

Costs of irritable bowel syndrome in European countries with universal healthcare coverage: a meta-analysis

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Abstract. – **OBJECTIVE:** To provide an overall estimate of the direct, indirect and total costs of irritable bowel syndrome (IBS) for the adult population of the European countries with universal healthcare coverage.

MATERIALS AND METHODS: We searched MedLine and Scopus databases (up to September 2018) to identify the European studies that evaluated the economic impact of IBS. Mean annual direct, indirect and total per-capita IBS costs were estimated using random-effect single-group meta-analyses of continuous data. All analyses were stratified by payer category (governments, insurance, societal), and the results were expressed as summary mean and 95% CI.

RESULTS: A total of 24 studies were included in the meta-analyses. Only two studies evaluated IBS costs in Italy. The pooled summary of direct IBS per-capita cost, obtained from 23 European datasets (n=15,157), was €1837/year (95% CI: 1480-2195), with large differences across payers (from €1183 to €3358, in countries with publicly-funded and insurance-based health systems, respectively). The mean indirect cost, extracted from 13 datasets (n=3978), was €2314/year (95% CI: 1811-2817), again with wide differences across payers. Finally, the meta-analysis estimating the total annual cost, based upon 11 European datasets (n=2757), yielded a summary estimate of €2889/year (95% CI: 2318-3460) per patient, ranging from €1602 (insurance-based health systems) to €3909 (studies adopting a societal perspective).

CONCLUSIONS: Considering a conservative estimate of 2,736,700 Italian adults affected by the syndrome, the minimum costs due to IBS in Italy – likely underestimated – range from 6 to 8 billion euro per year. Given the substantial economic burden for patients, healthcare systems

and society, IBS should be included among the priorities of the public health agenda.

Key Words

Irritable bowel syndrome, Direct costs, Indirect costs, Meta-analysis, Italy.

Introduction

Irritable bowel syndrome (IBS) is one of the most common functional disorder of the gastrointestinal tract (FGID)¹. However, in spite of formally established diagnostic criteria, IBS is often unrecognized², and epidemiological estimates widely vary, depending on the case-finding definition employed (Manning vs. Rome criteria) and the characteristics of the population^{1,3,4}. In industrialized countries, estimates range between 8 and 15%^{1,3}.

Clinically, IBS is characterized by abdominal pain and altered bowel habit, with either predominant diarrhea, constipation, or both^{4,5}. Although it has no attributable mortality, this disorder is associated with psychological distress and a drop in quality of life and work productivity⁶. As a result of its high prevalence, detrimental effect on quality of life and work productivity, and redundant medical procedures, IBS has the potential for creating a tremendous burden on the health care system⁷⁻⁹.

As a common trait, IBS patients consume a disproportionate amount of resources: only in the

USA, each year, over 3.6 million visits are attributable to IBS-related symptoms (accounting for up to 25% of all patients seen by gastroenterologists)^{3,9}, IBS care consumes over \$20 billion per year in both direct and indirect costs¹⁰, and patients spend over 50% more health care resources than matched controls without IBS³.

To quantify the disease burden and guide public health policies⁴, a number of studies sought to measure the economic and humanistic burden of this disorder across different countries and payers¹¹⁻⁶⁰, and a few reviews^{3,61-68} and systematic reviews^{1,9,69} have been published up to 2014. However, as regards Italy and European countries with universal healthcare coverage, no summary estimates of the economic impact imposed by IBS on the citizens are available to date. We thus performed a meta-analysis to provide an overall estimate of the financial burden of IBS for the adult population of Italy and other European countries with universal healthcare coverage.

Methods

Search Strategy and Selection Criteria

We searched MedLine and Scopus databases to identify the studies that evaluated the economic impact associated with IBS in European countries with universal healthcare coverage, either considering direct and productivity (indirect) costs. A search of the grey literature was also performed, in order to retrieve any relevant publication, such as government documents, reports, or conference abstracts not published in indexed journals^{70,71}. Searches were done by two independent investigators (LM, MEF), up to September 1, 2018 using various combinations of the following terms: (Irritable Bowel Syndrome OR IBS OR irritable colon OR functional bowel disease OR functional colonic diseases) AND (economic models OR economic* OR cost* OR health care costs OR health service costs OR health expenditure OR health resources OR health care utilization OR health service utilization OR productivity)⁵. The reference lists of reviews and retrieved articles were also screened for additional pertinent papers. No language restriction was used.

Studies were considered eligible for inclusion if they met the following criteria: (1) included adult subjects (≥ 18 years) with a diagnosis of IBS according to specific criteria, and/or reported by a physician; (2) were conducted in EU countries with universal healthcare coverage; (3)

assessed the economic impact of IBS in terms of: (a) direct costs – the prices charged by the provider and incurred by a third party paying for healthcare provision, such as a government or insurer, or the global societal costs regardless of payer; (b) indirect cost – the expenditures for the society that derive from reduced productivity in the workplace, but also from the time lost due to spillover effects on the patients' family^{5,72}; (c) both direct and indirect costs. The studies that evaluated the economic impact of a particular treatment i.e., studies where costs may be attributable to intervention rather than to the disease, or compared the cost-effectiveness of two or more drugs or diagnostic pathways, were not eligible for inclusion⁶⁹.

