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2023

Document Version:

Publisher's PDF, also known as Version of record

[Link to publication](#)

Citation for published version (APA):

Telborn, L. (2023). *Dietary aspects of Hirschsprung's disease*. [Doctoral Thesis (compilation), Department of Clinical Sciences, Lund]. Lund University, Faculty of Medicine.

Total number of authors:

1

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Dietary aspects of Hirschsprung's disease

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FACULTY OF MEDICINE | LUND UNIVERSITY



Dietary aspects of Hirschsprung's disease

Dietary aspects of Hirschsprung's disease

Lovisa Telborn



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DOCTORAL DISSERTATION

Doctoral dissertation for the degree of Doctor of Philosophy (PhD)
at the Faculty of Medicine at Lund University, Sweden.

To be publicly defended on December 8th 2023, at 13.00 in Belfragesalen, Lund

Faculty opponent

Associate professor Elisabeth Stoltz Sjöström
Umeå University, Sweden

Organization: LUND UNIVERSITY

Document name: DOCTORAL DISSERTATION

Date of issue: December 8th 2023

Author: Lovisa Telborn

Title: Dietary aspects of Hirschsprung's disease

Abstract:

Background Hirschsprung's disease is a congenital bowel motility disorder requiring surgery. Residual gastrointestinal complaints are frequently reported by patients, and dietary advice in management of gastrointestinal symptoms is requested. However, there is a gap of knowledge in the effects of diet on gastrointestinal symptoms in children in general. Also, disease-specific dietary guidelines for Hirschsprung's disease are lacking.

Aim The aim of this thesis was to expand knowledge of dietary impact on gastrointestinal symptoms in children with and without Hirschsprung's disease. The overall aim was to start building evidence on the effects of diet on gastrointestinal symptoms in children in order to support patients' dietary self-treatment with evidence-based knowledge.

Methods A qualitative focus group study with 10 parents to children with Hirschsprung's disease was conducted. Based on the results, a questionnaire was developed and qualitatively validated by cognitive interviews with 18 parents and 13 children, followed by structured refinements. Using the questionnaire, the qualitative results of the focus groups were quantitatively investigated by case control studies of 265 healthy children and 71 children with Hirschsprung's disease.

Results Parents in the focus groups emphasised diet as a strong influencer on their child's gastrointestinal complaints. Dietary restrictions were described to impact on the family and daily life. In the questionnaire, each question's relevance was ranked highly but most questions needed refining for clarity and comprehension. The Diet and Bowel Function questionnaire comprised 13 questions on dietary effects on gastrointestinal symptoms and daily life. Only a minority of healthy children reported diet to induce gastrointestinal symptoms. Children with Hirschsprung's disease reported dietary effects on gastrointestinal symptoms and daily life more frequently than controls, and other food items to induce symptoms. The differences remained when comparing children only with gastrointestinal complaints.

Conclusions Diet is an integral part of families' self-treatment of children with Hirschsprung's disease. Effects of diet on gastrointestinal symptoms differ between children with Hirschsprung's disease and healthy children. The results from the thesis indicate a profound need for evidence-based disease-specific dietary advice for families with children with Hirschsprung's disease.

Key words: Diet, Hirschsprung's disease, children, gastrointestinal symptoms, patient-reported outcome

Language: English

ISSN and key title: 1652-8220

Number of pages: 71

ISBN: 978-91-8021-491-9

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Dietary aspects of Hirschsprung's disease

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Lund University, Faculty of Medicine Doctoral Dissertation Series 2023:149

ISBN 978-91-8021-491-9

ISSN 1652-8220

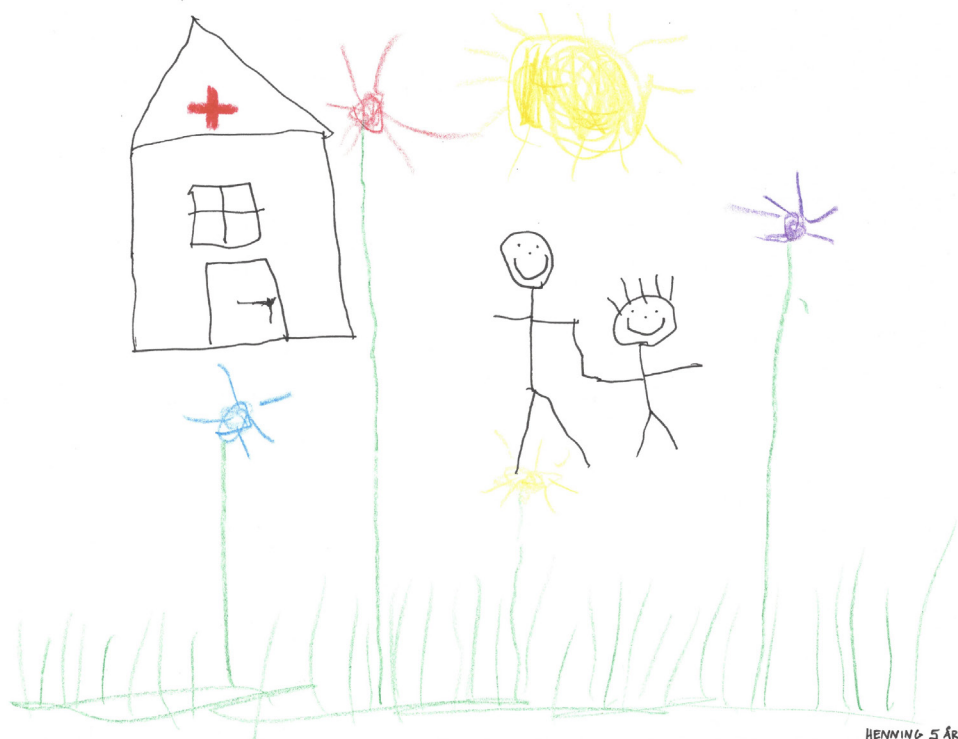
Printed in Sweden by Media-Tryck, Lund University

Lund 2023



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MADE IN SWEDEN 



*This thesis is dedicated to the children with
Hirschsprung's disease and to their families*

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List of publications

- I. **Telborn L**, Tofft L, Hallström I, Axelsson I, Brandström F, Stenström P. Diet plays a central role in parent's self-treatment of children with Hirschsprung's disease – a focus group study. *Acta Paediatrica* 2021;110(9):2620-2617.
- II. **Telborn L**, Kumlien C, Granéli C, Axelsson I, Stenström P. Diet and bowel function in children with Hirschsprung's disease: development and content validation of a patient-reported questionnaire. *BMC Nutrition* 2023;9,78.
- III. **Telborn L**, Axelsson I, Granéli C, Stenström P. Self-reported effects of diet on gastrointestinal symptoms in healthy children. *Journal of Pediatric Gastroenterology and Nutrition*. 2023;77:433-438.
- IV. **Telborn L**, Granéli C, Axelsson I, Stenström P. Children with Hirschsprung's disease report dietary effects on gastrointestinal complaints more frequently than controls. *Children*. 2023;10:1543

Abbreviations

BFS	Rintala Bowel Function Score
COREQ	Consolidated criteria for reporting qualitative research
ERNICA	European Reference Network for Health and Care Excellence
FODMAP	Fermentable Oligosaccharides Disaccharides Monosaccharides And Polyols
IBS	Irritable bowel syndrome
NICE	(British) National Institute for Health and Care Excellence

Thesis at a glance

	Aims	Methods	Key Results
I	To explore parental experiences of dietary effects on gastrointestinal complaints in children with Hirschsprung's disease	Qualitative focus group study analysed by content analysis	Parents emphasised diet as a strong influencer on their child's gastrointestinal complaints. The child's diet and gastrointestinal complaints impacted on the families' daily life.
II	To develop and qualitatively test content validity of a questionnaire for children with and without Hirschsprung's disease, to be able to later quantitatively explore experiences of dietary effects on bowel function.	Development of a questionnaire (based on results from Study I). Qualitative content validation through cognitive interviews analysed by informal analysis.	The Diet and Bowel Function questionnaire; 13 questions about dietary effects on gastrointestinal complaints and daily life and 90 specific food items.
III	To investigate self-reported dietary effects on gastrointestinal symptoms in healthy children.	Observational cross-sectional case control study of age and gender groups using self-reporting questionnaire (developed in Study II). Non-parametric and parametric statistical tests.	Only a minority (8%) of healthy children, regardless of their gastrointestinal symptoms, reported diet to induce gastrointestinal symptoms. They reported few food items that induced gastrointestinal effects.
IV	To investigate self-reported dietary effects on gastrointestinal symptoms and daily life, comparing children with Hirschsprung's disease and healthy children.	Observational cross-sectional case-control study using self-reporting questionnaire (developed in Study II). Non-parametric and parametric statistical tests.	A majority (77%) of children with Hirschsprung's disease reported diet to induce gastrointestinal symptoms. They reported a higher number of food items (n=7) compared to controls (n=2) and different foods to induce gastrointestinal symptoms.

Striving to regulate bowel function through dietary strategies

Restricting diet to control bowel function impact on family and daily life

Wishing for dietary and nutritional guidelines for facilitating self-treatment

Diet is a strong influencer on bowel function in Hirschsprung's disease

Conclusions

Diet plays a key role in parental self-treatment of gastrointestinal complaints in their children with Hirschsprung's disease.

Dietary guidelines for patients with Hirschsprung's disease are anticipated.

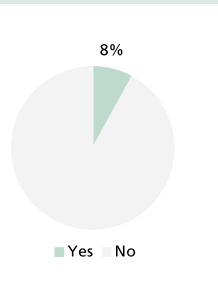
13 questions about dietary effects on gastrointestinal symptoms and daily life

90 specific food items' effects on gastrointestinal symptoms

The Diet and Bowel Function questionnaire

The Diet and Bowel Function can be used as a survey questionnaire to enhance understanding of dietary effects on gastrointestinal symptoms in children, but also as a clinical instrument to assess dietary focus of the family and the importance of specific food items for the patient,

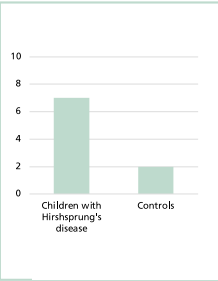
The questionnaire enables the children to answer.



Only a minority of healthy children reported diet to induce gastrointestinal symptoms

Few healthy children report that diet induces gastrointestinal symptoms. Children who already experience gastrointestinal symptoms to a higher extent than others report that diet impacts gastrointestinal symptoms, but still to a very limited extent.

Results can be used to determine accurate expectations and goals for dietary treatment of gastrointestinal symptoms in children.



Median seven food items per child were reported to induce gastrointestinal symptoms

Diet-induced gastrointestinal symptoms and dietary adjustments' impact on daily life are reported more frequently by children with Hirschsprung's disease than controls.

The results indicate a need for disease-specific dietary advice to improve support for families of children with Hirschsprung's disease.

Abstract

Background Hirschsprung's disease is a congenital bowel motility disorder requiring surgery. Residual gastrointestinal complaints are frequently reported by patients, and dietary advice in management of gastrointestinal symptoms is requested. However, there is a gap of knowledge in the effects of diet on gastrointestinal symptoms in children in general. Also, disease-specific dietary guidelines for Hirschsprung's disease are lacking.

Aim The aim of this thesis was to expand knowledge of dietary impact on gastrointestinal symptoms in children with and without Hirschsprung's disease. The overall aim was to start building evidence on the effects of diet on gastrointestinal symptoms in children in order to support patients' dietary self-treatment with evidence-based knowledge.

Methods A qualitative focus group study with 10 parents to children with Hirschsprung's disease was conducted. Based on the results, a questionnaire was developed and qualitatively validated by cognitive interviews with 18 parents and 13 children, followed by structured refinements. Using the questionnaire, the qualitative results of the focus groups were quantitatively investigated by case control studies of 265 healthy children and 71 children with Hirschsprung's disease.

Results Parents in the focus groups emphasised diet as a strong influencer on their child's gastrointestinal complaints. Dietary restrictions were described to impact on the family and daily life. In the questionnaire, each question's relevance was ranked highly but most questions needed refining for clarity and comprehension. The Diet and Bowel Function questionnaire comprised 13 questions on dietary effects on gastrointestinal symptoms and daily life. Only a minority of healthy children reported diet to induce gastrointestinal symptoms. Children with Hirschsprung's disease reported dietary effects on gastrointestinal symptoms and daily life more frequently than controls, and other food items to induce symptoms. The differences remained when comparing children only with gastrointestinal complaints.

