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SYSTEMATIC REVIEW

Systematic review and meta-analysis of anal motor and rectal sensory dysfunction in male and female patients undergoing anorectal manometry for symptoms of faecal incontinence

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Abstract

Aim: Manometry is the best established technique to assess anorectal function in faecal incontinence. By systematic review, pooled prevalences of anal hypotonia/hypocontractility and rectal hypersensitivity/hyposensitivity in male and female patients were determined in controlled studies using anorectal manometry.

Methods: Searches of MEDLINE and Embase were completed. Screening, data extraction and bias assessment were performed by two reviewers. Meta-analysis was performed based on a random effects model with heterogeneity evaluated by I^2.

Results: Of 2116 identified records, only 13 studies (2981 faecal incontinence patients; 1028 controls) met the inclusion criteria. Anal tone was evaluated in 10 studies and contractility in 11; rectal sensitivity in five. Only three studies had low risk of bias. Pooled prevalence of anal hypotonia was 44% (95% CI 32–56, I^2 = 96.35%) in women and 27% (95% CI 14–40, I^2 = 94.12%) in men. The pooled prevalence of anal hypocontractility was 69% (95% CI 57–81; I^2 = 98.17%) in women and 36% (95% CI 18–53; I^2 = 96.77%) in men. Pooled prevalence of rectal hypersensitivity was 10% (95% CI 4–15; I^2 = 80.09%) in women and 4% (95% CI 1–7; I^2 = 51.25%) in men, whereas hyposensitivity had a pooled prevalence of 7% (95% CI 5–9; I^2 = 0.00%) in women compared to 19% (95% CI 15–23; I^2 = 0.00%) in men.

Conclusions: The number of appropriately controlled studies of anorectal manometry is small with fewer still at low risk of bias. Results were subject to gender differences, wide confidence intervals and high heterogeneity indicating the need for international collective effort to harmonize practice and reporting to improve certainty of diagnosis.

KEYWORDS
anorectal manometry, faecal incontinence, hypersensitivity, hypocontractility, hyposensitivity, hypotonia

INTRODUCTION

Faecal incontinence (FI) is a debilitating condition with a prevalence of 8.4% in the general population [1]. Symptoms may be related to a sense of urgent need for bowel opening (urge incontinence), occur in the absence of a conscious need to defaecate (passive incontinence) or follow defaecation (post-defaecation leakage/soiling). Many patients suffer from mixed symptoms. While the nature of FI may suggest pathoaetiology [2], investigation of the physiological and structural mechanisms that help maintain continence is often necessary to establish pathophysiological factors that may be amenable to treatment [3–6].

Anal sphincter dysfunction is regarded as the most important pathophysiological mechanism in FI [7,8]. Meanwhile, factors including rectal reservoir function, stool form, defaecatory efficiency, and cognitive or physical ability may be as important [9], especially in men and in women who do not have evidence of obstetric anal sphincter injury [10,11].

Anorectal manometry is the best-established diagnostic tool to assess whether an individual's resting tone (considered reflective of internal anal sphincter function) and squeeze pressure (reflective of external anal sphincter function) are within or outside a normal range [12]. Such normal ranges should preferably comprise values seen in healthy volunteers (HVs) with similar demographics [13] using the same manometry equipment and set-up [14]. Ideally, manometry results should be interpreted uniformly with other centres [15].

To facilitate comparison of diagnostic findings between centres, the International Anorectal Physiology Working Group (IAPWG) recently published a consensus for the performance, terminology and interpretation of anorectal manometry [16]. The London Classification now provides standardized terminology for diagnosis/reporting of anal and rectal dysfunction; pathological terms (hypo, hyper) are based on a deviation from normal ranges rather than mean pressure. Reduced anal resting pressure, termed hypotonia, and reduced voluntary squeeze pressure, termed hypocontractility, are classed as major disorders of anal tone and contractility diagnosable by anorectal manometry. Likewise, routine determination of rectal sensitivity is also recommended in the consensus statement [16]. Rectal hypersensitivity (meaning a heightened sensory awareness) and hyposensitivity (diminished sensory awareness) are both classed as major disorders of sensation, as their potential to adversely affect continence is recognized [17,18].

Nevertheless, the prevalence of anal motor and rectal sensory dysfunction as diagnosed by the above approaches in patients with FI is currently uncertain. The specific aims of this review were (a) to determine the number of adequately controlled studies reporting on the prevalence of major classes of anal and rectal dysfunction; and (b) to calculate the pooled prevalence of anal hypotonia/hypocontractility and rectal hypersensitivity/hyposensitivity for men and women.

MATERIALS AND METHODS

Registration

The protocol for this systematic review was registered on PROSPERO (www.crd.york.ac.uk/PROSPERO: registration number CRD42020146507). The subsequent review was conducted in line with the protocol and is reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [19].

Eligibility

Original English language articles investigating adult patients (≥18 years old) with FI as the primary complaint using anorectal manometry and/or rectal balloon distension were considered. A pragmatic minimum sample size of 50 FI subjects and 20 HVs was imposed for eligibility. Crucially, control subjects had to be investigated using the same investigative technique; however, these data could be historical (referenced within the main article) or current. Eligible studies had to report the prevalence of at least one primary outcome: anal hypotonia, anal hypocontractility, rectal hypersensitivity and/or rectal hyposensitivity. Exclusion criteria were studies of children (age < 18 years) due the differences in aetiology of adult and child FI [20] and the lack of normative manometry data in children [21] and studies on homogeneous groups of adult patients with specific conditions that are known to impact anorectal function (e.g., Parkinson's, multiple sclerosis, spinal cord injury and diabetic neuropathy). Studies in which prevalence data could not be segregated by sex (i.e., the results in men and women were combined) were also excluded.

Information sources

MEDLINE (via OVID) and Embase libraries were searched for eligible studies published between 1966 and 2020. Searches were not restricted by language, but non-English-language articles were subsequently removed. The final search was performed on 6 July 2020. The reference lists of included articles were reviewed for any additional studies.

Search

Studies were searched by using the term ‘faecal incontinence’ with synonymous variants (as medical subject headings [MeSH] and free text terms). These were combined using the set operator AND with studies identified with the terms ‘resting pressure’ OR ‘squeeze’ both with synonymous variants (both as MeSH terms and free text terms). Results were then further combined with the operator AND

'anorectal manometry' OR 'rectal sensation' both with synonymous variants (both as MeSH terms and free text terms). The detailed search strategy can be found in Table S1. All records identified through database searches were downloaded and duplicate records were removed.

Study selection

All citations were imported into a bibliographic database. The title and abstract of all identified articles were screened against inclusion criteria independently by two authors (AR and KG). Subsequently, the full text of any title or abstract deemed potentially eligible by either investigator was retrieved. The two reviewers independently assessed the eligibility of each full-text article and disagreements were resolved by consultation with the senior author (SMS). Where necessary, the referenced article detailing a historical control group was also retrieved. In the case of inadequate information to assess eligibility, the corresponding author was contacted for relevant data.

