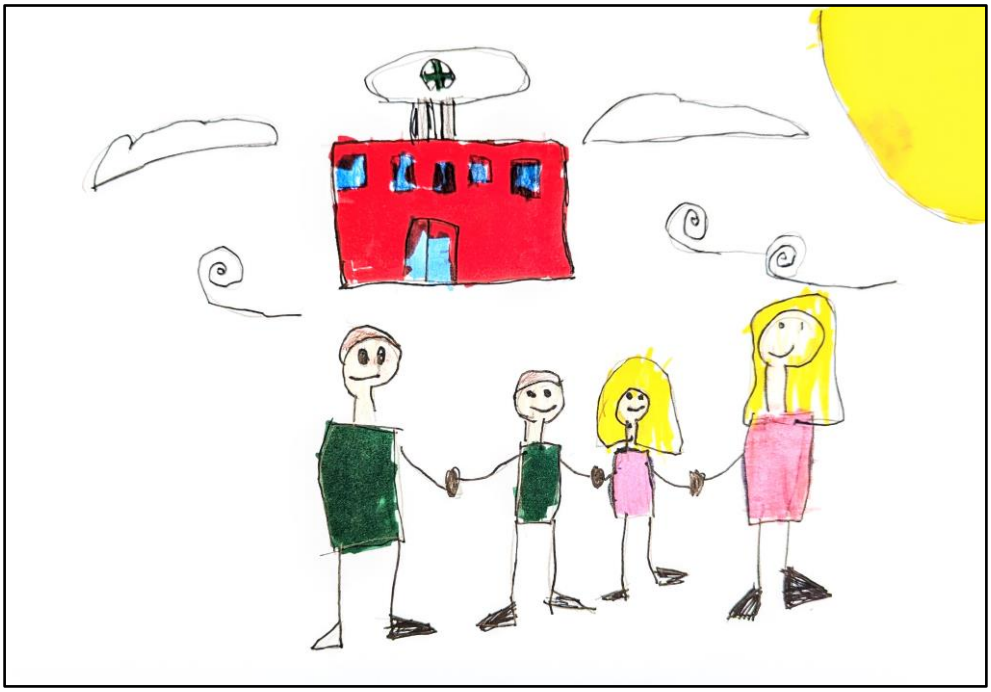
UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES



PhD Thesis

Gitte Færk

Children with atopic diseases

Care pathways, experiences of care and influence on family life

Supervisors: Susanne Reventlow, Lone Skov, Kirsten Skamstrup Hansen, and Jacob Pontoppidan Thyssen

This thesis has been submitted to the Graduate School of Health and Medical Sciences, University of Copenhagen on July 11th 2024

Children with atopic diseases

Care pathways, experiences of care and influence on family life

PhD Thesis

Author: Gitte Færk, Cand.med.

Centre for General Practice, Research Unit for General Practice Slagelse/Copenhagen, and Section of General Practice, Department of Public Health, University of Copenhagen, Denmark

Department of Dermatology and Allergy & Department of Pediatrics, Herlev and Gentofte Hospital, University of Copenhagen, Denmark

National Allergy Research Centre, Herlev and Gentofte Hospital, University of Copenhagen, Denmark

This PhD thesis is the product of a scientific collaboration between:

Supervisors:	Principal advisor: Professor Susanne Reventlow, MD, MSc anthropology, DMSc, Centre for General Practice, Research Unit for General Practice Slagelse/Copenhagen and Section of General Practice, Department of Public Health, University of Copenhagen, Denmark Primary co-supervisor: Professor Lone Skov, MD, PhD, DMSc, Department of Dermatology and Allergy, Herlev and Gentofte Hospital, University of Copenhagen, Denmark Co-supervisors: Chief physician Kirsten Skamstrup Hansen, MD, PhD, Department of Pediatrics, Herlev and Gentofte Hospital, University of Copenhagen, Denmark Professor Jacob Pontoppidan Thyssen, MD, PhD, DMSc, Department of Dermatology and Venereology, Bispebjerg Hospital, University of Copenhagen, Denmark
Assessment committee:	Professor Lene Heise Garvey, MD, PhD (Chair) Allergy Clinic, Department of Dermatology and Allergy, Copenhagen University Hospital – Herlev and Gentofte, Denmark Associate professor Bjarne Austad, MD, PhD General Practice Research Unit, Department of Public Health and Nursing, Norwegian University of Science and Technology, NTNU, Trondheim, Norway Associate professor Merethe Kirstine Andersen, MD, PhD Faculty of Health Sciences, Department of Public Health, Research Unit of General Practice, University of Southern Denmark, Odense, Denmark
Funding:	CAG (Clinical Academic Group) Fonden for Faglig Udvikling i Speciallægepraksis Lilly og Herbert Hansens Fond Region Hovedstadens Forskningsfond Tværspuljen
Cover picture:	Drawing made by my son, Peter Færk
Submitted on:	July 11th 2024

Acknowledgements

Completing this PhD project has been an exciting and challenging journey with twists and turns along the way and I am grateful for all the people, who made this work possible.

First and foremost, I would like to express my gratitude to all the participants, who took part in the questionnaire study and the interviews. Thank you for taking the time to complete the questionnaire. I am very grateful to the families, who welcomed me into their homes during the challenging times of COVID-19, and generously shared their detailed and often very personal experiences. The contributions of these participants are the foundation of this thesis, and it would not have been possible without them.

Thank you to the practicing specialists Susanne, Marta, Ida, Steffen, Steen and Anne in the Capital Region, who recruited informants from their practices to the questionnaire study. Thank you to the department of pediatrics and the department of dermatology and allergy for the opportunity to include participants at your sites.
Thank you, Viktoria for assisting with the recruitment of participants in the questionnaire study at the hospital departments and entering a portion of the questionnaires.
Malin, thank you for your assistance with the analysis in study 1 and for providing highly valuable feedback and input writing the manuscript for the questionnaire study.
Thank you, Ida, for transcribing all the interviews. Your work has been incredibly helpful.
Thank you, Elisabeth for your important input in the analytical process and writing manuscript II, as well as our collaboration on manuscript III. I have learned a great deal from you about analyzing and writing qualitative manuscripts. Additionally, I really appreciate the time we spent as office mates and your encouragement throughout this journey.

Thank you to my four supervisors, each with unique competences and personalities. A heartfelt thank you to Susanne, my primary supervisor and mentor, whom I deeply admire. You introduced me to qualitative research and you guided me on the journey into this new realm. It has been an exciting and highly enriching journey. Your ability to see things from different perspectives by combining your extensive knowledge within both family medicine and anthropology, and to see opportunities rather than limitations is truly inspiring. I am immensely grateful for your ability to see the whole person and your invaluable support and encouragement throughout the entire journey.

Lone, thank you very much for your motivation, support, kindness, and always responding promptly, when I write to you. I am grateful for the opportunity to be part of the dermatology research environment and for everything I have learned from you.
Kirsten, thank you for your extensive clinical knowledge, and our interesting discussions about atopic diseases. It has been inspiring to see a physician, who cares so deeply about her patients.
Jacob, thank you for your immense expertise in dermatology and for being a great source of new ideas.
Jeanne, thank you for the opportunity to be part of the research environment at the National Allergy Research Centre and the research collaboration CAG Allergy.
Thank you to the Department of Occupational and Social Medicine at Holbæk Hospital for providing me with the opportunity to dedicate some time to writing my thesis. Your support is truly appreciated.

Thank you to all the colleagues at the department of Dermatology and Allergy, the National Allergy Research Centre, and the Research Unit and Section for General Practice. I am grateful for being included in both the academic and social activities, although it changed along the way which department I was primarily associated with.

Finally, a special thank you to my family: My husband, Lasse, thank for your endless support and for managing additional responsibilities at home. To our children, Johannes, Peter and Maria – you and Lasse are the loves of my life and you all bring me immense joy.

Gitte Færk
Copenhagen, July 2024

Table of contents

Preface

This PhD thesis was part of a larger research collaboration CAG (Clinical Academic Group) Allergy. A CAG is an academic clinical research group with researchers and clinicians from the university, hospitals, specialist practices and general practices. The network was appointed in June 2017 as one out of the first four CAGs in the Region of Copenhagen/University of Copenhagen following evaluation by an international expert panel.

During my medical education, I developed an interest in atopic diseases, which became the focus of first my bachelor's project and later my master's thesis. Therefore, applying for the PhD position was an obvious choice for me, as it provided an excellent opportunity to further engage with this topic. Furthermore, my clinical experience in general practice and various hospital departments provided me with insights into referral pathways from different perspectives. I remember at times, while working in general practice as a junior general practitioner, it was challenging to guide patients to the appropriate services within the healthcare system. This often required firsthand experience with the wide range of healthcare services available in the specific geographical area, including the expertise areas and waiting times of individual practicing specialists, which I did not always have. My experiences made me wonder whether this could be organized differently.

The PhD project is based on both quantitative and qualitative research methods, and it has been my first opportunity to work as a qualitative researcher. It has been a continuous learning process strengthened by PhD courses in qualitative research methods and the extensive qualitative competences present at the Research Unit for General Practice and Section of General Practice in Copenhagen.

Included manuscripts

I. **Manuscript, study 1:** Færk G, Ahlström MG, Lura VH-E, Reventlow S, Johansen JD, Thyssen JP, et al. **Referral Pathways for Children with Atopic Diseases in Denmark**. Acta Dermato-Venereologica. 2024;104:adv34961. DOI: 10.2340/actadv.v104.34961.

II. **Manuscript, study 2:** Færk G, Søndergaard E, Skov L, Thyssen JP, Hansen KS, Reventlow S. **Parents of children with atopic diseases - experiences with care and the interaction with healthcare professionals over time**. Scandinavian Journal of Primary Health Care. 2024:1-10. DOI: 10.1080/02813432.2024.2357794.

III. **Manuscript, study 3:** Færk G, Søndergaard E, Skov L, Hansen KS, Reventlow S. **A "normal" life: a qualitative study exploring parents' experiences of everyday life with a child diagnosed with atopic dermatitis and atopic comorbidities**. Health: An Interdisciplinary Journal for the Social Study of Health, Illness and Medicine (Submitted) 2024.

List of abbreviations

AD	Atopic dermatitis
ADHD	Attention-deficit hyperactivity disorder
ARC	Allergic rhinoconjunctivitis
CAG	Clinical Academic Group
COVID-19	Coronavirus disease
CRF	Case report file
GINA	Global Initiative for Asthma
GP	General Practitioner
ICS	Inhaled corticosteroids
IgE	Immunoglobulin E
ISAAC	International Study of Asthma and Allergies in Childhood
LABA	Long-acting β2-agonists
OAS	Oral allergy syndrome
OFC	Oral food challenge
REDCap	Research Electronic Data Capture
SABA	Short-acting β2-agonists
STC	Systematic Text Condensation
VAS	Visual Analog Scale

Summary

English

Atopic diseases such as atopic dermatitis, food allergy, asthma, and allergic rhinoconjunctivitis (hay fever) are frequent among children. The severity of these diseases vary both among children and over time for the individual child. During their journey children with atopic diseases often need to interact with various healthcare professionals, but there is a limited knowledge about their care pathways and how these can be improved. The objective of this PhD-project was to explore dimensions of care for children with atopic diseases that could be strengthened.

In the first study, we completed a questionnaire survey exploring the present referral pathways in the Danish healthcare system for children with atopic diseases. We found that there was not a direct pathway to the hospital for children with three or more atopic diseases, but they were more often referred to the hospital compared with children with one or two atopic diseases. In addition, food allergy and to a smaller degree asthma were found to be main contributing factors for referral to a hospital, whereas the number of diseases, atopic dermatitis and allergic rhinoconjunctivitis did not have the same effect.

The second and third study were both based on individual interviews with parents of children with atopic dermatitis and another atopic disease (food allergy, asthma, and/or allergic rhinoconjunctivitis). In the second study, we examined parents' experiences with care and their children's care pathways within the healthcare system. The mapping revealed complexity and large variations in the children's care pathways even though they had the same atopic diseases. The allocation of responsibility, roles and tasks affected the interaction with healthcare professionals. The parents had a sense of care when the allocation of tasks and responsibilities matched both the families' expectations and experiences. The care pathway was experienced as segmented due to limited collaboration between healthcare professionals, which resulted in increased parental responsibility for coordination. The families felt supported, when healthcare professionals knew more about them than the child's diseases and individually adapted the level of provided care.

In the third study, we examined how the atopic diseases affected family life including the tasks parents assumed in response to their child's conditions. Tasks directly associated with the child's treatment only played a minor role in the total workload. The parents carried out numerous other tasks to modify family life in response to the child's atopic diseases, which stemmed from their aspiration for their child to have a childhood as normal as possible.

In conclusion, these three studies contribute to the understanding of the care pathway for children with atopic diseases with focus on the parents' perspective. While accessibility is a key factor, continuity and trust are essential in the care pathway from the parents' viewpoint. Having a child with multiple atopic diseases impact the entire family, and the child's overall care pathway extends beyond encounters with healthcare professionals and the biomedical aspects. It is important for healthcare professionals be aware of these broader implications, as knowledge of these represents a significant step towards improving parents' experiences of the care pathway for their children with atopic diseases.

Dansk

Atopiske sygdomme herunder atopisk dermatitis, fødevareallergi, astma og allergisk rhinoconjunctivitis (høfeber) er udbredte blandt børn. Sværhedsgraden af disse sygdomme varierer fra barn til barn, men også over tid hos det enkelte barn. Undervejs i et udrednings- og behandlingsforløb har børn med atopiske sygdomme ofte behov for at konsultere en række forskellige sundhedsprofessionelle, men der mangler viden om disse forløb og hvordan man kan forbedre forløbene. Formålet med dette ph.d.-projekt var at undersøge forløb og oplevet omsorg blandt forældre til børn med atopiske sygdomme med henblik på at identificere områder, der kan styrkes.

I det første studie gennemførte vi en spørgeskemaundersøgelse, hvor vi undersøgte det eksisterende forløb i sundhedsvæsnet i Danmark for børn med atopiske sygdomme. Vi fandt, at der ikke var en direkte henvisningsvej til hospitalet for børn med tre eller flere atopiske sygdomme, men at disse børn hyppigere blev henvist til hospitalet end børn med en til to atopiske sygdomme. Vi fandt også, at fødevareallergi og i mindre udstrækning astma var de væsentligste årsager til, at børnene blev henvist til hospitalet, hvorimod antallet af sygdomme, atopisk dermatitis og allergisk rhinoconjunctivitis ikke havde samme effekt.

Det andet og tredje studie var begge baseret på individuelle interviews med forældre til børn med atopisk dermatitis og en anden atopisk sygdom (fødevareallergi, astma og/eller allergisk rhinoconjunctivitis).

I det andet studie undersøgte vi forældres erfaringer med oplevelse af omsorg og deres børns forløb i sundhedsvæsnet. Kortlægningen viste, at børnenes forløb var komplekse og med stor variation, til trods for at de havde de samme atopiske sygdomme. Fordelingen af ansvar, roller og opgaver havde stor betydning for interaktionen med sundhedsprofessionelle. Forældrene havde en oplevelse af omsorg, når der i fordelingen af opgaver og ansvar var overensstemmelse

mellem det familierne forventede og faktisk oplevede. Forløbet blev oplevet som fragmenteret grundet begrænset samarbejde mellem de sundhedsprofessionelle, hvilket medførte at forældrene havde et øget ansvar for koordinering. Familierne oplevede omsorg og støtte, når de sundhedsprofessionelles kendskab til familien rakte ud over barnets sygdomme, og de tilpassede niveauet af ydet omsorg i forhold til den enkelte families behov.

