Functional defecation disorders in children
Kuizenga-Wessel, S.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Chapter three

FUNCTIONAL DEFECATION DISORDERS AND EXCESSIVE BODY WEIGHT

A systematic review


Pediatrics.
2016,138(3):e20161417
ABSTRACT

Context
Several studies have suggested an association between functional defecation disorders (FDDs) and overweight/obesity in children.

Objective
To synthesize current evidence evaluating the association between FDDs and overweight/obesity in children.

Study selection
PubMed, Medline, and Embase were searched from inception until January 25, 2016. Prospective and cross-sectional studies investigating the association between FDDs and overweight/obesity in children 0 to 18 years were included.

Data extraction
Data generation was performed independently by 2 authors and quality was assessed by using quality assessment tools from the National Heart, Lung, and Blood Institute.

Results
Eight studies were included: 2 studies evaluating the prevalence of FDDs in obese children, 3 studies evaluating the prevalence of overweight/obesity in children with FDDs, and 3 population-based studies. Both studies in obesity clinics revealed a higher prevalence of functional constipation (21%–23%) compared with the general population (3%–16%). In 3 case-control studies, the prevalence of overweight (12%–33%) and obesity (17%–20%) was found to be higher in FDD patients compared with controls (13%–23% and 0%–12%, respectively), this difference was significant in 2/3 studies. One of 3 population-based studies revealed evidence for an association between FDDs and overweight/obesity. Quality of 7/8 studies was rated fair or poor. Due to heterogeneity of the study designs, we refrained from statistically pooling.

Conclusions
Although several studies have revealed the potential association between FDDs and excessive bodyweight in children, results across included studies in this review differ strongly and are conflicting. Therefore, this systematic review could not confirm or refute this association.
INTRODUCTION

Functional defecation disorders (FDDs) are commonly encountered in pediatric health care and comprise functional constipation (FC) and functional non-retentive fecal incontinence (FNRFI). FC has a reported prevalence ranging from 0.7% to 29.6%. FNRFI is less prevalent and estimated to occur in <1% of children in the general population. FDDs are diagnosed according to the internationally accepted Rome III criteria (Table 1). These disorders are known to have a significant impact on the quality of life. The pathophysiology of FDDs is still incompletely understood, although genetic, biochemical, microbial, behavioral, and psychosocial factors have been suggested to potentially play a role. More recently, several studies have suggested that there is an association between FDDs and overweight and/or obesity in children.

Pediatric overweight and obesity have emerged as a serious public health concern in the 21st century. The global prevalence of childhood overweight and obesity has increased dramatically over the past decades; rising by 47% between 1980 and 2013: from 10% to 15%. Obesity is known to cause various comorbidities, such as hypertension, dyslipidemia, and fatty liver disease. Factors that may be involved in the pathophysiology of both FDDs and overweight in children include diet (e.g., a lack of fiber or a high-fat diet), a lack of physical activity, gut microbiota dysbiosis, psychological factors, and socioeconomic status. Since these factors are associated with both FDDs and excessive bodyweight in children, they could account for the commonly reported co-occurrence between these disorders.

To date, no comprehensive systematic review has been published to evaluate the potential association between FDDs and overweight/obesity in children. If an association exists, this could have important implications regarding early detection of FDDs in children with overweight and of overweight in children with FDDs in the clinical care setting. For both FDDs and overweight, early detection and intervention are of key importance since a delay in treatment increases the likelihood of poor long-term outcome. Therefore, our aim was to systematically review currently available literature regarding the association between FDDs and overweight/obesity in children.
PubMed, Medline, and Embase were searched from inception until January 2016. Publication language was restricted to English. Prospective and cross-sectional studies describing the association between FDDs and overweight/obesity in children (0–18 years) were included. Studies including a combination of children and adolescents (<21 years) were eligible for inclusion as long as the majority of subjects was <18 years of age. As a prerequisite for eligibility for inclusion, a clear definition for overweight/obesity and FDDs needed to be provided. For FC, this definition had to at least include defecation frequency (<3 times per week), FNRFI had to be described as fecal incontinence in the absence of FC and for overweight/obesity, the definition had to include the BMI. The primary outcomes of interest were the prevalence of FDDs and of overweight/obesity (in %). Exclusion criteria were organic causes of defecation disorders or of excessive body weight and insufficient data on the outcomes of interest. Search strategies included controlled vocabulary terms: Medical Subject Headings (MeSH) for PubMed and Medline and Emtree terms for Embase. Search terms included the following: constipation, fecal impaction, fecal incontinence, defecation, gastrointestinal motility; children, infants, adolescents, pediatrics; obesity, overweight, body size, BMI. The electronic search strategy, including the limits used, is provided in the Supplemental Information. Data generation was performed independently by 2 authors (Drs Koppen and Kuizenga-Wessel). This process involved searching literature, data selection, and data extraction. In case of disagreement between these authors, consensus was reached by discussion or by consulting a third author (Dr Tabbers). To identify additional studies, reference lists of reviews and included studies were searched.
Quality Assessment

