In-hospital costs associated with chronic constipation in Belgium: a retrospective database study

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Key Messages

- Analyses were performed using data from the year 2008 from the IMS Hospital Disease Database, which comprises data on about 34% of all acute hospital beds in Belgium and includes information on patient demographics, drug use, diagnoses, and admissions.
- The average cost of chronic constipation per day in hospital was €441, and the most common drug treatments prescribed were osmotically acting laxatives.
- There are significant costs associated with chronic constipation, which are often underestimated.
- Costs were higher for patients with constipation-associated complications than without.

Abstract

Background Real-life data on the economic burden of chronic idiopathic constipation are scarce. The objectives of this study were to assess hospitalization resource use and costs associated with chronic constipation and its complications in Belgium. **Methods** This was a single country, retrospective study using the IMS Hospital Disease Database (2008), which comprises data on 34% of acute hospital beds in Belgium and contains information on patient demographics, length of stay (LOS), billed costs, drug use, diagnoses, and procedures. Stays with a primary diagnosis of constipation, or a secondary diagnosis of constipation and a concomitant diagnosis of a constipation-related complication, were selected. Patients with diagnoses of colorectal cancer, ulcerative colitis or Crohn's disease, or who had stays involving potentially constipation-inducing procedures, were excluded as having secondary constipation. Patients receiving opioids, calcium-antagonists, antipsychotics or antidepressants were excluded as having drug-induced constipation. **Key Results** In total, 1541 eligible patients were identified. The average unadjusted cost per day in hospital for idiopathic constipation was €441 (€311 ± 1.4 in day clinic visits without overnight stays; €711 ± 14.0 in full hospitalizations with complications). The average LOS in a full hospitalization setting was 7.0 and 4.0 days in stays with and without complications, respectively. The most frequent drug and procedural treatments were osmotically acting laxatives (with complications: 42.61%; without complications: 35.69%), and transanal enema (2.32% and 2.03%), respectively. **Conclusions & Inferences** The burden of constipation is often underestimated; it is a condition reflected by hospital-related costs comparable to such indications as migraine, which increase when associated with complications.

Keywords chronic constipation, costs, drug use, economic burden.

Abbreviations: APR-DRG, All Patient Refined-Diagnosis Related Groups; ATC, Anatomical Therapeutic

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Chemical; HDD, IMS Hospital Disease Database; IBS, irritable bowel syndrome; ICD-9, International Statistical Classification of Diseases and Related Health Problems Version 9, Clinical Modification; LOS, length of stay; MBDS, minimum basic data set; MI, myocardial infarction.

Constipation is a very common symptom that affects most people at some point during their lifetime. It can be either primary (idiopathic) or secondary (when related to an organic or metabolic disease or to the use of medications). However, for about 17% of the population in Europe,[1] it can be much more than just a temporary discomfort. When constipation becomes a recurrent or chronic disorder, it can affect the patient's health-related quality of life in a way that is comparable to other severe chronic diseases (chronic allergies, diabetes, musculoskeletal conditions)[2] and can even be associated with worse survival when compared with patients without symptoms of chronic constipation.[3]

Chronic primary constipation is a typical functional disease; it presents as a combination of subjective and objective factors that often are not correlated with any demonstrable physiological abnormality. As with many functional diseases, the definition of chronic constipation has been subject to much debate. Currently, it relies on a consensus approach, resulting from ongoing discussions.[4] In recent years, the most widely recognized criteria for functional bowel disorders (including irritable bowel syndrome [IBS], functional bloating, functional diarrhea, functional constipation, and unspecified bowel disorder) have been the definitions proposed by the Rome Foundation. The latest version of the criteria (Rome III) was published in 2006,[5] and provides a symptom-based definition applicable to chronic constipation that has been adopted across Europe. The criteria pertaining to functional/chronic constipation require the presence of at least two from a list of six symptoms (straining during at least 25% of defecations; lumpy or hard stools in at least 25% of defecations; sensation of incomplete evacuation for at least 25% of defecations; sensation of anorectal obstruction for at least 25% of defecations; manual maneuvers required to facilitate at least 25% of defecations; fewer than three defecations per week) combined with an inability to obtain loose stools without the use of laxatives. In addition, no diagnosis of IBS should be present. For constipation to be considered as chronic, the criteria should be fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis, thus allowing clear separation between transient gut symptoms and true cases of chronic constipation.[6]