I det tredje studie undersøgte vi, hvordan de atopiske sygdomme påvirkede familielivet, herunder de opgaver som forældrene påtog sig i relation til deres barns sygdomme. Det viste sig, at de opgaver, som direkte vedrørte barnets behandling kun udgjorde en mindre del af den samlede arbejdsbyrde. Forældrene udførte talrige andre opgaver i forsøget på at tilpasse familielivet i forhold til barnets atopiske sygdomme ud fra et ønske om, at deres barn skulle have en så normal barndom som muligt.

Sammenfattende, så bidrager de tre studier med en større viden om de eksisterende forløb for børn med atopiske sygdomme med fokus på forældrenes perspektiv. Mens tilgængelighed er en vigtig faktor, så er kontinuitet og tillid essentielle elementer i forløbet set fra forældrenes synsvinkel. Det påvirker hele familien at have et barn med flere atopiske sygdomme, og børnenes udrednings- og behandlingsforløb omfatter mere end mødet med sundhedsprofessionelle og de biomedicinske aspekter. Det er vigtigt, at sundhedsprofessionelle er opmærksomme på disse omfattende implikationer, eftersom en opmærksomhed på dette er et væsentligt skridt mod at forbedre forældres oplevelser af forløbet for deres børn med atopiske sygdomme.

Introduction

Many parents find themselves navigating the challenges of raising a child with one or more chronic diseases. From the initial diagnosis to ongoing management, families of children with more severe symptoms often encounter various healthcare professionals to ensure their child receives the necessary treatment and support. While some children may experience mild symptoms requiring minimal attention, others may face severe symptoms necessitating constant vigilance from both parents and healthcare professionals. This PhD thesis will focus on children with atopic diseases, including atopic dermatitis (AD), food allergy, asthma, and allergic rhinoconjunctivitis (ARC).

Atopic diseases are very common. It is estimated that 10-40% of a population have one or more atopic diseases (1, 2). A study concerning Danish and Swedish children found that approximately 30% of children aged 0 to 15 years have or have previously had atopic diseases (3). Atopic diseases in childhood can vary greatly in terms of range of symptoms and severity, ranging from very mild cases to those were children have multiple concurrent atopic diseases with a chronic course requiring prolonged treatment and follow up.

Objective

The aim for this thesis is to identify areas for improvement of care for children with atopic diseases. To achieve this, we have examined the current referral pathways and, to integrate the parents' perspective, we explored their experiences with care and interactions with healthcare professionals. Furthermore, we explored how atopic diseases impact family life, acknowledging the family structure and the pivotal role parents play in the management of their child's atopic diseases.

I. *"To describe the current referral pathways in the Danish healthcare system for children with AD, food allergy, ARC, and/or asthma"* (Questionnaire study, manuscript I).

II. *"To explore how parents of children with AD and allergic diseases experience encounters with the healthcare system"* (Experiences with care and the interaction with healthcare professionals, manuscript II)

III. *"To explore the homework in the broadest sense: the tasks and care that parents perform every day that are related to their child's atopic diseases, both as part of the treatment and as part of the parents' wish for giving the child as normal a childhood as possible"* (Parents' experiences of everyday life, manuscript III)

Background

Atopic diseases

Atopic diseases included in this thesis are atopic dermatitis (AD), food allergy, asthma, and allergic rhinoconjunctivitis (ARC). There will be a particular emphasis on children with AD and atopic comorbidities.

Therefore, the following section will shortly address each disease covering aspects such as prevalence, duration, diagnostics and treatment. It will cover the aspects of having multiple atopic diseases, the organization and management of atopic diseases within the Danish healthcare system, patient experiences, the concept of care and the treatment burden. As this thesis focuses on children, parents are responsible for managing interactions with healthcare system, as well as providing daily care and treatment of the atopic diseases.

Atopic dermatitis

Atopic dermatitis (AD) is a chronic inflammatory skin disease (4). The prevalence has increased within the past century, but it has in recent years plateaued in high-income countries (5, 6). Almost 20% of children are affected by AD and approximately 10% of adults (4, 6). About 60% of individuals with AD have disease onset within their first year of life (7). It is common that AD persist into adulthood (8-11), which emphasizes, that AD for a substantial part is a long-term and chronic condition, requiring continuous attention and effort from both the parents/caregivers and healthcare professionals.

The severity, symptoms, and course of AD vary between individuals, and since there are currently no conclusive diagnostic tests, a clinical evaluation is used to make the diagnosis (4). Commonly used clinical diagnostic criteria for AD are based on Hanifin and Rajka criteria (12). The central criteria are itch, eczema with age-specific distribution and chronic/recurrent symptoms (4, 13). Furthermore, a substantial part of the individuals have early onset, dry skin, elevated Immunoglobulin E (IgE), and a family history of atopic diseases (4, 13).

The treatment is stepwise depending on the symptoms with emollients with a high lipid content being the mainstay frequently supplemented with intermittent periods with topical corticosteroids or calcineurine inhibitors (4). Most of the treatment can be managed by the parents in collaboration with general practice. If the symptoms are moderate to severe or persistent various healthcare professionals may be involved, including general practitioners, pediatricians or dermatologists. Additional treatment options, in more severe cases, such as

phototherapy, systemic anti-inflammatory and biological treatment (4), are managed by dermatologists. In case of severe or intractable AD, specialized care may be required, provided at the department of dermatology within a hospital (14).
As a result, diagnosing and treating AD may necessitate continual assessments and the involvement of healthcare professionals from various medical specialties and sectors. This calls for coordination and collaboration. The key question is how healthcare professionals can adjust the treatment approach to accommodate the individual disease course for each patient.

Food allergy

The term food allergy is used to describe when a food protein antigen causes a pathogenic immune response (15). Food allergy consists of allergies to a variety of different food items for example milk, eggs, peanuts, soy, tree nuts, fish, shellfish, and sesame (16). In childhood the most frequent allergens are milk, peanuts, eggs and tree nuts, but from childhood to adulthood, there is a shift in the most frequent allergens (17, 18). It has been estimated that 8% of children and 5% of adults have parent- or self-reported food allergy (17). Secondary food allergy caused by cross reaction with inhalant allergens is well-known (19). It is called oral allergy syndrome (OAS) and it is caused by cross reactive IgE pollen-antibodies reacting with a specific part on fruit and vegetable proteins (epitopes) (15, 20).
Food allergy can cause a range of symptoms; urticaria, OAS including itch, discomfort and a sense of swelling in the mouth and throat, gastrointestinal such as diarrhea, vomiting, and abdominal pain, anaphylaxis including hypotension and respiratory symptoms (15).
The clinical history and examination are supported by levels of specific IgE, skin prick tests, and oral food challenges (OFC) in the medical evaluation of food allergy (15, 19). Currently, the main treatment is avoiding allergens in the diet (16). Adrenaline auto-injectors are prescribed for immediate administration as emergency therapy (21), which must be brought along everywhere, requiring involvement from places like daycare and school. Avoiding food allergens can be particularly challenging when even trace amounts must be excluded, impacting the entire family.

Asthma

Asthma is a chronic disease typically characterized by inflammation and hyperreactivity of the airway passages in the lungs that results in airway obstruction (22). It is defined as intermittent episodes of breathlessness and wheezing which vary in frequency and severity (23). Children

with asthma frequently also experience concurrent cough (24). The prevalence of asthma is estimated to be approximately 14% among children (25).

The asthma diagnosis is based on a clinical history of fluctuating respiratory symptoms and for children ≥ 6 years of age verified variable expiratory airflow limitation (22). In children below 6 years of age wheezing/cough, that occurs simultaneous with exercise, laughing, crying, and in periods without a respiratory infection together with a history of atopic disease is indicative of asthma (22). According to the "Global Initiative for Asthma" (GINA) guidelines, asthma treatment varies by age, severity, and personal preference but generally includes inhaled corticosteroids (ICS) for prevention and either short-acting β2-agonists (SABA) or ICS combined with long-acting β2-agonists (LABA) for relief (22). The child may need to carry their reliever medication at all times, including at daycare and during leisure activities.

Allergic rhinoconjunctivitis

In this thesis, the notion ARC have been chosen, and this covers both allergic rhinitis and allergic rhinoconjunctivitis. ARC, also known as hay fever, is caused by allergy against inhalant allergens such as pollen from e.g., trees and grass, animal dander, molds, and dust mites (26). The worldwide cross-sectional study ISAAC has shown wide variations in prevalence from 4% and up to 45% of all children (13-14 years old) have ARC (2, 27). It often persists into adulthood, where studies show that 10 to 30% of adults have ARC (1, 28).

ARC is characterized by nasal itching, sneezing, rhinorrhea and/or nasal congestion. The nasal symptoms often occur with symptoms from the eyes including redness, itching and watery eyes (29). The diagnosis of ARC is based on the clinical history including description of the symptoms, where and when the symptoms appear, examination, skin prick test, and serum allergen-specific IgE (26). When possible, allergen avoidance is advised, such as avoiding particular animals if allergic to animal dander, although maintaining social interaction is essential (26). Management options for ARC vary by severity and include local and systemic antihistamines and intranasal corticosteroids, administered once or twice daily. For children aged 5 and older, allergen-specific immunotherapy can increase tolerance to allergens in moderate to severe cases (30).

Multiple atopic diseases

It is common for individuals to have more than one atopic disease, and there is an increased occurrence of food allergy, asthma, and ARC among both children and adults with (moderate-to-

severe) AD compared to those without AD (31-33). A meta-analysis study found a rhinitis prevalence of 37.2% among children with AD and 14.2% of individuals both children and adults with AD had rhinitis and asthma (31). Another study reported a prevalence of food allergy of 31.4% among children with AD (33). The severity of atopic diseases vary between individuals and typically also over time in the same individual (34), implying that the required level of treatment and support from healthcare professionals varies. The symptoms can range from mild to severe, and in rare cases of food allergy and asthma, they can be fatal (15, 35).

However, little is still known about the mechanisms behind the emergence of one or more atopic diseases, as well as predicting the severity. The concept of the Atopic March, proposing the sequential development of AD followed by asthma and later ARC, has been suggested to illustrate the time-dependent changes in prevalence, but studies have shown that different trajectories for atopic diseases exist (36-40). One study combining two children cohorts has described 8 different disease trajectories of AD, asthma and ARC with both transient and persistent disease patterns (36). Another recent study showed 7 disease trajectories for these three atopic diseases and influencing factors such as the early-life determinants (e.g. family history of allergy), genetic factors (e.g. filaggrin mutation) and food sensitization (40).

Having an atopic disease also increases the risk of other non-atopic diseases including infectious diseases (41), and among children with AD studies have shown that there is an increased risk of psychiatric diseases such as depression and ADHD (attention-deficit hyperactivity disorder) (42).

Early identification of children at high risk of developing severe and persistent atopic diseases can by aided by knowledge of disease trajectories and mechanisms (40). Furthermore, this early identification is an important step toward providing a more optimal level of care for each child and preventing progression of their diseases including the development of comorbidities. The differences in disease progression for children with multiple atopic diseases affect their healthcare needs. Therefore, gaining a better understanding of their care pathways is essential for optimizing disease management. As part of this effort, gaining deeper insights into parents' experiences both with the managing atopic diseases at home and navigating the healthcare system crucial.

Atopic diseases in the Danish Healthcare System

The healthcare system in Denmark is publicly funded by tax and it provides medical investigations, treatment, and preventive care through general practice, practicing specialists, and

hospitals (43). Additionally, subsidies cover a fraction of the cost of prescription medications, including some of those utilized in the treatment of AD, ARC, food allergy and asthma.
The vast majority of citizens are registered with a general practitioner (GP). The GP is available for all health issues an individual encounters at any age and is often the first contact to the healthcare system (44). The GP has a role as gatekeeper and most practicing specialists and hospital departments require a referral before consultation. A survey among Danish GP's identified great variations regarding diagnostics and treatment of patients with allergic disease including referral to other specialties and hospital departments (45). The variations depended on several different factors such as practice type (single handed versus more physicians) and clinical staff (45).
At the onset of symptoms the children and their parents may seek consultation at their GP, and it is estimated that the majority of children with atopic diseases can be fully treated by their GP (46). Depending on the symptoms, severity and complexity of the atopic disease (-s) a fraction of the children may be referred to a variety of practicing specialists or hospital departments including dermatology, pediatrics and allergy (46). According to pediatric specialty standard by the Danish National Health Authority, children with complex or severe allergic disease should be referred directly to a hospital or allergy center (47). Nevertheless, most children with allergy, asthma and other medical issues referred to a practicing pediatrician complete their medical assessment and treatment there and do not need a referral to a hospital department (47).
However, the number of patients with atopic diseases – both children and adults – receiving medical assessment and treatment at the hospitals has been increasing (46). There is a lack of knowledge about the referral pathways in the Danish Healthcare system, as only adequate disease-specific data from the hospitals are available in the official Danish disease registers (46).

In the Capital Region of Denmark, there are at this time clinical guidelines for single atopic diseases such as food allergy (anaphylaxis), asthma or ARC with treatment and referral recommendations, but there is not a disease management plan or clinical guideline for children with multiple atopic diseases neither regionally nor nationally (48). That is, when disease manifestations necessitate medical assessment and treatment across different medical specialties or healthcare sectors, healthcare professionals including GP's lack a description of when and where to refer these children. Additionally, there is not a description of how responsibilities for communication and coordination of the medical assessment and treatment are distributed. Thus, there is a pressing need for improved knowledge about care coordination and pathways for children with atopic diseases in the Danish Healthcare system.

Experiences with healthcare and the interaction with healthcare professionals

A Swedish study exploring the perspective of parents of children with severe atopic disease have described variations in access to care and received care depending of the region they resided in (49). According to the parents, the received care was influenced by the individual physician and they suggested that guidelines might support a more equal level of care (49).

Literature concerning parents' experiences with healthcare and the interaction with healthcare professionals have for the most part focused on children with a single atopic disease (50-52). One of the themes in these studies has been, that parents experienced receiving conflicting or insufficient AD advice from different healthcare professionals (51, 52). Another theme was parents were worried about the transition to another medical specialty, when the child became an adult (49, 50). A study examining both parents' and GP's experiences found that they had different disease understandings (52). On the other hand, parents expressed satisfaction when they experienced that they were involved in the decision-making, that there was enough time at consultations, and encountered competent healthcare professionals with good communication skills (50). Healthcare customized to the preferences, values and needs of individual patients and their families is the cornerstone in patient-centered care (53). As previously described, the course of atopic disease varies among individual children in terms of severity and the development of multiple conditions. These variations may be part of the explanation of parents' various experiences with care pathways and interactions with healthcare professionals. Therefore, it is crucial to thoroughly examine parents' experiences and challenges related to the treatment, care and daily life for children with long-term diseases. This will help shed light on current care pathways from various perspectives and identify areas for improvement. Integrating knowledge from various fields is essential to supplement biomedical understanding.

