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Drug substitution associated with a hospital stay in Belgium: a retrospective analysis of a claims database

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Abstract

Objectives This study measures the extent of drug substitution associated with a hospital stay in Belgium.

Methods Data were extracted from the 2006–2007 dataset of the Belgian Agency of Health Insurance Funds on drug use of patients hospitalized in acute hospitals. Reimbursed drugs received in ambulatory care during the 3 months prior to hospitalization were compared with drugs received during the 3 months following hospital discharge. Both a narrow definition and a broad definition were used for drug substitution. Narrow substitution (switches between generic and originator drugs) was computed for 14 drug classes for chronic conditions with the highest public expenditure. Broad substitution (changes between chemical substances within the drug class at ATC level 4, changes in brand name) was calculated for statins and proton-pump inhibitors only.

Key findings The database included 17 764 patients (mean age 66 ± 17 years; 60% female). In 71% of cases an originator drug was received prior to and following hospitalization. A generic drug was received prior to and following hospitalization in 25% of cases. Some form of narrow substitution occurred in 4% of cases: a generic drug was replaced by an originator drug in 2% of cases and an originator drug was replaced by a generic drug in 2% of cases. Some form of broad substitution occurred in 25% of cases for proton-pump inhibitors and 13% of cases for statins.

Conclusions Hospitalization was not a trigger for changes between originator and generic versions of a drug. Broad substitution associated with a hospital stay was relatively limited for statins and proton-pump inhibitors.

Introduction

Medication management is an essential element of seamless care; that is, the continuity of patient care across the spectrum of caregivers and healthcare settings.[1] As a result of a transition between healthcare settings, changes may occur in the type of drug that is prescribed by a physician: a specialist physician may prescribe an originator drug whereas a primary care physician may prescribe the generic version of that drug, and vice versa. The term 'originator drug' refers to the first version of a drug developed and patented by a pharmaceutical company, whereas 'generic drug' refers to a drug that is developed to be the same as the originator drug and is marketed once all relevant patents on the originator drug have expired. The transition between healthcare settings may also be associated with changes in physician prescriptions between drugs in the same therapeutic class due to different prescription rules in hospital and in ambulatory care.

In Belgium, the size of generic drug markets varies between healthcare settings. Generic drugs are increasingly being prescribed and dispensed in ambulatory care: the market share of generic drugs by volume (as measured by the number of defined daily dosages, DDDs) in the Belgian retail market rose from 0.6% in 1997 to 24.0% in 2008.[2] Although no data are publicly available about the market share, the use of generic drugs in hospitals is restricted due to, among other things, the existence of hospital-specific drug formularies

that tend to list one commercial preparation of a specific (originator or generic) drug/dosage as a result of tenders organized by hospitals. The limited availability of generic drugs with a suitable pharmaceutical formulation (e.g. for intravenous injection or perfusion, for intramuscular injection, etc.) might explain why so few generic drugs are on drug formularies, and hence why generic drugs are prescribed to a lesser extent in hospitals.

These differences in the availability of generic drugs in ambulatory care and in hospitals may lead to drug substitution associated with a transition between these settings. In this respect, this paper relates specifically to changes in physician prescriptions between originator and generic drugs associated with a transition between hospital and ambulatory care. It does not relate to generic substitution in the sense that a physician prescribes an originator drug and the pharmacist dispenses a generic version of that drug, a practice that is not allowed in Belgium.

To date, little is known about the frequency of drug substitution associated with a hospital stay.[3] This is an important issue because switches to medications on hospital lists or dosage changes following hospital discharge may cause drug-related problems.[4] Such problems may also result from inappropriate drug reconciliation at hospital admission and/or discharge, insufficient patient information and insufficient communication between healthcare providers in different settings.[5] To reduce drug-related problems, a recent conference presentation recommended a redesign of care processes focusing on medication reconciliation, patient counseling and coaching, follow-up after hospital discharge and an increased role for the pharmacist.[6] With respect to the latter, a pharmaco-economic literature review found that hospital discharge interventions mostly performed by pharmacists to improve seamless pharmaceutical care are likely to enhance compliance and decrease hospital re-admissions and healthcare costs, but the impact on quality of life or clinical outcomes was not clear.[7]

