

# Quality of life of patients with irritable bowel syndrome is low compared to others with chronic diseases

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**Background** Irritable bowel syndrome (IBS) is a prevalent functional gastrointestinal dysmotility disorder. This study aimed to estimate the burden of illness of a Dutch population of community dwelling patients suffering from IBS.

**Methods** Patients identified at community pharmacies, using mebeverine as a proxy for IBS, were administered a questionnaire regarding (1) the Rome II criteria for IBS, (2) predominant type of stool during complaints, (3) severity of symptoms (abdominal pain and discomfort), (4) generic and disease-specific quality of life, (5) current health status (utilities), and (6) loss of productivity.

**Results** Three hundred and seventy-five users of mebeverine were identified of which 169 patients met the Rome II criteria for IBS, and were included in the study. More than half (58%) of the IBS patients reported severe abdominal pain and complaints. Generic and disease-specific quality of life outcomes showed impairment on all dimensions. Current health status in IBS patients, calculated on the basis of the EQ-5D VAS, was perceived on 62% of full health (95% CI, 60–66%). A calculation of health status in these patients based on the SF-6D algorithm showed a comparable score of 0.67 (1 is full health; 95% CI, 0.65–0.68). The loss in productivity of IBS patients was 1.8 days (95% CI, 1.1–2.5) per month.

## Introduction

Irritable bowel syndrome (IBS) is a chronic and episodic functional gastrointestinal dysmotility disorder which is characterized by abdominal discomfort and pain, change of bowel habit and disordered defaecation. Although IBS is not a life-threatening disease it can have a disabling impact upon the patient's health and lifestyle [1–3].

Hungin *et al.* [1] reported a prevalence rate of 6.2% for patients suffering from IBS-like complaints in the Netherlands. Of these IBS patients, 2.0% were formally diagnosed with IBS. The impact of IBS on patients' well-being and daily functioning has not been assessed yet in a sufficiently large and well-defined population of IBS patients in the Netherlands [2,4–6]. Janssen *et al.* estimated health status in patients with non-specific abdominal complaints and reported that IBS patients were found to have a health status lower than patients

**Conclusions** This study confirmed that the burden of illness of IBS in the Netherlands is substantial. IBS patients treated with mebeverine experienced low quality of life and suffered from severe pain. Based on these results, more attention for the diagnosis and treatment of IBS seems to be justified. *Eur J Gastroenterol Hepatol* 18:475–481 © 2006 Lippincott Williams & Wilkins.

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**Keywords:** irritable bowel syndrome, burden of illness, health-related quality of life, SF-36, IBS-QOL, health status, EQ-5D VAS, SF-6D, loss in productivity

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with non-ulcer dyspepsia or other abdominal problems [6]. Additionally, IBS patients were found to experience the highest level of anxiety and depression symptoms of all patients with non-specific abdominal complaints [6]. Minderhoud *et al.* described an impairment of the quality of life in patients suffering from inflammatory bowel disease who experience IBS-like symptoms [5].

The burden of illness of IBS was assessed in the United Kingdom and in the United States (US) and found to be severe [7–9]. In the Netherlands, Goettsch *et al.* found that the use of medical resources and associated health care costs are increased in IBS patients using antispasmodic drug mebeverine (Duspatal), the only drug that is registered in the Netherlands for treatment of IBS [10–12] compared to matched controls [13]. In the current paper the results from a survey that was conducted to assess the burden of illness of IBS in a

Dutch population of IBS patients treated with mebeverine are presented. Burden of illness was assessed from a number of different viewpoints:

- On the basis of SF-36 methods we compared the general quality of life of the selected IBS patients to other chronically diseased.
- On the basis of IBS-QOL we compared the quality of life of the selected IBS patients in the Netherlands to other IBS populations in other countries.
- On the basis of utility assessments we compared the experienced health status of the selected IBS populations to the general population and other chronically diseased.

