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Living with VACTERL association

*From the perspectives of children, adolescents
and their parents*

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Abstract

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VACTERL association is a rare and complex congenital condition often requiring repeated surgery and entailing various physical sequelae. Knowledge is scarce regarding experiences of the health condition and health care, need of support at school, health-related quality of life (HRQoL), and psychological well-being in children, adolescents and their parents.

This thesis aims to investigate various aspects of living with VACTERL association, from the perspectives of children, adolescents and their parents.

Ten children aged five to eight years were interviewed using the computer-assisted interview technique *In My Shoes (Study I)*. They expressed awareness of their health history and felt proud but also different due to physical dysfunction. While happy to meet familiar staff in the hospital they voiced worries about medical procedures.

The nineteen parents interviewed described crisis reactions on the discovery of malformations in their child (*Study II*). Parental involvement in care was reported from the initial hospital admission until taking responsibility for treatments at home. Eventually the health condition became integrated in everyday life. Insufficient emotional and limited medical support were reported. Various levels of professionalism among healthcare professionals and discrepancies concerning knowledge and experience between the tertiary and local hospitals were described.

In ten evaluated pre-school children (*Study III*), intelligence measured by Wechsler-scales was within the normal range. Eight children had attention difficulties and two were later diagnosed with attention deficit hyperactivity disorder (ADHD). All children had physical dysfunctions affecting their nutrition, bowel or bladder functions. All needed extra support and adjustments at school.

Forty children and adolescents responded to validated questionnaires of DISABKIDS and Beck inventories (*Study IV*). The HRQoL was comparable to European children with chronic conditions. Their psychological well-being was similar to that of Swedish school children and significantly better than that of a clinical sample. Self-reported anxiety and depression in 38 mothers and 33 fathers were comparable to non-clinical samples.

In conclusion, regular follow-up by multi-professional team with continuity is crucial to optimise the physical function in children with VACTERL, to identify those in need of extra support at school and to detect reduced psychological well-being in children and parents. Fear of medical procedures may be reduced by carefully providing information and individual care strategies. For the parents psychological processing, support from medical experts and peers is essential to achieve self-confidence and adaptation. Transfer of knowledge and information between multi-professional teams at the local and tertiary hospitals could be improved by the use of video sessions.

Keywords: Congenital malformations, Experiences of health care, Health-related quality of life, Neurodevelopmental function, Physical dysfunction, Psychological well-being, VACTERL association

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*To my beloved husband Daniel for
his endurance in supporting me.*

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

- I Kassa, A-M., Engvall, G., Engstrand Lilja, H. (2017) Young children with severe congenital malformations (VACTERL) expressed mixed feelings about their condition and worries about needles and anaesthesia. *Acta Paediatrica*, 106(10):1694-1701
- II Kassa, A-M., Engstrand Lilja, H., Engvall, G. (2019) From crisis to self-confidence and adaptation. Experiences of being a parent of a child with VACTERL association – A complex congenital malformation. *PLoS One*, 14(4):e0215751
- III Kassa, A-M., Dahl, M., Strinnholm, M., Engstrand Lilja, H. (2018) Attention difficulties and physical dysfunction common in children with complex congenital malformations: a study of preschool children with VACTERL association. *Acta Paediatrica*, doi:10.1111/apa.14566 [Epub ahead of print]
- IV Kassa, A-M., Dellenmark-Blom, M., Thorsell Cederberg, J., Engvall, G., Engstrand Lilja, H. Children and adolescents with VACTERL association: health-related quality of life and psychological well-being in children and adolescents and their parents. *Accepted*

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Abbreviations

ACE	Antegrade Continence Enema
ADHD	Attention Deficit Hyperactivity Disorder
ANCOVA	Multivariable analyses of covariance
ARM	Anorectal Malformation
BAI	Beck Anxiety Inventory
BDI-II	Beck Depression Inventory, 2nd edition
BYI-A	Beck Youth Inventories – Anxiety
BYI-D	Beck Youth Inventories – Depression
BYI-S	Beck Youth Inventories – Self-concept
CHD	Congenital Heart Defect
CI	Confidence Interval
DCGM-37	DISABKIDS Chronic Generic Measure – long version
EA	Esophageal Atresia
EACH	European Association for Children in Hospital
HRQoL	Health-Related Quality of Life
ICC	Intraclass Correlation Coefficient
IMS	In My Shoes
IQ	Intelligence Quotient
NEPSY	Developmental NeuroPSYchological Assessment
PSARP	Posterior Sagittal Anorectoplasty
SD	Standard Deviation
SDQ	Strength & Difficulties Questionnaire
SPSS	Statistical Package for the Social Sciences
TSC	Tethered Spinal Cord
VACTERL	Vertebral anomalies, Anorectal malformations, Cardiac defects, Tracheo-Esophageal fistula, Renal anomalies and Limb deformities where at least three should be present for the diagnosis
WHO	World Health Organization
WHOQOL	WHO Quality of Life group
WISC-IV	Wechsler Intelligence Scale for Children, 4th edition
WPPSI-IV	Wechsler Preschool and Primary Scale of Intelligence, 4th edition
QoL	Quality of Life

Preface

During my years being a registered nurse my curiosity for research of the healthcare field was evoked by two situations in particular.

One of my favourite workplaces was the newly opened ward for day surgery and ambulatory treatments where the duties were both challenging and rewarding. One day I received a letter from a mother who had visited the ward together with her 4–5 year-old daughter who had undergone a minor surgical procedure under anaesthesia. The mother described how I had changed the girl's perception of hospital visits by meeting her as an individual and treating her as the main person in the situation. Her fear of hospital from previous experiences had been eliminated. Even afterwards the girl had said that she wanted to return to the hospital and go through all the procedures once again.

I was very surprised by this letter and I did not remember this particular family. I had just fulfilled my usual duties and furthermore I was probably, as usual, in something of a hurry the morning the girl attended the ward. For one nurse there were often 2-3 children to prepare for anaesthesia in a short time, with all the necessary procedures involved. There was not really much time for information and to get acquainted. So...What did I do? What did the girl perceive?

The other context was an in-patient ward abroad. I fell sick when I was on holiday and had to be admitted for one week. Although the ward was considered to be one of the best in the country I did not feel properly taken care of. I lacked assistance, felt ignored, not listened to and not respected.

I think both of these situations reflect the Swedish concept “bemötande” which is so difficult to translate to English. It was from this point of view I started my further studies in caring sciences and in my examination tasks I focused on patient experiences through literature studies and through interviews with children.

I tried to find an opportunity for doctoral studies shortly after my “Magister” Degree, but failed to find a suitable project. That is why I could not resist the challenge from my main supervisor to apply for a doctoral project emanating from the work we had started in value-based care. We recruited the associate supervisor and designed the research plan in which I could include my favourite subjects of experiences of health care in children and parents.

Now almost five years have passed since the application. Although there has been a great deal of hard work requiring a lot of endurance, I am grateful to have got this opportunity. The most valuable aspects of this process have

been the interviews with the children and their parents and the benefits of hearing their stories and experiences of living with VACTERL association. Through this generous sharing by the participants I have gained some knowledge in how it is to live with a complex congenital malformation.

Even though “bemötande” comprises a small part of this thesis I have gained knowledge about what will contribute to a good encounter with the healthcare providers, and this includes knowledge, competence, professionalism, information, engagement and sensitivity.

We have tried to shed some light on aspects of living with the condition of VACTERL association. It is my hope that this thesis can provide some benefit for children and adolescents with complex congenital malformations and for their parents through improved support and follow-up.

Introduction

VACTERL association

Definition, incidence and mortality

VACTERL association is a complex congenital condition with a combination of malformations including vertebral anomalies (V), anorectal malformations (A), cardiac defects (C), tracheoesophageal fistula (TE) with or without esophageal atresia, renal anomalies (R) and limb deformities (L). The condition was first described by Quan et al. 1973 (1) as the less extensive VATER association. Later cardiac and limb defects were included and the diagnosis name was changed to VACTERL (2, 3). The diagnosis is based on clinical features in which at least three of the above-mentioned malformations should be present and no evidence be found of an alternative condition. The denotation association implies that the combination of malformations occurs more often than could be expected by chance, but without an identified cause in common (4).

Since diagnostic criteria are not always used identically, incidence figures may not be exact but estimated to 1/10,000–1/40,000 live-born infants (5-7). Recent figures for estimated birth prevalence in Europe is 6.25/100,000 based on information from registers, national health institutes and published articles (8). According to these figures, less than 12 children with VACTERL association would be born in Sweden per year among the 115,000–120,000 births in total (9).

For survival most children require surgery during the first days of life and often repeated procedures under anaesthesia during childhood (4). Mortality has decreased with improvement in neonatal intensive care, anaesthesia and surgical techniques (4, 10), exemplified by 24% reported in a small cohort 1992 and 6–8% in a larger group of children born 2004–2012. The highest mortality rate occurs in children with cardiovascular defects and low birth weight (11, 12).

Malformations and potential sequelae

The malformations included in VACTERL association display a wide variation in severity. Depending of type and degree of their malformations patients with VACTERL association may experience long-term physical sequelae (4, 13, 14).

Vertebral anomalies, reported in approximately 60–80% of patients with VACTERL association (5, 15-18) are often combined with rib anomalies. The vertebral anomalies could appear as various altered shapes such as hemi-, butterfly or wedge vertebrae or as fusions, extra or missing vertebrae or other types of anomalies. For some of the patients, repeated surgery may be needed while others present with almost no symptoms. Development of scoliosis is common which might necessitate surgery (4, 19). Sequelae are reported as persistent back, shoulder and neck pain (14).

Anorectal malformations (ARM) of varying severity, which occur in approximately 55–90% of patients with VACTERL association (5, 15-18, 20), are classified according to presence and location of fistula and are frequently combined with genitourinary anomalies. Reconstruction of anus is usually performed by the method of posterior sagittal anorectoplasty (PSARP) most often at the age of 1–3 months after the infant has been provided with a colostomy during the first days of life. Daily dilatations are needed for several months to avoid constriction of the new anus and are performed by parents at home until necessary dimension is reached (21).

The most common complications from ARM are constipation and soiling (21) and sometimes gas incontinence (22). Daily use of enemas is often required treatment. To facilitate for the patient to independently perform these treatments a device for antegrade continence enema (ACE) can be constructed on the abdomen. Depending on the type of anorectal malformation, symptoms from the urinary tract might be present such as infections and functional disorders sometimes including urine incontinence (21).

Cardiac structural defects are similarly of various degrees of severity, from life threatening in need of immediate surgical treatment to minor defects not even observed in the new-born baby (14, 15). It is reported in approximately 40–80% of patients with VACTERL association (15-17, 20, 23). Cardiac defects requiring surgery have been reported as the most common cause of death in this patient group (12). Long-term sequelae can be observed as impaired cardiac function (4).

Tracheo-Esophageal fistula with or without esophageal atresia (EA) (4) is found in approximately 50–80% of patients with VACTERL association (5, 15-18, 20). EA is categorised depending on the presence and location of tracheoesophageal fistula. The most common type presents with an upper blind ending pouch of the esophagus and a lower part connected to trachea. In most cases surgery is required during the first days of life. Common sequelae are dysphagia, gastro-esophageal reflux and airway symptoms. Strictures in the esophagus requiring dilatation during anaesthesia are reported in approximately half of the children (24-30).