Data collection process

Data were extracted into a spreadsheet (Microsoft Excel 365, 2012) by KG and verified by AR. Any disagreements were resolved by consultation with the senior author (SMS). Outcome data included number of patients (men and women) and proportions with anal hypotonia and/or hypocontractility and/or rectal hypersensitivity and/or hyposensitivity. One study [22] provided individual data points for patients and controls. From these data, the reviewers calculated the lower limit of normal in health (fifth percentile) and applied this cut-off to the disease group to obtain prevalence in the absence of a defined normal range by the authors.

Two articles [23,24] included overlapping patient cohorts. As only one of these articles [23] included data on rectal sensitivity both studies were included; however, anal motor function data were only extracted from the article with a greater number of patients [24].

Where the prevalence of rectal hypersensitivity or hyposensitivity was reported using multiple sensory thresholds, data were extracted for the first sensation volume [25] or maximum tolerated volume [11,23,26–28], as these were presented most consistently in eligible studies. In one study [28], rectal hypersensitivity was based on either first sensation or urge volume. The study authors were contacted by email for the missing data.

Data items and summary measures

Outcome data were selected to reflect the specific aims of the review, namely to determine the pooled prevalence of anal hypotonia/hypocontractility and rectal hypersensitivity/hyposensitivity in male and female FI patients. These data (hereafter denoted primary outcomes) were extracted as the proportion of the patient population studied whose measures of anal motor function or rectal sensory function fell below the lower limit of normal defined in referenced healthy control subjects. In addition, data were collected on publication year, country of origin, study design, study period, mean or median age of study participants, types of FI, definitions of FI, total number of HVs, and cut-off values and definitions used to determine 'abnormal' for each outcome measure. Type of equipment and method used to perform anorectal manometry and/or rectal sensitivity testing were also recorded.

Assessment of risk of bias

Study quality was assessed using a modified version of the National Institutes of Health Quality Assessment Tool for Case–Control Studies (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools). Two reviewers independently scored included studies out of a maximum of 12 points, with 1 point gained for each 'yes' answer, indicating that the study met the quality condition being assessed. Disagreements were resolved through discussion and a third reviewer (SMS) was consulted if required for resolution. Parameters assessed were research question, methods of randomization, study population, sample size justification, random selection of study participants, concurrent controls, case and control definitions, statistical analysis, blinding of exposure/assessors. For clarity, studies were classed as having high (0%–33%), moderate (>33%–66%) or low (>66%–100%) risk of bias based on the percentage of points attained. However, study quality did not influence the 'weight' or 'worth' given to any individual study.

Data synthesis and statistical analysis

For each of the primary outcomes (hypotonia, hypocontractility, hypersensitivity, hyposensitivity) meta-analysis was performed using random effects models with a binomial distribution to model within-study variability. Results were accompanied by pooled estimates of the fixed (common) effect model [29] for transparency. Study-specific confidence intervals (95%) were calculated using the score method. Heterogeneity (based on chi-squared) and proportion of variability attributable to heterogeneity rather than chance (I^2) were assessed. All statistical analyses were performed using Stata 16 (StataCorp LLC) with the metaprop function to calculate pooled prevalences [29].

RESULTS

Study selection

The study selection process is summarized in Figure 1. Electronic and manual searches generated a total of 2116 records. Of these, 52 were duplicates, leaving 2064 screened records, of which 300

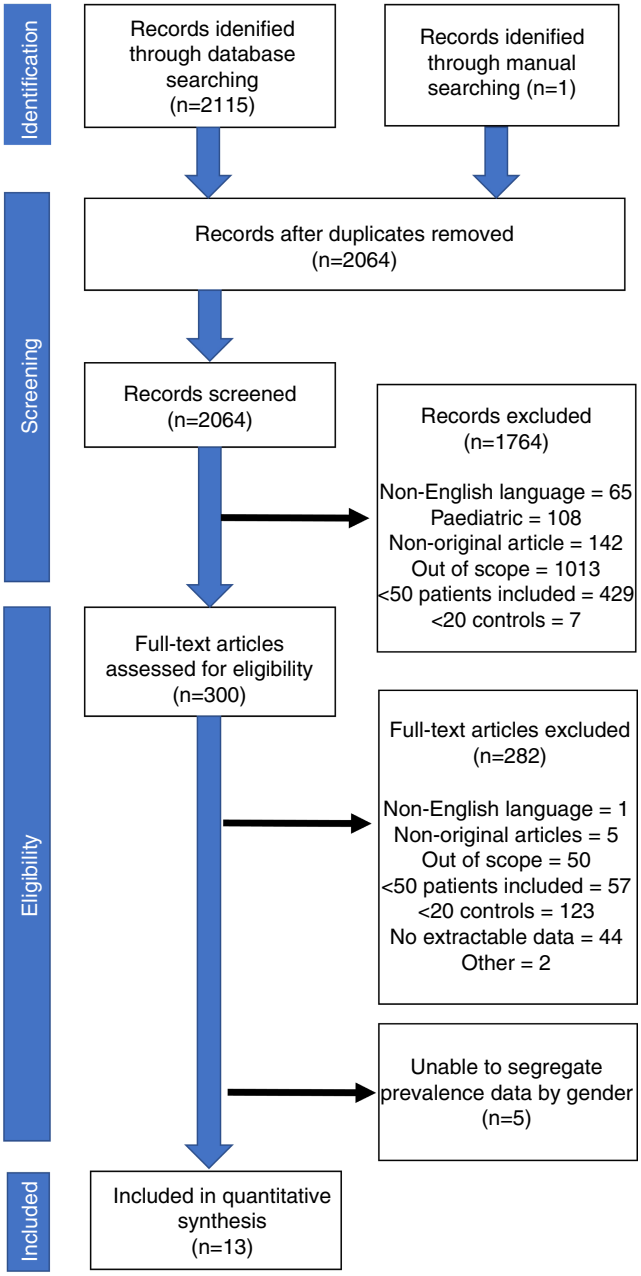


FIGURE 1 PRISMA flow diagram

were reviewed in full text and 287 did not meet study criteria. Five of these studies [30–34] included male and female patients, but prevalence data could not be segregated by sex and were subsequently excluded from the review. Two additional studies [35,36] were excluded as it was not possible to obtain required information relating to size of the control group. In total, 13 studies fulfilled the inclusion criteria; 12 were identified from database searches and one [37] was identified from screening of references.

Study characteristics

The features of the included studies are detailed in Table 1. Included studies were published between 1987 and 2019. A total of nine studies originated from European centres, one from the USA [38], two from Canada [25,37] and one from Australia [39]. Of the nine European studies, five originated from a single unit [11,23,24,26,27].

Study designs

The majority (7/13) of studies were cross-sectional, involving a retrospective review of data gathered into a patient database [23,24,26,27,39–41]. The remaining six studies were classed as prospective ($n = 4$) [22,28,37,38] or retrospective ($n = 2$) [11,25] case–control studies.