Daily life and care related to atopic diseases

When a child has one or more long-term diseases such as atopic diseases, they affect both the child, the parents and other family members e.g., siblings (54, 55). The primary caregivers of children with atopic diseases are the parents and they have a key position in the management of the diseases. Studies have shown, that having a child with an atopic disease affects both the child's and the parents' quality of life (54-57). Having a child with chronic diseases and the management of the diseases requires adaption of every day routines and family life (50). This process involves several tasks and activities for the parents. Some of these tasks are related directly to the diseases and are often referred to as "the treatment burden". There are different

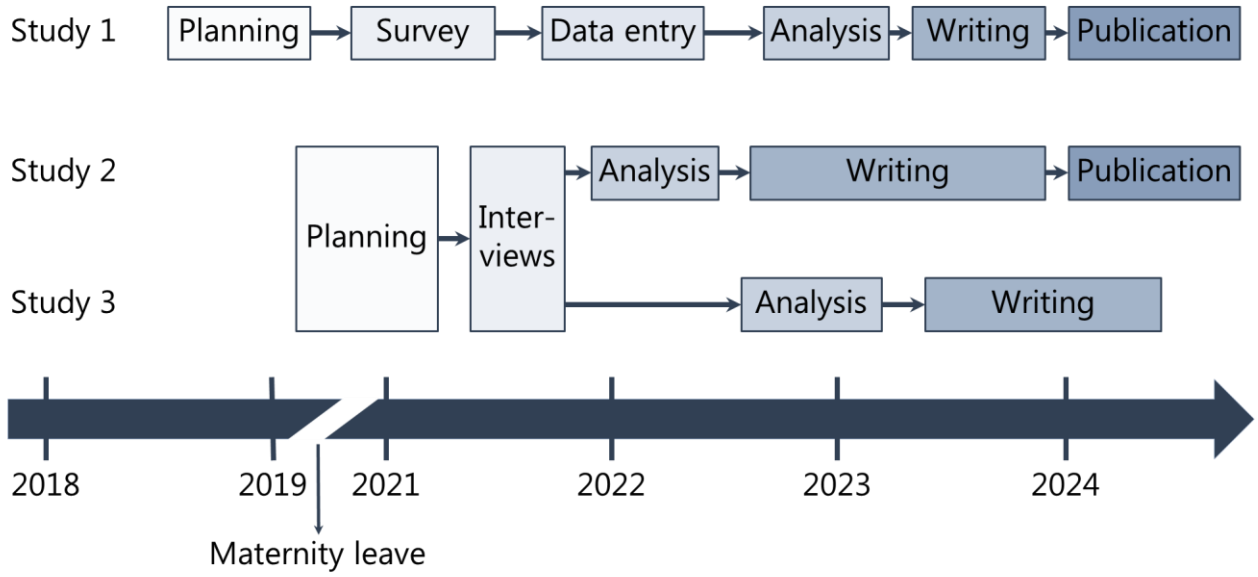
aspects and definitions of the concept treatment burden (58, 59). In a review they defined it as: "*Actions and resources patients devote to their healthcare, including difficulty, time, and out-of-pocket costs dedicated to the healthcare tasks such as adhering to medications, dietary recommendations, and self-monitoring*" (59). Adherence to the prescribed treatment regimen, consultations with several healthcare professionals, learning about diseases and treatments, and lifestyle changes are some examples (60). In a review by Teasdale et al. on the management of AD, is was found that the actual burden of AD was often not recognized by others, including healthcare professionals, who frequently downplayed the extent of the disease (61).
"Chronic homework" is another term used to characterize disease-related tasks (62). This notion includes a lot of the same tasks as indicated above, but it specifies that it applies to healthcare activities performed at home, and these involve both the child (patient) and their family (62), and thereby will impact the whole family.
For parents of children with atopic diseases, the tasks performed at home are an integral part of managing the child's long-term diseases. They shape the parents' expectations regarding their child's care and impact the care pathway. For instance, difficulties in adhering to the treatment regimen, such as applying emollients twice a day may contribute to a flare-up that requires medical attention. Learning more about parents' caregiving for a child with multiple atopic diseases, including their daily tasks, will shed light on how the child's conditions affect family life.

In summary, our understanding of existing care pathways for children with atopic diseases is limited. Despite many children being diagnosed with multiple atopic diseases, there is no clear framework for structuring communication and care. Examining how families cope with atopic conditions at home, and how encounters with the healthcare system are experienced, may suggest areas where care for these children can be enhanced.

Methods

The design for the studies included in this thesis used a mixed method approach. The application of both quantitative and qualitative methods provide a more nuanced understanding of the topic (63). The two methods were in this project used as complementary to examine different aspects of the focus area and the quantitative study 1 qualified the selection of participants for the qualitative studies 2 and 3 (64).

Figure 1: Timeline of the PhD project



Setting

Data collection for both the questionnaire study and the interviews took place in the Capital Region of Denmark. Stakeholders involved in the PhD-project included two hospital departments: the Department of Dermatology and Allergy, and the Department of Pediatrics at Herlev and Gentofte Hospital. Additionally five specialist clinics participated, comprising pediatricians, dermatologists, otorhinolaryngologists (ear, nose, and troat specialists), and allergists.

The participating hospital departments and practicing specialists were all situated in different parts of Greater Copenhagen. Only one of the specialist clinics was a group practice.

Both the hospital departments and practicing specialists mainly saw patients with residence in the Capital Region, but the exact distribution of patients from the Capital Region and Region

Zealand depended on differenct factors such as highly specialized hospital functions and their location. We chose to include only individuals from the Capital Region to avoid variations in health services provided to children with atopic diseases across the Regions.

Study 1

The data for Study I were collected as part of a larger questionnaire study involving participants of all ages. For consistency with the other two manuscripts in the thesis, we chose to exclusively analyze data from children and adolescents for Manuscript I. The following section describes the methods related to the part of the questionnaire concerning children.

Children and adolescents, who were referred for investigation and treatment of atopic diseases to different specialties in private practices and hospitals in the Capital Region of Denmark were invited to participate. Parents and adolescents were asked to complete a questionnaire about the child's or adolescent's journey through the healthcare system and to provide their evaluation of the process.

Inclusion criteria for participation in the study were:

- Diagnosed with one or more of the following diseases: AD, food allergy, ARC and/or asthma. At least one of them confirmed by a physician at the specialist clinics or hospital departments.
- <18 years and both genders
- Resident in the Capital Region, Denmark
- Parents and/or adolescent, who read, speak and understand Danish

Development of the questionnaire

The questionnaire was constructed for patients with atopic diseases aiming to examine their referral pathways. The questions concerning the specific diseases (AD, food allergy, ARC and asthma) were inspired by validated questionnaires (2, 36), whereas the questions concerning the referral pathways were developed specifically to this study.

We developed different versions of the questionnaire depending on the child's age (children 0-14 years, adolescents 15-17 years) and site of inclusion. The latter was to ensure the questions were adjusted to the patient's current position in the referral pathway.

Answers were multiple choice and with blank space for comments. Disease severity and impact on life was measured on a visual analog scale (VAS) with a range from 0 to 100 mm, where 0

was no symptoms/impact and 100 was the worst possible symptoms/impact. This was used to be able to compare across diseases.

The questionnaire was tested by colleagues from the Department of Dermatology and the Research Unit for General Practice, who were in the same age range as the participating parents and were parents of children of various ages. The colleagues did not necessarily have personal experience with having a child with atopic diseases. They received a brief introduction beforehand and provided oral feedback after completing the questionnaire. The questionnaire was then revised based on their feedback regarding their understanding of the questions, any phrasing issues, and the choice of response options.

The inclusion process

We included participants from August 2020 until June 2021. At the hospital departments, VHL and I recruited the participants.
All potentially eligible patients on a particular day were invited to participate either before or after their consultation with the physician/nurse and if they met the inclusion criteria.
The practicing pediatricians, allergist and otorhinolaryngologist recruited the participants themselves. The recruiter filled out a short case report file (CRF) regarding the inclusion criteria and the date for the child's first consultation. I also recruited the majority of participants at the practicing dermatologist.

Analysis

The questionnaire and CRF were manually entered in REDCap (Research Electronic Data Capture) by VHL and me after completion.
The study had a descriptive approach to gain a deeper understanding of referral pathways for children with atopic diseases. The questionnaire covered a wide range of topics, prompting a careful selection of the most relevant questions for describing current referral pathways, in addition to those addressing participant characteristics (Table 1). The comparison of groups focused on two key aspects: inclusion site (practicing specialist vs. hospital department) and the number of atopic diseases (1-2 diseases vs. ≥3 diseases). Additionally, we investigated the determining factors for referral to hospital departments. More detailed information regarding the statistical analysis can be found in manuscript I.

Table 1: An overview of items from questionnaire included in study 1.

Section	Items
General information	Age, gender
Disease: AD, ARC, asthma and food allergy	Diagnosis, disease severity, family history of atopic diseases
Pathway through the healthcare system	Referral pathways including medical specialties, practicing specialists and/or hospital departments involved, visits at private hospital, time away from daycare/school, need of urgent medical visits, and impact on family life.
Socio-economic status	Parents living together, parent education and employment, household income

Study 2 and 3

The informants

The informants in both study II and III were parents of children with AD and at least one allergic comorbidity: food allergy, asthma, and ARC. They were selected based on answers from the questionnaire in study 1. Since the aim was to recruit informants who had experience with cross-sectoral care, all participating children were receiving treatment at pediatric and/or dermatology departments at two larger hospitals in the Capital Region of Denmark. Other criteria for participation were that AD had been assessed or treated by a physician either at the time of the interview or within the prior two years and the children had to be below 7 years at the time of inclusion in the questionnaire study. These criteria were formulated to ensure that the diseases had recently been medically investigated.

In total twenty-three children from the questionnaire survey were potentially eligible for the study in the spring of 2021. It was not possible to make contact with three (contacted by phone at least three times), seven did not wish to participate and in two cases it turned out to be more than two years ago since the child had seen a physician with his/her AD. In total eleven families participated in the interviews.

For nine of the eleven children, all atopic disease diagnoses were based on hospital physician records. One of the diagnoses (AD and food allergy) for two children was recorded as a physician-

informed diagnosis in the questionnaire by their parents. A reason for the children's missing diagnosis in the hospital's medical record could be if they had only seen a practicing specialist, because medical information are not transferred between different medical record systems and healthcare sectors in Denmark.
Parent-reported severity of AD varied among the children, averaging 46 mm on a 0-100 mm visual analog scale (VAS). The majority of the children had food allergy.
The children's age ranged from one to five years. While the original goal was to recruit families with diverse backgrounds, this proved challenging during the COVID-19 period. Consequently, the families were relatively homogeneous in terms of socioeconomic background but resided in different municipalities within the Capital Region. Despite their apparent similarity, they provided varied experiences with care pathways and encounters with healthcare professionals.

The interviews

The study was originally planned to consist of focus group interviews, but due to COVID-19 and the derived recommendations for restricted gatherings, it was not possible nor responsible to summon the parents in the same location for the focus groups. Instead, individual in-depth interviews were conducted. All informants chose to have the interview carried out at home. Before the interview they received the written information material and the consent form, which both parents signed prior to the interview.
I conducted all the interviews and they took place from June to September 2021. The interviews lasted from 70 to 165 minutes.
I had met some of the informants when recruiting participants for study 1, but that was a brief encounter under less than 15 minutes and the primary focus had been on information about study 1 and whether they met the inclusion criteria. When we decided on the inclusion criteria for study 2 and 3 I had finished the inclusion at the hospital departments.
The interviews were explorative and the interview guide consisting of two parts, where the first part covered experiences with the atopic diseases and care. The second part covered experiences with encounters with healthcare professionals and their care pathways (see interview guide Supplementary table 1, manuscript II, Appendix II). Afterwards an assistant transcribed the audio recorded interviews verbatim.
I wrote immediate impressions and thoughts down after each interview. These notes included a description of the setting, nonverbal impressions (such as emotions like worry and frustration), and non-recorded statements (e.g., if the parents added a comment after the recorder was turned

off). All of this were written down to help remember the atmosphere of each interview and the context in which it took place. During the interviews, it was evident that the informants had extensive insights and experiences to share, as they could speak at length with only little stimulation. Based on my assessment, sufficient material on the focus areas was obtained after conducting nine interviews, with no new information emerging in the subsequent two interviews.

Analysis

For both manuscript II and III Systematic Text Condensation (STC) was applied (5). This method was developed by Kirsti Malterud and had its inspiration from Giorgi's phenomenological analysis (65). It was decided to use this method for the analysis, because it is suitable for descriptive cross-case studies and it supports the construction of new descriptions and concepts (66). In addition, it is well-suited as a point of departure for researchers with no prior experience with social sciences, while still providing possibilities for implementing theoretical perspectives at different levels of the analysis (66).

"The analysis consists of four steps:

1. *Total impression – preliminary themes*
2. *Identify and sort meaning units – from themes to codes*
3. *Condensation – from code to meaning*
4. *Synthesizing – from condensation to descriptions and concepts"* (65)

Although the process is described chronologically, emphasis is placed on the iterative aspect of the technique. The repetitive organization and reorganization of meaning units and sub groups have been the main focus of our application of the technique.

To get an overview of the material I started by reading all the transcribed interviews, while ES and SR read selected interviews. Thereafter, I began by systematizing the content and applying codes based on this discussion. All material was read line by line during this step to find text fragments containing information concerning the selected codes.

At a following meeting, the identified text parts for each code were reviewed and sorted into groups that supported each other. The process of discussing and reorganizing the meaning units in each code group to form sub groups was repeated at several meetings. This lead to result categories such as "Limited communication/collaboration between specialties" and "Unclear roles and tasks – responsibility a heavy burden". Two main themes were identified: "Care pathways – navigating the healthcare system" and "Responsibilities, decisions and roles" (67).

Theoretical perspectives were introduced to qualify the interpretation of the findings. During the analysis of data for manuscript II it became clear that a key component for the parents in their interactions with healthcare professionals was their experiences with provided care.
A substantial part of the care literature focuses on relations between patients (care receivers) and healthcare professionals (68). Annemarie Mol's theory "The Logic of Care" (68) can help us unravel whether care (work) involves the parents' experiences. Mol argues that it is not possible to apply a standard treatment and expect everything else to adapt to it (68). The concept "Tinkering" describes the process of individual tailoring that happens when a patient's treatment plan is fitted to accommodate the individual's needs, values and resources (68). In study 2, we applied Mol's ideas about care to nuance our understanding of the findings by integrating additional aspects of care into the discussion.

While identifying text elements that illuminated the main research question, a new group of themes emerged, highlighting the impact of the diseases and their derived consequences on family life. These themes extended beyond the encounters with the healthcare system and the treatment of the diseases. We followed the inductive process and analyzed these as described above. This work formed the basis for study 3, where we present three strategies that the parents apply in the everyday family life: risk avoidance, pursuing a normal childhood, and good parenting (69). These strategies are closely related to the parents' wish to give their child as normal a childhood as possible (69). We incorporated the concepts of chronic homework (62), and normalization (70) into our analysis to support a more comprehensive interpretation of the data concerning these tasks. Finally, we put the findings into perspective by connecting the individual parental experiences to broader patterns of present day's ideas and focus on the intensified parenthood (71, 72).

