples: - Patient B (SI = 3, MI = 1, RIW = 1.8314) + individual addition of ADR 1/3/4 => no impact - Patient B (SI = 3, MI = 1, RIW = 1.8314) + individual addition of ADR 2/5 => ↑ MI = 2 - Patient B (SI = 3, MI = 1, RIW = 1.8314) + addition of ADR 1 + 2 + 3 + 4 + 5 => ↑ SI = 4 + ↑ MI = 2 + ↑ RIW = 2.7629	1 [0–2]	1 [0–3]	0.9315 [0–1.4612]
				50.9%	35.1%	50.9%
4	Age	330	The impact of some ADRs is greater on a pediatric patient versus an adult patient. For examples: - Patient E (SI = 1, MI = 1, RIW = 1.8575, ages: 0/2/6/11/16 years old) + ADR15 => ↑ SI = 3 + ↑ RIW = 5.8278 - Patient E (SI = 1, MI = 1, RIW = 1.8575, age: 19 years old) + ADR15 => ↑ SI = 2 + ↑ RIW = 3,662 The impact is identical regardless of the age of the patient for other ADRs.	3.6%	0%	3.6%

TABLE 3. (Continued) Profile of the Eight Scenarios Used for Testing the Impact of Adding the ADR-Associated Drug-Manifestation Combinations on the Severity Index, the Mortality Index, and the Resource Intensity Weight

Scenarios with Variations of Variables		Total	Profile of Observed Impacts on the SI, MI, and RIW Specifically Related to the Studied Variable	SI	MI	RIW
				75th Percentile [Min–Max]% Simulation with Variation		
			For example: - Patient C (SI = 1, MI = 1, RIW = 0,3782, ages: 0/2/6/11/16/19 years old) + ADR14 => ↑ SI = 3 + ↑ MI = 4 + ↑ RIW = 1.1332			
5	Sex	330	No impact is observed on simulations	0 [0–0]	0 [0–0]	0 [0–0]
				0%	0%	0%
6	SI	12	An ADR sometimes has an impact with a fixed SI, if the basic SI of the patient is higher, then the ADR has no impact. Examples: - Patient D (SI = 1, MI = 1, RIW = 1.4285) + ADR4 => ↑ SI = 2 + ↑ RIW = 1,958 - Patient D (SI = 2, MI = 1, RIW = 1,958) + ADR4 => no impact is observed	1 [0–2]	0.75 [0–3]	0.136275 [0–0.5347]
				33.3%	25%	33.3%
7	MI	12	An increase in MI alone does not lead to an increase in SI and RIW in the simulations performed. Examples: - Patient D (SI = 3, MI = 1, RIW = 1.9632) + ADR14 => ↑ MI = 4	1 [0–1]	0,25 [0–3]	0.5778 [0–0.5778]
				41.7%	25%	41.7%
8	RIW	8	An increase in the SI systematically increases the RIW even if the basic RIW is higher. Examples: - Patient F (SI = 2, MI = 1, RIW = 1.7855) + ADR14 => ↑ SI = 3 + ↑ MI = 4 + ↑ RIW = 23,217 - Patient G (SI = 2, MI = 1, RIW = 7.2894) + ADR14 => ↑ SI = 3 + ↑ MI = 4 + ↑ RIW = 10.0142 Conversely, in the simulations carried out, the RIW never increases alone and is always linked to an increase in the SI.	0,25 [0–1]	0,75 [0–3]	0.13405 [0–2.7248]
				25%	25%	25%

ADR, adverse drug reaction; MDC, major diagnostic category; MI, mortality index; RIW, resource intensity weight; SI, severity index.

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The SI and RIW both increased in 30.7% (n = 482) of the 1,571 simulations, whereas the MI increased in 14.6% (n = 229) of the 1,571 simulations. We found that the same scenario could have a different impact depending on the particular patient profile used in the simulation.

DISCUSSION

To our knowledge, this is the first study simulating the impact of different ADRs in the form of an ADR-associated drug-manifestation combination on the coding of hospital stays and their effect on the SI, MI, and RIW. This study seems useful to us in a context of legislative changes requiring the reporting of serious ADR by Canadian health facilities starting in 2020 and the proposed reform for the funding of health facilities in Quebec.

Our study demonstrates that ADRs can affect the coding of hospital stays of patients. Observed MI, SI, and RIW changes are more marked in scenarios 1, 3, 4, 6, 7, and 8, while no changes are observed for scenarios 2 (effect of adding secondary diagnoses) and 5 (effect of sex).

These simulations highlight a number of key elements to remember: (1) the impact of adding an ADR varies according to the standardized patient profile. In our simulations, some ADRs have greater effects in sicker patients but the reverse is also observed. (2) The impact of adding an ADR varies according to the number of ADRs associated with a hospital stay. In our simulations, the addition of multiple ADRs may be associated with an increase in indicators, but not in all cases. (3) The impact of adding an ADR varies according to the age of the patient. In some cases, the impact is higher in pediatrics (young age) although our simulations have been limited in adult patients (>18 years). (4) The increase in SI is usually associated with an increase in RIW. (5) The increase in MI is not necessarily associated with an increase in SI and RIW.

