



UvA-DARE (Digital Academic Repository)

Defecation disorders and chronic abdominal pain in children. Pathophysiology and treatment

van Ginkel, R.

Publication date
2002

[Link to publication](#)

Citation for published version (APA):

van Ginkel, R. (2002). *Defecation disorders and chronic abdominal pain in children. Pathophysiology and treatment*. [Thesis, fully internal, Universiteit van Amsterdam].

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: <https://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 8

Childhood constipation: longitudinal follow-up beyond puberty

Rijk van Ginckel, Johannes B. Reitsma, Hans A. Büller, Michiel P. van Wijk, Jan A.J.M. Taminiau,

Marc A. Benninga

submitted for publication

1. Abstract

1.1 Background

There are sparse data about the prognosis of childhood constipation and its possible persistence into adulthood. Therefore, we initiated a prospective long-term follow-up study of children with chronic constipation.

1.2 Methods

From 1993 until 1999, 418 constipated patients older than 5 years at intake (279 boys; mean age 8.4 years) participated in several studies evaluating therapeutic modalities for constipation. All children were subsequently enrolled in the follow-up study, with prospective data collection, after an initial 6-week intensive treatment protocol, at 6 months and thereafter annually, using a standardized questionnaire.

1.3 Results

Follow up was obtained in more than 95% of the children. The median duration of follow-up period was 5 years (range, 1-8). The cumulative percentage of children who were successfully treated during follow up was 60% at 1 year, increasing to 80% at 8 years. Interestingly, successful treatment was more frequent in children without encopresis and in children with an age of onset of defecation difficulty older than 4 years. In the group of successfully treated children approximately 50% remained symptom-free during the follow up period, while the other half experienced at least one period of relapse. Relapses occurred more frequently in boys than in girls (RR 1.73, 95%CI 1.16 to 2.58). In the subset of children of 16 years and older, constipation was still present in circa 30%.

1.4 Conclusion

After an intensive initial medical and behavioral treatment, more than half of all children referred to a tertiary medical center for chronic constipation were successfully treated at one year of follow up. One third of the children followed up beyond puberty continued to have severe complaints of constipation. This finding contradicts the general belief that childhood constipation gradually disappears before or during puberty.

2. Introduction

Chronic constipation, often accompanied by encopresis (loss of feces in the underwear), is a common disorder in children, accounting for circa 3% of consultations in an average pediatric practice ⁽¹⁾. Pathophysiological mechanisms are hardly understood. This is largely due to the complex mechanisms involved in normal defecation and fecal continence and to the large diversity in the clinical presentation of children with chronic constipation. Treatment modalities are mainly based on empiricism rather than evidence. In 1984 it was already noticed, that “there are few long-term follow-up studies of the response to treatment of chronic constipation” ⁽²⁾. Almost 20 years later, this situation is not essentially changed and important questions remain to be answered. The general believe, that “they just do grow out of it” has never been substantiated. The difference in gender ratio between adult constipation (more women than men) and childhood constipation (more boys than girls) might point to different pathophysiologic mechanisms, however the possibility, that childhood constipation continues into adulthood accompanied by an increasing incidence of women in which defecation problems are the result of pregnancy or delivery, can not be excluded.

In the present study we report the long-term clinical outcome in a large cohort of referred constipated children over the past 10 years. Specific research questions are: 1) Does childhood constipation continue into young adulthood or will the majority of children overcome constipation during adolescence? and 2) Are there clinical characteristics associated with persistent constipation or relapse of symptoms after initial success?

3. Patients and Methods

3.1 Patients

All 418 patients who participated in one of the research protocols on childhood constipation between 1993 and 1999 were eligible. Patients were referred to the tertiary medical center with a gastro-intestinal motility outpatient clinic by family practitioners, pediatricians, psychiatrists and school doctors. At intake they had to fulfill the criteria for pediatric constipation as previously described ⁽³⁾. In short, at least 2 of the 4 following criteria had to be present: stool frequency less than three per week, two or more encopresis episodes per week, periodic passage of very large amounts of stool at least once every 7 – 30 days or a palpable abdominal or rectal mass on physical examination. In addition they must have had treatment with laxatives for a minimum period of 2 months before randomization in one of the protocols. Encopresis was defined as the voluntary or involuntary passage of a normal bowel movement in the underwear after the age of 4 years or was defined as the loss of loose stool in the underwear ⁽³⁾. At intake all children were at least 5 year of age, because they had to understand the anorectal manometric and biofeedback training procedures used in the research protocols.