The researcher's position

Reflexivity is the awareness of one's own assumptions, ideas, and attitudes and how they may impact the research process (73). Therefore, it is necessary to reflect on the researchers' background and position, as well as how earlier experiences may influence the research.
During my clinical experience in both general practice and various hospital departments I saw examples of good care pathways as well as examples of care pathways that may be improved. It became evident to me that a good care pathway also required the consideration of the patient perspective. Knowing the patient's experiences, preferences, and needs, in addition to knowledge

regarding the disease's severity and complexity, are crucial when making decisions concerning the patient's care pathway, such as a making a referral including determining where and when. This requires integration of two different perspectives by the physician. The first perspective is the positivistic paradigm, where knowledge is achieved by observation, measuring and counting followed by distribution of data into standardized categories and units (74). This requires a stable ontology, meaning how we experience the world is somewhat stable and objective (66). This paradigm is strongly embedded in my education as a medical doctor. The second perspective is the interpretive paradigm, where the world is perceived through reflectivity and interpretation (64). This paradigm's ontology is fluid, which means that how we see the world is dynamic and subjective, because we must interact with it in order to examine it (74).

The positivistic paradigm underpins quantitative research methods, while the interpretive paradigm underpins qualitative research. A significant distinction between the two methods is how data are transferred. With quantitative research methods the knowledge from the group level is transferred to the single individual e.g. the results of a randomized controlled trial of a novel treatment serves as the foundation for the treatment of an individual (66). On the opposite, with qualitative research methods the knowledge may be transferred from the individual to the group level or to similar settings, but this transfer depends on the specific context (66).

Ethics

Manuscript I was part of a larger study approved by both the Research Ethics Committee of the Capital Region of Denmark H-19041695. The adults from the questionnaire survey were originally scheduled to participate in a research biobank for future research, which was the reason for the approval by the Research Ethics Committee. However, due to COVID-19, the research biobank could not be launched because blood sampling proved to be very difficult with our project structure.

Qualitative research is not evaluated by the Danish Ethics Committees, because there is not a requirement for this in Denmark. All families (parents, adolescents and when it was possible children), who participated voluntarily in the studies received both verbal and written information before signing the consent form. They were also informed about the possibility of withdrawing their consent at any time without explanation. The Danish Ethics Committee of the Capital Region had approved that only one of the parents/caregivers in case of joint custody signed the consent form before the participation in the questionnaire study. For children aged <15 years the parent/caregiver gave the written consent and for adolescents 15-17 years of age

both the adolescent and parent/caregiver gave the written consent. Adolescents were encouraged to complete the questionnaire with their parent. Both parents signed the consent form before the interviews. The written information, consent forms, questionnaire, and CRF were all printed on paper.
We encouraged the adolescents to discuss their responses in the questionnaire with their parents. There were no potential risks or harms to the children/adolescents or their families.

Both the questionnaire study (manuscript I) and the interview study (manuscript II and III) are registered by "Videnscenter for dataanmeldelser Region Hovedstaden" (The Knowledge Center for Data Reviews, Capital Region) P-2020-659 and we received permission to collect, store, and handle the data.

All patient-specific information is stored in accordance with the regulations established by the Danish Data Protection Agency.

Results

Study 1

Title: Referral Pathways for Children with Atopic Diseases in Denmark (for full manuscript see Appendix I).

The aim was to explore how children with atopic diseases navigate the Danish healthcare system. Children aged ≤ 17 years, who were receiving treatment for atopic diseases from specialists in private practice or a hospital department within the Capital Region of Denmark, were invited to participate in a questionnaire study. The inclusion of participants took place between August 2020 and June 2021.

Statistical analysis involved the use of Chi-squared, Mann-Whitney U and logistic regression to analyze the collected data.

The study population consisted of 301 children. Of these 279 completed the questionnaire (92.7%), with 166 from a hospital department and 113 from practicing specialists.

The results showed that children from hospital departments more often had AD, food allergy and/or asthma. The self-reported severity of the atopic diseases did not differ between the two groups, nor did their impact on family life. Children from hospital departments experienced higher rates of missed days from daycare and school compared to those treated by practicing specialists (39% vs. 26%, P=0.02). They also exhibited a greater tendency to require urgent visits to their physician either due to flare-up of AD (10 % vs. 3%, P=0.02) or worsening of food allergy (8% vs. 2%, P=0.03).

In terms of referral patterns, the majority of children had consulted their GP only once or twice before being referred to either a practicing specialist or a hospital department. Notably, there was no consistent pattern of direct referrals to a hospital department for children with ≥3 atopic diseases. However, compared to children with ≤2 diseases, those with multiple atopic diseases were more frequently referred to hospital departments (OR 3.79 with 95% CI 2.07-7.24). Food allergy (OR 4.69 (95% CI 2.07-10.61)) and asthma (OR 2.58 (95% CI 1.18-5.63)) emerged as predictors of hospital treatment for children with multiple atopic diseases, whereas AD, ARC or having ≥3 diseases were not predictive factors.

Study 2

Title: Parents of children with atopic diseases - experiences with care and the interaction with healthcare professionals over time (for full manuscript see Appendix II).

The aim was to explore parents' experiences with encounters with healthcare professionals in Denmark, when the child has multiple atopic diseases.
We conducted individual in-depth interviews using a semi-structured approach with an interview guide. Analysis of the interviews was inspired by Systematic Text Condensation.
Parents of eleven children with AD and allergic diseases participated in the study. All children were receiving treatment at hospitals in the Capital Region of Denmark and their parents had experience with cross-sectoral care.
Our findings revealed that parents' understanding of diseases influenced their expectations regarding treatment and care pathways. Initially, many parents believed the atopic diseases could be cured, but over time, their perception gradually changed to an understanding of the long-term nature of these diseases.
There were substantial variations in the children's care pathways, even though they had the same diseases. The parents reported challenges with care transitions and noted limited collaboration between healthcare professionals from various specialties, leading to fragmented care experiences.
Many parents found it difficult to discern the areas of expertise and responsibility of healthcare professionals from the various specialties. Consequently, they struggled to navigate the healthcare system and often assumed roles as messengers and coordinators.
The unclear distribution of roles and tasks between parents and healthcare professionals, necessitated parents to take on roles, such as initiator, manager and navigator, contrary to their expectations. Limited collaboration among healthcare professionals further affected the task allocation.
Trust and a positive relationship with healthcare professionals were built upon the parents' perception that their child were well cared for and through consistent continuity of care. This continuity, particularly seeing the same physician consistently, facilitated this process. Conversely, encounters with different healthcare professionals undermined trust.
The parents described a learning curve in managing their child's diseases, supported by education provided by healthcare professionals and individualized hospital treatment plans tailored to the child and the family's needs.

Study 3

Title: A “normal” life: a qualitative study exploring parents’ experiences of everyday life with a child diagnosed with atopic dermatitis and atopic comorbidities (for full manuscript see Appendix III).

The aim was to explore the experiences of parents’ managing everyday tasks and care related to their child’s atopic diseases.
The study was based on individual in-depth interviews with parents of 11 children with atopic diseases and were analyzed with Systematic Text Condensation.
The results showed, that a minority of tasks were directly linked to treatment, such as applying emollients, which were often time-consuming and occasionally led to conflicts with the child. The main part of tasks involved broader aspects of daily life, and they included the need for meticulous planning, and adjusting family dynamics e.g., to accommodate altered eating habits. Furthermore, the atopic diseases and associated tasks had indirect implications for non-allergic siblings such as restricting the presence of allergens in the household food items. Parents also dealt with the unpredictability of managing their child’s conditions, frequently alternating leisure activities and postpone babysitting to maintain constant vigilance, particularly due to the child’s sleep disturbances resulting from itching caused by the AD lesions.
The tasks extended beyond the immediate family sphere. The parents sought knowledge and support from online sources such as social media groups, though they faced challenges validating the information. The diseases and associated tasks potentially affected parental employment both planned consultations with healthcare professionals and if the child was sent home from daycare due to allergy symptoms. The parents experienced that increased involvement in daycare and school was necessary and vigilance remained paramount, whether dining out at family and friends or visiting restaurants. Parents strove to create a sense of normality for their child while balancing the demands of managing atopic diseases and maintaining a fulfilling family life.

Discussion of methods

In this thesis both quantitative and qualitative methods have been applied. The following sections will elaborate on strengths and limitations of the studies included in this thesis, which were only briefly discussed in manuscripts I-III. The discussion of study 1 will primarily focus on the development and use of questionnaires, the research population, as well as strengths and limitations. The discussion of study 2 and 3 will be focused on reflectivity and internal validity of the two studies. Lastly, there will be a discussion of the mixed method approach and the external validity of all three studies.

Study 1

Development of the questionnaire

We chose to conduct a questionnaire study in order to include a large number of children, 279 in total, from both practicing specialists and hospital departments. In addition, it became possible to compare the referral pathways for these two groups of children. The questionnaire study included the viewpoint of parents of children and adolescents with atopic diseases, who are the receivers of the provided healthcare services. Other advantages of questionnaire studies are that they are cost effective for characterizing large groups of individuals, easy to administer at multiple inclusion sites, a faster response time compared with interviews and the standardized format is well suited to analyse with statistical software. There was no existing validated questionnaire. Therefore, the construction of questions concerning the referral pathways were based on literature studies and clinical experience from a broad research group of professionals working in the area. As a consequence, some of questions may be biased, since they were based on knowledge and assumptions about referral pathways.

The pre-testing of the questionnaire in study 1 may have lowered the likelihood of respondents misinterpreting questions and response categories, which is a common concern in questionnaire studies (75). During the evaluation of the questionnaire and data entry, it became evident that the sections that were simple and descriptive worked well, but there were also more challenging areas such as instances where participants did not understand a specific question as intended. For example, “Which disease affects the child the most, based on your assessment?” required each disease to be rated from 0 to 4. A rating of 1 indicated that the disease affects the child the most,

4 indicated the disease affects the child the least (if all four diseases present), and 0 indicated the child did not have the disease. This issue did not emerge during the pre-testing of the questionnaire. Optimally, focus group interviews prior to the questionnaire study, could have served as the foundation for the questionnaire's formulation and validation. Participants in the focus group could be asked to describe their care pathway chronologically to ensure that the questions covered their referral pathways, and we could also examine whether the questions were interpreted as intended during these interviews. However, this suggestion would also make the study much more time consuming. An alternative approach could have been to reverse the study order and conduct the qualitative studies first and subsequently design a questionnaire. Furthermore, cognitive interviews of the study population conducted concurrently with the questionnaire, could have reduced the risk of misinterpretation and avoided potentially confusing questions (76). However, this was not possible due to lack of time, and participant inclusion was not simultaneous at all inclusion sites (inclusion at hospital departments was initiated before at practicing specialists), therefore it would have been difficult to get a representative sample of the study population.

The questionnaire was printed on paper, and it raised the likelihood of non-response to questions, e.g., a participant inadvertently skipped questions. However, we chose that format because we had multiple inclusion sites, and it was more suitable and simpler for practicing specialists to administer a paper version. Furthermore, since no IT equipment was required we avoided technical difficulties and some studies have also found that paper questionnaires yield a better response rate than web-based questionnaires (77, 78).

Selection and recall bias

To obtain a representative group of participants and reduce selection bias, all eligible patients on a given day both at hospital departments and practicing specialists were asked to participate. The questionnaires were personally delivered. At least one of the atopic diseases was diagnosed by the physician they consulted at the time of enrollment, ensuring that an atopic disease was the reason for their referral pathway. There is a risk of misclassification of the atopic disease if it was not the primary reason for the consultation, since there might be participants, who for example had non-allergic rhinitis instead of ARC or wheezing symptoms interpreted as asthma but caused by an infection with no subsequent development of asthma (79). To minimize this

risk, all questions regarding an atopic disease were followed by a question whether the diagnosis was confirmed by a physician.

In Denmark, electronic medical record systems do not automatically share information across healthcare sectors making it very challenging to verify the participants' statements regarding referral pathways. Recall bias is an inevitable risk in retrospective questionnaire studies with recall often decreasing over time (80). This may decrease the reliability of some answers if the referral pathway occurred a few years ago compared with a recent referral pathway. Nonetheless, because all participants were children and adolescents, their disease onset and referral pathway had happened during the last few years.
Recall is affected by a variety of factors such as prior knowledge and experiences, including family history of atopic disease, the severity of the episode/disease and the parents' health perception (81). If the child had severe symptoms, the parents are more likely to recall them, and similarly, if the parents have the same disease, they will be more aware of the child's symptoms (81). The same factors are also likely to influence the parents' expectations of the referral pathway.

Considerations about the method selection

Referral pathways in the healthcare system can be assessed using different methods including register studies, interviews and questionnaires. As discussed, the questionnaire approach has its limitations. While interviews allow a detailed exploration of referral pathways, the large number of eligible children and extended response time rendered interviews unsuitable for study 1. Register studies, reliant on the information in the Danish national database, have constraints. Notable, children treated exclusively by general practitioners and practicing specialists are not registered in the database with an atopic disease diagnosis (82). Consequently, information about these children in a register study would rely heavily on disease proxies like treatment data. It is important to acknowledge that certain medications, such as topical corticosteroids can be used to treat skin conditions other than AD (83).
Therefore, in navigating these considerations and seeking balance between comprehensive data collection and practical feasibility, the questionnaire approach emerged as the best choice for study 1. It offered a broad scope for capturing insights into the pathways of a diverse group of children with atopic diseases while taking into account available resources and logistical considerations.

Study 2 and 3

We chose to conduct individual interviews. The application of this method provided in-depth descriptions of the parents' perceptions and experiences with care pathways, interaction with healthcare professionals and care, and how the child's atopic diseases impacted family life. The following discussion will focus on a discussion of reflexivity and internal validity.

Reflexivity

A core element of reflexivity is being aware of how knowledge is generated in the research process, including factors such as the researcher's background and preconceptions that influence this process (66, 84). The following section will discuss considerations regarding the individual interviews and subjective aspects that may affect the interviews and interpretation process.

Individual interviews allow the informants to talk confident about difficult matters concerning the child's atopic diseases, care pathways and the impact of the diseases. Studies comparing different interview approaches have shown that whether individual interviews is the optimal approach for the informants' self-disclosure of sensitive personal experiences compared with focus group interviews, is dependent on demographic factors such as gender, culture, socioeconomic status and the degree to which they are matched in a focus group (85, 86). Despite similarities, the parents in the present studies differed by ethnicity, culture, gender and municipality of residence, implying that the chosen approach encouraged verbalizations including self-disclosure of sensitive topics related to having a child with atopic diseases while the approach also ensured informants' anonymity.

The parents interviewed for study 2 and 3 included both mothers and fathers, with some interviews featuring both parents. However, we did not investigate how the gender of the parent and the family structure may influence their experiences, perspectives and expectations regarding their child's care pathway.

Additionally, individual interviews have logistic advantages, because it is easier to schedule since it only requires one informant per session and mostly only one data collector (85).

All of the interviews took place at the families' home, which provided a familiar interview setting for the parents and gave additional information about the families e.g., their housing conditions. This information and non-verbal impressions were registered as field notes.

