AN INFANT WITH FOOD ALLERGY AND ECZEMA IN THE FAMILY - THE MENTAL AND ECONOMIC BURDEN OF CARING

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To my Family

TABLE OF CONTENTS

ABSTRACT

Allergic diseases including food allergy and eczema in an infant in combination with the everyday activities of caring for a family will pose challenges to parents. Only fragments of these challenges are revealed to health care professionals. Families have varying mental, social and economic resources to help them care for an allergic infant, and all such resources are important in determining how families succeed in meeting these challenges and the quality of the infant's care.

This study evaluated the whole burden to the family caused by an infant's allergic disease during the first 24 months of life. As the primary caregiver during this period is usually the mother, her perspective was considered important. Ecocultural theory, which considers families as capable of modifying the positive and negative forces facing them, was taken as the frame of reference. Data were collected as part of an ongoing prospective mother-infant study, and the methods included severity scoring of atopic dermatitis, dietary records, health-related quality of life measurements and assessments of the use of health care services and medications for treating the infant's eczema, food allergy and asthma. Interviews with mothers were analysed by deductive content analysis on the basis of ecocultural theory and the family empowerment model.

The theme "Living an ordinary family life" guided the organization of family activities essential for treating the infant's food allergy and eczema. These activities were sources of both strain and support for the mothers, the allergy-related supporting factors being the mother's own knowledge of the allergy, hopes for an improvement in the infant's condition, social support and work. An infant's food allergy at the age of one year caused considerable strain for the mother in cases where the introduction of new foods into the child's diet was delayed. This delay was still causing the mother additional strain when the child was 24 months of age. The infants waking at night at the ages of 12 and 24 months because of itching related to eczema caused strain for the mothers.

The infants' health-related quality of life was impaired at ages of 6 and 12 months compared with healthy infants. The principal reasons for impairments were itching, scratching and sleep disturbances at 6 and 12 months and treatment difficulties at 6 months. Problems with getting to sleep were reported at all stages irrespective of eczema and were also present in healthy infants. The economic impact of the treatment of allergic diseases on families during the first 24 months was 131 EUR (2006 value) in cases of eczema and 525 EUR in cases of food allergy. From the societal perspective, the costs of food allergy were a median of 3183 EUR (range 628–11 560 EUR) and of eczema a median of 275 EUR (range 94–1306 EUR). These large variations in costs in food allergy and eczema indicate that disease varies greatly.

In conclusion, food allergy and eczema cause extra activities and costs to families which arrange these disease-related activities in such a way that they support the leading family theme "Living an ordinary family life". Health care professionals should consider this thematic character of family life and disease-related activities in order to ensure that new treatments are sustainable, meaningful and tailored to daily activities. In addition, those mothers who are experiencing difficulties with food allergic infants or infants with eczema should be recognized early and provided with individual encouragement and support from health clinics. In the light of the present results, early detection of symptoms and effective parental guidance can contribute to the well-being and health-related quality of life of the child and family.

ABBREVIATIONS

AD	Atopic dermatitis
AEDS	Atopic eczema/dermatitis syndrome
AUD	Australian dollar
CAD	Canadian dollar
CADIS	Childhood Atopic Dermatitis Impact Scale
CBA	Cost-benefit analysis
CDLQ	Children's Dermatology Life Quality Index
CEA	Cost-effectiveness analysis
CHQ-CF	Child Health Questionnaire-Child Form
CHQ-PF	Child Health Questionnaire-Parent Form
CIAD	The Childhood Impact of Atopic Dermatitis
CUA	Cost-utility analysis
DFI	Dermatitis Family Impact
DM	Deutsche mark
EASI	Eczema Area and Severity Index
EUR	Euro
FA	Food allergy
FAIM-CF	Food Allergy Independent Measure-Child Form
FAQL-PB	Food Allergy Quality of Life-Parental Burden
FAQLQ-CF	Food Allergy Quality of Life Questionnaire-Child Form
FAQLQ-PF	Food Allergy Quality of Life Questionnaire-Parent Form
FAQLQ-TF	Food Allergy Quality of Life Questionnaire-Teenage Form
FCFAQ	Family Coping with Food Allergy
FHS	Food hypersensitivity
GBP	British pound
HRQOL	Health-Related Quality Of Life
IDQOL	Infant Dermatitis Quality Of Life Index
PIQoL-AD	Parent's Index of Quality of Life in Atopic Dermatitis
PCFA	Parenting Children with Food Allergy
PedsQL^{TM}	Pediatric QOL Inventory 4.0
QALY	Quality-Adjusted Life Year
QLPCAD	Quality of Life in Parents of Children with Atopic Dermatitis
SASSAD	Six Area, Six Sign Atopic Dermatitis severity score
SCORAD	Severity Scoring of Atopic Dermatitis
QOL	Quality Of life
USD	American dollar
WHO	World Health Organization

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original publications, which are referred in the text by the Roman numerals I–IV.

