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Functional Constipation in Children: A Systematic Review on Prognosis and Predictive Factors

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ABSTRACT

Background and Aim: Knowledge regarding prognosis and factors influencing the clinical course of functional constipation in children is important to enable general practitioners and paediatricians to give accurate patient information, to compare treatment strategies, and identify children with high risk for unfavourable outcome. The objective of the study was to investigate and summarize the quantity and quality of evidence on prognosis of childhood constipation with and without treatment and its predictive factors.

Methods: An extensive literature search in MEDLINE and Embase was performed to identify prospective follow-up studies evaluating the prognosis or prognostic determinants of functional constipation. Methodological quality was assessed using a standardised list. Results on prognosis of constipation were statistically pooled, and the influence of prognostic factors was summarised in a best evidence synthesis.

Results: The search strategy resulted in a total of 2882 abstracts. Only 14 publications met our inclusion criteria, of which 21% scored high methodological quality. Included studies showed large heterogeneity in study populations and outcome measures. Without regard to these differences, 49.3% ± 11.8% of all of the children studied for 6 to 12 months were found to recover and taken off laxatives. The percentage of children who were free from complaints, regardless of laxative use, after 6 to 12 months was 60.6% ± 19.2%. There is substantial evidence that defecation frequency and a positive family history are not associated with recovery from constipation.

Conclusions: The few studies published on prognosis of childhood functional constipation and predictive factors showed large heterogeneity and poor methodological quality. Overall, 60.6% of children are found to be free from symptoms after 6 to 12 months. Recovery rate showed no relation with defecation frequency or positive family history. Based on the present literature, we are unable to identify a group of children with high risk for poor prognosis.

Key Words: childhood, constipation, prognosis, systematic review

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In childhood, functional constipation is a common complaint. In the general population prevalence is reported to vary from 0.7% to 29.6% (1). This large variation may be because of lack of a generally used definition to classify constipation. Consensus is hampered by the fact that clinical presentation is diverse and pathophysiology is multifactorial. Even though several internationally accepted guidelines such as those of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (2), the Paris Consensus on Childhood Constipation Terminology (3), and the Rome III criteria (4) have been developed to provide criteria for constipation; none of them have been implemented worldwide in research or clinical practice yet.

There are different concepts on the clinical course of constipation in children. Some authors suggest that constipation is a constitutional condition that gradually disappears (5). Others find that despite intensive therapy 30% to 50% of the children persist having severe symptoms even after 5 years of follow-up (6,7).

Knowledge regarding factors influencing the clinical course of functional constipation in children is important to enable general practitioners and paediatricians to give accurate patient information, to weigh treatment strategies, and to identify children with high risk for unfavourable outcome. However, no overview of these prognostic factors exists in the literature. Therefore, our aim was to investigate and summarise the quantity and quality of the existing evidence on the course of constipation in children with and without treatment, and determinants that predict this course.

METHODS

Search Strategy

The MEDLINE database was searched from 1965 to March 2009, and Embase from 1980 to March 2009. The key words (medical subheadings [MeSH] and text words) used to describe constipation were ''constipation,'' ''obstipation,'' ''coprostasis,'' ''encopresis,'' and ''soiling.'' The study population was identified by the words ''child,'' ''infant,'' and ''adolescent.'' For MEDLINE the following query was added: (incidence [MeSH] or follow-up studies [MeSH] or prognosis or predict*[Text Word] or course*[Text Word] or epidemiologic studies). For Embase we combined the search with the strategy for detecting prognostic studies recommended by Wilczynski et al (8). In addition, reference lists of review articles and included studies were searched. No language restriction was applied.

Two reviewers independently screened all of the abstracts of identified published articles for eligibility. For this purpose, 4 inclusion criteria were used: study population consisted of children between 0 and 18 years of age; a prospective observational study design; one of the aims of the study was to evaluate the prognosis of functional constipation expressed as duration or recurrence of functional constipation and determinants that influence prognosis; and follow-up was at least 8 weeks.

Excluded were articles concerning children with a developmental delay or mental health problems (ie, eating disorders), studies investigating children with organic causes of constipation, and children with functional nonretentive faecal incontinence.

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All potentially relevant studies, as well as the studies of which the abstracts did not provide sufficient information for inclusion or exclusion, were retrieved as full-text articles. Any disagreements regarding the inclusion of articles were resolved through consensus when possible or by arbitration of a third person.

Quality Assessment

To assess methodological quality of the included studies we developed a standardised list (Table 1). We modified an established criteria list used in systematic reviews of prognostic studies (9–12). Two reviewers independently rated the methodological quality with the 15 items of the quality score list. Each of the items had an answer option of ''yes''/''no''/''unclear'' (ie, insufficient information). A score of 1 point was given only to a criterion that is assessed with ''yes.'' Equal weights were applied to all items, resulting in a maximum score of 15 points. Disagreements were resolved through consensus or by arbitration of a third person.

Data Extraction

Two reviewers independently performed a structured data extraction from the original reports. Extracted information included (if available) items referring to setting, participants (diagnosis, age, sex, and withdrawal/dropouts), interventions, and outcome measures. Disagreements were resolved by consensus or by arbitration of a third person.

Data Analysis

Interassessor reliability on methodological quality was calculated using κ-scores (13). Our primary outcomes were the following: recovery from constipation or no constipation as defined by the authors of the included articles, and no laxative use, at the end of follow-up and successful outcome or no constipation as defined by the authors of the included articles, regardless of laxative use at the end of follow-up. Large clinical diversity among the included studies with regard to participants, disease definitions, and definition of outcomes existed. Furthermore, different statistical approaches and adjustments for different variables were used. Nevertheless results on prognosis of constipation were pooled using stratification to overcome large differences in duration of follow-up, study quality, and setting.

We refrained from statistical pooling of results with regard to prognostic factors (11), but carried out a best evidence synthesis for associations with recovery from constipation. Using the methodological quality list, quality scores were calculated as a percentage of the maximum score. High quality is defined as a score of 60% or more of the maximum score (ie, a score of $\geq$9 points).