In the written information to participants in study 1 my profession as a medical doctor was disclosed and some of the informants were enrolled in study 1 by me, therefore my medical qualifications were likewise declared to the informants in study 2 and 3. The interviewer's professional role has been shown to have an effect on the interview setting, where an interviewer with a medical profession is more likely to be asked about health related issues (87). It is impossible to eliminate this effect because knowledge in an interview is generated through interaction with the informant, but it is critical that the researcher is aware of their position (65).
As a medical doctor, conversations about sensitive topics such as disease were not unfamiliar to me, and the professional experience as well as the extensive comprehension of atopic diseases made it easier to ask detailed questions. Even though I was not involved in the clinical work at any of the hospital departments, one might expect that the informants could be hesitant to report dissatisfaction with their child's care pathway, interactions with healthcare professionals, alternative medicine or non-adherence to treatment. The interviews provided genuine thoughts on these topics, so this concern was likely without greater significance.

Members of the research team were involved in the different aspects of study 2 and 3, including design, planning, data analysis, and result interpretation, and my preconceptions were written down to reduce subjectivity and my preconceptions' influence on the interpretation process. Members of the research team with a non-medical background was involved in whole process to decrease the possibility of conceptual blindness.
With my preconceptions in mind, I tried to ask questions from both my own and other positions. This included being aware of internally agreed concepts used by healthcare professionals, where patients and their families may have a different grasp of these concepts, because they are rarely articulated, but simply assumed to be well-known and understood equally by all.

Internal validity

In this section, the study's internal validity will be discussed. This concerns whether the study design and methods were appropriately chosen to answer the research questions. Since the aim was to understand parents' experiences, a qualitative study using interviews was selected. Information power can be used to evaluate sample size and consists of five categories: *"a) study aim, b) sample specificity, c) use of established theory, d) quality of dialogue, and e) analysis strategy"* (88). In the context of both qualitative studies, the research objectives were broad, and a cross-case analysis was used, indicating a requirement for a larger sample size. Conversely, we

had a high sample specificity, because the informants represented the target group in the studies – parents of children with multiple atopic diseases, possessing experience with the healthcare system across sectors and medical disciplines. There was considerable variation in the explored experiences such as differences in the children's care pathways, disease duration, the parents' expectations, disease understanding and prior knowledge about the diseases, as well as the organization of the healthcare system.

Moreover, the interviews featured a strong and dynamic dialogue. Although the interviewer was untrained in qualitative interviewing, the robust quality of the dialogue was attributed to the researcher's clinical experience including extensive knowledge about atopic diseases, fostering enhanced mutual confidence. Theoretical perspectives were used to unfold the findings. By incorporating theoretical perspectives into our interpretation and in the discussion, our studies achieved a nuanced and more substantiated understanding of the factors influencing the care experienced by families and the extensive efforts they undertook to establish a sense of normalcy when dealing with a child's complex disease. Overall, the application of theoretical perspectives not only reduces the required sample size but it also serves to bridge to existing knowledge while concurrently challenging and renewing it (88).

Before and during the interviews, the research team carefully considered these aspects, and we anticipated that 10-15 informants would be necessary. In studies 2 and 3, we included 11 families. Following analysis, this number was assessed to be sufficient to meet the objectives of the studies. The experiences shared by these families brought forth new perspectives, enriching the existing knowledge.

All three studies

This section of the methodological discussion will examine the application of mixed methods, external validity, and transferability of the findings across all three studies to other contexts. However, it will initially address the impact of COVID-19 on the studies.

Impact of COVID-19

All three studies were influenced by the COVID-19 pandemic. The Research Ethics Committee of the Capital Region of Denmark granted approval for only one parent to sign the consent form in cases of joint custody. This approval was essential for the inclusion of participants in study 1, given that, at hospital departments in Denmark, only one parent was permitted to attend

consultations due to COVID-19 restrictions. During the interview period, Denmark still had COVID-19 restrictions in place, which affected our approach. Conducting focus group interviews with informants gathered in the same room, as initially planned, was not feasible. Another possibility could have been to conduct focus group interviews online. However, that approach brings other challenges such as responding to non-verbal cues during the interview and technical challenges (89). Furthermore, the social dynamics of a focus group, as well as nonverbal communication and reactions, may be affected differently in an online context compared with a face-to-face setting.

The parents could choose the location where they felt most comfortable particularly in terms of COVID-19. For example one family selected their covered terrace as the interview location.

Mixed methods

Different methods have been used in this thesis and could be described as a mixed methods study, necessitating some consideration on the advantages and disadvantages of this design. An important notion is that the quantitative and qualitative methodologies examine different aspects of the world. Correlation and causation in quantitative research cannot answer the "how" issues that qualitative research strives to answer (9). The research methods can be used to supplement each other: The questionnaire study aimed to describe the pathways in the healthcare system for children with atopic diseases and the interview study aimed to describe how these pathways and the impact of the diseases are experienced by these children's carers. Thus, the qualitative part of the thesis can be used to incorporate the parent perspective to the understanding of care pathways for these children.

Three types of mixed methods designs are recognized: explanatory sequential, exploratory sequential, and convergent (90). In a sequential design, researchers conduct either the quantitative (explanatory) or qualitative (exploratory) phase with data collection and analysis (90). The insights gained from this analysis then inform the design of the subsequent phase (90). With a convergent design both phases occur within the same timeframe, and this can save time compared with a sequential design (90). In this project the quantitative and qualitative studies were developed in parallel processes, where the informants for the qualitative study were selected from responses the quantitative study, but the interviews were conducted before the analysis of the questionnaire data. This strengthens internal validity of the studies.

The integration of quantitative and qualitative methods strengthens the robustness of the evidence and contributes to a higher level of confidence in the validity of the findings (63). This

approach allows for a more comprehensive exploration and richer understanding of the research questions (90). Furthermore, it mitigates the limitations inherent in each method.
The challenge is, that it necessitates a higher proficiency in managing different methods, highlighting the importance of a supervisor group with diverse expertise. Simultaneously managing both quantitative and qualitative approaches can be logistically complex, demanding effort to switch between them – particularly for those inexperienced with the one of the methods and needing to become acquainted with it.
Comparing two types of data and resolving discrepancies, if they arise, could pose challenges. In the questionnaire study, fully elucidating the details of the referral pathways within the heterogeneous group of participants proved challenging, as this became apparent during the data entry process. At the interviews, I asked the informants to describe their child's referral pathway, and these descriptions confirmed the complexity of the referral pathways even for a much more well-defined group.

External validity and transferability

Overall, all participating children with atopic diseases and their families in the three studies were residing in the Capital Region of Denmark, which meant that there was an equal distribution of provided healthcare services among the participants. However, provided healthcare services vary by region, since highly specialized hospital departments are only present in some of the Danish regions and the distribution of practicing specialists across the regions differ. It is possible to consult a practicing specialist or hospital department in another region, but this may necessitate more effort from the child's family including increased time consumption due to longer distances. As a consequence, the study population may not be representative of all Danish children with atopic diseases and their care pathways. Similarly, healthcare systems vary considerably across countries, even within Europe (91). This presumably results in diverse referral pathways for children with atopic diseases, making it challenging to transfer the questionnaire to a different country with a distinct healthcare setting. Despite variations in the healthcare organization, the presence of international guidelines for the assessment and treatment of atopic diseases (92-95) plays a crucial role in striving to harmonize care pathways. This, in turn, makes it relevant to compare the findings with those of other studies.
Eligible informants for study 2 and 3 were identified from questionnaire responses in study 1, but the inclusion of informants occurred prior to the analysis of the questionnaire data. Therefore, the sampling of parents of children with multiple atopic diseases consulting

physicians at hospital departments was based on the assumption that children followed there had more severe disease and thus interacted with healthcare professionals from different specialties and healthcare sectors to a greater extent than children followed at a practicing specialist. This suggests that the findings primarily apply to parents of children experiencing more severe and complex disease trajectories, and may not necessarily extend to parents of children with milder atopic diseases, who presumably are receiving treatment in primary care. However, the findings in this thesis can be compared to research findings related to other chronic illnesses in children that also require multi-sectoral treatment approaches.

The informants were similar in terms of educational level, income, and partnership status, and the families were generally resourceful (67, 69), which is a limitation of studies 2 and 3. Because the majority of study 1 participants were well-educated and did not have a low household income (96), it would be difficult to acquire greater diversity in these aspects among the participants using our study design. Even though the informants came from the same region of Denmark, there was variation in their municipality of residence. Other variation between informants included prior knowledge about the healthcare system and the cultural background in the family such as ethnicity and spoken languages in the family (67). Most notably, there was variation within the explored experiences with the interaction with healthcare professionals, care and the impact of the child's atopic diseases' on family life, and these experiences contributed with new insights to the existing knowledge. Moreover, the incorporation of theoretical perspectives into the interpretation not only reinforces the robustness of the findings, but also enhances the transferability of the results to diverse contexts.

Discussion of findings

Main findings

The main findings from the studies included in this PhD thesis are as follows:

- Children with three or more atopic diseases were nearly four times more likely to be referred to a hospital department than those with one or two atopic diseases (96). The primary factors were food allergy, with asthma playing a slightly lesser role (96). No direct track from general practice to a hospital department was observed for children with three or more atopic diseases (96).
- Care pathways for children with atopic diseases exhibited complexity, even among those with similar disease patterns (67, 96). Experiences of care were associated with coherence between expected and experienced roles, although parents' experiences of expanded responsibilities were common (67). Feeling cared for was linked to healthcare professional's dual knowledge – both biomedical and biographical knowledge – and the experience of personalized support (67).
- The parents experienced a comprehensive treatment burden (69). Beyond the immediate tasks linked to the child's treatments, various other tasks arose as families adapted to living with a child with atopic diseases (69). These tasks were closely tied to the parents' aspirations for providing their child with as normal a childhood as possible (69).

The subsequent discussion of the findings will be organized into three sections. The first section will concentrate on treatment burden and impact on daily lives, the second will concern care pathways, experiences of care and collaboration, and the final section will explore care pathways and the balance between access and continuity of care.

Treatment burden and impact on daily lives

In this section the findings pertaining the treatment burden and impact on family dynamics will be discussed including whether these findings align with those of similar studies focusing mainly on children with other long-term diseases.

While many studies have explored the experiences of parents with children facing a single long-term disease (50, 51, 56, 57, 61, 97, 98), only few previous studies concern children with more than one disease (49, 99).

A study focusing on children with both type 1 diabetes and celiac disease outlined additional management tasks and their implications for family life (99). This aligns with our findings that increased disease complexity resulted in parents taking on a greater number of tasks related to the care of the child (67, 69). The unclear distribution of roles and responsibilities in these intricate care pathways created uncertainty among the parents (67). Furthermore, multiple atopic diseases increased the treatment burden, such as requiring more time-consuming home care and typically concurrent consultations with healthcare professionals from different specialties (67, 69). In Study 3, we found that the tasks were both directly and indirectly related to the atopic diseases, and that the "visible" tasks directly related to the diseases only represented the tip of the iceberg (69). Additionally, the study concerning children with type 1 diabetes and celiac disease identified differences in parental knowledge about the two diseases, leading to a disproportionate focus on one of the diseases and heightened awareness of potential complications related to that specific disease (99). In our studies, we did not observe similar patterns, but we did find that parents had different point of departures regarding knowledge and understanding of atopic diseases and about the healthcare system (67).

The experience of having a child with long-term diseases has a profound impact on the entire family dynamic. As illustrated in study 3, families aspire to establish a sense of normalcy, a process revealed to be both extensive and complex (69). This process involves maneuvering through various challenges and adjustments. In this context, Iversen et al have proposed that support from healthcare professionals should go beyond biomedical aspects to include emotional support (100). Since the parent-child relationship may be influenced as parents navigate the delicate balance between maintaining control and enabling their child to have a childhood similar to other children (100).

Having a child with chronic diseases necessitates additional extensive activities, which are not directly related to the management of the diseases (69). These activities are carried out to maintain normalcy in the family's everyday life (69). To understand these activities and responses normalization as a framework can be applied. Normalization outlines a process in which parents continually select normalcy as a valued objective and devise strategies to create and preserve a family life that they perceive to be normal (70). Normalization can be used as a coping strategy (101), but it may also minimize or even conceal the actual impact of the child's diseases on family life. A recent review addressed the challenges and experiences faced by parents caring for a child diagnosed with type 1 diabetes (97). A recurring theme was the impact of the disease on the entire family and their daily lives, with parents exerting considerable effort

to normalize the child's life, often at their own expense (97). This aligned with study 3, where a substantial amount of the "invisible" tasks were performed to achieve normality (69).
Caring for a child with AD may impact family life to a greater extent than caring for a child with type 1 diabetes (102). Several studies have shown that caring for a child with AD may affect the parents' quality of life, for example, due to sleep loss, increased stress, affected mental health and social relationships (103-105). The psychosocial consequences may cause an increased use of medicine to treat mental health disorders and a greater need to consult a psychologist, which was explained by the overall burden in the family, not just by AD (106). This emphasizes that there is also a need for support to the family, where education and psychosocial support have been suggested to reduce this burden (107).

A recurring theme in a study was the perception of children with diabetes as being different, causing parents to worry about potential stigmatization (98). This concern led parents to accept additional tasks and consequences to ensure that their child could participate in activities on more equal terms with other children (98). The participants in our studies 2 and 3 were of a younger age group. However, had the children in our studies been within the same age range (6-15 years), stigmatization could potentially have emerged as a significant finding. A recent review indicated that stigmatization might be a concern among school-aged children with AD and other chronic skin diseases (108).
This perspective unveils additional layers of the complexity in the management of children's health challenges for parents, when the child has multiple atopic diseases. It highlights the intricate nature of caregiving and the additional burdens parents face in such circumstances. This underscores the importance for healthcare professionals to have increased awareness of these families and whether they may need additional (non-biomedical) support.

Care pathways, experiences of care and collaboration

The following discussion section will focus on the care pathways in the healthcare system.
The children's journey through the healthcare system differed depending on the number of atopic diseases with food allergy and asthma being the primary reasons for referral to hospitals (96). It involved the participation of healthcare professionals from different medical specialties both sequentially and in parallel (67). From the parents' perspective, this tortuous journey resulted in numerous tasks and frequently created uncertainty regarding the distribution of roles and responsibility (67). The uncertainty occurred not only between healthcare professionals and

parents, but it was also experienced by parents in relation to how care and responsibility were distributed among healthcare professionals from various specialties involved in the child's care (67). Most medical specialties primarily focused on their specific areas of expertise. However, this was not the case for general practitioners and pediatricians, who had a broader approach (67). While the overarching objective of collaboration is to achieve optimal health outcomes for the child, the specific agendas of the involved parties may diverge (109). Healthcare professionals may aim to foster collaboration through relationship-building to ensure adherence, whereas parents may focus on seeking access to the best care (109). Parents in study 2 felt that general practitioners lacked sufficient knowledge, diagnostic capabilities, and treatment options, particularly when multiple atopic diseases occurred simultaneously or when the conditions were more severe (67). Accordingly, some parents sought referrals to practicing specialists or hospital departments, valuing the specialized knowledge of healthcare professionals regarding atopic diseases and actively pursuing the best available care (67).