Renal anomalies reported in approximately 50–80% of patients with VACTERL association (5, 15-17, 20, 31), appear as one-sided renal agenesis, horse-shoe kidney, cystic or dysplastic kidneys. These anomalies cannot be diagnosed without imaging (4) and are sometimes combined with ureteral or

genitourinary anomalies (17, 32). Reported complications are urinary tract infections, nephrolithiasis and impaired renal function (14, 33).

Limb defects occurring in approximately 40–55% of the patients (5, 16-18, 20) were, for the VACTERL diagnosis, originally limited to radial anomalies with thumb aplasia or hypoplasia but later additional limb defects have been included in the diagnosis such as polydactylies and lower limb anomalies (4). Since the limb defects entail esthetical and functional impairment surgical correction is often necessary to reduce the impact on quality of life (34).

High incidence of tethered spinal cord (TSC) has been reported in children with VACTERL association including vertebral, ARM or urogenital anomalies. TSC might manifest as back or leg pain or disturbed motor or sensory function in legs, or as bladder and bowel dysfunction (35, 36).

Some malformations included in VACTERL association are not easily detected during childhood but could still cause long-term sequelae. Hence, it is recommended that thorough investigations are performed to identify potential further VACTERL features in children born with ARM, EA or two other components of VACTERL (37, 38).

In summary, VACTERL association may imply life-threatening health conditions and entail severe long-term complications. Physical health is often affected, and long-term care actions can be required which might result in impaired quality of life. In contrast, VACTERL in its least complicated presentation does not necessarily imply any long-term consequences.

Potential impact on Quality of Life

Health-Related Quality of Life

According to the World Health Organization (WHO), health is defined as not only the absence of disease or infirmity but also a state of complete physical, mental and social well-being (39). The concept of Quality of Life (QoL) was by the WHO Quality of Life (WHOQOL) group defined as “individuals’ perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” (40, p 1405). Thus, QoL is a subjective evaluation of both objective and subjective conditions, including physical, psychological and social dimensions with both positive and negative aspects (40). Health-Related Quality of Life (HRQoL) as one component of QoL has been defined as “a multidimensional construct covering physical, emotional, mental, social and behavioural components of well-being and function as perceived by patients and/or other observers” (41, p.1201). Hence, the concept of HRQoL includes physical, psychological and social aspects of health and could be described as a combination of the objective physical health status and the patient’s subjective perception of health. Expectations of health and ability to cope with limitations could influence this perception. Thus two persons with the same health status might have different

HRQoL (42). Psychosocial factors such as coping strategies, health locus of control and social support might have an important impact on QoL and might be more important than the impact of disease and treatment (43).

Physical aspects

Depending on the combination of malformations in children with VACTERL association, various physical sequelae entail medical difficulties in everyday life, which might affect HRQoL.

Difficulties in nutrition following EA often include dysphagia and strictures in the esophagus hindering food to pass which sometimes require dilations and endoscopic removal of stuck food (26, 27, 44). Time-consuming meals, need to drink significant amounts of fluid to facilitate food transportation, avoidance of some types of food and the need to vomit could be consequences of these sequelae (45).

For treatment of constipation in patients with ARM, the use of a daily enema will in many cases be necessary (21) which might hinder independency (46). Also urine incontinence or leakage connected to ARM (21) could entail the need to use nappies and other special arrangements. As a consequence of renal anomalies, repeated urinary tract infections, nephrolithiasis and reduced renal function (14, 33) might affect the HRQoL.

Reduced physical capacity and ability to be as active as other children could result from cardiac defects (47) but also after EA due to airway morbidity (26, 27, 29, 30).

Limb defects might lead to impairments (34) such as difficulties in meal situations and in other fine motor activities like writing and dressing.

Long-term back, neck and shoulder pain from vertebral malformations could be common and severe (14).

Psychological and social aspects

Consequently, various psychological and social consequences affecting HRQoL could be present in children with VACTERL association. Limited autonomy could be experienced due to sequelae such as the need for daily enemas due to ARM or (21, 46), the need of assistance for fine motor tasks during meals and in dressing due to limb deformities (34).

Negative social effects may be experienced when living with the consequences of ARM such as potential gas incontinence (22), soiling and odour all of which might entail bullying (48). Also, emotional problems such as more sadness, anger, fear and worries and less social competence than in healthy children has been described (49). Learned helplessness appearing as lower ability to express their own will might be a result of repeated enema procedures performed on the unwilling child with ARM (50).

Furthermore, a sense of being different from peers could originate from reduced physical capacity due to cardiac malformations or airway symptoms (27, 29, 30, 47). Limb defects might be the most obvious defect for peers (34,

51) but also other minor visible defects such as surgical scars and wing scapula after EA could be disturbing (52).

Neurodevelopment

Usually no cognitive impairments are linked to the diagnosis of VACTERL association (13, 14). Discussions are ongoing as to if and how, early anaesthesia and surgery in the new-born child have an adverse effect on neurodevelopment, and whether the contributing factors could be the anaesthetic drugs, other factors connected to anaesthesia, co-morbidity or the surgical procedure (53). Previous reports on single malformations have described adverse neurodevelopmental outcomes after early cardiac surgery and non-cardiac neonatal surgery suggesting risk factors such as multiple congenital anomalies, low birth weight, repeated surgery and long hospital stays (54, 55). Corresponding studies are scarce in children with EA (56-59) and ARM (57, 58, 60) and not found in children with VACTERL association.

Health care and the child

Children with VACTERL association will, during childhood, be exposed to repeated surgeries, examinations with or without anaesthesia e.g. radiology and endoscopy, needle-related procedures, treatments and medical procedures such as anal dilatations or enemas in hospital or at home (4, 19, 21, 24-28).

Even though the hospital environment might be perceived as enjoyable by providing opportunities for playing and making new friends (61), hospitalisation often entails negative experiences for children including worries and fears of painful and unpleasant procedures (61-63).

According to The European Association for Children in Hospital (EACH) Charter, children should be protected from unnecessary investigations and treatments and measures should be taken to decrease physical and emotional stress as much as possible (64). Continuity of caregivers meeting the child in the hospital could be an important factor to create trust and security in the child (64, 65). Children's participation in their health care should be assured by age appropriate information and their opinions taken into consideration according to their age and maturity (66, 67).

Parents' experiences of having a child with congenital malformations

The experience of becoming a parent could be described as an overwhelming event (68). Additionally, the disclosure of a congenital defect in the foetus or

in the new-born child induces a crisis reaction (69) with emotions of grief over the loss of an expected healthy child (70-72), shock (71) and sadness (73). To become a parent of a child in need of immediate surgery and care in neonatal intensive care unit entails huge stress, anxiety and worry related to the child's health condition, treatment and uncertain prognosis (72, 74, 75). Ambivalent emotions might arise, alternating between fear of losing the child and hope for successful treatment (73, 74). The psychological distress (76) could remain for many years (77) including acute and post-traumatic stress disorder (72, 78).

The development of the parent-child relationship could be delayed (79) due to difficulties in holding and feeding the child during the initial hospital stay (72, 74, 80).

Parents of a child with VACTERL association will be involved in the health care of their child throughout childhood and adolescence and they will be given the responsibility for medical treatment performed at home. These procedures might be experienced as hurting the child, particularly performing enemas and anal dilatations. Perceived suffering of the child could create suffering also in the parents. Hence, the physical dysfunction of the child and the daily treatments might affect the life of the whole family (48).

Drotar et al. (69) suggested a hypothetical model describing reactions in parents after the birth of a child with a congenital malformation. The first stage was defined as *shock*, followed by *denial* and further the third stage comprises *sadness and anger*. As the fourth stage follows *adaptation* and finally a *reorganisation* is attained. At the stage of adaptation the parents studied by the above-mentioned authors described satisfaction with their children and an increased ability to care for them. Adaptation to the new situation appeared to be a gradual process including coping with various issues (69).

Coping and adaptation

In the theory of stress, appraisal and coping, Lazarus and Folkman (81) defined coping as individuals' efforts to manage difficulties which challenge or surpass their capacity. Through primary appraisal the stressor is evaluated as significant or not, and by secondary appraisal evaluation what type of coping could be applied takes place. Coping is carried out with the use of thoughts and behaviours to handle the stressful internal or external situations (81, 82). Coping strategies can be divided in three categories. Active or primary control coping (problem-solving) include the aim of changing the source of stress or the reaction it evokes. Accommodative or secondary control coping (emotion-focused) aims to adapt to the stressor by e.g. positive thinking, acceptance or distraction. Passive avoidant or disengagement coping strives to evade the source of stress by avoidance and denial (83).

Infants are already from birth involved in the coping processes which are initially built on physiological reactions. Support seeking has been observed as the common coping strategy in infants and by activity, sounds and facial expressions and seeking eye contact they convey their stress. The caregivers respond to the reactions and perform the coping by discovering threats, protecting from and removing stressors and comforting the infant (84, 85). During childhood coping develops by applying different kinds of strategies. In the preschool age various coping strategies are used while support seeking followed by behavioural escape or avoidance are the most common back-up strategies when others are not effective. During middle childhood coping becomes more differentiated and includes cognitive strategies. The support seeking is no longer only limited to caregivers but also peers are included. In adolescence playful problem solving is added and the coping is more self-reliant and cognitive strategies more effective in the response to stressors (85). The effectiveness of coping depends on the combination of the type of stressor and the appraisal and coping response the individual applies – the goodness of fit (86).

A chronic health condition is a potentially acute and long-term stressor in children, adolescent and their parents (86). For adjustment to the chronic condition, secondary control or accommodative coping strategies are the most effective while the least effective coping strategy is the passive avoidant type. The coping strategies of primary control are most useful in managing stressors which are possible to control, such as treatment changes (83).

Adaptation could be defined as any beneficial change to respond to demands of the environment (87). Several conceptual models have been constructed to explain the adaption to chronic childhood illness where biomedical, psychological and socio-ecological processes contribute (86). The timing of onset of the illness is crucial for children's adjustment where children born with a condition adapt more easily than children with an acquired illness (88). Adjustment could be seen as a function of goodness of fit such as between parenting style and child characteristics and between demands and coping methods (86).

The process of a parent's psychological adjustment to a chronic condition in their child could be associated with the child's characteristics such as emotional and behavioural problems, with the parents' characteristics such as personality and coping styles, with family characteristics such as partner presence and supporting climate, and with informal social support (89).

Rationale

VACTERL association is a rare and complex condition comprising a combination of congenital malformations. Knowledge is scarce regarding experiences of the health condition, health care, treatments and follow up in young children with VACTERL association and in their parents. Also, little is known about need of support among these children when starting school. Furthermore, knowledge is scarce regarding the children's and adolescents' health-related quality of life and of psychological well-being and also of the psychological well-being of their parents.

Investigations into various aspects of living with the condition from the perspectives of children, adolescents and parents could contribute new insights and enhanced comprehension. Interviews with children and parents might provide increased understanding and knowledge of how health care could be improved from the perspective of the children and parents. Evaluation of the neurodevelopmental and physical function of preschool children with VACTERL association may display support requirements in school to optimise the learning process already from the start. Results from questionnaires measuring self-reported health-related quality of life and psychological condition might bring more understanding of the health condition's effect on health-related quality of life and psychological well-being in children and adolescents with VACTERL association, and their parents.

Overall and specific aims

The overall aim of this thesis was to investigate various aspects of living with the diagnosis of VACTERL association, from the perspectives of children, adolescents and their parents.