Outcomes and Data Analysis

We performed single-group meta-analysis of continuous data to estimate the following three outcomes: mean annual (1) direct, (or) (2) indirect or (3) total costs per patient due to IBS. Different studies may use different perspectives across countries and health systems, and this may lead to largely discrepant estimates^{1,9}. To account for this heterogeneity, we combined and analyzed separately data from single studies considering three main categories of payer: (a) governments or national health systems; (b) third-party payers, for the studies that assessed the costs from the perspective of insurers; (c) societal costs, for the studies that considered the costs on the welfare of the whole of society, regardless of payer. We thus performed a total of nine separate meta-analyses. For each outcome, the results were expressed as a summary mean and 95% CI. In two studies^{14,30}, the mean costs and their standard deviations (SD) were expressed as medians and interquartile ranges (IQR). In such cases, we used the method described by Hozo et al⁷³ to derive the corresponding means, and IQRs were divided by 1.35 to obtain the equivalent SD⁷⁴. To allow meaningful comparisons across countries, all the costs that were not reported in euros were converted from the respective currency to the corresponding euro value and were inflated to the specific exchange rates of the survey year or, when not available, of the publication year⁶⁴.

All meta-analyses were performed using a random-effects model to account for the inter-study heterogeneity and were carried out using Stata, version 13.1 (2013, Stata Corp., College Station, TX, USA).

Results

Characteristics of the Included Studies

Of the 1513 records initially retrieved, a total of 24 studies met our selection criteria and were included in the meta-analyses^{12-14,16,20,21,24,26,28,30-33,38,40,41,46,47,52,55,60,62,75,76}. Their main characteristics have been reported in Table I: all studies have been performed in the general population, with a combined overall sample of 16,378. Of the 24 publications, two provided data on the economic impact of IBS in Italy^{41,55}; the remaining studies were performed in the UK (9 studies)^{12,21,26,31,52,60,62,75,76}; Germany (n=2)^{32,40}; France (n=2)^{16,33}; Spain (n=2)^{38,47}; Netherlands (n=1)²⁴; Northern Europe (n=5)^{13,14,28,30,46}; and one publication analyzed a cohort from six European countries (France, Germany, Italy, Spain, Sweden, UK)²⁰. A total of eleven studies^{12,20,24,30,46,47,52,55,62,75,76} provided data only on direct IBS costs; two studies measured only indirect costs^{11,41}; and eleven studies reported data on both^{13,14,16,21,28,31-33,38,40,60}. One publication estimated the direct costs separately for Italy, France, and Germany⁵⁶: as such, in some analyses, the number of included datasets may not match the number of publications.

The two Italian studies enrolled a total of 990 subjects diagnosed with IBS-C^{41,55}. The first study enrolled 112 moderate-to-severe IBS subjects (diagnosed in the previous five years) and compared the mean annual direct costs per patient in Italy vs. France or Germany⁵⁵. The second study enrolled 878 subjects followed in 39 referral centers for gastrointestinal disorders, and quantified the per-capita annual indirect costs, considering the burden on the welfare of the whole of society, regardless of payer⁴¹.

Direct Costs

In the only Italian study that measured the direct economic burden of IBS, the estimated mean annual cost per patient for the national health system was €1761 (95% CI: 1339-2183), vs. €8256 (7674-8838) and €9162 (8720-9604) in France and Germany, respectively⁵⁵ ($p < 0.05$; Table I).

When the 23 datasets^{12-14,16,20,21,24,28,30-33,38,40,46,47,52,55,60,62,75,76} estimating the direct costs of IBS residents in European countries with universal health coverage were pooled, the overall mean cost was €1837 (95% CI: 1480-2195 – Table II and Figures 1-3). However, the summary estimates largely varied by

type of payer, with mean costs ranging from €1183 in countries with publicly-funded healthcare systems (13 studies, n=12,163), up to €3358 in the nations with an insurance-based health system (six studies, n=1494). Although the confidence intervals slightly overlapped, the difference between the mean annual direct costs between the above groups of countries was significant ($p=0.007$).

Indirect Costs

The mean annual indirect cost in Italy, due to productivity loss, was estimated to be €4905 (95% CI: 4681-5129 – Table I) per subject⁴¹.

In the 13 datasets from European countries with universal coverage^{13,26,28,31,41,16,32,33,40,14,21,38,60}, the estimated mean per-capita indirect cost was €2314 per year (95% CI: 1811-2817 – Table II; Figures 4-6). Also, the indirect costs largely differed by payer type, ranging from €139 per patient in countries with an insurance-based health system (four studies; n=1007), up to €3790 in the five studies adopting a societal approach (n=2196).

Notably, in three^{16,33,40} of the four studies performed in countries with an insurance-based health system, the indirect costs were very low (summary estimate: €38 per-capita), because the costs were computed considering only days-off work, and all the expenses related to productivity losses were not included. In the only other study from an EU country with insurance-based health system³², the indirect costs were estimated to be €2619. When the three studies above were excluded, the overall estimate of indirect costs from the ten remaining studies was €3068 (95% CI: €768-5368).