Nine studies [11,23–27,39–41] utilized normal values from previously investigated healthy controls; four studies recruited their own control group as part of the study design [22,28,37,38]. The normal cut-off or range in each study is shown in Table 2. Sources of funding were acknowledged in five studies [11,25,37–39]. Ethical approval was discussed in all but five studies [11,22,26,27,40].

Participants

A total of 2981 (75.1% women) FI patients were included across eligible studies. The number of participants included ranged from 52 to 538 (median 192). The number of control subjects included was 21–157 (median 80).

Four studies [24,26,38,41] included only female patients and one included only men [27], while the remaining eight studies included both men and women (Figure 2). In these studies, most patients were women who made up 50%–80% of the total.

The mean age reported across studies ranged between 52 and 67 years. Overall, the age of participants ranged from 13 to 97. Three studies [22,28,40] included a minority of patients under the age of 18 and were included in the review. Although it was not possible to ascertain the exact number of paediatric patients included, based on the information available their presence was deemed unlikely to have had any significant impact on overall prevalence data.

The severity of FI was evaluated in 10 studies using validated ($n = 8$) or unvalidated ($n = 2$) questionnaires. In the remaining studies, the evaluation of FI was based on clinical interview. Patients were described as having either isolated urge or isolated passive FI, or a mixed type of leakage in 5/13 studies [23,27,38,39,41]. In these studies, the proportion of patients with urge FI was 14% to 44%, passive incontinence was 6% to 52% and mixed FI was 19% to 53%.

Intervention characteristics

Details of the manometry set-up and rectal sensitivity protocol are presented in Table 1. Anorectal manometry was performed using a (conventional) water-perfused, station pull-through ($n = 6$), stationary ($n = 1$) or rapid pull-through ($n = 2$) technique in nine studies, and a solid-state high-resolution/high-definition technique in three

TABLE 1 Study characteristics of included papers

Authors	Publication year	Country	Study design	All patients (*n* =)	Female (*n* =)	FI assessment	Controls (*n* =)	Control type	Manometry technique	Balloon distension technique
McHugh and Diamant [37]	1987	Canada	Prospective case–control	143	97	Referral	157	Current	**1**	5
Felt-Bersma et al. [22]	1990	The Netherlands	Prospective case–control	178	122	Medical history/ referral	80	Current	**1**	8
Delechenaut et al. [40]	1992	France	Cross-sectional study	332	257	Unvalidated questionnaire	114	Historical published	**1**	nr
Sun et al. [28]	1992	UK	Prospective case–control	302	235	Medical history/ referral	65	Current	**2**	**6**
Bharucha et al. [38]	2005	USA	Prospective case–control	52	52	FICA scale	21	Current	**1**	na
Burgell et al. [27]	2012	UK	Cross-sectional study	160	0	Vaizey score	24* 41[ab]	Historical published and unpublished	**1**	**8**
Hotouras et al. [26]	2012	UK	Cross-sectional study	88	88	Unvalidated questionnaire	92	Historical published	1	**7**
Paramor et al. [25]	2014	Canada	Retrospective case–control	310	235	Vaizey score	50	Historical unpublished	**1**	**8**
Townsend et al. [11]	2016	UK	Retrospective case–control	200	100	Vaizey score	WP 82* SS 115* 91[ab]	Historical published	**1,3**	**8**
Carrington et al. [24]	2018	UK	Cross-sectional study	403	403	Vaizey score	85	Historical published	**3**	8
Leroi et al. [41]	2018	France	Cross-sectional study	83	83	Jorge–Wexner score	40	Historical published	**4**	6
Vollebregt et al. [23]	2019	UK	Cross-sectional study	192	154	Vaizey score	134	Historical published	3	**8**
Heitmann et al. [39]	2019	Australia	Cross-sectional study	538	423	Jorge–Wexner score	34	Historical published	**1**	7

Notes: 1, conventional, water perfused, stationary or rapid pull-through; 2, conventional, water perfused, stationary; 3, high-resolution, solid state; 4, high-definition, solid state; 5, incorporated balloon, nr; 6, incorporated balloon, stepwise distension; 7, non-incorporated balloon, stepwise distension; 8, non-incorporated balloon, ramp/continuous distension.

Bold indicates that prevalence data are reported.

Abbreviations: *manometry;a, hypersensitivity; b, hyposensitivity; FI, faecal incontinence; FICA, Faecal Incontinence and Constipation Assessment scale;na, not applicable; nr, not reported; SS, solid state; WP, water perfused.

TABLE 2 Table of normal values used in studies

Authors	Publication year	Measures (normative ranges or cut-off values)											
		Resting (mmHg)			Squeeze (mmHg)			Hypersensitivity (ml)			Hyposensitivity (ml)		
		Men	Women	Combined	Men	Women	Combined	Men	Women	Combined	Men	Women	Combined
McHugh and Diamant [37]	1987	26–142	9–142		113–399	38–261		nr	nr	nr	nr	nr	nr
Felt-Bersma et al. [22]	1990	>22	>31		>88	>38		nr	nr	nr	nr	nr	nr
Delechenaut et al. [40]	1992			Upper part > 24 Lower part > 2.2			>63	nr	nr	nr	nr	nr	nr
Sun et al. [28]	1992	nr	nr	nr	123–250	66–177		DDV 60–150 Pain 150–200	DDV 50–100 Pain 100–200		FCS 10–20	FCS 10–20	
Bharucha et al. [38]	2005			>25			>87	na	na	na	na	na	na
Burgell et al. [27]	2012			>37			>37	MTV > 80			FCS < 150 DDV < 190 MTV <320		
Hotouras et al. [26]	2012		>37			>37		MTV > 75	MTV > 75		MTV < 290	MTV <290	
Paramor et al. [25]	2014			>44			>131			FCS 38–58 DD 103–123			FCS 38–58 DD 103–123
Townsend et al. [11]	2016	WP > 24 SS > 37	WP > 24 SS > 30		WP > 26 SS > 60	WP > 26 SS > 42		MTV > 75	MTV > 75		FCS < 150 DDV < 190 MTV <325	FCS < 110 DDV < 200 MTV < 290	
Carrington et al. [24]	2018		>41			>29		MTV > 75			FCS < 150 DDV < 190 MTV < 320		
Leroi et al. [41]	2018		>67			>139			150–340			150–340	
Vollebregt et al. [23]	2019	>38	>33		>61	>45		MTV > 75	MTV > 75		FCS < 150 DDV < 190 MTV <325	FCS < 110 DDV < 200 MTV < 290	
Heitmann et al. [39]	2019			>40			>132			FCS 10–80 MTV 200			FCS 10–80 MTV 200

Abbreviations: DD, DDV, FCS, MTV, maximum tolerable volume; SS, solid state; WP, water perfused.