Constipation is a heterogeneous condition, involving multiple causes such as lifestyle, psychological factors, inadequate diet, dysfunction of the gastrointestinal tract, underlying medical condition or medication use. In particular, drug-induced constipation is often associated with the use of specific drugs[7] such as opioids,[8] calcium-antagonists, antipsychotics,[9,10] and antidepressants.[7]

Most of the published estimates of the prevalence of chronic constipation range from 2% to 27% depending on the definition used,[1] whereas 12% of the population worldwide reports self-defined constipation,[11] with a higher prevalence consistently reported in women than in men.[1] Besides behavioral measures such as diet and change in lifestyle, current treatment options for chronic constipation include the use of laxatives (osmotic, stimulant or bulk-forming) or prokinetic agents and biofeedback; surgery is recommended only when all other treatment options have failed.[12] There is currently no published evidence regarding the cost and resource use associated with in-hospital management of chronic constipation in Belgium.

The purpose of this descriptive study was to estimate the cost per hospitalization (full hospitalization or visit to a day clinic), the average length of stay (LOS) in hospital, and the use of drug and non-drug treatments in Belgian patients with chronic constipation using retrospective data from a hospital discharge database.

METHODS

Data source

This study was a single country (Belgium), retrospective database study of adult patients hospitalized in 2008 (the most recent available data at the time when the study was initiated) with idiopathic constipation or a constipation-related complication as the principal diagnosis. The source of information was the IMS Hospital Disease Database (HDD). Since 1991, Belgian hospitals have had to register case mix data for each admission in a minimum basic data set (MBDS), to receive funding from the health care payer. These MBDS are captured via a Trusted Third Party, which standardizes the data. Then, a subset of the national database, consisting of hospitals that have given written authorization to do so, is anonymized (on both the hospital and the patient level) and transmitted to IMS, constituting the HDD. The HDD comprises data on about 34% of all acute hospital beds in Belgium. The panel of hospitals is representative of the Belgian population in terms of geographical dispersion, hospital size, and type of center (general hospital vs academic hospitals), so national prevalence figures for Belgium can easily be extrapolated from the database.

The unit in the HDD is the 'hospital stay', either in a day clinic setting (meaning that the patient does not stay overnight) or as a full hospitalization (at least one overnight stay). Each stay receives a unique identification number. Data recorded at the stay level comprise the LOS, the International Statistical Classification of Diseases and Related Health Problems Version 9 (ICD-9) diagnoses and procedure codes, the type of admission, the LOS

in the different services, and the type of discharge. A separate table lists all the drugs that were invoiced over the course of the stay (number of units, dose, and cost; prescription dates are not available, however) with the corresponding Anatomical Therapeutic Chemical (ATC classification system) codes. The database also includes demographic data at the patient level (age and sex). Within one calendar year, all the stays related to the same patient can be tracked through a unique patient identification number attributed at the beginning of each calendar year. The database does not include any information about ambulatory care.

Population selection

The study population was selected in two steps. As a first step, hospital stays were selected based on ICD-9 diagnostic codes. Because there is no specific code in the ICD-9 nomenclature for chronic constipation, the code corresponding to constipation (564.0) was used. All adult patients (age ≥20 years) having that code as a principal diagnosis were retained. Due to the coding of age by ranges and the unavailability of exact ages in the HDD, 'adult' had to be defined according to the closest available age range (20 years and older).