Total Costs

No study estimated both direct and indirect costs of IBS in Italy; thus, the total costs were estimated only pooling the eleven studies from the other EU countries with universal health coverage^{13,14,16,21,28,31-33,38,40,60}. The summary per-capita total cost was €2889 per year (95% CI: 2318-3460) and again varied by payer type (Table III; Figures 7-9). The estimated mean annual total cost was €1602 per subject in countries with an insurance-based health system (4 studies; n=1007), €3597 in nations with publicly funded healthcare systems (4 studies; n=775), and €3909 in the three studies adopting a societal perspective (n=975).

Table 1. Characteristics of the included studies evaluating the economic burden (direct and/or indirect costs) of irritable bowel syndrome (IBS). To allow meaningful comparisons across studies, all costs have been converted from the respective currency to the corresponding value in euros and were inflated to the specific exchange rates of the survey year or, when not available, of the publication year.

Authors	Country	Population – Setting	IBS subtype	Perspective	Outcome(s)
Wells et al ²⁶	UK	Prevalence data extracted from the 1995 National Morbidity Survey; data on expenditure taken from the health databases of 360 GPs	NR	National Health Service	Mean total annual direct costs/patient: €113. Estimated annual costs for the NHS (million): - Overall: €57.2 - GP consultations: €16.4 - GP-prescribed medications: €15.7 - Outpatient setting: €20.8 - Inpatient admissions: €4.3
Hahn et al ²⁶	UK	Randomly selected members of the UK IBS Network support group contacted through postal questionnaire. (Total sample=343)	NR	Patient	Mean total annual indirect costs/patient - UK: €3794
Karampela et al ³¹	UK	12-week observational study on non-institutionalized IBS patients (total sample=19)	NR	Societal	Mean total annual cost/patient - Overall direct: €276 - Overall indirect: €816
Creed et al ²¹	UK	Patients with severe refractory IBS attending seven gastrointestinal out-patient clinics (total sample=257).	BS-C: 59 IBS-D: 74 IBS-M: 124	National Health Service	Mean annual costs/patient - Overall direct: €1870 - Overall indirect: €353
Akehurst et al ¹²	UK	Patients meeting Rome I criteria for IBS from 6 GP (total sample=161)	NR	National Health Service	Mean annual direct costs/patient - Overall: €477 Estimated annual costs for the total UK population: €302 million.
Muller-Lissner et al ⁴⁰	Germany	Randomly selected IBS patients with medical record data (total sample=200)	NR	Statutory Health Insurance	Mean annual costs/patient - Overall direct: €792 - Overall indirect: €203 ^y
Le Pen et al ³³	France	Patients identified through population survey (total sample=253).	IBS-C: 65 IBS-D: 72 IBS-M: 116	National Health Insurance; societal	Mean annual costs/patient* - Overall direct: €568 (NHS); €862 (societal) - Overall indirect: €40 (NHS) ^y
Brun-Strang et al ¹⁶	France	Randomly selected sample of IBS patients, from 264 French GPs, among those diagnosed in 2006 (total sample=452).	NR	National Health Insurance	Mean annual costs/patient - Overall direct: €756 - Overall indirect: €38 ^y

Continued

Table 1 (Continued). Characteristics of the included studies evaluating the economic burden (direct and/or indirect costs) of irritable bowel syndrome (IBS). To allow meaningful comparisons across studies, all costs have been converted from the respective currency to the corresponding value in euros and were inflated to the specific exchange rates of the survey year or, when not available, of the publication year.

Authors	Country	Population – Setting	IBS subtype	Perspective	Outcome(s)
Johansson et al ³⁰	Norway	IBS patients (from 26 GPs in one Norwegian county) selected among those who consulted their GP in the year 2001. Recruitment performed through questionnaire (total sample=164).	NR	National Health Service	Mean annual direct costs/patient ** - Overall: €260 - Outpatient setting: €40 - Inpatient setting: €180 - Medications: €11.4 - Complementary/alternative medicine: €6.4
Hillila ²⁸	Norway	Random sample of IBS patients, from non-institutionalized general population, recruited from postal survey (total sample=770)	NR	Societal	Mean annual costs/patient by IBS diagnostic criterion ^A - Overall direct: €497 (Rome II); €295 (Manning II) - Specialists visit: €209 (Rome II), €118 (Manning II) - Medications: €63 (Rome II); €42 (Manning II) - Endoscopies: €58 (Rome II); €40 (Manning II) - Overall indirect (absenteeism-related): €147 (Rome II); €82 (Manning II)
Andersson et al ¹³	Sweden	Random sample of IBS patients, from non-institutionalized general population, recruited through telephone interview (total sample=186)	NR	Societal	Mean annual costs/patient - Overall direct: €1192 - Outpatient setting: €1132 - Medications: €60 - Overall indirect (work loss/cutback, domestic capacity): €9291
Stamuli et al ⁷⁵	UK	Random sample of IBS patients from primary care in the English NHS (total sample=207)	NR	National Health Service	Mean annual costs/patient - Overall direct: €1153 - Complementary/alternative medicine (acupuncture): €382
Begtrup et al ¹⁴	Denmark	IBS patients from 307 Danish GPs, voluntarily enrolled at two facilities (total sample=302).	IBS-C: 61 IBS-D: 112 IBS-M: 129	National Health Service	Median annual costs/patient in positive and exclusion diagnostic approaches ^B - Overall direct: €155 - Overall indirect: €3046
Mearin et al ³⁸	Spain	Spanish branch of the IBIS-C Study; included all patients diagnosed with moderate-severe IBS (IBS-Severity Scale IBS-SSS ≥175) in the previous 5 years (total sample=112).	All IBS-C patients	National Health Service; out-of-pocket	Mean annual cost/patient - Overall direct: €1635 (€1067 for NHS; €568 for the patient) - Overall indirect (productivity loss): €1362
Neri et al ⁴¹	Italy	IBS outpatients consecutively enrolled in 39 Italian referral centers for GI disorders (total sample=878).	All IBS-C patients	Societal	Median annual indirect (productivity loss) costs/patient due to sick leave or presenteeism, expressed as Italian Purchase Power Parity (PPP) per capita Gross Domestic Product (expressed in 2010 USA \$). - Sick leave costs: €1150 - Presenteeism costs: €3755