In the best evidence synthesis (14,15), evidence was divided into the following levels: Strong–consistent findings ($\geq$75% of the studies report consistent findings) in at least 2 high-quality studies; moderate–consistent findings in 1 high-quality cohort and at least 2 low-quality studies; limited–findings of 1 high-quality cohort or consistent findings in at least 3 low-quality studies; conflicting–inconsistent findings (<75% of the studies report consistent findings); and insufficient–no high-quality studies and <3 low-quality studies available. The level of evidence was based on the results in high-quality studies only in case of $\geq$2 high-quality studies available. Only statistically significant associations are considered as associated prognostic factors in this synthesis.

RESULTS

Included Studies

The search strategy resulted in a total of 2882 abstracts. After eligibility, screening of 20 publications was judged potentially relevant (5–7,16–33). After reading the full-text articles, 6 studies were excluded (5,19–21,29,30) because the study design was not a prospective observational study but based on a retrospective chart review (5,20,21,29,30) or a cross-sectional survey (19). Only 3 studies were not published in English but in Polish (16) and Spanish (28,32). These articles were translated. Full characteristics of the included studies are described in Table 2.

TABLE 1. Methodological quality list

	Yes	No	Do not know
Study population			
1. Inception cohort			
2. Description of study population at least mentioned are setting; age; duration of constipation; and severity of constipation (described as defecation frequency or presence of faecal incontinence)			
3. Description of inclusion and exclusion criteria			
4. Description of setting			
Follow-up			
5. Prospective data collection			
6. FU of at least 12 mo			
7. Loss to FU <20%			
8. Information about loss to FU			
Outcome			
9. Standardised measurement of outcome (baseline and FU identically measured)			
10. Independent measurement of outcome (blinded for prognostic factors)			
Prognostic factors			
11. Presentation of prognostic factors at baseline (at least mentioned are age, sex, duration of constipation, and severity of constipation)			
12. Standardised measurement of prognostic factors (baseline and FU identically measured and presented)			
13. Independent measurement of prognostic factors (blinded for outcome)			
Analysis			
14. Measure of association and measures of variance given			
15. Multivariate analysis used			

FU = follow-up.

TABLE 2. Study characteristics

Study, setting	Population	Definition of constipation	Outcome measure (instrument)
Banaszkiewicz et al (16), paediatric gastroenterology department	**Incl**: Patients 2–16 y of age with constipation **Excl**: Enteric neuromuscular, anatomic, or metabolic diseases N = 84; mean age 96.0 ± 41.5 mo; sex: M/F: 36/48 Duration: 71.9 ± 41.7 mo Severity: defecation frequency/wk 2.2 ± 0.6	Defecation frequency <3/wk for at least 12 wk	Success: defecation frequency ≥3/wk with no faecal soiling and the use of laxatives during the last 6 mo (standardised questionnaire at 24 mo)
de Lorijn et al (17), paediatric gastroenterology department	**Incl**: Patients >5 y referred to the outpatient clinic between 1995 and 2000 with constipation **Excl**: Hirschsprung disease, spinal and anal anomalies, previous colon surgery, metabolic or renal abnormalities, mental retardation, use of drugs other than laxative N = 169; median age 8.4 y (25th–75th percentiles 7.0–10.5); sex: M/F: 109/60 Onset: median age 3.5 y (1.0–4.0) Severity: median defecation frequency/wk: 2.0 (1.0–2.0); for encopresis: 10.0 (5.5–21.0)	At least 2 of the following: defecation frequency <3/wk; >1 episode of encopresis/wk; passing of large stool every 7–30 day; palpable abdominal or rectal mass	Success: defecation frequency ≥3/wk, encopresis frequency <1/2 wk, and no laxatives for at least 1 mo (detailed medical history at baseline, 6 mo and 12 mo)
Elshimy et al (18), general paediatric department	**Incl**: Children <5 y with constipation referred as new patients **Excl**: no criteria presented N = 42; mean age 21 mo (range 1–58 mo); sex: not presented Duration: 12.5 mo (range 1–48 mo), severity: not presented	Unspecified	Resolved constipation with or without laxative use (hospital notes combined with information from the GP)
Loening-Baucke (22), general paediatric department	**Incl**: Children with encopresis and constipation for >1 y and presence of a large amount of stool in the rectum **Excl**: Age <5 y, hypothyroidism, Hirschsprung disease, mental deficiency, chronic debilitating disease, and previous colon surgery N = 25; mean age 9.9 y (range 5.8–15.4 y); sex: M/F:19/6 Duration >1 y, severity: encopresis frequency range 3–>10/day	Unspecified	Recovery: defecation frequency ≥3/wk, ≤2 smear/mo or no soiling at all, whereas off laxatives for at least 1 month (FU visit)
Loening-Baucke (23), general paediatric department	**Incl**: Children with chronic constipation and overflow incontinence who had their initial evaluation between January 1985 and December 1986 **Excl**: Age <5 y, hypothyroidism, Hirschsprung disease, mental deficiency, chronic debilitating disease, and previous colon surgery N = 104. Analysed children: mean age 9.0 y (±2.4 y); sex: M/F: 69/28 Duration: not presented Severity: mean soiling frequency: 15/wk, palpable faecal mass in the abdomen: 45%	Unspecified	Recovery: defecation frequency ≥3/wk, ≤2 smear/mo or no soiling at all, whereas off laxatives for at least 1 mo (mailed questionnaire 12 mo after start of treatment)
Loening-Baucke (24), general paediatric department	**Incl**: Children ≤4 y with idiopathic chronic constipation who were ≥6 y and had entered school at the time of FU in May 1999, who were seen by the investigator between 1980 and 1989 **Excl**: Disease states that placed limitations on the act of defecation such as hypotonia, cerebral palsy, severe mental retardation, Hirschsprung disease, anal atresia, or spinal disease N = 174; mean age 2.2 ± 1.3 y; sex: M/F: 87/87	Defecation frequency ≤3/wk or painful defecation, or rectal impaction, or an abdominal faecal mass	Resolution of constipation: no soiling, defecation frequency ≥3/wk, and received no drugs or treatment (history at baseline and questionnaire at FU)