Children with organic causes of constipation such as Hirschsprung’s disease, spina bifida (occulta), hypothyroidism or other metabolic or renal abnormalities, mental retardation and children using drugs influencing gastrointestinal function other than laxatives, were excluded.

3.2 Treatment protocols

All children participated in randomized trials comparing different treatment strategies. All patients were intensively treated during a 6 – 8 week intervention period with 3-6 out-patient visits lasting 30 minutes³⁸. Therapy consisted in all cases of a standard conventional treatment protocol including enemas, oral laxatives (started with lactulose 5 g/ 10 kg body weight per day, increasing the dose until soft stools were obtained), high fiber diet, fill in of diary cards, and education about constipation. Motivation was enhanced by praise and small gifts. Out of the 418 children, 297 children received additional treatment, consisting of 5 biofeedback training sessions or 2 anorectal manometric sessions as part of their treatment regimen of the randomized trial in which they participated. Laxative therapy was continued until successful treatment was achieved and then tapered over a period of 3 months. Subsequently, laxative therapy was discontinued over a 4-week period, while monitoring defecation frequency and encopresis episodes. During the first year of follow up every patient was frequently seen (frequency dependent on severity of constipation) in the out patient clinic and were asked to contact us when a relapse occurred. Relapses were managed by a second course of the same initial treatment.

3.3 Definition of clinical outcome

A good clinical outcome during follow-up was defined as ≥ 3 bowel movements per week for a period of 4 weeks with less than 2 encopresis episodes per month, while not receiving laxatives in the previous 4 weeks³⁹. This strict definition of success was used in all the studies (category 1). However, to further assess clinical outcome, a second, third and fourth category were defined: the second category of children had the same clinical success as the first group, but was using laxatives (category 2), whereas the two last groups did not fulfill the clinical criteria of success, whether without the use of laxatives (category 3) or with the use of laxatives (category 4). A child was considered to have a relapse, when the defecation frequency became less than 3 times per week, and/or the encopresis frequency became more than once per two weeks, and/or the reintroduction of laxatives was necessary, after initial successful treatment.

3.4 Follow-up and data collection

Follow up was carried out for each patient at 6 months and annually after the last visit of the initially intensive 6 – 8 week treatment protocol. A standardized questionnaire was obtained from the child and parents together during an out-patient visit or by telephone when the child had been discharged from the out-patient department. Data concerning defecation frequency, encopresis episodes, etc. were based on a six- week period prior to the moment of follow-up. In addition to this 6 week period all relapses between the previous and current follow-up time were documented.

4. Statistical analysis

4.1 Baseline characteristics

Baseline characteristics of the cohort were analyzed in a descriptive way. For each of the fixed time points of follow-up we computed the distribution of patients over the four possible categories of clinical outcome. Differences between groups were compared using Chi-square tests. The frequency and timing of first success was presented in a Kaplan Meier curve without adjustment for the discrete nature of the follow-up.

To gain insight into the clinical characteristics that are associated with clinical outcome during follow-up we set up two different analyses.

4.2 Prognostic factors for success

In the first model, prognostic factors for the occurrence of first clinical success were analyzed. We used a complementary log-log regression model to examine the relation between predefined baseline characteristics and the probability of a good clinical outcome ⁽⁹⁾. This model assumes that a continuous time, proportional hazards model has generated the underlying observations, but because we observe only data grouped in yearly intervals we use a discrete hazard model to estimate the contributions of the independent variables to the hazard. It has been shown that the discrete hazard model generates unbiased estimates of the coefficients of a continuous time proportional hazards model ⁽⁹⁾. A limited set of predefined baseline factors was entered into the model without any further selection strategy. These candidate factors were selected based upon previous research findings and own interest. The following factors were examined: gender, age of onset of complaints, total period of treatment before intake, family history and frequency of encopresis. Age of onset of defecation difficulties and total period of treatment before intake were subdivided in four categories. Encopresis frequency was considered as a continuous variable.

