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Constipation-related direct medical costs in 16 887 patients newly diagnosed with chronic constipation

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Background **Chronic constipation is a common condition, but the exact impact on healthcare budgets in Western Europe is poorly documented.**

Objectives **The aim of this study was to (a) investigate chronic constipation-related direct medical costs in patients with newly diagnosed chronic constipation and (b) study differences in costs according to natural history.**

Patients and methods **We identified 16 887 patients newly diagnosed with chronic constipation in a Dutch health insurance database (~1.3 million patients) in 2006–2009. Individuals with chronic constipation were selected on the basis of chronic laxative use (≥90 days/year) and diagnostic related groups for chronic constipation. On the basis of the episodes of laxative use and diagnostic related groups, individuals were categorized as having persistent, episodic, and nonrecurrent disease. Unadjusted costs for laxatives and hospital care for chronic constipation and constipation-related comorbidities were assessed and compared between patients with nonrecurrent, episodic, and persistent disease. Factors associated with costs were identified using Cox regression analyses.**

Results **The mean total chronic constipation-related direct medical costs in the first year after diagnosis were €310 ± 845 and consisted of laxatives (45%) and hospital care for chronic constipation (26%) as well as constipation-related comorbidities (29%). Costs were highest in patients with persistent disease (€367 ± 882) compared with patients with episodic (€292 ± 808) and nonrecurrent (€263 ± 613) disease ($P < 0.01$). Male sex was associated with higher costs, whereas increasing age, diabetes, and use of opioids were associated with lower costs.**

Conclusion **Pharmacy costs and hospital care costs for chronic constipation-related comorbidities were the largest cost drivers for total constipation-related direct medical costs in patients with newly diagnosed chronic constipation. Direct medical costs differed according to patient characteristics.** ***Eur J Gastroenterol Hepatol*** **26:1260–1266 © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

Constipation is a common cause of abdominal discomfort and painful defecation and is characterized by hard and infrequent stools, straining, and/or sensation of incomplete evacuation [1,2]. In all, 70–90% of patients with constipation report having symptoms for years [3,4] and it is therefore considered a chronic disorder. However, the natural history of chronic constipation may differ considerably between patients. The disease course of chronic constipation can be characterized as episodic or persistent [5]. Some patients can be treated successfully with lifestyle modification, dietary changes, and increased fiber and fluid intake [1,6]. For patients who fail to respond to these approaches, physicians typically prescribe laxatives [1,7].

Chronic constipation impacts the healthcare budget because of physician visits and procedures, medication use, and diagnostic procedures to identify underlying etiology. Currently, studies reporting the combined costs of healthcare utilization for chronic constipation have predominantly been carried out in the USA. In a study based on national healthcare visit surveys, it was shown that chronic constipation results in more than 2.5 million hospital and physicians visits per year in the USA [8]. In two previous studies, the mean annual direct medical costs for (chronic) constipation were estimated to be between $250 and $500 per patient in the USA in the period 1995–2003 [9,10], whereas out-of-pocket expenses approximated $400 per patient per year [9]. Because of a lack of studies, the exact impact of chronic constipation

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on healthcare budgets in Western Europe is largely unknown.

The primary aims of this study were to (a) estimate the incidence and prevalence of chronic constipation between 2006 and 2009 in the Netherlands and (b) investigate the overall and specific chronic constipation-related direct medical costs in patients newly diagnosed with chronic constipation.

Patients and methods

Data collection

For this retrospective cohort study, we studied data of the Achmea Health Database (AHD), a healthcare claims database covering ~1.2 million patients (8% of the Dutch population). In the Netherlands, inhabitants are obliged to have a basic healthcare insurance, which covers healthcare costs for physician visits, hospitalizations, diagnostic tests, procedures, and medication for chronic use. The population insured by Achmea Health Insurance represents the urbanized area of the Netherlands with respect to age, sex, and socioeconomic status [11].