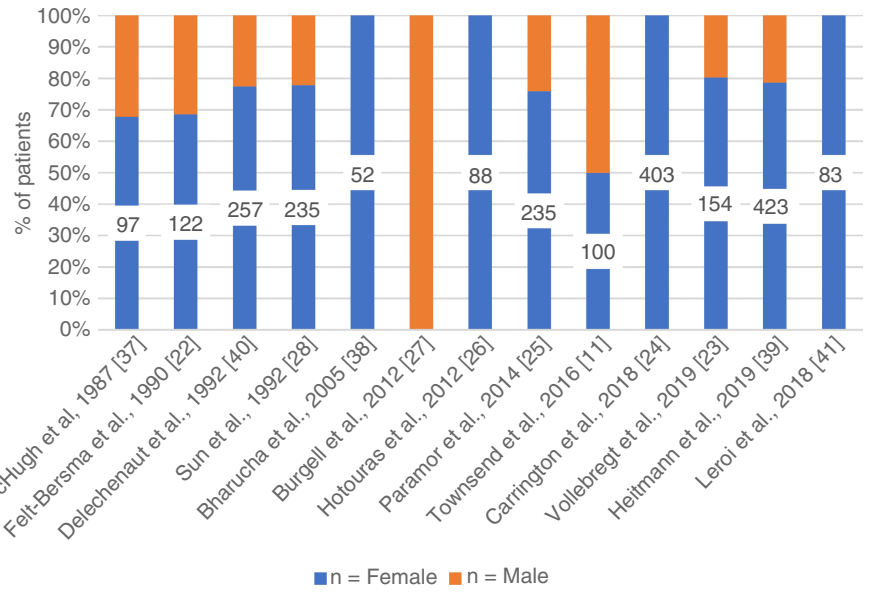


FIGURE 2 Proportion of men and women included [11,22-28,37-41]

studies. The catheter type and technique used was mixed in one study.

Rectal sensitivity was evaluated by balloon distension in 12 studies. Most studies used a balloon assembly made up of a balloon (latex $n = 5$, undefined $n = 3$) tied to a urinary catheter ($n = 6$) or other type of tubing ($n = 2$). In other studies, the balloon was attached to the tip of the manometry catheter ($n = 2$) or formed within the sheath covering the manometry catheter ($n = 1$). No details on balloon assembly or filling method were available in two studies [37,40]. All studies used air to distend the rectal balloon; four followed a stepwise filling protocol and the remaining six used continuous (ramp) distension. Most studies asked patients to report the following sensory thresholds: 'first sensation' (8/12 studies), 'desire to defaecate' (8/12) and/or 'maximum tolerable volume' (9/12 studies). Other sensory thresholds described included sensations of 'gas/wind' and 'pain'[28].

Outcomes

Anal tone and contractility

Overall, 11 studies reported prevalence data on anal tone and/or contractility. The prevalences of hypotonia and hypocontractility were each described in 10 studies [11,22,24,25,27,37–41]; one additional study described the prevalence of hypocontractility alone [28].

Resting pressure (hypotonia) and squeeze pressure (hypocontractility) were evaluated against the lower limit of normal defined by the fifth percentile in HVs in three studies [22,24,38], mean − 2SD in three studies [11,28,37] and the receiver operating characteristic cut-off defining the best sensitivity and specificity against health for a given measure in one study [41]. The remaining 6/15 studies with prevalence data on anal tone and contractility did not describe the cut-off definition used.

Rectal sensitivity

The prevalence of rectal hypersensitivity and hyposensitivity were each reported in only 5/12 studies that performed balloon distension. Only one study [11] stated the definition used to define the cut-off volume for hypersensitivity/hyposensitivity (mean − 2SD) in health. Communication with the senior author of three-quarters of the remaining papers [23,26,27] revealed that all studies performed in the same unit used mean − 2SD to define the normal cut-off.

Risk of bias in studies

Scores for each study are summarized in Figure S1 and further details can be found in Table S2. Of the 13 studies, six achieved ≤33% of attainable points and were considered as low quality, with high risk of bias, while four studies scored between 34% and 66% of available points (medium quality studies). Three studies [24,37,38] scored 67%–100% and were classed as good quality (low risk of bias). The median score was 55% (range 17%–75%).

Results of individual studies and data synthesis

Anal hypotonia

The pooled prevalence of anal hypotonia (Figure 3) was 44% (95% CI 32%–56%, $I^2 = 96.35\%$) in women ($n = 1767$) and 27% (95% CI 14%–40%, $I^2 = 94.12\%$) in men ($n = 624$). Within-study prevalence of hypotonia was always less in men (range 9%–58%) than in women (range 21%–80%), except for the studies by Heitmann et al. [39] who reported a similar prevalence between men (58%) and women (59%), and McHugh and Diamant [37] who reported a higher prevalence of hypotonia in men (45%) than women (36%). Leroi et al. [41] used the receiver operating characteristic cut-off for normal and reported the highest prevalence rate for hypotonia.