The aim of this study was to measure the extent of drug substitution associated with a hospital stay in Belgium by comparing reimbursed drugs received in ambulatory care during the 3-month period prior to hospitalization with drugs received during the 3-month period following hospital discharge. This study was part of a larger project on seamless care between hospital and home conducted by the Belgian Healthcare Knowledge Centre.[8] In addition to the study reported here, the seamless care project summarized Belgian data on drug-related problems related to discontinuity of care, examined the (cost-)effectiveness of initiatives aiming to improve continuity of care between healthcare settings and conducted focus groups to identify and evaluate systems to improve seamless care in Belgium.

Methods

Study setting

The study focused on drug substitution in ambulatory care of patients who had been admitted and discharged from Belgian acute hospitals.

Data source

Data were extracted from the 2006–2007 permanent sample dataset of IMA/AIM, the Belgian Agency of Health Insurance Funds. This is an anonymous sample of the Belgian population that includes data on demographic characteristics and healthcare claims (including all prescriptions for reimbursed drugs). The permanent sample consists of a 1/40 sample of patients aged below 65 years and a 1/20 sample of patients aged 65 years or older. As older patients are over-represented in the permanent sample the analysis weighted data so that the results were representative of the Belgian population. At the time of the study this sort of aggregated, descriptive analysis of a claims database did not require approval from an ethics committee.

Data

The study database extracted information about demographic characteristics, drug claims and hospitalizations from the IMA/AIM permanent sample dataset. The demographic characteristics of patients related to gender, year of birth and time of death, if applicable.

Data on reimbursed drugs received in ambulatory care were extracted for the 3-month period prior to hospitalization and for the 3-month period following hospital discharge. The time horizon was restricted to 3 months as this increases the probability that any drug substitution during this period is associated with a hospital stay. Yet the time horizon is sufficiently long to increase the probability that a physician prescribes one of the drugs under study (see below). For each 3-month period, variables included the Anatomical, Therapeutic and Chemical (ATC) drug code,[9] the number of packs received in ambulatory care and the number of DDDs of all drugs, and dispensing dates.

Two additional variables allowed identification of generic drugs and 'cheap' drugs (this is an official term used in Belgium to denote generic drugs and originator drugs that have dropped their price to the level of the reference price[10] or a lower level). The label 'generic drug' referred to generic drugs and copies, while the label 'originator drug' related to originator drugs, parallel imported drugs, reference specialties and orphan drugs. Cases where a patient took more than 25 packs of a specific drug during a 3-month period were considered to be outliers.

Also, data were gathered on start and end dates of patient hospitalizations. Day hospitalization, palliative care and stays in a psychiatric hospital were not considered. In Belgium, psychiatric hospitals are distinct and separate institutions that have different organizational and financing rules than acute hospitals. As only those hospitalizations could be included that had a 3-month period prior to and following the hospital stay during 2006–2007, hospitalizations needed to start on 1 April 2006 at the earliest and needed to end on 30 September 2007 at the latest. Patients may have experienced multiple hospitalizations during 2006–2007. Two hospital stays, for which there was a gap of 3 days at the most between two stays, were considered as one hospitalization. In order to have data on drug use in ambulatory care during a 3-month time period, no other hospitalization could occur in the 3 months prior to or following a hospitalization.

Medications under study

The study was limited to all medications in drug classes that met the following criteria: (a) that belonged to the top 30 drug classes in terms of public expenditure in 2008,[11] (b) that were included in the national agreement between physicians and health insurance funds, (c) that may lead to transition-related problems between ambulatory care and hospital,[12] (d) that are administered for chronic conditions and (e) that included generic drugs. The selected drug classes are presented in Table 1.