4.3 Prognostic factors for relapse

In the second model we examined the factors that were associated with relapse in patients, who had initially been cured. In this conditional model, the time since the first success till relapse was analyzed (including the re-start of laxatives). The same discrete time model and the same set of candidate factors were examined. All analysis were performed with SAS software version 8.2.

5. Results

5.1 Baseline characteristics

5.1.1 Cohort enrolment and baseline characteristics

Between January 1, 1993 and December 31, 1999, a total of 418 children (67% boys) met the inclusion criteria of childhood constipation and were enrolled. The median age at intake was 8.0 years, whereas the median age of onset of defecation problems was 3 years. The median period of symptoms before intake was 5 years and 5 months and the median period of treatment before intake, including laxatives, enema's, psychological intervention etc., was 15 months. At intake, successful toilet training for bowel control, bladder control at day and at night was established in 65%, 92%, and 82%, respectively. Further characteristics are presented in Table 1.

The median age at intake was not different between boys and girls. However, there were some statistical significant differences in baseline characteristics between boys and girls. The median defecation frequency at intake was higher in boys than in girls (4.2 vs. 3.2 times per week; $p < 0.05$) as was the median frequency of daytime encopresis frequency (7.0 vs. 5.5; $p < 0.05$).

The total period of treatment before intake was significant longer in girls (median of 24 months) compared to boys (13 months) ($p = 0.006$), while the total period of symptoms of constipation before intake was not different.

At intake more boys than girls presented with encopresis (68 vs. 52%, $p = 0.03$). Furthermore, children with encopresis at intake reported more often a positive family history (25 vs. 11%, $p = 0.01$) compared to children without encopresis.

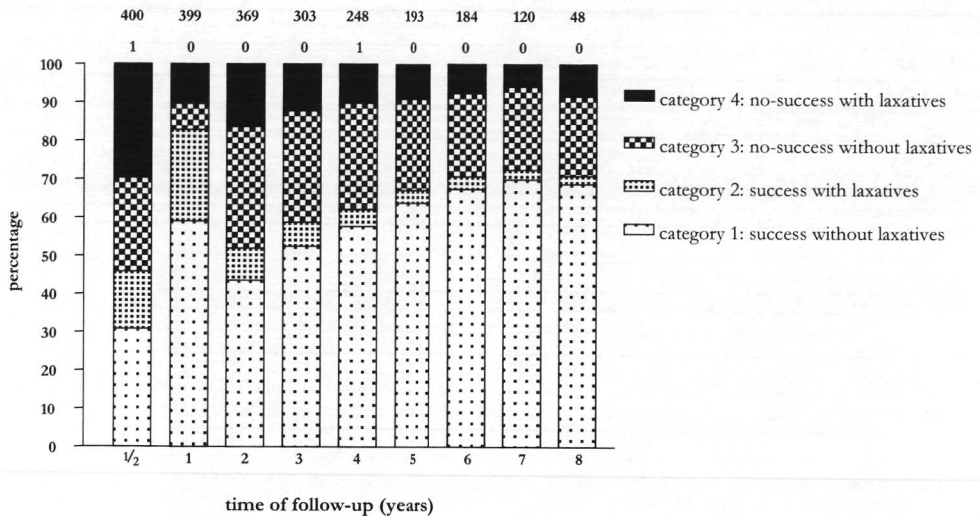
5.1.2 Clinical outcome during follow-up

Of the 418 children originally included in the study, 15 children were lost to follow up, due to drop out of the original studies during the first half year due to lack of compliance to the treatment protocols or due to development of evident psychological problems. The overall follow-up percentage was 96% due to the 15 patient who dropped out early in the study. Except these patients we missed one patient at 0.5 year follow-up and 1 at 4 years of follow-up (Table 1). Figure 1 shows the distribution of the patients over the four defined categories.

