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Research Article

**CHRONIC CONSTIPATION, CAUSES, DIAGNOSIS AND
MANAGEMENT****Mohamed Elsayed Seifalyazal¹, Sameh Said Mohammed², Ayman M H T Elsayed³, Naif G Mahrous⁴, Khalid R Muminah⁴, Mohammed A Gedhnan⁴**

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Abstract:

In this review, we intend to perform an integrative evaluation of the literary works to supply a better understanding of the pathophysiology, diagnosis and management of chronic constipation. As a matter of fact, suitable understanding of this disease can play a key duty in managing disease and planning higher quality therapies. We conducted a narrative review of articles published up to January 2018, in following databases; PubMed, and Embase investigating causes, diagnosis and management of Chronic constipation. We restricted our search to only English published articles with human subjects concerning surgical management mainly. Constipation is a typical trouble that might be acute or chronic. There are many definitions. It might be idiopathic or primary, or secondary to a selection of clinical or metabolic diseases. History and physical examination are the most important initial methods to the analysis of those with constipation. In the absence of any type of alarm attributes or ideas of an involved disorder, a restorative trial with bulking agents or basic laxatives is an ideal primary step. Diagnostic examinations can be done in a selective fashion directed at either defining the nature of transportation with the colon or evacuation with the anorectum or verifying the absence of a primary ailment bring about the signs of constipation.

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INTRODUCTION:

Constipation is a disease in the gastrointestinal system, which can lead to the irregular stools, difficult stool passage with ache and tightness. Acute constipation might cause closure of the intestinal tract, which might also require surgery [1]. It is worth keeping in mind that there is currently no optimal meaning for constipation; thus, history and physical examination can be thought about the main preliminary techniques. Several definitions are defined by utilizing a self-reported constipation and the formal standards. Numerous definitions of chronic constipation relate to scientific considerations such as secondary causes (medicines), neurological, or systemic illness. Nonetheless, it is considered primary or idiopathic [1]. Pathogenesis is multifactorial with focusing on genetic proneness, socioeconomic status, low fiber usage, lack of ample fluid intake, absence of mobility, disturbance in the hormone balance, side effects of drugs, or anatomy of the body, etc [1]. Constipation is a usual gastrointestinal problem, which creates lots of expenses for the community with an approximated prevalence of 1% to 80%, worldwide, where the condition is defined by a broad geographical variation [2]. It is significant that the varieties of interpretations have caused a large range of occurrence. Chronic constipation is a difficult problem among older individuals, which is defined by difficult stool passage [3]. Hereof, this condition has a close

relationship with the patients' quality of life and taking in health sources [3].

In this review, we intend to perform an integrative evaluation of the literary works to supply a better understanding of the pathophysiology, diagnosis and management of chronic constipation. As a matter of fact, suitable understanding of this disease can play a key duty in managing disease and planning higher quality therapies.

METHODOLOGY:

We conducted a narrative review of articles published up to January 2018, in following databases; PubMed, and Embase investigating causes, diagnosis and management of Chronic constipation. We restricted our search to only English published articles with human subjects concerning surgical management mainly. Search strategies used following MeSH terms in searching via these databases: "Chronic constipation", "diagnosis", "Management", "surgical intervention". Then we also searched the bibliographies of included studies for further relevant references to our review.

DISCUSSION:

- **Pathophysiology**

Constipation may be primary (idiopathic) or secondary to other factors (Table 1).

Table 1. Causes of secondary constipation [4].

Cause	Example
Organic	Colorectal cancer, extra-intestinal mass, postinflammatory, ischemic or surgical stenosis
Endocrine or metabolic	Diabetes mellitus, hypothyroidism, hypercalcemia, porphyria, chronic renal insufficiency, panhypopituitarism, pregnancy
Neurological	Spinal cord injury, Parkinson's disease, paraplegia, multiple sclerosis, autonomic neuropathy, Hirschsprung's disease, chronic intestinal pseudo-obstruction
Myogenic	Myotonic dystrophy, dermatomyositis, scleroderma, amyloidosis, chronic intestinal pseudo-obstruction
Anorectal	Anal fissure, anal strictures, inflammatory bowel disease, proctitis
Drugs	Opiates, antihypertensive agents, tricyclic antidepressants, iron preparations, anti-epileptic drugs, anti-Parkinsonian agents (anticholinergic or dopaminergic)
Diet or lifestyle	Low fiber diet, dehydration, inactive lifestyle

- **Diagnosis**

The duration and qualities of the patient's symptoms have to be evaluated to differentiate chronic from transient constipation. Short-term constipation is conveniently acknowledged by history, showing constipation started each time of modification in nutritional habits, mobility or way of life. Second

constipation, as a consequence of other factors (Table 1), need to be recognized and treated appropriately.

