Six-year-old children had greater risks of functional gastrointestinal disorders if their parents had mental health conditions

Signe Heuckendorff1,2 | Martin Nygård Johansen3 | Charlotte Overgaard4 | Søren Paaske Johnsen2,5 | Janus Laust Thomsen5,6 | Kirsten Fonager1,5

1Department of Social Medicine, Aalborg University Hospital, Aalborg, Denmark
2Danish Center for Clinical Health Services Research, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark
3Unit of Clinical Biostatistics, Aalborg University Hospital, Aalborg, Denmark
4Public Health and Epidemiology Group, Department of Health Science and Technology, Aalborg University, Aalborg, Denmark
5Department of Clinical Medicine, Aalborg University, Aalborg, Denmark
6Center for General Practice, Aalborg University, Aalborg, Denmark

Correspondence
Signe Heuckendorff, Department of Social Medicine, Aalborg University Hospital, Havrevangen 1, 9000 Aalborg, Denmark. Email: s.heuckendorff@rn.dk

Funding information
This study was funded by The Danish Regions Fund for research in prevention (grant no A3224). The funder had no involvement in an aspect of the study or paper

Abstract

Aim: This study examined any associations between parents' mental health conditions and hospital diagnoses of functional gastrointestinal disorders (FGIDs) in offspring at the age of six. We also examined any associations between children who met these criteria and attended routine Danish preventive child health examinations.

Methods: Nationwide registers identified all children born in Denmark from 2000 to 2011 and parents' mental health conditions. Negative binomial regression analyses estimated the incidence rate ratios (IRRs) with 95% confidence intervals (CIs) of children receiving their first hospital diagnosis for an FGID at the age of six.

Results: We identified 750,379 children and 38% had at least one parent with a mental health condition: 24% were minor, 12% were moderate, and 2% were severe. These children faced a higher risk of an FGID diagnosis than children whose parents did not have mental health conditions. The IRRs were highest for maternal exposure: minor (1.35, 95% CI 1.29–1.42), moderate (1.58, 95% CI 1.48–1.67) and severe (1.58, 95% CI 1.38–1.81). Attending routine preventive child health examinations was associated with a higher risk of FGIDs associated with parents' mental health conditions.

Conclusion: Paediatric FGIDs were associated with parents' mental health conditions, especially mothers, and attending routine preventive child health examinations.

KEYWORDS
Gastrointestinal diseases, mental health, parents, preventive health services

1 | INTRODUCTION

Functional gastrointestinal disorders (FGIDs) are common in children and are defined by the Rome IV criteria.1 The most common FGIDs are functional abdominal pain disorders, which affect about 13.5% of all children,2 followed by functional defecation disorders (11–18%),3 and functional nausea and vomiting disorders (0.2–4.2%).3 The majority (90%) of children with abdominal pain or constipation have no discernible organic pathology,4 and it is preferable that FGIDs are treated by primary care doctors.5,6

Abbreviations: ATC, anatomical therapeutic chemical; FGID, functional gastrointestinal disorder; ICD-10, International Classification of Diseases, 10th Revision; IR, incidence rate; IRR, incidence rate ratio.
Functional gastrointestinal disorders are multifactorial and influenced by biological, psychological and social factors. Early adverse childhood events, such as the loss of a parent, parental divorce or alcohol abuse, can play an important role in the development of FGIDs. Family characteristics, such as socioeconomic status and parental functional problems, appear to influence how chronic abdominal pain is. Parental anxiety and maternal depression have been shown to be associated with recurrent abdominal pain, but it is unknown whether other parental or general mental health conditions are associated with an increased risk of FGIDs. Mental health conditions are common in parents, and have been associated with adverse child health.

In Denmark, all children aged 0–5 years are offered seven routine preventive child health appointments by primary care doctors, to ensure they have the best physical, mental and social conditions for healthy development. In addition, primary care doctors play a central role in identifying children and families with special care needs at an early stage. It has been reported that children have a greater risk of morbidity if their parents have mental health conditions than if they do not. Therefore, these children may particularly benefit from child health appointments that include preventive healthcare, early detection and counselling from primary care doctors with knowledge of both the parents and the child. These examinations have been referred to as interventions to reduce inequality in child health. Children who attend preventive child health examinations may have a lower risk of a hospital diagnosis of an FGID than those who do not, especially if their parents have mental health conditions. However, the impact of preventive child health visits has been poorly studied and this theory has never been explored.