Table 1. Clinical characteristics of the children at the moment of intake

Characteristics	Value
Age – yr	
Median	8
Percentiles	
25	6
75	10
Sex – no. (%)	
Female	139 (33)
Male	279 (67)
Defecation frequency / week	
Median	2
Percentiles	
25	1
75	5.5
<3 times per week – no. (%)	240 (60%)
Encopresis frequency / week (daytime)	
Median	7
Percentiles	
25	3
75	14
≥ 2 times per week	84%
no encopresis	10%
Encopresis frequency (night)	27%
Large stools	62%
Rectal scybalus	28%
Abdominal scybalus	22%
Abdominal pain	51%
Painful defecation	41%
Rectal blood loss	4%
Rectal loss of mucus	5%
Anal fissures	<1%
Pos. family history	13%

Figure 1. (No)-Success full outcome with and without laxatives



This figure shows the distribution of the patients over the 4 defined clinical outcome categories in the different years of follow-up. The number on the top of each bar shows the number of patients available for follow up in that year. The second row shows the patient missed for follow-up in that year, except the 15 patients who dropped out the study before the first follow-up visit

At 1 year follow-up, 59% of the patients was successfully treated according to the strict criteria, increasing to 83%, when including the patients without symptoms but still using laxatives. Between one and two years of follow-up a decrease in successfully treated children was observed, but a slow increase was observed in the years thereafter. After 5 years the percentage was more or less stable around 70%.

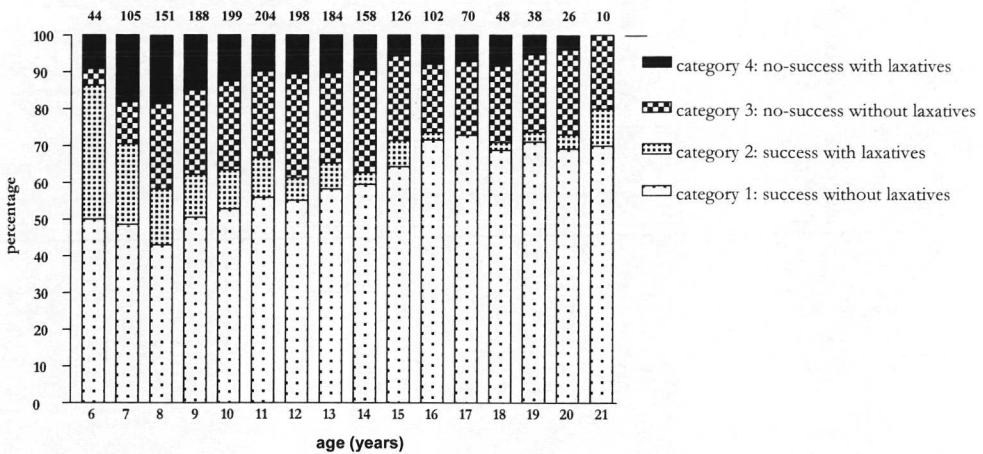
The observed changes in distribution of the children among the 4 groups between 1 and 2 years of follow-up were analyzed. Eighty-four of the 96 children who were successfully treated with laxatives at one year follow up, did also reach the follow-up of 2 years. These 84 children were equally distributed over the 4 defined categories at 2 years of follow-up. The total group of 117 children who were unsuccessfully treated without laxatives (category 3) at 2 years follow-up, consisted mainly (62%) of children who were successfully treated without the use of laxatives at 1 year follow-up (category 1).

From 2 years follow up circa 10% of the children were not successfully treated while getting laxative treatment (category 3), whereas circa 20% of the children were not successfully treated, but were also not getting any laxative therapy (category 4).

At 5 years of follow-up there were no statistical differences between boys and girls concerning successful treatment ($p = 0.7$; χ -square) or successful treatment with the use of

laxatives ($p = 0.2$; χ -square). Figure 2 shows the distribution of these four groups according to biological age.

Figure 2. (No)-Success full outcome with and without laxatives



This figure shows the distribution of the patients over the 4 defined clinical outcome categories at different ages. The number on the top of each bar shows the number of patients having reached that age during the total period of follow-up.

