Gastroenterology and Hepatology From Bed to Bench.
2024 **RIGLD**, Research Institute for Gastroenterology and Liver Diseases

ORIGINAL ARTICLE

p-ISSN: 2008-2258 e-ISSN: 2008-4234

Translation, cultural adaptation, reliability, and validity of the Persian version of the Constipation Severity Instrument

Zeinab Moradi[1], Farhad Azadi[1], Jalil Shoa Hasani[2], Mohsen Vahedi[3]

[1]Department of Physical Therapy, Faculty of Rehabilitation Sciences, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran
[2]Colorectal Surgery Fellowship, Private Medical Practice, Rasht, Iran
[3]Department of Biostatistics and Epidemiology, faculty of Rehabilitation Sciences, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran

ABSTRACT

Aim: The aim of this study was to translate and cross-culturally adapt the Constipation Severity Instrument (CSI) and assess its reliability and validity in the Iranian Persian language with chronic functional constipation.

Background: Chronic functional constipation is a common complaint characterized by a range of symptoms. The use of a validated tool adapted to the culture is an important part of the treatment process.

Methods: CSI was translated into Persian language according to Beaton's guidelines. One hundred and twenty-five patients with chronic functional constipation, according to ROME IV criteria, completed the questionnaires. Face validity was assessed in two qualitative and quantitative forms (impact score), internal consistency and test-retest reliability were assessed by Cronbach's alpha coefficient and intraclass correlation coefficient (ICC), respectively. Convergent validity was assessed by correlating the total scores of the CSI and the WCSS. The floor/ ceiling effects of the questionnaire were also assessed.

Results: The impact score of all questions was greater than 1.5. The Cronbach's alpha coefficient for the total score was 0.90 and the ICC was 0.90. The total score of the CSI was significantly correlated with the total score of the WCSS (Spearman's p=0.74). No floor/ceiling effects were found.

Conclusion: The Persian version of the CSI is a reliable and valid tool that can be used for psychometric evaluation. Clinicians can also benefit from this questionnaire when assessing treatment outcomes in Iranian patients.

Keywords: Constipation, Validity, Reliability, Questionnaire, Persian version.

(Please cite as: **Moradi Z, Azadi F, Shoa Hasani J, Vahedi M. Translation, cultural adaptation, reliability and validity of the Persian version of the Constipation Severity Instrument. Gastroenterol Hepatol Bed Bench 2024;17(2):198-205. https://doi.org/10.22037/ghfbb.v17i2.2867).**

Introduction

Chronic functional constipation is a common public health problem with an estimated prevalence of 2.4% to 11.2 % in the Iranian population (1). Chronic severe constipation has a significant impact on the quality of life and the downstream economic effects of lost work days, reduced productivity, and associated with high healthcare costs (2-4).

According to the ROME IV criteria for functional constipation, functional constipation is diagnosed when the following three criteria are met 1) At least 2 of the following must be present: infrequent bowel movements (<3 per week), constipation is often associated with other symptoms such as incomplete evacuation, straining, lumpy and hard stools, sensation of anorectal blockage, manual maneuvers to evacuate stools, all of which must occur in at least 25% of bowel movements. 2) Loose stools are rarely present without the use of laxatives. 3) Insufficient criteria for irritable bowel syndrome, criteria met for the last 3 months with onset of symptoms at least 6 months before diagnosis (5).

Received: 01 October 2023 *Accepted*: 03 December 2023
Reprint or Correspondence: **Farhad Azadi**, *Department of Physical Therapy, Faculty of Rehabilitation Sciences, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.*
E-mail: fa.azadi@uswr.ac.ir
ORCID ID: 0000-0003-1754-2730

Copyright © 2024, Gastroenterology and Hepatology From Bed to Bench (GHFBB). This is an open-access article, distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/) which permits others to copy and redistribute the material just in noncommercial usages, provided the original work is properly cited.

ROME IV criteria were developed for the diagnosis of constipation, but they could not determine the severity of constipation. There are several self-reported questionnaires to assess the severity of constipation, such as wexner constipation score (WCSSS), patient assessment constipation scoring system (PAC-SYM), constipation assessment scale (CAS) and constipation severity instrument (CSI) (6-9). WCSS has been translated in Iran twice by Mirbehrsi et al. and Majidi Rad et al., its validity and reliability have been assessed (10, 11).