Quality of the studies was assessed by using quality assessment tools from the National Heart, Lung, and Blood Institute (NHLBI); the choice for the applied tool was based on the study designs. We used 1 tool for observational cohort and cross-sectional studies and another tool for case-control studies. Both tools assessed the internal validity and risk of bias in a similar manner. Two authors (Drs Koppen and Kuizenga-Wessel) applied these tools; they independently evaluated the items of the tools as “yes,” “no,” “not applicable,” “cannot determine,” or “not reported.” This was used to guide the overall rating for the quality of each study as “good,” “fair,” or “poor.” In case of disagreement, consensus was reached through discussion or by consulting a third author (Dr Tabbers).

RESULTS

A flowchart of the selection process is depicted in Fig 1. Eight studies were included, which were categorized into 3 groups: (1) studies that evaluated the prevalence of FDDs in obese children (n = 2; Table 2); (2) studies that evaluated the prevalence of overweight/obesity in children with FDDs (n = 3; Table 3); (3) population-based studies assessing the association between FDDs and overweight/obesity (n = 3; Table 4). Studies were conducted in 6 different countries across 4 continents. Five studies were conducted in tertiary care centers, 2 studies were conducted in schools, and 1 study was conducted in primary care centers. In total, 5442 children were described (1–20 years, 49.5% boys), this number reflects all study group children in the different studies and not only those with conditions of interest. Only 3 studies had a case-control design, and the total number of children in the control groups was 1870 (2–20 years, 49.3% boys). The quality assessment for all included studies is presented in Tables 5 and 6.

GROUP 1  FDDS IN OBESE CHILDREN

Fishman et al. administered a self-developed bowel questionnaire to 80 consecutive pediatric patients presenting at an obesity clinic. They found a prevalence of FC of 23%, which was higher than the previously reported prevalence of 8.9% in the general population. They also observed that 12 (15%) obese children suffered from fecal incontinence; in 6 of them this was associated with FC. However, in the other 6 children (7.5% of the total obese population), it was not associated with FC and they were diagnosed as having nonretentive soiling, a disorder now referred to as FNRFI.
Two studies were excluded due to insufficient details on the outcomes of interest: Kiefte et al. was excluded due to insufficient information. The authors performed a large prospective birth cohort study and reported outcomes at 24, 36 and 48 months of age. However, follow-up response rate differed per time point and the exact total number of children with FC and/or overweight/obesity at each of these ages was not provided. The authors reported that prevalence of overweight was almost similar in children with and without constipation (8% vs. 11%; p=0.46, 13% vs. 10%; P=0.10 and 8% vs. 9%; P=0.60 at the age of 24, 36 and 48 months, respectively). More information is not available. Chien et al. was excluded because recalculation of the data provided in the tables resulted in different results than those provided by the authors, indicating that the authors performed an analysis that was not described clearly and could not be repeated by us. Furthermore, in this study an odds ratio was reported without a confidence interval, thereby making it impossible to interpret. This study had other methodological weaknesses; obesity was based on self-reported height and weight via a questionnaire and low defecation frequency (assessed by a questionnaire) was used as an indicator of constipation.
Van der Baan-Slootweg et al. evaluated the bowel habits of 91 morbidly obese children included in an obesity treatment trial, using questionnaires and a 2-week bowel diary. A physical examination was performed in all children, and a rectal examination was performed in 69 (76%) children. Nineteen of 91 (21%) morbidly obese children were found to have FC according to the Rome III criteria. In addition, colonic transit time (CTT) was determined in all study subjects by using a radiopaque marker test using the method described by Bouchoucha et al. A prolonged CTT (>62 hours) was found in 2 (11%) children with constipation and in 6 (8%) children who did not have FC according to the Rome III criteria. FNRFI was found in 1 patient and, as expected, CTT was normal in this child. Furthermore, food intake was measured by using a 7-day diary record kept by the children after instructions from a dietitian; no difference was found between the diet of children with or without constipation, including regarding fiber and fat intake.