The specific aims of the included studies were to:

- I** Describe experiences of the health condition and health care in young children with VACTERL association and to describe their suggestions to improve hospital care.
- II** Describe experiences of being a parent of a child with VACTERL association.
- III** Evaluate neurodevelopmental and physical function in pre-school children with VACTERL association and to identify potential need of extra support in school.
- IV** Investigate HRQoL, self-reported anxiety, depression and self-concept in children and adolescents with VACTERL association and self-reported anxiety and depression in their parents.

Material and Methods

Overview of the included studies

This thesis consists of four studies whereof two with qualitative and two with quantitative design. An overview of the designs, participants and applied methods is presented in Table 1.

Table 1. *Overview of the included studies*

Study	Design	Participants	Data collection	Analysis
I	Qualitative interview study	10 children aged 5–8 years	Semi-structured interviews using the computer based software In my Shoes	Qualitative content analysis with inductive approach
II	Qualitative interview study	10 mothers, 9 fathers of children in Study I	Semi-structured interviews face-to-face or by telephone	Qualitative content analysis with inductive approach
III	Quantitative cross sectional observational study	10 children aged 5–7 years	Evaluation of neurodevelopmental and physical function. Review of medical records.	Descriptive statistics
IV	Quantitative cross sectional questionnaire study	40 children and adolescents aged 8–17 years, 38 mothers, 33 fathers	Questionnaires: DISABKIDS, BYI-A, BYI-D, BYI-S, BAI, BDI-II, reported symptoms	Descriptive and comparative parametric statistics: independent, paired and one-sample t-tests, Intraclass correlation coefficient (ICC), Multivariable analyses of covariance (ANCOVA), Pearson correlation

Participants

Children diagnosed with VACTERL association and their parents were recruited from one tertiary paediatric surgical centre for Studies I, II and III. For Study IV recruitment was performed from three out of four tertiary paediatric surgical centres in Sweden. Additionally, participants were invited through a peer organisation including families with a child with VACTERL association for Studies I, II and IV.

Study I

An invitation letter was sent to parents of 12 children with VACTERL association aged 5-8 years. Additionally one child was recruited through the peer organisation and the family itself contacted the researcher. Totally, 10 families accepted to participate and five girls, aged 5–8 years and five boys 5–6 years old were interviewed between December 2015 and October 2016.

Study II

Parents of the children with VACTERL association participating in Study I were invited. One parent was excluded due to language difficulties. Totally 10 mothers and nine fathers were interviewed from December 2015 until November 2016.

Study III

Children with VACTERL association aged 5–7 years were recruited. Through information letters 13 families were invited and 10 agreed to participate. The study group consisted of four girls and six boys and the evaluations took place in the regional habilitation centre between 2015 and 2017.

Study IV

Children and adolescents aged 8–17 years with VACTERL association were invited, together with their parents, to participate in the questionnaire study during 2015–2019. Furthermore, three families were recruited by an invitation conveyed through the peer organisation. Questionnaires addressed to children, mothers and fathers respectively, were sent to all 64 families identified as eligible and were returned by 40 children or adolescents, 38 mothers and 33 fathers.

Data collection

Study I

The In My Shoes software (IMS) (Child and Family Training Limited, York, UK) was used to facilitate the interviews (90, 91). IMS has been suggested as a feasible method to help children to describe their experiences of health care (92). Furthermore, it has been validated by comparing results with a standard forensic interview approach (93) and also found to be a helpful tool when interviewing shy children (94). A number of modules with simplified drawings were used to ask about emotions, places, people and experiences (90). Parallel to IMS a semi-structured interview guide was used consisting of open-ended questions concerning experiences of health and health care and suggestions for improving hospital care. Follow-up questions were used to expand the answers. The PhD student, who was not involved in the treatment of the children, performed the interviews.

Study II

A semi-structured interview guide was constructed by the authors and used to cover the aim of the study. The open-ended questions concerned the parents' experiences of being a parent of a child with VACTERL association, experiences of hospital care and healthcare support for the child at home. Follow-up questions were used to enlarge upon the answers. The PhD student, who was not involved in the regular treatment of the children, performed the interviews, whereof three were accomplished face-to-face and 16 by telephone.

Study III

Evaluations of the children were performed in the regional habilitation centre in the tertiary Children's Hospital. The children were evaluated over a period of three days by a psychologist and a paediatric neurologist.

The Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition (WPPSI-IV) (95) or the Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV) (96) were used according to the age of the children. A full-scale IQ was obtained from the included scales with mean 100 and standard deviation (SD) 15 and classified by using SD intervals as average (93–107), low average (85–92), borderline (70–84) and extremely low (< 70) (95). The visual attention and auditory attention tests from Developmental Neuropsychological Assessment, commonly known as NEPSY (97) were used in four children. Observation of the child's behaviour including focused and sustained attention, signs of inattention, hyperactivity or difficulties with impulse control was carried out during testing.

To obtain information about the child's health, medical problems and physical function in daily life, parents were interviewed and anamneses obtained by a paediatric neurologist. Data was collected from the medical records including patient characteristics, former and present physical function, growth and number of surgeries and anaesthesia. General physical and neurological examination of the child was performed by a paediatric neurologist.

Study IV

The DISABKIDS Chronic Generic Measure – long version (DCGM-37) was used to assess the HRQoL of children and adolescents aged 8–17 years and a corresponding proxy version was applied for each parent. The questionnaires cover mental, social and physical domains of HRQoL. Results from a European field study sample including children with chronic conditions of asthma, arthritis, dermatitis, diabetes, cerebral palsy, cystic fibrosis and epilepsy, and their parents were available as reference material (98, 99). The DCGM-37 comprises 37 items with a 5-graded Likert scale worded: “never” “seldom”, “quite often”, “very often” and “always” which are transformed to numerical values 1–5, where higher values indicate better HRQoL. To make the results more comprehensible, we used positive names for the subscales in line with suggestion from Chaplin et al. (100) namely: *independence*, *inner strength* (originally emotion), *social inclusion*, *equality* (originally social exclusion), *physical ability* (originally limitation) and *treatment*. The raw scores (RS) received from each subscale and the total summed up score were recoded to transformed raw scores (TRS) ranging from 0–100. Internal consistency has been reported as Cronbach's alpha 0.70–0.87 in the six subscales and test-retest reliability has been found to be satisfactory (99).

Beck Youth Inventories (BYI) measure emotional and social impairment in children and adolescents 7–18 years. The subscales used in this study were Beck Youth Inventories – Anxiety (BYI-A), measuring worries and anxiety related to school, own health and the future, Beck Youth Inventories – Depression (BYI-D), measuring sadness, hopelessness and guilt related to self-image and physical symptoms and Becks Youth Inventories – Self-concept (BYI-S) measuring perceived own competence, skills and self-worth (101). Internal consistency for the scales has been shown to be $\alpha = 0.89–0.94$ and test-retest reliability has been demonstrated as satisfactory. Each scale consists of 20 items with a 4-graded Likert scale from 0 = “never” to 3 = “always”. For the BYI-A and the BYI-D high values indicate higher levels of anxiety and depression respectively. For the BYI-S, a high value implies a more positive self-concept. Reference values are provided for a norm group of Swedish school children ($n=2358$) and a Swedish clinical sample of children with psychiatric diagnoses ($n=149$) (101).

Beck Anxiety Inventory (BAI) (102) and Beck Depression Inventory second edition (BDI-II) (103) were used to measure self-reported anxiety and

depression in each parent. Both instruments consist of 21 items with a 4-graded Likert scale from 0 = “never” to 3 = “always”. Internal consistency has been reported to be $\alpha = 0.88$ for the BAI and $\alpha = 0.91$ for the BDI-II in Norwegian non-clinical samples and temporal stability has been demonstrated for both scales (102, 103). Reference values for BAI were found from Finnish (104), US (105) and Spanish (106) non-clinical samples and for BDI from a Norwegian non-clinical sample (103).

In addition to the questionnaires, a parent-reported form was attached with an open question concerning physical complications or symptoms of the child/adolescent during the previous year.

Analysis

Studies I and II

Qualitative content analysis with an inductive approach (107) was used, as described by Graneheim et al. (108). The text was carefully read through repeatedly to achieve a sense of the whole content. According to the aim, meaning units were identified, condensed and given a code. Subcategories and categories were formulated by the process of comparing, grouping and abstracting codes, while including similarities in and excluding disparities from the categories. NVivo 11 Pro for Windows software (QSR International Pty Ltd, Victoria, Australia) was used to organise and visualise the material. To ensure correct understanding of the content, a movement between the whole content of the interviews and the identified codes was performed during the analysis process. In Study I the analysis was limited to the manifest content while analysis of latent content was included in Study II with formulation of a theme describing the underlying meaning (108). The analysis was performed through collaboration between all the authors and a consensus was reached.

Study III

Descriptive statistics were used. Categorical data were presented as counts and analysis of the numeric results was performed by calculating the medians and ranges. Deviations in weight and height were presented as standard deviations, with calculated medians and ranges. Results from the Wechsler tests were grouped and categorised according to standard deviations in the general Scandinavian population (95). Due to the small study sample, no percentage calculations or significance testing of the results were performed.

Study IV

For descriptive statistics IBM SPSS Statistics for Windows, version 25.0. (IBM Corp, Armonk, NY) was used and for statistical tests, R version 3.5.0 (R Foundation for Statistical Computing, Vienna, Austria). The study group was described by descriptive statistics such as mean (M), min and max and standard deviation (SD) for continuous variables and number (n) and percentage (%) for categorical. Parametric tests were used for statistical analysis. Comparisons between diagnoses and gender (independent groups) were performed by using t-test, comparisons between parents (dependent groups) by paired t-test and comparisons with reference groups' values by using one-sample t-test. In order to evaluate agreement in ratings between children, adolescents and mothers and fathers, the intraclass correlation coefficient (ICC) was calculated using the ICC function in package psych. ICC coefficients were interpreted as <0.40 poor, 0.40–0.59 fair, 0.60–0.74 good and 0.75–1.0 excellent agreement (109). Multivariable analyses of covariance (ANCOVA) were used to evaluate factors related to the rating scales. Variables included as possible independent predictors were gender, age, gestational age, the presence of anorectal malformation or not, number of procedures in anaesthesia up to 8 years, mother's BAI score and mother's BDI score. Correlations between overall HRQoL in DCGM-37 and the results from BYI-A, BYI-D and BYI-S, between parents' BAI and BDI and further between parents' BAI and BDI and their assessment of their children's HRQoL were estimated by using Pearson correlation and were, according to Cohen (110), interpreted as strong if $r \geq 0.50$. The significance level was set to $p < 0.05$. No adjustment for multiplicity was performed.

Ethical considerations

The included studies were approved by the Regional Ethical Review Board in Uppsala (registration number 2015/264, amendments 2015/264/1, 2015/264/2, and 2015/264/3) and by the Swedish Ethical Review Authority (amendment 2019-00139).

According to the ethical principles for research in humans, the Declaration of Helsinki states that research involving vulnerable groups is only justified if it is not possible to perform in a non-vulnerable group and provided the included group stands to benefit from the outcomes (111). Since the children with VACTERL association form a unique group the choice of participants can be justified. Moreover it is possible that the outcomes can be beneficial for this group of children. All medical research involving humans should be voluntary and consent should be obtained from participants after adequate information (111). For these studies informed consent was obtained from all parents and adolescents aged 15–17 years. Children below the age of 15 were provided

with age-adapted information, while their formal consent was provided by their parents. The voluntariness of participation was emphasised and information provided regarding the possibility to refrain from participation at any time. Before the interviews in Study I started, the voluntariness of the child was confirmed, and the child was given the option of a parent's presence or not.