## Methods and patient selection

### Patient selection

Community pharmacies contributing to the PHARMO Record Linkage System (PHARMO RLS) were asked to cooperate in the study. The PHARMO RLS is a network of medical databases including the UEXPO database which contains detailed drug-dispensing records from community pharmacies. The UEXPO database represents more than 2 million inhabitants of representative and well-defined demographic areas in the Netherlands. From March 2003 until December 2003, patients presenting a prescription for mebeverine (first or refill) at the pharmacy were asked to participate in the study. Because mebeverine is the only drug labelled for IBS treatment in the Netherlands, its use was used as a proxy for IBS. After consent, patients completed a questionnaire, assisted by a pharmacy technician or a pharmacist. The Rome II criteria for diagnosis of IBS were applied to confirm the diagnosis of IBS [14].

### Questionnaire

The questionnaire consisted of the Rome II criteria for IBS, questions regarding previous diagnosis of IBS, type of symptoms, severity of symptoms, health-related quality of life, current health status (utilities) and loss of productivity. Due to privacy legislation, age and gender could not be retrieved directly through the questionnaire. This information was retrieved from the PHARMO RLS.

### Characterization

IBS patients were selected on the basis of the Rome II criteria: (1) suffering at least 12 weeks, which need not be consecutive, in the preceding 12 months of abdominal discomfort or pain, and (2) two out of three of the following features: (a) relief of symptoms with defaecation, (b) onset of symptoms associated with a change in frequency of stool and (c) onset of symptoms associated with a change in form of stool [14]. Additional to the Rome II criteria patients were asked if they were previously diagnosed with IBS by their general

practitioner. Information on the type of IBS regarding predominant stool was retrieved by asking patients to characterize the dominant type of stool (diarrhoea predominant, constipation predominant or a combination of both) they suffered from during complaints. The severity of the symptoms was estimated using an anchored 100 mm visual analogue scale (VAS) for pain and abdominal complaints, on which six states of severity were indicated: absent (0 mm), very mild, mild, moderate, severe and very severe (100 mm) [15]. Patients were asked to rate pain and abdominal symptoms experienced in the past week. For analyses the patient were classified regarding severity of symptoms as asymptomatic (0–30 mm), low (31–40 mm), moderate (41–60 mm) and severe (more than 60 mm).

### Burden of illness

Health-related quality of life was estimated with a generic and disease-specific instrument. The Medical Outcome Study 36-item Short Form Health Survey (SF-36) was used as generic instrument [16]. The SF-36 questionnaire consists of 36 questions regarding eight dimensions of health perception. In Table 1 the instrument is described in short. Outcomes of the SF-36 were described in terms of mean scores per dimension and regarding physical and mental health by the physical component summary (PCS) and mental component summary (MCS). The outcomes of the distinct SF-36 dimensions were compared to data from two samples of the general Dutch population (Amsterdam and national populations) and to samples of Dutch migraine and cancer patients [17], and to data from a US population of IBS patients that were seen at functional bowel clinic [18]. The PCS and MCS were compared to summary component measures for the Dutch population [19], and the US population of IBS patients [18].

Disease-specific health-related quality of life was assessed with the Irritable Bowel Syndrome Quality of Life questionnaire (IBS-QOL) [20]. The IBS-QOL instrument consists of 34 questions regarding eight dimensions of health. In Table 1 the IBS-QOL instrument is described in short. Mean scores were calculated per dimension of the IBS-QOL, with a score of 0 for worst quality of life and a score of 100 for best quality of life. An overall mean score, taking into account all dimensions, was calculated following the instruction of the designers of the instrument [20]. IBS-QOL outcomes were compared to results from a British and a German population of IBS patients, recruited respectively at general practitioner offices and from an IBS focus group [11,21].