Conclusions Diet is an integral part of families' self-treatment of children with Hirschsprung's disease. Effects of diet on gastrointestinal symptoms differ between children with Hirschsprung's disease and healthy children. The results from the thesis indicate a profound need for evidence-based disease-specific dietary advice for families with children with Hirschsprung's disease.

Populärvetenskaplig sammanfattning

Den här avhandlingen visar att mat har en central betydelse för familjer med barn som har Hirschsprungs sjukdom. Med hjälp av maten försöker föräldrarna få kontroll över barnens magbesvär, vilket påverkar familjernas dagliga liv. Hos barn överlag verkar matens påverkan på magbesvär vara begränsad, men barn med Hirschsprungs sjukdom tycks uppleva en större effekt av maten än friska barn. Barn med Hirschsprungs sjukdom får även andra magsymtom av mat än friska barn. Avhandlingen visar på ett stort behov av forskningsbaserade kostråd vid magbesvär, speciellt för barn med Hirschsprungs sjukdom.

Hirschsprungs sjukdom är en medfödd tarmsjukdom. Trots att den sjuka delen av tarmen opereras bort under de första levnadsmånaderna har de flesta barn med Hirschsprungs sjukdom besvär med magen under uppväxten; till exempel genom förstoppning, spänd och svullen mage, gaser, magsmärtor och/eller avföringsläckage. Behandling för magbesvären är till exempel läkemedel eller lavemang, men barnen och deras föräldrar frågar ofta sjukvården om vilken mat de ska äta för att må bättre. Det finns väldigt lite kunskap om vilken mat som lindrar magbesvär hos barn och framförallt hos barn med Hirschsprungs sjukdom. Det finns idag inga speciella kostråd för barn med Hirschsprungs sjukdom.

I denna avhandling har matens påverkan på magbesvär hos barn undersökts genom att studera både barn med och utan Hirschsprungs sjukdom. Målet är att sjukvården på sikt ska kunna ge familjer forskningsbaserat stöd i frågor om mat och magbesvär.

Matens betydelse och påverkan på magbesvär undersöktes genom diskussionsgrupper med föräldrar till barn med Hirschsprungs sjukdom och genom en enkät till de barn med Hirschsprungs sjukdom som behandlas vid Skånes Universitetssjukhus. Eftersom maten kan antas påverka magbesvär hos alla barn fick även friska barn utan tarmsjukdom svara på samma enkät.

Maten visades ha stor betydelse för barn med Hirschsprungs sjukdom; en majoritet (77%) svarade att maten påverkar deras magbesvär, vilket var fler jämfört med friska barn där ungefär hälften svarade att maten påverkar magbesvär i någon utsträckning. Det var också fler barn med Hirschsprungs sjukdom som anpassade maten för att må bättre; 69% jämfört med 32% bland friska barn. Barnen med Hirschsprungs sjukdom

rapporterade fler livsmedel som påverkade magbesvär, sju livsmedel per barn jämfört med två livsmedel per barn för friska barn. Det var skillnad i vilka livsmedel som påverkade magbesvär och även skillnad i vilken typ av magbesvär som barnen rapporterade. De vanligaste livsmedlen som rapporterades av barn med Hirschsprungs sjukdom var mjölk, banan och majs, medan friska barn rapporterade bönor, plommon och grädde.

Även om många barn svarade att maten påverkar magbesvär i någon utsträckning, så var det få barn som svarade att maten ofta eller alltid påverkar magbesvär. Möjligheten att kontrollera magbesvär enbart genom anpassningar av maten verkar vara väldigt begränsad. Resultaten från avhandlingen kan användas i individuell kostrådgivning till barn med magbesvär, men med försiktighet eftersom matens effekt tycks vara begränsad och individuell. För att med större säkerhet veta på vilket sätt mat påverkar magbesvär hos barn med Hirschsprungs sjukdom behövs mer forskning. Resultaten från avhandlingen kan användas för att planera undersökningar med kostbehandling för magbesvär.

Background

Introduction

“We talk about poop all the time! And what to eat, or not to eat.”

This citation reflects the ever-present focus of gastrointestinal symptoms and food, and was expressed by a mother to a child with Hirschsprung’s disease.

In my work as a dietician, specialized in paediatrics at the Department of Paediatric Surgery at Skåne University Hospital in Lund, I often meet children with Hirschsprung’s disease. The children and their parents frequently request dietary counselling, in order to improve gastrointestinal complaints. The importance of diet for patients was reflected in our prioritization study, conducted in collaboration with the National Hirschsprung’s Disease Patient Organization of Sweden, in which diet was the highest ranked requested research topic by families of children with Hirschsprung’s disease.

Bowel management in Hirschsprung’s disease includes laxative drugs and/or enemas to improve gastrointestinal complaints. Recently, dietary management was included in the European guidelines; however, there is a paucity of knowledge about if and which foods actually have an impact on gastrointestinal symptoms in children in general, and in children with Hirschsprung’s disease in particular.

My motivation for this thesis derives from the lack of evidence regarding the role of diet for gastrointestinal complaints in children with Hirschsprung’s disease. Thus, the overall aim of the thesis was to explore and increase the understanding of dietary impact on gastrointestinal symptoms, in order to improve the evidence-based support for patients’ self-treatment.

Hirschsprung's disease

Hirschsprung's disease is a congenital intestinal motility disorder (1-5). In Sweden, about 25 children are born with Hirschsprung's disease per year; the global incidence is 1:5,000 (1-2,4-6). The disease is characterized by an absence of ganglia cells (nerve cells) in the intestinal wall (1,3-5). The aganglionic part of the bowel always stretches orally from the anus. Rectosigmoid aganglionosis, or short-segment Hirschsprung's disease, presents in approximately 80% of cases (1,4). Long-segment Hirschsprung's disease extends beyond the sigmoid colon, still not involving the caecum. Total colon aganglionosis, affecting 2-5% of all patients with Hirschsprung's disease, refers to when the colon and up to 50 centimetres of the small intestine is aganglionic (7-8). The anatomic parts of the colon are displayed in **Figure 1**.

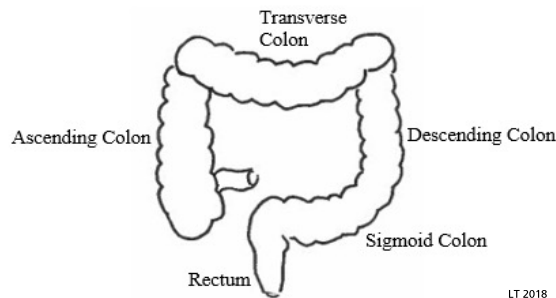


Figure 1. The different parts of the colon and rectum.

Physiology of the colon and rectum

The colonic primary functions are absorption of water and electrolytes, production and absorption of vitamins, and moving chyme (from here on described as stools) toward the rectum. Up to 90% of the water and most nutrients are absorbed in the small intestine, the remaining water and nutrients are absorbed in the ascending colon (9). Intestinal microbiota impact nutrition, for example, by production of short fatty acids, being involved in vitamin synthesis and lipid and protein metabolism (10). Stools are stored in the rectum. An internal and an external sphincter interact in controlling defecation and preventing faecal incontinence. When the rectum is distended, the involuntary internal sphincter relaxes. The stool passes to the anal canal, discriminating between solid, liquid and gas. Defecation may then occur by voluntary relaxation of the external sphincter (11).

Pathophysiology, symptoms and diagnosis

The absence of ganglia cells in Hirschsprung's disease results in a loss of intestinal motility; the aganglionic segment becomes contracted and fails to relax during peristalsis, leading to functional obstruction (1,3-5). Symptoms of Hirschsprung's disease include abdominal distention, vomiting and delayed passage of meconium (after the first 24-78 h of life) (4-5). The vast majority (90%) present during the neonatal period. Diagnosis is made by rectal biopsy. In cases of Hirschsprung's disease, the histopathological evaluation will reveal a lack of ganglion cells (1,12).

Hirschsprung's associated enterocolitis

Hirschsprung's associated enterocolitis can appear both pre- and postoperatively, and in most cases within two years after definitive surgery. Specifically, the perioperative prevalence is 18%. Hirschsprung's associated enterocolitis is one of the major complications of Hirschsprung's disease, associated with morbidity and mortality rates of up to 30%. The condition is characterised by diarrhoea, distended abdomen, lethargy and fever. The pathogenesis of enterocolitis is not completely known, but has been reported to associate with bowel obstruction, genetics, and general infections (2,13). Rectal irrigations and botulinum toxin injections after surgery are used to prevent enterocolitis. Treatment includes rectal irrigations, antibiotic treatment, and hydration (1-2).

Initial and surgical treatment

After diagnosis of Hirschsprung's disease, the initial treatment aims to prevent Hirschsprung's associated enterocolitis and ensure bowel emptying. For this purpose, rectal irrigations are performed one to three times a day by using a rectal tube. The treatment can be done by the parents at home, with healthcare support at regular follow-up visits at the out-patient clinic (1-2). For children with long segment aganglionosis, rectal irrigations are usually not enough to manage bowel emptying, as it is difficult to reach the ganglionic part of the bowel. These children need an early operation establishing an enterostomy (7-8).

Surgical treatment aims to remove the aganglionic segment of bowel to relieve the functional obstruction, and to preserve the continence mechanism by sparing the anal canal and sphincter mechanism. There are several different surgical techniques, all of which have in common that ganglionic bowel is brought down to the anal canal for anastomosis. Surgery is usually performed electively 2-12 weeks after diagnosis when the bowel has been decompressed and the infant is stable (1,5).

Dietary management of gastrointestinal complaints in Hirschsprung's disease

Despite surgical treatment, residual gastrointestinal complaints are frequently reported (1-8,14-16). Gastrointestinal symptoms can prevail to varying degrees into adulthood, although several studies show that functional outcomes may improve with age (3-4,16). Gastrointestinal complaints may impact social functioning and quality of life in the individual with Hirschsprung's disease and their family (1-5,7-8).

Physiological factors affecting the outcome

There are several physiological factors affecting the outcome and gastrointestinal complaints in children with Hirschsprung's disease. Since aganglionosis even involves the anal canal, part of this also needs resection. Loss of the anal canal is reported to lower the anal sensibility, causing loss of discrimination between stool and gas. The preservation of the aganglionic anal canal is essential for continence but can also cause obstructive symptoms (2,5). Contributing to these obstructive symptoms is the absence of the internal sphincter relaxation, which is disease typical for Hirschsprung's disease (17). It is also well known that bowel movements in a high frequency of children operated on for Hirschsprung's disease, are faster than in the general population (18). The combination of fast bowel movements and obstruction can lead to abdominal distention, but also soiling and faecal incontinence (2,5,19-20). In literature, children with short-segment Hirschsprung's disease more often report constipation and obstructive symptoms while children with long-segment aganglionosis more often report loose stools, diarrhoea and incontinence because absorption of water is diminished due to the shorter colon (2-3,7-8).

Growth and nutritional status may be concerns, especially in children with total colon aganglionosis, while loss of intestinal length and dysmotility might impact the absorption of nutrients (7-8,21-24).

Dietary guidelines

There are currently no guidelines or evidence-based recommendations for dietary management of Hirschsprung's disease. However, dietary management of gastrointestinal complaints is of great relevance for the children and families living with Hirschsprung's disease (21,25). In a Canadian prioritization study, caregivers of children with Hirschsprung's disease ranked the topic Bowel management highest

priority, while the topic Nutrition and growth is ranked second highest priority of concern for them. They requested disease-specific information regarding optimal diet, eating behaviours, gaining weight, food intolerances, and food allergies (21).

The European consensus guidelines for the management of rectosigmoid Hirschsprung's disease were published in 2020 and include recommendations on dietary modifications within bowel management (1). Dietary treatment is also included in a small number of other bowel management programs (2,18,26). However, any evidence for whether diet actually improves gastrointestinal complaints in patients, and then which diet, is lacking. There's a paucity of knowledge of dietary effects on gastrointestinal symptoms in general (27-30), and especially in children with Hirschsprung's disease, which is only rarely studied (31-33).

Dietary effects on unspecified gastrointestinal symptoms in Hirschsprung's disease

In a cross-sectional questionnaire study, 64% patients with Hirschsprung's disease (mean age 12 years, range 2-42 years old) reported that diet impacted their gastrointestinal symptoms. There were no significant differences in the frequency of reported dietary effects between participants with short-segment and long-segment Hirschsprung's disease, or any differences with age. The most frequently reported foods were fruit (59%), fatty or fast food (44%), vegetables (28%), dairy products (28%), and grains/bread/cereals (26%). Dietary restrictions because of the dietary effects on their gastrointestinal symptoms, were reported by 44% participants (31).