The main aim of this study was to examine associations between parents’ mental health conditions and hospital diagnoses of FGIDs in their offspring at 6 years of age. We also wanted to examine any associations between children who met these criteria and attended preventive child health examinations.

2 METHODS

2.1 Study design, setting and participants

This cohort study used nationwide registers. Data linkages were achieved via the personal identity number that is assigned to all Danish residents at birth or when individuals become residents. The register keepers at Statistics Denmark carried out the data collection and register linkage. All the data were deidentified before the researchers received access.

We followed up children in Denmark who were born from 2000 to 2011 when they reached 6 years of age to see whether a first hospital diagnosis of an FGID had been recorded. This age was chosen because previous research identified a peak in FGID prevalence at the age of six. Most children undergo their routine 5-year examination during their sixth year and before they turn 6 years old. Therefore, the follow-up period was between the children’s sixth and seventh birthday.

Key Notes

- This study examined associations between diagnoses of functional gastrointestinal disorders (FGIDs) and parents’ mental health conditions and attending routine Danish preventive child health examinations.
- We identified 750,379 children born from 2000 to 2011 and the 38% with at least one parent with a mental health condition faced a higher risk of FGID.
- Children with a higher risk of FGIDs associated with parents’ mental health conditions were more likely to attend preventive examinations.

We searched the parents’ health records to see whether they had received a mental health diagnosis between the child’s first and sixth birthdays. Children were excluded if the parents’ identification number was missing, meaning that they could not be linked to the parents, or if the children or parents were not living in Denmark between the child’s first and seventh birthdays.

2.2 Data sources

Information on the children’s date of birth, sex, country of origin, municipality and the parents’ cohabitation status was obtained from the Danish Civil Registration System. The parents’ highest level of completed education was extracted from the Population Education Registry. The National Patient Register provided information on inpatient and outpatient contacts and diagnoses that used the International Classification of Diseases, Tenth Revision (ICD-10) codes. The Danish National Prescription Registry provided information on reimbursed drug prescriptions, using the Anatomical Therapeutic Chemical (ATC) classification system. The Danish Health Service Register for Primary Care provided information on primary care doctor services, as well as contacts with private psychologists and psychiatrists practising outside a psychiatric hospital.

2.3 Parents’ mental health

We measured the severity of the parents’ mental health based on the treatment they received. Parents with minor mental health conditions were treated solely in primary healthcare settings. Moderate mental health conditions required a higher level of mental healthcare. The most severe mental health conditions were placed in a separate category. The Danish Health Service Register for Primary Care provides information from the primary health sector where minor or the least complex mental health conditions in Denmark are treated by primary care doctors and psychologists. However, this register does not contain information on...
diagnoses and this meant that minor mental health conditions had to be identified in a different way. Mental health services, such as talk therapy and psychometric tests performed by primary care doctors and contacts with psychologists, are registered and were used. Furthermore, prescriptions of antidepressants and anxiolytics were used.

The criteria for minor mental health conditions included at least two prescriptions of antidepressant medication (ATC N06AB and N06AX) and at least two prescriptions of anxiolytics (benzodiazepines: ATC N03AE, N05BA, N05CD and N05CF). They also included at least two sessions of talk therapy with the primary care doctor, at least two psychometric tests by the primary care doctor and/or at least one contact with a private psychologist. The criteria did not include contacts with a psychiatrist, at, or, outside a psychiatric hospital. The criteria for moderate mental health conditions were mental health conditions treated by psychiatrists practising outside a psychiatric hospital, including child and adolescent psychiatrists and/or any psychiatric diagnosis (ICD-10 F00-99) registered at a psychiatric hospital. These excluded the diagnoses included in the severe group.

The severe category included the following ICD-10 diagnoses registered at psychiatric hospitals: F20-22 (schizophrenia), F30-31 (bipolar disease) and F32-34 (unipolar depression) if combined with a registered psychiatric inpatient admission, and F60.3 (emotionally unstable personality disorder) if combined with a registered psychiatric inpatient admission.

The three exposure groups were mutually exclusive, and the reference group contained those parents who did not meet any of the criteria for minor, moderate or severe mental health conditions.

2.4 | Preventive child health examinations

In Denmark, all children are offered seven examinations during their first 5 years of life. The first three examinations are during the first year, followed by one examination a year at the ages of two, three, four and five. The last four examinations were included in the present study.