I   Alanne S, Laitinen K, Paavilainen E. Living ordinary family life with an allergic child – the mother's perspective. Submitted.

II   Alanne S, Laitinen K, Söderlund R, Paavilainen E. Mothers' perceptions of factors affecting their abilities to care for infants with allergy. *J Clin Nurs* 2012;21(1–2):170–179.

III   Alanne S, Nermes M, Söderlund R, Laitinen K. Quality of life in infants with atopic dermatitis and healthy infants: a follow-up from birth to 24 months. *Acta Paediatr* 2011;100(8):e65–e70.

IV   Alanne S, Maskunitty A, Nermes M, Laitinen K, Pekurinen M. Costs of allergic diseases from birth to two years in Finland. *Public Health*; *In Press*.

1 INTRODUCTION

Families of infants similar in terms of the infant's food allergy and eczema may express the burden imposed by the disease to health care professionals in different ways. This observation raises questions about general life situations and parents' personal and economic resources for caring for their infants. Besides families, the state, local authorities (municipalities, health care providers) and society at large all carry part of the economic burden. The societal point of view is important, since the prevalence of food allergy and eczema are high during the first three years of life. The cumulative incidence of eczema ranges from 16.5% in Norway (Smidesang et al. 2008) to 21.5% in Germany (Illi et al. 2004), and 5–6% of children suffer from food hypersensitivity by the age of three years in United Kingdom (Venter et al. 2008). In Finland the lifetime prevalence of physician-diagnosed food allergy has been reported to be 9% and that of parent-perceived food hypersensitivity (FHS) 21% based on birth cohorts of 1 to 4-year-old children (Pyrhönen et al. 2009).

Living with an infant with food allergy and eczema in combination with other everyday activities may be a real challenge for many parents. From this perspective it is not surprising, that a certain "impact of the disease" prevails. One possible approach that can be used to understand the impact of food allergy and eczema on families is ecocultural theory (Gallimore et al. 1989), which regards families as active subjects who are capable of modifying various internal forces such as their economic status, social relations, values, characteristics of their members, and reacting to various external conditions, such as the state of the economy and political measures. Families consider forces either constraints or resources, negative or positive, on the basis of leading family themes which organize and guide their daily routines. Food allergy and eczema in an infant can be considered a characteristic of one family member which creates a need to reorganize the activities in the family's daily routines so that they are meaningful. The mother and father need certain personal resources in order to implement allergy treatment, and economic resources are needed from both the family and society for the treatment of food allergy and eczema to be successful. Society has a direct role in this by providing health care services and through public and private insurance and day care. National health policy and governmental decisions thus affect families in many ways, e.g. with respect to treatment, health care availability and family's economic resources for caring for the infant with food allergy and eczema and the equality of it's status relative to that of families with healthy infants. The national Finnish Allergy Programme 2008–2018 focusing

on children and families aims to reduce the burden of allergy in patients and society. The purposes are to prevent the development of allergic symptoms, to increase tolerance against allergens, to improve diagnostics, to allocate resources to manage severe allergies and to decrease costs due to allergic diseases (Haahtela et al. 2008, von Hertzen et al. 2009).

However, more information is needed, how food allergy and eczema in early childhood is cared for and experienced   in families, and what factors lie behind the differently experienced parental burden and how families can be supported. Such answers can be expected to help in the evaluation of the success of care and the social support provided and the identification of points at which improvement is needed. This study aims to evaluate the challenge posed to the family by an infant's food allergy and eczema, the parental resources available, the well-being of the infant and economic impact of these diseases.

2 REVIEW OF THE LITERATURE

2.1 Allergic diseases in early childhood

The main allergic symptoms in infancy are atopic dermatitis, gastrointestinal symptoms and recurrent wheezing, whereas bronchial asthma and allergic rhino conjunctivitis are the main problems later in childhood (Høst and Halken 2000). Food allergy also may cause these symptoms (Lack 2008).