CSI developed in 2008 by Varma et al. and consists of 16 questions and 3 subscales and a score range of 0-73. Obstructive defecation subscale (ODS) has 6 questions and a score of 0-29. Colon inertia subscale (CI) has 6 questions and a score of 0-28. Pain subscale has 4 questions and score of 0-16. This questionnaire identifies different types of constipation including obstructive defecation and colonic inertia based on pathophysiology and in both sections there are questions about the degree of irritation of the person from related condition (9).

To the best of our knowledge, this questionnaire has not been translated into Persian language yet.

The aim of this study was to provide a Persian version of the CSI and to determine the psychometric properties, validity and reliability of the Persian version.

Methods

Cultural adaptation

The questionnaire was translated based on Beaton's guidelines, the questionnaire was independently translated into Persian language by three translators with expertise in the field of medicine. Then the researchers and translators compared two Persian translations with the original text of the questionnaire and came to an acceptable Persian translation.

In the next stage, a psychologist and a pelvic floor physiotherapist who are fluent in English, were requested to back translate the questionnaire. These individuals were not aware of the original questionnaire.

In a meeting attended by translators and researchers, by comparing two English translations with the original version, an English version was prepared and sent to the main author of the questionnaire for approval.

After approval of the English version in the presence of researchers and translators with discussion and consultation, the pre-final Persian version was prepared and given to 10 patients with chronic functional constipation problem (qualitative face validity). Patient opinions on writing style, comprehensibility, and clarity were gathered at the final meeting. Feedback was considered and the final Persian version was created (12).

Based on the opinions collected from the patients in the face validity, and with the permission of the main author of the questionnaire, to make the options more understandable to the Iranian population in the Persian language, a brief explanation was given for some items. For example, the word "rarely" was written as "less than once a month".

Participants

The sample was selected from patients with functional constipation who were referred by colorectal and gastroenterology specialists to a specialized pelvic floor physiotherapy center in Rasht city, Guilan province, Iran, from March 2021 to September 2022.

Inclusion criteria

Iranian Persian-language people over the age of 18 years who met the Rome IV criteria for chronic functional constipation and who had the ability to read and write in the Persian language.

Exclusion criteria

People with cognitive problems, secondary constipation, irritable bowel syndrome, drug addiction, history of neurodegenerative disease (i.e. multiple sclerosis, spinal cord injury, stroke), and people who did not want to complete the questionnaire were excluded from the study. The sample size was considered to be 125 people, considering 20% attrition (13, 14).

Validity and reliability methods

The Persian version was studied for face validity, convergent validity, discriminate validity, internal consistency, and test-retest reliability.

Validity

Quantitative face validity

Quantitative face validity was done by measuring the impact score. Five colorectal surgeons, gastroenterologists, and general surgeons who visit patients with functional constipation were asked to give a score of 1 to 5 based on the importance of each question in the questionnaire. Score 1 indicates the least importance and score 5 indicates the most importance.

The impact score of each question is calculated as the product of the importance of each question and the number of times it was repeated (that is, the percentage of individuals who gave the question a score of 4 and 5 multiplied by the average score obtained for each question). An impact score greater than 1.5 is considered appropriate (15).

Convergent validity

Convergent validity was assessed using data from 125 patients with chronic functional constipation. The convergent validity of the questionnaire was evaluated in two ways:

1- The patients completed both the CSI and WCSS questionnaires. Then correlation between two questionnaires were evaluated using Spearman Rho correlation coefficient.

2- To confirm convergent validity, a correlation was made between the scores on the pain subscale of the CSI questionnaire and the scores obtained from the pain rating based on the VAS index, and this correlation was assessed using the Spearman Rho correlation coefficient.

Discriminate validity

In order to perform discriminate validity, the difference in the severity of constipation in the groups of the number of physician visits during the last two years was investigated (16). Patients were divided into 4 groups depending on the number of visits to the physician (group 1 (0-1 visit), group 2 (2-3 visits), group 3 (4-5 visits), group 4 (more than 6 visits)). The statistical difference between the groups was verified by a one-way ANOVA test.