Constipation

Constipation is reported in up to 44% of patients with Hirschsprung's disease (2-8). Diagnostic criteria for paediatric functional constipation, according to Rome IV criteria, includes two or fewer defecations per week, faecal incontinence at least once per week, history of painful or hard bowel movements, presence of a large faecal mass in the rectum and/or history of large diameter stools that can obstruct the toilet. At least two of the criteria must occur at least once a week for a minimum of one month (34). However, in studies of gastrointestinal symptoms in Hirschsprung's disease, the Rintala Bowel Function Score (BFS) is frequently used, and here constipation is reported from a treatment point of view; as the need for dietary, laxative or enema management (35-37).

In children with Hirschsprung's disease, the underlying cause of symptoms of constipation might be obstruction but, as in other children, painful passage of stools can also lead to withholding behaviour (2,30,38). International guidelines for

management of functional constipation include laxative treatment and toilet training as first-step treatment (38).

Dietary management of constipation

In international guidelines, a normal fibre and fluid intake is advised for management of functional constipation (30,38-39). There is only one previous study, which was observational on 84 patients (mean age 12 years old, range 2-42 years old), on dietary effects in Hirschsprung's disease in which 64% reported experienced dietary effects on gastrointestinal symptoms. Diarrhoea was reported to be induced by fruits, vegetables, dairy, grains/bread/cereals and fatty/fast food. Constipation was reported to be induced by fruits and dairy (31).

Obstruction

Obstruction is reported in up to 53% of patients with Hirschsprung's disease (2). Obstructive symptoms can give rise to abdominal distension, bloating, vomiting, failure to thrive, enterocolitis and difficulties in passing stools. The obstruction might result from anatomic causes, such as anastomosis, or functional causes, such as dysmotility or non-relaxing sphincter. While most children learn to overcome and control the non-relaxing sphincter with age, for example by pushing the stool out with increased intraabdominal pressure, it may contribute to persistent obstructive symptoms in others (1-2,5,17-18).

Management of obstruction

Anatomical causes of obstruction need to be ruled out before further regimes are implemented, and they often require surgical correction. Functional obstruction is usually first line treated by intra-sphincteric injections with the muscle-relaxing drug botulinum toxin, to achieve relaxation of the internal sphincter. Further, bowel management can also be applied (1-2,5,17-18). Examples and description of treatment alternatives considering the child's age and sphincter relaxation are displayed in **Table 1**.

Table 1. Choice of bowel management considering the child's age and sphincter relaxation

	Infant	Child	Adolescent
Characteristic	Non-relaxing anal sphincters	Using other defecation manoeuvres	Desire for independence or if management failed
Bowel management	Rectal irrigations	Laxatives Rectal enemas	Antegrade continence enema
	+ Botulinum toxin injections as needed		

Dietary management of obstruction

Water-soluble fibre binds water and makes the stool bulkier, thus these fibres can be added to the diet to change the viscosity of stools. This has been evaluated as part of a bowel management program, but separate dietary effects have never been evaluated (2,18). However, if giving laxatives or laxative diet to patients with nonrelaxing sphincters, stools may accumulate in the distal colon, worsening obstructive symptoms (2).

Faecal incontinence

Faecal incontinence is reported in up to 59% of patients with Hirschsprung's disease (2), and is characterized by soiling (staining) and involuntary bowel movements (faecal accidents with uncontrolled loss of larger volume of stools) (1-2,5,26). Faecal continence depends on anal sensation, sphincter tone and colonic motility (2,26). Faecal incontinence might result from obstruction with an overflow faecal incontinence or non-retentive faecal incontinence. An overflow incontinence refers to when stool is accumulated in the distal colon and watery stool leaks around. Non-retentive faecal incontinence refers to a condition where the child has faecal incontinence, without the presence of rectal stool. In Hirschsprung's disease, the latter may be caused by injury during surgery, a too-low anastomosis, or by hypermotility in the bowel. It can also appear in cases of loss of rectal sensitivity (2,19-20).

Management of faecal incontinence

In children with dilated colon and overflow faecal incontinence caused by obstruction, management of the obstruction is needed (2). In children with non-retentive faecal incontinence and impaired anatomy, surgical management could be considered. In children with non-retentive faecal incontinence, normal anatomy and hypermotility, the treatment recommendations include medication and a constipating diet (1-2,5). In the latter circumstance, laxatives should be avoided since soft stools or bowel motility stimulation may worsen the incontinence (2,5).

Dietary management of faecal incontinence

A constipating diet in management of hypermotility has been recommended as part of bowel management programs for children with soiling (1-2,5,26). Still, as for other gastrointestinal symptoms in Hirschsprung's disease, no separate evaluation has been reported on.

In an interventional study in a small group of selected children (n=10) with Hirschsprung's disease, the effect of a low FODMAP (Fermentable Oligosaccharides,

Disaccharides And Polyols)-diet was investigated with regard to effects on faecal incontinence. In the included children, any anatomical cause for faecal incontinence had been excluded, and hypermotility had been diagnosed. An exclusion diet led to resolution or improvement of faecal incontinence in 9 out of 10 children (32).

Abdominal pain and flatulence

Abdominal pain has been reported in adult patients with Hirschsprung's disease (40). Flatulence, which in some cases could cause abdominal pain or social inhibition, is reported in up to 47% of patients with Hirschsprung's disease (7-8).

Dietary management of abdominal pain and flatulence

In children with functional abdominal pain, fibre supplement has been shown to be efficacious in improving symptoms (28,39). However, dietary effects on abdominal pain in children with Hirschsprung's disease have not been specifically investigated. For dietary impacts on flatulence in Hirschsprung's disease there is one observational study, in which dietary effects on gastrointestinal symptoms were reported by 64% respondents (31). Abdominal discomfort was reported to be induced by vegetables, dairy, grains/bread/cereals and fatty/fast food (31).

Dietary management of functional gastrointestinal disorders

Lacking disease-specific dietary guidelines for Hirschsprung's disease, the dietary advice and recommendations given by healthcare professionals for children with the disease has usually mimicked the traditional dietary advice for irritable bowel syndrome (IBS). Up to 93% of children with IBS report that diet affects their gastrointestinal complaints (41). The first-line dietary treatment in IBS is the NICE-guidelines (National Institute for Health and Care Excellence), including eating habits such as consuming regular meals, adjusting the intake of dietary fibre, and limiting trigger foods such as spicy food (42) (see **Table 2**). However, similar effects on gastrointestinal complaints in Hirschsprung's disease remain to be evaluated.

Referring to the section Faecal incontinence, the low-FODMAP diet has been investigated in one interventional trial on children with Hirschsprung's disease (32). The low-FODMAP diet is an established treatment option for adults with IBS and has also been used in children with IBS respective functional abdominal pain (29).

FODMAPs are carbohydrates typically not fully absorbed in the intestine and instead fermented by gut bacteria – a process leading to gas production and distended abdomen. Since the unabsorbed carbohydrates tend to bind water, this leads to loosening of stool consistency. Excluding FODMAPs has been shown to improve gastrointestinal symptoms in children with IBS. However, due to insufficient evidence, and since the low-FODMAP diet is very restrictive, it is not recommended routinely for children (29). Examples of dietary recommendations in the NICE-diet and the low-FODMAP diet are displayed in **Table 2**.

Table 2. Examples of dietary recommendations in the NICE-diet and the low-FODMAP diet

NICE-diet		Low-FODMAP diet		
Overarching recommendations			Avoid	Choose
Consume regular meals	Trial lactose-free diet	<i>Oligosaccharides</i>	Corn, banana	Gluten-free bread
Take time to eat	Drink water	<i>Disaccharides</i>	Dairy	Lactose-free dairy
Eat max three fruits/day	Choose soluble fibre	<i>Monosaccharides</i>	Mango, dried fruit	Kiwi, cucumber
Restrict soda	Limit fat intake	<i>Polyols</i>	Plum, sorbitol	Orange, zucchini

Food items' effect on gastrointestinal symptoms

The effect of certain food items and nutrients on gastrointestinal symptoms have been investigated, to some extent, in children with functional constipation, abdominal pain and IBS (27-30,41,43). An overview of examples of dietary interventions for improvement of gastrointestinal symptoms is displayed in **Table 3**. A high-fibre diet, such as one rich in fruits and vegetables, is frequently recommended to treat constipation (30,44-47), and is included in the first-line guidance for the Swedish population and in guidelines for primary care (48-49). Self-imposed dietary changes are reported to be common in parental self-treatment of children's gastrointestinal symptoms (50,51). However, evidence for its efficacy is lacking (30,38-39,52). The effectiveness of foods on gastrointestinal symptoms in healthy children has never been described.

Self-reported effects of food items on gastrointestinal symptoms were frequently reported in Swedish adults with IBS; 84% participants reported diet-related symptoms (53). Especially foods containing incompletely absorbed carbohydrates (high content of FODMAP's) and fat were considered important, reported by 71% and 52% respectively. Further, histamine-releasing food such as pork (28%), chocolate (17%)

and orange (17%) as well as food rich in biogenic amines such as wine/beer (31%), salami (22%) and cheese (20%) were reported to induce symptoms. The study questionnaire included food items relevant to food intolerance/allergy (53), specific food items (i.e., apricot, cherry, lingonberry, melon, nectarine, peach, apple, avocado, pepper, parsley, celery, chicken, salami, shellfish, wine/beer, fried food, curry, cayenne, chili/tabasco, chamomilla, sesame seeds, hazelnut, peanut, chestnut, almond, brazil nut, walnut, soy) were added to the Diet and Bowel Function questionnaire, developed and validated in Study II.

In children with IBS, 93% reported at least one food item to induce gastrointestinal symptoms (41). The ten most frequently reported food items were, in descending order, cow's milk, fast food, cheese, ice cream, spicy food, beans, pizza, sodas, chocolate and fried foods (41). Specific food items included in the study questionnaire (41,50) (i.e., cabbage, sausage, diet soda) were added to the Diet and Bowel Function questionnaire, developed and validated in Study II.

Table 3. Overview of examples of dietary interventions for improvement of gastrointestinal symptoms

Category	Dietary intervention	Population	Findings	Reference
Constipation				
	Fibre	Children	No evidence that high-fibre diet is beneficial Some evidence that addition of specific fibres (e.g., glucomannan, guar gum, fructo-oligosaccharides) may be more effective as placebo or as effective as laxative treatment	30,38-39
	Extra fluid intake	Children	No evidence for effect of increased water intake on stool frequency	30,38-39
	Cow's milk	Children	A cow's milk free diet may be beneficial in children with previous diagnosis of cow's milk protein allergy	30,39
	Probiotics	Children	Specific probiotic strains (e.g., <i>Bifidobacteria</i> and <i>Lactobacilli</i>) might be effective	30
	Flaxseed seeds	Children	May be just as effective as osmotic laxatives, but with worse taste	30
	Kiwi	Adults	2 kiwifruits/d improved stool frequency and consistency	54
	Prunes	Adults	100 g/d = 12 prunes/d improved stool frequency and increased stool weight	55
Abdominal pain				
	Low-FODMAP diet	Children	Limited evidence of efficacy. Some studies have shown improvement in abdominal pain.	29,39
	Fibre	Children	Addition of specific fibres (e.g., psyllium, glucomannan, ispaghula husk) may improve abdominal pain, especially at intake of at least 5 g/d of soluble fibres	39
	Lactose-free diet	Children	Very limited evidence of efficacy. Few studies have shown improvement.	39
Flatulence				
	Diet low in fermentable residues	Adults	Decreased intake of for example beans, cauliflower, broccoli, cabbage, onion, garlic and prunes led to decrease of gas-related symptoms	56

Growth and nutritional needs

Growth and nutritional needs are scarcely reported in children with Hirschsprung's disease, but nevertheless an issue of uttermost concern for their parents, according to the findings in this thesis. Moderate to severe malnutrition has been reported in 16% of children with Hirschsprung's disease at admission to hospital for surgery (23). Preoperative malnutrition has been associated with an increased risk for Hirschsprung's associated enterocolitis (23). In general paediatric populations, preoperative malnutrition has been shown to be associated with higher rates of prolonged intubation, infectious complications, and longer length of hospital stay after major paediatric surgery (57).