The examinations were organised into three categories: attending all or just missed one, missed two or three and missed all four examinations.

2.5 | Functional gastrointestinal disorders

We defined offspring FGIDs based on primary or secondary ICD-10 diagnoses recorded during inpatient and outpatient hospital visits. The following diagnoses were identified, based on the Rome IV criteria, paediatric guidelines and paediatrician guidance: nausea and vomiting (DR11), functional dyspepsia (DK30), irritable bowel syndrome (DK58), abdominal pain (DR100-108), other specified general symptoms and signs, gastrointestinal (R688A9B2), constipation (DK590), faecal incontinence (DR15) and gastro-oesophageal reflux disease without oesophagitis (DK219).

2.6 | Other covariates

We included the following parental characteristics: their age, whether they lived with a partner or not and the mental health condition of the other parent, namely none, minor, or moderate to severe. Education was based on the levels of the International Standard Classification of Education (2011) and grouped into three categories according to the parent’s highest educational attainment. These were level 0–2 if they had 10 years of mandatory education or below, level 3–4 for 10–14 years of education, such as high school, and level 5–8 for more than 14 years of education, such as a bachelor’s degree.

To account for geographic variations in access to healthcare services, we divided the municipality into four categories: outer, rural, intermediate and city. We also included the child’s sex, the calendar year they were born in and their country of origin, broken down into Nordic, Western European and other. We used restricted cubic splines with three knots to adjust for the parents’ age and calendar year. All covariates were extracted at baseline.

2.7 | Statistical methods

The numbers and percentages of the covariates and the outcomes by any parents’ mental health condition were calculated. The following analyses were conducted separately for the mother and the father: the number of children with outcomes, namely the cases, and the incidence rates (IRs). Adjusted incidence rate ratios (IRR)s were estimated using negative binomial regression on the first hospital diagnosis of an FGID due to overdispersion of data. To account for siblings, the estimates were fitted using generalised estimating equations with an exchangeable correlation structure.

The association between preventive child health examination participation and hospital diagnosis of an FGID was examined by calculating the IRRs for the strata of the parents’ mental health conditions, with attending routine child health appointments as the independent variable. Due to too few observations in these strata, moderate and severe mental health conditions were combined into one category for these analyses.

We also wanted to examine whether the association between the parents’ mental health condition and hospital diagnoses of FGIDs applied to both acute and planned hospital contacts. To do this, separate analyses were conducted for FGID diagnoses from hospital admissions and outpatient contacts.

A sensitivity analysis that excluded children with an FGID diagnosis before baseline was performed. We also analysed three strata of birth years: 2000–2003, 2004–2007 and 2008–2011.
3 | RESULTS

The analyses comprised 750,379 children, as we excluded 24,035 (2.8%) children due to a missing parental personal identification number and 72,463 (8.6%) because the child and/or the parents were not living in Denmark at baseline or during the exposure period (Figure 1).

Table 1 shows the sociodemographic characteristics by parents’ mental health conditions at baseline. Almost a quarter (23.7%) of the children had at least one parent with a minor mental health condition, 11.9% had at least one parent with a moderate condition, and 2.1% had at least one parent with a severe mental health condition.

In the exposed groups, 1.4%, 1.6% and 1.7% of the children had a hospital FGID diagnosis during the follow-up period. In the reference group, which was no mental health conditions in the parents, 1.0% of the children had an FGID diagnosis. Furthermore, 71.4% of the children in the reference group attended all the preventive child health appointments or only missed one, compared with 67.6%, 57.7% and 53.4% of the children with at least one parent with a minor, moderate or severe mental health condition, respectively.

For both maternal and paternal mental health conditions, the IR of an FGID diagnosis was higher for the exposed groups than for the reference group (Figure 2) and highest for the mothers’ mental health conditions.

The adjusted IRRs showed an increase of 36% (IRR 1.36, 95% CI 1.30–1.42) for the children of mothers with minor mental health conditions compared with the reference group. The figures were a 57% increase (IRR 1.57, 95% CI 1.48–1.67) for the children of mothers with moderate conditions and 58% (IRR 1.58, 95% CI 1.38–1.81) for the children of mothers with severe conditions. The respective figures for the father’s mental health conditions were an increased risk of 10% for minor (IRR 1.10, 95% CI 1.04–1.16), 14% for moderate (IRR 1.14, 95% CI 1.06–1.23) and 13% for severe mental health conditions (IRR 1.13, 95% CI 0.96–1.32).