Reliability

Internal consistency and reproducibility were investigated to evaluate reliability of the CSI.

a- Internal consistency

Internal consistency was investigated while considering each subscale and total score. The internal consistency of total score and three subscales was assessed by Cronbach's alpha, the value equal to or greater than 0.7 was considered acceptable (17).

b- Reproducibility

The test-retest method was used to assess the reproducibility of the CSI. 20 participants completed the CSI questionnaire again after one week. These people did not receive any new treatment during this time period. Intraclass correlation coefficient (ICC) of total score and subscales were calculated. A high

Table 1. Demographic characteristics of the participants (n=125)

Characteristics		N (%)
Gender	Female	98 (78.4)
	Male	27 (21.6)
Age (year)	18-45	76 (60.8)
	46-60	29 (23.2)
	+61	20 (16)
Type of delivery	Natural childbirth	34 (34.7)
	Cesarean	41 (41.8)
	Natural childbirth and cesarean	15 (15.3)
	Without childbirth	8 (8.2)
Educational level	Less than diploma	19 (15.2)
	Diploma	31 (24.8)
	University	75 (60)
Occupational status	Employed	61 (48.8)
	Housewife	44 (35.2)
	Retired	9 (7.2)
	Unemployed	11 (8.8)
Income	Low*	15 (12)
	Middle**	22 (17.6)
	High***	53 (42.4)
	No answer	35 (28)
Number of physician's visits in the last two years	Group 1 (0-1 visit)	25 (20)
	Group 2 (2-3 visits)	51 (40.8)
	Group 3 (4-5 visits)	30 (24)
	Group 4 (+6 visits)	19 (15.2)

* Less than 60 USD per month, ** 60 to 110 USD per month, *** more than 110 per month [1USD = 500000 Rials (Iran's currency)]

positive correlation coefficient (>0.7) was taken as evidence of reproducibility (17).

Floor/ceiling effects

If more than 15% of the participants received the lowest or highest score, there were a ceiling and floor effects. The existence of floor and ceiling effects indicates that the questions of minimum and maximum intensity of the phenomenon are not included in the questionnaire and it reduces the content validity and reliability of the questionnaire (17).

Statistical analysis

Quantitative variables were described in mean±SD and qualitative variables as frequency and percentage. Distribution pattern of variables assessed by Kolmogorov-Smirnov test, and based on their patterns (normal or non-normal), statistical analyses were performed using SPSS version 23, by Cronbach's alpha, intraclass correlation coefficient, Spearman's correlation coefficient, ANOVA, independent t-test. Confidence interval was 95% and P-value < 0.05 was considered significant.

Ethics

Email approval was obtained from Madhulika G. Varma for the translation of CSI into Persian language.

Results

One hundred and twenty-five patients with chronic functional constipation participated in the study. The mean age was 42.91±14.42 years (range 19-80 years). The majority of the participants were female (N=98, 78.4%) and age of 60.8% of participants were aged between 18 and 45 years. Detailed demographics of the participants are summarized in Table 1.

Reliability

The Cronbach's α coefficient of the total score of the CSI questionnaire was 0.90. For the subscale scores, the Cronbach's α coefficients ranged from 0.85 to 0.89 (Table 2). Based on the values obtained for Cronbach's alpha, the internal consistency of the total score and the subscales is also determined.

The test-retest reliability of the CSI shows in Table 3 that the ICC value for all questions is 0.90 with 0.78 for ODS, 0.89 for CI, 0.95 for pain and the results are satisfactory.

Face validity

The mean impact score for all items was was 2/56 (ranging from 1/8 to 4/8) and no item had an impact score lower than 1.5.

There were no patients with a CSI score of 0 or 73, thus, there were no floor-ceiling effects in the total score of the questionnaire.

Convergent validity

Positive correlation between the scores obtained from the CSI Constipation Questionnaire and the WCSS Questionnaire (Spearman's correlation coefficient =0.74, P<0.001), that, it confirms the existence of an adequate convergent validity of the CSI questionnaire. The correlation between the pain subscale of the CSI and the VAS was also significant (Spearman's correlation coefficient =0.75, P< 0.001).