Postoperative growth outcome in the short- and long-term has been reported to be similar among different surgical pull-through methods at definitive surgery (22). At one year of age, one Australian study showed weight, height and head-circumference to be within the normal range for age and sex, with no differences between children with short- and long-segment aganglionosis (22). In the long-term, children with total colon aganglionosis have been reported to be at risk for growth impairment and nutritional deficiencies (7-8,58-60). In a Nordic multicentre study of long-term outcomes of 20 years in patients with total colonic aganglionosis, 21% of patients had low BMI-for-age, 23% had low height-for-age and 36% had low BMI-for-age or low height-for-age (8). Only half of the participants with growth impairment reported any use of nutritional supplements. Previous and present need of nutritional supplements was reported by 55% of respondents, and 35% had ongoing parenteral nutrition (8).

Figure 2 displays the previous and present need of specific nutritional supplements.

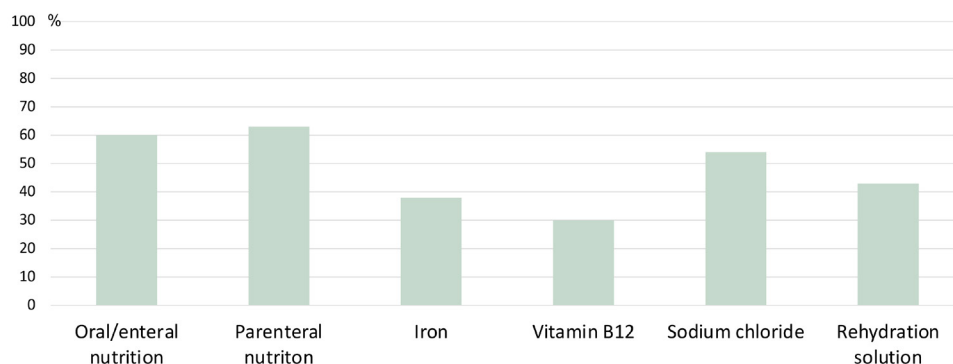


Figure 2. Need of specific nutritional supplements as reported by patients with total colonic aganglionosis

Surgery and healthcare of children with Hirschsprung's disease in Lund and Sweden

In Lund, children with Hirschsprung's disease are included in a structured follow-up program at the Department of Paediatric Surgery. The children and their families receive regular follow-up visits by specialist nurses and paediatric surgeons. Included in the multi-disciplinary team are paediatric gastroenterologists, dieticians, psychologists, social workers and physiotherapists as needed and requested by families. The children are monitored more closely during the first few years after surgery. A transition to adult healthcare takes place at the age of 15 (61).

The paediatric care in Lund is a tertiary children's hospital serving a region of two million residents. Since 2018, Lund is one out of two national referral centres for Hirschsprung's disease, with a catchment area of five million residents (62). The Department of Paediatric Surgery in Lund is a member of ERNICA – European Reference Network for rare inherited and congenital digestive disorders, including Hirschsprung's disease. European Reference Networks are networks for caregivers and researchers, with the aim of improving care of patients with rare and complex diseases (63).

Aims

- I** To explore parental experiences of dietary impact on bowel function in children with Hirschsprung's disease
- II** To develop and qualitatively test the content validity of a patient-reported outcome instrument, in order to explore experiences of dietary effects on bowel function and daily life in children with and without Hirschsprung's disease
- III** To investigate healthy children's experiences of whether, and how, diet and specific food items induce gastrointestinal symptoms
- IV** To investigate whether experiences of dietary effects on gastrointestinal symptoms and daily life differ between children with Hirschsprung's disease and healthy children

Methods

Study design

The thesis includes four studies. Study I was a qualitative focus group study, revealing dietary aspects relevant to the patient group. In Study II, a self-reporting questionnaire was developed based on the results from the focus group study and then qualitatively validated. In Study III and Study IV, the questionnaire was used to quantitatively investigate the themes that emerged in Study I. An overview of the study design is shown in **Table 4**.

Table 4. Overview of the design of the studies

	Design	Data collection	Subjects	Analysis
I	Exploratory qualitative study	Focus groups	10 parents to children with Hirschsprung's disease in three focus groups	Content analysis
II	Development and qualitative content validation of a questionnaire	Focus groups (Study I), cognitive interviews, pilot study	One child with Hirschsprung's disease 13 parents to children with Hirschsprung's disease 12 healthy children Five parents to healthy children	Content analysis Informal analysis
III	Observational cross-sectional study	Self-reporting questionnaires (Study II)	265 healthy children	Non-parametric and parametric statistical tests
IV	Observational cross-sectional case-control study	Self-reporting questionnaires (Study II)	71 children with Hirschsprung's disease 265 healthy children	Non-parametric and parametric statistical tests

Study setting

The studies were conducted at Skåne University Hospital in Lund, a tertiary children's hospital serving a region with 2 million residents. The Department of Paediatric Surgery was appointed as a national referral centre for Hirschsprung's disease in 2018, covering a catchment area of 5 million residents.

The focus group discussions were held in December 2018 and analyses performed in 2019. Study II was conducted 2019; the final version of the questionnaire was completed February 2020. Study III and Study IV were conducted 2020-2023, with data collection performed from March 2020 to March 2021.

Study population and recruitment process

Study I and Study II: Focus groups

Parents of children with Hirschsprung's disease treated at the national centre for Hirschsprung's disease were invited. A total of 26 parents of children with Hirschsprung's disease aged 1-12 years were invited by letters in the post. A study announcement was published online by the National Hirschsprung's Disease Patient Organization Sweden (64). A purposive sampling (65) was made to obtain a wide variation in experiences.

Study II: Questionnaire development and validation

Participants in the validation study were purposively selected (65) regarding age, gender and whether they/their child had Hirschsprung's disease or not, to secure a diversity of participating responders in the cognitive interviews. Patient representatives were recruited from the patient organization. Healthy children and parents were recruited among children admitted to the hospital for orthopaedic emergency procedures after accidental traumas.

Study III: Healthy children

Healthy children (n=300) aged 1-18 years old and their parents were invited to participate. The number of healthy children was based on the number of children with Hirschsprung's disease (n≈100); the case:control ratio in Study IV was set at 1:3. The study group included children admitted to the hospital for orthopaedic emergency

procedures as a result of accidental traumas. In addition, their siblings, and offspring of professionals were invited to participate. “Healthy” was defined as being without any gastrointestinal, nephrological, metabolic, or other disorders, being without enteral tube feeding or parenteral nutrition support, and not having any medically treated allergy. Children with possible food allergies and/or food intolerances that did not require any medication were included in the study in order to reflect a general, healthy population.

Study IV: Children with Hirschsprung’s disease

All children (n=85) aged 1-18 years treated for Hirschsprung’s disease were identified in the local register and invited to participate in the questionnaire study, together with their parents. Invitations and questionnaires were sent by post, and a study announcement was published online by the patient organization.

Data collection

Study I and Study II: Focus groups

Three focus groups discussions were conducted, consisting of three, four and three participants, respectively. The study was conducted at the Department of Paediatric Surgery. The discussion moderator was a social worker and family therapist employed at the department. She had experience of treating families with children with Hirschsprung’s disease, but had not met any of the participants in a clinical setting. It was considered important that the moderator had insight into issues related to Hirschsprung’s disease, but not be too engaged in the research question. The moderator initiated, encouraged, and facilitated discussions through fictional case histories (66) and open-ended follow-up questions. The focus groups’ discussions were audio-recorded and transcribed verbatim by L. Telborn. All personal data were removed.

Study II: Questionnaire development and validation

Items for the questionnaire were generated from the focus groups’ discussions in Study I. In addition, foods previously reported (41,50,53) to induce gastrointestinal symptoms in other gastrointestinal disorders were added. The questionnaire questions were created together with representatives from the patient organization (67).

Cognitive interviews were carried out to assess the content validity (68-71) and performed in a semi-structured manner following an interview guide, including: 1.

Comprehension and relevance of each item; 2. Wording; and 3. Overall assessment (**Table 5**). Participants' answers were recorded using field notes. Interviews were conducted by L. Telborn in two rounds, with different participants in each round. The results from the cognitive interviews were used to refine the questionnaire.

Table 5. Semi-structured interview questions in the cognitive interviews

Questions	
Comprehension and relevance	<ol style="list-style-type: none"> 1. In your own words, can you explain what the question means to you (open answer) 2. Do you find the question easy or hard to understand? (Easy/Hard) 3. Do you find the question easy or hard to answer? (Easy/Hard) 4. Do you find the question relevant to ask? (Yes/No) 5. Do you have any comments about the question? 6. Read each of the options for answers, and tell me what they mean to you? 7. What do you think about the options for answers? 8. Could you find your first-choice answer among the options for answers? 9. Were there any words that you found hard to understand?
Wording	<ol style="list-style-type: none"> 10. What do you think about the form of questioning "you/your child"? 11. What does the term "bowel function" mean to you? Would you prefer another term? If yes, which term? 12. What does the term "psychological" (round 1) / "emotional" (round 2) mean to you? Would you prefer another term? If yes, which term?
Overall assessment	<ol style="list-style-type: none"> 13. What do you think about the instructions for filling in the questionnaire? 14. How long did it take for you to fill in the questionnaire? 15. Do you have any other comments that could help us improve the instrument?

Study III and Study IV: Study questionnaire

The study questionnaire ended up including 32 questions in total. Children and parents were asked to answer the questionnaire together. The questionnaire comprised three sections:

Background information was investigated by nine questions on growth, other diseases, medications and allergies (7) (**Table 6**, Questions 1-9).

Gastrointestinal symptoms were assessed by both the Rintala Bowel Function Score (BFS) (35-36) (**Table 6**, Questions 10-16) and specific questions on the gastrointestinal symptoms of constipation, abdominal pain and bothersome gases (7) (**Table 6**, Questions 17-19). The BFS is frequently used and includes, in total, seven questions generating a total score of 1-20 (20=best function). A BFS of 18-20 suggests normal bowel function

and 1-17 impaired bowel function. Only answers for study participants aged 4-18 years who had answered all the BFS questions were included in the BFS analyses.

Diet-induced gastrointestinal symptoms were assessed by the Diet and Bowel Function questionnaire (developed and validated in Study II). It consisted of 13 questions on the impact of diet on gastrointestinal symptoms and daily life. To assess specific gastrointestinal symptoms of food items, questions on 90 specific food items were posed. The questionnaire is described in detail in the results section, Study II.

Table 6. Questions included in the study questionnaire: Background information, Rintala Bowel Function Questionnaire and gastrointestinal symptoms

Questions	
Background information	<ol style="list-style-type: none"> 1. Age 2. Gender 3. Height 4. Weight 5a. Do you have any disease, allergy or any gastrointestinal congenital malformation? 5b. If yes, what allergy/disease? 6a. Do you take any treatment for bowel symptoms? 6b. If yes, what type of treatment? 6c. If yes, for what reason? 7. Have you ever had impaired growth? 8. Have you ever had the need for nutritional supplements? 9a. Do you have any special diet? 9b. If yes, what type of special diet?
Bowel Function Questionnaire and gastrointestinal symptoms	<ol style="list-style-type: none"> 10 a. How often do you/your child poop? 10 b. How many times a week do you/your child poop? 11. Do you/does your child have hard poop and troubles to push it out? 12. Do you/does your child ever experience difficulties in school or in their spare time, for example doing what you/your child wants, or seeing friends, due to problems with stool coming in underwear or the risk of it happening? 13. Do you/does your child feel the urge to poop and verbalizes when you/he or she will poop? 14. Are you/your child able to hold back defecation? 15. Do you/does your child ever soil (staining in underwear)? 16. Do you/does your child ever have accidents where a lot of poop comes out in the underwear? 17. Do you experience abdominal pain? 18. Do you suffer from bothersome gases? 19. Do you experience difficulties in passing stools despite soft poop?

Data analysis

Study I and Study II: Focus groups

The focus groups were analysed through qualitative content analysis (65). On a manifest level, analyses were made on participants' directly expressed sentences. On a latent level, interpretation of the underlying meanings was performed (72-73). Transcripts were read several times, ensuring comprehension of overall meaning. Then, meaning units were identified, condensed without loss of content, and abstracted into sub-categories and categories. Describing the overall underlying meaning on a latent level, a theme was formulated. Examples from the analysis process are shown in the audit trail (**Table 7**).