Concomitant diagnoses (i.e., at the time of constipation-related hospitalization) corresponding to constipation-related complications were also retrieved for these patients. The constipation-related complications retained for this analysis were 'anal fissure and fistula' (ICD-9 diagnosis code 565), 'fecal impaction' (560.39), 'impaction of intestine' (560.30), 'rectal prolapse' (569.1), 'hemorrhoids' (455), or 'peri-anal thrombosis' (453.8). 'Intestinal obstruction' (560, excluding 560.30 and 560.39) was not included as ICD-9 coding does not allow obstruction resulting from constipation to be distinguished from obstruction resulting from another organic cause such as stenosis. Adult patients having constipation as a secondary diagnosis but in combination with a primary diagnosis corresponding to one of the above-mentioned constipation-related complications were also included in the study population.

As a second step, exclusion criteria were applied. Because diagnoses are coded at the moment of discharge, we assumed that patients hospitalized with a principal diagnosis of constipation were likely to suffer from chronic constipation. The same assumption was made for patients who experienced one of the complications of interest, as such complications are not likely to occur in cases of acute constipation. However, as the study focused on patients with primary/idiopathic constipation, cases where constipation was likely to be directly attributable to another condition were excluded. Therefore, stays during which a concomitant diagnosis (principal or secondary) of colorectal cancer (ICD-9 codes 153 and 154), ulcerative colitis (ICD-9 code 556) or Crohn's disease (ICD-9 code 555) had been recorded were removed from the study sample. Similarly, stays where a dilatation of rectum (ICD-9 code 96.22) or a dilatation of anal sphincter (ICD-9 code 96.23) was performed were also withdrawn from the sample, as these procedures were possible extraneous causes of secondary constipation.

The identification of cases of possibly drug-induced (as opposed to idiopathic) constipation was based on the documented administration of specific drugs well described in the literature as prone to inducing constipation:[7–10] opioids (ATC code N02A), calcium-antagonists (ATC C08), antipsychotics (ATC N05A), and antidepressants (ATC N06A). Patients receiving one of these drugs during any hospitalization over the course of the calendar year (not necessarily related to constipation) were assumed to be 'drug-induced' constipation patients. Idiopathic cases were considered the main population of interest while potentially drug-induced cases were analyzed as a separate cohort.

Study endpoints

The primary study endpoints were the average cost per day and the average LOS in hospitalizations related to chronic idiopathic constipation. For a given stay, the hospitalization costs consist of three components: drug costs, room/bed costs, and procedure costs. Drug costs were extracted directly from the database. Room/bed costs and procedure costs were obtained by merging the data from the database with average costs per All Patient Refined-Diagnosis Related Groups (APR-DRG)/severity level as calculated from the financial data files that all the Belgian hospitals are legally required to send twice a year to the Belgian authorities. These costs are published on the website of the Ministry of Public Health (latest available: data year 2008).[13] Costs were then extrapolated to 2011 based on the progression in costs per APR-DRG as observed between 2001 and 2008 in the same published data using a geometric extrapolation.

Different variables reflecting the burden of the disease were also calculated as secondary endpoints: mortality during the stay, laxative drug use, and use of surgical procedures in patients with chronic idiopathic constipation.

All results were stratified per group age and gender. Age groups taken into account in this study were adult patients below and above 65 years.

Treatment of constipation

The use of laxatives was tracked in the database using the ATC codes as available in 2011. The following categories of laxatives were taken into consideration: softeners and emollients (ATC A06AA), contact laxatives (A06AB), bulk producers (A06AC), osmotically acting laxatives (A06AD), enemas (A06AG), and glycerol (A06X01).

Procedures used to treat constipation were retrieved using ICD-9 procedure codes. The list of procedures of interest, established after discussions with an expert gastroenterologist, included the following items: 'Manual reduction of rectal prolapse' (ICD-9 code 96.26), 'Proctoclysis' (ICD-9 code 96.37), 'Removal of impacted feces' (ICD-9 code 96.38), 'Other transanal enema' (ICD-9 code 96.39), and 'Biofeedback' (ICD-9 code 94.39).

Analytical approach

Data were analyzed using SAS software version 9 (SAS Institute, Cary, NC, USA). All unadjusted average values are reported with standard errors. Given the skewed distribution, average costs are also reported with their range (minimum and maximum).