Definitions of drug substitution

Both a narrow definition and a broad definition were used for drug substitution. In the primary analysis, narrow substitution was defined as a switch from a generic drug to an originator drug or vice versa between the pre- and post-hospitalization periods. A switch had to involve the same active substance as defined at ATC level 5 (for example, the generic drug Simvastatin Teva versus the originator drug Cholemed). When more than one medication of the same drug class (at ATC level 4) or chemical substance (at ATC level 5) was received during the pre- and post-hospitalization periods, in each case the medication received at the time closest to the hospitalization was used; that is, the last purchase of a drug prior to the hospitalization was compared with the first purchase following hospital discharge. Patients who died or stopped taking a drug at some point during the 3 months following hospital discharge were not excluded from the analysis. This is because such patients still provided relevant data about possible substitution associated with a hospital stay.

A secondary analysis explored broad substitution associated with a discharge from hospital. Broad substitution could involve:

1 changes between chemical substances within the same drug class at ATC level 4 (for example, a switch from simvastatin to atorvastatin),
2 changes in brand name of the product with the same composition (for example, switch from the originator drug

Table 1 Frequencies of generic and originator drugs prior to and following hospitalization

ATC code and name	Generic–generic drug	Generic–originator drug	Originator–generic drug	Originator–originator drug
A02B Drugs for peptic ulcer and gastro-oesophageal reflux disease	69 260 (56%)	2160 (2%)	1140 (1%)	51 900 (42%)
A10B Blood glucose lowering drugs, excluding insulins	7880 (10%)	1580 (2%)	680 (1%)	69 520 (87%)
C03B Low-ceiling diuretics, excluding thiazides	5960 (48%)	360 (3%)	220 (2%)	5760 (47%)
C03C High-ceiling diuretics	10 300 (23%)	1200 (3%)	1020 (2%)	32 420 (72%)
C03D Potassium-sparing agents	6380 (28%)	740 (3%)	520 (2%)	15 000 (66%)
C07A Beta-blocking agents	42 960 (28%)	4700 (3%)	1820 (1%)	101 700 (67%)
C08C Selective calcium-channel blockers with mainly vascular effects	10 020 (17%)	1680 (3%)	1100 (2%)	46 880 (78%)
C09A ACE inhibitors, plain	15 680 (19%)	1320 (2%)	840 (1%)	66 620 (78%)
C10A Lipid-modifying agents, plain	32 960 (28%)	1960 (2%)	920 (1%)	79 800 (69%)
M01A Anti-inflammatory and anti-rheumatic products, non-steroids	12 460 (24%)	3200 (6%)	2540 (5%)	34 660 (65%)
M05B Drugs affecting bone structure and mineralization	40 (0%)	0 (0%)	60 (1%)	17 820 (99%)
N02A Opioids	6800 (12%)	1420 (3%)	1500 (3%)	46 920 (83%)
N05A Antipsychotics	3280 (7%)	120 (0%)	100 (0%)	40 300 (93%)
N06A Antidepressants	34 260 (22%)	4020 (3%)	2440 (2%)	111 980 (73%)
Total	258 240 (25%)	24 460 (2%)	14 900 (2%)	721 280 (71%)

ACE, angiotensin-converting enyme.

Cholemed to the generic drug Simvastatin Teva), including the changes already analysed above (same chemical substance with a generic or originator label).

A change in tablet dosage (for example, switch from a tablet of 20 mg to a tablet of 40 mg of simvastatin) was not included in our definition of drug substitution because such a change may arise from a change in the patient's condition rather than relating to drug substitution.

The extracted database contained information about brand name and dosages, but not in separate fields. All marketed drugs therefore first had to be manually coded according to brand name and dosage separately to identify any possible change in brand name prior to and following hospitalization. The secondary analyses were restricted to the two specific drug classes of statin and proton-pump inhibitor. These drug classes were selected because they are administered for chronic conditions, generated the highest public expenditure in 2008[11] and are reported to lead to transition-related problems between ambulatory care and hospital.[12]

Data analysis

A descriptive analysis was carried out of the demographic characteristics of the patient sample. Characteristics were reported as relative frequencies for categorical data, and mean and standard deviation for normally distributed continuous data. The age was calculated as the difference between the year in which the most recent hospitalization took place and the year of birth.