The number of children with VACTERL association in Sweden is limited and to avoid identifying the children in the reported results, the individuals are represented by codes created separately for each study. The recorded and transcribed interviews were identified only by a code and do not contain any personal information except gender and age of children and gender of parents. Similarly, the returned questionnaires were coded. All results were stored in data files with participants identified only by a code and the code key is kept locked up separately. Only the research group has access to the data and the code key.

Answering questionnaires about psychological well-being as in Study IV, might activate psychological distress. A letter was sent to those children, adolescents and parents who displayed very elevated or severe levels of anxiety and depression. In this letter their ratings were acknowledged and information was given about available health services to contact if needed.

Results

Study I: Experiences of health condition and health care in young children with VACTERL association

The mean length of the interviews was 50 minutes (28–70) with 32 minutes (16–53) addressing health issues and hospital experiences. The analysis resulted in five categories containing three to six subcategories each, describing experiences of living with the health condition and hospital visits (Table 2).

Table 2. *Categories and subcategories describing children's experiences*

Categories	Subcategories
Everyday life with the health condition	Being aware of their health history
	Continuing treatment at home was both hard and easy
	Experiencing physical signs and symptoms
	Sharing with peers
	Feeling different and not understood
Experiences of hospital visits	Feeling happy and proud
	Feeling happy or unhappy when going to hospital
	Remembering the physical environment
	Experiencing good things and situations
Experiences of medical procedures	The disadvantages of being in hospital
	Worrying in advance
	Knowing or not knowing the reason
	Managing well
	Experiencing physical sensations from medication
Coping with stressful situations	Suffering unpleasant examinations and treatments
	Using their own psychological strategies
	Gaining control by participating in decisions
	Seeking support from parents
	Comforting themselves using objects or toys
Suggestions for improving care	Distracting activities
	Sedation before needle-related procedures
	All family members staying together
	Pleasant environment

Everyday life with the health condition

The children described awareness of their health condition regarding previous surgery, continued treatment, physical symptoms and consequences due to their health condition. Treatments performed at home were described. Some of these were associated with pain and discomfort e.g. repeated widening of anus. *"The pins ... it hurt quite a lot, my booty hole was too small ... it really hurt"* (Child 3, age 5). The children described signs and symptoms affecting them like stomach pain, difficulties in swallowing, being slow and feeling palpitations.

Descriptions were given of how experiences of illness and health care in other situations were shared with peers. The children expressed sadness at being different and also anger and anxiety about being teased. However and on the contrary feelings of happiness and pride were also expressed.

Experiences of hospital visits

According to the children visiting the hospital entailed mixed feelings. Happiness was expressed in meeting familiar staff but also worry and uncertainty about what was going to happen in the hospital. *"Daddy doesn't know if there's going to be needle sticks"* (Child 7, age 5). Many other positive experiences were described such as receiving gifts, meeting clowns and playing with other children cared for at the hospital. On the other hand, there were descriptions of negative aspects due to being excluded from normal daily life such as difficulties in sleeping on account of not having their usual bed equipment, missing friends to play with, and not having the opportunity to work with school subjects.

Experiences of medical procedures

Unpleasant feelings were expressed in connection with hospital procedures. The children recounted worrying in advance since they did not know why and how procedures would be performed nor their possible outcome. Nervousness was expressed before anaesthesia and worries that the staff would make a mistake so it would be impossible to wake up again.

Nevertheless, satisfaction was expressed when the child managed well in some procedures that did not cause suffering. Receiving anaesthesia was described as something positive and it was considered to be an advantage to sleep during procedures.

Among the unpleasant procedures, the children most frequently expressed fear of needle-related ones; described as being difficult, tough, scary and painful. *"Getting a needle stick ... I don't like it ... it's horrid"* (Child 10, age 8).

Pain was also described during procedures such as examinations, dilations of anus and removing catheters.

Coping with stressful situations

Psychological strategies to cope with stressful situations were described by the children such as thinking about something positive and encouraging themselves. Strategies for relaxation and endurance were expressed. *“It hurts quite a lot ... then it’s just ... to wait until it’s over ... then you just have to relax”* (Child 3, age 5).

The children also described processing unpleasant treatments by repeating the same procedure on their own dolls. Furthermore, the children recounted how one way to handle the situation was by clearly presenting their wishes to the healthcare providers. According to the children the presence of and closeness to the parents helped them through the procedures. Comforting objects such as cuddly toys or comforter were described. Distractions provided by the staff, such as watching a film were described as helping the children through needle-related procedures.

Suggestions for improving care

The children made suggestions how needle-related procedures could be facilitated by sedating medication always being given in advance. *“Give me something to calm me down every time! ... but not in my bottom!”* (Child 5, age 7).

A wish was expressed that there should be big rooms available in the hospital ward to make it possible for all the family to stay together with the child. Another suggestion was to make the hospital environment more pleasant by creating a special cosy corner with cuddly toys for relaxing.

Study II: Being a parent of a child with VACTERL association

Median length of the interviews was 54 minutes (27–155), mothers’ 56 minutes (27–155) and fathers’ 45 minutes (27–82) without significant difference between genders.

From the analysis an overarching theme was formulated: *From crisis through struggles with rays of hope, to self-confidence and adaptation*. The crisis represents the shock and reactions; the struggles are all the effort needed to handle a child with malformations at the hospital and at home. The hope derives from professionalism among healthcare providers, improvements in the child’s health and shared experiences with peers until self-confidence and adaptation are reached and the health condition becomes an integrated part of life.

Two categories and 10 subcategories describe the experiences of being a parent of a child with VACTERL association (Table 3).

Table 3. *Categories and subcategories describing mothers' and fathers' experiences of being a parent of a child with VACTERL association*

Categories	Subcategories
Becoming and being a parent of a child with a complex congenital malformation	Experiencing acute crisis and delayed psychological reactions
	Being involved in the child's care from providing closeness to taking active responsibility
	Experiencing existential reflections and ambivalent emotions about procedures and complications
	Perceiving their child's acceptance and dislike of health care in hospital and at home
	Sharing experiences with others and gaining strength to handle the situation
Experiences of health care in conjunction with treatment of the child	Accepting and integrating the health condition into the life of both parents and children
	Experiencing more or less professionalism from healthcare professionals
	Receiving both appropriate and inappropriate medical and practical information
	Experiencing both adequate and insufficient support
	Dealing with more or less suitable practical arrangements

Becoming and being a parent of a child with a complex congenital malformation

The parents described how they at the discovery of the malformations in the child reacted with a state of shock with worries, anxiety and uncertainty of the prognosis of the child, *"Then I didn't know how many hours he would survive ... and I didn't expect him to get through ... the surgery ... I was pretty sure that we would be parting ... a natural sadness"* (9M). Hope was experienced when the parents realised that surgery was possible and when the child was recovering. However, it was described how psychological reactions could be delayed for several years and be manifested as panic attacks or fatigue depression.

During the initial hospital stay the parents described how they tried to stay as close as possible to the child although the difficulties to lift up and hold the child were experienced as a hindrance to attachment. A sense of having got an illness instead of a child was expressed *"It took quite a long time before we ... bonded with him as our child ... it felt ... we said to each other ... like we've got a disease ... that's like going to ruin ... our family and this wasn't how we'd thought it*

would be, that was our first thought” (2M). The parents described how the healthcare professionals involved them in the care of the child from the beginning but also how too much responsibility changed their focus from the child to practical issues. Gradually, the parents took more active part in the care and could influence treatment decisions. Performing procedures at home entailed feelings of great responsibility and were sometimes described as difficult, particularly administering enemas and dilating anus. In conjunction with hospital visits the parents described how they actively prepared the child, strived to stay close during procedures and encouraged the child by arranging something positive like playing or rewards.

The parents described struggling with thoughts about the meaning of having a child who had to suffer difficult procedures but still they could perceive every procedure as a step towards improvement in the child’s health. In spite of repeated experiences, the parents described worries about every episode of general anaesthesia the child went through and further about complications and adverse events.

Parents described the child’s perception of hospital care as being a natural part of their life but entailing mixed feelings. Positive aspects were described such as playing and meeting the healthcare professionals while dislike was based on uncertainty and not knowing the plan for the visit. According to the parents, the most negative feelings were associated with needle procedures. Furthermore, again as described by the parents, the children experienced procedures of dilatations performed at home as hard and painful especially when performed after the first year.

Meeting other families with a child with VACTERL association brought recognition and hope to the parents. Additionally, the parents described how they gained strength by experiencing their child’s wellbeing and development and through the relationships within the family.

The parents expressed how the health condition of their child and the related procedures eventually became incorporated into their daily life. *“Now A [the child], he’s A and not his illness, but we don’t think so much about the disease ... it was much more so when he was little ... now you don’t feel that you need to ... we simply don’t think so much about it”* (2M). According to the parents, the health condition had become an integrated part of life for the child as well, and the parents described their children as being positive, having friends and enjoying talking about their health history.

Experiences of health care in conjunction with treatment of the child

The parents perceived varying degrees of professionalism among the healthcare professionals who showed diverse levels of dedication, sensitivity

and calm. Even though the healthcare professionals were described as knowledgeable and competent, the parents sometimes experienced a lack of confidence in their ability to handle emergency situations. Further the parents described limited knowledge and experience in the local hospitals with respect to congenital malformations. *"They didn't know themselves ... it was some nurse who was going to make a hole, there was no anal opening ... so she stood there with the thermometer and tried"* (6F). However, the parents also described child competence among the healthcare professionals, demonstrated by respect and direct communication with the child and through various ways of preparing the child ahead of procedures.

According to the parents, good explanatory, honest and continually updated medical information was provided. However, information in the local hospitals was sometimes experienced as simplified and incorrect. The parents wanted even more and recurring information which should be realistic and include potential complications, preferable provided in writing. They also wished to have more detailed information ahead of planned visits.

The parents referred to good medical support provided in the hospital, and good accessibility to healthcare professionals after discharge, including valued support from specialist nurses. Conversely, other parents described difficulties in receiving support with the child's various health conditions and assistance in practical care procedures. Some parents missed functioning coordination of the follow up of the child and wished for a person coordinating all contacts. According to the parents, emotional support was provided initially in the hospital but the counselling sometimes focused more on practical issues than the core experience of having a sick child. Suggestions were made that counselling should be routine during the initial hospital stay and should comprise repeated invitations.

The parents described how at least one of them could also stay close to the child during the nights in the neonatal ward. An alternative that was appreciated was accommodation in the parents' quarters with the possibility to meet other parents in similar situations. Less appropriate settings were described, such as maternity wards or ordinary hotels where the parents were surrounded by happy people, while they themselves were doubtful about their child's survival. Furthermore, wishes were conveyed that both parents should have the possibility to stay with the child in the hospital ward, also when the child grew older.

Study III: Neurodevelopmental and physical function in pre-school children with VACTERL association

Patient characteristics, surgeries and episodes of anaesthesia

The study group consisted of four girls and six boys with a median age of 5.71 (4.90–7.25). All the children had gone through major surgery within the first three days of life due to congenital heart disease (CHD), EA or ARM. Patient characteristics, surgeries and episodes of anaesthesia are presented in Table 4.