Average daily cost and LOS were also adjusted for age, gender, and other descriptive variables (presence of a concomitant diagnosis of cancer, presence of constipation-related complications, use of constipation-related medications/treatments, and admission through emergency unit) with multivariate regression models, using a gamma distribution and a log-link function. Adjusted values are reported with 95% confidence intervals (CI). Statistical significance was assessed with reference to an *a priori* α level of 0.05.

RESULTS

Eligible population

A total of 2694 stays with a principal diagnosis of constipation or constipation-related complication were

retrieved from the Belgian database for the full year 2008, corresponding to 2615 unique patients (one patient could have more than one stay over the course of the year; Table 1). After exclusion of non-adult patients/patients with a diagnosis of colorectal cancer, ulcerative colitis or Crohn's disease documented over the course of the calendar year, the sample comprised 2101 eligible patients, corresponding to 2172 stays. Among all patients with constipation, 1541 (~73.3%) were identified as cases of idiopathic constipation (corresponding to 1574 stays), while the remaining 560 (~26.7%) patients had drug-induced constipation (corresponding to 598 stays). Thirty patients (1.9%) in the main cohort had more than one constipation-related hospitalization during the study period.

Of the eligible patients in the study cohort, 1052 (~68.3%) were women and 948 (~61.2%) were younger than 65 years. The largest subgroup was female patients younger than 65 years old, accounting for 41.8% of the eligible population. The percentage of stays corresponding to full hospitalizations was 33.5% (Table 2) and relevant complications were recorded in 12.8% of the stays ($n = 202$), the most common being hemorrhoids ($n = 139$; 8.8%) and fecal impaction ($n = 31$; 2.0%).

Average cost per day in hospital

The average unadjusted estimated cost per day in hospital with a principal diagnosis of constipation/constipation-related complication was €441 ± 4.9 in

patients with idiopathic constipation (ranging from €311 ± 1.4 in stays in day clinic without overnight stay to €711 ± 14.0 in full hospitalizations with complications; Table 3). The average daily cost of hospitalization was significantly higher in patients with complications (€499 ± 15.5) than in patients without complications (€433 ± 5.1; $p < 0.001$). Age greater than 65 years was consistently associated with higher daily costs ($p < 0.001$).

Average LOS in hospital, admission through an emergency unit, and mortality in patients with a principal diagnosis of constipation

The average unadjusted LOS in patients with idiopathic constipation admitted in a full hospitalization setting was 4.6 (±0.47) days (Table 4). The average LOS was significantly higher in patients experiencing complications than in patients with no recorded complications (7.0 ± 2.4 days vs 4.0 ± 0.3 days; $p > 0.001$). When adjusted for age, gender, and such factors as admission through the emergency room, the presence of a codiagnosis of cancer or the use of constipation-related medications or procedures, the adjusted LOS was 6.1 days [95% CI 5.2–7.2] in patients with a complication and 4.1 days [95% CI 3.6–4.6] in patients without a complication. Thirty percent of patients (both full hospitalizations and visits to a day clinic) were admitted through an emergency unit. In-hospital mortality was 0.32%.

Treatment of constipation

A record of laxative administration or an invasive procedure was found in 42.1% of stays (70.2% of full hospitalizations and 27.9% of visits to a day clinic). In the overall population, the most frequently used drugs were osmotically acting laxatives (given in 36.79% of stays), enemas (16.16% of stays), and contact laxatives combined with osmotically acting laxatives (5.20% of stays).

The most common surgical/invasive procedure was transanal enema (2.07% of stays). For all types of treatments, except proctoclysis and contact laxatives, the rate of use was higher in patients with complications than in those without (Table 5).