The AHD contains anonymized data on demographic characteristics, reimbursed diagnostic related groups (DRGs), and ambulatory pharmaceutical prescriptions. DRGs are based on the International Classification of Disease, ninth revision (ICD-9). DRGs are reimbursed per episode of care provided by secondary care physicians for all hospital care services including diagnostic and therapeutic procedures, hospitalizations, outpatient visits, and medication provided during hospitalizations. The available data do not allow identification of laboratory tests, endoscopies, and other services that were provided to individual patients. In addition, in the Dutch DRG system, there are no data available on visits to general practitioners for chronic constipation.

Data on reimbursed pharmaceutical prescriptions contain information on type of drug (ATC codes), date the drug was filled, amount of daily defined doses (DDDs), prescribed daily dose (PDD), and costs reimbursed by the third paying party to the pharmacist. The DDD is the average maintenance dose per day for a drug used for its main indication in adults [12]. The PDD is the fraction of DDD per day that is actually prescribed by the treating physician. Over-the-counter medication is not reimbursed and is therefore not available in this study. A complete list of laxatives and enemas with the corresponding ATC codes and DDDs is provided in Appendix Table 1. The prescribed amount of days for medication was calculated as follows: prescribed days = DDD/PDD. For laxative prescriptions where the PDD was unknown (15.6%), we assumed that the prescribed amount of days was equal to the amount of DDD. For prescriptions in which the amount of DDD was unknown (3.8%), which mainly involved enemas (48.3%), we assumed that the prescribed amount of days was equal to 1.

Chronic constipation diagnosis and natural history

The complete database was systematically searched for adult (≥18 years) patients who were newly diagnosed with chronic constipation in the period January 2006 to December 2009. Chronic constipation was defined as a minimum of two prescriptions for laxatives/enemas for cumulative 90 days or more (not necessarily consecutive) within a period of 1 year and/or the presence of a DRG for chronic constipation. The date of chronic constipation diagnosis was set as the index date and was defined as the date of the first laxative prescription that fulfilled the above criteria for chronic constipation or the date of the first DRG for chronic constipation. The individual start of observation for patients included in the AHD began in 2005 for patients who were already part of the cohort before 2005 or in later years for patients who joined the Achmea Health Insurance after 2005. Cases that fulfilled the above criteria for chronic constipation in the first year after the individual start of observation ($n = 23\,984$) were excluded to ensure that only patients with newly diagnosed chronic constipation were included. Patients with DRGs for inflammatory bowel disease or colorectal cancer before or within 1 year after the diagnosis of chronic constipation were excluded from this study.

The use of laxatives, enemas, and chronic constipation hospital care was divided into episodes for each individual patient. A new constipation episode was defined as a period with laxatives and/or a DRG for chronic constipation that was not filled/registered within 90 days after the end of the last laxative supply or the end of the latest DRG for chronic constipation. Patients with chronic constipation were divided into three groups: patients with 'nonrecurrent disease' (single constipation episode and > 1 year free of constipation), patients with 'episodic disease' (multiple constipation episodes with ≥ 90 days' intervals), and patients with 'persistent disease' (single constipation episode until the end of follow-up). Patients with less than 1 year of follow-up after the end of a single episode of chronic constipation (12% of chronic constipation patients) could not be classified into either of these groups and were excluded from subgroup analyses, but were included in the entire cohort analyses.

Other variables

Clinical factors previously reported to be associated with a risk of chronic constipation [13] were identified through DRG and ATC codes between 90 days before and 90 days after the diagnosis of chronic constipation. These risk factors included multiple sclerosis, Parkinson's disease, diabetes, hypothyroidism, and use of opioids, β-blocking agents, calcium antagonists, antidepressants, and psycholeptic agents for 30 days or more. For this study, we defined DRGs for irritable bowel syndrome

(IBS), hemorrhoids/anal fissures, and ileus/volvulus starting from 3 months before the diagnosis of chronic constipation as being related to chronic constipation [14].

Outcomes

The primary outcomes of this study were (a) a diagnosis of new chronic constipation and (b) total and specific chronic constipation-related direct medical costs (euros) up to 3 months before and after (first year and per 3 months) the diagnosis of chronic constipation in new chronic constipation cases. The presented costs are the actual unadjusted, unstandardized costs, meaning that the presented costs were not corrected for inflation. Chronic constipation-related direct medical costs were calculated using laxative and enema prescriptions, DRGs for chronic constipation, and DRGs for constipation-related comorbidities that were reimbursed by the third-party payer Achmea Health Insurance to pharmacists and secondary care physicians.

