

Systematic review: the economic impact of irritable bowel syndrome

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SUMMARY

Background: Although little mortality is associated with irritable bowel syndrome, curative therapy does not exist and thus the economic impact of this disorder may be considerable.

Methods: A systematic review of the literature was performed. Studies were included if their focus was irritable bowel syndrome, and direct and/or productivity (indirect) costs were reported. Two investigators abstracted the data independently.

Results: One hundred and seventy-four studies were retrieved by the search; 11 fulfilled all criteria for entry into the review. The mean direct costs of irritable bowel syndrome management were reported to be UK£90, Canadian\$259 and US\$619 per patient annually, with total annual direct costs related to irritable bowel

syndrome of £45.6 million (UK) and \$1.35 billion (USA). Direct resource consumption of all health care for irritable bowel syndrome patients ranged from US\$742 to US\$3166. Productivity costs ranged from US\$335 to US\$748, with total annual costs of \$205 million estimated in the USA. Annual expenditure for all health care, in addition to expenditure limited to gastrointestinal disorders, was significantly higher in irritable bowel syndrome patients than in control populations.

Conclusions: Despite the lack of significant mortality, irritable bowel syndrome is associated with high direct and productivity costs. Irritable bowel syndrome patients consume more gastrointestinal-related and more total health care resources than non-irritable bowel syndrome controls, and sustain significantly greater productivity losses.

INTRODUCTION

Irritable bowel syndrome is a prevalent functional gastrointestinal disorder characterized by abdominal pain or discomfort associated with abnormal patterns of defecation.^{1–9} Although not a cause of significant mortality, irritable bowel syndrome has been shown to be associated with significant detrimental effects on the health-related quality of life.^{10, 11} Definitive treatment

of this disorder remains elusive. Although a variety of pharmacological agents have been utilized to treat irritable bowel syndrome, few have been subject to rigorous testing.¹² As a result of the high prevalence, detrimental impact on the quality of life and absence of curative therapy, irritable bowel syndrome has the potential for creating tremendous economic pressure on the health care system.^{13–15}

It has been estimated that 3.5 million physician visits are made annually in the USA for irritable bowel syndrome, accounting for up to 25% of all patients seen in gastroenterologists' practice.¹⁶ Irritable bowel syndrome is the seventh most prevalent diagnosis

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amongst all physicians and the most common diagnosis made by gastroenterologists.¹⁶ Despite these impressive numbers, it has been estimated that only 10–25% of all subjects with symptoms consistent with irritable bowel syndrome seek medical care.^{13, 17, 18} There is therefore the potential for substantial economic impact resulting from the direct consumption of health care resources, as well as the loss of productivity and reduction in the quality of life, even amongst those not seeking health care.

Cost determination is a complex process due to multiple factors. The identification of the cost of providing a service requires an understanding of the perspective of the analysis. Potentially different perspectives include those of a third-party payer (insurance company, government), a hospital, an individual patient or society as a whole. Costs must be differentiated from charges, which vary greatly and may include a mark-up for profit and cost shifting for coverage of non-reimbursed services or other losses.^{19–21} It must be stated what direct health care costs are included in the analysis, such as hospitalizations, out-patient or emergency visits, procedures and medication. Differentiation between the resources utilized for diagnostic evaluation and the resources consumed for therapeutic interventions should be performed. In addition, assumptions regarding the direct non-health care and productivity (indirect) costs that are incorporated must be provided. Finally, costs may be derived from hospital accounting systems, claims databases, insurance reimbursements or other administrative databases that were not originally designed for research purposes. Despite these limitations and challenges, it remains an important task to estimate the magnitude of resource expenditure required to manage irritable bowel syndrome so that the economic impact of this disorder may be compared with that of other diseases, and any new treatment interventions may be evaluated for efficacy and economic viability.

We performed a systematic review of the published literature with the primary intent of determining the economic impact of irritable bowel syndrome. Specifically, we sought to determine the total costs, including direct and productivity (indirect) costs, associated with irritable bowel syndrome in adults. In addition, we aimed to determine what types of cost were included in published economic analyses of irritable bowel syndrome. Our search included international sources of data and was not restricted to the monetary description of economic impact.

METHODS

Literature review

A systematic review of the literature was performed to ascertain the economic impact of irritable bowel syndrome. Guidelines for the conduct of systematic reviews have been published previously.^{22, 23} The focused clinical question we wished to address was: 'what are the direct, productivity (indirect) and total costs associated with irritable bowel syndrome?' A computer-assisted search of five online bibliographic databases was performed. The MEDLINE database from 1966 to June 2002, the EMBASE database from 1988 to 2002, Current Contents, the Cochrane Library and PreMEDLINE were interrogated using the MESH term (exploded) Colonic disease, functional OR keywords irritable bowel syndrome OR irritable colon OR spastic colon AND MESH terms (exploded) cost and cost analysis; cost of illness; health care costs; cost-benefit analysis; economics; economics, hospital; economics, medical; economics, pharmaceutical OR keywords cost OR costs. Bibliographies of identified articles were also reviewed to trace other potential studies not revealed by the search.