- **Diagnostic resources**

- **Rome III criteria**

The Rome III category system is widely recognized as the only standard symptom-based diagnostic standards for functional GI disorders (FGIDs), including chronic constipation (Table 2). Various other interpretations of

chronic constipation follow the Rome III requirements but are much less quantitative and extra subjective [6]. Although clinicians understand the Rome criteria, these are used primarily for study functions and are not widely applied in clinical practice, with the feasible exemption of IBS [7]. Nonetheless, the Rome Foundation analysis algorithm project has actually just

recently released a brand-new collection of clinical algorithms for FGIDs, consisting of chronic constipation, which make active use the Rome standards for diagnostic and healing management (gone over in area qualified Review of presently offered guidelines, recommendations and algorithms).

Table 2. Rome III criteria for chronic constipation [5].

Criteria fulfilled for the last 3 months and symptom onset at least 6 months prior to diagnosis
Presence of ≥ 2 of the following symptoms:
• Lumpy or hard stools in $\geq 25\%$ of defecations
• Straining during $\geq 25\%$ of defecations
• Sensation of incomplete evacuation for $\geq 25\%$ of defecations
• Sensation of anorectal obstruction/blockage for $\geq 25\%$ of defecations
• Manual maneuvers to facilitate $\geq 25\%$ of defecations (digital manipulations, pelvic floor support)
• < 3 evacuations per week
Loose stools rarely present without the use of laxatives
Insufficient criteria for irritable bowel syndrome

Bristol Stool Form Scale

The Bristol Stool Form Scale (BSFS) is a beneficial visual help that was made to assist in the evaluation of patients with constipation [8]. Making use of easy visual descriptors, it shows the common stool forms and consistency on a 7-point scale. It has been validated in several research studies and has been found to be conveniently comprehended by patients,

allowing them to recognize and thus identify the stool type that a lot of carefully represents their own experience. The form of the stool depends on the time that it spends in the colon; as a result, the BSFS is a fast and trusted indicator of transit time. It is especially valuable in patients with self-reported irregularity who do not have irregular bowel movements, to develop that difficult or lumpy stools are, certainly, present.

Table 3. Bristol Stool Scale Data adapted from reference [9].

Type	Description
1	Separate hard lumps, similar to nuts (difficult to pass)
2	Sausage shaped but lumpy
3	Like a sausage but with cracks on its surface
4	Like a sausage or snake, smooth and soft
5	Soft blobs with clear cut edges (passed easily)
6	Fluffy pieces with ragged edges, a mushy stool
7	Watery, no solid pieces, entirely liquid

• Evaluation

A careful history and physical checkup are most important in the analysis of a patient complaining of constipation. The history ought to consist of an understanding of the patient's perception of their existing bowel habit compared with the past, perhaps aided by a two-week stool diary that would certainly include stool frequency, character or form, and flow of

stool. Use of the Bristol Stool Scale may serve as a layout to define stool form (Table 3) [10]. One ought to obtain an understanding of what measures, including kind, dosage and duration of laxatives, were formerly attempted. It is useful to recognize the problems and assumptions the patient has for their bowels, and what objectives they have for their bowel pattern. Many are just seeking peace of mind.

A look for 'alarm system' functions such as unintended weight-loss, anal bleeding or new onset of signs, particularly after 50 years of age, is required. The history needs to include a drug history, both recommended and over the counter, and an evaluation for systemic or neurological ailments that may relate to A careful history and physical checkup are most important in the analysis of a patient complaining of constipation. The history ought to consist of an understanding of the patient's perception of their existing bowel habit compared with the past, perhaps aided by a two-week stool diary that would certainly include stool frequency, character or form, and flow of stool. Use of the Bristol Stool Scale may serve as a layout to define stool form (Table 3) [10]. One ought to obtain an understanding of what measures, including kind, dosage and duration of laxatives, were formerly attempted. It is useful to recognize the problems and assumptions the patient has for their bowels, and what objectives they have for their bowel pattern. Many are just seeking peace of mind.