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Table 1 (Continued). Characteristics of the included studies evaluating the economic burden (direct and/or indirect costs) of irritable bowel syndrome (IBS). To allow meaningful comparisons across studies, all costs have been converted from the respective currency to the corresponding value in euros and were inflated to the specific exchange rates of the survey year or, when not available, of the publication year.

Authors	Country	Population – Setting	IBS subtype	Perspective	Outcome(s)
Raya et al ¹⁷	Spain	Data extracted from the 2011 primary care LASIST database, including several primary care sites and >3 mln citizens. IBS patients identified through ICD codes and drug prescriptions (total sample=5649).	All IBS-C patients	National Health Service	Mean annual direct costs/patient:*** - Overall: €842 - GP consultations: €494 - Hospitalization: €108 - Specialist visits: €98.5 - ER visits: €87 - Medications: €54.1
Coffin et al ²⁰	France; German; Italy; Spain; Sweden; UK	French branch of the IBIS-C Study, providing also data for the entire Eu cohort; included all patients diagnosed with moderate-severe IBS (IBS-SSS ≥175) in the previous five years (total Europe sample=525; French sample=59).	All IBS-C patients	Societal	Mean annual cost/patient - Overall direct: €4639 (Europe cohort); €4128 (French cohort)
Flik et al ²⁴	Netherlands	Data extracted from the Achmea Health Insurance database (>1 mln citizens included). Included patients from 23 GPs with a diagnosis of IBS made between 2006 and 2009 either in primary care (total sample=326) or in secondary care setting (total sample=9274)	NR	Third-party payer (social insurance)	Mean annual direct cost/patient in primary and secondary care setting ^p - Overall: €2639
Layer et al ³²	Germany	German branch of the IBIS-C Study; included all patients diagnosed with moderate-severe IBS (IBS-SSS ≥175) in the previous five years (total sample=102).	All IBS-C patients	Statutory Health Insurance; out-of-pocket	Mean annual cost/patient - Overall direct: €1423 (NHS); €539 (patient) - Overall indirect (work productivity loss): €2619
Soubieres et al ³²	UK	Data extracted from Hospital Episode Statistics (HES) database, including all admissions for IBS and IBS-related symptoms (identified through ICD codes) in 2012-2013 throughout all Clinical Commissioning Groups (total sample=1982 and 3517 for outpatient and inpatient settings, respectively).	NR	National Health Service	Mean annual direct cost/patient in outpatient and inpatient setting ^E - Overall costs: €502

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Table 1 (Continued). Characteristics of the included studies evaluating the economic burden (direct and/or indirect costs) of irritable bowel syndrome (IBS). To allow meaningful comparisons across studies, all costs have been converted from the respective currency to the corresponding value in euros and were inflated to the specific exchange rates of the survey year or, when not available, of the publication year.

Authors	Country	Population – Setting	IBS subtype	Perspective	Outcome(s)
Stanghellini et al ⁵⁵	Italy; France; Germany	IBS patients with moderate-severe IBS-C diagnosed in the last five years (total sample: Italy=112; France=59; Germany=102).	All IBS-C patients	National Health Service	Mean annual cost/patient - Overall direct: €1761 (Italy) - Overall direct: €8256 (France)** - Overall direct: €9162 (Germany)**
Yiannakou et al ⁶⁰	UK	UK branch of the IBS-C study; included all patients diagnosed with moderate-severe IBS (IBS-SSS \geq 175) in the previous five years (total sample=104).	All IBS-C patients	National Health Service; out-of-pocket	Mean annual cost/patient - Overall direct: €2250 (NHS); €404 (patient) - Overall indirect (work productivity loss): €4374
Canavan et al ⁶²	UK	Data extracted from HES and Clinical Practice Research (CPR) database, including >600 GPs, including all IBS patients referred to a GI specialist during 2008-2009 (total sample=2076).	NR	National Health Service	Mean annual direct costs/patient (1 year after diagnosis) - Overall €1668 - GP attendances: €431 - Medications: €2600 - Endoscopies: €90 - Outpatient appointments: €740
Poulsen et al ⁴⁶	Denmark	IBS patients selected among those included in two population-based longitudinal studies enrolling non-institutionalized adult subjects (total sample=677)	NR	National Health Service	Mean annual direct costs/patient: €3600

GI = Gastro-intestinal; GP = General practitioner; NR = Not reported; US = Ultrasound.