Study selection criteria

Requirements for study inclusion in this systematic review included the following: (i) disease limited to irritable bowel syndrome (chronic abdominal pain, pelvic pain or dyspepsia without irritable bowel syndrome were excluded); (ii) presentation of economic impact, including direct or productivity (indirect) costs; (iii) adult population; (iv) original data (reviews of other studies excluded); and (v) English language. Costs were not limited to the US currency and could be expressed in non-monetary terms. As study assessment could not be performed on abstracts, this study was limited to publications in full manuscript form. One investigator (J.M.I.) reviewed all the articles captured in the search for relevance to the study question.

Data abstraction

A standardized data abstraction form was prepared for this study. Two reviewers (J.M.I. and M.B.F.) performed independent data abstraction for each manuscript meeting the entry criteria. The data abstracted included: manuscript authors, journal, year of publication, study setting (geographical location and study environment), patient population, method of verification of irritable

bowel syndrome, method of cost calculation, standardized cost year, study perspective (third-party insurer, societal, hospital or practice), direct costs, productivity (indirect) costs and total costs. Discrepancies in data abstraction were resolved by consensus.

Statistical analysis

Due to the heterogeneity of the basis upon which costs amongst studies were identified, a quantitative meta-analysis to aggregate cost data could not be performed. Specifically, the resources used to derive direct health care-related costs and productivity costs varied substantially between the studies, as did the monetary basis (\$US, £UK, \$Canadian). The data are presented quantitatively and descriptively in tabular form. The manner in which costs were defined is detailed in the Appendix. It should be noted that no study attempted to quantify intangible costs (potential costs associated with decrements in the quality of life), and thus these were not included in this review.

RESULTS

Characteristics of the selected studies

The search strategy yielded 95 published manuscripts from the MEDLINE database. Seventy-four additional references were obtained from the EMBASE database

and five additional studies through PreMEDLINE. No additional published studies were noted in the databases of Current Contents or the Cochrane Library. When duplicate entries had been accounted for, there were 174 published manuscripts identified. The review of each manuscript identified 11 articles that met all the inclusion criteria (Tables 1 and 2). There were six studies using data derived from the USA, three from the UK and one each from Canada and Italy. Nine studies reported mean or median per patient direct costs, one reported total direct costs for the entire US population, and one stated both per patient and total (UK) costs. Productivity costs were stated per patient in three studies, total for the US population in one study, and were not reported in the remaining seven studies.

The studies presented in this review used several methods of cost calculation. The most common method was to abstract mean patient resource utilization, such as the number of clinic visits, hospitalizations and procedures, through chart reviews or insurance databases, and to combine these data with the mean unit costs of each resource, derived from local or national accounting databases. An alternative method was to follow a cohort of subjects via a cost-accounting system to capture the charges or costs incurred over time to manage irritable bowel syndrome-related symptoms. Two studies looked only at the cost of evaluation to obtain a diagnosis of irritable bowel syndrome, model-

Table 1. Studies fulfilling the entry criteria

Reference	Setting	Patients	IBS diagnosis	Costs or charges
Talley <i>et al.</i> ²⁴	US population-based survey	IBS subjects identified by postal survey	Manning criteria	Charges
Coremans <i>et al.</i> ²⁵	Italian National Health Service	Estimate of IBS patients in Italy	Prevalence estimate	Costs
Wells <i>et al.</i> ²⁶	UK National Health Service	Estimate of IBS patients in UK	Prevalence estimate	Costs
Bentkover <i>et al.</i> ²⁷	Canadian cohort study	Estimate of IBS patients in Canada	Prevalence estimate	Costs
Levy <i>et al.</i> ²⁸	HMO	IBS patients treated in HMO	IBS diagnostic code assigned by provider	Costs
Creed <i>et al.</i> ³⁰	Secondary/tertiary GI clinics in the UK	Severe IBS non-responsive to standard therapy	Rome criteria	Costs
Suleiman and Sonnenberg ³¹	USA	Hypothetical IBS patients	Prevalence estimate	Costs
Levy <i>et al.</i> ²⁹	HMO	IBS patients treated in HMO	ICD-9 code 564.1	Costs
Patel <i>et al.</i> ³²	HMO	IBS patients treated in HMO	ICD-9 code 564.1	Charges
Akehurst <i>et al.</i> ³³	General practice	IBS patients treated in general practice	Rome criteria	Costs
Sandler <i>et al.</i> ¹⁰	US population	Estimate of IBS patients in USA	ICD-9 codes (564.1, 564.5, 564.8, 564.9)	Costs

GI, gastrointestinal; HMO, health maintenance organization; IBS, irritable bowel syndrome; ICD-9, International Classification of Diseases, Ninth Revision.