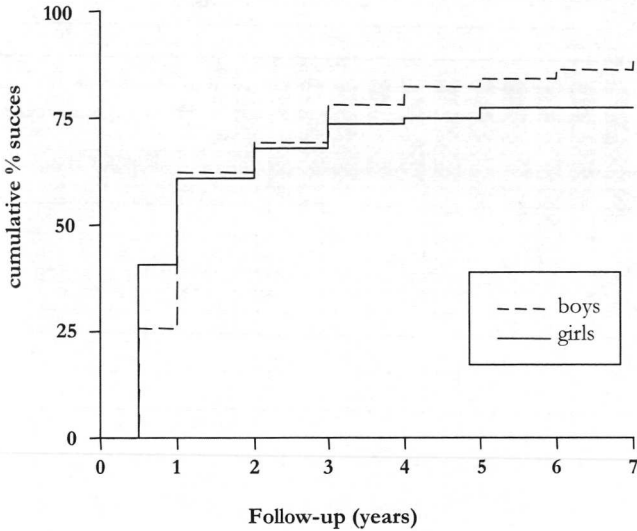
From the age of 9 years to 16 years a steady increase in successfully treated children is found, from 50% at age 9 to 70% at age 16. Thereafter this percentage remains stable up into young adulthood.

5.2 Timing, frequency and prognostic factors for first success and relapse after initial successful treatment

5.2.1 Success

Figure 3 shows the cumulative percentage of children achieving at least once successful treatment during follow-up.

Figure 3. Cumulative percentage of children achieving successful treatment



This figure shows the cumulative percentage of children who achieve successful treatment, showing no difference between boys and girls.

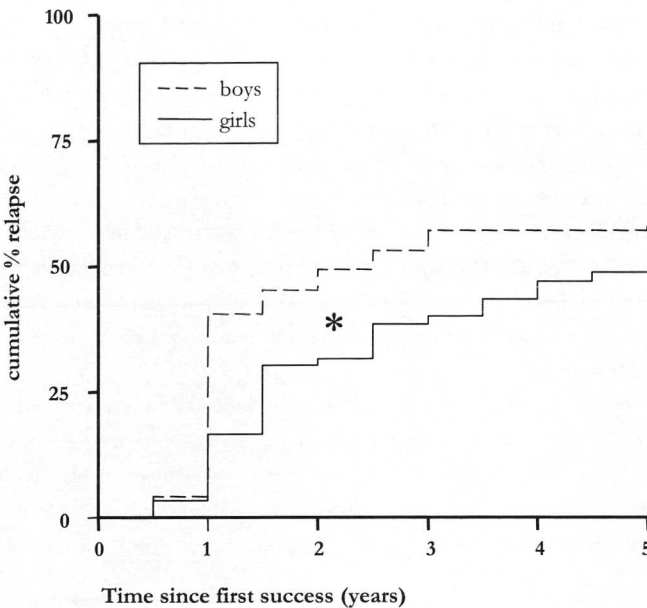
Within one year after the 6-8 weeks intervention period, clinical success is obtained in 63% of all patients. Thereafter, the increase in success rate is considerably slower. After 7 years of follow-up the percentage of children that did experience a successful treatment once during follow-up was 80%.

We found two factors significantly related to first treatment success in our multivariate model. First, successful treatment occurred more often in children in whom the symptoms of constipation developed after the age of 4 years compared to children in whom symptoms developed before their first birthday (RR 1.53, 95% CI 1.11 to 2.11). Second, encopresis frequency was negatively associated with a good outcome. A difference of encopresis frequency at intake of 7 episodes changed the probability of having a good outcome by 15% (RR 0.85, 95% CI 0.79 to 0.92). In addition, there was a trend towards a diminished number of successfully treated children in those with a longer period of symptoms before entry into the study (see table 2). Gender and a positive family history were not associated with achieving a good clinical outcome.

5.2.2 Prognostic factors for relapse after initial successful treatment

Figure 4 shows the timing and frequency of relapse after initial success.