The current health status (utilities) was assessed with the VAS from the Euroqol-5D instrument (EQ-5D VAS) on which a score of 0 indicated the worst imaginable

**Table 1 Characteristics SF-36 [16] and IBS-QOL [20]**

Instrument	Type	Number of questions		Dimensions	Measurement
SF-36	Generic	36 on 8 dimensions	Physical functioning (PF)	Limitations in walking, climbing, for example	Scores for dimensions are generated from the score for the different questions contributing to the dimension. Scores are between 0 and 100, with 0 indicating poor health and 100 indicating good health.
			Role limitations because of physical health (RP)	Limitations in work and activities due to physical impairment	
			Bodily pain (BP)	Pain experienced in past 4 weeks	
			General health perception (GH)	Indication of current health status	
			Vitality (VT)	Energy, fatigue	
Social functioning (SF)	Limitations in social activities in the past 4 weeks				
			Role limitations because of emotional health (RE)	Limitations in work and activities due to mental impairment	
			Mental health (MH)	Indication of current personal feeling	
		2 summary measures	Physical component summary (PCS)	Considers the dimensions physical functioning, role limitations because of physical health, bodily pain and general health	Summary measures are derived from the distinct dimension using norm-based scoring techniques. The score are compared to the norm (mean=50, SD=10)
			Mental component summary (MCS)	Considers the dimensions vitality, social functioning, role limitations because of emotional health and mental health	
IBS-QOL	Disease-specific	34 on 8 dimensions	Dysphoria	Feeling about life with IBS	Scores for dimensions are generated from the scores of the different questions contributing to the dimension. Scores are between 0 and 100, with 0 indicating poor health and 100 indicating good health. An overall score is calculated from all the separate scores of the different questions.
			Interference	Change in daily activities due to IBS	
			Body image	Feeling about body	
			Health worry	Puzzling about health	
			Food avoidance	Patient can eat less due to IBS	
Social reaction	Patients ideas what other people think of him being ill				
Sexual Relationships	Change in sexual desire/activity Matter in which relationships with others are affected by IBS				

health status and a score of 100 the best imaginable health status [22].

Additionally, community valuations were calculated from the SF-36 outcomes, using the SF-6D algorithm developed by Brazier *et al.* [23,24]. A SF-6D index of 0 represents the worst imaginable health status and an index of 1 represents the best imaginable health status [23,24]. Both health status valuations were calculated as mean scores with 95% CI. The loss of productivity, calculated as the average number of days per month with 95%CI, was assessed by asking patients to estimate the number of days on which they had been unable to perform their daily activities due to IBS complaints in the period of 3 months before the questionnaire.

### Analysis

All statistical analyses were performed using SAS version 8.2 (SAS Institute Inc., Cary, NC, USA).

### Results

In the 33 community pharmacies that participated in the study 375 current users of mebeverine consented and the questionnaire was completed by 315 patients, of whom 169 (53.7%) met the Rome II criteria for IBS and were therefore eligible for analysis. The total population that

was dispensed mebeverine in the participating pharmacies during the study period included 1288 patients (Table 2). On average, the respondents were 4 years older and contained a comparable percentage of females compared to all users of mebeverine (Table 2). The included respondents did not differ from the excluded respondents regarding age and gender (Table 2). Age and gender could not be retrieved from the PHARMO RLS for 20% of the patients.

The majority of the patients (75%) reported to be previously diagnosed with IBS by their general practitioner. Of the patients who did not meet the Rome II criteria for IBS, 60% also reported to be diagnosed with IBS. An alternating stool pattern was reported most often as predominant type of stool: 51% of the IBS patients suffered from diarrhoea and constipation, 18% reported predominantly diarrhoea, 19% reported predominantly constipation and 12% reported a normal stool. The average VAS score for severity of symptoms was 66.3 (95% CI, 63.0–69.5). Fifty-eight percent of the patients was classified as severe. The distribution of the severity of symptoms is presented in Fig. 1.