Table 7. Examples of meaning units, condensed meaning units, sub-categories, categories, and overall theme from the content analysis

Meaning unit	Condensed meaning unit	Sub-categories	Categories	Theme
<i>"Fruits: kiwi, pears, oranges. We use them to loosen the stools"</i>	Choice of food for improving bowel function	Using food to obtain bowel function effects	Striving to regulate bowel function through dietary strategies	Diet is a strong influencer on bowel function in Hirschsprung's disease
<i>"He gets constipated when eating white bread., If he has bread for breakfast, it's no more bread that day"</i>	Choice of food for avoiding worsened bowel function			
<i>"We give him a lactose-free diet. It has improved his bowel function a thousand times"</i>	Avoidance of food for avoiding worsened bowel function			
<i>"We give him probiotics. His bowel function has become more balanced"</i>	Use of probiotics for improving bowel function	Using nutritional supplements to secure growth and improve bowel function		
<i>"If you have a child who always has stools like soft ice-cream, how will you know if it is because of food?"</i>	Difficulties in finding correlations between diet and bowel function	Striving to establish an association between diet and bowel function		
<i>"If we start to eat a lactose-free diet, what if he gets constipated?"</i>	Fear of introducing new foods			
<i>"We must renounce some things in life. The advantages are superior"</i>	Choice of habits for improving bowel function	Adjusting family habits to improve the child's bowel function	Restricting diet to control bowel function impact on family and daily life	
<i>"We talk about poop all the time! And what to eat, or not to eat"</i>	Bowel function and diet always in mind	Reacting emotionally to diet and bowel dysfunction		
<i>"To make the dietary habits and bowel function work is extremely strenuous"</i>	Feelings of exhaustion			
<i>"She looks healthy, but what is her nutritional status?"</i>	Uncertainty regarding nutritional status	Feeling anxiety about possible nutritional deficiencies	Wishing for dietary and nutritional guidelines for facilitating self-treatment	
<i>"There should be information regarding foods that could improve bowel function"</i>	Presumptions of existing knowledge about diet's role in bowel function	Expecting healthcare support in parental self-treatment		
<i>"It's the hospital's responsibility to give you an overall view of the child, and support all the different aspects of their care"</i>	Desire for dietary support from the healthcare service			

Study II: Questionnaire development and validation

Cognitive interviews were analysed using informal analysis (74). Results from the cognitive interviews guided decisions about keeping, modifying, or deleting items. Questions for which respondents identified difficulties were revised based on participants' responses and suggestions. Quantitative data were reported as total numbers and medians for continuous variables and as total numbers for discrete variables.

Study III and Study IV: Questionnaire studies

The statistical design was planned in collaboration with a statistician. Only questionnaires with a minimum of 90% (29/32) questions answered were included in the study. Descriptive data were reported as n (%). Data on continuous variables did not fulfil assumptions for normal distribution and were therefore reported as median (range). The non-parametrical Mann-Whitney U-test was used for continuous variables and for graded data on an ordinal scale. Binary categorial variables were analyzed by means of the Chi-square test. Statistical significance was set at $p < 0.05$. The program IBM SPSS Statistics Version 27 for MacOS was used. Answers to questions about constipation were dichotomized to No versus Yes (including experienced but no treatment, or treated with diet, medication, enemas, other). Gastrointestinal complaints were defined as constipation (Yes), abdominal pain (Often/Always) and/or bothersome gases (Often/Always).

Preunderstanding

Preunderstanding refers to the researcher's prior understanding of the phenomena under investigation (75). It can be, for example, knowledge, experience, ideas, perspectives, assumptions or interests of the topic. Preunderstanding underlies all research but especially research using qualitative methodologies. Left without reflection, preunderstanding can jeopardize the validity of a study (75).

When I started the work on the thesis, I had been working as a clinical dietician for 16 years, 11 of which were at the Department of Paediatric Surgery. In my clinical work, I had met children with Hirschsprung's disease and their families. My preunderstanding of the topic was associated with clinical counselling to patients and their parents. To ensure that my preunderstanding did not permeate the analyses, I regularly reflected on, and continuously discussed, my preunderstanding with my supervisors and co-authors.

Ethical considerations

The studies were conducted in accordance with the Declaration of Helsinki developed by the World Medical Association in 2013. The studies had received ethical approval from the Swedish Ethical Review Authority (registration number 2018/720). Patients were identified in the local disease register and pseudo-anonymized with a code. In the control group, children and parents answered fully anonymously.

Participants received age-adapted oral and written information. Written information included study aim, methods, benefits and risks. Risks considered were a potential increased focus on diet in families, especially for children with Hirschsprung's disease. Specifically, for participants in the focus groups, emotions arising during the discussions were considered. All participants were informed about the possibility to contact the research team, with guidance to for help. Participants were ensured confidentiality and that the choice to take part in the studies was voluntary. They were also informed of their right to refuse to participate at any time, without reprisal. Written consent was obtained from legal guardians to children aged younger than 15 years, while adolescents aged 15 years or over gave their own consent.

*“I think it’s hard – how do I know it’s exactly this food?
It’s not that way, they eat just bananas for one day.”*

Parent to a child with Hirschsprung’s disease

*“We give him a lactose-free diet. It has improved his
bowel function a thousand times.”*

Parent to a child with Hirschsprung’s disease

*“You get stressed when you find a lot of information on
the internet. For me, if I get advice from the hospital,
I feel safe.”*

Parent to a child with Hirschsprung’s disease

Results

Study I

Participating parents described that they constantly tried to deduce causes for their child’s gastrointestinal complaints. Factors that they had identified to influence gastrointestinal symptoms were, for example, cold, stress, physical activity and diet. Parents described diet to be the extrinsic factor with the greatest impact on their child’s gastrointestinal symptoms. They explained how they adapted the diet by choosing or avoiding certain foods, adjusting meal times and the composition of meals. The participants agreed that their constant awareness of the diet was required to optimise their child’s gastrointestinal function. Despite a belief in both positive and negative effects of diet on gastrointestinal symptoms, the parents also described a frustration caused by difficulties in ascertaining gastrointestinal effects of specific foods. This meant that they carried a concern about what food could possibly affect and worsen their child’s gastrointestinal complaints. The parents expressed a strong desire for dietary guidelines from the healthcare system, to support them in self-care.

The parents’ experiences of dietary impact on gastrointestinal complaints in their children with Hirschsprung’s disease were merged in one overall theme and three categories (**Figure 3**).



Figure 3. Sub-categories, categories and overall theme derived from the content analysis

Study II

The questionnaire development and qualitative content validation process resulted in the Diet and Bowel Function questionnaire (**Table 8**). The final version of the questionnaire contained 13 questions assessing the impact of diet on gastrointestinal symptoms and daily life, and 90 specified foods items with possible effects on gastrointestinal symptoms.

The questionnaire's content and structure were made up according to the overall theme and the categories of the focus groups' discussions in Study I. During the validation process, using cognitive interviews, all questions were reported to be highly relevant. Still, a majority of the questions needed reformulation to become clearer and increase understanding. In particular, it was requested that the terminology be changed to be suitable both for children and parents, with and without Hirschsprung's disease, respectively, so that key concepts could be perceived equally by the participants. Questions that touched emotions gave rise to discussions among the participants, and needed refining several times. The final questionnaire is, according to the suggestion of participants, answered by children and parents together.

Table 8. Questions included in the Diet and Bowel Function questionnaire

Questions	
Dietary habits and gastrointestinal symptoms	<ol style="list-style-type: none">1. Would you agree that your diet affects your stomach?2. Would you agree that how you eat affects your stomach?3a. Do you adjust your diet for your stomach's sake?3b. If yes, why?4. Do you choose specific types of food to help your stomach?5. Do you avoid specific types of food to help your stomach?6. Is there anyone else in your family who adjusts their diet to help their stomach?7. Does your diet limit you (in school, when you are with friends, or in general)?8. Do you think about how your diet affects your stomach?9. To parents: Do you think about your child's diet and how it affects his/her stomach?10. Does your diet affect you emotionally?11. To parents: Does your child's diet affect you emotionally?12a. Would you be interested in finding out more information about how your diet affects your stomach?12b. If yes, who would you turn to to find out more information?
Specific food items and gastrointestinal symptoms	<ol style="list-style-type: none">13a. Does the food item affect your stomach?13b. If yes, in which way? (Laxative effect/Constipating effect/Gives gases/Gives pain) <p>Food items listed:</p> <p>Fruits: pineapple, apricot, orange, banana, clementine, strawberry, kiwi, cherry, lingonberry, melon, nectarine, peach, plum, pear, dried fruit, grapes, apple, fruit peel</p> <p>Vegetables: avocado, cauliflower, broccoli, beans, cabbage, lentils, onion, corn, carrot, pepper, parsley, potato, rhubarb, celery, asparagus, mushroom, tomato, peas</p> <p>Dairy: cream, ice cream, lactose-free milk, milk, cheese, butter, yoghurt</p> <p>Bread, flour, rice: bread with grains/seeds, Swedish cracker, cornmeal, pasta, rice, flour, white bread</p> <p>Meat, fish, egg: fish, pork, beef, sausage, chicken, salami, shellfish, egg</p> <p>Sweets and snacks: pastry, chips, chocolate, candy, popcorn, rice cakes, pretzel sticks</p> <p>Beverages: soda (with sugar), soda (free from sugar), water, carbonated drink, wine/beer, formula</p> <p>Cooking effects: deep fried food, spicy food, fried food, soup</p> <p>Spices and seeds: curry, cayenne, chili/tabasco, chamomilla, sesame, sunflower seeds, poppy seeds</p> <p>Nuts etc: cashew, hazelnut, peanut, chestnut, almond, brazil nut, walnut, soy</p>

Study III

This study reports only on healthy children. Gastrointestinal complaints (defined as constipation, abdominal pain and/or troublesome gases Often/Always) were reported by 29% children.

An overwhelming majority of these healthy children (92%) reported that diet never or only seldom induced gastrointestinal symptoms. The statement that diet induced gastrointestinal symptoms was reported more frequently by children with gastrointestinal complaints, compared to children without gastrointestinal complaints: 22% versus 2% ($p \leq 0.001$). Children with gastrointestinal complaints adjusted diet more often than children without gastrointestinal complaints: 21% versus 4% ($p \leq 0.001$).

The median number of foods reported as inducing gastrointestinal symptoms was two out of 90 food items. Children with gastrointestinal complaints reported that more food items induced gastrointestinal symptoms compared to children who reported gastrointestinal symptoms Never/Seldom (3 versus 1; $p = 0.001$).

The most common food items reported to induce symptoms were beans (24%), plums (21%) and cream (14%) (**Table 9**). **Table 9** also displays the most frequently reported foods inducing laxative and constipating effects, as well as pain and gas. Specific food items reported to induce gastrointestinal symptoms differed between the children with different gastrointestinal complaints (**Figure 4**).

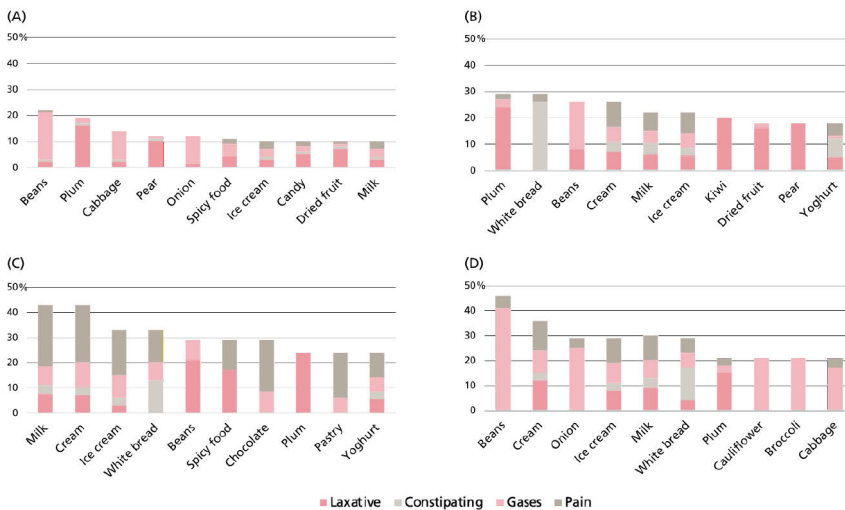


Figure 4. Frequencies of the 10 most commonly reported food items to induce gastrointestinal symptoms and their specific gastrointestinal effects reported by children 1-18 years old with: (A) No/Seldom gastrointestinal symptoms, (B) Constipation, (C) Abdominal pain, and (D) Gases, using the Diet and Bowel Function questionnaire

Table 9. Ranking of the 10 most frequently reported food items to induce any (unspecified) gastrointestinal symptom, laxative effect, constipating effect, rising pain and/or rising gases, respectively, reported by healthy children (n=265) 1–18 years old using the Diet and Bowel Function questionnaire