Data analyses

The incidence and prevalence of chronic constipation were calculated by dividing the number of new and existing chronic constipation cases per year by the total number of patients insured by Achmea Health Insurance in that particular year.

Differences in baseline characteristics were analyzed using Pearson's χ^2-test and one-way analysis of variance where applicable. The Wilcoxon signed-rank test was used to analyze differences in costs. Multivariable Cox regression analyses were used to identify independent risk factors for high chronic constipation-related direct medical costs and provided hospital care. Patients whose direct medical costs exceeded the 90th percentile were classified as patients with high costs. The date of diagnosis of chronic constipation and the date of end of follow-up were used as the underlying time variables. Statistical analyses were carried out using Statistical Analyses System (SAS) software package version 9.2 (SAS Institute, Cary, North Carolina, USA). Two-sided *P*-values less than 0.05 were considered statistically significant.

Results

Between January 2006 and December 2009, we identified 16 887 patients with new chronic constipation (64.6% female, mean age at diagnosis 64.0 ± 17.9 years), corresponding with a mean annual incidence of 0.32% (range 0.30–0.37%). Patient characteristics are shown in Table 1. The mean annual prevalence of chronic constipation was 2.1% and increased from 1.9% in 2006 to 2.4% in 2009. Of all patients with new chronic constipation, 94.4% were identified on the basis of the chronic use of laxatives, 0.2% on the diagnosis and treatment by a secondary care physician (DRG for chronic constipation), and 5.4% by a combination of these. Of all patients with new chronic constipation, 2133 (12.6%) were classified as having nonrecurrent disease, 10 058 (59.6%) as having episodic disease, and 2659 (15.7%) as having persistent disease, whereas 2037 (12.0%) could not be classified into either of these groups.

Chronic constipation-related direct medical costs in the first year after diagnosis

Chronic constipation-related healthcare utilization and direct medical costs in the first year after chronic constipation diagnosis are shown in Table 2. Almost all patients (99.8%) were treated with laxatives/enemas, whereas 5.6% received inpatient or outpatient hospital care (gastroenterologists, internists, or surgeons) for chronic constipation and 6.2% for constipation-related comorbidities (e.g. IBS, hemorrhoids/anal fissures, and/or ileus/volvulus). The mean total costs per patient in the first year after diagnosis were €310 ± 845, consisting of laxative/enema prescriptions (mean €138 ± 101, 45%) and hospital care for chronic constipation (mean €82 ± 514, 26%) and constipation-related comorbidities (mean €90 ± 650, 29%). The mean hospital care costs only including treated individuals were €1471 ± 1637 for chronic constipation and €1456 ± 2208 for constipation-related comorbidities.

Stratified analyses for natural history are summarized in Fig. 1 and available in more detail in Appendix Table 2. The mean total chronic constipation-related direct medical costs were the highest ($P < 0.01$) in patients with persistent disease (€367 ± 882) compared with patients with nonrecurrent (€263 ± 613) and episodic disease (€292 ± 808).

Costs per 3 months and cumulative costs

Costs per 3 months in all new chronic constipation cases and stratified for disease course are shown in Fig. 2, Appendix Figs 1–3, and Appendix Tables 3 and 4. In the 3 months before the diagnosis of chronic constipation, 1.7% of the patients were treated with laxatives/enemas, 1.9% were treated for constipation-related comorbidities, and the mean total costs were €38 ± 488, almost fully consisting of hospital care costs for constipation-related comorbidities. In the total population of patients with new chronic constipation, as well as stratified for disease course, chronic constipation-related direct medical costs were the highest in the first 3 months after diagnosis and decreased thereafter. The mean cumulative chronic constipation-related direct medical costs after 3, 6, 9, and 12 months were €154 ± 610, €214 ± 694, €267 ± 782, and €316 ± 834, respectively.