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Physical checkup should consist of palpation of the abdomen in search for palpable stool indicating fecal loading. A mindful rectal evaluation is vital. This may determine proof of anal diseases such as strictures, fissures, inflammation, rectocele or masses. Neurological disorders might manifest as a gaping or patulous anus or reduced perianal feeling. Failing of perineal descent when the patient bears down suggests pelvic floor dysfunction [11].

From the history and checkup one can normally identify or think those with new-onset or secondary bowel irregularity due to medications, and/or neurological or endocrinological diseases, IBS or those with obstructive pathology such as cancer. The remainder would be detected with primary or idiopathic constipation (Table 1). Background should likewise assist to separate IBS from chronic constipation, with the previous normally including constipation alternating with diarrhea and,

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• Tests

Laboratory tests

Serum thyroid function, glucose, electrolytes and calcium, complete blood count and urinalysis are frequently recommended, but there is no literary works to sustain their effectiveness in the workup of patients with chronic constipation [12].

Endoscopy

In the lack of alarm features, such as bleeding or new-onset constipation, there is no boosted diagnostic yield with using either adaptable sigmoidoscopy or colonoscopy beyond what would be expected in asymptomatic individuals going through colorectal cancer testing [16]. However, one may take into consideration and offer age- and interval-appropriate testing to patients with constipation as one would to asymptomatic individuals.

Radiological tests

Plain abdominal x-ray:

Even with the typical use plain abdominal x-rays to evaluate 'fecal loading', there is no literature sustaining it. As a matter of fact, there is no typical action of a 'typical' fecal load where to contrast.

Barium enema:

There is no existing literature to assist the use of barium enemas in the workup or examination of patients with chronic constipation. Presently, these are rarely performed and have been replaced by endoscopy or computed tomography colonography, where there is a need to eliminate obstructive pathology within the colon.

Endoscopic ultrasound:

While useful in assessing the integrity of the anal sphincter and extrarectal or presacral space, it has not yet found a place in the evaluation of constipation.

Defecography:

This test, not normally done in medical technique because of patient discomfort and the lack of standardized methods or measurements, is created to disclose physiological variants in the anorectum that could contribute to constipation from outlet delay. Barium paste is placed in the anus to imitate natural stool consistency and fluoroscopically observed to be gone by the patient on a particularly designed and fluoroscopically easily accessible commode [17]. Numerous dimensions of the movement of the pelvic floor and anus can be taken throughout this procedure. In particular, this test must demonstrate the normal 'opening' of the anorectal angle and proper pelvic floor descent throughout the act of defecation. Lack of these changes suggests dyssynergic defecation. Its only usage is in defining the anatomical and functional composition of the anorectum after dyssynergic defecation is already identified and must not be used as an initial or sole test in the evaluation of constipation [12], [15].

Magnetic resonance imaging

Comparable to endoscopic ultrasound, magnetic resonance imaging is vital in the analysis of the perirectal tissue planes; nonetheless, to date, it is not beneficial or conveniently available in examining practical constipation [17].

Physiological testing

These tests are the only investigations that actually attempt to measure the physiological movement of stool within the colon and anus.

Colon transit study:

While constantly eating a high-fibre diet and preventing laxatives, an individual swallows' numerous radiopaque pens that are followed through the colon with plain x-rays. A variety of methods have been proposed since they were initially defined in 1969 [18]. The easiest, calling for the least radiation direct exposure, entails ingesting a commercially available capsule including the 24 markers (this can be made by introducing 242 mm to 3 mm pieces of a radiopaque nasogastric tube in gelatin capsules) and obtaining a stomach x-ray after six days. With 'regular transit', less than 5 markers will certainly continue to be in the colon; with 'slow transit', six or even more markers will continue to be and be scattered throughout the colon. The third pattern, showing dyssynergic defecation or

outlet delay, will certainly be revealed by discovering 6 or more markers gathered in the rectosigmoid [14]. Although an easy and relatively inexpensive test that is widely performed, radiopaque marker research studies have restrictions [19]. Initially, they really measure complete oral-anal transit, not just colon transit. Second, the meaning of 'normal' is based upon a minimal variety of researched healthy topics, with a broad variety of outcomes that are not well standardized [19]. A methodical testimonial of the literary works showed poor reproducibility for these examinations, particularly in patients with slow transportation or dyssynergic defecation compared to those with typical transportation, which suggests low specificity [12].