GROUP 2 OVERWEIGHT AND OBESITY IN CHILDREN WITH FDDS

In a prospective case control study, Kavehmanesh et al. compared 124 children with FC with 135 controls (patients admitted for other diseases). Obesity (18% vs 12%) and overweight (33% vs 23%) were more prevalent in the FC group compared with the controls, but these differences were not statistically significant. The authors mentioned that the prevalence of both overweight and constipation found in this study (both in constipated children and controls) was much higher than found in a nationwide study (4% and 9%, respectively).

Teitelbaum et al. performed a prospective case-control study to investigate the association between functional gastrointestinal disorders and overweight. They compared 757 children who presented to their pediatric gastroenterologist for upper and lower functional gastrointestinal disorders with 2 healthy control groups from a local pediatric practice (control group 1) and a high school (control group 2), comprising 1691 controls. 30 Out of all children with FC ($n = 196$), 37 (19%) were considered to be overweight and 45 (23%) were obese; the obesity rate in the FC group was significantly higher compared with the healthy controls (8% in control group 1 and 11% in control group 2, $P < .001$ for both comparisons). For fecal incontinence (with or without FC), overweight and obesity were both significantly more prevalent in the patient group (25% and 25%, respectively) compared with both healthy control groups (overweight control group 1: 13%; overweight control group 2: 15%; obesity control group 1: 8%; overweight control group 2: 11%; comparisons are further specified in Table 3).
<table>
<thead>
<tr>
<th>Author, year</th>
<th>Country, setting</th>
<th>Population (P)</th>
<th>Controls (C)</th>
<th>Definition OW/OB and measurement</th>
<th>Definition FC and measurement</th>
<th>n (%) FC</th>
<th>n (%) FI</th>
<th>Conclusion</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fishman et al. 2004</td>
<td>USA, prospective observational study at obesity clinic</td>
<td>n=80 1-18 years ♂: 39%</td>
<td>n/a</td>
<td>OW: n/a OB: BMI &gt; 95th percentile Weight and height measurements Not reported which reference values were used</td>
<td>2 or more of the following, ≥25% of the time, ≥3 months, hard or pellet-like stools, infrequent stools (less than 3 per week), straining, painful defecation, or sense of incomplete evacuation. Soiling was defined as presence of fecal material in underwear or pajamas in a child older than 48 months of age for at least 3 months</td>
<td>18/80 (23%) Total: 12/80 (15%)</td>
<td>-FNRFF: 6/80 (8%) FC: 6/18 (3.3%)</td>
<td>Prevalence of FC in OB children (23%) higher than previous reports (5-16%)</td>
<td>BMI adjusted for age and gender, not reported which reference values were used Discrepancy number of males: 30 according to text and 31 according to table</td>
</tr>
<tr>
<td>Van der Baan-Slootweg et al. 2011</td>
<td>The Netherlands, prospective observational study at obesity clinic</td>
<td>n=91 8-18 years ♂: 34%</td>
<td>n/a</td>
<td>OW: n/a OB: BMI ≥35, or BMI ≥30 in the presence of obesity-related morbidity Methods of anthropometric data collection not reported</td>
<td>Rome III criteria Assessed with standardized questionnaire</td>
<td>19/91 (21%) Total: 5/91 (5%)</td>
<td>-FNRFF: 1/91 (1%) FC: 4/19 (21%)</td>
<td>Higher frequency of FC in children with obesity (21%) compared to worldwide prevalence (8%)</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Country, setting</td>
<td>Population (P)</td>
<td>Controls (C)</td>
<td>Definition FC and measurement</td>
<td>Definition OW/OB and measurement</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>-------</td>
<td>-----------------</td>
<td>----------------</td>
<td>-------------</td>
<td>-------------------------------</td>
<td>--------------------------------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>Kavehmanesh et al. 2015</td>
<td>Iran, prospective case control study in children admitted to the hospital</td>
<td>n=124 2-14 years 52%</td>
<td>n=155 52%</td>
<td>Rome II criteria</td>
<td>Patients in the same age group without FC or weight/height affecting disease</td>
<td>Rome II criteria</td>
<td>OW BMI &gt;85th percentile 124/124 (100%)</td>
<td>P: 51/124 (53%)</td>
<td>P: 22/124 (15%)</td>
</tr>
<tr>
<td>Tertelbaum et al. 2009</td>
<td>USA, prospective case control study at pediatric gastroenterology clinic (GI group)</td>
<td>n=757 2-20 years 51%</td>
<td>n=255 51%</td>
<td>Rome III criteria</td>
<td>Methods of anthropometric data collection not reported</td>
<td>Methods of anthropometric data collection not reported</td>
<td>OW BMI 85-95th percentile 757/196 (78%)</td>
<td>P: 129/196 (66%)</td>
<td>P: 196/757 (26%)</td>
</tr>
<tr>
<td>Tertelbaum et al. 2009</td>
<td>USA, prospective case control study at pediatric gastroenterology clinic (GI group)</td>
<td>n=757 2-20 years 51%</td>
<td>n=255 51%</td>
<td>Rome III criteria</td>
<td>Methods of anthropometric data collection not reported</td>
<td>Methods of anthropometric data collection not reported</td>
<td>OW BMI 85-95th percentile 757/196 (78%)</td>
<td>P: 129/196 (66%)</td>
<td>P: 196/757 (26%)</td>
</tr>
</tbody>
</table>