Participation in preventive child health examinations, compared with no participation, was associated with an increased risk of an FGID diagnosis in the overall population (Figure 3). The same association was seen for all three levels of mental health conditions. For the children of mothers with no mental health conditions, the risk was increased by 15% (IRR 1.15, 95% CI 1.02–1.30) if they attended all examinations or missed one compared with missing all examinations (reference). The estimate was even higher in the exposed children: 24% (IRR 1.24, 95% CI 1.02–1.49) in the children of mothers with minor mental health conditions and 30% (IRR 1.30, 95% CI 1.06–1.60) in the children of mothers with moderate-to-severe conditions. The same pattern was observed for the children of fathers with mental health conditions, but mostly without statistical significance.

The separate analyses for inpatient and outpatient hospital contacts yielded similar estimates (Table S1). For example, if the mothers had minor mental health conditions, the adjusted IRR for a child with a hospital diagnosis of FGID was 1.33 (95% CI 1.23–1.43), whereas for an outpatient FGID diagnosis, it was 1.37 (95% CI 1.29–1.44).

Excluding the 38,382 children with a previous hospital diagnosis of an FGID did not change the estimates markedly (Table S2). The adjusted IRRs were 1.34 (95% CI 1.27–1.41) for maternal minor mental
### Table 1: Sociodemographic characteristics, numbers and percentages, by parents' mental health condition (at least one parent with a mental health condition)

| Parental mental health condition | None       | Minor      | Moderate   | Severe     |
|----------------------------------|------------|------------|------------|------------|
| Number of children (%)           | 466,826 (62.2) | 178,097 (23.7) | 89,463 (11.9) | 15,993 (2.1) |
| Child sex, %                     |            |            |            |            |
| Boys                             | 51.1       | 51.3       | 51.5       | 51.9       |
| Diagnosis of functional gastrointestinal disorder, % | 1.0       | 1.4       | 1.6       | 1.7       |
| Preventive child health examinations (age 2-5), % |          |            |            |            |
| Attending all or missing one exam | 71.4       | 67.6       | 57.7       | 53.4       |
| Missing 2-3 examinations         | 24.4       | 27.7       | 35.1       | 38.1       |
| Missing all (4) examinations     | 4.2        | 4.7        | 7.2        | 8.5        |
| Socioeconomic characteristics    |            |            |            |            |
| Maternal age at birth of the child, % |          |            |            |            |
| <25                              | 9.8        | 12.0       | 22.5       | 26.0       |
| 25–32                            | 50.7       | 48.8       | 44.9       | 43.6       |
| >32                              | 39.5       | 39.1       | 32.6       | 30.3       |
| Missing                          | 0.1        | 0.0        | 0.0        | 0.1        |
| Paternal age at birth of the child, % |          |            |            |            |
| <25                              | 4.4        | 5.7        | 11.6       | 13.6       |
| 25–32                            | 38.6       | 37.9       | 37.9       | 37.7       |
| >32                              | 56.8       | 56.3       | 50.5       | 48.7       |
| Missing                          | 0.1        | 0.0        | 0.1        | 0.1        |
| Maternal educational level, %    |            |            |            |            |
| ISCED 0–2                        | 11.8       | 14.8       | 30.6       | 37.3       |
| ISCED 3–4                        | 37.8       | 38.9       | 38.2       | 36.6       |
| ISCED 5–8                        | 49.5       | 45.5       | 29.8       | 24.5       |
| Missing                          | 1.0        | 0.7        | 1.4        | 1.6        |
| Paternal educational level, %    |            |            |            |            |
| ISCED 0–2                        | 14.2       | 17.2       | 29.7       | 34.5       |
| ISCED 3–4                        | 45.5       | 46.5       | 43.8       | 42.2       |
| ISCED 5–8                        | 39.1       | 35.0       | 24.1       | 20.2       |
| Missing                          | 1.2        | 1.2        | 2.4        | 3.1        |
| Country of origin, %             |            |            |            |            |
| Nordic                           | 91.8       | 93.5       | 86.1       | 85.3       |
| Western Europe                   | 0.5        | 0.3        | 0.3        | 0.4        |
| Other                            | 7.7        | 6.1        | 13.6       | 14.3       |
| Missing                          | 0.0        | 0.0        | 0.0        | 0.0        |
| Municipality, %                  |            |            |            |            |
| Outer                            | 8.3        | 8.0        | 7.5        | 9.1        |
| Rural                            | 27.2       | 28.3       | 28.0       | 29.2       |
| Intermediate                     | 16.3       | 18.0       | 16.4       | 17.1       |
| City                             | 47.8       | 45.6       | 47.9       | 44.6       |
| Missing                          | 0.4        | 0.2        | 0.1        | 0.1        |
health conditions, 1.45 (95% CI 1.35–1.55) for moderate conditions and 1.50 (95% CI 1.27–1.76) for severe conditions.