TABLE 2. (Continued)

Study, setting	Population	Definition of constipation	Outcome measure (instrument)
	Duration: mean age of onset 11 ± 13 mo Severity: defecation frequency <1/wk: 13%, ≤1 wk: 32%, </wk: 58%		
Loening-Baucke (25), general paediatric department	**Incl**: Consecutive healthy children with functional constipation and encopresis who were examined in the University of Iowa Encopresis Clinic with the balloon defecation test between 1985 and 1993 **Excl**: Hirschsprung disease, hypothyroidism, mental deficiency, chronic debilitating diseases, or neurological abnormalities, and previous surgery of the colon N = 232; mean age 9 ± 3 y; sex: M/F: 176/56 Duration: not presented, severity: not presented for whole group	Unspecified	Recovery: defecation frequency ≥3/wk and ≤2 soiling episodes/mo, whereas off laxatives for at least 1 mo, successfully treated: defecation frequency ≥3/wk and ≤2 soiling episodes/mo, no abdominal pain, irrespective of laxative use (clinic visit, mailed questionnaire, or telephone interview)
Michaud et al (26), paediatric gastroenterology department	**Incl**: Children 6 mo to 14 y of age. Referred between 1990 and 1992 for constipation **Excl**: Hirschsprung disease, anal atresia, spinal disease, cerebral palsy, severe mental retardation, or previous colonic surgery N = 72; mean age 4 y (range/SD not presented); sex: M/F: 40/32 Duration: not presented; severity: not presented	Defecation frequency <3/wk, painful defecation, and hard stools	Recovery: defecation frequency ≥3/wk, no painful defecation, no hard stools
Miele et al (27), general paediatric department	**Incl**: Children presenting to 1 of the 13 participating paediatricians from the Campania region in Italy from April 1 to June 30, 1999, diagnosed with a FGID according to the Rome criteria **Excl**: No criteria presented N = 66; mean age 3.9 ± 2.8 y; sex: M/F: 30/36 Duration: age at onset: 2.1 ± 1.8 y, severity: not presented	FGID according to the Rome criteria	Improvement (unspecified)
Polanco et al (28), paediatric gastroenterology department	**Incl**: Consecutive children with constipation **Excl**: No criteria presented N = 154; mean age 6.3 ± 3.3 y; sex: M/F: 72/82 Duration: age of onset 2–4 y: 23.8%, onset >4 y: 39.5% Severity: abdominal pain: 53.2%, palpable abdominal mass: 8.15%	Defecation frequency <3/wk for at least 3 mo, with difficult and painful defecation	Response: defecation frequency ≥3/wk
Staiano et al (6), not specified	**Incl**: Consecutive children who reported constipation for at least 6 mo between March 1983 and June 1986 **Excl**: Hypoparathyroidism, hyperparathyroidism, spinal, and anal anomalies, and mental retardation. Secondary constipation was excluded by clinical interview, physical examination, laboratory investigations, barium enema, and anorectal motility studies N = 103; median age 4.7 y (range 1.3–11.3 y); sex: M/F: 61/42 Duration: at least 6 mo; severity: median defecation frequency 2/wk (range 1–4 wk)	Unspecified	Recovery: defecation frequency >4/wk and/or TGTT <33 h whereas off laxatives for at least 1 mo (visit to outpatient clinic initially monthly, after 2 y of FU once/y)
van den Berg et al (31), paediatric gastroenterology department	**Incl**: Children referred between 1999 and 2003 to the tertiary outpatient clinic of the AMC with a suspicion of Hirschsprung disease and in whom constipation had started during the first year of life, in whom Hirschsprung disease was excluded by anorectal manometry and rectal suction biopsy	At least 1 of the following: defecation frequency <3/wk, painful defecation, and use of laxatives	Successful outcome: at least 4 wk with defecation frequency ≥3/wk, no pain during defecation, and no laxative use (standardised questionnaire)

TABLE 2. (Continued)

Study, setting	Population	Definition of constipation	Outcome measure (instrument)
	Excl: Organic causes of constipation such as gastroinestinal malformations, spinal abnormalities, and cerebral palsy N = 47; median age 3.5 mo (25th–75th percentiles 2.0–13.5); sex: M/F: 28/19 Duration of symptoms: median 3 mo (1.2–9.2), Severity: median defecation frequency/wk: 2 (0–7)		
van Ginkel et al (7), paediatric gastroenterology department	**Incl**: Patients participating in 1 of the research protocols on childhood constipation between 1993 and 1999 and referred to the tertiary centre gastrointestinal motility program by fam, practitioners, paediatricians, psychiatrists and school doctors. Patients must have had treatment with laxatives for minimum of 2 mo before randomisation into 1 of the protocols **Excl**: Organic causes of constipation and children using drugs influencing gastrointestinal function other than laxatives N = 418; median age 8 y (25th–75th percentiles 6–10); sex: M/F: 139/279 Duration: median period of symptoms before intake: 5 y+5 mo Severity: median defecation frequency/wk: 2 (1–5.5); for encopresis: 2 (3–17)	At least 2 of the following: defecation frequency <3/wk, ≥2 episodes of encopresis/wk, periodic passage of large amounts of stool at least once every 7–30 days, palpable abdominal or rectal mass	Successful outcome without laxatives: at least 4 wk with defecation frequency ≥3/wk, with ≤2 encopresis episodes/mo, no laxative use; successful outcome with laxatives: at least 4 wk with defecation frequency ≥3/wk, with ≤2 encopresis episodes/mo, and laxative use; relapse: defecation frequency became <3/wk and/or reintroduction of laxatives was necessary after initial successful treatment (standardised questionnaire)
Martinez-Costa et al (32), paediatric gastroenterology department	**Incl**: Children >4 y referred between June 2002 and January 2004 with chronic functional constipation **Excl**: Organic causes of constipation such as encefalopathy, Hirschsprung disease, etc N = 62; median age 6.1 y (range 1–14 y); sex: M/F: 25/37 Duration: ≥2 mo, severity: encopresis 31%, faecal impaction 27%	Defecation frequency ≤3/wk since the previous 2 mo; voluminous or scybalous stools; pain or straining; ≥2 soiling episodes/wk	Positive outcome: defecation frequency ≥3/wk, no pain, <2 soiling episodes/mo (structured questionnaire)