DISCUSSION

This study presents an estimation of the unadjusted average daily cost associated with a hospitalization for chronic idiopathic constipation in Belgium in 2011. It also provides an estimation of the average LOS asso-

Table 1 Attrition table identifying patients included in the final study population

Group of patients	Number of patients	Number of stays
Initial population: with a primary diagnosis of constipation/constipation-related complication	2615	2694
Patients younger than 20 years	492	500
Adult patients (≥20 years)	2123	2194
With a diagnosis of colorectal cancer during the calendar year	15	15
With a diagnosis of ulcerative colitis during the calendar year	1	1
With a diagnosis of Crohn's disease during the calendar year	6	6
Adult patients with no organic cause of constipation	2101	2172
Patients receiving potentially constipation-inducing drugs during the calendar year (≈ drug-induced constipation)	560	598
Final eligible population: adult patients with idiopathic constipation	1541	1574

Table 2 Description of study sample: number of stays with idiopathic constipation (percentages between brackets show the proportion of stays in full hospitalization setting)

	Men (20–65 years)	Men (>65 years)	Women (20–65 years)	Women (>65 years)	All adults
Without complication	225 (30.2%)	217 (45.6%)	624 (19.9%)	306 (47.1%)	1372 (31.7%)
With complications (all)	38 (36.8%)	22 (59.1%)	86 (34.9%)	56 (62.5%)	202 (45.5%)
With anal fissure and fistula (565[*])	4 (75.0%)	2 (50.0%)	9 (55.6%)	5 (100.0%)	20 (70.0%)
With fecal impaction (560.39)	7 (71.4%)	6 (100.0%)	8 (100.0%)	10 (90.0%)	31 (90.3%)
With impaction of intestine (560.30)	1 (100.0%)	1 (100.0%)	–	1 (100.0%)	3 (100.0%)
With rectal prolapse (569.1)	–	–	2 (50.0%)	7 (85.7%)	9 (77.8%)
With hemorrhoids (455)	26 (19.2%)	13 (38.5%)	67 (23.9%)	33 (42.4%)	139 (28.8%)
All stays	263 (31.2%)	239 (46.9%)	710 (21.7%)	362 (49.4%)	1574 (33.5%)

[*]Complications are identified with the ICD9 codes specified between brackets.

ciated with these hospitalizations. Finally, it estimates other resource use and potential cost drivers associated with hospital admissions for chronic constipation, such as LOS in intensive care units, rate of admission through an emergency room, mortality, use of laxatives, and use of surgical procedures.

A total of 2172 stays with constipation or a constipation-related complication as a principal diagnosis (and no concomitant diagnosis of colorectal cancer, ulcerative colitis or Crohn's disease) corresponding to adult patients were found in the database; extrapolated to the whole Belgian population, this would represent a total of 6388 stays over the course of the calendar year. In 598 (27.5%) of these stays, one potentially constipation-inducing drug was administered and it was assumed that constipation was drug induced. Projection to the total Belgian population suggests that there are ~4600 hospitalizations for idiopathic constipation per year in Belgium. As a reference point, there are about 20 000 hospitalizations for heart failure per year.[13]

Costs and resource use appear to be consistently higher in cases where constipation was associated with a complication. First, the LOS was significantly higher in patients with a constipation-related complication than in patients with no complication (7.0 days *vs* 4.0 days). This result was confirmed when adjusting the LOS for confounding factors (adjusted LOS of 6.1 days [95% CI 5.2–7.2] in patients with a complication *vs* 4.1 days [95% CI 3.6–4.6] in patients without a complication).

Secondly, there were a higher proportion of patients being hospitalized in a full hospitalization setting (thus requiring higher resource use) in the population with a complication than without (45.5% *vs* 31.7%). Finally, the average daily cost of hospitalization, adjusted for gender, age, and other confounders, was significantly higher in stays with a complication (€498 [95% CI 490–507]) than in stays without a complication (€433 [95% CI 428–438]). The combination of these three factors

resulted in an average unadjusted cost per stay that was significantly higher in patients with complications than in patients without complications (€2128 *vs* €1036; *p* < 0.001), thus clearly demonstrating the incremental burden of complications.

Patients tagged as 'cases of drug-induced constipation' were not included in the main analyses as part of the cost, and resource use related to these cases may have been due to other serious underlying conditions (e.g. cancer) that could have explained at least part of the cost rather than the constipation itself.