**Table 3:** Prevalence of overweight and obesity in children with functional defecation disorders
Wagner et al. recently published a prospective case-control study describing 43 children who presented with fecal and/or urinary incontinence problems, including 17 children (40%) with fecal incontinence. Of these 17 children with fecal incontinence, 14 (82%) were found to have FC based on the Rome III criteria. The authors compared children with incontinence (both urinary incontinence and fecal incontinence) to 44 matched healthy controls. There was no statistically significant difference in FC prevalence between BMI groups. In children with fecal incontinence (both FNRFI and FC-associated fecal incontinence), the rate of obesity was high (24%) compared with controls (0% obese, 14% overweight; no statistical analysis reported).

GROUP 3 OVERWEIGHT, OBESITY, AND FDGS IN PEDIATRIC POPULATION-BASED STUDIES
In a survey study among 450 healthy children in the United States, Phatak et al. found that FC was significantly more prevalent in overweight and obese children (44/91, 23%) than in normal-weight children (36/259, 14%). The odds ratio for having FC in the combined overweight and obese population was 1.83 (P = .01). An important feature of this study was that a logistic regression analysis was performed after including factors such as age, gender, ethnicity, and recruitment site.

Costa et al. performed a study in 1077 adolescents (10–18 years) in Brazil. They defined constipation according to a combination of pediatric and adult Rome III criteria (Table 4). Overweight was defined as a BMI >85th percentile, and this study did not differentiate further between obesity and overweight. They found no association between overweight and constipation in adolescents. However, in a sub-analysis in constipated adolescents, an association between overweight and fecal incontinence was confirmed; fecal incontinence occurred in 8/28 (29%) of overweight patients versus 14/168 (8%) in non-overweight patients.

In the most recent study on this topic, our research group investigated 2820 Colombian school children by using a Spanish translation of the Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III Version and anthropometric measurements. In this sample, FC was not significantly more prevalent in children who were obese (28/188, 15%) or overweight (71/542, 13%) compared with children with normal weight (269/2090, 13%).