Risk factors

Male sex was associated independently with high total chronic constipation-related direct medical costs [hazard ratio (HR) 1.13, 95% confidence interval (CI) 1.02–1.25], whereas increasing age (HR 0.72, 95% CI 0.64–0.82; for

Table 1 Baseline characteristics of 16 887 patients with new chronic constipation

Patient characteristics	Total[d]	Nonrecurrent	Episodic	Persistent	*P*-value[e]
Patients [*n* (%)]	16 887	2133 (12.6)	10 058 (59.6)	2659 (15.7)	–
Follow-up (person years)	45 562	6412	30 505	5240	–
Age (mean ± SD)	64.0 ± 17.9	58.8 ± 18.5	63.4 ± 17.8	68.5 ± 16.1	< 0.01
Female sex [*n* (%)]	10 902 (64.6)	1407 (66.0)	6649 (66.1)	1610 (60.6)	< 0.01
Medical history [*n* (%)][a,b]					
Hypothyroidism	1083 (6.4)	103 (4.8)	666 (6.6)	178 (6.7)	< 0.01
Parkinson's disease	496 (2.9)	50 (2.3)	305 (3.0)	79 (3.0)	0.23
Multiple sclerosis	168 (1.0)	16 (0.8)	116 (1.2)	18 (0.7)	0.04
Diabetes mellitus[c]	2863 (17.0)	351 (16.5)	1733 (17.2)	398 (15.0)	0.02
Medication use [*n* (%)][a,c]					
Opioids	3186 (18.9)	312 (14.6)	1675 (16.7)	746 (28.1)	< 0.01
β-Blocking agents	4305 (25.5)	479 (22.5)	2558 (25.4)	727 (27.4)	< 0.01
Calcium antagonists	2672 (15.8)	269 (12.6)	1606 (16.0)	476 (17.9)	< 0.01
Antidepressants	2911 (17.2)	314 (14.7)	1759 (17.5)	470 (17.7)	< 0.01
Psycholeptics	5159 (30.6)	539 (25.3)	3073 (30.6)	949 (35.7)	< 0.01

[a]Present between 90 days before and 90 days after the diagnosis of chronic constipation.
[b]On the basis of diagnostic related groups.
[c]On the basis of medication use of cumulative 30 days or more.
[d]12.1% of patients could not be classified as having nonrecurrent, episodic, or persistent disease.
[e]One-way analysis of variance and Pearson's χ^2-test were applicable for baseline differences between nonrecurrent, episodic, and persistent disease.

Table 2 Chronic constipation-related medication use, secondary healthcare utilization, and direct medical costs (euros) in the first year after the diagnosis of chronic constipation

Healthcare claims	Number of patients [*n* (%)]	Total costs	Costs per patient (mean ± SD)	Costs per patient (median, 10–90%)
Laxatives/enemas				
Total (≥1 laxatives/enemas)	16 856 (99.8)	2 333 638	138 ± 101	114 (43–260)
Stool softeners	17 (0.1)	561	0 ± 1	0 (0–0)
Bulk laxatives	2718 (16.1)	163 495	10 ± 34	0 (0–25)
Osmotic laxatives	315 (1.9)	7762	0 ± 5	0 (0–0)
Poorly absorbed sugars	16 207 (96.0)	2 112 406	125 ± 99	102 (26–250)
Stimulant laxatives	1460 (8.7)	18 654	1 ± 10	0 (0–0)
Enemas	1274 (7.5)	30 760	2 ± 22	0 (0–0)
Hospital care				
Chronic constipation[a]	946 (5.6)	1 391 438	82 ± 514	0 (0–0)
Constipation-related comorbidities[a]				
Total (≥1 comorbidities)	1041 (6.2)	1 515 601	90 ± 650	0 (0–0)
IBS	679 (4.0)	682 709	40 ± 279	0 (0–0)
Hemorrhoids/anal fissures	264 (1.6)	223 905	13 ± 150	0 (0–0)
Ileus/volvulus	117 (0.7)	608 986	36 ± 569	0 (0–0)
Total	16 887 (100.0)	5 240 677	310 ± 845	122 (45–598)

IBS, irritable bowel syndrome.
[a]On the basis of diagnostic related groups.