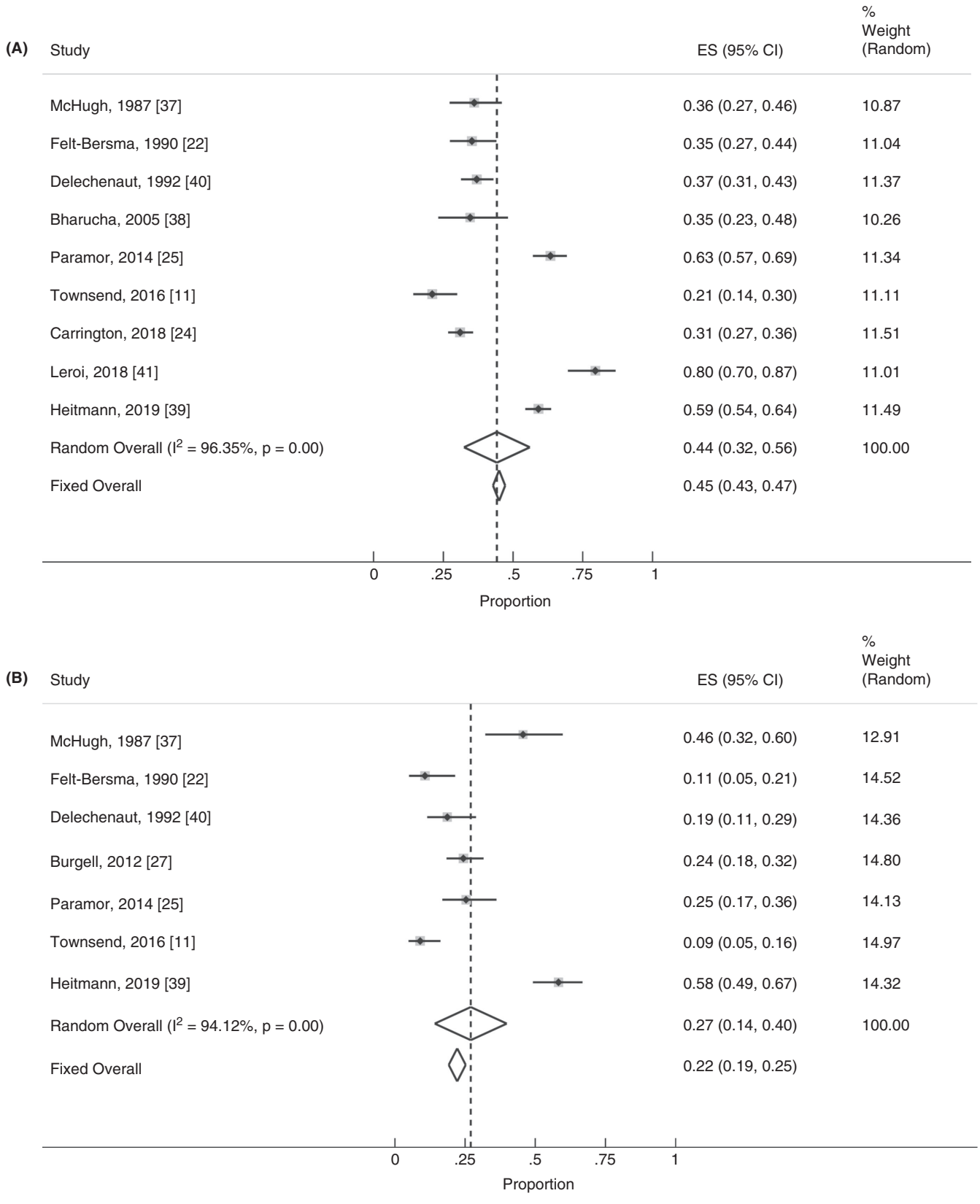


FIGURE 3 Forest plot of female [11,22,24,25,37-41] (A) and male [11,22,25,27,37,39,40] (B) anal hypotonia

Anal hypocontractility

The pooled prevalence of anal hypocontractility (Figure 4) was 69% (95% CI 57%–81%, I^2 = 98.17%) in women (n = 2007) and 36% (95% CI 18%–53%, I^2 = 96.77%) in men (n = 696). Within-study prevalence of hypocontractility was nearly always significantly greater in women than in men (over double that in men in 4/6 studies). It also generally exceeded hypotonia prevalence. Hypocontractility prevalence was highest in the paper by Sun et al. [28] at 94% in women and 87% in men.

Rectal hypersensitivity

The pooled prevalence of rectal hypersensitivity (Figure 5) was 10% (95% CI 4%–15%, I^2 = 80.09%) in women (n = 577) and 4% (95% CI 1%–7%, I^2 = 51.25%) in men (n = 373). In women, the prevalence of hypersensitivity was highest (17% vs. 5%–10% in other studies) in the study by Paramor et al. [25]. This study, unlike others, based the diagnosis on volume at first sensation or urge sensation rather than maximum tolerable volume.

Rectal hyposensitivity

The pooled prevalence of rectal hyposensitivity (Figure 6) was 7% (95% CI 5%–9%) in women (n = 577; I^2 = 0%, P = 0.88) and 19% (95% CI 15%–23%) in men (n = 373; I^2 = 0%, P = 0.46). The prevalence of hyposensitivity was higher in men than women in all studies. The majority of data (3/4 studies in men and 3/4 studies in women) came from a single institution at different time points [11,23,26,27].

Sensitivity analysis

As per our inclusion criteria, defined a priori, only studies with appropriate control data based on at least 20 HVs were included in the meta-analysis. Over due concern for the number of studies excluded on the basis of this criterion, we conducted a sensitivity analysis to include those seven [35,42–47] studies with sex-stratified FI data in >50 patients, irrespective of the number of HVs. Overall, the inclusion of these studies did not majorly impact the pooled prevalences (see Table S3 and Figures S2–S5 for detailed results).

DISCUSSION

Summary of findings

This systematic review and meta-analysis on the prevalence of major disorders of anal motor and rectal sensory function found only 13 original, English-language studies in patients with FI which met inclusion criteria. This illustrates the paucity of FI studies with large sample sizes and the consideration of gender differences, and highlights the limited numbers of included HVs upon which generation of prevalence data depends.

Anal sphincter dysfunction was the most prevalent pathophysiological finding. According to pooled results, 44% of women and 27% of men had anal hypotonia and 69% of women and 36% of men had anal hypocontractility. In women, these results support the popular notion that inadequate barrier function (whether of neurological/functional or structural origin) is the leading cause of FI. In contrast, only a minority of men present with attenuated anal sphincter function; other (suprasphincteric) mechanisms warrant consideration especially in this group. Nevertheless, it may be that measures of resting tone and squeeze pressure lack sensitivity to convey all degrees of anal sphincter dysfunction.

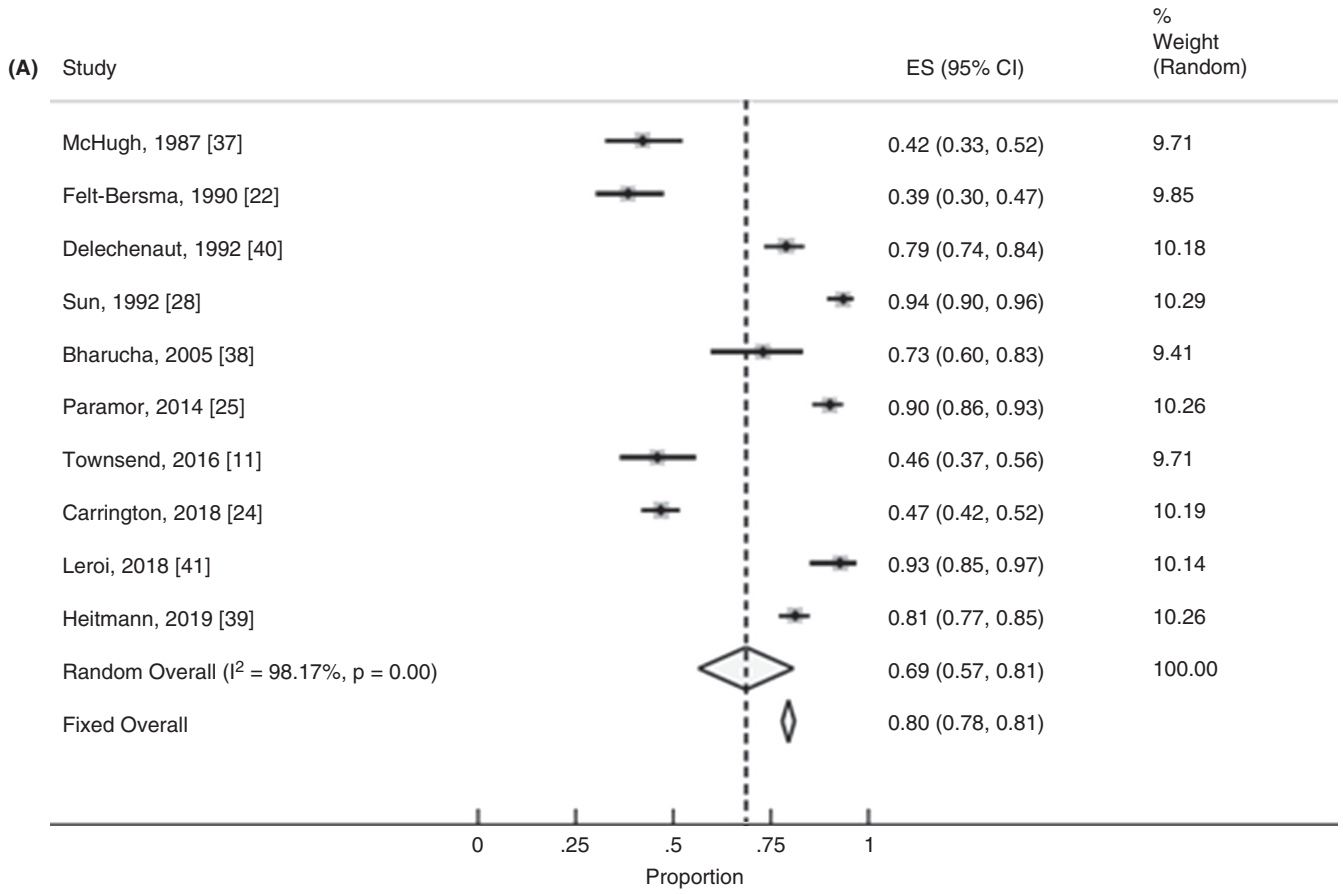
Rectal sensory dysfunction was present in up to one-fifth of men (hyposensitivity) and a tenth of women (hypersensitivity). This highlights the need to evaluate rectal capacity and afferent pathway function in at least a proportion of individuals to determine the pathoaetiology of impaired sensation.