*Annual costs were obtained multiplying by 12 the reported monthly costs.

**Annual costs were obtained doubling the reported 6-month costs.

***Annual costs were obtained dividing the reported total costs by the total sample size.

ψ In this study, only days off work as recorded by physicians were considered to compute the overall indirect costs, thus the true costs, also due to productivity loss, are likely to be considerably higher.

A Only data from the Rome II criteria were included in the analyses.

B To obtain total annual direct and indirect costs, both positive and exclusion strategy costs were multiplied by a specific weight, corresponding to the percentage of the total sample assigned to each strategy (0.497 and 0.503 respectively); the resulting amounts were summed up to obtain an overall weighted value.

C Only data from the European cohort were included in the analyses.

D To obtain total annual direct costs, both primary and secondary costs were multiplied by a specific weight, corresponding to the percentage of the total sample that, according to the most recent literature, may be hypothetically diagnosed and followed in a primary and secondary care setting (0.77 and 0.23, respectively); the resulting amounts were summed up to obtain an overall weighted value.

E To obtain total annual direct costs, both outpatient and inpatient costs were multiplied by a specific weight, corresponding to the percentage of the total sample that, according to the most recent literature, may be hypothetically followed in outpatient and inpatient setting (0.977 and 0.023 respectively); the resulting amounts were summed up to obtain an overall weighted value.

Costs of IBS in Italy

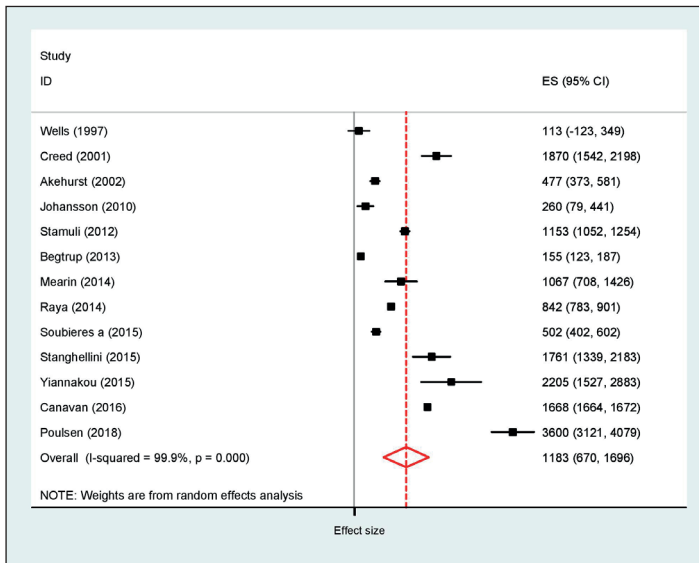


Figure 1. Direct costs: weighted mean annual costs/patient/year (€); perspective: National Health Service.

Figure 2. Direct costs: weighted mean annual costs/patient/year (€); perspective: third party-payer.

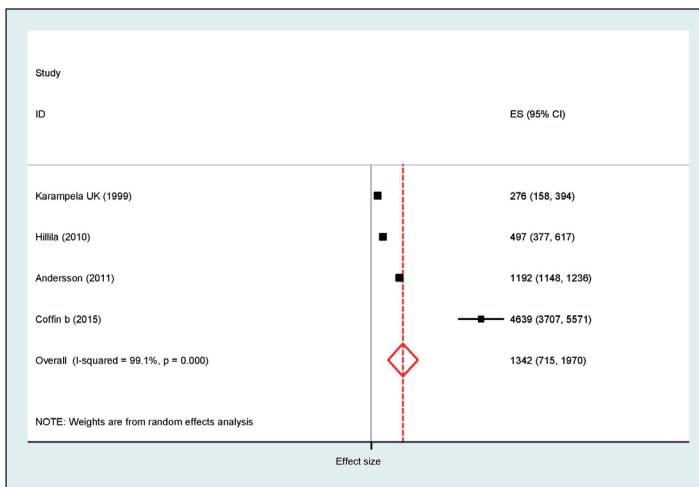
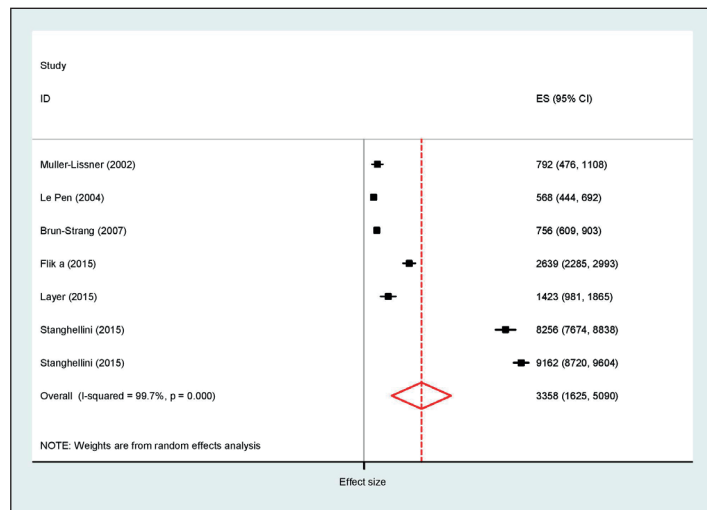