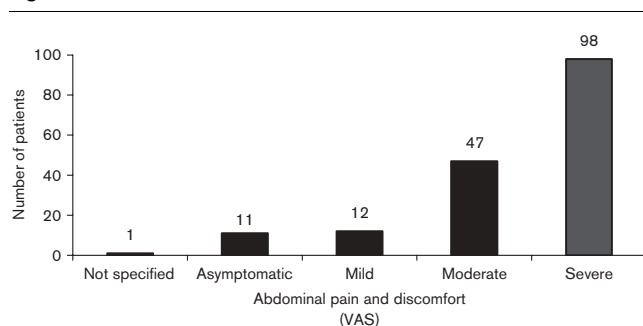
In Table 3 the estimates for generic quality of life (SF-36) of IBS patients are presented and compared to other

**Table 2 Characteristics of the study population**

	Users of mebeverine eligible for participation (inclusive consenters)		Respondents (included and excluded patients)		Included patients	
	n	Age, years (SD)*	n	Age, years (SD)*	n	Age, years (SD)*
All	1288	50.2 (20.2)	250**	54.5 (18.1)	136**	55.0 (17.1)
Male	333 (25.9%)	50.8 (18.9)	69 (27.6%)	52.7 (17.4)	31 (22.8%)	54.3 (16.7)
Female	955 (74.1%)	50.0 (20.6)	181 (72.4%)	55.2 (18.3)	105 (77.2%)	55.2 (17.3)

\*The patient's age at the first dispensation of mebeverine in 2003 was taken for this analysis.

\*\*It was not possible to retrieve information on age and gender of 65 respondents (20%), of which 33 were included in the study.

**Fig. 1**

Number of patients with irritable bowel syndrome, by severity of symptoms [15].

populations. Eighty-six percent of the included subjects provided answers on all items of the SF-36, enabling the calculation of summary scores for these patients. IBS patients had lower scores on all dimensions of the SF-36 compared to the samples of the Dutch population [17]. Compared to Dutch migraine and Dutch cancer patients [17], IBS patients reported a lower quality of life especially regarding bodily pain and vitality. Dutch IBS patients scored worse regarding role functioning physical and vitality than US IBS patients. In contrast, Dutch IBS patient reported a better score for role functioning emotional than the US IBS patients [18]. Both summary measures for IBS patients were significantly lower than the reference value for the Dutch national population reported by Ware *et al.* [19]. The summary measures for the Dutch IBS patients were very similar to the US IBS patients.

All IBS-QOL questions were completed by 73% of the patients, enabling an overall score for these patients (Fig. 2) to be calculated. The outcomes of the IBS-QOL were significantly different from the score of 100, which corresponds to no impairment, for all distinct dimensions and the overall mean score (75.4). The results for the separate dimensions and the overall score were similar to the IBS-QOL outcomes of British IBS patients (Fig. 2) for whom an overall score of 71.6 was reported [11]. German IBS patients reported lower disease-specific

quality of life than Dutch IBS patients with an overall score 59.8 [21].

Patients reported a current health status on the EQ-5D VAS of 62% (95% CI, 60–66%,  $n = 166$ ) of the best imaginable situation. Application of the SF-6D algorithm resulted in a similar, but somewhat higher estimate for current health status: 0.67 (95% CI, 0.65–0.68,  $n = 133$ ). On average, IBS patients reported a loss of productivity of 1.8 (95% CI, 1.1–2.5,  $n = 150$ ) days per month.

## Discussion

The results of this study showed that the burden of illness of IBS in the Netherlands was substantial. The quality of life of IBS patients was impaired on all dimensions regarding generic and disease-specific health-related quality of life. Summary components measures revealed that both physical and mental components of health are impaired. Severe abdominal pain and symptoms were reported by 58% of the patients. Utility measurement showed a current health status of 62%. Patients were unable to perform daily activities for 1.8 days per month.