Quality Assessment
Quality assessment tools from the NHLBI were used to assess the methodological quality of the included studies (Tables 5 and 6). Outcomes were used to assess the internal validity and risk of bias for each study and the overall
quality was rated as good, fair, or poor. Only 1 study had an overall rating of good.\textsuperscript{9} Four studies were rated fair,\textsuperscript{12,13, 21, 31} and the remaining 3 articles were rated poor.\textsuperscript{28, 30, 32} In general, studies lacked sample size justification, some studies did not differentiate between overweight and obesity and all but 1 study did not adjust for key potential confounding variables. In addition, some items of the quality assessment tools were not reported across studies (Tables 5 and 6).
<table>
<thead>
<tr>
<th>Study</th>
<th>Country, setting</th>
<th>Population (N)</th>
<th>Definition FC and measurement</th>
<th>Definition OW/OB and measurement</th>
<th>n (%)</th>
<th>n (%)</th>
<th>n (%)</th>
<th>n (%)</th>
<th>Conclusion</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phatak et al.</td>
<td>USA, pediatric and adolescent clinic</td>
<td>n=450 4-18 years</td>
<td>Rome III criteria</td>
<td>OW BMI 85-95th percentile</td>
<td>P: 80/450 (18%)</td>
<td>P: 88/450 (19%)</td>
<td>P: 123A/450 (27%)</td>
<td>Probability of having FC in OW/ OB population 25% vs 14% in normal weight population (OR=1.85, p=0.001)</td>
<td>In the text of the article by Phatak et al., 15% of NW children are mentioned to have FC, in the table of this same article this number is reported to be 13.9%. (the latter number is adapted in this systematic review)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Assessed using questionnaire (interview)</td>
<td>OB BMI &gt;95th percentile</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Weight and height were measured</td>
<td>NW: 36/259 (14%)</td>
<td>FC: n/a</td>
<td>FC: n/a</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Standard data from the Center for Disease control and Prevention were used as reference</td>
<td>OW/OB</td>
<td>44/191 (23%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Modified Rome III criteria, combination of pediatric and adult criteria: 2 of the following: 2 or fewer defecations in the toilet per week, a history of painful, or hard bowel movements, hard stools that resembled a sausage but have cracks on their surface or separate hard lumps, a sensation of incomplete evacuation, a history of large diameter stools that may obstruct the toilet and a history of fecal incontinence</td>
<td>OW BMI ≥85th percentile</td>
<td>P: 196/1077 (18%)</td>
<td>P: 25/1077 (2%)</td>
<td>P: 144/1077 (14%)</td>
<td>No significant difference between BMI of adolescents with/without FC (medians 19.4 vs 19.3 kg/m², p=0.001)</td>
<td>According to the table, the number of children with OW in the study population is 144 (and not 145 as mentioned in the article)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Assessed using validated questionnaire</td>
<td>OB: n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costa et al.</td>
<td>Brazil, cross-sectional survey conducted at schools</td>
<td>n=1,077 10-18 years</td>
<td>Rome III criteria</td>
<td>OW BMI z score between +1 and +2</td>
<td>P: 36/1077 (15%)</td>
<td>P: 188 (7%)</td>
<td>P: 542 (7%)</td>
<td>P: 368 (7%)</td>
<td>No association between FC and OW/ OB was found</td>
<td>Authors state that the questionnaire is validated, but do not provide a reference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Assessed using a Spanish translation of the Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III Version (QPGS-RIII)</td>
<td>OB BMI z score &gt; +2</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Weight and height were measured</td>
<td>OW: 269/2,090 (13%)</td>
<td>FC: 71/566 (19%)</td>
<td>FC: 28/566 (8%)</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>WHO reference values were used</td>
<td>O/W: 71/542 (13%)</td>
<td>non-FC: 471/2,452 (19%)</td>
<td>non-FC: 160/2,452 (7%)</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 5  NHLBI Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Was the research question or objective in this paper clearly stated?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>Was the study population clearly specified and defined?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>Was the participation rate of eligible persons at least 50%?</td>
<td>Yes</td>
<td>Yes</td>
<td>CD</td>
<td>CD</td>
</tr>
<tr>
<td>4</td>
<td>Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>Was a sample size justification, power description, or variance and effect estimates provided?</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>9</td>
<td>Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?</td>
<td>CD</td>
<td>CD</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>10</td>
<td>Was the exposure(s) assessed more than once over time?</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>12</td>
<td>Were the outcome assessors blinded to the exposure status of participants?</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>13</td>
<td>Was loss to follow-up after baseline 20% or less?</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>14</td>
<td>Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Rating</td>
<td>Fair</td>
<td>Fair</td>
<td>Poor</td>
<td>Good</td>
<td>Fair</td>
</tr>
</tbody>
</table>