Figure 3. Direct costs: weighted mean annual costs/patient/year (€); perspective: societal.

Table II. Mean annual direct and indirect costs/patient due to IBS, overall and by healthcare payer (studies' perspective). Overall means were obtained combining data from individual studies to perform meta-analyses of single-group continuous data. All costs are expressed in euros. CI = Confidence Interval.

Perspective	Mean annual costs/patient (€)	
	Direct costs Overall mean (95% CI)	Indirect costs Overall mean (95% CI)
References	12,14,21,30,38,46,47,52,55,60,62,75,76	14,21,38,60
N. datasets (sample)	13 (12,163)	4 (775)
National Health Service	1183 (670-1696)	2180 (382-3978)
References	16,24,32,33,40,55	16,32,33,40
N. datasets (sample)	6 (1494)	4 (1007)
Third-party payer*	3358 (1625-5090)	139 (12-266)
References	13,20,28,31	13,26,28,31,41
N. datasets (sample)	4 (1500)	5 (2196)
Societal**	1342 (715-1970)	3790 (253-7327)
References	12-14,16,20,21,24,28,30-33,38,40,46,47,52,55,60,62,75,76	13,26,28,31,41 16,32,33,40 14,21,38,60
N. datasets (sample)	23 [‡] (15,157)	13 (3978)
Overall	1837 (1480-2195)	2314 (1811-2817)

*Studies assessing the costs from the perspective of insurers (e.g., French or Germany National Health Insurance).

**Studies considering the costs on the welfare of the whole of society, regardless of payer.

[‡]Although the included publications are 22, one study⁵⁵ reported separately data for more than one country, thus a total of 23 separate datasets have been included in the analyses.

Discussion

Based on the estimates of Italy and other European countries with universal healthcare coverage, this meta-analysis estimated a total per capita cost, due to IBS, of almost €3,000 per year. Notably, the total annual per capita costs of other high-prevalence chronic diseases, such as persistent asthma⁷⁷, chronic obstructive pulmonary

disease⁷⁸ or diabetes⁷⁹, which are considered as major public health priorities, have been estimated to be lower or comparable (€1183, €3291 and €2991, respectively). To obtain a raw estimate of the overall cost of IBS for the national health system of each of the European countries with universal healthcare coverage, the summary per capita cost should be multiplied by the total number of patients with IBS of the country.

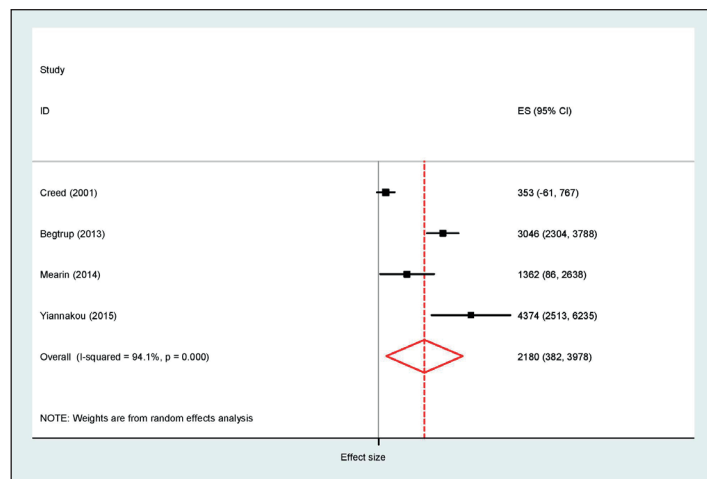


Figure 4. Indirect costs: weighted mean annual costs/patient/year (€); perspective: National Health Service.