The list of laxative drugs and invasive procedures of interest was established based on expert opinion. However, in 57.9% of the eligible stays (29.8% of the full hospitalizations and 72.1% of the visits to a day clinic), none of these invasive procedures had been performed and none of these laxative drugs had been administered. This could be due to the fact that 'watchful waiting' was the chosen approach or that the physician did not complete all actions and only diagnostic tests were performed (which are not collected in the database). Also, in 12% of the stays tagged as day clinic in our analyses, the patients were admitted through an emergency unit; it is possible that they went to the emergency room due to constipation and were sent back home with a prescription for laxative drugs.

The study showed that 0.32% of patients with idiopathic constipation died during stays where constipation was recorded as the principal diagnosis (as a comparison, the overall in-hospital mortality rate as calculated from the whole HDD—i.e., also including the most severe pathologies—during the same year was 1.56%). However, it was not possible to determine whether death was related to the constipation or any comorbidity or underlying indication, so these figures should be interpreted cautiously.

The study was descriptive, but the main endpoints (cost and LOS) were also adjusted for possible confounders. The main limitation of this study was that it was not possible to identify cases of chronic constipa-

Table 3 Average daily cost (in Euros) of hospitalization with a principal diagnosis of constipation

| | Unadjusted cost estimates* | | | | | Adjusted cost estimates† |
	Men (20–65 years)	Men (>65 years)	Women (20–65 years)	Women (>65 years)	All adults	All adults
Without complication	426 (±12.3) [278–1019]	484 (±13.7) [233–1206]	390 (±6.7) [250–1533]	489 (±11.3) [250–866]	433 (±5.1) [233–1533]	433 [428–438]
Full hospitalization	699 (±8.6) [554–1019]	693 (±8.9) [529–1206]	702 (±5.7) [573–978]	692 (±5.1) [551–866]	696 (±3.4) [529–1206]	695 [686–705]
Day clinic	309 (±1.1) [278–360]	308 (±2.2) [233–453]	313 (±2.5) [250–1533]	309 (±1.3) [250–405]	311 (±1.4) [233–1533]	311 [308–314]
With complication	502 (±43.4) [263–1218]	523 (±36.8) [273–739]	462 (±23.4) [250–1047]	541 (±26.8) [250–1008]	499 (±15.5) [250–1218]	498 [490–507]
Full hospitalization	802 (±54.7) [616–1218]	654 (±12.8) [575–739]	725 (±25.7) [527–1047]	684 (±16.0) [535–1008]	711 (±14.0) [527–1218]	715 [702–728]
Day clinic	328 (±14.6) [263–554]	334 (±28.4) [273–557]	319 (±7.1) [250–555]	303 (±4.7) [250–335]	319 (±5.4) [250–557]	317 [312–323]
All stays	437 (±12.3) [263–1218]	487 (±12.9) [233–1206]	399 (±6.6) [250–1533]	497 (±10.4) [250–1008]	441 (±4.9) [233–1533]	441 [436–447]
Full hospitalization	716 (±12.3) [554–1218]	689 (±8.0) [529–1206]	707 (±6.8) [527–1047]	690 (±5.2) [535–1008]	699 (±3.7) [527–1218]	699 [688–709]
Day clinic	311 (±2.2) [263–554]	310 (±2.9) [233–557]	313 (±2.4) [250–1533]	309 (±1.2) [250–405]	312 (±1.4) [233–1533]	312 [308–315]

*All unadjusted values are given with SE (between brackets) and range.
†All adjusted values are given with 95% confidence intervals. Costs were adjusted for gender, age category (20–65 years/older than 65 years), presence of cancer diagnosis, admission through an emergency unit, and presence of a constipation-related medication/procedure documented in the patient's data.

tion conclusively. The content of the database did not allow a strict application of the Rome III criteria; the chronic character of constipation cases cannot be established based solely on ICD-9 coding. Different criteria were included in the database search strategy to alleviate this limitation as much as possible.