Table 2. Studies fulfilling the entry criteria

Reference	Source of cost/charge estimates	Calculation method	Resources included	Study perspective
Talley <i>et al.</i> ²⁴	Olmstead County accounting database	Charge data	Out-patient, in-patient and emergency services Laboratory and radiology charges	Hospital
Coremans <i>et al.</i> ²⁵	National cost data	Estimated cost of diagnostic tests	Laboratory tests, sigmoidoscopy, lactose intolerance test	National Health Service
Wells <i>et al.</i> ²⁶	National data of resource utilization and unit costs	National and mean patient resource consumption	Out-patient (general practitioner and gastroenterologist) and in-patient services, medication	National Health Service
Bentkover <i>et al.</i> ²⁷	Medical record abstraction of resource use	Markov model	Out-patient, in-patient and emergency services, procedures, medication Productivity losses	Societal
Levy <i>et al.</i> ²⁸	Unit costs derived from provincial reimbursement registers Medical records	Mean patient resource consumption	Total out-patient and in-patient services and medication, not limited to IBS treatment	Not stated
Creed <i>et al.</i> ³⁰	Medical record abstraction of resource use	Mean patient resource consumption	Out-patient, in-patient and emergency services Prescription medication, alternative therapy, direct non-health care and productivity costs	Societal
Suleiman and Sonnenberg ³¹	Unit costs derived from local service providers and national data	Decision analysis of strategies	Diagnostic tests only	Third-party insurer
Levy <i>et al.</i> ²⁹	Local cost-accounting system	Mean patient resource consumption	Out-patient, in-patient and emergency services Laboratory, procedures, medication	Managed care
Patel <i>et al.</i> ³²	Claims database	Mean patient resource consumption	Out-patient, in-patient and emergency services, medication, procedures, laboratory	Managed care
Akehurst <i>et al.</i> ³³	Medical records abstraction of resource use Unit costs derived from local provider units and national estimates	Mean patient resource consumption	Out-patient, in-patient and emergency services, medication, home visits Productivity losses from time off work	Hospital
Sandler <i>et al.</i> ¹⁰	In-patient costs: National Hospital Discharge Survey Out-patient visits: National Ambulatory Medical Care Survey Emergency room and procedures: National Hospital Medical Care Survey Medication costs: Scott-Levin database Other costs: The Group Health Cooperative of Puget Sound claims database	National and mean patient resource consumption	Out-patient, in-patient and emergency services, medication, procedures Productivity losses from time off work	Societal

IBS, irritable bowel syndrome.

ling the resource use of hypothetical cohorts of patients and national cost data. It should be emphasized that, whilst some studies evaluated the resource utilization directly related to irritable bowel syndrome care, other studies reported resource consumption for all health care of irritable bowel syndrome patients, thereby including costs incurred for the management of non-irritable bowel syndrome diagnoses.

Economic impact of irritable bowel syndrome

Direct costs of irritable bowel syndrome. Combined data on direct health care resource utilization are presented in Table 3. Talley *et al.* performed a population-based study using postal surveys to identify subjects who had irritable bowel syndrome by the Manning criteria.²⁴ This was the only study included in this review that examined subjects even if they had not consulted a physician for symptoms of irritable bowel syndrome. Two previously validated surveys (Bowel Disease Questionnaire and Elderly Bowel Symptoms Questionnaire) were administered to the population of Caucasians living in Olmstead County, MN, USA. The economic impact was based on charge data (not costs) from the Mayo Clinic and Olmstead Medical Group, and included out-patient, emergency room, in-patient and procedural services (facility and physician) and laboratory and radiology charges, but excluded out-patient medication. The authors reported charges accumulated for all health care, thereby potentially including charges for

the management of non-irritable bowel syndrome diagnoses. Median direct health care charges were estimated at US\$742 per irritable bowel syndrome patient annually (25–75% quartiles, US\$177–1654).

Coremans *et al.* estimated the initial cost of diagnostic tests to the Italian National Health Service in the evaluation of patients with irritable bowel syndrome.²⁵ Providing a complete blood count with differential, erythrocyte sedimentation rate, faecal occult blood test, flexible sigmoidoscopy and lactose tolerance test would translate to US\$55, equating to 0.093% of the Italian National Health Service budget. The costs of management for irritable bowel syndrome beyond the initial diagnosis were not considered in this study.