The 15 ADR-associated drug-manifestation combinations tested are very varied given their diversity of clinical manifestations and they show very different impacts on the indicators. Some couples have no impact, while others result in increases in SI to 3 and MI to 4. Among the very high-impact couples, opioid-induced respiratory arrest and related analgesics (ADR # 14) cause an increase in the MI to its maximum (i.e., 4) on each simulation performed. Conversely, other ADR-associated drug-manifestation combination did not have any effect on any of the simulations performed. For example, these are generalized rashes secondary to other systemic antibiotics (ADR # 3) and respiratory abnormality secondary to antiepileptic drugs (ADR # 6).

The results obtained in these simulations are consistent with what might have been expected. Considering the physiological differences between an adult patient and a pediatric patient, it is not surprising that some ADRs have a more serious impact in pediatrics. In our examples, it was acute pancreatitis that showed a higher impact in pediatrics (i.e., increase in SI from 1 to 3 vs. 1 to 2 in adults and increase in RIW from 1.8575 to 5.8278 vs. 1.8575 to 3.662 in adults). According to the same reasoning, one would also expect higher impacts of some ADRs in the geriatric population. It would be interesting to test such scenarios in a hospital with a geriatric population of patient. Moreover, the age appears in phases I and III of rules of assignment of the SI, according to the normative framework in force.[14] Indeed, this framework specifies that the impact of age plays not only at the first level during the assignment of the SI of each secondary diagnosis of the patient, but also at the third level with impact according to the main diagnosis.

In addition, the use of CMG applicable to all patients, specified and reviewed (commonly referred to as APR-DRG), makes it possible to apply a subclass of clinical severity (i.e., from 1 to 4) and a subclass of mortality (i.e., from 1 to 4) at

each secondary diagnosis.[15] An algorithm taking into account all the SIs of each secondary diagnosis also makes it possible to establish the subclass of the patient's clinical severity. The ADRs that did not show any impact in our simulations are in line with our predictions because they are also those that we qualified as "less serious" according to their clinical presentation. For example, this is the case with generalized systemic antibiotic eruptions (i.e., ADR # 3) and opioid-induced constipation (i.e., ADR # 13). However, as the simulations have shown, the combination of several ADRs sometimes leads to greater impacts on the indicators. The assignment figure of the SI specifies that all the SIs of the secondary diagnoses are taken into account to determine the patient's SI. However, other observations challenge us. Indeed, in our simulations, some ADRs have a greater impact on MI depending on the patient's primary diagnosis. Thus, a metabolic acidosis will result in a higher risk of mortality according to the MDC (i.e., passage of 1–2 of MI in a patient with an MDC6 = diseases and disorders of the digestive tract vs. stabilization of MI to 1 in a patient with an MDC17 = lymphatic tumors).

Strengths

This descriptive study has strengths. This is a unique study that confirms the importance of proactively identifying ADRs when coding a hospital stay. In our hospital, a pharmacovigilance program has been set up under the auspices of the pharmacy department. This program includes a proactive detection of ADR by clinical pharmacists and a close link with the archive service to optimize the coding of the summary sheet completed at the end of each hospital stay.[16] Therefore, pharmacists can play an increased role in the quality of coding medical records.

Limitations

This descriptive study has limitations. This is an exploratory study. The study does not provide a definitive confirmation of the ADRs and baseline conditions that may lead to more variation in hospital stay indicators. The proposed scenarios represent a weak part of all possible combinations in a health facility (i.e., combination of four of the 25 possible MDCs and seven of the 283 CMGs applicable to our health facility). However, these scenarios represent interesting cases (e.g., MDC16 and MDC17) at risk of ADR in a mother-to-child Quebec institution.[17] Further work could better describe the extent of the relationship between ADRs and their impact on the coding of hospital stay records. Unlike the calculation of the SI, the explanations and calculation rules of the RIW available are very complex and deserve a deeper understanding. According to the Ministry of Health and Social Services, the RIW is obtained by averaging, on all APR-DRG, the adjusted cost, weighted by the number of typical cases of the case mix (3 years).[18] With regard to MI, there is little data available to understand its assignment rules.

CONCLUSION

This study has presented simulation data on the impact of the coding of ADRs on the hospital stay of a patient in Quebec. The SI and RIW both increased in 30.7% (n = 482) of the 1,571 simulations, whereas the MI increased in 14.6% (n = 229) of the 1,571 simulations. The addition of an ADR significantly increases SI, MI, and RIW in several simulated patients.

CONFLICTS OF INTEREST

All authors declare that they have no conflicts of interest.

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DATA AVAILABILITY STATEMENT

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

COMPLIANCE WITH ETHICAL STANDARDS

This article does not contain any studies involving human participants. The protocol was approved by the Institutional Research Ethics Board.

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