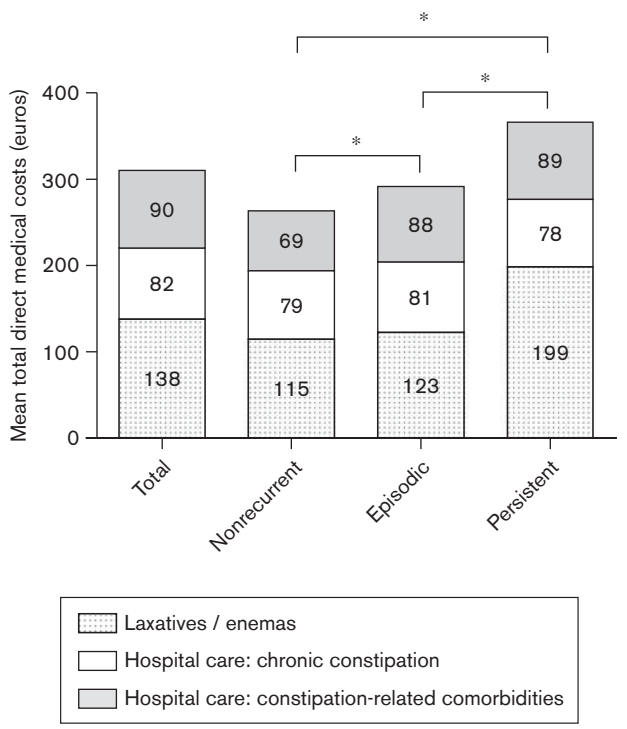
age > 70 years vs. < 50 years), diabetes (HR 0.69, 95% CI 0.59–0.80), and opioid use (HR 0.74, 95% CI 0.63–0.86) were associated with lower total costs. Further analyses for individual components of costs are shown in Table 3.

Discussion

Here, we report the costs of chronic constipation in a large cohort of patients newly diagnosed with chronic constipation in the Netherlands. Our main finding is that the mean annual total chronic constipation-related direct medical costs are €310 per new chronic constipation patient and mainly consisted of pharmacy costs (45%) and hospital care for chronic constipation-related comorbidities (29%) including IBS, hemorrhoids/anal fissures, and ileus/volvulus. However, this is probably a conservative estimation because we did not include primary care visits in our analyses. Costs are highest in the first year after diagnosis, especially in the first 3 months, but gradually decrease in the second and third year. The mean annual incidence of new chronic constipation between 2006 and 2009 was 0.32% and the mean annual prevalence was 2.1%. The latter finding is lower compared with previous studies in Western Europe, although these studies had a different study design and used self-reported questionnaires [15].

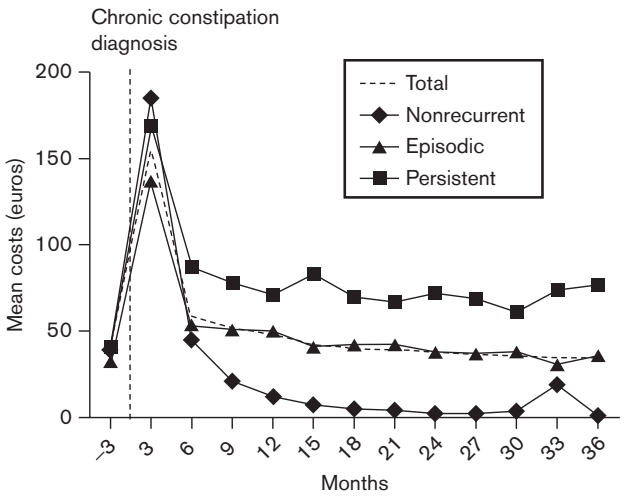
Although differences exist in study populations, our results are similar to those of two previous large US cohort studies carried out in 2007 [9,10]. A study by Nyrop *et al.* [9] in more than 525 000 members of a Health Maintenance Organization found that the mean annual direct medical costs related to the 'lower GI' in patients with constipation were $487. However, individual components of these costs (i.e. pharmacy and treatment) directly related to chronic constipation were not reported. Singh *et al.* [10] investigated direct medical costs in patients with constipation on the basis of

Fig. 1



Individual components of the mean chronic constipation-related direct medical costs (euros) in the first year after the diagnosis of chronic constipation. *Tested with Wilcoxon signed-rank test ($P < 0.01$).