Table S3 shows that the numbers and risks of an FGID diagnosis increased in the three time periods. The association between the parents’ mental health condition and a child FGID diagnosis was stronger in 2004–2007 and 2008–2011 than 2000–2003.

4 | DISCUSSION

This study demonstrated an association between parents having minor, moderate or severe mental health conditions and their children facing an increased risk of a hospital diagnosis of FGID at 6 years of age. The association was most evident if the mothers had mental health conditions. Furthermore, we found an association between attending routine preventive child health appointments and a higher risk hospital FGID diagnosis in children. This was seen in both the overall population and the children of parents with mental health conditions. The association between preventive child health examination participation and FGID tended to be stronger for the children of parents with mental health conditions.

4.1 | Interpretation

We previously reported associations between minor and moderate-to-severe mental health conditions in parents and higher child healthcare use in general. This also seems to apply to paediatric FGIDs treated in hospital settings. As well as showing an increased number of hospital contacts, the current study also supports earlier findings of an association between maternal depression and higher prevalence of child somatic health complaints, including stomach ache and constipation. They also show an association between maternal and paternal anxiety and child recurrent abdominal pain. Furthermore, our results may indicate an increased risk of more severe or complex cases of FGIDs in exposed children. This is because a hospital FGID diagnosis could be interpreted as a severe FGID, as these cases require referral from primary care doctors. The results could also reflect help-seeking behaviour in exposed parents. However, on the contrary, these findings could also indicate an inappropriately high number of referrals from the primary care doctor. These could lead to the excess use of hospital services, and this issue would need action and prevention. Further studies are needed to explore this, for example by including information on FGID severity.

Parents’ poor mental health could affect the occurrence of children’s FGIDs via numerous potential mechanisms. First, parental involvement is crucial when handling paediatric FGIDs because central elements in FGID treatment, such as education and psychological therapy, include both the child and parents. Many mental health conditions can affect cognitive functions and parental skills. For example, one study reported that depression was associated with a range of difficulties in parenting behaviour. These included high rates of negative interactions, fewer positive interactions with the child and being less responsiveness to
child behaviour. Therefore, handling paediatric FGIDs might be even more demanding for parents with mental health conditions. Furthermore, evidence suggests that parental anxiety has an adverse effect on the severity and chronicity of symptoms, and that having an accepting family that supports child’s coping skills improves symptoms.

Second, stressors might play an important role. Several studies have found an increased prevalence of abdominal pain in children with high stress levels and identifying stressors is an important part of an FGID diagnosis. Having parents with poor mental health is often referred to as a childhood stressor or adverse childhood event, associated with a wide range of negative child health outcomes. It could be hypothesised that this could affect child FGID by increasing their stress levels.

Third, gastrointestinal and mental health problems often co-occur and mental health problems are frequently seen in children if their parents have mental health problems. Thus, FGIDs in children could reflect a predisposition to mental health conditions or transmission of functional disorders across a generation through genetics and social learning mechanisms.

Attending routine preventive child health examinations was associated with an increased risk of a hospital diagnosis of FGIDs in the children of parents with mental health conditions. Primary care doctors play a key role in handling paediatric FGIDs, because they have knowledge of both the children and parents. However, handling FGIDs in children when their parents have poor mental health may be time consuming and require extensive knowledge. One study examined the attention that Danish primary care doctors paid to the children of parents with depression. The authors reported that more than half of the primary care doctors referred to lack of time and almost half wanted to learn more about the potential consequences of the parents’ depression. The study also found out that the primary care doctors were six times more likely to give the child the attention they needed if they felt knowledgeable about the impact that parental depression had on children. Another study reported that parents rarely mentioned their worries about their
child’s psychosocial health or their own mental well-being during preventive child health examinations and the primary care doctors did not ask.28  

Moreover, the findings of our study might reflect help-seeking behaviour in parents and children attending preventive child health examinations. When children attend preventive child health examinations parents might be more anxious about any symptoms the child has and demand further assessments in hospital settings. This can happen regardless of whether the parents have mental conditions.