Joan Tronto describes care as a practice, because it includes both *"thought and action"*(110). This perspective can be used to elaborate the findings concerning parents' care experiences and how these are conditioned by an overlap between expected and experienced responsibility distribution (67). According to Tronto care is an ongoing process and consists of four dimensions: 1) *"Caring about: Recognizing a need and that care is necessary, 2) Taking care of: Assuming responsibility for the recognized needs and decide how to respond, 3) Care-giving: The needs for care are directly met, 4) Care-receiving: Assuming that care given will be acknowledged as such"* (110). Tronto's theory emphasizes the importance of both a caring attitude from healthcare professionals and material work (110). A caring attitude involves continually acknowledging and addressing the families' needs, while material work includes providing families with tangible advice to meet their care needs (110).
The initial period after the child's diagnosis is often characterized by a steep learning curve, as the family adjusts to the new demands imposed by the disease (111). In study 2, we found that support needs undergo changes over time as parents gradually acquire expertise in disease management (67). Comparable findings regarding the transformation of preferences and needs of the healthcare recipients were observed in research concerning other long-term conditions among children, where they also suggested shared decision-making as a strategy to adapt to the families' evolving needs and preferences (112). Additionally, the changes in needs can be influenced by fluctuations in the atopic diseases within the individual child (67). Likewise, a study conducted by Khoury et al. focusing on adults with psoriasis, observed that the individual needs change

over time in response to variations in disease severity, with heightened support requirements during periods of flare-ups (113).

In a study by Kimbell et al., parents of children with diabetes were generally content with the supplied care from healthcare professionals, but they also brought attention to occasional discrepancies in the information received from healthcare professionals (97). Similar experiences were reported by the parents in our study 2, however, this discrepancy in information primarily occurred between healthcare professionals from different specialties (67). Information discrepancies may pose challenges to the decision-making process. Parents may feel uncertain about whose advice to follow, and experience being unable to share the responsibility of decision-making (67).
Healthcare professionals are the key providers of information and education for families with children facing long-term diseases (114). Despite a shared interest in alternative and complementary medicine across various diseases, obtaining information on these approaches from healthcare professionals proved to be challenging (69, 114). In response, parents sought information from other sources, including social media groups, both for topics related to alternative medicine and other aspects concerning the diseases (69). However, this approach also raised concerns about the reliability of the information (69).

In the context of pediatric patients, the patient perspective encompasses both the child's viewpoint and that of the parents. Incorporating parents' perspective in the present studies facilitated a comprehensive understanding of the broader context of a child's care and the whole family's healthcare experiences. This included the family's essential involvement in decision-making and support, and impact on family dynamics. While the focus of study 2 and 3 was the parents' perspective, another study has explored the viewpoint of children aged 3 to 6 years with long-term diseases (115). The findings from this study indicated that these children did not feel invited to actively participate in their care, as part of a child-centered approach the authors suggest to build relational trust as a way to increase the children's experiences of agency and competences (115). In sum, research representing both the parents' and children's perspectives indicate a desire for an active role in the child's care pathway such as shared decision-making (52, 115). Having an active and balanced role was also requested by the parents in our studies, as there was a clear expectation that the responsibility should be shared and that healthcare professionals would apply their specialist knowledge (67).

While a care pathway can be perceived as primarily involving the journey through the healthcare system and the individual's encounters with healthcare professionals, it can also be viewed more broadly. Study 2 highlights the complexity and often inadequate coordination of the care pathway within the healthcare system, especially for children with multiple atopic diseases (67). Moreover, the study shows that the care pathway extends beyond the healthcare system, encompassing elements of the process that occur in settings like the home, daycare, and school (67). Supporting this broader perspective requires the acknowledgement of the inherent interconnectedness and concurrent processes between the components within the healthcare system and those occurring outside. Each component plays an integral role in shaping the overall trajectory of the care pathway for a child with atopic diseases. In another study with parents of children with two chronic diseases, instances are noted, where the parents felt that the healthcare professionals lacked awareness of this broader impact, including the extensive tasks related to the home management of the diseases (97). The first step could therefore be to raise the awareness among healthcare professionals of the extended care pathway and the additional complexity posed by multiple atopic diseases. Combining this awareness with knowledge of the additional tasks these families take on to achieve normality for the child could improve the ability to provide the best support and advice to each family e.g., prioritization of tasks.

Care pathways, access and continuity of care

There are continuous ongoing discussions revolving around reorganizing the healthcare system to address societal demands such as shifts in demographic composition, and the evolving needs of healthcare recipients at both group and individual levels (116, 117). The organization of the healthcare system is pivotal for the framework for care pathways, and if we aim to optimize care pathways, whether for specific diseases and in a broader context, we need to consider what constitutes a "good care pathway". This concept can be approached from various perspectives. As discussed by Olsen et al, there is the public management viewpoint emphasizing standardization, efficiency and equality as central elements, while, on the other hand, individualized patient-centered care is emphasized (118). Healthcare professionals find themselves navigating the crossroads of these differing perspectives, attempting integration (118). Yet this integration also requires reflections on how the elements should be prioritized as well as what is possible within the given framework. Our studies provide the parents' perspective on care pathways, highlighting important elements and potential areas for improvement.

In Denmark, chronic care initiatives, particularly for adults with chronic diseases have implemented principles from the Chronic Care Model (119). The Chronic Care Model is a proactive approach incorporating clinical practice guidelines and self-management support (120). However, its main focus is on adult individuals with a single disease, and in its original form, it does not fully acknowledge the complex interplay of multiple diseases (121). Recognizing the prevalence of individuals with multiple long-term diseases, there is a pressing need for more individualized and flexible care approaches. Findings from the studies included in this thesis on children with multiple atopic diseases support this.
Notably, health policymakers are shifting towards a more patient-centered focus (116). However, this shift challenges the desire for standardization with a relatively simple measurement of outcome indicators. Research have demonstrated that the framework of a standardized consultation with a healthcare professional inadequately supports adaptation to the individual needs of each patient (113). The parents in our study 2 highly valued personalized modifications to the care they received, accommodating their needs and preferences (67).

A good care pathway can be characterized by different key elements such as patient-centered, coordinated care, continuity, accessibility, timeliness, empowerment and collaboration (122). Patient-centeredness and coordinated care including collaboration have been addressed in the manuscripts and previously in the thesis. Manuscript 1 discussed the importance of providing timely tailored healthcare to the right patients at the right moment (96). In continuation of patient-centered care is empowerment. This involves equipping the individual healthcare recipient with knowledge and tools to actively participate in the care process through disease education as well as reinforcing of shared decision-making and self-management (123). In the process of empowerment, the parents' evolving needs and the described learning curve should be considered, as parents initially rely more on the expertise of healthcare professionals (67).
Continuity of care encompasses seamless transitions in healthcare and the establishment of an ongoing relationship with the same healthcare professional (124). Continuity of care is particularly crucial in instances of long-term and complex diseases, where multiple interactions with healthcare professionals are required (124). Our findings indicate that parents highly valued continuity, as it not only contributed to an enhanced care experience, but also allowed healthcare professionals to be familiar with their personal history (67). This familiarity facilitated discussions beyond biomedical concerns, encompassing broader aspects related to parenting a child with long-term diseases (67). It has been indicated that continuity of care also increases adherence to treatment (125).

Accessibility, on the other hand, refers to easy access to healthcare services with the primary objective is to minimize potential barriers, such as waiting time, distance and socioeconomic status (117). In a study with parents of children with diabetes, the significance of easy access to healthcare professionals was highlighted, but also the necessity for consistent and dependable communication (112). The prioritization between continuity and accessibility by healthcare recipients hinges on the nature of the medical need. At the beginning of the disease course access to specialist care was of great importance especially in more severe cases (67). However, later on, to evolve trust continuity became pivotal (67). Yet, continuity was challenged by the involvement of multiple healthcare professionals in the child's care pathway, and in some instances, the child saw a new healthcare professional at each consultation (67). In cases were urgent medical assistance is needed, easy accessibility takes precedence to ensure timely care (126). Conversely, in regular follow-up consultations, the emphasis may shift towards continuity of care. In these instances, maintaining a consistent and ongoing relationship with healthcare professionals becomes essential for delivering patient-centered care, as the healthcare professional gains a more comprehensive knowledge about the individual needs and preferences of the healthcare recipient. Therefore, it should not be perceived as a rigid either-or prioritization; instead the balance between continuity and accessibility varies based on the specific situation and medical context.

Acknowledging these aspects and challenges, our exploration of a "good care pathway" underscores the importance of balancing key elements including accessibility and continuity of care, offering a dynamic approach that adapts to the individual needs of each patient and situation.

Conclusion

This PhD thesis has provided insight into current referral pathways in the Danish healthcare system. It was found that children with multiple atopic diseases were more frequently referred to a hospital department. The primary explanations for this were shown to be food allergy and, to a lesser extent, asthma.

We found that the care pathways were complex and characterized by limited coordination. It was of great significance that healthcare professionals undertook the role as coordinators, mainly in the initial phase.

Parents experienced a substantial treatment burden and the diseases had a major impact on the daily life of the entire family. Much of the parents' caregiving extended far beyond the specific treatment in an effort to create as normal a childhood as possible for the child. Access to care was important, but trust and continuity were crucial as parents developed their competences. The thesis emphasizes the relevance for healthcare professionals to be knowledgeable and curious about the overall care pathway, including aspects beyond the biomedical.

Implications for future research

This thesis encourages further investigation in several areas, suggesting additional dimensions that could be explored.

In relation to study 1, it could be interesting to investigate whether the current referral pathways for children with atopic diseases differ in other regions in Denmark, where there presumably is a different distribution of practicing specialists and specialized hospital departments.

The interviews conducted for study 2 and 3 were singular, occurring at a specific moment in time for each family. To delve deeper into the evolving experiences, needs, and preferences of families of children diagnosed with atopic diseases, conducting sequential interviews over time would be valuable, ideally beginning from the initial diagnosis of the diseases. This longitudinal approach would offer insight into how the families' perspectives shift over time, influenced by fluctuations in the child's diseases and the families' growing understanding of them.

Additionally, exploring variations in socioeconomic status and place of residence, such as different regions, would be beneficial to capture a more comprehensive understanding of the impact of these factors on the families' experiences. Understanding these variations could inform efforts to address inequalities and improve the overall quality of care for children with atopic diseases and their families.

Another possibility is to explore the potential impact of gender and family structure on parental roles, coping mechanisms, and support networks. Understanding these variations could provide nuanced insights into the challenges encountered by families of children with atopic diseases. In addition, the children's perspective could be incorporated by conducting individual or focus group interviews with children diagnosed with atopic diseases. These interviews could aim to explore the children's understanding of their diseases, their experiences with healthcare professionals, and their perspectives on treatment and care. Including the children's voices could help ensure that interventions and support services are more aligned with their unique needs and preferences.

To develop improved care pathways, collaboration, and coordination across sectors, the results of this study can be further enhanced by gaining deeper insights into the professionals' perspectives. This can be followed by a co-design phase that incorporates both professional and child/caregiver viewpoints. Drawing on the insights gained from study 2, one intriguing possibility is to organize focus group interviews with healthcare professionals from various sectors and specialties such as general practitioners, pediatricians, and dermatologists. These interviews could explore their perspectives on interacting with families of children diagnosed with atopic diseases. Following this, joint workshops could be arranged involving both healthcare professionals and affected families. These workshops would provide a platform to discuss strategies for advancing and strengthening these interactions, with the aim of fostering greater coherence and a more patient-centered approach.

Implications for practice

Based on the findings outlined in the studies included in this thesis, several implications for practice emerge.

Improving healthcare providers' knowledge of referral pathways for children with atopic diseases, along with factors influencing them, enables them to assess the need for optimizing current referral practices. This, in turn, ensures more timely access to specialized care when it is required.

Recognizing the complexity of care pathways for children with atopic diseases, healthcare providers should aim to ensure coordinated care and collaboration across sectors and specialties. Furthermore, healthcare professionals should aim to align families' expected roles and responsibilities with their actual experiences within the healthcare system. This alignment may

improve the overall experience and promote better outcomes. Moreover, providing personalized support that integrates both biomedical and biographical knowledge can enhance feelings of being cared for among families, further improving their overall care experience.

In addition to addressing the immediate treatment needs of children with atopic disease, healthcare professionals should be attentive to the broader challenges faced by families as they adapt to life with a child with chronic diseases. It is important to be aware of support services available, including those outside the healthcare system, such as those provided by municipalities, and patient and family associations. By addressing these broader challenges, healthcare professionals can enhance the overall well-being of both child and the family.

References

1. Pawankar R, Canonica GW, Holgate ST, Lockey RF, Blaiss MS. Chapter 2 The burden of allergic diseases. In: World Allergy Organization (WAO) White Book on Allergy. Update 2013.2013. 240 p. ISBN 978-0-615-92915-6

2. Asher MI, Montefort S, Bjorksten B, Lai CK, Strachan DP, Weiland SK, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet. 2006;368(9537):733-43. DOI: 10.1016/S0140-6736(06)69283-0.

3. Henriksen L, Simonsen J, Haerskjold A, Linder M, Kieler H, Thomsen SF, et al. Incidence rates of atopic dermatitis, asthma, and allergic rhinoconjunctivitis in Danish and Swedish children. J Allergy Clin Immunol. 2015;136(2):360-6 e2. DOI: 10.1016/j.jaci.2015.02.003.

4. Langan SM, Irvine AD, Weidinger S. Atopic dermatitis. Lancet. 2020;396(10247):345-60. DOI: 10.1016/S0140-6736(20)31286-1.

5. Bylund S, Kobyletzki LB, Svalstedt M, Svensson A. Prevalence and Incidence of Atopic Dermatitis: A Systematic Review. Acta Derm Venereol. 2020;100(12):adv00160. DOI: 10.2340/00015555-3510.

6. Laughter MR, Maymone MBC, Mashayekhi S, Arents BWM, Karimkhani C, Langan SM, et al. The global burden of atopic dermatitis: lessons from the Global Burden of Disease Study 1990-2017. Br J Dermatol. 2021;184(2):304-9. DOI: 10.1111/bjd.19580.

7. Weidinger S, Novak N. Atopic dermatitis. Lancet. 2016;387(10023):1109-22. DOI: 10.1016/S0140-6736(15)00149-X.

8. Margolis JS, Abuabara K, Bilker W, Hoffstad O, Margolis DJ. Persistence of mild to moderate atopic dermatitis. JAMA Dermatol. 2014;150(6):593-600. DOI: 10.1001/jamadermatol.2013.10271.

9. Mortz CG, Andersen KE, Dellgren C, Barington T, Bindslev-Jensen C. Atopic dermatitis from adolescence to adulthood in the TOACS cohort: prevalence, persistence and comorbidities. Allergy. 2015;70(7):836-45. DOI: 10.1111/all.12619.

10. Thyssen JP, Corn G, Wohlfahrt J, Melbye M, Bager P. Retrospective markers of paediatric atopic dermatitis persistence after hospital diagnosis: A nationwide cohort study. Clin Exp Allergy. 2019;49(11):1455-63. DOI: 10.1111/cea.13487.

11. Abuabara K, Yu AM, Okhovat JP, Allen IE, Langan SM. The prevalence of atopic dermatitis beyond childhood: A systematic review and meta-analysis of longitudinal studies. Allergy. 2018;73(3):696-704. DOI: 10.1111/all.13320.

12. Hanifin JM, Rajka G. Diagnostic Features of Atopic Dermatitis. Acta Dermato-Venereologica. 1980;60(92):44-7. DOI: 10.2340/00015555924447.

13. Eichenfield LF, Tom WL, Chamlin SL, Feldman SR, Hanifin JM, Simpson EL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. J Am Acad Dermatol. 2014;70(2):338-51. DOI: 10.1016/j.jaad.2013.10.010.