AMC = Amsterdam Medical Center; Excl = exclusion criteria; Fam = family practitioner; FGID = functional gastrointestinal disorder; FU = follow-up; GP = general practitioner; Incl = inclusion criteria; TGTT = total gastrointestinal transit time.

Setting

Of the 14 included studies, 6 were conducted in a general paediatric department (18,22–25,27), 7 in a paediatric gastroenterology department (16,17,26,28,31,32), and in 1 article no setting was stated (6). None of the included studies were conducted in a primary care centre.

Outcome Measures

All of the studies described a composed definition of recovery, resolution, or successful treatment of constipation as positive outcome, except for 2 studies that did not specify their outcome (18,27). Definitions of outcome measures varied strongly, nevertheless all of the studies took into account defecation frequency: in 1 study, having more than 4 bowel movements per week was a requirement for success (6); all of the other studies applied the criterion of at least 3 bowel movements per week. Frequency of faecal incontinence was included in the success definitions of 8 studies: in 5 studies (7,22,23,25,32) the success definition required <2 episodes per month, 1 study (17) allowed 1 episode per 2 weeks, and in 2 studies (16,24) children were not allowed to have any faecal incontinence. No abdominal pain or no pain with defecation was included in the success definition of 3 studies (7,25,32). All but 3 of the studies (27,28,33) took laxative use into account in their definition of success. Six studies (7,16–18,25,31) presented recovery rates of children taken off laxatives, as well as success rates including children still using laxatives.

Study Population

In total, 1752 children participated in the included studies. Age was reported in mean (16,18,22–28) (mean 72.2 ± 37.6 months, range 21.0 to 118.8 months) or median (6,17,31,32) (66.0 ± 39.3 months, range 3.5 to 100.8 months) values. Distribution of sex of all randomised children was reported in all but 2 of the studies (18,23): 51.2% of participants were boys (M/F: 822/784). Duration of constipation before start of the study was reported in 12 articles (expressed in mean or median duration before start of the study) (7,16,18,31), mean or median age of onset (17,24,26–28), or defined in the inclusion criteria (6,22,32). Two studies did not report duration (23,25). Numbers on severity of constipation at baseline (eg, defecation frequency, frequency of faecal incontinence episodes, presence of abdominal pain) were not presented in 4 studies (18,25–27). All of the other included studies used symptoms of constipation to express severity of constipation.

Follow-up Time

Most articles expressed follow-up time in mean number of months (mean 32.5 ± 34.7 months). Two studies presented

follow-up time in median number of months (7,31), and 1 study presented a range (22).

Methodological Quality

The 3 reviewers (M.A.M.P., M.E.J.B., and M.Y.B.) initially agreed on 85.6% of the items of the methodological quality list. Interobserver reliability of methodological quality assessment (0.71) was high. Overall methodological quality score of all of the included studies ranged from 4 to 10 out of a maximum of 15 points, with a mean score of 6.8. Only 21% of the included studies (n = 3) (7,17,31) were considered of high quality. Most prevalent shortcomings of the studies were the following: outcome measurement was not independent of prognostic factors (100%, n = 14), unstandardised and dependent measurement of prognostic factors (both 85.7%, n = 12), no presentation of association measures and measures of variance, or no multivariate analysis performed (both 78.6%, n = 11).

Prognosis

Of all of the children followed for 6 to 12 months (7,16,17, 22–25,31), 49.3% ± 11.8% (mean ± SD) recovered and were taken off laxatives at the time of follow-up. The percentage of children who were free from complaints, regardless of laxative use, after 6 to 12 months was 60.6 ± 19.2 (7,16,17,22–25,27,28,31,32).

Children followed for 1 to 2 years showed a recovery rate of 58.0% ± 14.1% (7,16,18), and 69.3% ± 19.0% were recovered with or without laxative use (2,4,18). After a follow-up period of 5 to 10 years, 56.0% ± 11.3% of the children recovered and were no longer taking laxatives (6,7); 56.3% ± 10.4% of the children had successful outcomes regardless of laxative use (6,7,26).

A total of 74.2% ± 14.5% of the children included in a paediatric gastroenterology department (n = 979) had successful outcomes regardless of laxative use at the time of follow-up (mean follow-up: 28.8 ± 35.8 months) (7,16,17,26,28,31,32). Studies performed in general paediatric departments (18,22–25,27) (n = 643) showed a lower recovery rate of 57.8% ± 19.5% ($P = 0.11$) (mean follow-up: 13.0 ± 2.5 months, $P = 0.31$).

Studies of high methodological quality (17,31,32) (n = 634) showed a success rate of 70.9% ± 5.3%, compared with 63.8% ± 20.4% ($P = 0.57$) in low-quality studies (6,16,18,22–28,32) (n = 1118).

Prognostic Factors

In the present review a total of 22 prognostic factors were analysed in 63 associations with recovery. In 44 evaluations no significant association was found, whereas in 19 evaluations a statistically significant association was reported. The mean sample size of studies that reported ''no association'' was not significantly different from the mean sample size of studies that reported a significant association (mean sample size: 130.9 ± 94.5 vs 145.6 ± 115.3, $P = 0.60$). All of the results of the best evidence syntheses on the prognostic factors are presented in Tables 3 and 4.