The cost of caring for irritable bowel syndrome patients in the UK was reported in a study by Wells *et al.*²⁶ The mean unit costs of medication and of out-patient or in-patient services provided by general practitioners and gastroenterologists were combined with national irritable bowel syndrome prevalence and resource utilization data to estimate the total direct health care costs. National records were also used to calculate the annual number of visits to general practitioners per irritable bowel syndrome patient, and the average cost per visit. A market research study of general practitioners estimated the number of medications prescribed per year, and these data were combined with the average cost per prescription to determine the pharmaceutical expenditure for irritable bowel syndrome. Additional surveys were conducted to determine the number of

Table 3. Direct resource consumption

Reference	Reported values	Resources included	Cost year	Direct resources
Talley <i>et al.</i> ²⁴	Median charges	Total health care	1992 US\$	US\$742 per patient annually*
Coremans <i>et al.</i> ²⁵	Mean costs	IBS-related	Not stated	US\$55 per patient†
Wells <i>et al.</i> ²⁶	Mean costs	IBS-related	1995 UK£	£90 per patient annually (£45.6 million in UK annually)
Bentkover <i>et al.</i> ²⁷	Mean costs	IBS-related	1996 Canadian\$	Canadian\$258.82 per patient annually
Levy <i>et al.</i> ²⁸	Mean costs	Total health care	Not stated	US\$3166 per patient annually
Creed <i>et al.</i> ³⁰	Mean costs	Total health care	Not stated	US\$1743 per patient annually (converted from UK£)
Suleiman and Sonnenberg ³¹	Mean costs	IBS-related	2000 US\$	Least costly strategy: US\$320; most costly strategy: US\$1212†
Levy <i>et al.</i> ²⁹	Mean costs	IBS-related	1995 US\$	US\$619 per patient annually
Patel <i>et al.</i> ³²	Median charges	Total health care	1998 US\$	US\$2237–2504 per patient annually
Akehurst <i>et al.</i> ³³	Mean costs	Total health care	1997/1998 UK£	£316.20 per patient annually
Sandler <i>et al.</i> ¹⁰	Total national costs	IBS-related	1998 US\$	US\$1 353 000 000 USA annually

IBS, irritable bowel syndrome.

* Non-consulters with IBS symptoms included.

† Diagnostic evaluation only.

irritable bowel syndrome patients seen yearly by gastroenterologists and the proportion admitted to hospital. National data were used to determine the number of gastroenterology consultants in the UK and the average cost per consultant visit and hospital admission to determine in-patient and out-patient costs. Through the compilation of these cost data, it was estimated that £45.6 million was spent annually in the UK for irritable bowel syndrome care, translating into approximately £90 annually in costs per patient.

The annual mean direct costs of caring for irritable bowel syndrome patients in Canada were estimated at Canadian\$259.²⁷ In this study by Bentkover *et al.*, the investigators reviewed the medical records of 120 irritable bowel syndrome patients to estimate resource utilization for medical services, including physician fees, procedures and drugs. They calculated the unit costs of providing these services from provincial reimbursement registers and private insurance plan reimbursement, and combined these data with the prevalence of irritable bowel syndrome to calculate the total direct costs expended in Canada. This study limited costs to those directly related to irritable bowel syndrome care.

Levy *et al.* reported the total direct costs of providing all health care in 373 patients identified in medical records as having been diagnosed with irritable bowel syndrome (criteria for diagnosis not stated).²⁸ The costs were from the perspective of the health maintenance organization in the state of Washington, and included out-patient, in-patient and prescription drug costs. Total mean costs per patient were estimated to be US\$9497 over the 3-year period of analysis, and included not only irritable bowel syndrome care costs but also costs of unrelated medical diagnoses. The authors found that the total costs of health care delivery in irritable bowel syndrome patients were significantly greater than those expended for non-irritable bowel syndrome patients. In a related study, the authors examined direct costs limited to the management of irritable bowel syndrome-related diagnoses.²⁹ Using the same health maintenance organization database, 3153 patients with an irritable bowel syndrome diagnosis [identified by International Classification of Diseases, Ninth Revision (ICD-9) codes] were tracked via a cost accounting system to calculate the expenditure 1 year prior to (to capture evaluation costs) to 2 years after the first health care encounter for irritable bowel syndrome. They estimated the mean direct cost of irritable bowel syndrome care to be US\$619 per patient annually. It

should be noted that the total cost of all health care for irritable bowel syndrome patients remained significantly greater than that of health maintenance organization enrollees without an irritable bowel syndrome diagnosis, but only 33% of the difference in the total cost of care was due to lower gastrointestinal-related services.