Rank	Any gastrointestinal symptom	Laxative effect	Constipating effect	Rising pain	Rising gases					
1	Beans	63 (24)	Plum	49 (19)	Banana	23 (9)	Cow's milk	20 (8)	Beans	47 (18)
2	Plum	55 (21)	Pear	30 (11)	White bread	19 (7)	Cream	19 (7)	Onion	28 (11)
3	Cream	38 (14)	Dried fruit	22 (8)	Cream	8 (3)	Ice cream	17 (6)	Cabbage	27 (10)
4	Cabbage	37 (14)	Kiwi	21 (8)	Cow's milk	8 (3)	Yoghurt	9 (3)	Cauliflower	18 (7)
5	Cow's milk	37 (14)	Grapes	18 (7)	Yoghurt	8 (3)	Chocolate	9 (3)	Lentils	17 (6)
6	Ice cream	35 (13)	Cream	17 (6)	Formula	7 (3)	Candy	8 (3)	Cream	17 (6)
7	Pear	33 (13)	Cow's milk	15 (6)	Corn	6 (2)	Spicy food	7 (3)	Ice cream	17 (6)
8	Onion	33 (13)	Ice cream	14 (5)	Ice cream	6 (2)	Chili/tabasco	7 (3)	Cow's milk	15 (6)
9	Spicy food	33 (13)	Cherry	12 (5)	Cheese	5 (2)	Lactose free milk	6 (2)	Egg	15 (6)
10	White bread	30 (11)	Spicy food	12 (5)	Bread: grain/seeds	5 (2)	White bread	6 (2)	Soda	13 (5)

Study IV

This case-control study reports on children with Hirschsprung's disease compared to healthy children. Gastrointestinal complaints (defined as constipation, abdominal pain and/or troublesome gases Often/Always) were reported more frequently by children with Hirschsprung's disease (72%) than by healthy children (29%) ($p \leq 0.001$).

Dietary effects on gastrointestinal symptoms were reported more frequently by children with Hirschsprung's disease (77%) than by healthy children (52%) ($p \leq 0.001$) (**Table 10**). Children with Hirschsprung's disease also reported that they adjusted their diet to improve gastrointestinal complaints more frequently than healthy children (69% versus 32%, $p \leq 0.001$). These differences remained in the sub-analyses including only children with gastrointestinal complaints (**Table 10**).

Social limitations as a result of dietary adjustments were reported more frequently by children with Hirschsprung's disease (42%) than by healthy children (18%) ($p = 0.002$). A vast majority (89%) of parents to children with Hirschsprung's disease reported concerns about how diet affected their child's gastrointestinal complaints, compared to 63% of parents to healthy children ($p \leq 0.001$). These differences remained in the sub-analyses including only children with gastrointestinal complaints.

Children with Hirschsprung's disease reported a median of seven food items that induced gastrointestinal symptoms, compared to two food items per healthy child ($p \leq 0.001$). Specific gastrointestinal effects as a result of consuming selected types of foods are shown in **Figure 5**.

Table 10. Dietary effects on gastrointestinal symptoms in children aged 1-18 years old with and without Hirschsprung's disease (HD) using the Diet and Bowel Function questionnaire. Gastrointestinal complaints were defined as constipation (Yes), abdominal pain (Often/Always), and/or bothersome gases (Often/Always). Values are n (%) of children.

	All children n=336			Children with gastrointestinal complaints n=128		
	HD n=71	Control n=265	p-value	HD n=51	Control n=77	p-value
Diet induces gastrointestinal symptoms						
No	16 (23)	127 (48)	<0.001 ¹	10 (20)	25 (33)	0.004 ¹
Sometimes	29 (41)	116 (44)		18 (35)	35 (46)	
Often	13 (18)	18 (7)		12 (24)	14 (18)	
Always	13 (19)	3 (1)		11 (22)	3 (4)	
Missing	0 (0)	1 (0)		0 (0)	0 (0)	
Eating habits induce gastrointestinal symptoms						
No	38 (55)	164 (62)	0.126 ¹	23 (47)	44 (58)	0.130
Sometimes	21 (30)	86 (33)		16 (33)	24 (32)	
Often	5 (7)	10 (4)		5 (10)	6 (8)	
Always	5 (7)	4 (2)		5 (10)	2 (3)	
Missing	2 (3)	1 (0)		2 (4)	1 (1)	
Adjusting diet to improve gastrointestinal symptoms						
No	22 (31)	181 (68)	<0.001 ¹	16 (24)	33 (43)	0.003 ¹
Sometimes	23 (32)	60 (23)		18 (35)	28 (36)	
Often	11 (16)	14 (5)		9 (18)	11 (14)	
Always	15 (21)	10 (4)		12 (24)	5 (7)	
Missing	0 (0)	0 (0)		0 (0)	0 (0)	
Choosing food to improve gastrointestinal symptoms						
Yes	27 (38)	41 (16)	<0.001 ²	20 (39)	23 (30)	0.273 ²
No	44 (62)	223 (85)		31 (61)	54 (70)	
Missing	0 (0)	1 (0)		0 (0)	0 (0)	
Avoiding food to improve gastrointestinal symptoms						
Yes	44 (62)	47 (18)	<0.001 ²	32 (63)	23 (30)	<0.001 ²
No	27 (38)	217 (82)		19 (37)	53 (70)	
Missing	0 (0)	1 (0)		0 (0)	0 (0)	

¹Mann-Whitney U-Test

²Chi-square test

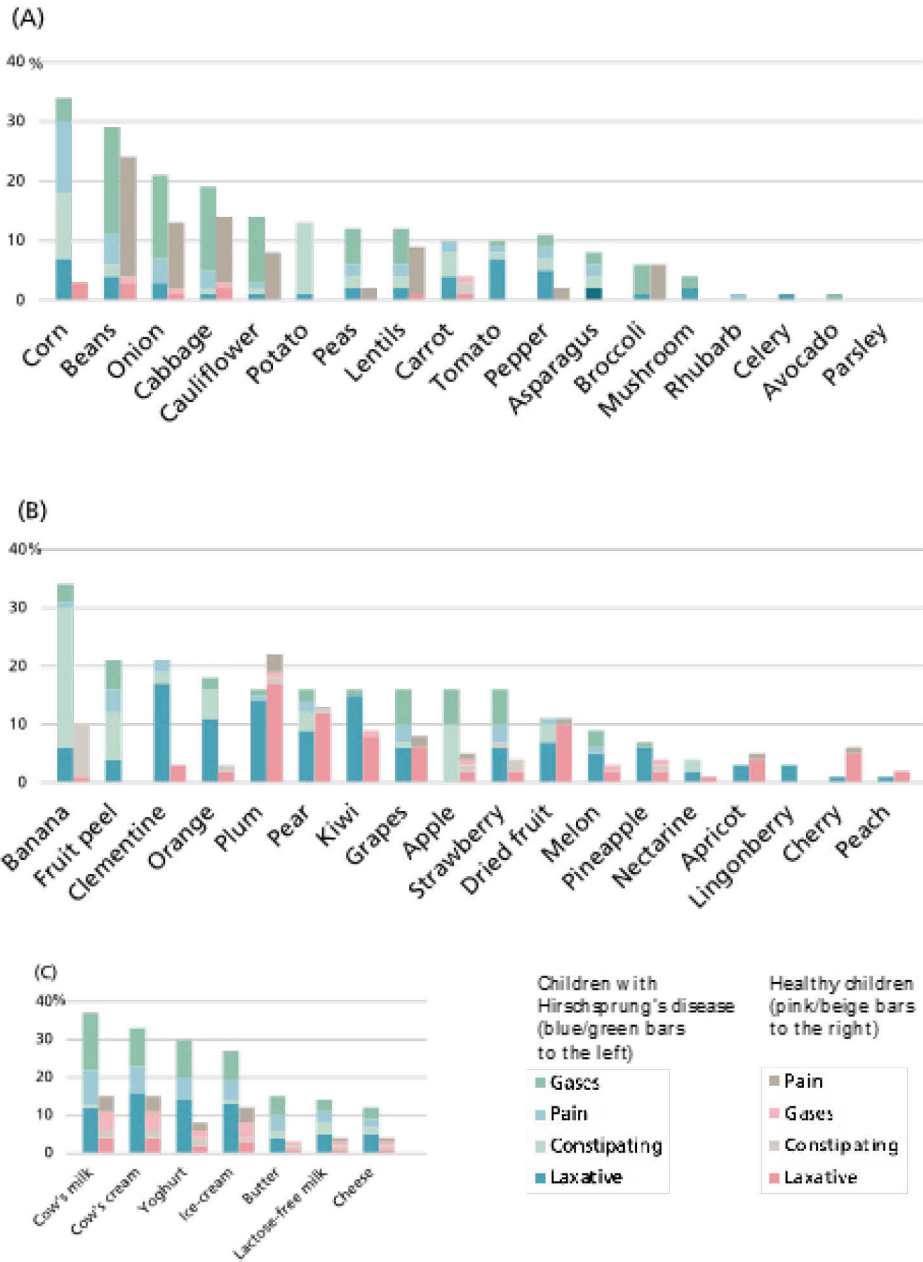


Figure 5. Comparison of frequencies of foods inducing gastrointestinal symptoms and each food's specific gastrointestinal effect, as reported by children with Hirschsprung's disease (n=71) and healthy children (n=265) using the Diet and Bowel Function questionnaire. (A) vegetables, (B) fruits, and (C) dairy products

Discussion

Main findings

This thesis reveals that diet plays a very central role in self-treatment of gastrointestinal complaints in Hirschsprung's disease. Specifically of importance, and previously unknown, is that dietary effects on gastrointestinal symptoms differ between children with Hirschsprung's disease and healthy children. This difference is also present when comparing only children with gastrointestinal complaints.

Diet in self-treatment of gastrointestinal complaints in children with Hirschsprung's disease

That diet was reported to be a key component in self-treatment, was especially demonstrated in Study I and IV. The parents participating in the focus groups (Study I) advocated diet to be the dominating extrinsic influencer on gastrointestinal complaints in their child. This was confirmed by that a majority (77%) of children with Hirschsprung's disease reported that diet induced gastrointestinal symptoms and that 69% reported adjustment of diet as a means to improve gastrointestinal complaints. These frequencies of dietary effects and adjustments of diet were higher in our study than in others, where 58-64% patients (both children and adults) with Hirschsprung's disease reported diet to induce symptoms and 44% restricted at least one food item from their diet (31).

In the thesis' studies, as a result of dietary adjustments, 42% children with Hirschsprung's disease reported social limitations and especially parents (89%) reported concerns about dietary effects on their child's gastrointestinal complaints (Study IV). Having a child with chronic functional impairment might lead to considerable parental stress (76-77). Similar social and emotional effects of diet have not been shown previously in children with Hirschsprung's disease, although comparable psychosocial concerns regarding diet have been reported in families of children with food allergies (78-79). A constant struggle to find a suitable diet has been reported in adults with Hirschsprung's disease (40), revealing that dietary impact on gastrointestinal symptoms and beliefs in the diet's potential to regulate gastrointestinal complaints persist into adulthood.

This thesis contributes with new knowledge on food items' gastrointestinal effects in Hirschsprung's disease. For example, in Study IV detailed results on effects (i.e., laxative effect, constipating effect, inducing pain and/or inducing gases) of 90 specific food items was revealed. The top 10 most frequently reported food items reported to induce gastrointestinal symptoms are displayed in **Table 11** (unpublished data). This information can be helpful in clinical counselling of the child's gastrointestinal symptoms, especially in dietary management of constipation, abdominal pain and flatulence. However, interventional studies are needed to further explore specific food items effects on gastrointestinal symptoms. Knowledge gaps regarding dietary management of obstruction and faecal incontinence remain. Further analysis of the data gained in Study IV will be performed outside the scope of this thesis. These analyses will contribute with detailed results especially regarding food items' effects on gastrointestinal symptoms in Hirschsprung's disease.

Difference in dietary effects on gastrointestinal symptoms between children with Hirschsprung's disease and healthy children

Comparing children with Hirschsprung's disease with healthy children, Study IV revealed that dietary effects were more profound in children with Hirschsprung's disease. Children with Hirschsprung's disease more frequently than healthy children reported that diet induced gastrointestinal symptoms (77% versus 52%) and that they made dietary adjustments accordingly (69% versus 32%), which influenced their daily life more frequently compared to healthy children (42% versus 18%). Furthermore, specific food items inducing gastrointestinal effects were also reported more frequently by children with Hirschsprung's disease (median 7 versus 2 food items), and the food items differed between the groups. These differences remained in the sub-analyses including only children with gastrointestinal complaints.