Fig. 2



Mean total chronic constipation-related direct medical costs (euros) per 3 months in all patients with new chronic constipation and stratified for disease course.

longitudinal data from Medi-Cal (California Medicaid Program, Sacramento, California, USA). During a 15-month period, the total constipation-related direct medical costs were $246. Costs for laxatives/enemas were responsible for only 2% of the total costs compared with 45% in the present study. However, Medi-Cal is a Medicaid Program, providing healthcare coverage for low-income and disabled persons, and their expenditures per adult are approximately two to three times lower compared with the total US Medicaid expenditures per adult [16]. Therefore, the results of this US study cannot be extrapolated directly to the total US population or be compared directly with the population of the present study.

As can be expected, significant differences were found in costs between patients with nonrecurrent, episodic, and persistent disease. During the complete follow-up, both total and pharmacy costs were significantly higher in patients with persistent disease compared with patients with nonrecurrent and episodic disease. Patients with episodic and persistent disease were also more frequently treated for constipation-related comorbidities after the first 3 months after diagnosis, resulting in significantly higher costs compared with patients with nonrecurrent disease. These results emphasize that hospital care costs for chronic constipation are higher in patients with ongoing disease compared with patients with episodic or nonrecurrent disease.

A remarkable finding of our study is the inverse associations between multiple clinical factors, direct medical costs, and hospital care. Increasing age and use of opioids, antidepressants, and psycholeptic drugs were associated with high laxative costs, but inversely associated with hospital care for chronic constipation and constipation-related comorbidities. All of these clinical factors have been found to be associated with an increased risk of developing chronic constipation [15,17,18], and may, in theory, lead to increased constipation-related costs. However, these specific patients may also have had laxatives prescribed to prevent constipation and constipation-related comorbidities, resulting in a lower probability of receiving hospital care. In contrast, patients with secondary chronic constipation may also be prescribed laxatives for constipation as part of the treatment for the underlying disease. In those cases, DRGs for chronic constipation might not be claimed, leading to an underestimation of the actual chronic constipation-related direct medical costs.

The strengths of the present study include the high number of patients, the availability of complete and accurate data, and the possibility of investigating risk factors for high chronic constipation-related direct medical costs and healthcare utilization [11]. A possible limitation includes the risk of misclassification because of administrative errors, although we expect this to be minimal [19] because of the economic function of the database [11]. DRGs and pharmacy costs are only reimbursed after extensive control of the electronic

Table 3 Independent risk factors for high chronic constipation-related direct medical costs and hospital care