Eczema

It has been proposed that atopic eczema and atopic dermatitis should be grouped together as one atopic eczema/dermatitis syndrome (AEDS), which can then be further divided into IgE-associated and non-IgE-associated forms (Johansson et al. 2001). In the revised nomenclature of the World Allergy Organization, it was then proposed that AEDS should be replaced by the term eczema (Johansson et al. 2004), which is used generally in this thesis to denote atopic eczema and atopic dermatitis. Severity of eczema has been defined by the scoring of atopic dermatitis (SCORAD) (European Task Force on Atopic Dermatitis 1993) or by objective SCORAD without subjective items. Objective SCORAD may be categorized as mild (<15 SCORAD), moderate (15<SCORAD<40) or severe (SCORAD>40) (Kunz et al. 1997). Other measures of severity exist, e.g. the Nottingham Eczema Severity Score (Emerson et al. 2000), the Eczema Area and Severity Index (EASI) (Cherill et al. 1998), the Six-Area, Six Sign Atopic Dermatitis severity score (SASSAD) (Berth-Jones 1996) and grading of the severity of atopic dermatitis (Rajka and Langeland 1989).

Eczema is a common health problem for children throughout the world, with symptoms that exhibit wide variations in prevalence both within and between countries (Williams et al. 1999). The cumulative incidence of eczema at the age of two-years has ranged from 16.5% (Smidesang et al. 2008) to 21.5% in birth cohort studies (Illi et al. 2004). Forty-three percent of these children with early eczema were in complete remission by the age of three years (Illi et al. 2004).

The progression of skin region involvement in infants who develop eczema begins at the scalp, forehead, ear and neck (Halkjær et al. 2006). Other previously reported symptoms include itching and scratching, sleep disruption and poor sleep quality, and irritated skin (Chamlin et al. 2004, Chamlin et al. 2005a). Sleep disturbances in children with eczema are

likely to be due to itching and scratching, but sleep fragmentation in children with a remission of eczema was not related to the act of scratching (Reuveni et al. 1999). Adverse reactions to food have been reported in 71% of children with severe eczema initially and in 51% of children who had less severe eczema (Gustafsson et al. 2000). Eczema is most often mild in infants, in about 70% (Smidesang et al. 2008, Halkjær et al. 2006), while the prevalence of severe eczema is less than 5% (Smidesang et al. 2008). The cornerstones of disease management are the reactive use of topical corticosteroids to treat the inflammation in conjunction with emollients to treat dry skin (Darsow et al. 2005).

Food allergy

An adverse reaction to food is referred to as food hypersensitivity (FHS), or food allergy, when immunological mechanisms can be demonstrated. All other reactions to food are non-allergic food hypersensitivities (Johansson et al. 2001, Johansson et al. 2004). The term food allergy is used in this thesis and refers to food allergy diagnosed by a physician. A systematic review has indicated that food allergy affects more than 1% of the population but less than 10% (Chafen et al. 2010), although there are large discrepancies between reported and diagnosed allergies. The point prevalence of parentally perceived food allergy in the general population across Europe is said to be 4.7%, the most affected age group (7.2%) being 2 to 3-year-olds (Steinke et al. 2007). Based on double-blinded, placebo-controlled food challenge and a good clinical history, it has been determined that 5–6% of children suffer from food allergy by the age of three years (Venter et al. 2008).

The prevalence of cow's milk allergy as identified by food challenge tests varies between 0 to 3% (Rona et al. 2007). Milk and egg are the most common forms of food allergy in the first 3 years of life (Venter et al. 2008), but most children grow out of cow's milk allergy (Høst et al. 2002, Venter et al. 2008) and egg allergy (Venter et al. 2008), whereas the prevalence of pollen-related reactions to food increases with age (Östblom et al. 2008a).

The symptoms of food-induced allergic reactions range from localized hives to life-threatening anaphylaxis. The organ systems most commonly involved include the skin, gastrointestinal tract and respiratory tract (Lack 2008). Anaphylaxis is a severe, generalized hypersensitivity reaction (Johansson et al. 2004) requiring prompt treatment of the symptoms with rapid-acting antihistamines and intramuscular epinephrine injector (Muraro et al. 2007). The cornerstone of the management of food allergies is avoidance of the relevant food

allergens. Clear and accurate diagnoses, instruction on avoidance diets and the development of emergency care plans for the treatment of allergic reactions remain the key elements of such care (Wood 2007). Children diagnosed with food allergy need a consultation with a dietician to prevent growth problems and inadequate nutrient intake (Christie et al. 2002). According to the Finnish Allergy Programme 2008–2018 a new approach to allergy from avoidance to tolerance means that the instructions given to families are timely and quantitatively individualised based on allergic symptoms and their severity (von Hertzen et al. 2009).