Comment on major findings

Overall, anal hypocontractility was the most common abnormality both in women and in men. In individual studies, prevalence of anal hypocontractility generally exceeded that of anal hypotonia, and rates of hypocontractility were nearly always greater in women than in men. The risk for anal sphincter barrier dysfunction is greatest in women due to obstetric injuries (including structural defects and pudendal neuropathy), whilst in men sphincter barrier dysfunction is generally considered to be iatrogenic [8]. However, even in the absence of structural sphincter defects, chronic straining at stool and subsequent pelvic floor denervation may also lead to hypocontractility in both men and women [48]. Constipation and FI are known to coexist in a sizeable proportion of patients with FI [49].

While the prevalence of male hypotonia was reduced in more recent studies (perhaps due to more sphincter sparing surgery [11]), the prevalence of anal hypotonia and hypocontractility in women remained consistent over the duration of included studies (>30 years). This is probably because the lag between sphincter injury and symptom occurrence in women is usually several decades [50] meaning that the benefits of any change in obstetric practice (e.g., the move from posterior to mediolateral episiotomy) has yet to translate to observed changes in physiology. Notably, excluding patients with sphincter defects did not reduce the prevalence of hypocontractility in relation to other studies [40]. Bharucha et al. [38] was the only other study to specifically exclude patients with sphincter defects, although they did include patients with a history of forceps delivery, stitches and sphincter repairs.

Of the major disorders, rectal hyposensitivity was the only condition to have higher prevalence in men compared with women. Altered rectal sensitivity, especially in the presence of weak



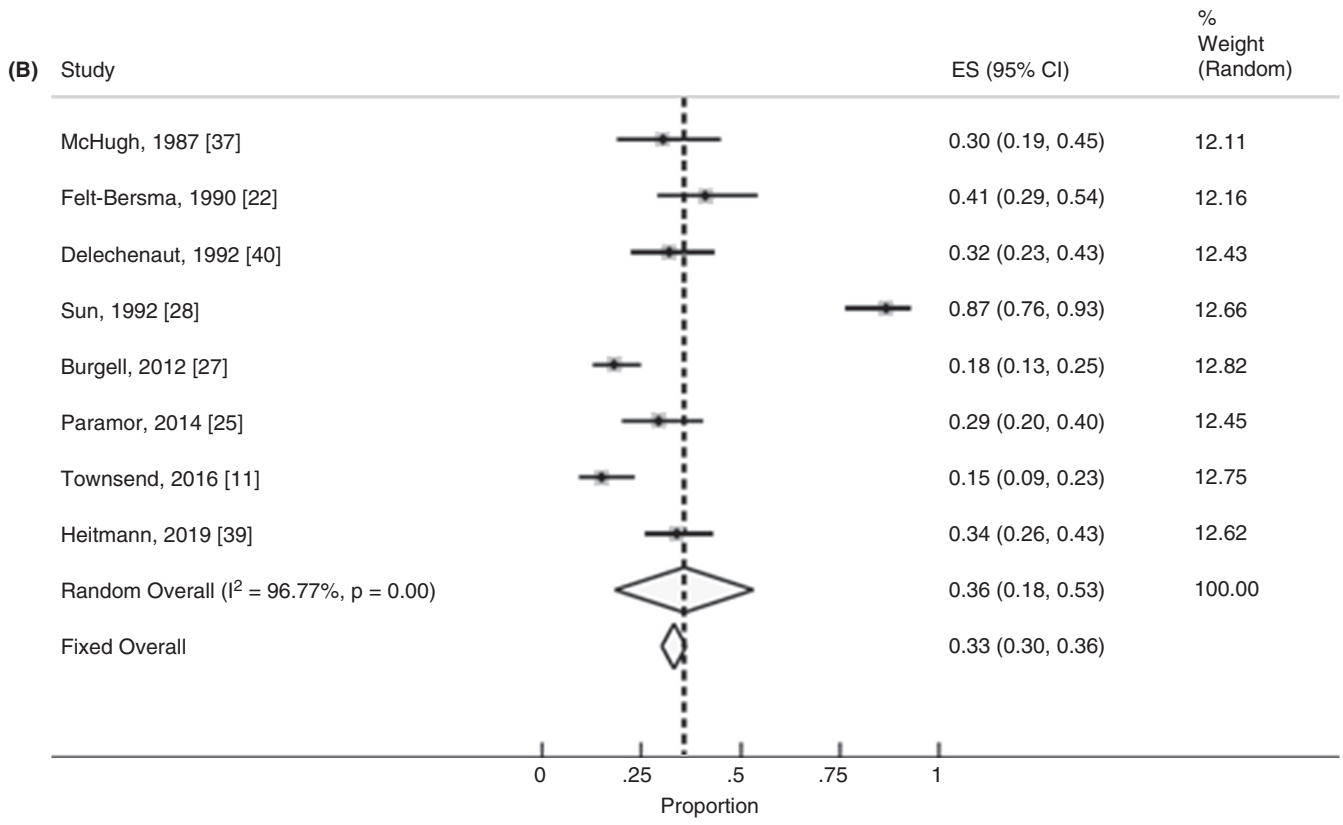


FIGURE 4 Forest plot of female [11,22,24,25,28,37-41] (A) and male [11,22,25,27,28,37,39,40] (B) anal hypocontractility