Table 4. *Patient characteristics, (N=10)*

Characteristics	Counts, Median (range)
Female/Male	4/6
Gestational age at birth, full weeks	35.5 (33–41)
Birth weight (BW), grams	2290 (1780–4094)
Small for gestational age (BW SD < -2)	1
APGAR 5 minutes (9 values found)	9 (5–10)
Age at first surgery, days	2 (1–3)
Age at evaluation, years	5.71 (4.90–7.25)
Weight at evaluation (SDS)	-1.3 (+2.1– -3.9)
Height at evaluation (SDS)	-1.6 (+2.3– - 4.3)
Major surgeries prior to evaluation	3.5 (1–9)
Episodes of anaesthesia prior to evaluation	7 (3–52)

Neurodevelopmental evaluation

Results from WPPSI-IV and WISC-IV indicated that IQ was within the normal range in all the children, two of which were at borderline level. The visual attention and auditory attention tests were used for four children, but the results were impossible to calculate in three of them, due to the attention problems described below. Observing the children during two to five sessions showed that eight of the 10 children had attention difficulties. These emerged as problems in focused, divided, shifting and sustained attention, as well as inattention to a task, hyperactivity or difficulties with impulse control. After evaluation, two of the children with attention difficulties were diagnosed with attention deficit hyperactivity disorder (ADHD) following extended investigations.

Physical evaluation

All of the children were found to have normal motor function and the only neurological deviation was a minor finding of abducens nerve palsy in one child. Underweight (<-2 SD) was found in three of the children and four had short stature (<-2 SD). The children's parents reported several problems with

physical function in the children's daily lives. Nutritional problems were described in nine children manifested as selective or slow eating or eating too quickly and risking food obstruction. Gastrostomy was used in one of the children. Bowel dysfunction was reported in seven children, including constipation, and five experienced faecal soiling. The bladder dysfunction issues in five children with anorectal malformations comprised of urinary incontinence or passing urine into a nappy. In one child this was continuous and in three children it was intermittent. Furthermore, one child depended on continuous suprapubic drainage. Reduced physical capacity was described in four of the children; two had previously undergone cardiac surgery and two had asthma or frequent respiratory infections. Surgery for a tethered spinal cord had previously been performed in two children and another two had symptoms of pain in their back and legs requiring further investigations.

Recommendations of support

All the included children needed some cognitive or physical adjustments and assistance in school (Table 5). Support was recommended during meals, for toilet visits and some of the children needed full-time rather than part-time support. Further, the children with attention difficulties required distinct instructions and structured measures such as short working periods, breaks, varied school tasks and reminders.

Table 5. *Recommendations of support, (N=10)*

	Type of support needed	n
Assistance	Support at meals	7
	Support for toilet visits	7
	Attention support	6
	Resource person	2
Structure	Short working periods, breaks, variation	4
	Clear instructions	5
	Reminders	4
Other	Medical investigations and treatments	7

Study IV: HRQoL and self-reported anxiety, depression and self-concept in children and adolescents with VACTERL association and self-reported anxiety and depression in their parents

Patient characteristics

Out of the children and adolescents, 39 were diagnosed with VACTERL association and one child with VACTERL with hydrocephalus (VACTERL-H). Patient characteristics are presented in Table 6.

Table 6. *Characteristics of children /adolescents (N=40)*

Characteristics	n (%) mean (min–max)
Sex, Boy/Girl	22/18
Age, years	12.8 (8.1–17.7)
GA, full weeks ^a	37 (30–41)
Malformations, total number in the group	
Vertebral	28 (70.0)
Anorectal	26 (65.0)
Cardiac	23 (57.5)
Tracheo-Esophageal	24 (60.0)
Renal	18 (45.0)
Limb	11 (27.5)
Anorectal + Tracheo-Esophageal	11 (27.5)
Number of procedures with anaesthesia ^b	
Until 1 year of age ^a	3.8 (1–13)
Until 5 years of age ^a	7.8 (1–25)
Until 8 years of age ^c	9.5 (1–28)
Until study ^c	11.3 (2–33)

^a 37 values available

^b Imaging procedures not included

^c 36 values available

Health-related quality of life in children and adolescents

The mean (M) overall self-reported HRQoL in children and adolescents in the study group was 80.4, and comparable to children with asthma (M=80.2) and diabetes (M=79.5) in the European reference sample (98). Significantly higher scores were found in the subscales of independence and inner strength, compared to the European reference sample of children with various chronic diseases, $p < 0.05$. Lowest scores were reported in the study group in the subscales of social inclusion and physical ability (Table 7).

The children's and adolescents' mean overall HRQoL reported by their parents was 74.7 and comparable to the parents' scoring in the European sample

of children with various chronic conditions (98). No significant differences were found between the HRQoL scores of mothers and fathers. In accordance with the children, the parents reported the lowest scores in social inclusion and physical ability (Table 7).

Table 7. HRQoL measured by DISABKIDS (DCGM-37) results in the study group compared to European reference sample with various chronic conditions (The DISABKIDS Group Europe) (98)

Subscale	Study group, children n=40	European children n=1152	Study group, parents n=69 ^a	European parents n=1061
Independence	81.6 (14.4)*	76.9 (18.3)	74.5 (16.1)	76.6 (17.2)
Inner strength	83.4 (17.3)*	76.7 (20.6)	74.8 (18.6)	71.6 (20.5)
Social inclusion	74.1 (16.3)	75.2 (17.8)	70.6 (16.9)	74.3 (17.6)
Equality	86.8 (15.9)	85.2 (15.6)	80.7 (18.4)	80.9 (16.8)
Physical ability	75.4 (24.4)	73.8 (18.2)	71.2 (20.3)	70.2 (18.3)
Overall HRQoL	80.4 (15.0) ^b	77.0 (14.2)	74.7 (16.1) ^b	74.9 (14.6)

Transformed raw score 0 – 100. Mean (SD). Higher values indicate better HRQoL.

*Significant difference from European reference sample, $p < 0.05$. One-sample t-test.

^a n=68 in equality, overall HRQoL, n=70 in social inclusion

^b Based on 31 items in DCGM

To evaluate agreement of the HRQoL scores rated by children/adolescents and mothers and fathers, the intraclass correlation coefficient (ICC) was calculated for 29 complete triads. Agreement in overall HRQoL was excellent between children and mothers and good between children and fathers (Table 8).

Table 8. Intraclass correlation coefficient (ICC) with 95% confidence interval (CI) between children's/adolescents', mothers' and fathers' reports in DISABKIDS in 29 families

Subscale	Children–mothers		Children–fathers		Mothers–fathers	
	ICC	95% CI	ICC	95% CI	ICC	95% CI
Independence	0.58	0.27–0.78	0.58	0.28–0.78	0.80	0.62–0.90
Inner strength	0.72	0.48–0.86	0.53	0.20–0.74	0.71	0.47–0.85
Social inclusion	0.66	0.38–0.82	0.53	0.22–0.75	0.92	0.84–0.96
Equality	0.76	0.55–0.88	0.74	0.52–0.87	0.76	0.56–0.88
Physical ability	0.71	0.47–0.85	0.57	0.26–0.77	0.87	0.74–0.94
Overall HRQoL	0.75	0.54–0.88	0.62	0.34–0.80	0.87	0.74–0.94

Interpretation of ICC according to Cicchetti (109): < 0.40 poor, 0.41–0.59 fair, 0.60–0.74 good, 0.75–1.00 excellent

Anxiety, depression and self-concept in children and adolescents

There were no significant differences between the study group and the Swedish norm group in self-reported anxiety, depression and self-concept as meas-

ured by BYI-scales. The study group reported significantly lower anxiety, depression and significantly higher self-concept than a Swedish clinical sample ($p < 0.001$) (Table 9).

Table 9. Mean scores in the BYI-scales of the children and adolescents in the study group compared to Swedish norm group and clinical sample (Beck et al. 2004) (101)

Group	BYI-A	BYI-D	BYI-S
Study group	9.4***	9.8***	43.9***
Swedish norm group	10.3	10.5	40.8
Swedish clinical sample	16.6	20.2	31.6

***Significant difference from Swedish clinical sample, $p < 0.001$. One-sample t-test

Anxiety and depression in parents

In the parents' self-reported anxiety and depression as measured by BAI and BDI-II, the mothers scored significantly higher on depression than the fathers, while no significant difference was found in anxiety (Table 10).

Table 10. Scoring of anxiety and depression among mothers (M) and fathers (F) in BAI-and BDI-II-scales, mean (SD)

BAI			BDI-II		
Mothers	Fathers	M+F	Mothers	Fathers	M+F
10.7 (11.8)	6.4 (9.9)	8.7 (11.1)	9.9 (11.1)*	5.7 (7.0)	8.0 (9.6)

*Significant difference between mothers and fathers, $p < 0.05$. Paired t-test

The scores of anxiety were comparable to Finnish (104), US (105) and Spanish (106) non-clinical samples. With regards to the parents' reported depression, the scores were comparable to a non-clinical Norwegian sample (103).

Discussion

Summary of main findings

In this thesis we have investigated and shed light on aspects of living with the rare and complex condition of VACTERL association from the perspectives of children, adolescents and their parents. The studies covered personal experiences, neurodevelopmental and physical functions, HRQoL and psychological well-being.

Young children with VACTERL association described mixed feelings about their health condition and its consequences by expressing emotions of pride but also a sense of being different from peers. They enjoyed visiting the hospital to meet familiar healthcare professionals, but also pronounced fear and worries about medical procedures. The children described various ways of coping with the difficult situations and gave some suggestions for improvements in hospital care.

The parents of the young children described crisis reactions at the discovery of the malformations in their child and uncertainty of the child's survival. Reactions could be delayed and be manifested as panic attacks or fatigue depression. Hope was gradually perceived through support from healthcare providers, peers and family, and by observing the child's well-being and development. Gradually the parents actively took increasing responsibility for treatments of the child and performed procedures at home, which were sometimes considered to be demanding. Eventually the health condition became an integrated part of everyday life. The parents described varying standards of professionalism among healthcare professionals, difficulties at times in receiving medical support and adequate emotional support and in practical arrangements regarding accommodation.

Assessment of neurodevelopmental and physical function in 10 pre-school children indicated that intelligence was within the normal range; but that the majority of the children had obvious attention difficulties and two of them were subsequently diagnosed with ADHD. Furthermore, all children displayed physical dysfunction. We found that all children in the study group would need extra support and adjustments when starting primary school.

The self-reported HRQoL in children and adolescents was basically comparable to the European reference sample with chronic conditions while significantly higher scores were found in the subscales of independence and inner

strength. The psychological well-being was similar to the norm group of Swedish school children and more favourable than that of a clinical sample. Self-reported anxiety and depression in the parents was comparable to non-clinical samples.

Favourable outcomes in children and adolescents

Living with VACTERL association from the perspectives of children and adolescents displays favourable outcomes in the areas of intelligence and psychological well-being comparable to normal samples and in HRQoL similar, or in some subscales better than samples with chronic health conditions. Furthermore, the children in Study I described emotions of pride and the parents in Study II described their children's adjustment and integration of their health condition into their lives.

The results of the subscales of independence and inner strength in HRQoL were significantly higher than those of the reference sample which was also reflected in the results of BYI, displaying psychological well-being similar to Swedish school children. Similarly, significant higher scores in independence and inner strength subscales were found in Swedish children and adolescents with limb reduction deficiency (112) while children with diabetes (100, 113), and juvenile idiopathic arthritis (114) reported results comparable to the European reference sample with chronic diseases. These favourable findings in our study might to some extent be explained by the congenital nature of VACTERL association where the malformations have been present since birth and the children have no experience of living without these disorders. According to Jardine et al. (115) children with conditions of congenital origin or onset early during infancy often report HRQoL similar to healthy controls. Pless et al. (88) stated that children born with a chronic condition more easily adjust to it compared to children who acquire a lasting condition later in childhood. Similarly, Bogart (116) described how congenital onset of a disability predicted higher satisfaction with life compared to later acquirement of a similar condition (116). Hence, the congenital nature could at least partly be the reason for well-being in our study group.