When the same active substance was used prior to and following hospitalization (based on paired comparisons), the primary analysis quantified the extent of narrow substitution by calculating the percentage of generic drug to originator drug switches and the percentage of originator drug to generic drug switches between pre- and post-hospitalization periods. Also, the percentage of cases where a generic drug was received prior to and following hospitalization was computed. A similar percentage was calculated for originator drugs.

The secondary analysis focused on broad substitution and computed the frequency and percentage of possible changes (i.e. change within the drug class, change in brand name and no change) by type of drug (generic or originator drug) between pre- and post-hospitalization periods (based on paired comparisons). All analyses were conducted in SAS Enterprise Guide 4.

Results

The database related to 17 764 patients: the mean age of patients was 66 years (standard deviation 17 years) and 60% of patients were women. Patients had between one and four hospitalizations during 2006 and 2007. Cases where a patient took more than 25 packs of a specific drug during a 3-month period were considered to be outliers and, hence, seven cases were excluded from the dataset.

Drug substitution: narrow definition

The study database included 41 633 records where the patient received the same active substance prior to and following a hospitalization. Table 1 reports the extrapolated frequencies of generic drugs and originator drugs received during the 3-month periods prior to and following a hospitalization in 2006–2007. In 71% of cases an originator drug was received prior to and following hospitalization. Similarly, a generic drug was received prior to and following hospitalization in 25% of cases. Some form of narrow substitution occurred in 4% of cases: a generic drug was replaced by an originator drug in 2% of cases and an originator drug was replaced by a generic drug in 2% of cases.

With respect to individual drug classes, narrow substitution was most likely to occur for the following drug classes according to their ATC classification: M01A anti-inflammatory and anti-rheumatic products (11% of cases), N02A opioids (5%), C03D potassium-sparing agents (6%), C03B low-ceiling diuretics (5%), C03C high-ceiling diuretics (5%), C08C selective calcium-channel blockers with mainly vascular effects (5%) and N06A antidepressants (4%).

Drug substitution: broad definition

For the drug class of proton-pump inhibitors, Table 2 presents the frequency and percentage of broad substitution, broken down by the type of drug (originator or generic) delivered prior to the hospitalization. In general, no change occurred in 75% of cases, the name of the same chemical substance (at ATC level 5) changed in 13% of cases and changes between chemical substances within drug class at ATC level 4 happened in 12% of cases. When a generic drug was received prior to hospitalization, the name of the same chemical substance changed in 21% of cases and changes between chemical substances within the drug class occurred in 11% of cases. When an originator drug was received prior to hospitalization, the name of the same chemical substance changed in 2% of cases and changes between chemical substances within the drug class occurred in 13% of cases.

The frequency and percentage of broad substitution involving statins are presented in Table 3, broken down by the type of drug delivered prior to hospitalization. Considering both generic and originator drugs, no changes occurred in 87% of cases, name of the same chemical substance (at ATC level 5) changed in 9% of cases and changes between chemical substances within the drug class at ATC level 4 occurred in 4% of cases. When a generic drug was received prior to hospitalization, name of the same chemical substance changed in 23%

Table 2 Frequencies of changes by type of proton-pump inhibitor drug delivered before hospitalization

	Type of change after hospital discharge		
Type of drug delivered prior to hospitalization	Change between chemical substances within drug class (ATC level 4)	Change in brand name within ATC level 5	No change
Generic drugs	6720 11%	12 740 21%	40 640 68%
Originator drugs	5120 13%	760 2%	34 240 85%
Total	11 840 12%	13 500 13%	74 880 75%

Table 3 Frequencies of changes by type of statin drug delivered before hospitalization

	Type of change after hospital discharge		
Type of drug delivered prior to hospitalization	Change between chemical substances within drug class (ATC level 4)	Change in brand name within ATC level 5	No change
Generic drugs	1600 5%	7600 23%	24 200 72%
Originator drugs	2440 4%	1020 2%	62 020 94%
Total	4040 4%	8620 9%	86 220 87%

of cases and changes between chemical substances within the drug class occurred in 5% of cases. When an originator drug was received prior to hospitalization, name of the same chemical substance changed in 2% of cases and changes between chemical substances within the drug class occurred in 4% of cases.