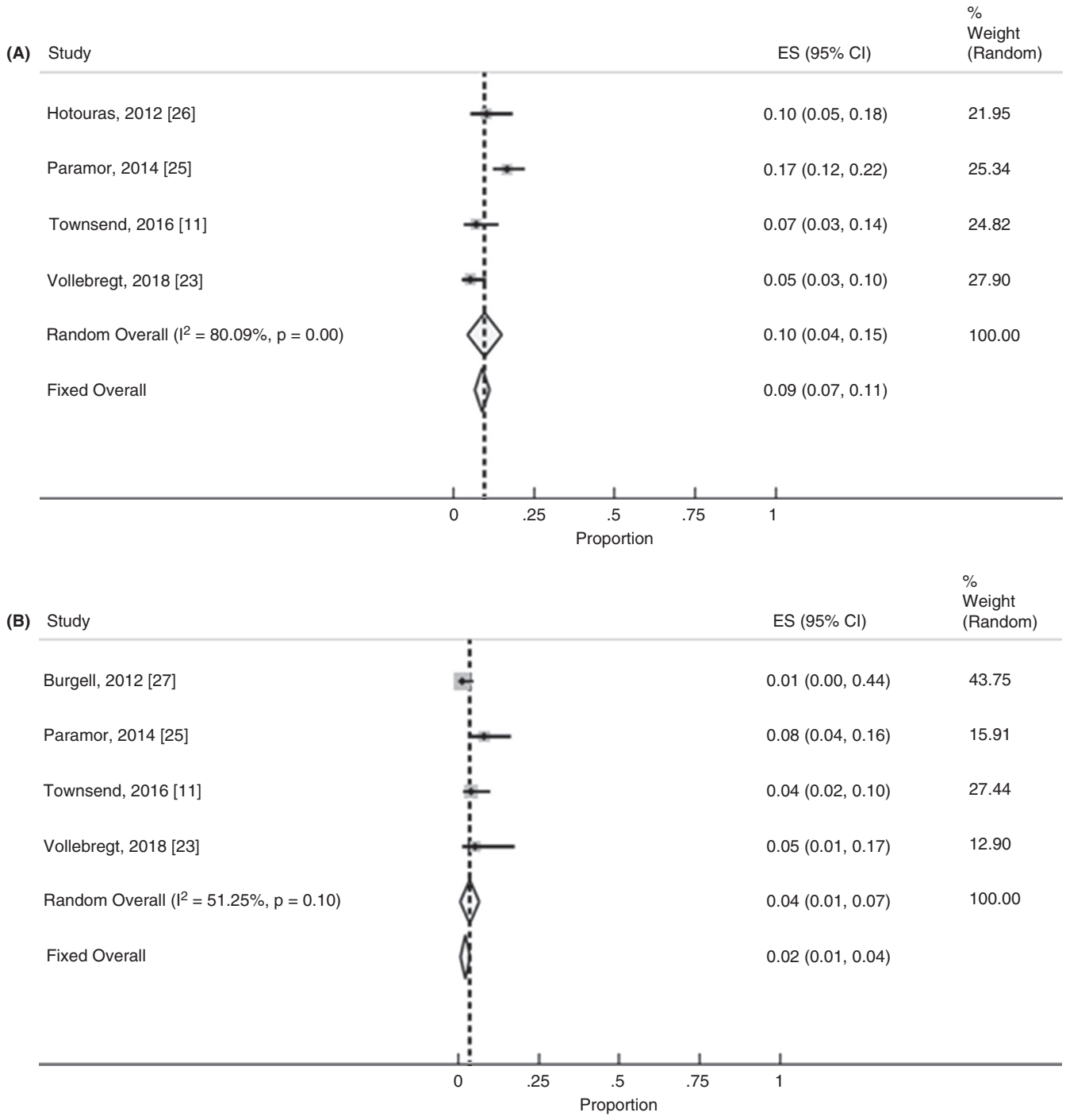


FIGURE 5 Forest plot of female (A) [11,23,25,26] and male [11,23,25,27] (B) rectal hypersensitivity

sphincters [28] may lead to incontinence due to reflex inhibition of the internal anal sphincter before the patient perceives the presence of stool in the rectum [51]. This may be of particular importance for some patients who complain of mainly passive leakage, which is more likely to be associated with a weak internal anal sphincter [30]. Meanwhile, hypersensitivity may result from altered rectal compliance, sensitization of extrinsic peripheral pathways and/or central afferent mechanisms, or abnormalities in perceptual and behavioural processes causing hypervigilance [52]. Often this leads to urgency and urge incontinence associated with an inability to defer defaecation [52]. Rectal hypersensitivity was more prevalent in women than men.

Comment on heterogeneity

The prevalence rates for anal hypotonia, hypocontractility, rectal hypersensitivity and hyposensitivity varied greatly. To reduce