Before results of Study IV, it was unknown whether the dietary effects at all differed between children with and without Hirschsprung's disease. The results of Study III and IV showed that, in healthy children, diet appeared to have a very limited impact on children's gastrointestinal symptoms. This was contrary to the findings observed in children with Hirschsprung's disease. The dietary effects were somewhat higher in children with gastrointestinal complaints and even higher in children with Hirschsprung's disease. Even though differences are clearly evident, expectations of being able to improve gastrointestinal complaints by only dietary treatment are still connected to uncertainties. More studies are needed on specific dietary items' role for inducing gastrointestinal symptoms. Realistic goals need to be set up, including social circumstances and age of the child and all dietary treatments need a close individual guidance over time.

Table 11. Ranking of the 10 most frequently reported food items to induce any (unspecified) gastrointestinal symptom, laxative effect, constipating effect, rising pain, and/or rising gases, respectively, reported by children with Hirschsprung's disease 1–18 years old using the Diet and Bowel Function questionnaire

Rank	Any gastrointestinal symptom	Laxative effect	Constipating effect	Rising pain	Rising gases				
1	Cow's milk	26 (37)	15 (21)	Banana	20 (28)	Cow's milk	9 (13)	Beans	18 (25)
2	Banana	24 (34)	13 (18)	White bread	13 (18)	Corn	8 (11)	Cow's milk	14 (20)
3	Corn	24 (34)	12 (17)	Rice	8 (11)	Cow's cream	6 (9)	Onion	27 (10)
4	Cow's cream	23 (32)	12 (17)	Candy	7 (10)	Beans	5 (7)	Cabbage	11 (16)
5	Beans	21 (30)	11 (16)	Yoghurt	7 (10)	Potato	7 (10)	Cow's cream	11 (16)
6	Yoghurt	21 (30)	10 (14)	Kiwi	7 (10)	Pasta	7 (10)	Ice cream	9 (13)
7	Ice cream	19 (27)	9 (13)	Pastry	6 (9)	Flour	6 (9)	Candy	8 (11)
8	White bread	19 (27)	8 (11)	Plum	5 (7)	Apple	5 (7)	Pastry	8 (11)
9	Candy	18 (25)	7 (10)	Chocolate	4 (6)	Chips	4 (6)	Chips	8 (11)
10	Pastry	17 (24)	7 (10)	Clementine	4 (6)	Fruit peel	4 (6)	Chocolate	6 (9)

Methodological considerations

Choice of research methods

In the structured literature search for the background of this thesis, only a few publications were found on the topic diet in Hirschsprung's disease. Therefore, to collect deep and dynamic data from the patient group was essential. With that purpose focus group methodology was chosen since it is considered suitable in gaining research questions for subsequent studies in exploratory research (80). Then, to quantitatively investigate the concerns that had emerged in the focus group study, the specific questionnaire was developed. Using focus group discussion to generate items in questionnaire development, is a recommended and frequently used method (68-69,81-82). One positive aspect of generating disease or symptom specific questionnaires is a high internal validity (69). However, their generalisability could be low implying that the use of the Diet and Bowel questionnaire might be questioned for other diseases, for example anorectal malformations or inflammatory bowel disease. To evaluate the generalisability to other diseases further validations are needed.

One of the issues of dietary management in Hirschsprung's disease, is that there's a lack of knowledge about the true impact of diet on gastrointestinal symptoms. This was apparent both in the paediatric population in general, and especially in children with diseases, such as Hirschsprung's disease. In order to create a point of reference for children with Hirschsprung's disease, it became of great importance to also investigate healthy children.

The overall aim of this thesis was to improve the evidence-based support of patients' self-treatment. This mission was completed, and although much remains unknown, we now know for sure that food in Hirschsprung's disease plays a central role for the families. A greater knowledge was required to be able to carry out dietary interventional randomized controlled studies, and these can now – leaning on the thesis results - be planned. The ultimate aim is to clarify the impact of specific diet's role for gastrointestinal complaints in Hirschsprung's disease.

Trustworthiness

To enable evaluation of the trustworthiness of the focus group results, the COREQ (Consolidated criteria for reporting qualitative research) checklist (83) was used throughout the planning, execution and reporting of the study. The checklist and its trustworthiness criteria included credibility, dependability, confirmability and transferability (72-73,83-84). Credibility refers to if both results and the researcher

could be considered true and credible. Examples of strategies used to achieve credibility in the assessment of focus groups were ensuring a sufficiently prolonged engagement with each focus group, to be able to engage with participants and to build trust. Triangulation was performed by both conducting multiple focus groups and by that the analyses were performed by multiple researchers; four researchers of different professions were involved in analysis and interpretation decisions. Member checks were made by using probing questions and asking for participants' feedback during focus group discussions. Furthermore, after focus groups discussions, one participant from each focus group checked the summaries of the discussions, to ensure agreement between participants and researchers. Transferability refers to the degree to which the results can be transferred to other context or settings, which can be achieved through a thick description. Our strategies used were for example description of data collection through a purposeful sampling method, but especially through a thorough description of the analysis and related results. Dependability refers to the stability of findings over time. In Study I, this was ensured by a constant comparison and connection to raw data (the transcribed text) during analysis. Confirmability refers to the degree to which the findings could be confirmed by other researchers, and that the findings are clearly derived from the data collected. Strategies used in Study I were researcher triangulation and analysis transparency in the audit trail.

Likewise, in the qualitative validation of the questionnaire; credibility was ensured by multiple rounds of cognitive interviews with feedback from the representatives of the patient organization after each revision of the questionnaire, and by researcher triangulation. Transferability was ensured by transparency of data collection in the interviews, analysis and related results. Confirmability was ensured especially by transparency of analysis in the full track overview of changes and rewording in all the steps of the validation process.

Validity and reliability

The overall credibility and internal validity of the thesis were ensured by method triangulation, i.e., using mixed methods (qualitative and quantitative) for data collection (84). The content validity of the Diet and Bowel Function questionnaire was assessed by cognitive interviews, in which the participants' perception of each question's relevance, clarity and comprehension were thoroughly penetrated and structurally noted. Regardless of which methods were used (focus groups, cognitive interviews, questionnaire studies), similar results appeared; namely that diet has a great importance for gastrointestinal symptoms in children with Hirschsprung's disease and that dietary effects differ between children with Hirschsprung's disease and healthy children. Since

these results repeatedly appeared, their validity is considered as very high. The high level of agreement of the results, permeating the entire thesis, also reflects a high degree of reliability.

Strengths and limitations

The main strengths of this thesis were the inclusion of both qualitative and quantitative methods and the involvement of patients early in the process. The qualitative focus group study generated research questions that were quantitatively investigated. The results from the case-control study both confirmed and explained the results from the focus groups, namely that experiences of diet to induce gastrointestinal symptoms were frequently reported and that specific dietary items induced gastrointestinal effects differently compared to healthy children. The parents' profound and dynamic perspectives emerging in the focus groups, of diet's role in impacting the child's gastrointestinal complaints in daily life, ensured a deeper understanding of the results in the case-control study. The collaboration with the patient organisation secured research questions of high relevance for the patient group, in accordance with previous studies (21,25). Involving children with and without Hirschsprung's disease respectively, and their parents, in the development and validation of the questionnaire, ensured a user-friendly questionnaire with relevant and clear questions. Involving patients in the design of studies has been shown to generate higher-quality and more relevant research (85). Furthermore, the multi-professional research group contributed to enhanced medical, emotional and social aspects of diet in Hirschsprung's disease, in addition to the detailed information on diet's and food items' effect on gastrointestinal symptoms.

Limitations to consider are that mainly the parental view was taken into consideration, when developing the questionnaire and maybe also in answers of the questionnaire. To catch the children's true experiences and views on diet and their own perception of importance, would be of great interest and concern. This would need another round of a qualitative study, and maybe also a quantitative validation of the questionnaire from a child perspective. Since the concepts for the questionnaire were collected from the focus groups, the parents' concerns might have come to permeate the questionnaire although the children's concern also were really emphasised to be in focus. To reduce the risk of any analytic bias, clear information on how to answer the questionnaire; i.e.; by-proxy was included in the questionnaire instructions. Still, whose perspective is most represented; the child's or the parent's, remains unclear and needs to be taken into consideration. Another limitation was the cross-sectional design in the case-control study, implying that neither causalities nor changes over time were investigated. In the

case-control study, we couldn't detect any significant differences in dietary effects on gastrointestinal symptoms between children with various extensions of aganglionosis; i.e.; severity of disease. This may be attributed to the limited number of children with long-segment aganglionosis and consequently a type 2 error. The weak power could, hypothetically, in turn also lead to the absence of differences regarding dietary effects on gastrointestinal symptoms between subgroups (age or sex) of children with Hirschsprung's disease. In order to confirm or exclude that dietary effects on gastrointestinal symptoms do not associate with the severity of disease, larger multicentre studies are needed. The generalizability of the questionnaire studies could be questioned, since the questionnaire was only provided in Swedish and the food items listed in it reflected a typical Nordic diet. This may have contributed to uncertainty in the questionnaire responses about which food choices affect gastrointestinal symptoms. This needs to be taken in consideration especially in children with a food culture at home and a different food culture in preschool and school, and especially in younger children where the parent is assumed to have greater participation in answering the questionnaire. In order to confirm the results in a wider context, linguistic and cultural adaptations are required.

Clinical implications

The overall results from this thesis support the inclusion of a multi-professional discussion about diet in bowel management programs within Hirschsprung's disease guidelines. The results show that, on group level, diet and specific food items appear to have a limited effect on gastrointestinal complaints, why recommendations about using food alone to control gastrointestinal symptoms should be questioned. Since food is a great part of daily and social life, it still deserves a careful consideration within a dialogue and counselling between a dietician competent in Hirschsprung's disease and parents and/or patients. This is of special importance since results from the focus groups showed dietary impact also on emotional and social life. Restrictions of diet, may lead to negative consequences for the child with no beneficial gastrointestinal effect.

The overall results in this thesis revealed a discrepancy between the parent's focus on dietary adjustments to improve their child's gastrointestinal complaints, and the healthcare service's common practise in focusing on laxative drugs and enemas to improve gastrointestinal complaints. Especially in Study I, multi professional support was described as important, consistent with previous studies (7,21,40). The results of this thesis have led to a change in our follow-up program, with the inclusion of a dietician and social worker in the multi-professional team at key follow-up visits during childhood.

Applying the results to specific clinical counselling about diet, the results support that recommendations should preferably be given on specific food items, for example beans, instead of on a food group category, for example “fruits” or “vegetables”. This is because specific food items within a food group were shown to induce gastrointestinal symptoms differently. This was especially evident in children with Hirschsprung’s disease. Furthermore, because of the reported high incidence of side effects as gas and stomach pain of fibre-rich foods (which are usually recommended for children with constipation), we could say from results that such a diet might even be contraindicated in children with Hirschsprung’s disease suffering from obstruction. This information needs to be handled in preschools and schools where fibre-rich food is increasingly served, since it, on a population level, has several health implications.

In clinical counselling, not only the sort of food but also the amount needs to be taken into account. The impact of food on gastrointestinal symptoms may be affected by the quantity of a specific food item, or of the combination of different food items (86). Potential efficacy on constipation has been shown in adults, after intake of large amounts of food items with laxative effect, for example, 12 prunes per day (55) or 2 kiwi fruits per day (54). For a child, it could be difficult to eat such large amounts regularly. Furthermore, it has been shown that children’s compliance to food recommendations has been reported to be low (87), which needs to be taken into consideration in counselling. In addition, most Swedish adolescents were reported to consume fruit, vegetables, and dietary fibre at levels far below official recommendations (88-89). Therefore, it may be difficult to encourage children to increase their intake of fruit, vegetables and dietary fibre in order to improve gastrointestinal symptoms.

Also, of importance to take into consideration as a clinical dietician is that there are several conditions in Hirschsprung’s disease leading to gastrointestinal complaints, that cannot be managed by diet. For example, an anatomical cause of obstruction or faecal incontinence could instead need surgical treatment. The multi-professional team-work is essential to assess and manage the condition for the individual child. A clear communication within the team is of importance in order to limit any unnecessary efforts by food regulation. The flow-chart displayed in **Figure 6** can be used as a pedagogic tool in counselling, to get an overview of the management alternatives of different gastrointestinal symptoms. The conditions where diet might be a treatment alternative are marked in pink.