Subjects were included in the study if they used mebeverine and if they met the Rome II criteria for IBS. Mebeverine is the only drug labelled for the treatment of IBS in the Netherlands, but it is also labelled for the treatment of secondary irritable colon due to diverticulitis or Crohn's disease [12], for example. The Rome II criteria for IBS are constructed with consensus on which disease symptoms are characteristic for IBS in order to diagnose patients. This criteria can be used to select IBS patients from a population of patients with functional gastrointestinal dysmotility disorders [14]. The patients included in this study were diagnosed and medically treated IBS patients.

Hungin *et al.* [1] reported that 2.0% of the Dutch population suffered from IBS. Goettsch *et al.* [13] found that 1.2% of the Dutch population used mebeverine. We found that half (53.7%) of the mebeverine users met the Rome II criteria for IBS. Based on these results it can be estimated that 0.6% of the total Dutch population and one third of the total Dutch IBS population would use

**Table 3 SF-36 outcomes for patients with irritable bowel syndrome (IBS), two samples of the Dutch population [17], Dutch migraine [17] and Dutch cancer patients [17], and a US population of IBS patients [18]**

Dimension	IBS (n=169) mean (SD)	National (n=1742) mean (SD)	Migraine (n=423) mean (SD)	Cancer (n=485) mean (SD)	IBS US (n=877) mean (SD)
PF (SD)*	66.3 (26.0)	83.0 (22.8)	82.4 (21.3)	63.6 (25.1)	79.2 (22.4)
RP (SD)*	43.5 (42.9)	76.4 (36.3)	62.2 (40.8)	35.0 (40.3)	49.9 (41.5)
BP (SD)*	47.7 (19.8)	74.9 (23.4)	64.9 (22.4)	69.3 (26.6)	53.6 (24.9)
GH (SD)*	48.8 (22.9)	70.7 (20.7)	67.5 (20.5)	52.5 (21.4)	54.5 (23.3)
VT (SD)*	47.5 (20.0)	68.6 (19.6)	61.1 (18.6)	60.1 (22.3)	64.8 (19.8)
SF (SD)*	64.8 (27.2)	84.0 (22.4)	76.2 (20.9)	73.9 (24.1)	64.8 (40.9)
RE (SD)*	60.9 (43.2)	82.3 (32.9)	74.5 (37.8)	58.4 (43.6)	44.0 (23.2)
MH (SD)*	64.7 (20.1)	76.8 (17.4)	72.0 (18.7)	68.0 (19.8)	62.7 (27.7)
PCS (SD)**	41.1 (10.8)	49.7 <sup>†</sup> (9.3)	NA	NA	42.7 (10.5)
MCS (SD)**	44.9 (13.0)	52.1 <sup>†</sup> (9.6)	NA	NA	43.4 (11.4)

NA=not available.