14. Sundhedsstyrelsen [Danish National Health Authority]. Specialeplan for dermato-venerologi [Dermato-venerology Specialty Standard] 2023 [Available from: https://sst.dk/-/media/Viden/Specialplaner/Specialeplan-for-dermato-venerologi/Specialevejledning-for-Dermato-venerologi-den-23-august-2023.ashx.

15. Yu W, Freeland DMH, Nadeau KC. Food allergy: immune mechanisms, diagnosis and immunotherapy. Nat Rev Immunol. 2016;16(12):751-65. DOI: 10.1038/nri.2016.111.

16. Sicherer SH, Sampson HA. Food allergy: A review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. Journal of Allergy and Clinical Immunology. 2018;141(1):41-58. DOI: 10.1016/j.jaci.2017.11.003.

17. Sicherer SH, Sampson HA. Food allergy: Epidemiology, pathogenesis, diagnosis, and treatment. J Allergy Clin Immunol. 2014;133(2):291-307; quiz 8. DOI: 10.1016/j.jaci.2013.11.020.

18. Peters RL, Koplin JJ, Gurrin LC, Dharmage SC, Wake M, Ponsonby AL, et al. The prevalence of food allergy and other allergic diseases in early childhood in a population-based study: HealthNuts age 4-year follow-up. J Allergy Clin Immunol. 2017;140(1):145-53 e8. DOI: 10.1016/j.jaci.2017.02.019.

19. Muraro A, Werfel T, Hoffmann-Sommergruber K, Roberts G, Beyer K, Bindslev-Jensen C, et al. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. Allergy. 2014;69(8):1008-25. DOI: 10.1111/all.12429.

20. Rosenlund H, Kull I, Pershagen G, Wolk A, Wickman M, Bergstrom A. Fruit and vegetable consumption in relation to allergy: disease-related modification of consumption? J Allergy Clin Immunol. 2011;127(5):1219-25. DOI: 10.1016/j.jaci.2010.11.019.

21. Cardona V, Ansotegui IJ, Ebisawa M, El-Gamal Y, Fernandez Rivas M, Fineman S, et al. World Allergy Organization Anaphylaxis Guidance 2020. World Allergy Organization Journal. 2020;13(10):100472. DOI: 10.1016/j.waojou.2020.100472.

22. Reddel HK, Bacharier LB, Bateman ED, Brightling CE, Brusselle GG, Buhl R, et al. Global Initiative for Asthma Strategy 2021: executive summary and rationale for key changes. Eur Respir J. 2022;59(1). DOI: 10.1183/13993003.02730-2021.

23. Porsbjerg C, Melén E, Lehtimäki L, Shaw D. Asthma. The Lancet. 2023;401(10379):858-73. DOI: 10.1016/s0140-6736(22)02125-0.

24. Martin J, Townshend J, Brodlie M. Diagnosis and management of asthma in children. BMJ Paediatr Open. 2022;6(1). DOI: 10.1136/bmjpo-2021-001277.

25. Pearce N, Ait-Khaled N, Beasley R, Mallol J, Keil U, Mitchell E, et al. Worldwide trends in the prevalence of asthma symptoms: phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax. 2007;62(9):758-66. DOI: 10.1136/thx.2006.070169.

26. Bousquet J, Anto JM, Bachert C, Baiardini I, Bosnic-Anticevich S, Walter Canonica G, et al. Allergic rhinitis. Nat Rev Dis Primers. 2020;6(1):95. DOI: 10.1038/s41572-020-00227-0.

27. Bjorksten B, Clayton T, Ellwood P, Stewart A, Strachan D, Group IPIS. Worldwide time trends for symptoms of rhinitis and conjunctivitis: Phase III of the International Study of Asthma

and Allergies in Childhood. Pediatr Allergy Immunol. 2008;19(2):110-24. DOI: 10.1111/j.1399-3038.2007.00601.x.

28. Bauchau V, Durham SR. Prevalence and rate of diagnosis of allergic rhinitis in Europe. Eur Respir J. 2004;24(5):758-64. DOI: 10.1183/09031936.04.00013904.

29. Blaiss MS, Hammerby E, Robinson S, Kennedy-Martin T, Buchs S. The burden of allergic rhinitis and allergic rhinoconjunctivitis on adolescents: A literature review. Ann Allergy Asthma Immunol. 2018;121(1):43-52 e3. DOI: 10.1016/j.anai.2018.03.028.

30. Bousquet J, Pfaar O, Agache I, Bedbrook A, Akdis CA, Canonica GW, et al. ARIA-EAACI care pathways for allergen immunotherapy in respiratory allergy. Clin Transl Allergy. 2021;11(4):e12014. DOI: 10.1002/clt2.12014.

31. Knudgaard MH, Andreasen TH, Ravnborg N, Bieber T, Silverberg JI, Egeberg A, et al. Rhinitis prevalence and association with atopic dermatitis: A systematic review and meta-analysis. Ann Allergy Asthma Immunol. 2021;127(1):49-56 e1. DOI: 10.1016/j.anai.2021.02.026.

32. Ravnborg N, Ambikaibalan D, Agnihotri G, Price S, Rastogi S, Patel KR, et al. Prevalence of asthma in patients with atopic dermatitis: A systematic review and meta-analysis. J Am Acad Dermatol. 2021;84(2):471-8. DOI: 10.1016/j.jaad.2020.02.055.

33. Christensen MO, Barakji YA, Loft N, Khatib CM, Egeberg A, Thomsen SF, et al. Prevalence of and association between atopic dermatitis and food sensitivity, food allergy and challenge-proven food allergy: A systematic review and meta-analysis. Journal of the European Academy of Dermatology and Venereology. 2023;37(5):984-1003. DOI: 10.1111/jdv.18919.

34. Amat F, Soria A, Tallon P, Bourgoin-Heck M, Lambert N, Deschildre A, et al. New insights into the phenotypes of atopic dermatitis linked with allergies and asthma in children: An overview. Clin Exp Allergy. 2018;48(8):919-34. DOI: 10.1111/cea.13156.

35. Vestergaard C, Thyssen JP, Barbarot S, Paul C, Ring J, Wollenberg A. Quality of care in atopic dermatitis - a position statement by the European Task Force on Atopic Dermatitis (ETFAD). J Eur Acad Dermatol Venereol. 2020;34(3):e136-e8. DOI: 10.1111/jdv.16092.

36. Belgrave DCM, Granell R, Simpson A, Guiver J, Bishop C, Buchan I, et al. Developmental Profiles of Eczema, Wheeze, and Rhinitis: Two Population-Based Birth Cohort Studies. PLoS Medicine. 2014;11(10):e1001748. DOI: 10.1371/journal.pmed.1001748.

37. Li H, Dai T, Liu C, Liu Q, Tan C. Phenotypes of atopic dermatitis and the risk for subsequent asthma: A systematic review and meta-analysis. J Am Acad Dermatol. 2022;86(2):365-72. DOI: 10.1016/j.jaad.2021.07.064.

38. Paternoster L, Savenije OEM, Heron J, Evans DM, Vonk JM, Brunekreef B, et al. Identification of atopic dermatitis subgroups in children from 2 longitudinal birth cohorts. J Allergy Clin Immunol. 2018;141(3):964-71. DOI: 10.1016/j.jaci.2017.09.044.

39. Haider S, Fontanella S, Ullah A, Turner S, Simpson A, Roberts G, et al. Evolution of Eczema, Wheeze, and Rhinitis from Infancy to Early Adulthood: Four Birth Cohort Studies. Am J Respir Crit Care Med. 2022;206(8):950-60. DOI: 10.1164/rccm.202110-2418OC.

40. Kilanowski A, Thiering E, Wang G, Kumar A, Kress S, Flexeder C, et al. Allergic disease trajectories up to adolescence: Characteristics, early-life, and genetic determinants. Allergy. 2023;78(3):836-50. DOI: 10.1111/all.15511.

41. Pols DHJ, Bohnen AM, Nielen MMJ, Korevaar JC, Bindels PJE. Risks for comorbidity in children with atopic disorders: an observational study in Dutch general practices. BMJ Open. 2017;7(11):e018091. DOI: 10.1136/bmjopen-2017-018091.

42. Thyssen JP, Halling AS, Schmid-Grendelmeier P, Guttman-Yassky E, Silverberg JI. Comorbidities of atopic dermatitis-what does the evidence say? J Allergy Clin Immunol. 2023;151(5):1155-62. DOI: 10.1016/j.jaci.2022.12.002.

43. Tikkanen R, Osborn R, Mossialos E, Djordjevic A, Wharton G. International Profiles of Health Care Systems 2020. Available from: https://www.commonwealthfund.org/sites/default/files/2020-12/International_Profiles_of_Health_Care_Systems_Dec2020.pdf.

44. Allen J, Gay B, Crebolder H, Heyrman J, Svab I, Ram P. The European Definition of General Practice/Family Medicine WONCA Europe 2023 Edition 2023 [Available from: https://www.woncaeurope.org/kb/european-definition-gp-fm-2023.

45. Hansen DG, Jarbol DE, Munck AP. Variation in examination and treatment offers to patients with allergic diseases in general practice. Qual Prim Care. 2010;18(3):181-7. DOI n/a, https://www.ncbi.nlm.nih.gov/pubmed/20659402.

46. Sundhedsstyrelsen [Danish National Health Authority]. Status på allergi-området. Rapportering til Sundheds- og Ældreministeriet [Overview of the allergy area. Reporting to the Health and Senior Citizen Ministry]2017. 92 p. ISBN 978-87-7104-869-8

47. Sundhedsstyrelsen [Danish National Health Authority]. Specialeplan for pædiatri [Pediatric Specialty Standard] 2023 [Available from: https://www.sst.dk/-/media/Viden/Specialplaner/Specialeplan-for-p%C3%A6diatri/Specialevejledning-for-Paediatri-den-14-februar-2023-_D10161971_.ashx.

48. sundhed.dk. Almen praksis - Patientbehandling [General Practice - Patient Treatment Plans] 2024 [cited 2024 June 26]. Available from: https://www.sundhed.dk/sundhedsfaglig/information-til-praksis/hovedstaden/almen-praksis/.

49. Lagercrantz B, Persson A, Kull I. "Healthcare seems to vary a lot": A focus group study among parents of children with severe allergy. J Asthma. 2017;54(7):672-8. DOI: 10.1080/02770903.2016.1258079.

50. Fawcett R, Porritt K, Stern C, Carson-Chahhoud K. Experiences of parents and carers in managing asthma in children: a qualitative systematic review. JBI Database System Rev Implement Rep. 2019;17(5):793-984. DOI: 10.11124/JBISRIR-2017-004019.

51. Santer M, Burgess H, Yardley L, Ersser S, Lewis-Jones S, Muller I, et al. Experiences of carers managing childhood eczema and their views on its treatment: a qualitative study. Br J Gen Pract. 2012;62(597):e261-7. DOI: 10.3399/bjgp12X636083.

52. Powell K, Le Roux E, Banks J, Ridd MJ. GP and parent dissonance about the assessment and treatment of childhood eczema in primary care: a qualitative study. BMJ Open. 2018;8(2):e019633. DOI: 10.1136/bmjopen-2017-019633.

53. Barry MJ, Edgman-Levitan S. Shared decision making--pinnacle of patient-centered care. N Engl J Med. 2012;366(9):780-1. DOI: 10.1056/NEJMp1109283.

54. Ali F, Vyas J, Finlay AY. Counting the Burden: Atopic Dermatitis and Health-related Quality of Life. Acta Derm Venereol. 2020;100(12):adv00161. DOI: 10.2340/00015555-3511.

55. Cibella F, Ferrante G, Cuttitta G, Bucchieri S, Melis MR, La Grutta S, et al. The burden of rhinitis and rhinoconjunctivitis in adolescents. Allergy Asthma Immunol Res. 2015;7(1):44-50. DOI: 10.4168/aair.2015.7.1.44.

56. Stensgaard A, Bindslev-Jensen C, Nielsen D, Munch M, DunnGalvin A. Quality of life in childhood, adolescence and adult food allergy: Patient and parent perspectives. Clin Exp Allergy. 2017;47(4):530-9. DOI: 10.1111/cea.12849.

57. Taminskiene V, Alasevicius T, Valiulis A, Vaitkaitiene E, Stukas R, Hadjipanayis A, et al. Quality of life of the family of children with asthma is not related to asthma severity. Eur J Pediatr. 2019;178(3):369-76. DOI: 10.1007/s00431-018-3306-8.

58. Powell P, Saggu R, Jones S, Clari M, Saraiva I, Hardavella G, et al. Discussing treatment burden. Breathe (Sheff). 2021;17(1):200284. DOI: 10.1183/20734735.0284-2020.

59. Alsadah A, van Merode T, Alshammari R, Kleijnen J. A systematic literature review looking for the definition of treatment burden. Heliyon. 2020;6(4):e03641. DOI: 10.1016/j.heliyon.2020.e03641.

60. Sav A, Salehi A, Mair FS, McMillan SS. Measuring the burden of treatment for chronic disease: implications of a scoping review of the literature. BMC Med Res Methodol. 2017;17(1):140. DOI: 10.1186/s12874-017-0411-8.

61. Teasdale E, Muller I, Sivyer K, Ghio D, Greenwell K, Wilczynska S, et al. Views and experiences of managing eczema: systematic review and thematic synthesis of qualitative studies. Br J Dermatol. 2021;184(4):627-37. DOI: 10.1111/bjd.19299.

62. Mattingly C, Gron L, Meinert L. Chronic homework in emerging borderlands of healthcare. Cult Med Psychiatry. 2011;35(3):347-75. DOI: 10.1007/s11013-011-9225-z.

63. Guetterman TC, Fetters MD, Creswell JW. Integrating Quantitative and Qualitative Results in Health Science Mixed Methods Research Through Joint Displays. The Annals of Family Medicine. 2015;13(6):554-61. DOI: 10.1370/afm.1865.

64. Jørgensen T, Christensen E, Linneberg A. Klinisk Forskningsmetode. 4 ed. København: Munksgård Danmark; 2016. 272 p. ISBN 9788762814783

65. Malterud K. Systematic text condensation: a strategy for qualitative analysis. Scand J Public Health. 2012;40(8):795-805. DOI: 10.1177/1403494812465030.

66. Malterud K. Kvalitative metoder for medisin og helsefag: en innføring [Qualitative Methods for Medical and Health Sciences: An Introduction]. 4 ed: Universitetsforlaget; 2017. 256 p. ISBN 9788215028286

67. Færk G, Søndergaard E, Skov L, Thyssen JP, Hansen KS, Reventlow S. Parents of children with atopic diseases - experiences with care and the interaction with healthcare professionals over time. Scandinavian Journal of Primary Health Care. 2024:1-10. DOI: 10.1080/02813432.2024.2357794.

68. Mol A. The logic of care : health and the problem of patient choice. London ; New York: Routledge; 2008. 129 p. p. ISBN 9780203927076

69. Færk G, Søndergaard E, Skov L, Hansen KS, Reventlow S. A "normal" life: a qualitative study exploring parents' experiences of everyday life with a child diagnosed with atopic dermatitis and atopic comorbidities. Health: An Interdisciplinary Journal for the Social Study of Health, Illness and Medicine (Submitted)2024.