Anorectal motility:**Manometry:**

This method is additionally a straight step of physiological function-- however just within the anus-- and makes it possible for the analysis of rectal compliance, rectal sensation and the visibility of anorectal reflexes. Thus, its objective is the verification and analysis of outlet hold-up or dyssynergic defecation. Its best worth is in dismissing Hirschsprung's illness. It is most recently examined in detail in the American Gastroenterological Association clinical position statement on anorectal screening techniques [15]. A lot more recent organized review emphasized the poor level of sensitivity for anorectal manometry and absence of clear criteria and meaning for dysynergic defecation [12].

Balloon expulsion:

Initial defined in 1985, this timed examination analyzes the ability of the patient to get rid of a standard-size thing- typically a 50 mL fluid-filled balloon-- from the anus [20]. The balloon can typically be passed within 3 min; failing to do so recommends dyssynergic defecation. There is a selection of protocols for this treatment, but it is limited by patient embarrassment and its usual efficiency in the left side decubitus setting, which is much removed from the typical resting placement for defecation. The lack of standardization stays a weakness of this test.

Scintigraphy:

This test uses nuclear medicine and measurement of the transit of radiolabelled stool with the colon. It is hardly ever done outside of a research setting and, consequently, is not a clinically practical or readily available test to many medical professionals [19].

Electrophysiology:

These examinations, including pudendal nerve terminal motor latency dimensions and electromyography of the exterior rectal sphincter or puborectalis, presently belong in the sector of clinical research [13].

• OVERALL APPROACH IN MANAGENT:

Dietary fiber and laxatives

Fiber consumption has been demonstrated to boost practical constipation. It has been shown that diets with soluble fiber (psyllium 15 g every day or ispaghula) may profit patients suffered from chronic constipation and IBS [21]. There have been research studies that suggested much less efficiency of supplements in patients suffered from sluggish defecatory conditions or slow-transit constipation (STC), whereas patients tend not to react to fiber intake [21]. On the other hand, a number of research studies reported that fiber supplements might boost bowel symptoms in patients with chronic constipation [21]. Supplements and/or an affordable osmotic agent have been introduced for irregular bowel movements (e.g., milk of magnesia 1 or two times daily, or polyethylene Glycol (PEG) 17 g day-to-day).

Regarding existing evidence, osmotic, and stimulant laxatives should be utilized as initial treatment techniques in patients with chronic constipation [32]. Furthermore, there is great proof of effectiveness for using PEG with considerable osmotic activity such as a controlled test with period of 6 months [22].

Newer treatment options

A new agent is required when the laxatives are ineffective in reducing signs and symptoms; therefore, lubiprostone and linaclotide can be taken into consideration 2 beneficial medicines. Lubiprostone is a bicyclic fatty, which was advised at dose of 24 µg p.o. twice daily as a gelatin capsule. Lubiprostone can be an ideal and tolerable medication for patients that need long-term treatment of constipation [23].

Linaclotide is a guanylate cyclase 2C receptor agonist, which is mainly advised for healing additional endpoints such as stool consistency, discomfort, bloating, and straining [33].

Prucalopride has actually been called a careful high affinity 5-HT₄ receptor agonist, which works as a stimulator of gut motility. It is suitable for eliminating the primary signs and symptoms of chronic constipation. The security profile was persuaded, especially the absence of arrhythmogenic capacity. It has had encouraging results in patients that did not

react to standard laxatives. Long-term examination and postsales information will certainly be important in demining the therapeutic advantages and threats of this combination [24].

Colchicine is an alkaloid material, which is used as an anti-inflammatory agent. It can boost the frequency of bowel movements, where it might be suggested as a treatment for the therapy of chronic constipation. Alvimopan and methylnaltrexone have been lately suggested as new agents for the therapy of constipation caused by opioid.