The routine preventive child health examinations are complex interventions that depend on the primary care doctor, the parents and the child. The effect of these examinations has been poorly studied, and explanations of any associations are needed.

4.2 | Implications

Our study emphasises the importance of parents’ mental health when handling paediatric FGIDs. Although the association was strongest for maternal exposure, the father’s exposure showed an independent association and his role should not be ignored.

Further studies are needed to explore the association between parents’ mental health and child FGIDs. However, the present study highlights the relevance of public health, due to the high prevalence of children with parental mental health conditions and the consequences of FGIDs. These include school absences, further FGIDs and anxiety.29 We suggest that primary care doctors, paediatricians and others working with children with FGIDs enquire about parents’ mental health, along with other potential stressors.8,18 Furthermore, providing tailor-made education about FGIDs for parents and children, based on the family’s needs and resources, must be prioritised. This will support families to handle FGIDs. Attention should be paid to the parents’ possible anxiety about the child’s symptoms, along with patterns of help-seeking behaviour.

Although the routine child health examinations provide primary care doctors with extensive, preventive opportunities, our findings may indicate they did not make full use of these. This may indicate the need for them to receive further training and possibly improved guidelines.

Having said that, we found no comparable studies and this means that the results of this study regarding preventive child health examinations must be interpreted with caution and further examined in future studies.

4.3 | Strengths and limitations

One major strength of this study was the use of the nationwide registers, ensuring complete the follow-up on an entire birth cohort in Denmark and allowing for powerful statistical analyses.

The limitations included the lack of validated FGID diagnoses and potential differences in coding strategies. However, a study that reviewed the data quality of the Danish National Patient Registry reported correct categorisation of primary diagnoses, at the three-digit level, for 82% of the cases in paediatrics. This increased to 89% when alternative diagnoses were accepted.30

Paediatric FGIDs may also be treated by paediatricians practising outside hospitals.18 However, data on diagnoses from practising paediatricians are not available in the registers.

Furthermore, we were only able to identify parents with mental health conditions who had sought medical care during the relevant periods of their child’s life. The absence of any data on clinical assessments and medication would have meant they were placed in the reference group. This may have led to any associations between parents’ mental health conditions and offspring FGID diagnosis being underestimated.

5 | CONCLUSION

Children of parents with minor, moderate or severe mental health conditions faced an increased risk of a hospital FGID diagnosis at 6 years of age. Our main findings highlight the negative impact of parents’ poor mental health on paediatric FGIDs.

The findings of associations between taking part in routine preventive child health examinations and higher risks of paediatric FGID hospital diagnosis for all groups of mental health conditions should be interpreted with caution. Further studies are needed.

ACKNOWLEDGEMENTS

The authors are grateful to paediatrician Charlotte Eggertsen for her support.

ORCID

Signe Heuckendorff  https://orcid.org/0000-0002-4074-064X

REFERENCES

1. Hyams JS, Di Lorenzo C, Saps M, Shulman RJ, Staiano A, Van Tilburg M. Childhood functional gastrointestinal disorders: child/adolescent. Gastroenterology. 2016;150(6):1456-1468.e2. doi:10.1053/j.gastro.2016.02.015

2. Korterink JJ, Diederen K, Benninga MA, Tabbers MM. Epidemiology of pediatric functional abdominal pain disorders: a meta-analysis. PLoS One. 2015;10(5):e0126982. doi:10.1371/journal.pone.0126982

3. Mugie SM, Benninga MA, Di Lorenzo C. Epidemiology of constipation in children and adults: a systematic review. Best Pract Res Clin Gastroenterol. 2011;25(1):3-18. doi:10.1016/j.bpg.2010.12.010

4. Andrews ET, Beattie RM, Tighe MP. Functional abdominal pain: what clinicians need to know. Arch Dis Child. 2020;105(10):938-944. doi:10.1136/archdischild-2020-318825

5. Berger MY, Gietelink MJ, Benninga MA. Chronic abdominal pain in children. BMJ. 2007;334(7601):997-1002. doi:10.1136/bmj.39189.465718.BE

6. Flik CE, Laan W, Smout AJPM, Weusten BLAM, de Wit NJ. Comparison of medical costs generated by IBS patients in primary and secondary care in The Netherlands. BMC Gastroenterol. 2015;15(1):168. doi:10.1186/s12876-015-0398-8