Thus, there is a need for caution when recommending dietary modifications in children with Hirschsprung’s disease. Since dietary intervention studies have not been conducted, except for the study on children with faecal incontinence (19), we still cannot tell for sure about any efficacy of the dietary modifications. For this invention studies are needed. Failing to implement goals of dietary advice risk imposing

considerable guilt on children and their families. If introducing a dietary change, a close clinical follow up is a must in order to support or restrict further adjustments. If the desired effect is not achieved, the food should be reintroduced. This should be respectfully acknowledged by health care professionals and be accompanied by individualized counselling.

Gastrointestinal complaints in children with Hirschsprung's disease

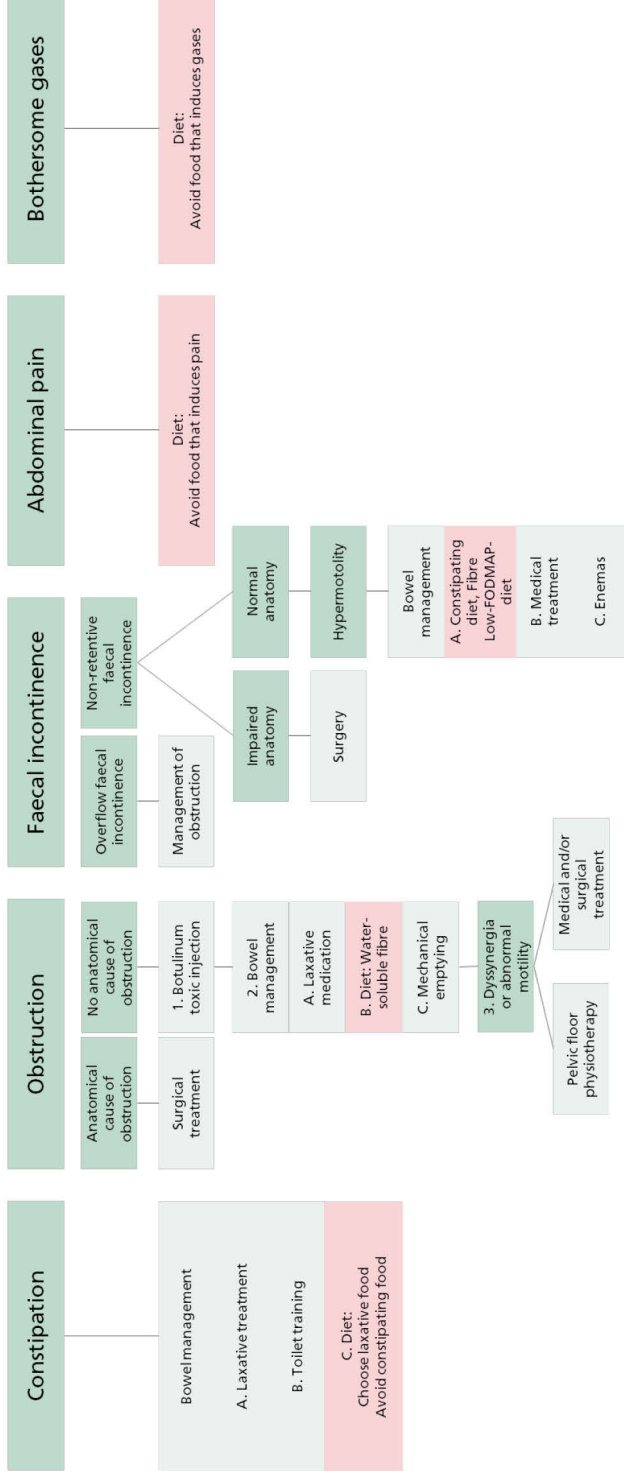


Figure 6. Overview of management of gastrointestinal complaints in children with Hirschsprung's disease. Conditions where dietary management might constitute a treatment option are marked in pink.

Future perspectives

The results of this thesis provide increased knowledge about the effects of diet on gastrointestinal symptoms in children with Hirschsprung's disease. In order to clarify the diet's fruitful pathways or blind alleys in the management of Hirschsprung's disease, and before any evidence-based recommendations can be given, dietary interventional studies urgently need to be carried out. The results from this thesis can form a stable base for future planning of dietary interventional studies.

Diets of interest in interventional studies in Hirschsprung's disease could include the traditional IBS-diet as per the NICE-guidelines and/or the low FODMAP-diet. (The diets are described in the Background section of the thesis). Dietary effects in Hirschsprung's disease, as reported in this thesis, largely mimic the theory of NICE-guidelines, and it would be of importance to investigate any possible beneficial effects of such diets. Also, the food items most frequently reported by children with Hirschsprung's disease in this thesis have a high content of FODMAP's. In one small interventional study, a low FODMAP-diet in children with Hirschsprung's disease led to a decrease of faecal incontinence (32). Therefore, it would be of great interest to investigate if the low FODMAP-diet could lead to improvement of gastrointestinal complaints also in a larger group of children and with a wider spectrum of gastrointestinal symptoms.

Since Hirschsprung's disease is rare, to increase power and enable analyses of subgroups of children with Hirschsprung's disease, multi-centre studies are needed. The extension of aganglionosis, sex and age are variables that possibly could impact the outcome. To confirm the results of this thesis in other cultural contexts, international multi-centre studies are preferable but of course complicated to perform. This is since a diet not only consists of one type of food, but a spectrum, and since dedicated dieticians need to be in place to guide families and patients during the whole intervention course.

The Diet and Bowel Function questionnaire can be used as a clinical tool to assess dietary effects on gastrointestinal complaints in Hirschsprung's disease. In research, the questionnaire could be used in a Nordic setting. For the use in an international setting, an adaptation of the food items would be necessary.

In accordance with the National highly specialized care, collaboration in research and in clinical care are essential cornerstones for the two national referral centres for Hirschsprung's disease (62). Since the assignment started in 2018, national cooperation has expanded. This is essential in order to provide equal care for patients and to increase overall knowledge about Hirschsprung's disease although being a rare condition. Already on board on the national multidisciplinary cooperation are paediatric surgeons,

paediatricians and paediatric nurses. Based on the thesis' results, there are now strong reasons also to include paediatric dieticians and to promote networks for dietitians. Incentives for networks for dietitians in paediatric surgery have started slowly locally, nationally and internationally but the networks need to be better defined and settled. A first step might be to design a structured care and time scheduled regime specifically for dietary key control in clinical counselling of children with Hirschsprung's disease and their parents.

Conclusion

Diet constitutes an integral part of families' self-treatment of children with Hirschsprung's disease. This was repeatedly shown no matter which method was applied. Effects of diet on gastrointestinal symptoms overall seem to be limited although children with Hirschsprung's disease experience a greater impact than that observed in healthy children. The specific gastrointestinal effects induced by food also seem to differ between children with Hirschsprung's disease and healthy children. Trying to control children's gastrointestinal complaints by self-treatment with food has an impact on daily life in families of children with Hirschsprung's disease. The results from this thesis indicate a profound need for evidence-based disease-specific dietary advice within a multi-professional follow-up programme for children with Hirschsprung's disease.

Acknowledgements

First of all, I want to thank the *patient organisation Hirschsprung disease Sweden*, our collaboration is very meaningful to me. I want to thank all the *children without Hirschsprung's disease and their families*, for taking your time to participate in the studies. Foremost, I want to thank all the *children with Hirschsprung's disease and their families* for participating in the studies and sharing your experiences. I hope that you and other children will benefit from the results of this thesis.

Pernilla Stenström, my main supervisor. Thank you for your tremendous support during my PhD-studies. I am grateful for all the opportunities you have given me. Thank you for your curiosity, warmth and enormous commitment. You inspire me, in life and in research. I look forward to continuing working with you, and just as much, when you are no longer my supervisor, I look forward to nurturing the friendship I have in you.

Irene Axelsson, my co-supervisor. Thank you for supporting me, despite retirement. Our clinical collaboration inspired me to start my PhD-studies. You have strengthened my clinical skills and my scientific reasoning. I value your warmth, enormous experience, childlike and sharp mind. I appreciate our friendship a lot.

Christina Granéli, my co-supervisor. Thank you for your great knowledge in Hirschsprung's disease, which you so generously share with me. Your contribution in planning the studies and writing the manuscripts are clearly anchored in the clinic and in your research, and I am so grateful for that. I look forward to our future collaborations!

My other co-authors: Inger Hallström. Thank you for sharing your vast experience in qualitative research methodology. *Frida Waldenvik*. I can't think of a better moderator for the focus groups. The result would never have been so rich without you. *Louise Tofft*. Thank you for our collaboration with the focus group study. I really enjoy all the laughs with you! *Christine Kumlien*. Thank you for believing in the questionnaire development and for your words of encouragement along the way.

David Ley, at the last minute you took your time to proofread my manuscript. Thank you for your generosity and kindness!

Ros Kenn, thank you for proofreading my manuscripts.

My managers: Maria Mårtensson. Your support, especially in recent years, has meant a lot to me. Thank you for your curiosity, calmness and courage. *Charlotte Brattström.* I enjoy laughing with you and I appreciate you enormously. Let's keep raising our glasses of sparkling water and celebrate the events of everyday life! *Elisabeth Olhager.* Thank you for giving me opportunities to finish my master's thesis. I really appreciate our small but meaningful conversations.

My fellows from Bengt Ihre Research School: Emma Svensson, Hanna Tufvesson, Ida Henriksson, Soran Bozorg, Gullik Gulliksson. It has been a pleasure to develop as a researcher while spending time with you. Thank you for "the Bengt Ihre spirit"!

Emma Svensson. Thank you for all the laughter and inspirational conversations about research, clinical work and life. I saw a chance and I took it! And on top of that, I got a friend for life.

My dietician colleagues, especially Patricia Fröslin, Siyin Gao, Lisa Olsson, Mikael Nilsson, Viktoria Schiöler, Maria Medrano Savvidou, Marika Kanthe, Martina Engström, Tove Diswall, Lotta Söderberg, Anna Hansson, Elin Malmberg Hård af Segerstad. Thank you for your support and for all the laughter! I'm grateful for our discussions about paediatric nutrition, science and clinical issues. I look forward to be back in the clinic with you again!

The staff at the Department of Paediatric Surgery in Lund, especially at the outpatient clinic and on ward 65: Magnus Anderberg, Helena Arnadottir, Einar Arnbjörnsson, Torbjörn Backman, Anna Börjesson, Emma Eklund Grotting, Lars Hagander, Kristine Hagelsteen, Mette Hambraeus, Ann Nozohoor Ekmark, Erik Omling, Martin Salö, Morten Vigen, Gunnar Westbacke and Hans Winberg. Thank you for your never-ending encouragement! I look forward to continue working with you. *Matilda Wester Fleur.* Thank you for our clinical collaboration, I appreciate it immensely. It will be so much fun to follow you during your PhD-studies – imagine how much we will learn together! *Maja Hernborg, Emma Tiseus, Helen Sjövie, Anna Sjögren, Monica Wedbäck, Agneta Svensson, Elin Öjerholm and Ingrid Billström.* Thanks for all your kindness and warmth!

The physiotherapists and occupational therapists. Thanks for your encouragement. I really enjoy working with you. *Ingrid Pupp.* I appreciate you as a colleague and as a friend. *Pia Karlsland Åkeson.* I appreciate our clinical collaboration a lot. *Björn Sigurdsson and Gunnar Sigurdsson.* Thank you for the conversations and your company while writing this thesis. *Niclas Rudolfsson,* thanks for sharing your thesis template with me.

Minna, Maria, Anja, Ulrika, Mia, Lisa, Marie, Helen & Jesper, Linda & Erik & Glimminge-friends. Thank you for all that we share and experience together. Thank you for making such a positive impact on my life.

Britten Telborn and Johan Falk. Thank you for all your love and support, both then and now. I appreciate you enormously as persons and I am so happy to have you as parents.

Klas Telborn. My older brother and childhood star. Thank you for all the laughs we share. *Josefin Telborn,* my sister-in-law. Thanks for talks about knitting and other essentials in life.

Bengt Jönsson. Thank you for all the good times, for hikes, walks and talks where you made me look at things in a new way. Thank you for the most precious we have – the children.

Signe Telborn and Henning Telborn. You are my greatest love, gratitude and inspiration. I love to discover with you. You fill my life with joy!

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Studies I–IV



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Paediatrics
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Lund University, Faculty of Medicine
Doctoral Dissertation Series 2023:149
ISBN 978-91-8021-491-9
ISSN 1652-8220