Demographics

Sex

Seven studies reported on the association between sex and recovery from constipation. Two studies of high methodological quality (7,31) found no statistically significant association, and 1 high-quality study (17) found that male sex was negatively associated with recovery. In addition, 4 studies of low methodological quality (6,23,24,26) found no significant association. In conclusion, there is conflicting evidence that sex influences recovery rate.

Age at Intake

Based on 4 low-quality studies reporting no significant association between age and recovery, limited evidence for no association was found (6,22–24).

Medical History

Age of Onset/Duration

One high-quality (31) and 4 low-quality studies (22–24,26) concluded that age of onset of constipation and recovery are not statistically significantly associated. In contrast, a high-quality study (7) showed that onset between 1 and 4 years of age is not significantly associated with recovery, but onset at the age of 4 years or older gives a higher recovery rate rather than onset before the age of 1 year. A low-quality study (6) supports the finding that an older age at onset was associated with a higher recovery rate. Based on these 7 articles, we conclude that evidence is conflicting.

Family History

Two high-quality studies (7,31) found no significant association between a positive family history for childhood constipation and recovery. In contrast, 1 low-quality study (6) found a negative association. Based on these 3 studies, we found strong evidence for no association.

Clinical Symptoms

Defecation Frequency at Intake

Two high-quality studies (17,31) found no statistically significant association between defecation frequency and recovery. We found 3 low-quality studies (6,23,24) that support this finding. In conclusion, these studies provide strong evidence that there is no association between defecation frequency and recovery.

Presence of Faecal Incontinence at Intake

Two low-quality studies reported on the association between the presence of faecal incontinence and recovery from constipation. One of them (25) found a positive association; the other (6) found no significant association. Therefore, evidence for this association is insufficient.

Frequency of Faecal Incontinence

We included 1 high-quality (17) and 1 low-quality (22) study that found no significant association between the frequency of episodes of faecal incontinence and recovery. In contrast, a high-quality (7) and a low-quality (23) study showed that in recovered children the frequency of episodes of faecal incontinence was significantly lower at baseline than in children who did not recover during follow-up (negative association). Overall, this provides conflicting evidence.

Abdominal Pain

We found 3 low-quality studies reporting on history of abdominal pain or abdominal pain at presentation (19,21,22). All 3 show the same results, together providing limited evidence for no

TABLE 3. Results of the included studies

Study, follow-up	Population	Prognosis	Prognostic factors, instrument	Results (n, % or mean ± SD)
Banaszkiewicz et al (16), 24 mo	n = 84 Age: mean 96.0 ± 41.5 mo Boys: 42.9%	Recovery*: 60% Success†: 70%	None presented	
de Lorijn et al (17), 12 mo	n = 169 Age: median 8.4 y (25th–75th percentiles 7.0–10.5) Boys: 64.5%	Recovery: 57.7% Success: 67.7%	Male sex (history) Presence of a rectal or abdominal mass (PE) CTT>100 h (ingestion of markers+radiography) Defecation frequency Encopresis frequency Presence of nighttime encopresis Production of large stools (history)	OR 0.34 (95% CI 0.16–0.70) OR 3.39 (95% CI 1.30–8.83) OR 0.31 (95% CI 0.12–0.85) No statistically significant association
Elshimy et al (18), 18 mo	n = 42 Age: mean 21 mo (range 1–58 mo) Sex not presented	Recovery: 71% Success: 88%	Complicating psychosocial factors (only investigated for nonresponders by chart review)	No statistical analysis performed
Loening-Baucke (22), 9–16 mo	n = 25 Age mean 9.9 y (range 5.8–15.4 y) Boys: 76%	Recovery: 36%	Age at presentation Time of onset of constipation Time of onset of encopresis Soiling frequency History of severe abdominal pain Presence of a palpable abdominal faecal mass Ability to relax external sphincter (electromyographic activity with 3 surface electrodes) Ability to defecate rectal balloon (balloon defecation test)	No association measures presented; not statistically significantly associated $P < 0.0001$ Recovery 70% (yes) vs 13% (no) Recovery 64% (yes) vs 14% (no)
Loening-Baucke (23), 12 mo	n = 104 Analysed children n = 97 Age mean 9.0 ± 2.4 y Boys: 71.1%	Recovery: 43%	Sex Age at presentation Time of onset of constipation and soiling Defecation frequency History of severe abdominal pain Nighttime urinary incontinence Previous urinary tract infection Mean soiling frequency/wk (recovered vs nonrecovered) Presence of a palpable abdominal faecal mass (initial evaluation and history) Inability to defecate rectal balloons (balloon defecation test) Abnormal contraction of the external anal sphincter during act of bearing down for defecation (electromyographic activity with 3 surface electrodes)	No association measures presented; not statistically significantly associated (10 vs 18) $P < 0.002$ (26% vs 62%) $P < 0.0006$ Relates to treatment failure ($P < 0.04$) Relates to treatment failure ($P < 0.01$)
Loening-Baucke (24), 6.9 y	n = 174 Age mean 2.2 ± 1.3 y Boys: 50%	Recovery at 12 mo: 63%	Sex Age at presentation Time of onset of constipation Defecation frequency Stool withholding Urinary tract infection Abdominal or rectal mass	No association measures presented for the whole group; no statistically significant differences between recovered children and nonrecovered children or children with soiling
Loening-Baucke (25), 12 mo	n = 232 Age mean 9 ± 3 y Boys: 75.9%	Recovery: 41.7% Success: 47.5%	Ability to defecate a 100-mL rectal balloon (balloon defecation test) Secondary encopresis (medical history)	OR 2.13 (95% CI 1.06–4.29) $P < 0.04$ OR 2.09 (95% CI 1.04–4.23) $P < 0.04$

TABLE 3. (Continued)