Figure 4. Cumulative percentage of relapse after initial success



This figure shows the cumulative percentage of children who relapses after initial successful treatment, showing a significant larger relapse percentage in boys compared with girls (RR 1.71, 95% CI 1.15 to 2.55)

The conditional analysis of patients with an initial success (80% of the children) showed that relapse of symptoms is common: 17% of the girls and 41% of the boys had a relapse within the first year after success. The percentage of boys and girls without a relapse after 5 years after their initial successful treatment was respectively 41.8% and 51.2%.

The multivariate model of the risk of relapse confirmed that boys were more likely to experience a relapse than girls (RR 1.71, 95% CI 1.15 to 2.55). No other factors were associated with a higher frequency of relapses, in particular no detrimental effect of encopresis was found.

6. Discussion

This long-term follow-up study of chronically constipated children shows the persistence of complaints of constipation into young adulthood in one third of all patients. The cumulative percentage of children successfully treated during the total follow-up time of 8 years was 80%, whereas 60% was already achieved at 1 year follow up. Successful outcome was higher in children without encopresis at intake and in children with an age of onset older than 4 years. Fifty percent of the children had at least one relapse within the first 5 years after initial treatment success. Relapse was more common among boys than girls.

The higher prevalence of boys with constipation compared to girls, as observed in almost all studies in constipated children might not be the result of a difference in incidence (an 1:1 ratio was observed in children younger than one year ⁽¹⁰⁾), but might be due to a difference in initial start of treatment. The significant difference in treatment delay between girls and boys might suggest that symptoms of constipation, such as encopresis, are less accepted in girls than in boys. This earlier treatment of girls might result in the cure of a substantial number of girls, leading to the over-presentation of boys at a secondary or tertiary medical center.

As shown in figure 1 there is a remarkable shift in the 4 categories of treatment outcome between follow up at one versus two years. Analysis of the results show that this shift is mainly due to the transition of patients from successful treated patients (category 1) to unsuccessfully treated children not using laxatives (category 3). This suggests that successfully treated children who relapse do not restart the use of laxatives. Therefore, it seems important to continue frequent follow up visits at least for one year after successful treatment, to prevent or treat a possible relapse with laxatives.

Analyzing the total group by biological age, no increase in success rate was observed during puberty. After the age of 16 years, no apparent changes occurred leaving circa 30% of children unsuccessfully treated from which 65% does neither take any medical treatment nor visit a physician. They are often tired of taking medical therapy for long periods without any result. Thus, the onset of puberty is not accompanied by a spontaneous disappearance of symptoms of constipation.

It is clear from quality of life studies in children and young adults with fecal incontinence as result of Hirschsprung's disease or anorectal malformations that the involuntary loss of feces has a major negative impact on the psycho-social functioning of these children ⁽¹¹⁻¹³⁾.

We identified two negative prognostic factors for success; age of onset and presence of encopresis. The observed negative relation between an early age of onset and treatment success is in accordance with a previous study ⁽¹⁴⁾. It suggests a primarily organic underlying pathophysiological mechanism in these young children in contrast with children who have shown normal defecation for many years before experiencing symptoms of constipation. In contrast, the duration of symptoms before intake does not have a prognostic value.

The other negative prognostic factor implies that children with encopresis are more difficult to treat. In the majority this is the result of a large rectal scybalus (due to stool withholding or primary rectal dysfunction) leading to frequent soiling episodes. It underscores the need of rigorous and long-lasting laxative treatment and if necessary enema's to prevent rectal re-accumulation of feces.

Although other follow-up studies have been performed ^(2,10,14-18) comparison is difficult, as many of them have disadvantages such as using a cross-sectional instead of a longitudinal follow-up method, low follow-up percentages (40 – 74%), small number of patients (32 – 137 patients) or unclear inclusion criteria ⁽¹⁹⁾.

The advantages of this study are the uniform inclusion criteria and prospective data collection and the high percentage of follow-up (96%), excluding a possible bias in the studied population. A possible draw back is that the therapeutic regimen in the initial 6-8 weeks of treatment was not uniform, due to the participation in different trials. Nevertheless the basic therapeutic regime was the same in all studies. ^(3, 6,18)

In conclusion, successful treatment was achieved in 3 out of 4 children with chronic constipation, but relapses occur frequently. The large percentage of relapse during the first year of initial successful treatment stresses the importance of intensive follow-up. Constipation was still present in a substantial proportion (30%) of children after puberty.