Table 6  NHLBI Quality Assessment of Case-Control Studies

<table>
<thead>
<tr>
<th></th>
<th>Kavehmanesh et al.</th>
<th>Telebaum et al.</th>
<th>Wagner et al.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Was the research question or objective in this paper clearly stated and appropriate?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>Was the study population clearly specified and defined?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>Did the authors include a sample size justification?</td>
<td>No</td>
<td>CD</td>
</tr>
<tr>
<td>4</td>
<td>Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?</td>
<td>Yes</td>
<td>CD</td>
</tr>
<tr>
<td>5</td>
<td>Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls valid, reliable, and implemented consistently across all study participants?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>6</td>
<td>Were the cases clearly defined and differentiated from controls?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>7</td>
<td>If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomly selected from those eligible?</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>8</td>
<td>Was there use of concurrent controls?</td>
<td>CD</td>
<td>CD</td>
</tr>
<tr>
<td>9</td>
<td>Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case?</td>
<td>CD</td>
<td>CD</td>
</tr>
<tr>
<td>10</td>
<td>Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same time period) across all study participants?</td>
<td>CD</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>Were the assessors of exposure/risk blinded to the case or control status of participants?</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>12</td>
<td>Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis?</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Rating: Poor Poor Fair

DISCUSSION

This systematic review could not confirm or refute the association between FDDs and overweight/obesity because results are conflicting across the studies. Both studies in obesity clinics revealed a high prevalence (21%–23%) of FC compared with the general population (3%–16%), and 2 out of 3 case-control studies in children with defecation disorders revealed a higher prevalence of overweight and obesity in patients with FDD (12%–33% and 17%–20%, respectively) compared with controls (13%–23% and 0%–12%, respectively). On the other hand, only 1 of 3 population-based studies revealed evidence for an association.

There are multiple factors that may partially explain these different and conflicting results. As is shown in Tables 2, 3, and 4, the definitions of overweight and obesity differed among studies. Some studies have used the 85th and 95th percentiles of BMI for age and sex published in a study from the United States as cutoff points to identify overweight and obesity. Other studies have used centile curves on the basis of data from multiple countries (the International Obesity Task Force cutoff values) or the Centers for Disease Control and Prevention growth charts. One study used the cutoff values provided by the World Health Organization (WHO), these gender-specific BMI-for-age percentile curves use z scores. The WHO Child Growth Standards are now widely implemented worldwide in clinical care. It has been shown that using different definitions of overweight and obesity may lead to different results in epidemiologic studies. This could partially explain the different findings among the studies included in this systematic review.

In addition, studies used different definitions for FDDs. Although in all studies, the diagnosis of FDDs was based on the Rome criteria, some used the Rome II criteria, others used the Rome III criteria, and some studies had modified the criteria. It has been shown that using different criteria can lead to major differences in the evaluation of the prevalence of FDDs. Furthermore, only 1 study was rated to be of good quality on the basis of an assessment of the internal validity and risk of bias, whereas most studies were rated to be of fair or poor quality. Thus, most of these studies are at some risk of bias and should be interpreted with caution. Future high-quality studies are needed to shed more light on this issue.

Although evidence from studies performed in tertiary hospital settings seems indicative for an association between FC and overweight, evidence from
population-based studies is much less convincing. Potentially, patients in tertiary care centers may not be representative of the population as a whole. These patients may represent a subset of patients with risk factors for FDDs and overweight/obesity that were not accounted for in the studies.

Lifestyle factors such as diet and a physical activity are assumed to play an important role in the pathophysiology of both FC and overweight,\(^\text{20, 26, 41 - 44}\) which may explain why some studies have revealed an association between these disorders. For overweight and obesity, the pathophysiological importance of dietary factors (eg, high-caloric diet and low fiber intake) and a sedentary lifestyle is well recognized.\(^\text{20, 45 - 49}\) Therefore, treatment of childhood obesity mainly consists of dietary and physical activity modifications, often utilizing behavioral interventions.\(^\text{50, 51}\) The suggested role of dietary factors, especially the role of fiber, in the pathogenesis of FC is generally well-accepted, although pediatric data are scarce.\(^\text{20, 25, 41, 42, 52}\) The pathophysiological role of physical exercise is less well described and may be disputable.\(^\text{25, 26, 43, 44}\) Studies on fiber supplementation in the treatment of FC in children have resulted in conflicting results\(^\text{53}\) and no randomized controlled trials on the effect of increased physical activity on FC in children have been performed.\(^\text{54}\) Interestingly, studies conducted in developed countries (Germany, the Netherlands, and the United States) seem to demonstrate an association between FDDs and excessive bodyweight, whereas studies in developing countries (Brazil, Colombia, and Iran) were unable to confirm this finding. This raises the question whether there are pathophysiological differences between developing countries and more economically developed countries regarding the association between FDDs and excessive body weight. Possible shared etiological factors involved in the pathogenesis of overweight/obesity and FDDs are eating behavior, low fiber intake, physical exercise, hormonal dysfunction, gut microbiota, genetic predisposition, psychological factors, and socioeconomic status.\(^\text{1, 9, 13, 16, 21}\) Many of these factors likely differ between developed and developing countries. Potentially, a high-calorie, high-fat, low fiber diet and a sedentary lifestyle, which are common in developed countries, impact body weight and FDDs differently compared with lifestyle habits in developing countries.