Alvimopan has been suggested for postoperative ileus after surgical procedures by Food and Drug Administration (FDA), while FDA suggested that methylnaltrexone could be requested patients suffering from opioid-induced constipation. Nonetheless, tests of alvimopan in the validated use methylnaltrexone in inopioid-induced constipation stand for seriously hazardous cardiovascular reasons with opposite lead to regards to efficiency [25]. Additionally, the effectiveness of readily available synbiotic elements has been formerly reviewed for the treatment of useful constipation in males [26].

Biofeedback therapy

Previous studies reported that biofeedback therapy could be properly efficient by using neuromuscular training, aesthetic, and verbal feedback. It has top priority over other treatments such as laxative and sham training [27].

Biofeedback session implicates placing a probe right into the anus to offer feedback of muscle tension using a computer screen. Psychophysiological feedback therapy is an efficient and multidisciplinary strategy without unfavorable impacts of treatment [27]. It has been observed that greater than 70% of patients with gastrointestinal disorders get rid of signs by treating psychophysiological feedback treatment [34].

It has actually been exposed that psychophysiological feedback therapy could be valuable for improving bowel signs and symptoms and dyssynergic defecation when it comes to specialist motivation, training (for relaxing pelvic floor muscle mass), extent of re-training program, neuromuscular synchronisation, visual, sounds, and verbal comments techniques [34]. It has been reported that the physiotherapy procedure could be efficient for getting rid of some signs and symptoms utilizing pelvic floor muscular tissue training in female patients struggled with functional constipation [28].

Surgical Treatment

Surgical treatments might be utilized as an option if clinical treatment was fallen short in constipated patients and mechanical emptying of the colon may be recommended in patients with slow bowel movements using an enema program [29]. Colectomy with ileorectal anastomosis has been presented to be the treatment choice in patients dealing with refractory slow transit constipation (i.e., colonic inertia), where dyssynergic defecation was accepted [31]. In addition to slow transit constipation (STC), a pelvic flooring retraining with biofeedback must be thought about prior to surgical treatment in patients suffering from evacuation condition. Additionally, patients that suffer from considerable rectocles and intussusception need to be advised repair and pelvic floor retraining [30].

CONCLUSION:

Constipation is a typical trouble that might be acute or chronic. There are many definitions. It might be idiopathic or primary, or secondary to a selection of clinical or metabolic diseases. History and physical examination are the most important initial methods to the analysis of those with constipation. In the absence of any type of alarm attributes or ideas of an involved disorder, a restorative trial with bulking agents or basic laxatives is an ideal primary step. Diagnostic examinations can be done in a selective fashion directed at either defining the nature of transportation with the colon or evacuation with the anorectum or verifying the absence of a primary ailment bring about the signs of constipation.

REFERENCE:

1. Benninga M, Candy DC, Catto-Smith AG, et al. The Paris Consensus on Childhood Constipation Terminology (PACCT) Group. *J Pediatr Gastroenterol Nutr* 2005;40:273–5.
2. Sanchez MI, Bercik P. Epidemiology and burden of chronic constipation. *Can J Gastroenterol* 2011;25: 11B-L 15B.
3. Suares NC, Ford AC. Systematic review: the effects of fibre in the management of chronic idiopathic constipation. *Aliment Pharmacol Ther* 2011;33:895–901.
4. Eoff JC. Optimal treatment of chronic constipation in managed care: review and roundtable discussion. *J Manag Care Pharm*. 2008;14:1–15.
5. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology*. 2006;130:1480–91.
6. American College of Gastroenterology Chronic Constipation Task Force. An evidence-based approach to the management of chronic

constipation in North America. *Am J Gastroenterol*. 2005;100:S1–4.