Costs of IBS in Italy

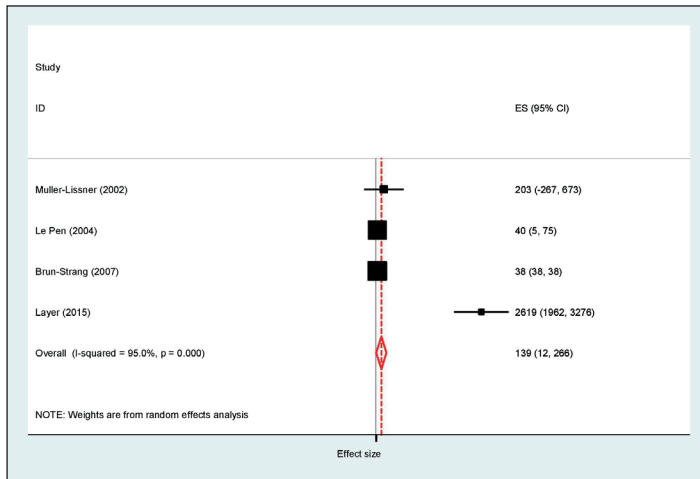


Figure 5. Indirect costs: weighted mean annual costs/patient/year (€); perspective: third party-payer.

Figure 6. Indirect costs: weighted mean annual costs/patient/year (€); perspective: societal.

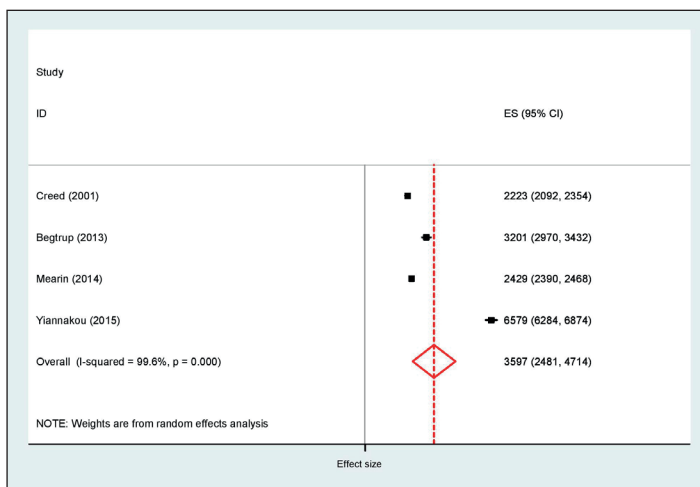
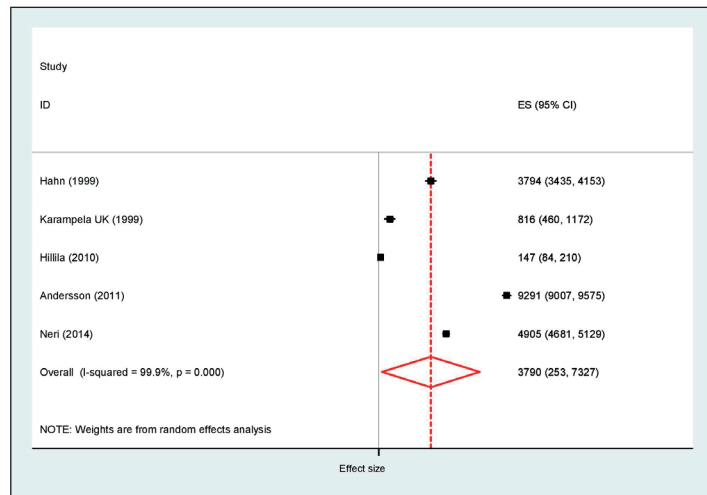


Figure 7. Total costs: weighted mean annual costs/patient/year (€); perspective: National Health Service.

Figure 8. Total costs: weighted mean annual costs/patient/year (€); perspective: third party-payer.

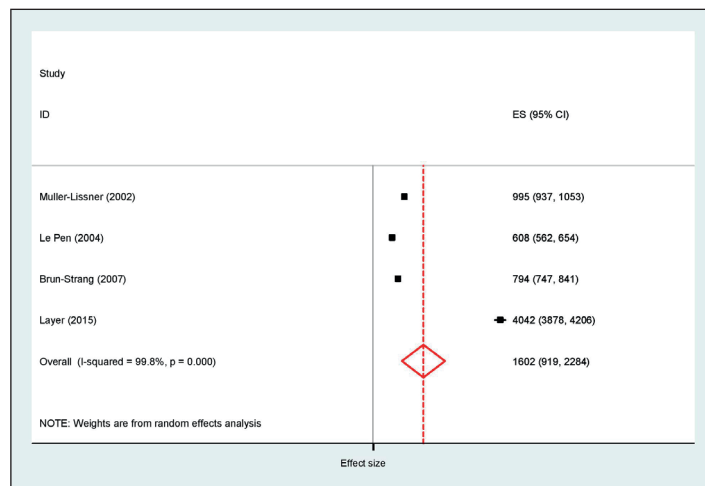
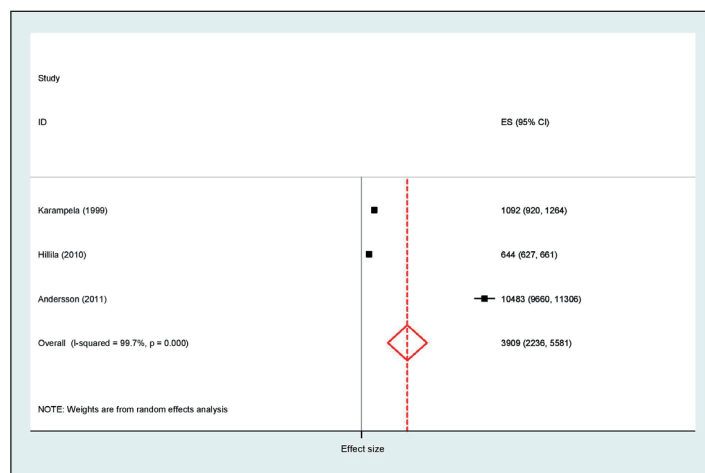


Figure 9. Total costs: weighted mean annual costs/patient/year (€); perspective: societal.