Discriminate validity

80% of the participants in this research were visited two times or more by a specialist physician during the last two years, and patients with acute pain and active bleeding were referred after partial control of symptoms. Using the one- way ANOVA test, it was

Table 2. Internal consistency of the CSI

CSI subscale	Questions	Mean ±SD	Cronbach' s α
ODS	1-6	19.58±4.96	0.85
CI	7-12	15.25±5.80	0.85
Pain	13-16	6.57±4.58	0.89
CSI	1-16	40.86±12.29	0.90

Table 3. Intraclass correlation coefficient for Constipation Severity Instrument (n=20)

Items	ICC	95% confidence interval	
		Lower bound	Upper bound
ODS	0.78	0.45	0.91
CI	0.89	0.74	0.96
Pain	0.95	0.88	0.95
CSI	0.90	0.84	0.96

found that there was a statistically significant difference between the mean scores obtained from the CSI questionnaire and the number of physicians' visits in the last two years (P<0.001) (Tables 4 and 5).

Differences in the severity of constipation were examined by age, level of education, income, occupational status and type of birth group. As shown in Table 6, there were no significant differences between the groups.

Discussion

Constipation covers a range of symptoms with different treatments including medication, pelvic floor physiotherapy and surgery (18-20). The need for a questionnaire with simple, understandable, and short sentences provides a common language between researchers and therapists in the clinical stages and evaluation of clinical outcomes (21).

When the original CSI questionnaire was developed, people were classified into 4 groups based on ROMEII criteria: functional constipation, pelvic floor dyssynergia, constipation predominant irritable bowel syndrome and no specific criteria. The participants in our study were patients with functional constipation according to Rome IV criteria. The questions asked in the CSI provide valuable data for assessing the patient's current condition and for following up the patient's condition after medical and physiotherapeutic interventions.

The CSI questionnaire is one of the newest and most reliable tools for measuring the severity of constipation and has advantages over the WCSS questionnaire. The main advantage of this questionnaire is that it has subscales to help the therapist determine

Table 4. Discriminate validity of the CSI

Number of physician's visits in the last two years	N	Mean ±SD	F	P value
0-1 visit	25	33.08±10.17	8.85	P<0.001
2-3 visits	51	39.24±11.83		
4-5 visits	30	45.07±11.13		
+6 visits	19	48.79±11.28		

Table 5. The comparison of the number of physician's visits during the last two years

	0-1 visit	2-3 visits	4-5 visits	+6 visits
0-1 visit		P=0.119	P= 0.001	P=0.0001
2-3 visits	P=0.119		P=0.116	P=0.011
4-5 visits	P=0.001	P= 0.116		P=0.674
+6 visits	P=0.0001	P= 0.011	P=0.674	

Table 6. Relationship between CSI scores and demographic variables

	Mean±SD of the CSI scores	P/t value
Gender	Female :41.57±12.72 Male:38.26±10.39	t=1.24
Age (year)	18-45 years old :41.92±12.42 46-60 years old:42.03±12.57 61+ years old: 35.1±10.10	P=0.72
Educational level	Less than diploma :41.11±11.46 Diploma :40.52±12.00 University: 40.93±12.75	P=0.98
Occupational status	Employed: 32.91±9.79 Housewife: 41.59±11.93 Retired: 38.67±13.03 Unemployed: 32.91±9.79	P= 0.12
Income	Low: 43.60±12.38 Middle: 44.32±11.44 High: 39.15±12.44 No answer: 40.09±12.40	P=0.30
Type of birth	Natural childbirth: 40.52±12.27 Cesarean: 42.91±16.06 Natural childbirth and caesarean section: 42.09±10.91 Without childbirth: 37.35±11.79	P=0.92

the treatment plan.

In both the WCSS and CSI questionnaires, obstructive defecation was discussed with different questions, but the CSI questionnaire also asked about the severity and inconvenience of having to defecate and straining.

Only one question in the WCSS questionnaire dealt with colonic inertia, whereas the 6 questions in the CSI questionnaire dealt extensively with regular bowel movements, frequency of bowel movements, the intensity and discomfort, the feeling of the needing to defecate, and the degree of discomfort (9). Considering that a large percentage of people with functional constipation have problems with colonic inertia problems (22), it seems that diverse and complete questions and an appropriate scoring system for colonic inertia are needed.