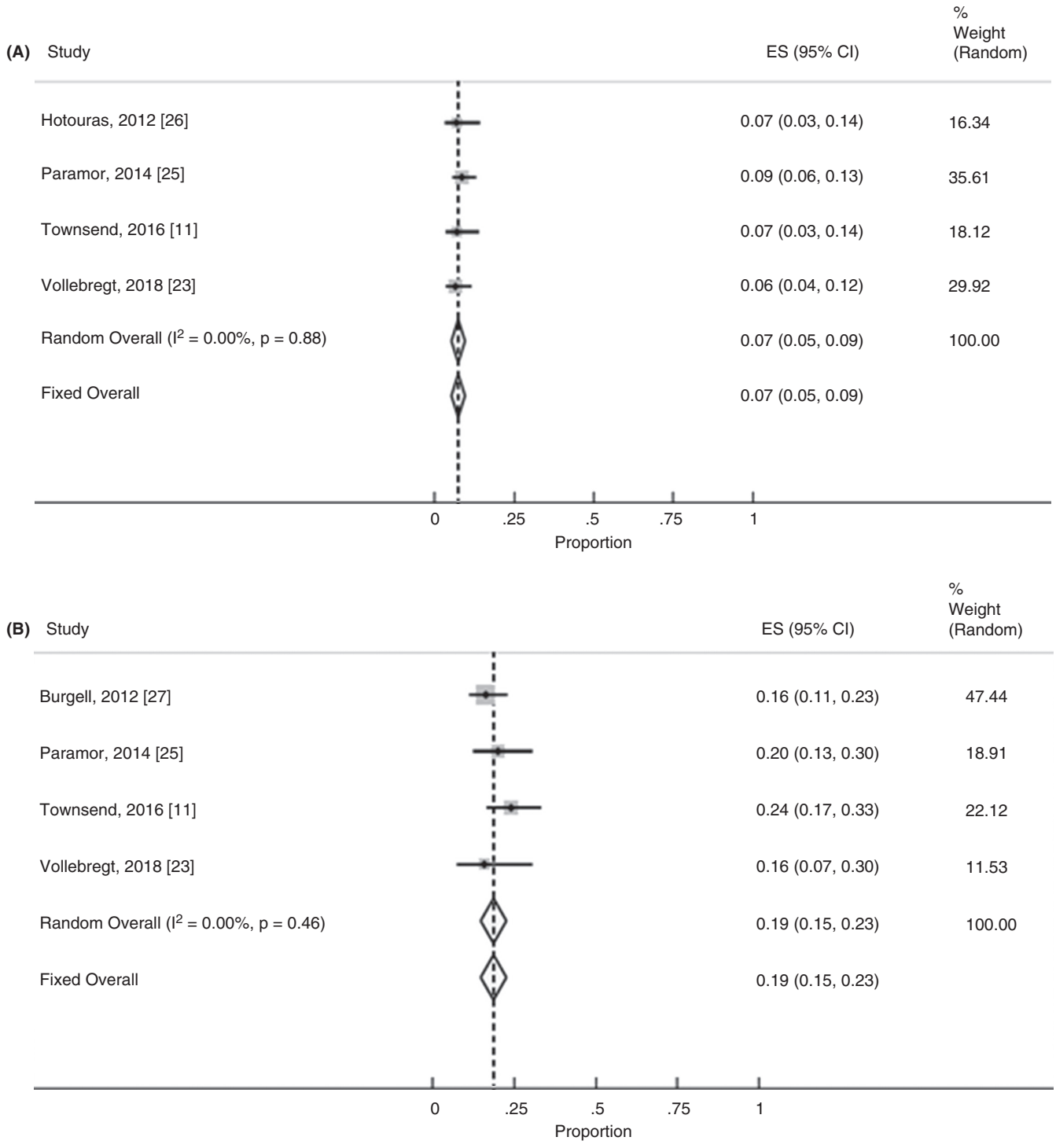


FIGURE 6 Forest plot of female [11,23,25,26] (A) and male [11,23,25,27] (B) rectal hyposensitivity

clinical heterogeneity resulting from the choice of manometric or balloon distension technique, we considered only those studies with institution-derived or -identified control values to ensure appropriate normal ranges were included. However, we did not set criteria for the method or definition of normality used between studies, which may explain some of the variability observed. For example, studies that define abnormal cut-offs based on the sensitivity and specificity of each test report generally higher prevalence rates, since these cut-offs may be different from normal values in a larger population of HVs [41]. Indeed, it was much more common that a value depicting only extreme outcomes in health (typically the fifth percentile or mean − 2SD) was used. Reassuringly, when studies used the same method and definition for the lower limit of normal, as demonstrated in the pooled analysis of rectal hyposensitivity, findings between studies remained consistent over time and statistical heterogeneity disappeared [11,23,25–27]. This observation calls

for international standardization of not only the parameters studied (as per the IAPWG protocol [16]) but also the definition of normal cut-offs.

LIMITATIONS

Our review has several limitations. In choosing search terms, we did not consider 'anal incontinence' due to its association with more minor forms of leakage including soiling and flatus incontinence [53]. Meanwhile, some eligible studies included a proportion of patients with lesser forms of FI [25]. One study [26] included only FI patients eligible for percutaneous tibial nerve stimulation, which may be offered to patients with more minor FI, dependent on hospital policy. For consistency, we did not impose set criteria for FI, relying on the authors' definition of FI. One exception was the study by Paramor et al. [25] who included an FI and faecal leakage (FL) group (defined as leakage up to two tablespoons). For this study, we chose to combine the two groups as it was felt that their definition of FL was comparable to FI in other studies. However, it should be noted that Paramor et al. [25] themselves concluded that pathophysiology in men with FL is different from that in men with FI and in women with FI and/or FL.

A high degree of coexistent symptoms amongst patients may influence rates of pathophysiology. Several of the included studies had large proportions of patients with coexistent constipation symptoms, irritable bowel syndrome, rectal prolapse etc. Although it was our intention to study patients with 'idiopathic' FI (thus excluding studies in homogeneous groups of patients with conditions known to impact anorectal function), many studies included a proportion of patients with neurological or surgical risk factors, which could have influenced the results. For example, in considering the 40% of included patients with 'idiopathic' FI, Burgell et al. [27] observed that normal sensation was more likely than hyposensitivity (i.e., prevalence of hyposensitivity was lower in patients with idiopathic FI) compared to other causes of FI. One of the main problems in limiting any study of FI to 'idiopathic' FI is that only very rarely do patients present clinically with no precipitating factors to FI. Our results are therefore generally reflective of patients attending tertiary sector care for the investigation of FI.

Regarding the primary outcomes, we did not impose the definition used for hypo/hyper within the selected studies and relied upon the definition used in individual studies. On occasion, the direction of results was difficult to interpret, especially for sensation. Having standardized definitions for the pathological terms 'hyper' and 'hypo' will help future studies communicate these results [16]. To include the study by Felt-Bersma et al. [22], we applied the fifth percentile in health to data presented based on this being the most widely employed definition for the lower limit. Although an alternative cut-off could have been chosen, using the fifth percentile resulted in a small percentage of FI men and women with sphincter dysfunction in line with the authors' observation of 'near complete overlap between incontinent and control subjects'.

Application of minimum eligibility criteria regarding the sample and control group size was intended to ensure that studies included came from departments with sufficient experience in techniques and knowledge of normal ranges. Five included studies originated in a single unit while a large proportion of studies were excluded due to a small sample size; inclusion of such smaller studies may have yielded different results. On the other hand, while we imposed a criterion for the overall number of participants, we did not consider the numbers of male and female patients individually. In one study [23], the number of included men was <50, meaning that this study met inclusion criteria for the systematic review solely based on the number of women in the study.

A total of five studies [30–34] comprising both male and female patients were excluded from the review because prevalence data were reported as a single result (rather than specific values by sex). These studies represent some of the largest conducted, so the data loss is considerable. However, our aim was to specifically compare prevalence by gender (a decision justified by the widely differing results between men and women) and such data could not be accurately extracted from excluded studies. Overall, the number of male patients included in the meta-analysis was considerably fewer than women, reflective of the clinical population typically investigated for FI.

CONCLUSION

These results convey clear gender disparity in the rates of sphincter barrier dysfunction and rectal sensory dysfunction. Poor voluntary sphincter control remains the most prevalent abnormality observed, especially in women. However, the number of appropriately controlled studies was small and few were judged as having low risk of bias. Consistent technique and definition of normal improved certainty of diagnosis (e.g., hyposensitivity) but overall wide confidence intervals and high levels of heterogeneity were observed. This indicates the need for large-scale prospective studies to be performed using a standardized protocol (e.g., the IAPWG protocol [16]) and calls for a collective effort to harmonize practice.

CONFLICT OF INTERESTS

AMP Rasijeff: none to declare. K Garcia-Zermeno: none to declare. GL Di Tanna: none to declare. JM Remes-Troche has served as a speaker, a consultant and an advisory board member for Takeda, Medtronic, Asofarma, Chinoin and Alfasigma. CH Knowles has received financial remuneration from Medtronic Inc. as speaker fees and for expert advisory committees. SM Scott has received honoraria for teaching for Laborie.

AUTHOR CONTRIBUTIONS

AMPR, KGZ and SMS contributed to study design. AMPR and KGZ performed study screening and data extraction. AMPR, KGZ and GLDT performed data analysis. AMPR, KGZ, CHK and SMS wrote

the paper. All authors contributed to data interpretation and read and approved the final version of this article including the authorship list.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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