70. Knafl KA, Darney BG, Gallo AM, Angst DB. Parental Perceptions of the Outcome and Meaning of Normalization. Research in Nursing & Health. 2010;33(2):87-98. DOI: 10.1002/nur.20367.

71. Furedi F. Paranoid Parenting: Why Ignoring the Experts May be Best for Your Child: Chicago Review Press; 2002. ISBN 9781556524646

72. Hays S. The cultural contradictions of motherhood. New Haven: Yale University Press; 1996. 252 p. ISBN 0300066821

73. Jamieson MK, Govaart GH, Pownall M. Reflexivity in quantitative research: A rationale and beginner's guide. Social and Personality Psychology Compass. 2023;17(4). DOI: 10.1111/spc3.12735.

74. Guassora AD, Reventlow S, Malterud K. 22 temateorier til kvalitativ forskning [22 substantive theories for qualitative research]. København: FADL's Forlag; 2022. 138 p. ISBN 9788793810617

75. Choi BC, Pak AW. A catalog of biases in questionnaires. Prev Chronic Dis. 2005;2(1):A13. DOI n/a, https://www.ncbi.nlm.nih.gov/pubmed/15670466.

76. Willis GB, Artino AR. What Do Our Respondents Think We're Asking? Using Cognitive Interviewing to Improve Medical Education Surveys. Journal of Graduate Medical Education. 2013;5(3):353-6. DOI: 10.4300/jgme-d-13-00154.1.

77. Sebo P, Maisonneuve H, Cerutti B, Fournier JP, Senn N, Haller DM. Rates, Delays, and Completeness of General Practitioners' Responses to a Postal Versus Web-Based Survey: A Randomized Trial. J Med Internet Res. 2017;19(3):e83. DOI: 10.2196/jmir.6308.

78. Van Gelder MMHJ, Bretveld RW, Roeleveld N. Web-based Questionnaires: The Future in Epidemiology? American Journal of Epidemiology. 2010;172(11):1292-8. DOI: 10.1093/aje/kwq291.

79. Doss AMA, Stokes JR. Viral Infections and Wheezing in Preschool Children. Immunol Allergy Clin North Am. 2022;42(4):727-41. DOI: 10.1016/j.iac.2022.05.004.

80. Naleway AL, Belongia EA, Greenlee RT, Kieke BA, Jr., Chen RT, Shay DK. Eczematous skin disease and recall of past diagnoses: implications for smallpox vaccination. Ann Intern Med. 2003;139(1):1-7. DOI: 10.7326/0003-4819-139-1-200307010-00006.

81. Brick T, Hose A, Wawretzka K, Von Mutius E, Roduit C, Lauener R, et al. Parents know it best: Prediction of asthma and lung function by parental perception of early wheezing episodes. Pediatric Allergy and Immunology. 2019;30(8):795-802. DOI: 10.1111/pai.13118.

82. Ali Z, Ulrik CS, Egeberg A, Thyssen JP, Thomsen SF. Association of Childhood Atopic Dermatitis With a Higher Risk of Health Care Utilization and Drug Use for Asthma: A Nationwide Cohort Study. Dermatitis. 2022;33(4):257-63. DOI: 10.1097/DER.0000000000000724.

83. Stacey SK, McEleney M. Topical Corticosteroids: Choice and Application. Am Fam Physician. 2021;103(6):337-43. DOI n/a, https://www.ncbi.nlm.nih.gov/pubmed/33719380.

84. Baarts C, Tulinius C, Reventlow S. Reflexivity--a strategy for a patient-centred approach in general practice. Fam Pract. 2000;17(5):430-4. DOI: 10.1093/fampra/17.5.430.

85. Guest G, Namey E, Taylor J, Eley N, Mckenna K. Comparing focus groups and individual interviews: findings from a randomized study. International Journal of Social Research Methodology. 2017;20(6):693-708. DOI: 10.1080/13645579.2017.1281601.

86. Kruger LJ, Rodgers RF, Long SJ, Lowy AS. Individual interviews or focus groups? Interview format and women's self-disclosure. International Journal of Social Research Methodology. 2019;22(3):245-55. DOI: 10.1080/13645579.2018.1518857.

87. Richards H, Emslie C. The 'doctor' or the 'girl from the University'? Considering the influence of professional roles on qualitative interviewing. Fam Pract. 2000;17(1):71-5. DOI: 10.1093/fampra/17.1.71.

88. Malterud K, Siersma VD, Guassora AD. Sample Size in Qualitative Interview Studies: Guided by Information Power. Qual Health Res. 2016;26(13):1753-60. DOI: 10.1177/1049732315617444.

89. Thunberg S, Arnell L. Pioneering the use of technologies in qualitative research - A research review of the use of digital interviews. International Journal of Social Research Methodology. 2022;25(6):757-68. DOI: 10.1080/13645579.2021.1935565.

90. Fetters MD, Curry LA, Creswell JW. Achieving Integration in Mixed Methods Designs—Principles and Practices. Health Services Research. 2013;48(6pt2):2134-56. DOI: 10.1111/1475-6773.12117.

91. Schwettmann L, Hamprecht A, Seeber GH, Pichler S, Voss A, Ansmann L, et al. Differences in healthcare structures, processes and outcomes of neighbouring European countries: the example of Germany and the Netherlands. Research in Health Services & Regions. 2023;2(1). DOI: 10.1007/s43999-023-00031-9.

92. Chu DK, Schneider L, Asiniwasis RN, Boguniewicz M, De Benedetto A, Ellison K, et al. Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on

Practice Parameters GRADE– and Institute of Medicine–based recommendations. Annals of Allergy, Asthma & Immunology. 2024;132(3):274-312. DOI: 10.1016/j.anai.2023.11.009.

93. Santos AF, Riggioni C, Agache I, Akdis CA, Akdis M, Alvarez-Perea A, et al. EAACI guidelines on the diagnosis of IgE-mediated food allergy. Allergy. 2023;78(12):3057-76. DOI: 10.1111/all.15902.

94. Levy ML, Bacharier LB, Bateman E, Boulet L-P, Brightling C, Buhl R, et al. Key recommendations for primary care from the 2022 Global Initiative for Asthma (GINA) update. npj Primary Care Respiratory Medicine. 2023;33(1). DOI: 10.1038/s41533-023-00330-1.

95. Bousquet J, Schunemann HJ, Togias A, Bachert C, Erhola M, Hellings PW, et al. Next-generation Allergic Rhinitis and Its Impact on Asthma (ARIA) guidelines for allergic rhinitis based on Grading of Recommendations Assessment, Development and Evaluation (GRADE) and real-world evidence. J Allergy Clin Immunol. 2020;145(1):70-80 e3. DOI: 10.1016/j.jaci.2019.06.049.

96. Færk G, Ahlström MG, Lura VH-E, Reventlow S, Johansen JD, Thyssen JP, et al. Referral Pathways for Children with Atopic Diseases in Denmark. Acta Dermato-Venereologica. 2024;104:adv34961. DOI: 10.2340/actadv.v104.34961.

97. Kimbell B, Lawton J, Boughton C, Hovorka R, Rankin D. Parents' experiences of caring for a young child with type 1 diabetes: a systematic review and synthesis of qualitative evidence. BMC Pediatrics. 2021;21(1). DOI: 10.1186/s12887-021-02569-4.

98. Haegele JA, Holland SK, Hill E. Understanding Parents' Experiences with Children with Type 1 Diabetes: A Qualitative Inquiry. International Journal of Environmental Research and Public Health. 2022;19(1):554. DOI: 10.3390/ijerph19010554.

99. Erickson K, Freeborn D, Roper SO, Mandleco B, Anderson A, Dyches T. Parent experiences raising young people with type 1 diabetes and celiac disease. J Pediatr Nurs. 2015;30(2):353-63. DOI: 10.1016/j.pedn.2014.09.011.

100. Iversen AS, Graue M, Haugstvedt A, Råheim M. Being mothers and fathers of a child with type 1 diabetes aged 1 to 7 years: a phenomenological study of parents' experiences. International Journal of Qualitative Studies on Health and Well-being. 2018;13(1):1487758. DOI: 10.1080/17482631.2018.1487758.

101. Amaro LM. Emotional Experiences and Communal Coping among Mothers of Children with Eczema. J Fam Commun. 2020;20(3):221-35. DOI: 10.1080/15267431.2020.1753745.

102. Su JC, Kemp AS, Varigos GA, Nolan TM. Atopic eczema: its impact on the family and financial cost. Archives of Disease in Childhood. 1997;76(2):159-62. DOI: 10.1136/adc.76.2.159.

103. Na CH, Chung J, Simpson EL. Quality of Life and Disease Impact of Atopic Dermatitis and Psoriasis on Children and Their Families. Children. 2019;6(12):133. DOI: 10.3390/children6120133.

104. Pustišek N, Vurnek Živković M, Šitum M. Quality of Life in Families with Children with Atopic Dermatitis. Pediatric Dermatology. 2016;33(1):28-32. DOI: 10.1111/pde.12698.

105. Yang EJ, Beck KM, Sekhon S, Bhutani T, Koo J. The impact of pediatric atopic dermatitis on families: A review. Pediatric Dermatology. 2019;36(1):66-71. DOI: 10.1111/pde.13727.

106. Vittrup I, Droitcourt C, Andersen YMF, Skov L, Egeberg A, Delevry D, et al. Family burden of hospital-managed pediatric atopic dermatitis: A nationwide registry-based study. Pediatric Allergy and Immunology. 2022;33(1). DOI: 10.1111/pai.13693.

107. Carroll CL, Balkrishnan R, Feldman SR, Fleischer AB, Manuel JC. The Burden of Atopic Dermatitis: Impact on the Patient, Family, and Society. Pediatric Dermatology. 2005;22(3):192-9. DOI: 10.1111/j.1525-1470.2005.22303.x.

108. Kelly KA, Balogh EA, Kaplan SG, Feldman SR. Skin Disease in Children: Effects on Quality of Life, Stigmatization, Bullying, and Suicide Risk in Pediatric Acne, Atopic Dermatitis, and Psoriasis Patients. Children. 2021;8(11):1057. DOI: 10.3390/children8111057.

109. Smith J, Kendal S. Parents' and Health Professionals' Views of Collaboration in the Management of Childhood Long-term Conditions. J Pediatr Nurs. 2018;43:36-44. DOI: 10.1016/j.pedn.2018.08.011.

110. Tronto JC. Moral boundaries : a political argument for an ethic of care. New York: Routledge; 1993. 226 p. p. ISBN 0415906415

111. Holmström Rising M, Söderberg S. Experiences of transitions in daily life for parents of children with type 1 diabetes: An interpretive description. Research in Nursing & Health. 2023;46(3):313-22. DOI: 10.1002/nur.22303.

112. Boogerd EA, Maas-Van Schaaijk NM, Noordam C, Marks HJG, Verhaak CM. Parents' experiences, needs, and preferences in pediatric diabetes care: Suggestions for improvement of care and the possible role of the Internet. A qualitative study. Journal for Specialists in Pediatric Nursing. 2015;20(3):218-29. DOI: 10.1111/jspn.12118.

113. Khoury LR, Skov L, Møller T. Facing the dilemma of patient-centred psoriasis care: a qualitative study identifying patient needs in dermatological outpatient clinics. British Journal of Dermatology. 2017;177(2):436-44. DOI: 10.1111/bjd.15292.

114. Currie GR, Kennedy BL, S. M. B, R. S. M. Y, J. F. S, S. J. V, et al. Managing juvenile idiopathic arthritis within the context of their life: What we learnt from children and youth living with juvenile idiopathic arthritis and their parents. Musculoskeletal Care. 2023;21(4):1248-60. DOI: 10.1002/msc.1805.

115. Decosta P, Skinner TC, Sørensen JL, Topperzer MK, Grabowski D. Young children's perspectives on treatment and care: A qualitative study using narrative and play-based interviewing. Journal of Pediatric Nursing. 2023;73:211-20. DOI: 10.1016/j.pedn.2023.10.014.

116. Indenrigs- og sundhedsministeriet [Ministry of the Interior and Health of Denmark]. Sundhedsstrukturkommissionen n.d. [cited 2024 January 20]. Available from: https://sum.dk/temaer/sundhedsstrukturkommissionen.

117. Jonsson F, Blahed H, Hurtig AK. More than meets the eye: a critical discourse analysis of a Swedish health system reform. Bmc Health Services Research. 2023;23(1). DOI: ARTN 1226 10.1186/s12913-023-10212-4.

118. Olsen CF, Bergland A, Debesay J, Bye A, Langaas AG. Patient Flow or the Patient's Journey? Exploring Health Care Providers' Experiences and Understandings of Implementing a Care Pathway to Improve the Quality of Transitional Care for Older People. Qualitative Health Research. 2021;31(9):1710-23. DOI: Artn 10497323211003861 10.1177/10497323211003861.

119. Schlünsen ADM, Christiansen DH, Fredberg U, Vedsted P. Patient characteristics and healthcare utilisation among Danish patients with chronic conditions: a nationwide cohort study in general practice and hospitals. BMC Health Services Research. 2020;20(1). DOI: 10.1186/s12913-020-05820-3.

120. Bodenheimer T. Improving Primary Care for Patients With Chronic Illness. JAMA. 2002;288(14):1775. DOI: 10.1001/jama.288.14.1775.

121. Boehmer KR, Abu Dabrh AM, Gionfriddo MR, Erwin P, Montori VM. Does the chronic care model meet the emerging needs of people living with multimorbidity? A systematic review and thematic synthesis. PLOS ONE. 2018;13(2):e0190852. DOI: 10.1371/journal.pone.0190852.

122. World Health Organization. Continuity and coordination of care: a practice brief to support implementation of the WHO Framework on integrated people-centred health services. Geneva: World Health Organization; 2018. 76 p. ISBN 978-92-4-151403-3

123. Castro EM, Van Regenmortel T, Vanhaecht K, Sermeus W, Van Hecke A. Patient empowerment, patient participation and patient-centeredness in hospital care: A concept analysis based on a literature review. Patient Education and Counseling. 2016;99(12):1923-39. DOI: 10.1016/j.pec.2016.07.026.

124. Miller AR, Condin CJ, Mckellin WH, Shaw N, Klassen AF, Sheps S. Continuity of care for children with complex chronic health conditions: parents' perspectives. BMC Health Services Research. 2009;9(1):242. DOI: 10.1186/1472-6963-9-242.

125. Rehman N, Morais-Almeida M, Wu AC. Asthma Across Childhood: Improving Adherence to Asthma Management from Early Childhood to Adolescence. J Aller Cl Imm-Pract. 2020;8(6):1802-+. DOI: 10.1016/j.jaip.2020.02.011.

126. Hallgren J, Bergman K, Klingberg M, Gillsjö C. Implementing a person centred collaborative health care model-A qualitative study on patient experiences. Int Emerg Nurs. 2021;59. DOI: ARTN 101068 10.1016/j.ienj.2021.101068.

Appendices I, II, and III

Appendix I: Manuscript I

Referral Pathways for Children with Atopic Diseases in Denmark

Appendix II: Manuscript II

Parents of children with atopic diseases - experiences with care and the interaction with healthcare professionals over time

Appendix III: Manuscript III

A “normal” life: a qualitative study exploring parents’ experiences of everyday life with a child diagnosed with atopic dermatitis and atopic comorbidities