One of the most common consequences of obstructive defecation is severe pelvic floor pain and rectal bleeding, which have a very negative impact on people's quality of life. The CSI questionnaire has a separate section with 4 questions and a scoring system from 0 to 16 that deals with these symptoms of the patient in the present and past month. Although 2 questions in the WCSS questionnaire deal with pain in the anus and abdomen, the questions in the CSI questionnaire are more specific and also ask about the severity of bleeding in the past month.

It is important to note that in the article by Varma et al, the range of questionnaire scores is between 0-73, whereas 4 questions of the Obstructive Defecation subscale and 2 questions of the Colonic Inertia subscale started from option 1, unlike the rest of the questions. Therefore, the range of questionnaire scores is between 6 -73.

When the internal consistency and reproducibility of the questionnaires were examined, the results of all three studies were close to each other. The results of this study showed that the Persian version of the CSI questionnaire had a high positive correlation with the WCSS questionnaire, and a positive correlation was found between the score of the pain subscale of the CSI questionnaire and the VAS. Therefore, the questions in the pain subscale of this questionnaire are reliable in determining the severity of pain associated with constipation symptoms.

In the original questionnaire, the correlation between the CSI and the PAC-SYM and in the Chinese version, the correlation between the CSI and the WCSS was assessed as convergent validity. Validity results were consistent across all three studies.

There is a positive relationship between the severity of constipation and the number of visits to the physician, and the highest severity is associated with patients who have visited the physician more than 6 times in the last 2 years (discriminant validity). It is noteworthy that the severity of constipation in the two adjacent groups (in terms of number of visits to the physician) does not have a statistically significant difference, although in terms of severity of constipation, with increasing number of visits, the average score of severity of constipation has increased. Future research (es) is needed to investigate this concept in more detail.

In the Varma and Tsai studies, the difference between the scores of the healthy and sick groups was examined for discriminative validity (9, 14).

None of the questions in the questionnaire were included in the upper and lower limits, so the content of this questionnaire can measure the lowest and highest levels of constipation (17). The ceiling and floor effects were not investigated in the original and Chinese studies.

Conclusion

The results of the current study showed that there was no significant difference in the severity of constipation between men and women, and there was no significant difference in the severity of constipation between different age groups, occupational status, level of education, income, and type of birth. In many researches, it has been determined that the severity of constipation depends on people's lifestyle more than anything else, and education about proper lifestyle and diet will reduce the severity of constipation and improve people's quality of life (23, 24). Research results have also shown that the severity of constipation increases with decreased health care (25).

One limitation of this study was the lack of a control group. Although we looked at the severity of people's constipation according to the number of the physician’s visits, the presence of a control group may give us a more complete picture in addition to the existing findings. Other limitation of the study included the fact that most of the participants in the study were referrals from a colorectal specialist's office, and

choosing samples from a larger community can provide a broader view of the research variables. Another limitation was the small number of male participants. It is suggested that future studies could investigate the validity and reliability of the CSI questionnaire in other groups with constipation, including functional defecation disorders, irritable bowel syndrome with constipation predominance. The correlation of the colonic inertia subscale of this questionnaire with the Bristol Stool Scale and Colon Transient Time (CTT) findings could be investigated in the future. The relationship between the severity of constipation and people's quality of life and disability could also be investigated, too.

Acknowledgment

The authors would like to thank Dr. Ghazal Kharaji and Fatemeh Moradi for their help in translating the questionnaire.

Conflict of interests

The authors declare that they have no conflict of preferences.

References

1. Iraji N, Keshteli AH, Sadeghpour S, Daneshpajouhnejad P, Fazel M, Adibi P. Constipation in Iran: SEPAHAN Systematic Review No. 5. Int J Prev Med 2012;3:34-41.

2. Frank L, Schmier J, Kleinman L, Siddique R, Beck C, Schnelle J, et al. Time and economic cost of constipation care in nursing homes. J Am Med Dir Assoc 2002;3:215-23.

3. Sun SX, Dibonaventura M, Purayidathil FW, Wagner JS, Dabbous O, Mody R. Impact of chronic constipation on health-related quality of life, work productivity, and healthcare resource use: an analysis of the National Health and Wellness Survey. Dig Dis Sci 2011;56:2688-95.