One other potential pathophysiological factor that has been under increased attention over the past decades is the gut microbiota. It has been well established that obesity is associated with changes in the composition of the gut microbiota.\(^\text{55 - 62}\) Studies in mice and humans strongly suggest that the gut microbiota plays an important role in energy metabolism and that there is
a causative role for the microbiota in the development of obesity.\textsuperscript{55,56,61} Gut microbiota involvement in children with constipation has also been suggested.\textsuperscript{63} Although it is yet unclear whether the gut microbiota plays a causative role, it has been suggested that biochemical substances related to the gut microbiota may influence motility.\textsuperscript{8,65-66} It is highly likely that dietary factors also play an important role in these microbiota-associated biochemical processes.\textsuperscript{67-69}

However, further studies in this field are needed to further elucidate the association between the gut microbiota, FDDs, and excessive body weight.

Several studies specifically revealed that fecal incontinence (FNRFI, FC-associated fecal incontinence, and fecal incontinence not otherwise specified) was more common in children with excessive body weight.\textsuperscript{13,30-32} However, not all included studies reported on fecal incontinence; therefore, it is difficult to draw firm conclusions from these pediatric data. A high prevalence of fecal incontinence has been previously described in obese adults, and in the adult population fecal incontinence may improve after weight loss due to bariatric surgery.\textsuperscript{70,71}

The underlying pathophysiological mechanism behind this association is incompletely understood, but it has been hypothesized that this is due to pelvic floor dysfunction.\textsuperscript{72,73} Most likely, the excessive weight on the pelvic floor causes direct mechanical and neurologic dysfunction together with indirect effects of obesity such as diabetes, nerve conduction abnormalities, and intervertebral disc herniation.\textsuperscript{71,72} Whether the same mechanisms apply in children is yet to be sought out. These findings warrant further studies, especially because fecal incontinence is known to have a major negative impact on quality of life.\textsuperscript{5,6}

This is the first systematic review evaluating the association between FDDs and overweight/obesity in children. Because both FDDs and overweight/obesity are such significant pediatric health care problems, it is of key importance to investigate a potential association between them to improve pediatric health care worldwide. However, there are some limitations to this systematic review. First of all, the included studies have adopted a variance of definitions for FDDs and overweight/obesity and are conducted in different settings using different study designs; therefore, it is difficult to draw firm conclusions. Moreover, we were unable to perform a quantitative analysis due to the heterogeneity of the data. By including only articles written in English, this systematic review is at risk for some level of selection bias. However, we consider this risk to be very low, because most relevant literature is likely published in English. Finally, there is a potential risk of publication bias, although negative studies were identified and included in this systematic review, we may potentially have been unable to identify unpublished negative data.
CONCLUSIONS

Although several studies have reported on the potential association between FDDs and excessive body weight in children, the results from studies included in this systematic review are conflicting. Moreover, only 1 study was rated to be of good quality on the basis of an assessment of the internal validity and risk of bias, whereas most studies were rated to be of fair or poor quality. Therefore, we cannot draw firm conclusions. There is a need for high quality prospective cohort studies using uniform definitions and well-defined inclusion and exclusion criteria according to accepted guidelines.

Future studies assessing the association between FDDs and overweight in children should aim to further investigate the role of factors such as dietary factors, physical exercise, and psychological factors. Furthermore, the differences in study results between developed and developing countries warrants further investigation into the role of social economic status and the indirect consequences thereof. In addition, the potential risk of pelvic floor dysfunction in obese children needs to be sought out further. Finally, the field of microbiome studies is relatively young, but very promising and future studies investigating the potential role of the gut microbiota would seem to be of much interest.
REFERENCES


21 Koppen IJN, Velasco-Benítez CA, Benninga MA, et al. Is there an Association between


37 de Onis M. Update on the implementation of the WHO child growth standards. World Rev Nutr Diet. 2013;106:75–82