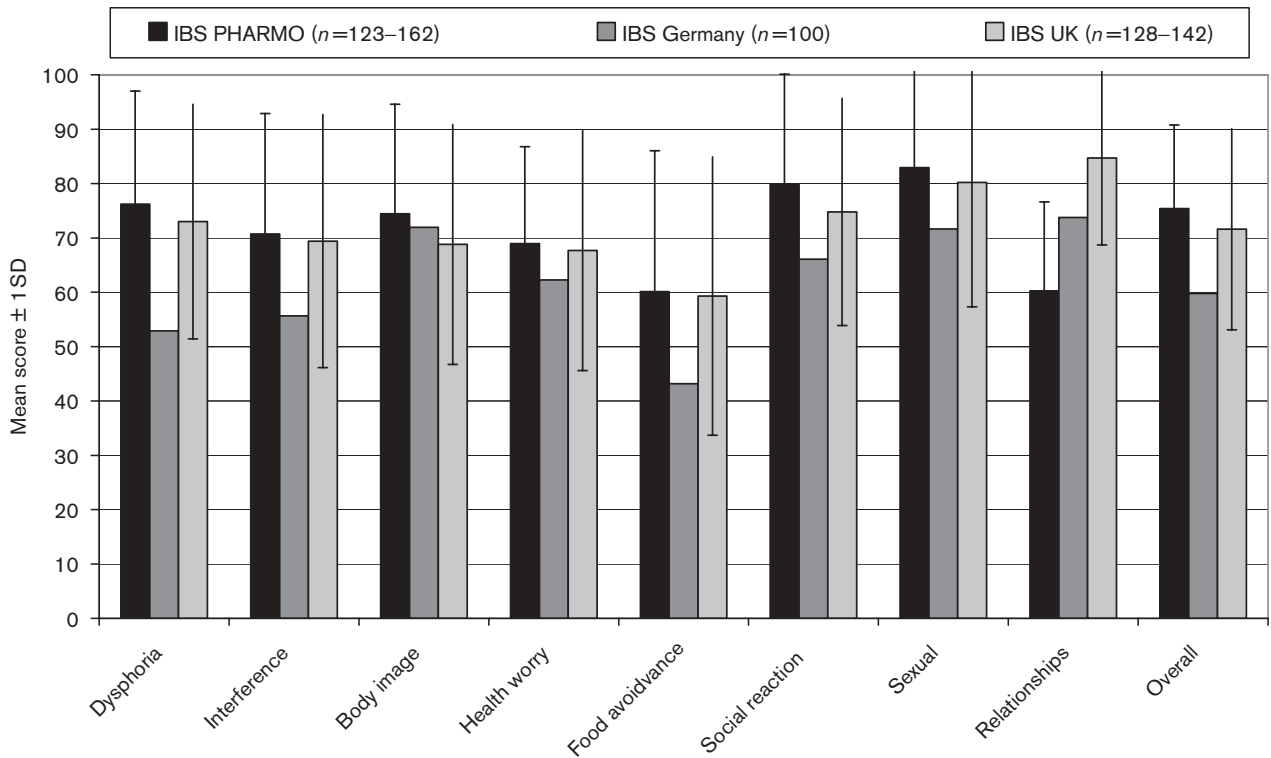
\*PF=physical functioning, RP=role-functioning physical, BP=bodily pain, GH=general health, VT=vitality, SF=social functioning, RE=role-functioning emotional, MH=mental health.

\*\*PCS=physical component summary, calculated regarding norms for the United States, mean score=50, SD=10<sup>16</sup>.

\*\*\*MCS=mental component summary, calculated regarding norms for the United States, mean score=50, SD =10<sup>16</sup>.

<sup>†</sup>Summary scores for the 'national population' were reported separately from the scores from the distinct dimensions, by Ware *et al.* [19].

**Fig. 2**



Irritable bowel syndrome (IBS) quality of life outcomes for Dutch, German [21] and British IBS patients [11]. A score of 100 on a dimension of IBS-QOL corresponds with no impairment of disease-specific quality of life. See Table 1 for clarification of the x-axis categories. The dimension score could not be calculated for all patients because some failed to answer the question regarding this scale. This explains the variation in number of patients (n) for the Dutch and UK patients.

mebeverine. We must take into account that IBS patients treated with mebeverine may be more severely affected than average Dutch IBS patients, since the Dutch guidelines for treatment of IBS advise reassurance of the patient and optimization of food intake as first

treatment before starting therapy with mebeverine [10]. Moreover, our results showed that the included IBS respondents were somewhat older than the total group of patients using mebeverine (Table 2). Therefore, our data may overestimate the severity of disease of the general

Dutch IBS population to some extent. However, it may be assumed that medically treated IBS patients are most relevant in terms of loss of quality of life on a population level. Subsequently, they will also be primarily indicated for an alternative or new medical IBS treatment.