4. Chou AB, Cohan JN, Varma MG. Differences in symptom severity and quality of life in patients with obstructive defecation and colonic inertia. Dis Colon Rectum 2015;58:994-8.

5. Mearin F, Lacy BE, Chang L, Chey WD, Lembo AJ, Simren M, et al. Bowel disorders. Gastroenterology. 2016:0016-5085.

6. Agachan F, Chen T, Pfeifer J, Reissman P, Wexner SD. A constipation scoring system to simplify evaluation and management of constipated patients. Dis Colon Rectum 1996;39:681-5.

7. Frank L, Kleinman L, Farup C, Taylor L, Miner P, Jr. Psychometric validation of a constipation symptom assessment questionnaire. Scand J Gastroenterol 1999;34:870-7.

8. McMillan SC, Williams FA. Validity and reliability of the Constipation Assessment Scale. Cancer Nurs 1989;12:183-8.

9. Varma MG, Wang JY, Berian JR, Patterson TR, McCrea GL, Hart SL. The constipation severity instrument: a validated measure. Dis Colon Rectum 2008;51:162-72.

10. Majidirad F, Hadian MR, Asl Soleimani H, Jalaie S, Ahadi T, Bazaz Bebahani R, et al. Cross-cultural adaptation, validity, and reliability of the Wexner questionnaire in patients with functional constipation in an Iranian population. Gastroenterol Hepatol Bed Bench 2021;14:243-9.

11. Mirbehresi P, Nikjooy A, Sarrafzadeh J, Mohsenifar H. Cultural adaptation, validity, and reliability of the Persian Version of Wexner constipation scoring system. Func Disabil J 2020;3:17-26.

12. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine 2000;25:3186-91.

13. Bonett DG. Sample size requirements for estimating intraclass correlations with desired precision. Stat Med 2002;21:1331-5.

14. Tsai YJ, Yang YW, Lan YT. Translation and validation of the traditional Chinese version of the Constipation Severity Instrument. J Chin Med Assoc 2021;84:299-302.

15. Taghizadeh Z, Ebadi A, Montazeri A, Shahvari Z, Tavousi M, Bagherzadeh R. Psychometric properties of health related measures. Part 1: Translation, development, and content and face validity. Payesh 2017;16:343-57.

16. Nojomi M, Baharvand P, Moradi lakeh M, Patrick DL. Incontinence quality of life questionnaire (I-QOL): translation and validation study of the Iranian version. Int Urogynecol J 2009;20:575-9.

17. Terwee CB, Bot SD, de Boer MR, van der Windt DA, Knol DL, Dekker J, et al. Quality criteria were proposed for measurement properties of health status questionnaires. J Clin Epidemiol 2007;60:34-42.

18. Gokce AH, Gokce FS, Iliaz R, Gulaydin N. Transcutaneous tibial nerve stimulation as therapy for functional constipation. Turk J Gastroenterol 2022;33:565-9.

19. Bretagnol F, Hain E, Moszkowicz D, Giovinazzo D. Colorectal surgery for functional bowel disorders. J Visc Surg 2022;159:35-9.

20. Jalanka J, Major G, Murray K, Singh G, Nowak A, Kurtz C, et al. The effect of psyllium husk on intestinal microbiota in constipated patients and healthy controls. Int J Mol Sci 2019;20.

21. Chan DS, Saklani A, Shah PR, Lewis M, Haray PN. Rectal irrigation: a useful tool in the armamentarium for functional bowel disorders. Colorectal Dis 2012;14:748-52.

22. Soares ASGF, Barbosa LER. Colonic Inertia: approach and treatment. J Coloproctol 2017;37.

23. Nour-Eldein H, Salama HM, Abdulmajeed AA, Heissam KS. The effect of lifestyle modification on severity of constipation and quality of life of elders in nursing homes at Ismailia city, Egypt. J Family Community Med 2014;21:100-6.

24. Ozturk MH, Kılıc SP. Effective of education on quality of life and constipation severity in patients with primary constipation. Patient Educ Couns 2019;102:316-23.

25. Neri L, Basilisco G, Corazziari E, Stanghellini V, Bassotti G, Bellini M, et al. Constipation severity is associated with productivity losses and healthcare utilization in patients with chronic constipation. United European Gastroenterol J 2014;2:138-47.