Reference list

1. Loening-Baucke V. Chronic constipation in children. *Gastroenterology* 1993;105(5):1557-64.
2. Abrahamian FP, Lloyd-Still JD. Chronic constipation in childhood: a longitudinal study of 186 patients. *J Pediatr Gastroenterol Nutr* 1984;3(3):460-7.
3. Van der Plas RN, Benninga MA, Buller HA, Bossuyt PM, Akkermans LM, Redekop WK et al. Biofeedback training in treatment of childhood constipation: a randomised controlled study. *Lancet* 1996;348(9030):776-80.
4. Van der Plas RN, Benninga MA, Redekop WK, Taminiu JA, Buller HA. Randomised trial of biofeedback training for encopresis. *Arch Dis Child* 1996;75(5):367-74.
5. Van Ginkel R, Benninga MA, Blommaart PJ, Van der Plas RN, Boeckxstaens GE, Buller HA et al. Lack of benefit of laxatives as adjunctive therapy for functional nonretentive fecal soiling in children. *J Pediatr* 2000;137(6):808-13.
6. Van Ginkel R, Buller HA, Boeckxstaens GE, Van der Plas RN, Taminiu JA, Benninga MA. The effect of anorectal manometry on the outcome of treatment in severe childhood constipation: a randomized, controlled trial. *Pediatrics* 2001;108(1):E9.
7. Benninga MA, Buller HA, Taminiu JA. Biofeedback training in chronic constipation. *Arch Dis Child* 1993;68(1):126-9.
8. Benninga MA, Buller HA, Heymans HS, Tytgat GN, Taminiu JA. Is encopresis always the result of constipation? *Arch Dis Child* 1994;71(3):186-93.
9. Prentice RL, Gloeckler LA. Regression analysis of grouped survival data with application to breast cancer data. *Biometrics* 1978(34):57-67.
10. Loening-Baucke V. Constipation in early childhood: patient characteristics, treatment, and longterm follow up. *Gut* 1993;34(10):1400-4.
11. Hanneman MJ, Sprangers MA, De Mik EI, Ernest van Heurn LW, de Langen ZJ, Looyard N et al. Quality of life in patients with anorectal malformation or Hirschsprung's disease: development of a disease-specific questionnaire. *Dis Colon Rectum* 2001;44(11):1650-60.
12. Diseth TH, Bjornland K, Novik TS, Emblem R. Bowel function, mental health, and psychosocial function in adolescents with Hirschsprung's disease. *Arch Dis Child* 1997;76(2):100-6.
13. Bai Y, Chen H, Hao J, Huang Y, Wang W. Long-term outcome and quality of life after the Swenson procedure for Hirschsprung's disease. *J Pediatr Surg* 2002;37(4):639-42.
14. Sraiano A, Andreotti MR, Greco L, Basile P, Auricchio S. Long-term follow-up of children with chronic idiopathic constipation. *Dig Dis Sci* 1994;39(3):561-4.
15. Keuzenkamp-Jansen CW, Fijnvandraat CJ, Kneepkens CM, Douwes AC. Diagnostic dilemmas and results of treatment for chronic constipation. *Arch Dis Child* 1996;75(1):36-41.

16. Sutphen JL, Borowitz SM, Hutchison RL, Cox DJ. Long-term follow-up of medically treated childhood constipation. *Clin Pediatr (Phila)* 1995;34(11):576-80.
17. Loening-Baucke V. Persistence of chronic constipation in children after biofeedback treatment. *Dig Dis Sci* 1991;36(2):153-60.
18. Loening-Baucke V. Biofeedback treatment for chronic constipation and encopresis in childhood: long-term outcome. *Pediatrics* 1995;96(1 Pt 1):105-10.
19. Bellman M. Studies on encopresis. *Acta Paediatr Scand* 1966:Suppl 170.