Associations between HRQoL and coping have been reported (117) and it has been suggested that more effective coping patterns reduce the negative effect of the health condition on HRQoL (118, 119). Oppenheimer et al. (119) found that coping patterns were stronger predictors of HRQoL than the disease itself and that they differed according to the type of disease. Coping patterns of more acceptance and distance and less avoidance were associated with higher HRQoL (119). Furthermore, Hampel et al. (120) reported that children with chronic conditions used less passive, avoidant coping than healthy peers and thus coping with chronic conditions might lead to better coping with eve-

ryday stressors (120). According to Compas et al. (83) secondary control coping aiming to adapt to a stressor is related to better adjustment to chronic illness while primary control coping intending to change a stressor is most effective for circumstances possible to control, such as influencing methods of treatments (83). By evolving effective coping strategies including support-seeking from parents, the children with VACTERL association might have adapted to the difficulties, and the health condition has been integrated into life. Thus, the evolvement of coping patterns in the children might be a contributing factor to the positive results in our study.

Another factor contributing to the favourable outcomes might be the organisation of the Swedish healthcare system providing access to care for all, without the requirement of private insurance. Specialised care is provided with national follow-up programmes implemented for various congenital malformations such as ARM and EA, including monitoring and treatment of potential physical sequelae and dysfunctions, which may also to some extent explain the positive study results.

Potential difficulties in children and adolescents

Living with VACTERL association might imply physical, psychosocial and neurodevelopmental difficulties. Fear of being different or of encountering teasing due to physical dysfunction, as described by the children in Study I, could originate from sequelae of the malformations as reported in similar studies including children with single malformations (47, 48, 51). All the 10 children evaluated in Study III had some physical dysfunction affecting daily life, in nutrition, bowel or bladder functions. Difficulties in meal situations were not only reported in children with EA who often suffer from dysphagia (27) but also in children with difficulties to concentrate. Furthermore, physical dysfunctions were described in bowel, urine bladder function and restricted physical capacity, which might according to previous studies be related to emotionally, socially and psychologically reduced well-being and HRQoL (49, 121-124).

Attention difficulties were found in eight out of 10 children in Study III and such problems have also been reported in previous studies of children born with various congenital malformations (60, 125, 126). Through later investigations, two children in our study group were diagnosed with ADHD. Van den Hondel et al. (60) found this diagnosis in five out of 43 children (12%) with colorectal malformations while international prevalence has been reported to approximately 6–7% among children and adolescents (127). The prevalence in our study group cannot be compared to larger studies due to few participants.

All but two children in the study groups included in this thesis were exposed to at least two previously described risk factors for neurodevelopmental

dysfunction, namely multiple congenital anomalies and neonatal surgery where contributing factors could be general anaesthesia, comorbidity or the surgery itself (53, 54). The impact of general anaesthesia on future neurodevelopmental function is debated. A randomised trial using spinal versus general anaesthesia lasting less than one hour in children having surgery for hernia repair (128, 129) and a study comparing a large sibling cohort (130) did not find any differences in neurodevelopmental outcomes between children exposed or unexposed to general anaesthesia. On the other hand, Castellheim et al. (131) reported from a twin study that exposure to anaesthesia and surgery may be a risk factor for ADHD traits (131). These results are difficult to compare with our study group since the exposures to anaesthesia and surgery usually occur earlier than in the reported studies, namely in the first few days of life, and often last longer than one hour.

Need of follow up and support of children and adolescents

Considering the potential difficulties affecting children and adolescents with VACTERL association, careful medical follow up by multi-professional teams is crucial to optimise the health and functional status and to detect affected HRQoL and psychosocial functioning. Furthermore, neurodevelopmental evaluation of pre-schoolers is essential to identify children in need of extra support in school. Such follow-up programmes are implemented in the Netherlands for children with congenital anomalies (132), in Sweden for children born prematurely (133) and in Norway for children with CHD (134). Still no formal follow-up programme including physical, psychosocial and neurodevelopmental functioning in children with VACTERL association is available in Sweden but ought to be implemented for children with multiple congenital anomalies in accordance with these above-mentioned models.

All the children included in Study III needed extra support and adjustments when starting primary school. Hence, cooperation between the healthcare providers, parents and the school is essential to evaluate the need for assistance and to provide appropriate support for the children, such as enough time for meals, assistance in toilet visits and adjustments to improve cognitive functioning as described in Study III.

Future research on this group will probably be limited to observational prospective studies since early surgery is inevitable and requires general anaesthesia. To gain knowledge from larger cohorts, the use of a national or when available international quality register is essential. Neurodevelopmental outcomes could be registered in addition to physical data such as type of malformations and their outcomes, type, length and episodes of anaesthesia and surgery.

Children's experiences of health care

The children in Study I mostly expressed a positive view of hospital visits where their acquaintance with the healthcare professionals was of great importance in achieving trust. Creating continuity so that the children know who they will meet, as stated in article 9 in the European Association for Children in Hospital Charter (64), could, according to other authors, be a relevant factor in reducing fear and increasing a sense of safety in the children (65). Furthermore, this acquaintance with the staff might induce courage in the child to convey their wishes concerning the methods of performing procedures.

Even though many good aspects and situations in the hospital were described by the children in Study I, anxiety was expressed due to uncertainty concerning the plan for the visit. Also ahead of routine follow-up visits it is important to provide children and their parents with detailed information to prepare them and reduce their worry (62, 135).

The children in Study I expressed fear of medical procedures, particularly those needle-related, in consistency with findings from other studies (135, 136). This fear could originate not only from the pain from the needle but also from removing the local anaesthetic patch, squeezing the finger or a general fear of the unknown (137). Since children with VACTERL association will often be followed lifelong and be exposed to repeated procedures, it is necessary to minimise the perceived stress in conjunction with health care. Administration of sedating medication before needle-related procedures was suggested by the children and also the use of nitrous oxide could be considered (138).

Although we did not systematically study coping strategies, children in Study I as young as 5 years described their ways of coping with stressful situations. Emotion-focused coping strategies were described, such as using positive thinking, relaxation, endurance, encouraging themselves, seeking support in parents and using comforting toys similar to the strategies of preschool children described by Salmela et al. (139). Problem-focused coping to influence treatment was described by one child who wrote a letter about her desire for anaesthesia. The healthcare professionals need to recognise, support and strengthen these coping strategies and to find individualised strategies suitable for the age and development of each child (85). Most important is to listen to the individual child ahead of procedures to find out what coping strategies he/she prefers. As suggested by Salmela et al. (139) a list of different coping strategies could be presented to the parents in order to identify the most effective and preferred coping strategies for each child. This list could be sent home with the information letter ahead of hospital visits and the chosen coping strategies be subsequently documented.

Parents' experiences of initial crisis

The crisis reactions described by the parents in Study II at the discovery of malformations in their child are in many ways similar to previous reports. The experience of fear that their child would die, regardless of whether he/she was born with malformations that were immediately life-threatening or not, are in line with previous studies (69, 72, 74). As also reported by Jones et al. (70) and Cantwell-Bartl et al. (72) the parents' expectations of having a healthy baby were not fulfilled and in our study they instead described an initial feeling of having an illness destroying their family life. The psychological reactions resulted for some parents in panic attacks and fatigue depression similar to reports of parents of children with long-term health conditions describing physical and emotional burdens resulting in chronic fatigue (140).

Although there might be other factors besides the health condition of the child contributing to psychological distress such as unemployment and economic factors (77, 141), it is important to assist parents in their crisis. First and foremost it is imperative to provide emotional support during the initial hospital stay, preferably provided by a psychologist, to parents of children born with chronic conditions. Probably the psychological ill-health could be alleviated by creating an opportunity to process the traumatic event of having a sick child already from the beginning. Furthermore, this counselling and support could provide an opportunity to identify those parents in need of continued support after discharge.

Early initiation of the relationship with their child might reduce the anxiety of the parents (69). One contributing way of handling the crisis could be to stay as close as possible to the child and from the beginning be involved in the care of the child, as also described by parents studied by Sjöström-Strand et al. (142). To participate in the care or at least be close to the child could be one way of coping in this stressful situation and could be perceived as doing something important for the child by initiating bonding.

Above all it is essential to provide the parents with hope. Medical information given initially should, according to the parents, not be simplified but honest and realistic. Furthermore, the parents described hope for the future of their child when they met older children with similar conditions. Thus, it is important to provide the parents with an invitation to a diagnosis specific peer association and information of a contact family as soon as possible (143), to enable them to make an appointment when they find it suitable.

Practical solutions are required regarding the described needs of the parents. When arranging accommodation during the initial admission, the parents' fear of losing their child should be taken into consideration by not mixing them with happy parents and new-born healthy babies. Rooms in parental quarters intended for parents of sick infants should be the first choice, which might also provide contacts with other parents of children with similar conditions.

Parents' subsequent psychological well-being

Long-standing psychological impact in parents of children with congenital malformations has been reported. Skreden et al. (77) found clinically important psychological distress and state anxiety in approximately 30% of the parents 9 years after the birth of the child. Even though the parents included in Study IV reported mean anxiety and depression similar to non-clinical samples, a considerable number scored moderate or severe anxiety and depression. Whereas no significant differences in the results of anxiety were found between mothers and fathers in Study IV, scores of nine out of 34 (26%) among mothers indicated moderate or severe anxiety and likewise 3/30 (10%) among fathers. Corresponding classifications for depression were 6/34 (18%) among mothers and 2/29 (7%) among fathers. Similarly, previous studies including parents of children with congenital malformations have reported higher scores in depression and anxiety (141), and psychological distress (77) and more depressive symptoms in mothers than in fathers (144). However, in a Swedish randomly selected sample, women showed significantly higher stress levels which were associated with depression (145) and in the latest national public health survey in Sweden, 9% of women and 5% of men reported severe worry and anxiety (146). Furthermore, the responsibility for the care of children with a chronic condition may not be equally divided between the parents (147). Hence, the fact that more mothers than fathers reported elevated levels of anxiety and depression in our study group might be associated partially with generally more anxiety and depression among females in the population and partially with the mothers taking greater responsibility for the medical and daily care of the child. Since some parents of children with complex health conditions might suffer from increased anxiety and depression it is important that those in need of support are detected by healthcare providers during the follow up of the children and adolescents.

Parents' roles and adjustment

After discharge the parents were given the responsibility to carry out medical procedures at home particularly in children with ARM. Since the parents need knowledge and guidance in performing specialised treatment, an individualised care plan should be created with tailored care for each child and for the training and support of parents. The specialist nurses and stoma therapists play a significant role in supporting the parents and providing practical advice on how to perform procedures and treatments.

The parents described how, through their experiences, they became the experts regarding their child's health condition and expressed self-confidence and ability to influence the treatment. They described how they eventually became adapted to the health situation as an integrated part of life. It has been

suggested that active participation in the treatment of the child might reduce the symptoms of post-traumatic stress disorder (78). Furthermore, parents might have developed in their parental role through the hardships they have overcome and through coping with the situation, as also described in parents of children with anorectal malformations (148). The stressor of the child's condition could here be met by problem-focused coping through providing treatment which will benefit the child. Through coping the parents included in Study II had probably reached to the stage of adaptation and even reorganisation according to the model suggested by Drotar et al. (69). Like the parents studied by the above-mentioned authors, (69) they described how they actively took responsibility for the care of the child and could observe the child's well-being.