Discussion

This study has observed a low rate of drug substitution associated with a stay in a Belgian acute hospital during 2006 and 2007 for the selected medications. Narrow substitution occurred in 4% of cases only, with substitution of an originator drug for a generic drug more likely to occur than vice versa. This may reflect the limited use of generic drugs in Belgian hospitals. A more detailed analysis for statins and proton-pump inhibitors showed that broad substitution at ATC level 4 (any changes in brand name and/or chemical substance) occurred in 13% of cases for statins and 25% of cases for proton-pump inhibitors. Unfortunately, the reason for changes (medical or other reasons) could not be retrieved from these administrative data. However, such changes create the potential for medication errors following hospital discharge.

To the best of the authors' knowledge, this is one of the few studies quantifying the frequency of drug substitution associated with a hospital stay. [3] Our analysis was able to draw on a large database of drug prescriptions that is representative of the Belgian population. Yet, our analysis suffered from a number of limitations. Our dataset was restricted to drugs that are reimbursed by RIZIV/INAMI, the Belgian third-party payer. Therefore, our results apply to substitution of reimbursed drugs only. Data on substitution of, for example, over-the-counter drugs and non-reimbursed prescription drugs associated with a hospital stay were not available. However, the issue of substitution is primarily relevant to reimbursed drugs, as few generic over-the-counter drugs are available in Belgium. Another limitation of this study is that it only gives information on changes between drugs received in ambulatory care: between the drugs prescribed before and after hospitalization. Intramural substitutions have not been studied. Finally, this study quantified the extent of drug substitution, but was not able to identify the rationale for substitution or to explore the possible health and cost impact of substitution between healthcare settings.

Few data are available about the extent of drug substitution associated with a hospital stay. A Dutch study investigated discontinuities in drug use upon hospital discharge.[13] Drugs of discharged patients that were dispensed by a community pharmacy were compared with the latest hospital medication. Forty per cent of prescriptions gave rise to some form of discontinuity, with 27% involving therapeutic substitution.

Schemes have been developed to enhance seamless care with a focus on narrow substitution. For instance, the Safe Therapeutic Economic Pharmaceutical Selection method (STEPS) was implemented in Northern Ireland.[14] This scheme reached agreement among specialist physicians, general practitioners, hospital and community pharmacists and prescribing advisers with regard to the use of seven generic drugs that had equivalent clinical efficacy as the originator drugs. In primary care, prescribing advisers actively promoted this substitution scheme with general practitioners. Community pharmacists were key players with regard to availability and stock management. In secondary care, contractual arrangements were put in place, ensuring that the agreed products were utilized in hospital and detailed on discharge. This process proved to be effective in achieving the objective of seamless care between secondary and primary care. Furthermore, the increased use of generic drugs was estimated to generate savings of £3.5 million.[14]

The larger project on seamless care between hospital and home (of which this study was one component)[8] also included focus groups that proposed recommendations for policy and for practice on how seamless care focusing on medication can be improved in Belgium. These recommendations included a national guideline about seamless care focusing on medication; a national campaign to increase awareness among healthcare professionals and patients about seamless care focusing on medication; a uniform, complete and up-to-date drug history of each patient and electronic infrastructure to support the exchange of drug data.[15]

Conclusions

This study has focused on the issue of drug substitution associated with a stay in a Belgian acute hospital during 2006 and 2007. It has shown that hospitalization is not a trigger for changes between originator and generic versions of a drug. More detailed analyses for statins and proton-pump inhibitors indicated that broad substitution associated with a hospital stay was relatively limited.

Declarations

Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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Authors' contributions

All authors contributed to the design of the study. CD analysed the data, SS wrote the draft manuscript and all co-authors provided feedback on the manuscript. All Authors state that they had complete access to the study data that support the publication.

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