Only hospital stays with a principal diagnosis of constipation or a constipation-related complication were retained; this first criterion ensured that constipation was the main reason leading to the hospitalization, and not just a potentially acute symptom resulting from an underlying condition. Stays with a concomitant diagnosis of colorectal cancer, ulcerative colitis, or Crohn's disease were excluded from the study population because these concomitant indications were assumed to be the cause of the constipation. On the other hand, some other malignancies that might result in severe constipation due to peritoneal carcinomatosis (e.g., gastric, ovarian or pancreatic cancers) were not excluded as we could not identify them in the database (no specific code for peritoneal carcinomatosis) and might account for some of the severe cases.

The study also applied a differentiation between patients hospitalized for idiopathic constipation or for drug-induced constipation; hospital stays where opioids, calcium-antagonists, antipsychotics or antidepressants had been prescribed were assumed to relate to drug-induced constipation. However, as the database did not register dates of prescription, it was not possible to establish whether the patient was already receiving the potentially constipation-inducing drug when the diagnosis of constipation was registered, or whether the drug was prescribed later during the course of the hospitalization (as an example, opioids can be the cause of constipation if the patient was under treatment at hospital admission, but they can also be administered during the hospitalization to relieve the pain resulting from surgery performed for a constipation-related complication). Conversely, some patients might have been hospitalized for opioid-induced constipation but the opioid treatment could have been disrupted at the moment of the hospitalization (and hence not recorded in the database); these cases of drug-induced constipation were not identified as such. As a consequence, the criterion used for differentiation should be considered as a proxy that might be questionable in some situations.

Two more limitations resulting from the nature of the database have to be acknowledged. Firstly, by definition, the database only contains information related to hospitalizations (full hospitalization and

Table 4 Length of stay (LOS), percentage of admissions through emergency room (ER), and mortality in hospitalizations with a principal diagnosis of constipation

	Average LOS (in days)		Admission through ER (%)	Mortality (%)
	Unadjusted*	Adjusted†		
Without complication	1.3 (±0.1)	1.3 [1.1–1.5]	30.32	0.29
Full hospitalization	4.0 (±0.3)	4.1 [3.6–4.6]	66.67	0.92
Day clinic	–	–	13.45	0.00
With complications (total)	3.2 (±1.1)	2.8 [2.4–3.3]	24.75	0.50
Full hospitalization	7.0 (±2.4)	6.1 [5.2–7.2]	50.00	1.09
Day clinic	–	–	3.64	0.00
All stays	1.5 (±0.2)	1.5 [1.3–1.7]	29.61	0.32
Full hospitalization	4.6 (±0.5)	4.4 [3.9–5.1]	63.76	0.95
Day clinic	–	–	12.42	0.00

*All unadjusted values are given with standard errors (between brackets) and range.
†All adjusted values are given with 95% confidence intervals. Costs were adjusted for gender, age category (20–65 years/older than 65 years), presence of cancer diagnosis, admission through an emergency unit, and presence of a constipation-related medication/procedure documented in the patient's data.

Table 5 Use of laxatives and surgical procedures in hospitalizations with a principal diagnosis of constipation. Data are presented as the percentage of stays where a drug was administered or the surgical procedure performed

	Without complications			With complications			All		
	All	Full hospitalization	Day clinic	All	Full hospitalization	Day clinic	All	Full hospitalization	Day clinic
Laxatives									
Softeners and emollients	0.33	0.78	0.00	5.51	8.64	0.00	1.15	2.53	0.00
Contact laxatives combined with osmotically acting laxatives	4.76	11.04	0.19	7.54	11.82	0.00	5.20	11.21	0.17
Contact laxatives only	1.42	3.25	0.09	1.16	1.82	0.00	1.38	2.93	0.08
Osmotically acting laxatives only	35.69	48.31	26.49	42.61	55.00	20.80	36.79	49.80	25.89
Bulk producers	0.33	0.78	0.00	1.45	2.27	0.00	0.51	1.11	0.00
Enema	14.61	29.74	3.60	24.35	37.27	1.60	16.16	31.41	3.38
Others	0.11	0.26	0.00	0.29	0.45	0.00	0.14	0.30	0.00
Surgical procedures									
Manual reduction in rectal prolapse	0.00	0.00	0.00	1.45	2.27	0.00	0.23	0.51	0.00
Proctoclysis	0.22	0.52	0.00	0.00	0.00	0.00	0.18	0.40	0.00
Removal of impacted feces	0.93	1.69	0.38	2.90	4.55	0.00	1.24	2.32	0.34
Other transanal enema	2.03	2.86	1.42	2.32	2.73	1.60	2.07	2.83	1.44
Biofeedback	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