Study, follow-up	Population	Prognosis	Prognostic factors, instrument	Results (n, % or mean ± SD)
Michaud (26), 10 y	n = 72 Age mean 4 y (range/SD not presented) Boys: 55.6%	Success: 53%	Sex Age of onset <2 y Sporting activity ''Good'' food habits Initial good response to treatment Laxative use Anorectal dyssenergia	No association measures presented, no statistically significant differences between recovered and constipated children $P < 0.05$
Miele (27), 12 mo	n = 66 Age mean 3.9 ± 2.8 y Boys: 45.5%	Success: 70%	None presented	
Polanco (28), 6 mo	n = 154 Age mean 6.3 ± 3.33 y Boys: 46.8%	Success: 98.4%	None presented	
Staiano (6), 5 y	n = 103 Age median 4.7 y (range 1.3–11.3 y) Boys: 59.2%	Recovery: 48%	History of constipation in the first year of life Positive family history Presence of abdominal pain at 1 y from diagnosis Age of onset Soiling at presentation Age at presentation Presence of abdominal pain at presentation Sex Defecation frequency Megarectum/megacolon at diagnosis TGTT at diagnosis	Recovered 33.3% vs constipated 53.1% ($P < 0.05$) Recovered 26.6% vs constipated 40.6% ($P < 0.05$) $P < 0.05$ with persistence Recovered 3.0 ± 2.9 vs constipated 1.8 ± 1.4 ($P < 0.05$) Not statistically significantly associated
van den Berg et al (31), median 20 mo (range 6–52)	n = 47 Age median 3.5 mo (25th–75th percentiles 2.0–13.5). Boys: 59.6%	At 12 mo: Recovery: 60% Success: 77%	<2 mo of treatment before presentation <3 mo of symptoms before intake Sex Age of onset Defection frequency at presentation Prematurity at birth Delayed passage of meconium Positive family history (standardised questionnaire)	RR 2.4 (95% CI 1.2–4.8) RR 2.5 (95% CI 1.1–3.7) Not statistically significantly associated
van Ginkel et al (7), median 5 y (range 1–8)	n = 418 Age median 8 y (25th–75th percentiles 6–10) Boys: 33.3%	At 12 mo: Recovery: 59% Success: 83%	Male sex Age of onset of complaints 1–≤4 y (<1 y = reference category) Age of onset of complaints >4 y (<1 y = reference category) Duration of symptoms 4–≤12 (0–<4 mo = reference category) Duration of symptoms >12 (0–<4 mo = reference category) Positive family history Difference of 7 encopresis episodes/wk at intake Hard faecal bolus found on physical examination (standardised questionnaire and PE)	RR+ 95% CI for first success 1.08 (0.82–1.42) 1.00 (0.75–1.32) 1.55 (1.11–2.15) 0.95 (0.66–1.35) 0.81 (0.59–1.11) 1.14 (0.79–1.64) 0.87 (0.80–0.94) 0.97 (0.74–1.28)
Martinez-Costa et al (32), 12 mo	n = 62 Age median 6.1 y (range 1–14 y) Boys: 40.3%	Success: 85%	None presented	None presented

OR = odds ratio; CI = confidence interval; CTT = colonic transit time; PE = physical examination; RR = relative risk; TGTT = total gastrointestinal transit time; SD = standard deviation.

* Recovery: no constipation as defined by the authors of the included study, and no laxative use.

† Success: no constipation as defined by the authors of the included study, with or without laxative use.

TABLE 4. Prognostic factors (best evidence synthesis)

Prognostic factor		Methodological quality	Results	Association with recovery	Best evidence synthesis	Reference
Demographics	Sex	High	OR 0.34 (0.16–0.70)	neg	Conflicting	de Lorijn et al (17)
			No association measures presented	no		van den Berg et al (31)
			OR 1.08 (0.82–1.42)	no		van Ginkel et al (7)
		Low	No association measures presented	no		Loening-Baucke (23)
			No association measures presented	no		Loening-Baucke (24)
			No association measures presented	no		Michaud (26)
			OR 1.71 (0.62–4.77)	no		Staiano (6)
	Age at intake	Low	No association measures presented	no	Limited evidence for no association	Loening-Baucke (22)
			No association measures presented	no		Loening-Baucke (23)
			No association measures presented	no		Loening-Baucke (24)
			Recovered 11.1 ± 3.4 vs constipated 10.3 ± 3.1 ($P = 0.34$)	no		Staiano (6)
Medical history	Age of onset	High	No association measures presented	no	Conflicting	van den Berg et al (31)
			>4 y (<1 y = ref): RR 1.55 (1.11–2.15)	pos		van Ginkel et al (7)
		Low	No association measures presented	no		Loening-Baucke (22)
			No association measures presented	no		Loening-Baucke (23)
			No association measures presented	no		Loening-Baucke (24)
			<2 y (>2 y ref): no association measures presented	no		Michaud (26)
			Age of onset recovered 3.0 ± 2.9 y vs constipated 1.8 ± 1.4 y ($P < 0.05$)	pos		Staiano (6)
	Positive family history for childhood constipation	High	No association measures presented	no	Strong evidence for no association	van den Berg et al (31)
			RR 1.14 (0.79–1.64)	no		van Ginkel et al (7)
		Low	Recovered 26.6% vs constipated 40.6% ($P < 0.05$)	neg		Staiano (6)
	Duration of symptoms <3 mo before presentation	High	No association measures presented	pos	Limited	van den Berg et al (31)
	Treatment duration <2 mo before presentation	High	No association measures presented	pos	Limited	van den Berg et al (31)
	Premature birth	High	No association measures presented	no	Limited	van den Berg et al (31)
	Delayed passage of meconium	High	No association measures presented	no	Limited	van den Berg et al (31)
	History of constipation in the first year of life	Low	Recoverd 33.3% vs constipated 53.1% ($P < 0.05$)	neg	Insufficient	Staiano (6)
Clinical symptoms	Defecation frequency	High	≥3/wk OR = 1 (ref)		Strong evidence for no association	de Lorijn et al (17)†
			>1–3/wk: 1.48 (0.54–4.08)			
			0–1/wk: 1.06 (0.40–2.80)	no		
			No association measures presented	no		van den Berg et al (31)
		Low	Recovered 5 ± 4 BM/wk vs nonrecovered 4 ± 5 BM/wk ($P = 0.28$)	no		Loening-Baucke (23)
			No association measures presented	no		Loening-Baucke (24)
			Recovered 2.3 ± 1.7 BM/wk vs constipated 1.9 ± 1.8 BM/wk ($P = 0.37$)	no		Staiano (6)
	Presence of faecal incontinence episodes	Low	OR 2.09 (1.04–4.23) $P < 0.04$	pos	Insufficient	Loening-Baucke (25)
			Recovered 6.6% vs constipated 12.5%, OR 1.81 (0.34–11.82)	no		Staiano (6)