Due to the generic character of the SF-36 it is possible to compare health-related quality of life of IBS patients with data from the general population and from populations of patients suffering from other diseases. Comparison of the mean scores of the eight SF-36 dimensions of the population of IBS patients to data reported by Aaronson *et al.* for two samples of the general Dutch population and data from Dutch populations of migraine and cancer patients provided an estimate of the relative impact of IBS on health-related quality of life [17]. IBS patients, especially, scored relatively low for the dimensions bodily pain and vitality. In addition, the majority of the included patients reported experiencing severe pain and abdominal complaints. Therefore the suggestion that pain is an important determinant in the experience of health of medically treated IBS patients is worth further investigation with a focus on the relationship between the burden of illness and pain. Both SF-36 summary component scores indicated that IBS patients were significantly impaired regarding physical and mental health compared to the Dutch population. The summary measures for Dutch IBS patients were similar to summary measures reported by Gralnek *et al.* for US IBS patients [18].

Additionally, we compared our results to other Dutch populations of chronic diseased patients using data from Alonso *et al.* who presented summary component scores for patient groups suffering from allergies, arthritis, chronic lung disease, congestive heart failure, diabetes, hypertension and ischaemic heart disease, respectively [25]. The summary component scores for these populations were derived from the summary component scores for a population of Amsterdam residents that reported not to suffer from any of the mentioned chronic conditions (PCS 53.4, MCS 55.2), with a regression model. Consequently, the deviation from this estimate for 'healthy subjects' was calculated for the different patients groups. The PCS estimates for arthritis, chronic lung disease and congestive heart failure patients were most decreased, as were the MCS estimates for allergies, diabetes and hypertension [25]. All PCS and MCS estimates for patients with chronic conditions reported by Alonso *et al.* [25] were substantially higher than the results for our Dutch IBS group. However, comparison of the summary scores calculated by Alonso *et al.* [25] with the estimates for IBS patients from the current study must be done with caution because the summary scores in the study of Alonso *et al.* [25] were calculated with a regression model taking into account several variables and were primarily aimed to compare quality of life of the different groups of chronic diseased patients between

European countries. (Alonso, December 2004, personal communication).

IBS-QOL results showed (Fig. 2) that the overall score and the separate dimensions were similar for Dutch and the British IBS patients, who were both medically treated IBS patients [8]. German IBS patients reported lower disease-specific quality of life than Dutch IBS patients with an overall score 59.8 [21]. This may be related to the fact that in the latter the patients of an IBS focus group were included, who may be patients with a more severe form of IBS.

To our knowledge, a single preference based index (SF-6D) presenting the current health status experienced by patients suffering from IBS has never been derived from the SF-36 before. Brazier *et al.* [26] discussed utility measures for different patients groups of chronic diseased patients and reported SF-6D indices for patients suffering from leg ulcers (0.65) and lower back pain (0.66) that corresponds with a similar health status as experienced by IBS patients [26].

In conclusion, the results on the severity of symptoms, health-related quality of life, the current health status and the loss of productivity reveal that suffering from IBS has a high impact on every dimension of quality of life of Dutch IBS patients treated with mebeverine. We also demonstrate that the impact of IBS on the quality of life in these patients is even higher than in other patients with chronic diseases and is primarily related to pain complaints. Combined with the fact that IBS is a prevalent disease it can be concluded that the burden of illness of IBS is of major concern for Dutch health care.

## Acknowledgements

We especially thank all community pharmacies that contributed to PHARMO and participated in this study.

### Conflict of interest

Guido van den Boom is employed by Novartis NL. Wim G. Goetsch and Ron M.C. Herings received project funding from Novartis. André J.P.M. Smout was a member of the national and international advisory board for Tegaserod.

### Authors' contributions

Maarten J. ten Berg carried out the statistical analysis of the data and wrote the first draft of the manuscript. Wim G. Goetsch developed the design of the study, recruited the participating pharmacists, and was involved in interpreting the study results and preparing the manuscript. Guido van de Boom assisted with developing the study design, reviewing the study results and preparing the manuscript. André J.P.M. Smout helped to develop the study design and to review the study results and the manuscript. Ron M.C. Herings developed the study design, recruited the participating pharmacists, interpreted the study results and prepared the manuscript.

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