Creed *et al.* examined patients in the UK with severe disease, defined as irritable bowel syndrome patients (Rome criteria) with persistent symptoms despite medical therapy including education, dietary advice, anti-spasmodic agents, laxatives or anti-diarrhoeals.³⁰ The records of 257 patients in a prospective trial of medical vs. psychotherapy were abstracted to determine the resource use related to in-patient, out-patient and non-hospital health care encounters, prescription medication and alternative medical therapy (such as reflexology). Unit costs were assigned to these services, as well as to direct non-health care costs such as travel, non-prescription drugs, childcare and housework or personal care. The mean per patient cost over a 12-month period was estimated to be US\$1743. This figure represented the total health care costs that were incurred annually and was not limited to irritable bowel syndrome management.

The costs of providing a diagnosis of irritable bowel syndrome in patients were also estimated through computer modelling by Suleiman and Sonnenberg.³¹ The costs of diagnosis from the perspective of a third-party insurer ranged from US\$320 for providing a history and physical examination, basic laboratory tests and a breath test for bacterial overgrowth, to US\$1212 for adding colonoscopy with biopsy and radiological small bowel study. No further management costs were considered in this modelling analysis.

A managed care perspective of irritable bowel syndrome costs was studied by Patel *et al.*³² Health care utilization of irritable bowel syndrome patients was captured during the year before and the year after the first clinical encounter in which an ICD-9 code (564.1) was documented. The investigators tracked emergency department, in-patient, out-patient, medication, procedural and laboratory charges (not costs) through a claims database. The reported values represented the total health care expenditure and were not limited to irritable bowel syndrome management. Median charges per patient were US\$2237 during the year preceding and US\$2504 during the year following the index encounter.

Akehurst *et al.* reviewed the medical records of irritable bowel syndrome patients (Rome I criteria) in six practices in the UK to determine resource use, including medication, in-patient, out-patient, emergency department or home visits.³³ Unit costs for these resources were derived from nationally published estimates and local provider unit financial returns. Costs were not limited to irritable bowel syndrome-related health care encounters, and thus total health care consumption was reported in this study. The mean direct cost per patient per year was calculated to be £316 (median cost, £160).

Most recently, Sandler *et al.* provided an estimate of the total cost of irritable bowel syndrome to the US health care system.¹⁰ In this study, four databases (National Hospital Discharge Survey, National Ambulatory Medical Care Survey, National Hospital Medical Care Survey and the Group Health Cooperative of Puget Sound claims database) were used to estimate resource use and unit costs for each resource. The costs included hospital facility costs, out-patient and in-patient physician costs, out-patient hospital costs for procedures and pharmaceutical therapy costs that were derived from charge data using cost-to-charge ratios. In addition, costs were weighted on the basis of whether irritable bowel syndrome was the primary or secondary diagnosis for each health care encounter. The total direct cost for irritable bowel syndrome care in the US was estimated to be over \$1.3 billion annually.

The proportions of direct health care resources expended through in-patient and out-patient services and for medication are shown in Figure 1. Only studies reporting these sub-categories were included. The estimates vary widely, with in-patient services accounting for 7–80% of the total direct health care costs, out-patient services responsible for 16–68% of the costs and medication use responsible for 2–27% of the costs.

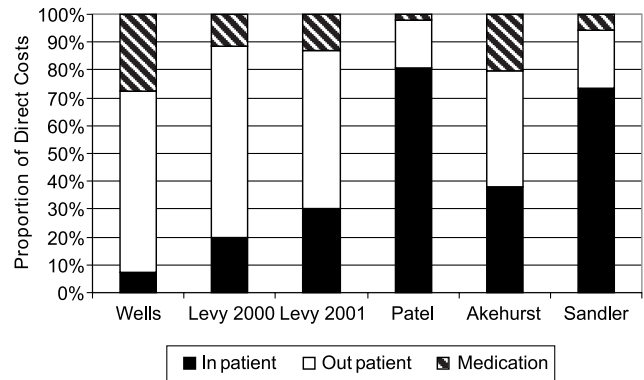


Figure 1. Proportion of direct health care resources allocated to in-patient or out-patient services or medication.

It should be noted that the studies varied geographically, by the perspective of the analysis, in reporting costs vs. charges and by the source of their cost estimates, thus affecting not only the absolute value but also the relative proportion spent in each cost category.

Productivity (indirect) costs of irritable bowel syndrome. Four studies reported the productivity costs associated with irritable bowel syndrome (Table 4). The study by Akehurst *et al.* reported that 46/102 (45%) irritable bowel syndrome patients had taken time off work related to symptoms of their disease, and that 15% had taken more than 1 week off work in the previous 3 months prior to entry into the study.³³ This study did not translate the productivity losses into monetary units.