The mothers and fathers participating in the interview study shared their experiences of being a parent of a child with VACTERL association and both genders provided statements in all subcategories. Furthermore, no significant differences were found between mothers' and fathers' ratings of the children's HRQoL in Study IV while similar ratings in previous studies have reported differences between parents (149). Closer agreement has been found between fathers' and children's reporting than between mothers' and children's, which Petsios et al. (150) suggested could be partially explained by cultural factors, overprotection by mothers and fathers' increased involvement in the child (150). Conversely, other studies have reported closer concordance between mothers' and children's scoring than between fathers' and children's (151). The mothers might more often than the fathers take closer care of the child both in the treatment of their health condition (147) and in their daily care, which could contribute to the closer proxy reports of mothers (151). Due to the limited samples of participants these differences might not be detected in our study. An alternative explanation might be that both parents were actively involved in the treatment and care. Around the birth of a child with a malformation in Sweden, the close participation of both parents is possible since one of them benefits from parental leave and the other parent has access to sick leave in accordance with the social welfare system. Further, the parents may continue to share responsibility during the child's upbringing.

Parents' experiences of health care and need of support

According to the parents in Study II, routines for adequate actions at the birth of a child with a malformation were lacking in the delivery room. Also parents interviewed by Nisell et al. (48) perceived insecurity among healthcare professionals in similar situations (48). Consequently, a manual describing how to handle various malformations is required together with training to improve the routines.

Even though some parents reported good support from the local and tertiary hospital directly after discharge other parents described lack of necessary support and assistance. There may be limited experience of the diagnoses included in VACTERL association in the local hospitals. To transfer knowledge, video sessions could be implemented at discharge and at follow up of the child. Additionally, the parents could rest assured through their observation of the exchange of information and agreement of treatment between the tertiary and the local health professionals during these sessions.

VACTERL association usually entails various sequelae (13, 14) and difficulties in daily functions with the need for lifelong follow up. The parents described how they had to keep track of all the different healthcare contacts. As suggested in Study II, it would be worthwhile for parents of children with VACTERL association to have access to one coordinator with an overview of the planning of all the child's healthcare contacts.

Methodological considerations

This thesis is based on qualitative and quantitative investigations of children and adolescents with VACTERL association and their parents. To our knowledge these studies are the first exploring experiences of health and health care in young children, evaluating neurodevelopmental and physical outcome in pre-school children and investigating HRQoL and psychological well-being in children and adolescents, all with VACTERL association. Furthermore, these studies are, as far as we know, the first investigating parental experiences and the psychological well-being of mothers and fathers of children and adolescents with VACTERL association.

Participants

Since VACTERL association is a rare diagnosis with low birth prevalence and estimated less than twelve children born per year in Sweden (8, 9), the recruitment base is limited, thus hindering large study samples.

Several factors could impede definite conclusions valid for those children and adolescents diagnosed with VACTERL association. The group is heterogeneous with various types and severities of malformations, which might contribute to significant variations in the findings. More numerous and severe malformations may result in more frequent and longer hospital admissions. Moreover, the children and adolescents may have additional health conditions which we have not taken into consideration when assessing HRQoL and psychological well-being. There might also be some uncertainty about the accuracy of the diagnosis since it is not based on a specific test method but on the identification of features of the malformations which may not always be consistent.

Nevertheless, the characteristics the children in these studies have in common are the congenital nature of the health condition, malformations predominantly requiring surgery during the first days of life, the need of follow up due to sequelae of physical dysfunctions and in most cases repeated episodes of anaesthesia. Consequently, considering the diversity of the study group, the findings from the studies provide some insight into life with congenital malformations and could be used as starting point for identifying potential difficulties in children with similar diagnosis of congenital malformations and for designing a follow-up programme to detect those who need extra support.

The participants in the included studies were recruited mainly from one tertiary paediatric surgical centre. Study IV was strengthened by the multicentre design including patients from three out of four tertiary paediatric surgical centres in Sweden, which enabled the evaluation of a fairly large sample size considering the low birth prevalence. In Study I a purposive sampling was applied to obtain a mixed sample according to age and sex while in Studies III and IV families of all eligible children and adolescents were invited. There might be a risk of selection bias due to non-participants. In Studies I and III, three invited families declined to participate and in Study IV response rate was around 60%. Dropout analyses were not possible to perform due to lack of ethical permission and the reason for not participating can only be speculated in. The families declining to participate could be those with a child with either poorer or better outcomes.

Data collection and data analysis Studies I and II

In qualitative studies the researcher acts as the instrument for data collection and analysis (152). The content is created through the interaction between the interviewer and the informant in the interview and between the text and the researcher in the analysis phase (153). The analysis should represent the experiences provided by the informants and not be a product of the researcher's subjective interpretation. Thus it is essential to describe the process of the research to demonstrate trustworthiness. The criteria of trustworthiness are according to the framework of Lincoln and Guba as described by Polit et al.: *credibility, dependability, confirmability, transferability* and *authenticity* (152).

Credibility addresses the truth of the findings and could be demonstrated by descriptions of selection of participants, data collection and analysis process (108). The sample was purposive to obtain as mixed a sample as possible. The interviews were carried out by one researcher who was not involved in the regular care of these children. This may have contributed to the children and parents freely sharing their experiences, which in turn resulted in rich data of both positive and negative experiences. Even though the interviewer had some pre-understanding, the ambition was to keep an open mind and encourage the informants to elaborate on their answers. Furthermore, an additional

strength was that both parents were interviewed in Study II and the content was covered by both mothers and fathers providing statements in all subcategories, thus contributing data from both genders.

In Study I, the software *In My Shoes* (90, 91) was found to be a useful tool to enable the interviews with the young children. Through the multiple modules it was possible to confirm the children's expressed feelings and experiences. The telephone was used in 16 of the 19 interviews with parents in Study II. No participant hesitated in using this interviewing method and no disadvantage was experienced by the interviewer. The impression was that the parents in this interview setting vividly shared their experiences. Even though the wordless communication was lost between the interviewer and the parent, the telephone interviews provided information of probably a similar amount and quality as face-to-face interviews (154). Furthermore, the informants might have been more relaxed, found it easier to discuss sensitive subjects (155-157), been more honest (156) and not least appreciated the more practical way to participate (154, 156).

During the process of the inductive manifest analysis, efforts were made to represent the children's and parents' viewpoints by staying close to the transcribed interviews when extracting the meaning units. The interviews were read repeatedly and by recurrently moving back and forth between the created categories and the original transcription the concordance was checked. No data responding to the aim of the studies was systematically excluded. In addition, disparity as well as similar aspects were described within subcategories, supporting good saturation of data (108). Representative quotations were chosen to further strengthen the credibility (108).

In eight of the interviews with the children, one parent was present and sometimes gave cues and shared their own experiences. This was considered during the analysis process, and the meaning units were carefully chosen to include only the experiences of the child.

Dependability refers to stability over time and conditions. To enhance stability, the interviews were performed by one interviewer, during a limited time period and with the use of the interview guide to ensure that the interviews were performed in a uniform way. Even though an interview guide was used parallel to *In My Shoes* (90, 91) in Study I it was not always possible to discuss all the questions planned due to the young children's inability to stay alert. Also, some of the children were distracted by their great interest in the computer programme itself.

Confirmability as for the objectivity of the analysis, was increased by the cooperation between the interviewer and the co-authors during the analysis process to reduce the risk of making subjective interpretations. Considerations and discussions of the content of the categories and subcategories took place repeatedly among the authors until consensus was reached.

Transferability is the denotation corresponding to generalisability used in quantitative research and refers to the degree to which the result could be applicable in other groups and contexts. The small study groups including 10 children with a rare diagnosis and their 19 parents might reduce the transferability of the findings to other groups and contexts. Nevertheless, the descriptions of the children's feelings of being different (47, 48, 51) and experiences of hospital care are in line with results from other studies (61-63, 135, 136, 158). Thus, the findings might be transferable to this patient group in similar contexts and patient groups requiring recurring hospital care. Likewise, our findings from the interviews with the mothers and fathers were confirmed by other parents' similar reactions to the diagnosis of their child (69-75, 148), experiences during initial hospitalisation (74, 75, 79, 80, 159) and of taking responsibility for treatments (48, 160), comprising various diagnoses. These experiences might be common in parents of children diagnosed with various congenital malformations or other chronic health conditions, which strengthens the transferability to similar contexts (108).

Authenticity refers to how well the researcher reports the realities of the participants. This was enhanced by providing thorough descriptions of experiences and expressive quotations to convey as much and well as possible the emotions and experiences of the informants.

Data collection and data analysis Studies III and IV

In Study III the evaluations were carefully carried out by professionals who were much experienced in performing such assessments in children with various diagnoses, neurodevelopmental conditions and ages. However, the visual and auditory tests from NEPSY (97) were not found to be suitable in this group. As a complement to the observations of the children, parental reports through a behavioural screening instrument such as The Strength & Difficulties Questionnaire (SDQ) (161) could be suggested in line with a follow-up programme of Swedish premature children (133).

Furthermore, in Study IV the choice of HRQoL-instruments must be considered in the interpretation of results, since generic and diagnosis-specific instruments might reveal different outcomes. Moreover, no comparison of HRQoL with healthy children and adolescents was possible, since no instrument was included with such reference values.

To estimate the total admission time in hospital we used the proxy of number of procedures in anaesthesia. A detailed data collection of number of days in hospital might have provided different outcomes in the multivariate analysis of predictors of HRQoL and psychological well-being.

In Study III, the statistical methods applied for analysis were limited to descriptive statistics due to the low number of participants. A statistics consultant was engaged for assistance with the analysis of the results in Study IV and parametric statistics were applied.

Significantly higher scores in all subscales and overall HRQoL were found in children and adolescents with vertebral anomalies compared to those without this malformation. Conversely, the presence of other specific malformations such as ARM was expected to affect HRQoL and psychological well-being. However, no significant differences were found between the children and adolescents with ARM compared to those without, nor were any effects of ARM demonstrated in the multivariable analysis. These outcomes are difficult to explain but important to consider in further studies. Our limited study sample of 40 children and adolescents might contribute to difficulties in demonstrating significances. Furthermore, the multiple statistical tests performed on the material and many potential independent predictor variables included in the multivariable analysis, might result in false significances. Since no adjustment for multiplicity was performed all p-values should therefore be interpreted with caution.

The participants in Study IV were children and adolescents of wide spread ages between 8 and 17 years. There might be differences in HRQoL and psychological well-being according to age where adolescents with congenital malformations might be more affected than children (118, 121, 162). In the analysis of the result in Study IV we did not compare different age groups such as children versus adolescents, but the multivariable analysis did not show any significant impact of age on any outcome variable.

Conclusions and implications

In a family including a child with VACTERL association not only the child is affected but also the parents. The objectives for the provision of health care for these families should be to optimise the physical and psychosocial function in the children and adolescents, to support the parents in the acute crisis at the birth of the child, to optimise the parents' role as the carers for the special needs of their child and to support the family in adapting to the situation.