7. Kellow JE. Introduction: a practical evidence-based approach to the diagnosis of the functional gastrointestinal disorders. *Am J Gastroenterol*. 2010;105:743–6.
8. Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. *Scand J Gastroenterol*. 1997;32:920–4.
9. O'Donnell L, Virjee J, Heaton K. Detection of pseudodiarrhea by simple clinical assessment of intestinal transit rate. *Br Med J*. 1990;300:439–40.
10. Barnett JL, Hasler WL, Camilleri M. American Gastroenterological Association medical position statement on anorectal testing techniques. *Gastroenterology*. 1999;116:732–60.
11. Talley NJ. How to do and interpret a rectal examination in gastroenterology. *Am J Gastroenterol*. 2008;103:820–2.
12. Rao SSC, Ozturk R, Laine L. Clinical utility of diagnostic tests for constipation in adults: A systematic review. *Am J Gastroenterol*. 2005;100:1605–15.
13. Locke GR, III, Pemberton JH, Phillips SF. American Gastroenterological Association medical position statement: Guidelines on constipation. *Gastroenterol*. 2000;119:1761–78.
14. Rao SSC. Constipation: Evaluation and treatment of colonic and anorectal motility disorders. *Gastroenterol Clin North Am*. 2007;36:687–711.
15. Barnett JL, Hasler WL, Camilleri M. American Gastroenterological Association medical position statement on anorectal testing techniques. *Gastroenterology*. 1999;116:732–60.
16. Pepin C, Ladabaum U. The yield of lower endoscopy in patients with constipation: Survey of a university hospital, a public county hospital and a Veterans Administration medical center. *Gastrointest Endosc*. 2002;56:325–32.
17. Savoye-Collet C, Korning E, Dacher JN. Radiologic evaluation of pelvic floor disorders. *Gastroenterol Clin North Am*. 2008;37:553–67.
18. Hinton JM, Lennard-Jones JE, Young AC. A new method for studying gut transit times using radioopaque markers. *Gut*. 1969;10:842–7.
19. Dinning PG, Smith TK, Scott SM. Pathophysiology of colonic causes of chronic constipation. *Neurogastroenterol Motil*. 2009;21(Suppl 1):20–30.
20. Preston DM, Lennard-Jones JE. Anismus in chronic constipation. *Dig Dis Sci*. 1985;30:413–8.

21. Soares NC, Ford AC. Systematic review: the effects of fibre in the management of chronic idiopathic constipation. *Aliment Pharmacol Ther* 2011;33:895–901.
22. Mueller-Lissner S, Kamm MA, Wald A. Multicenter, 4-week, double-blind, randomized, placebo-controlled trial of sodium picosulfate in patients with chronic constipation. *Am J Gastroenterol* 2010;105:897–903.
23. Lacy BE, Levy LC. Lubiprostone: a novel treatment for chronic constipation. *Clin Interv Aging* 2008;3:357–64.
24. Quigley EM. Prucalopride: safety, efficacy and potential applications. *Therap Adv Gastroenterol* 2012;5:23–30.
25. Rodriguez RW. Off-label uses of alvimopan and methylnaltrexone. *Am J Health Syst Pharm* 2014;71:1450–5.
26. Fateh R, Iravani S, Frootan M, et al. Synbiotic preparation in men suffering from functional constipation: a randomised controlled trial. *Swiss Med Wkly* 2011;141:w13239.
27. Rao SSC. Biofeedback therapy for constipation in adults. *Best practice & research. Clin Gastroenterol* 2011;25:159–66.
28. Remes-Troche JM, Paulson J, Yamada T, et al. Anorectal cortical function is impaired in patients with dyssynergic defecation. *Gastroenterology* 2007;108:A20.
29. Dehghan FM, Frootan M, Javanbakhti M, et al. The effects of a physiotherapy program based on education and pelvic floor muscle training on chronic functional constipation. *J Med Council Islamic Republic Iran* 2013;30:400–7.
30. Levitt MA, Mathis KL, Pemberton JH. Surgical treatment for constipation in children and adults. *Best Pract Res Clin Gastroenterol* 2011;25:167–79.
31. Hassan I, Pemberton JH, Young-Fadok TM. Ileorectal anastomosis for slow transit constipation: long-term functional and quality of life results. *J Gastrointest Surg* 2006;10:1330–7.
32. Basilisco G, Coletta M. Chronic constipation: a critical review. *Dig Liver Dis* 2013;45:886–93.
33. Rao SS, Go JT. Update on the management of constipation in the elderly: new treatment options. *Clin Interv Aging* 2010;5:163–71.
34. American Gastroenterological Association Medical Position Statement on Constipation. *Gastroenterology* 2013;144:211–7.