	HR (95% CI)			
Patient characteristics	High total costs	High laxative costs	Hospital care for chronic constipation	Hospital care for constipation-related comorbidities
Age at diagnosis (years)				
<50	Ref.	Ref.	Ref.	Ref.
50–60	0.98 (0.85–1.13)	1.17 (1.01–1.36)	0.90 (0.74–1.10)	1.01 (0.84–1.21)
60–70	0.94 (0.81–1.08)	1.20 (1.03–1.39)	0.80 (0.66–0.98)	0.91 (0.76–1.10)
>70	0.72 (0.64–0.82)	1.03 (0.90–1.17)	0.76 (0.65–0.90)	0.64 (0.54–0.76)
Male sex	1.13 (1.02–1.25)	1.19 (1.08–1.32)	1.10 (0.96–1.26)	1.13 (0.99–1.29)
Medical history[a,b]				
Hypothyroidism	0.86 (0.70–1.07)	1.15 (0.96–1.38)	1.10 (0.85–1.42)	0.70 (0.52–0.94)
Parkinson's disease	0.68 (0.44–1.05)	1.10 (0.80–1.51)	0.77 (0.44–1.33)	0.60 (0.33–1.09)
Multiple sclerosis	0.80 (0.35–1.82)	0.51 (0.24–1.05)	1.79 (0.80–4.01)	0.39 (0.09–1.74)
Diabetes mellitus[c]	0.69 (0.59–0.80)	0.95 (0.83–1.09)	0.77 (0.63–0.95)	0.69 (0.56–0.84)
Medication use[a,c]				
Opioids	0.74 (0.63–0.86)	1.18 (1.04–1.34)	0.70 (0.57–0.87)	0.83 (0.69–1.00)
β-Blocking agents	0.95 (0.84–1.08)	0.85 (0.75–0.96)	0.85 (0.72–1.01)	0.99 (0.85–1.16)
Calcium antagonists	0.94 (0.81–1.10)	1.06 (0.92–1.22)	1.10 (0.91–1.33)	0.85 (0.69–1.04)
Antidepressants	0.97 (0.85–1.11)	1.12 (0.99–1.27)	0.93 (0.78–1.12)	0.99 (0.83–1.17)
Psycholeptics	0.96 (0.85–1.08)	1.34 (1.20–1.49)	0.94 (0.80–1.10)	0.86 (0.74–1.00)

CI, confidence interval; HR, hazard ratio; Ref, reference.
[a]Present between 90 days before and 90 days after the diagnosis of chronic constipation.
[b]On the basis of diagnostic related groups.
[c]On the basis of medication use of cumulative 30 days or more.

registration. Second, the definition of chronic constipation was based on laxative use for at least 90 days per year and approximates the Rome III criteria in which patients are required to have symptoms for at least 3 months. As we could only identify patients on the basis of their claims and not by their symptoms, misclassification of patients with secondary constipation, IBS constipation, or other functional abdominal disorders may have occurred. Another possible drawback is that patients with constipation, who are prescribed laxatives for less than 90 days per year, were not included in our study. This may have underestimated the incidence and prevalence of chronic constipation in our study. Third, the amount of days for which laxatives were prescribed was calculated using the PDD and DDD. For laxative prescriptions where the PDD was unknown (15.6%), we assumed that the prescribed amount of days was equal to the DDD. Although this approach may have led to biased results, sensitivity analysis showed that in cases where the PDD was known, the calculated amount of days was similar to the DDD (data not shown). Fourth, data on out-of-pocket expenditures for medication and costs for chronic constipation specific primary care and physiotherapy visits are not available. Our results are therefore a conservative estimation of the total chronic constipation-related medical costs. Fifth, we only have data on overall direct medical costs that were made and we do not have data on what specific diagnostics tests were performed. Finally, we defined constipation-related comorbidities as the presence of DRGs for IBS, hemorrhoids/anal fissures, and/or ileus/volvulus. It is, however, debatable whether these conditions can fully be attributed to chronic constipation in patients included in the present study as causality cannot be proven. Despite the fact that constipation-related comorbidities also occurred in the 3 months before the diagnosis of chronic constipation, indicating they might not be fully related to chronic constipation, these comorbidities may still have been caused by constipation [14], although not chronic yet according to our definitions.

This study should create awareness among physicians and third-party payers that chronic constipation-related direct medical costs largely depend on a relatively small number of patients (~6%) who receive hospital care for constipation or constipation-related conditions. To lower direct medical costs, new and effective therapeutic agents for constipation are required that can help in preventing expensive hospital care treatment for chronic constipation and constipation-related comorbidities.

Conclusion

We showed that pharmacy costs and hospital care costs for chronic constipation-related comorbidities are the most important cost drivers for the total constipation-related direct medical costs reimbursed by third-party payers in patients with new chronic constipation. Direct medical costs differed considerably according to the natural history, comorbidities, and medication. Despite the fact that only a relatively small number of patients with new chronic constipation received hospital care for chronic constipation and constipation-related comorbidities, both have a huge impact on the total direct medical costs.

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Conflicts of interest

A.J. and P.H. are employees and owns stock options of Shire. For the remaining authors there are no conflicts of interest.

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