The analysis by Bentkover *et al.* estimated productivity costs of Canadian \$748 annually.²⁷ This estimate was based on lost time at work valued at the mean Canadian wage rate. Creed *et al.* likewise limited productivity costs to work productivity losses, estimated to be US\$335 annually.³⁰ Finally, Sandler *et al.* calculated productiv-

Table 4. Indirect resource consumption

Reference	Resources included	Cost year	Productivity losses
Bentkover <i>et al.</i> ²⁷	Lost time at work due to IBS symptoms	1996 Canadian\$	Canadian\$748.16 per patient annually
Creed <i>et al.</i> ³⁰	Lost time at work due to any illness	Not stated	US\$334.50 per patient annually (converted from UK£)
Akehurst <i>et al.</i> ³³	Lost time at work due to any illness	Not applicable	46/102 (45%) had taken time off work 15/102 (14.7%) had more than 1 week off work in previous 3 months
Sandler <i>et al.</i> ¹⁰	Lost time at work due to IBS symptoms	1998 US\$	US\$205 million USA annually

IBS, irritable bowel syndrome.

Table 5. Total resource utilization

Reference	Resources included	Cost year	Total resource utilization
Bentkover <i>et al.</i> ²⁷	IBS-related resource use	1996 Canadian\$	Canadian\$1006.98 per patient annually
Creed <i>et al.</i> ³⁰	Total health care resource use	Not stated	US\$2077.50 per patient annually (converted from UK£)
Sandler <i>et al.</i> ¹⁰	IBS-related resource use	1998 US\$	US\$1 558 000 000 USA annually

IBS, irritable bowel syndrome.

ity costs by combining the time away from work due to health care encounters for clinic visits, hospitalizations and procedures with National Statistical Abstract 2000 data on age- and gender-specific wage estimates.¹⁰ The total productivity cost for the US was estimated to be US\$205 million annually. It should be noted that none of the studies identified in this review were able to report data concerning decreases in work productivity due to disease morbidity, nor intangible costs incurred as a result of pain or decrement in the quality of life.

Total costs of irritable bowel syndrome. Three studies reported both direct and productivity costs of irritable bowel syndrome care (Table 5). The annual mean costs related to irritable bowel syndrome management were estimated to be Canadian\$1007 per patient.²⁷ The total health care costs for 'severe irritable bowel syndrome patients' in the UK were equivalent to US\$2078.³⁰ The total (direct and productivity) cost related to irritable bowel syndrome management in the USA was estimated to be US\$1.56 billion annually (1998 dollars).¹⁰ It is reiterated that these cost data may be underestimates due to the lack of inclusion of additional productivity costs, such as those due to impaired ability to work or to enjoy leisure activities.

Comparison of health care expenditure

Several studies reported the difference in health care expenditure between individuals with irritable bowel syndrome or irritable bowel syndrome symptoms and control populations without irritable bowel syndrome symptoms. The study of subjects with irritable bowel syndrome in Olmstead County, MN, USA showed that the odds of incurring some direct medical cost were significantly greater in subjects with irritable bowel syndrome symptoms than in those without symptoms.²⁴ In this study, median annual charges amongst subjects identified with irritable bowel syndrome were US\$742, compared with US\$429 spent on controls without irritable bowel syndrome. In the two studies

performed by Levy *et al.*, direct health care costs were significantly higher in irritable bowel syndrome patients than in population controls.^{28, 29} Annual per person costs related to lower gastrointestinal diagnoses were higher amongst irritable bowel syndrome patients than in controls (US\$619 vs. US\$102, respectively; $P < 0.05$), as were costs for all health care provided (US\$4044 vs. US\$2719; $P < 0.05$). Similar results based on charges were obtained by Patel *et al.*; patients with irritable bowel syndrome had significantly higher out-patient, drug and total charges compared with controls without irritable bowel syndrome.³² Lastly, National Health Service costs in the UK were found to be significantly higher in irritable bowel syndrome patients (£316.20; s.d., £474.66) than in non-irritable bowel syndrome control patients (£192.87; s.d., £373.29).³³