	Frequency of faecal incontinence episodes	High	No encopresis: OR = 1 (ref) <1/day: 0.58 (0.14–2.43) 1–2/day: 0.44 (0.11–1.68) ≥2/day: 0.44 (0.12–1.68)	no	Conflicting	de Lorijn et al (17)†
			Difference of 7 encopresis episodes/wk at intake: RR = 0.87 (0.80–0.94)	neg		van Ginkel et al (7)
		Low	No association measures presented	no		Loening-Baucke (22)
			Recovered 10/wk vs nonrecovered 18/wk, $P < 0.002$	neg		Loening-Baucke (23)
	Abdominal pain at presentation/ history of abdominal pain	Low	No association measures presented	no	Limited evidence for no association	Loening-Baucke (22)
			Recovered 49% vs nonrecovered 44%, OR 1.22 (0.55–2.74)	no		Loening-Baucke (23)
			No association measures presented	no		Staiano (6)
	Production of large stools	High	OR 1.09 (0.51–2.30)	no	Limited evidence for no association	de Lorijn et al (17)
	Urinary tract infection	Low	OR 0.35 (0.09–1.27)	no	Insufficient	Loening-Baucke (23)
			No association measures presented	no		Loening-Baucke (24)
	Nighttime urinary incontinence	Low	No association measures presented	no	Insufficient	Loening-Baucke (23)
	Stool withholding	Low	No association measures presented	no	Insufficient	Loening-Baucke (24)
Physical examination	Absence of a rectal or abdominal mass	High	Rectal mass: OR 3.39 (1.30–8.83)	pos	Conflicting	de Lorijn et al (17)
			Abdominal mass: OR 1.23 (0.49–3.10)	no		van Ginkel et al (7)
			Hard faecal bolus on PE: RR 0.97 (0.74–1.28)	no		
		Low	Presence of abdominal mass related to nonrecovery: $P < 0.0001$	neg		Loening-Baucke (22)*
			Abdominal mass: recovered 26% vs nonrecovered 62%, ($P < 0.0006$)	neg		Loening-Baucke (23)
			Abdominal or rectal mass: no association measures presented	no		Loening-Baucke (24)
Additional examination	Balloon defecation	Low	Ability to defecate at least 2/3 balloons: no association measures presented	pos	Insufficient	Loening-Baucke (22)
			Inability to defecate a 100-mL balloon in ≤1 min related to treatment failure: $P < 0.04$	pos		Loening-Baucke (23)*
			Ability to defecate balloon: OR 2.13 (1.06–4.29) ($P < 0.04$)	pos		Loening-Baucke (25)
	Relaxation of external sphincter	Low	Ability to relax external sphincter: no association measures presented	pos	Insufficient	Loening-Baucke (22)
			Abnormal contraction of external sphincter related to treatment failure: $P < 0.01$	pos		Loening-Baucke (23)*
	CTT/TGTT	High	CTT >100 h OR 0.31 (0.12–0.85)	neg	Limited evidence for a negative association	de Lorijn et al (17)
		Low	TGTT (h) recovered: 87.6 ± 22.0 vs constipated 89.3 ± 19.9 ($P = 0.75$)	no		Staiano (6)
	Megarectum and/or megacolon at diagnosis	Low	Recovered 53.3% vs constipated 62.5%	no	Insufficient	Staiano (6)

BM = bowel movement; CTT = colonic transit time; neg = negative; OR = odds ratio; pos = positive; RR = relative risk; SD = standard deviation; TGTT = total gastrointestinal transit time.
* Not included in best evidence synthesis.
† Results summarised as "no."

association between abdominal pain and recovery from constipation.

Urinary Tract Infection

Both of the 2 low-quality studies (23,24) found no significant association between previous urinary tract infections and recovery from constipation. Evidence for this association is insufficient.

Physical Examination

Palpable Rectal or Abdominal Mass

Two high-quality studies (7,17) evaluated the relation between absence of a rectal or abdominal mass on physical examination and recovery from constipation. One study (7) found no statistically significant association, whereas the other study (17) found absence of a palpable rectal mass to be positively associated but absence of palpable abdominal mass not significantly associated with recovery. These findings provided conflicting evidence for an association. In addition, 1 low-quality study found no significant association between absence of an abdominal or rectal mass and recovery (24), another low-quality study found a negative association (23), and yet another low-quality study (22) investigated the association between presence of an abdominal mass and treatment failure, and found a negative association.

Additional Examination

Balloon Defecation

On the association between the ability to defecate a rectal balloon and recovery, 2 low-quality studies (22,25) reported a positive association that provides insufficient evidence. Another low-quality study (23) that reported on the association between the disability to defecate a rectal balloon and treatment failure found a positive association as well.

Relaxation of External Anal Sphincter

One low-quality study (22) found a positive association between the ability to relax the external sphincter and recovery. Another low-quality study (23) investigated the association between an abnormal contraction of the external sphincter and treatment failure, and also found a positive association. This provides insufficient evidence.

Colonic Transit Time/Total Gastrointestinal Transit Time

We found 2 studies reporting on the association between colonic transit time or total gastrointestinal transit time and recovery. One high-quality study (17) found a negative association, and 1 low-quality study (6) found no significant association. In conclusion, we found limited evidence that children with a longer transit time have a lower recovery rate.