As an example, in Italy, a recent meta-analysis reported a lowest, extremely conservative estimate of 2,736,700 Italian adults with IBS⁴. Multiplying the estimated per capita cost (€2889) for this value, the overall cost for the Italian adults approximates 8 billion euro per year (€ 7,906,326,000). Even if the lowest, logically plausible estimate is used (the lowest confidence interval of the summary estimate – €2318), the overall cost of IBS for the Italian national health system is higher than 6 billion euro (€ 6,343,670,000). This estimate can be used as a minimum, most likely underestimated basis for targeted public health policies, which should recognize that IBS is associated with substantial costs to the patients, healthcare systems and society. In addition, it is important to note that the costs associated with IBS in Italy may be considerably underestimated. First, the true prevalence of IBS is likely to be even higher than the above estimate⁴: it has been observed that more than half

of the IBS patients in the USA are undiagnosed². Second, the evidence on the economic burden of IBS in Italy relies mainly on two studies that focused on IBS-C^{41,55}. However, it is commonly accepted that the economic burden of IBS-D may be higher¹⁸, because it requires more complex diagnostic tests to comply with Rome IV criteria⁸⁰ (endoscopy, imaging, microbiology, serology), with a consequent increase of the direct costs. Also, diarrhea urgency or faecal incontinence in the workplace may cause higher indirect costs due to increased absenteeism and reduced productivity. Some actions may be helpful to decrease the large economic burden associated with IBS in the healthcare settings of Italy and other European countries with universal healthcare coverage. Firstly, promoting dietary control and a healthy lifestyle may facilitate better management of IBS at a primary care level. The adult population could be educated to avoid some behaviours that are

Table III. Mean annual total (direct + indirect) costs/patient due to IBS, overall and by healthcare payer (studies' perspective). Overall means were obtained combining data from individual studies to perform meta-analyses of single-group continuous data. All costs are expressed in euros. CI = Confidence Interval.

<i>Perspective</i>	Mean annual costs/patient (€) Overall mean (95% CI)
References N. datasets (sample) National Health Service	14,21,38,60 4 (775) 3597 (2481-4714)
References N. datasets (sample) Third-party payer*	16,32,33,40 4 (1007) 1602 (919-2284)
References N. datasets (sample) Societal**	13,28,31 3 (975) 3909 (2236-5581)
References N. datasets (sample) Overall	13,14,16,21,28,31-33,38,40,60 11 (2757) 2889 (2318-3460)

*Studies assessing the costs from the perspective of insurers (e.g., French or Germany National Health Insurance).

**Studies considering the costs on the welfare of the whole of society, regardless of payer.

known to generate or exacerbate IBS symptoms, such as: (a) the indiscriminate and/or unnecessary use of pharmaceutical compounds (e.g., nonsteroidal anti-inflammatory drugs⁸¹ or proton pump inhibitors⁸²), which can alter gut microbiota richness and diversity up to small intestine bacterial overgrowth⁸³; (b) poor hygiene and careless food preparation and/or cooking, which may increase the risk of enteric infections⁸⁴. Secondly, the general practitioners should be trained to apply Rome IV criteria during IBS diagnostic process, thus avoiding unnecessary and redundant tests in the absence of alarming clinical features. Thirdly, once the diagnosis is made, evidence-based lifestyle modifications, symptom-driven pharmacological treatments, and psychological support should be started according to international guidelines and best-evidence practices^{6,85,86}. Finally, other strategies aimed at improving medication adherence – typically low in IBS patients⁸⁷ – might also help to decrease the absenteeism-related indirect costs and the loss of productivity. Some limitations must be taken into account when interpreting the study findings, which are to be considered preliminary and require confirmation. First of all, despite an

updated systematic search performed according to PRISMA guidelines, we might have missed some studies or data from the grey literature. Then, as in most cost-of-illness studies⁸⁸, the methodologies used across the included European studies varied substantially. In particular, the costs of IBS and their calculation were not standardized, and the approaches used to distinguish IBS and non-IBS costs differ across studies. Finally, due to the lack of important patient-level data, it was not possible to ascertain the association between individual patient's characteristics and related costs.

Conclusions

The minimum costs due to IBS in Italy – likely underestimated – range from 6 to 8 billion euro per year. Given the substantial economic burden for the patients, healthcare systems and society, IBS should be included among the priorities of the public health agenda.

Ethics Approval

The study did not involve human subjects and no approval from Ethics Committee was thus requested.

Authors' Declaration of Personal Interests

None of the authors declare any potential conflict of interests.

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