Two studies compared the costs of irritable bowel syndrome with the costs required to manage other gastrointestinal diseases.^{10, 29} Compared with the estimated US\$1.56 billion (1998 dollars) for direct and indirect irritable bowel syndrome costs, Sandler *et al.* estimated gastro-oesophageal reflux disease to be associated with total costs reaching US\$9.8 billion. Other notable diseases with high costs included gall-bladder disease (US\$6 billion), colorectal cancer (US\$5 billion) and peptic ulcer disease (US\$3.3 billion).¹⁰ Levy *et al.* reported that the annual mean direct health care costs for patients with irritable bowel syndrome [US\$4376; 95% confidence interval (CI), US\$4039–4713] were substantially less than those of patients with inflammatory bowel disease (US\$7237; 95% CI, US\$6539–7935), but similar to those of patients with gastro-oesophageal reflux disease (US\$5144; 95% CI, US\$4877–5411).²⁹ It should be noted that the latter study did not include indirect costs, and that the Sandler *et al.* study reported national expenditure that takes into account the prevalence of irritable bowel syndrome. These differences may account for the discrepancy in the estimates of the costs between the studies.

Several studies examined demographic variables associated with resource use in irritable bowel syndrome. Increasing age,²⁴ higher education²⁴ and female gender^{29, 30} were associated with higher costs, although one study reported that gender was not a significant predictor of costs.²⁴ Mean costs between irritable bowel syndrome sub-groups did not differ significantly in one study, although pain-predominant subjects experienced a trend towards higher costs than constipation- or diarrhoea-predominant subjects.³⁰

DISCUSSION

The costs of managing irritable bowel syndrome are considerable, although the precise impact remains elusive. The estimates of the direct costs related to irritable bowel syndrome care ranged from Canadian\$259 to US\$619 annually, with charge data ranging from US\$742 to US\$2504 annually. The subgroup of patients with severe symptoms of irritable bowel syndrome required as much as US\$1743 in direct costs per year. It was estimated that \$1.3 billion are expended annually in direct costs associated with irritable bowel syndrome care in the USA, whereas a similar estimate in the UK was £45.6 million. Productivity cost estimates ranged from US\$335 to Canadian\$748 per patient annually, with total annual productivity losses for the USA estimated at \$205 million. Total costs from a societal perspective, including both direct and productivity values, ranged from Canadian\$1007 to US\$2078 per patient per year, whilst the total annual expenditure in the USA was estimated to be \$1.56 billion.

Although irritable bowel syndrome is not associated with significant mortality, the direct and productivity costs associated with the management of this disorder place it within the 10 most expensive gastrointestinal diseases in the USA.¹⁰ It is likely that the presence of chronic symptoms without adequate treatment options in a non-fatal disorder actually increases the cost of management, as the absence of significant mortality acts to increase the prevalence of the disorder. A significant decrement in the health-related quality of life has been demonstrated in irritable bowel syndrome. A recent systematic review illustrated that the impact of irritable bowel syndrome was similar to that of gastro-oesophageal reflux disease or depression.¹¹ Whilst the severity of irritable bowel syndrome symptoms correlated with decrements in the perceived

quality of life, respondents who met the criteria for irritable bowel syndrome but who had not sought health care reported a similar quality of life to non-irritable bowel syndrome controls.

It should be noted that the economic burden of irritable bowel syndrome is not limited to the USA. Even in countries in which a national health service provides care, the costs associated with irritable bowel syndrome are high.^{25, 26, 30, 33, 34} Although it is difficult to directly compare health care costs across national borders due to differences in economic structure and currency, the studies evaluated in this review consistently illustrate that the magnitude of direct health care resource consumption and productivity losses that are sustained internationally as a result of this disorder is similar.

Five studies reported in this review compared health care utilization in subjects with symptoms of irritable bowel syndrome with that in populations without irritable bowel syndrome symptoms. In each report, direct health care costs were significantly higher amongst subjects with irritable bowel syndrome or irritable bowel syndrome symptoms than in control populations without irritable bowel syndrome symptoms.^{24, 28, 29, 32, 33} In those studies evaluating the total costs of all health care in addition to irritable bowel syndrome-related expenditure, it was consistently noted that total health care resource utilization was greater amongst irritable bowel syndrome patients than in matched control patients without irritable bowel syndrome.

This study utilized an evidence-based approach to summarize the data regarding irritable bowel syndrome costs. Specifically, a systematic review was conducted using previously published methods.^{22, 23} In a systematic review, unlike conventional non-systematic reviews, bias is limited by establishing criteria for the performance of the literature search and for the inclusion of the studies in the review in an a priori manner. It should be noted that, although there were a large number of published studies on this topic, few met the pre-defined criteria for inclusion in this review.