In addition, there are several prognostic factors that were investigated in 1 high-quality study. We found limited evidence that premature birth (31), delayed passage of meconium (31), and production of large stools (17) are not associated with recovery. There is also limited evidence that children with duration of symptoms of <3 months before presentation and children with treatment duration of <2 months have a higher recovery rate than children with longer treatment or symptom duration (31).

DISCUSSION

To our knowledge, no previous reviews on prognosis or prognostic factors of childhood constipation have been performed. In the present systematic review, only 14 articles concerning the course of childhood constipation and its determinants could be included. The majority of these studies showed poor methodological quality. Furthermore, studies were heterogeneous, encompassing different definitions, populations, outcome measures, and follow-up periods. Without regard to these differences, $60.6\% \pm 19.2\%$ of the children who were diagnosed with constipation are free of symptoms after 6 to 12 months. In addition, $49.3\% \pm 11.8\%$ of the children studied for 6 to 12 months recovered and were taken off laxatives. After a follow-up period of 1 to 2 years, $58.0\% \pm 14.1\%$ of the children recovered and were taken off laxatives, and after 5 to 10 years, this percentage does not rise any further, being $56.0\% \pm 11.3\%$. Children included in a specialist setting show a higher success rate ($74.2\% \pm 14.5\%$) than children included in general paediatric departments ($57.8\% \pm 19.5\%$).

Based on the present literature, there is substantial evidence that defecation frequency and a positive family history are not associated with recovery of constipation. With limited level of evidence, a short duration of symptoms and treatment before presentation results in better prognosis, whereas studies evaluating other factors in the medical history showed no relation or were insufficient to draw firm conclusions. Conflicting evidence exists on the prognostic value of sex, age of onset, and faecal incontinence. Furthermore, there is insufficient evidence available to determine the role of prognosis for one third of the prognostic factors described in literature.

Limitations

A potential shortcoming of this systematic review is the literature search. To minimise the risk of missing relevant publications as much as possible, we performed an extensive and sensitive literature search without language restrictions.

Various outcome measures have been used in the included studies. A definition of recovery, resolution, or success was described by every author except for 2 (4,12), but no uniformity among these definitions existed. Of all of the symptoms that may occur with constipation, only defecation frequency was consistently included in the recovery definitions, but not all of the studies applied the same limiting value.

Because there were large variations in presentation of outcome and prognostic factors between the studies, it was impossible to perform a true meta-analysis on prognostic factors. In the best evidence synthesis we present a summary of the studies reporting on a prognostic factor. We assessed the methodological quality of the included studies for the best evidence synthesis using a standardised list. Because of misclassification of items, bias may occur. However, of the 14 included studies, only 3 scored as having high quality. Because of the low-quality scores of most studies, misclassification of 1 item would not change the classification into a high methodological quality. Therefore we assume that the effect of a possible bias on the results is minimal. Nevertheless, published results per prognostic factor were scarce. Therefore, the results of the evidence-based synthesis should be interpreted with caution.

In the best evidence synthesis, we only considered statistically significant associations as associated prognostic factors. We included several studies with a small sample size (implying low statistical power), of which misclassification could have occurred because their results did not reach statistical significance. Statistically pooling of data would have been a solution to this problem, but it was not possible because of the large clinical heterogeneity.

However, we found that small sample size did not influence the results of our best evidence synthesis.

Prognosis

Despite differences between the studies included, we statistically pooled data to summarise results on prognosis of constipation. Although the overall 6- to 12-month success rate of constipation in children was found to be 60.6%, a large variation (range 36.0%–98.4%) (22,28) among included studies was found. Interpretation of these pooled recovery rates is biased because studies were heterogeneous with regard to study populations and definitions of constipation and outcome measures used.

The finding that prognosis is more favourable for children in specialised centres than for children in general paediatric departments is somewhat surprising. Previous research showed that prognosis is better the earlier the treatment starts after the onset of constipation (1). Because children usually first present to their general practitioner or paediatrician before being referred to a more specialised centre, one would expect better prognosis in first- and second-line settings. Furthermore, children with constipation referred to a tertiary centre are most likely children with more severe symptoms of constipation unresponsive to conventional treatment. Children seen in specialist settings may receive more advanced or more aggressive treatment than children in general paediatric settings. Because of the large diversity between the studies, it was impossible to make a valid comparison of study populations. This also counts for the treatment regimens applied, although the evidence for an effect of treatment of functional constipation is not sufficiently proven (34).

Prognostic Factors

The present literature shows strong evidence that a positive family history is not associated with recovery of constipation. Strong evidence also exists that defecation frequency is not an influence on prognosis of constipation. This finding supports the idea that functional constipation is a disease entity that has more aspects than defecation frequency only, as described in the Rome III criteria (4).

The present review does not provide insight into the prognostic value of faecal incontinence. A negative influence would be expected based on experience, but at the moment evidence is conflicting because of a lack of studies evaluating its role.

Future Research

The results of our review show that further research by means of large follow-up studies on prognosis of childhood constipation and factors of influence on prognosis is necessary. We recommend using clear definitions for both the diagnosis of constipation and the recovery from constipation. This definition preferably is a uniform definition used worldwide, taking into account all aspects of constipation, such as the Rome III criteria (4). It is important to investigate prognosis not only in children seen in specialised settings but also in a more general population to gain insight into possible differences between these settings and the prognosis of constipation of recent onset. In addition, more detailed registration of symptom severity and treatment regimens applied is needed.

CONCLUSIONS

The few studies published on prognosis of childhood functional constipation and its predictive factors showed large clinical diversity and poor methodological quality. Overall 6- to 12-month recovery rate of constipation in children was found to be 60.6% regardless of laxative use, but large variation ranging from 36.0% to 98.4% among the included studies was found. Children included in a specialist setting show a higher recovery rate than children included in general paediatric departments. Recovery rate showed no relation to defecation frequency or positive family history. Based on the present literature, we are not able to identify a group of children at risk for poor outcome.

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