day clinic); conversely, it is not possible to collect data on ambulatory visits or on out of hospital drug use. As a consequence, the use of procedures that are widely performed in an ambulatory setting might be considerably underestimated. That restriction may explain the very low percentage of use observed for certain procedures (such as biofeedback or manual disimpaction). Secondly, while all stays related to the same patient can be tracked through a unique patient identification number attributed at the beginning of each calendar year, it is not possible to follow up patients for more than one calendar year because patients' identification numbers are reinitialized at the beginning of each year. This should not be a drawback, however, as we calculated the average annual cost associated with a chronic condition in general and not linked to a specific episode.

To benchmark this cost of chronic constipation, a comparison was made with the average cost of a hospitalization for migraine and for acute myocardial infarction (MI) using the same database and the same methodology (the lack of detailed demographic information in the database did not allow for conducting a full case–control study). Migraine (ICD-9 code 346) was chosen because it is a symptomatic indication, similar to idiopathic constipation and therefore a good benchmark group.[14] Myocardial infarction (ICD-9 code 410) was selected because it is a resource-intensive indication that constitutes a well referenced upper threshold when discussing hospitalization costs. An extrapolation from the HDD showed that the number of patients hospitalized in 2008 for MI or migraine was 19 000 and 2500, respectively. The average cost of a full hospitalization for MI and migraine was €6698 ± 118.9 and

€2027 ± 88.5, respectively, whereas it was €2891 ± 257 for a full hospitalization for chronic idiopathic constipation.

It might be argued that most constipated patients would be treated in ambulatory setting and that hospitalization costs only represent a marginal portion of the economic burden of constipation. According to an American case–control study following a cohort of 168 women suffering from chronic constipation and comparing it with a matched control group (n = 336) over a 15-year period,[15] the average number of visits to hospital (including inpatient visits, outpatient visits, and admission through emergency unit) was 0.54 visits per patient-year in the case group vs 0.36 visits per patient-year in the control group. The difference (0.18 visits to hospital per patient-year) can be used as a proxy to estimate the incremental rate of hospitalizations due to chronic constipation. This estimate is consistent with the rates provided by a European study, showing an incremental rate of hospitalization attributable to chronic constipation equal to 0.44 and 0.32 visits/patient-year in a population of patients with constipation-predominant IBS in France and the United Kingdom, respectively.[16] This confirms the fact that most of the constipation patients would seek treatment in an ambulatory setting and be treated for instance with laxatives available as over-the-counter drugs. However, the higher proportion of constipation patients treated in ambulatory setting is compensated by the low cost related to these patients as compared with hospitalized patients; Caekelbergh et $al.$ (2009) estimated that the cost of an episode of constipation related to opioid use treated in ambulatory setting in Belgium was €130 (95% CI: 108–153), including the cost of laxatives that are not reimbursed by the Belgian public health care payer.[17] As a consequence, hospitalization costs remain an important component of the economic burden of constipation, despite the relatively low rate of hospitalization.

DISCLOSURE

IMS HEOR, employer of PC and ML, has received consulting fees to conduct the research that resulted in this manuscript. AJ is an employee of Shire AG based in Nyon, Switzerland. DD and GB have no conflicts of interest to declare.

AUTHOR CONTRIBUTION

PC and ML contributed to study conception and design, data analysis, and interpretation of the results; AJ and DD contributed to study conception and interpretation of the results; GB contributed to interpretation of the results. All authors were involved throughout the development of the manuscript and approved the final version.

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