There was great variation in the estimated costs of irritable bowel syndrome between the various studies. The reasons for this variation are multiple. The studies were performed in different countries, with different health care systems and different costs for the same services or products. The studies used different methodologies to ascertain costs. Different direct and indirect

costs were included in the different studies. Different assumptions were made in the cost estimates. Different irritable bowel syndrome patient groups were included in the various studies, with many studies limited only to the small percentage of irritable bowel syndrome patients who seek care. Finally, different perspectives were used in the various studies. With the wide variation in study methodology and assumptions, it is not surprising to find a wide range of estimates for the costs of irritable bowel syndrome. The one common factor in all of the studies was the conclusion that irritable bowel syndrome is a disease that imposes large direct and indirect costs on the health care system and society. Although the exact costs are difficult to calculate, there is no doubt that the financial impact of this disease is extremely high.

Several other considerations should be made with regard to cost determination in irritable bowel syndrome. The lack of effective therapy has the effect of decreasing the estimated pharmaceutical component of direct health care costs. As opposed to gastro-oesophageal reflux disease, where drug costs are estimated to account for 63% of the total direct costs, only 6% of irritable bowel syndrome direct costs are attributed to medication.¹⁰ On the other hand, 21% of the total direct costs of management of gastro-oesophageal reflux disease are consumed through hospital admissions, whereas 63% of irritable bowel syndrome-related direct costs are attributed to in-patient stays for evaluation, diagnosis and treatment.¹⁰ A significant shift in costs may occur if effective therapy is made available, away from health care encounters or diagnostic tests and towards pharmaceuticals. It should also be recognized that many pharmaceutical therapies for irritable bowel syndrome are available over the counter, imposing costs on patients, but often not captured in estimates of third-party health care costs.

Further research to examine the economic burden of irritable bowel syndrome should focus on several aspects highlighted by this article. It would be ideal to perform the analysis from a societal perspective, so that not only direct health care costs, but also productivity (indirect) costs may be included, as the latter are especially critical when analysing a disease such as irritable bowel syndrome that is associated with more morbidity than mortality. Costs should be reported in a format that reflects the skewed distribution of costs amongst patients, which may include using median

values, bootstrapping methods or other non-parametric forms of analysis. The source from which costs are derived should consist of a validated cost-accounting system or claims database. A control group without irritable bowel syndrome, with or without other gastrointestinal disorders, may be useful to more fully assess the economic impact of irritable bowel syndrome. Although irritable bowel syndrome patients exhibit a wide variation in symptom severity, comparison of resource expenditure stratified by this factor is lacking. Finally, total medical care costs, in addition to costs incurred for irritable bowel syndrome care, should be reported, as several studies have noted significantly higher total medical costs in patients with irritable bowel syndrome.

In summary, the economic impact of irritable bowel syndrome is substantially greater than its effect on mortality, illustrating that a disorder need not be lethal in order for tremendous health care resources to be expended in its management. The productivity losses incurred as a result of morbidity contribute in addition to direct health care costs, and the combined losses far exceed those incurred by non-irritable bowel syndrome patients. Geographical boundaries are spanned by this disorder and the impact on national health care in countries other than the USA accounts for considerable deficits. As therapeutic options at the present time are limited, productivity at work and leisure activities suffer, neither of which is quantifiable by present means. The development of effective therapy may dramatically shift resource use away from costly diagnostic evaluations, decrease the productivity (indirect) costs incurred by this disorder and improve the quality of life.

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APPENDIX — COST IDENTIFICATION

Costs associated with disease can be broken down into two broad categories: direct and productivity (indirect) costs.³⁵ It must be emphasized that costs are different from charges, as the latter reflect mark-up specific to an institution that relates to profit, non-reimbursed resource allocation and other factors. Direct costs include the value of all goods, services and other resources consumed in the provision of an intervention, its side-effects and all current or future consequences. Direct costs have been traditionally sub-divided into fixed and variable costs. Fixed costs (designated as such as they do not vary with the quantity of health care product delivered) include wages, salaries and lease or rent of

equipment and space. Variable costs include supplies or non-reusable items, which vary with the quantity of product provided. Another method of sub-dividing direct costs, which may be more applicable to health care, is to characterize them as direct health care costs and direct non-health care costs. Direct health care costs include the costs of medical facilities, personnel, tests, supplies and medication. Direct non-health care costs include the costs incurred through transportation, childcare or home care that are accrued due to health care encounters. Indirect or productivity costs refer to the economic losses resulting from disease-related morbidity and mortality, and include lost work time,

decreased work productivity and long-term disability. Also included are the costs associated with lost or decreased ability to engage in leisure activities due to morbidity. It should be noted that some authors include the non-medical costs of transportation, lodging or family care which result from health care encounters in indirect costs, but prevailing opinion states that these costs should be included in direct non-health care costs. A third category of costs, intangible costs, are incurred as a result of pain, suffering or decrements in the quality of life; however, it is unusual to see intangible costs reported in cost identification or cost-effectiveness analyses.