The following conclusions and implications would be worth consideration

- Careful follow up by the same multi-professional team continuously is crucial to optimise the physical function in children and adolescents. Preferably, a psychologist could be included in the team to detect children and adolescents with reduced psychological well-being. Such formal programmes are already implemented for some types of malformations but need to be extended to all types of included malformations.
- Including the evaluation of neurodevelopmental and physical function in a follow-up programme ahead of school start is essential, the aim being to identify any need of extra physical and cognitive support in the school situation. These evaluations should be implemented in cooperation between healthcare providers, parents and school professionals.
- Fear of medical procedures may be reduced through detailed and clear information, sensitivity for children's wishes and by offering individually adjusted caring strategies.
- Parents should be provided with psychological processing of the stressful event of having a non-healthy child, preferably by a psychologist. Through this support parents in need of long-term emotional support could be identified.
- A care plan should be developed with individualised, tailored care for each child including a training and support plan for the parents. Contact with a specialist nurse (contact nurse) should be established

during the first hospital stay. For accessible medical support, a paediatrician and a specialist nurse should be identified and designated in the local hospital soon after discharge.

- Parents should, as soon as possible, be provided with the possibility to get into contact with a family with a child with VACTERL association and an invitation to a diagnosis-specific peer association, to further induce hope for the future of the child.
- Video sessions with the participation of the parents, the child and responsible professionals at the local and tertiary hospital could be implemented for the transfer of information and knowledge between the hospitals, at discharge and follow up of the child.

Recommendations for future research

Children born with VACTERL association are, in most cases, in need of life-long follow up due to sequelae and physical dysfunctions. Transition to adult health care is currently insufficient, sometimes non-existent, and the grown-up patient could face difficulties in finding an adequate healthcare provider when facing complications. Since knowledge is scarce of expectations and of experiences of transition in adolescents and young adults with VACTERL association, a planned interview study may provide important aspects in connection with transition to adult health care.

For some years now video sessions have been implemented in our tertiary surgical centre at discharge and follow up of children with congenital malformations. The impression is that the parents appreciate these arrangements. Qualitative or quantitative studies could be performed to evaluate advantages and disadvantages of video sessions compared to the physical follow up at the tertiary hospital.

The large proportion of children in Study III displaying attention difficulties motivates studies of prevalence of ADHD in children and adolescents with VACTERL association and other types of congenital malformations. An indication of the prevalence could be obtained through data from the diagnosis register of the Swedish National Board of Health and Welfare.

Furthermore, to follow the outcomes of children with congenital surgical conditions, the development of a national quality register for advanced paediatric surgery is essential. In addition to physical data such as type of malformations and their outcomes, type and length of treatments, neurodevelopmental outcomes and HRQoL could also be registered. From this register research on larger cohorts could be performed.

From our Study II both mothers and fathers seem to be involved in the care of the child but knowledge is scarce about their roles in taking responsibility for the medical care of children with chronic health conditions. By using qualitative and/or quantitative methods, further studies could explore psychosocial aspects of mothers and fathers, such as involvement in the child's care, emotions and coping, and the process of acceptance and integration of the child's health condition in their daily life.

Svensk sammanfattning

Bakgrund

VACTERL association är ett medfött tillstånd som innefattar missbildningar i ryggkotor (V), ändtarm (A), hjärta (C) luft- och matstrupe (TE), njurar (R) och extremiteter (L). För att ställa diagnosen krävs missbildningar i minst tre av dessa organ. Tillståndet är sällsynt med färre än 12 barn födda per år i Sverige. Operation under de första levnadsdagarna är i de flesta fall nödvändig och upprepade operationer och procedurer i narkos kan behövas under barndomen. Trots avancerad kirurgi kan olika fysiska resttillstånd kvarstå exempelvis krokig ryggrad, försämrad tarmfunktion, backflöde från magsäcken till matstrupen, luftvägssymtom och nedsatt funktion i hjärta, njurar och extremiteter.

VACTERL association kan medföra påverkan på hälsorelaterad livskvalitet (HRQoL) och psykologiskt välbefinnande men studier omfattande barn och ungdomar med medfödda enstaka missbildningar rapporterar motstridiga resultat. Samband har rapporterats mellan kirurgi under spädbarnsperioden och nedsatt utvecklingsneurologisk funktion hos barn med missbildningar. Riskfaktorer för detta har beskrivits såsom multipla missbildningar, låg födelsevikt, upprepade kirurgi och långa sjukhusvistelser. I djurstudier har negativa effekter av generell narkos på hjärna under utveckling påvisats medan motsvarande påverkan på hjärnan hos spädbarn är okänd.

På grund av de fysiska resttillstånden utsätts de flesta barn med VACTERL association för upprepade sjukhusvistelser vilka kan medföra oro och rädsla för obehagliga behandlingar och procedurer. Upptäckten av missbildningar hos barnet kan orsaka en krisreaktion hos föräldrarna med sorg över förlusten av ett förväntat friskt barn och oro för barnets tillstånd, behandling och prognos.

Få studier återfinns som innefattar barn och ungdomar med VACTERL association. Kunskapen är begränsad om hur hälsotillstånd och sjukvård upplevs av barnen och deras föräldrar och lite är känt om dessa barns behov av stöd i samband med skolstarten. Vidare är tillgänglig kunskap om HRQoL och psykologiskt välbefinnande bland barn och ungdomar och deras föräldrar begränsad.

Syfte

Det övergripande syftet för denna avhandling var att undersöka och beskriva olika aspekter av att leva med VACTERL association utifrån barns, ungdomars och föräldrars perspektiv.

Material och metod

I studie I beskrevs små barns upplevelse av sin hälsa och av sjukvård och tio barn i åldrarna 5–8 år intervjuades med hjälp av den datorstödda intervju-tekniken In My Shoes. En intervjuguide användes innehållande öppna frågor som behandlade upplevelser av hälsotillståndet, av sjukvård och förslag till förbättringar av vården. Intervjuerna spelades in, skrevs ut ordagrant och analyserades med kvalitativ innehållsanalys.

I studie II beskrevs erfarenheter av att vara förälder till ett barn med VACTERL association och 19 föräldrar intervjuades personligen eller per telefon. En intervjuguide användes med öppna frågor som behandlade deras upplevelser av att ha ett barn med missbildningar och erfarenheter av sjukvård och sjukvårdsstöd i hemmet. Intervjuerna spelades in, skrevs ut ordagrant och analyserades med kvalitativ innehållsanalys.

I studie III bedömdes förskolebarns utvecklingsneurologiska och fysiska funktion samt behov av extra stöd i skolan. Tio barn i åldrarna 5–7 år deltog. Åldersanpassade intelligenstest användes (WPPSI-IV, WISC-IV) och för test av uppmärksamhet visuellt och auditivt test från NEPSY. Beteende och uppmärksamhet observerades och fysisk funktion bedömdes genom generell och neurologisk kroppsundersökning och med hjälp av föräldrarnas beskrivningar. I analysen användes deskriptiv statistik.

I studie IV undersöktes självrapporterad HRQoL, ångest, depression och självbild hos barn och ungdomar och ångest och depression hos deras föräldrar. Frågeformulär skickades ut till barn och ungdomar i åldrarna 8–17 år och deras föräldrar. DISABKIDS generiska formulär användes för självrapporterad och föräldrarapporterad HRQoL. För barns och ungdomars självskattning av psykologisk påverkan användes delskalorna ångest, depression och självbild från Beck ungdomsskalor. För föräldrarnas självskattning av ångest och depression användes Becks motsvarande skalor för vuxna (BAI, BDI-II). Frågeformulären besvarades av 40 barn och ungdomar, 38 mammor och 33 pappor. För analysen av resultaten användes parametriska statistiska test.

Resultat

Barnen i studie I beskrev blandade känslor för sitt hälsotillstånd och uttryckte stolthet men också en känsla av att vara annorlunda än sina kamrater. De uppskattade sjukhusbesök och att träffa bekant personal men beskrev också rädsla och oro inför medicinska procedurer. Barnen beskrev olika sätt att hantera svåra situationer och gav förslag till förbättringar av sjukvården.

Föräldrarna i studie II beskrev krisreaktioner vid barnets födelse och osäkerhet om barnets chans att överleva. Reaktionerna var ibland fördröjda och kunde senare yttra sig som panikattacker och utmattningsdepression. Föräldrarna upplevde efterhand hopp genom stöd från sjukvårdspersonal, från andra familjer i liknande situationer och från den egna familjen och genom att se barnets utveckling och välbefinnande. Gradvis tog föräldrarna ökat ansvar för barnets behandlingar och genomförde procedurer i hemmet som ibland upplevdes som krävande. Barnets hälsotillstånd blev så småningom en integrerad del av vardagen. Föräldrarna beskrev varierande grad av professionalism bland sjukvårdspersonalen, svårigheter att få tillräcklig medicinskt och känslomässigt stöd och problem med praktiska arrangemang som transport och föräldraboende.

Bedömning av utvecklingsneurologisk och fysisk funktion hos tio förskolebarn i studie III visade att intelligensen var inom normalområdet. Åtta av barnen uppvisade svårigheter med uppmärksamhet och två av dem fick vid senare utredning diagnosen ADHD. Alla barnen hade någon form av fysisk påverkan inom områdena nutrition, tarm och/eller blåsfunktion. Barnen som deltog bedömdes alla vara i behov av extra stöd vid skolstarten.

Självrapporterad HRQoL hos barnen och ungdomarna i studie IV var jämförbar med det Europeiska referensmaterialet omfattande barn med kroniska sjukdomstillstånd men signifikant bättre i delskalorna självständighet och inre styrka. Psykologiskt välbefinnande självskattades i samma nivå som hos svenska skolbarn och signifikant bättre än i en grupp barn med psykiatriska diagnoser. Självrapporterad ångest och depression hos föräldrarna var jämförbar med andra grupper ur normalbefolkningar. Trots det fanns det individer bland barn, ungdomar och föräldrar med tecken på ångest och depression i behov av stöd.

Slutsatser

I en familj med ett barn med VACTERL association är inte enbart barnet påverkat utan även föräldrarna. Syftet med hälso- och sjukvården för dessa familjer bör vara att optimera den fysiska och psykosociala funktionen hos barn och ungdomar, att stödja föräldrarna i den akuta krisen vid barnets födelse, att optimera föräldrarnas roll som vårdare för barnens särskilda behov och att stödja familjen i anpassningen till situationen.

- Noggrann uppföljning av den fysiska hälsan utförd av ett multiprofessionellt team med kontinuitet bland personalen i teamet, är nödvändig för att optimera barnens och ungdomarnas fysiska funktion. Önskvärt är att även en psykolog ingår i teamet för att fånga upp barn och ungdomar med nedsatt psykiskt välbefinnande.
- Bedömning av utvecklingsneurologisk och fysisk funktion behövs inför skolstart för att identifiera barn i behov av extra stöd.

- Rädslan för medicinska procedurer kan minskas genom noggrann information, lyhördhet för barnets önskemål och anpassade vårdåtgärder.
- Känslomässigt stöd och hjälp med bearbetning av upplevelsen att få ett barn som inte är friskt bör ges till föräldrarna, lämpligen från en psykolog. Härigenom kan föräldrar i behov av långsiktigt stöd identifieras.
- En individuell vårdplan inkluderande träning och stöd till föräldrar bör utformas. Kontakt med en specialistsjuksköterska (kontaktsjuksköterska) bör etableras under den första sjukhusvistelsen. För tillgängligt medicinskt stöd bör en barnläkare och specialistsjuksköterska utses som kontaktpersoner vid hemsjukhuset helst i samband med utskrivningen.
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- Videokonferenser med medverkan av föräldrar, barnet och ansvarig sjukvårdspersonal på hemsjukhus och specialistsjukhus i samband med barnets utskrivning och senare uppföljning är önskvärt för att förbättra överföring av information och kunskap mellan sjukhusen.

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