2.2 Theories and models related to parental and family psychosocial resources

Theories and models are needed when qualitative approaches to families are used. Ecocultural theory (Gallimore et al. 1989) places the family in a cultural context in which positive and negative forces affecting it are considered. This approach helps to reveal how challenges are experienced by family members.

2.2.1 Ecocultural theory

Ecocultural theory proposes that the key adaptation problem in the face of the constraints and opportunities that families experience in the world around them is the organization of the activity settings of daily routines so that they are sustainable, meaningful and congruent with the individual needs of all the family members (Gallimore et al. 1989, Gallimore et al. 1993b). In this thesis the focus is on characterization of family activities of daily routines that are essential for successful management of food allergy and eczema. The theory emphasizes the family as an active subject able to modify the influencing forces. These forces can be divided into forces operating within the community, such as the state of the economy and political measures, and forces within the family including economic pressures, social relations and the values, beliefs and characteristics of the family members. Families aim to balance these forces so that the activity settings of their daily routines contribute themes that give meaning to the parents' decisions. Such themes are not detected only because the families clearly articulate them, but also because they are trying to implement them across these activity settings. To construct and maintain activity settings that express their thematic goals, parents must balance various constraints against their resources while at the same time accommodating the personal characteristics of the family members (Gallimore et al. 1989). In this accommodation process families must respond in various ways to their sometimes conflicting circumstances in order to create and sustain daily routines (Gallimore et al.1993b). Although most people have little direct control over their broader economic and social

ecology, the accommodation process gives parents a way in which to influence how these forces affect their families. Guided by their cultural and personal values and goals, they create activity settings that mitigate and shape the effects of the broader ecology (Gallimore et al. 1989).

From a mix of social and economic forces and actions, families construct their ecocultural niches. Each econiche reflects an element of their material ecology, such as income, public health conditions, housing and living space, transportation and distances from relatives and services. The niche is also influenced by cultural features that human beings use to understand their everyday lives. This means that an ecocultural niche manifested in an everyday routine and its constituent activity settings is not static. At the household level it is constantly being changed and shaped as a result of family accommodation (Gallimore et al. 1989).

Ecocultural theory suggests that one of the best predictors of child and family outcomes will be the sustainability of activity settings across time and multiple situations (Gallimore et al. 1989). The socially constituted meaning of an activity setting is a mix of ecological, cultural, interactional and psychological features, which can be observed in terms of the person's present, cultural values, tasks, scripts for conduct, motives and the purposes of actions (Gallimore et al. 1993a). This theory applies to all children in all families, a generality that does not accept the assumption that developmentally delayed children or their families are necessarily different from non-delayed children and their families (Gallimore et al. 1989). All the same, this theory has been applied to mothers with young children who have disabilities (Kellegrew 2000) and families caring for adolescents with disabilities (Schneider et al. 2006). The challenges for families revealed in the latter were changing family roles and relationships and service discontinuity in the adolescents (Schneider et al. 2006).

2.2.2 The family empowerment model

A family's resourcefulness can be seen to derive from the balance between supporting and straining factors (Pelkonen and Hakulinen 2002), where support can be defined as something providing immaterial assistance to a person and strain as a difficulty that causes worry or emotional tension (Visual Thesaurus). The family empowerment model is based on a previous theory about the concept of empowerment and the study of family resources (Pelkonen and Hakulinen 2002). In this approach a parent can empower him or herself or be empowered by something outside the family. Empowerment is seen as both an individual, personal process and a social process that is not transferable to another person (Siitonen 1999). In one study, empowerment was conceptualized as a personal process in which mothers of chronically ill

children developed and employed the necessary knowledge, competence and confidence for making their voices heard. This process of empowerment in mothers took the form of discovering reality, critical reflection, taking charge and holding on. Critical reflection was necessary for the mothers to be able to take charge of their situation and develop a sense of personal power. Finally, as a result of their awareness of their strengths, competences and capabilities, the mothers were able to maintain their own sense of power even under changing circumstances (Gibson 1995). Empowerment is also a helping process whereby groups or individuals are enabled to alter their situation and are given the skills, resources, opportunities and authority to do so. Individuals have the power and freedom to make choices and to accept responsibility for actions should they wish to do so. Empowerment involves a partnership and mutual decision-making (Rodwell 1996).

In the empowerment model for family nursing, a parent's strengths are divided into those arising from personal abilities and those arising from the family's internal and external capabilities (Pelkonen and Hakulinen 2002). The personal abilities implied in the model include the mother's physical and psychological condition, level of education, sense of competence (Tarkka 2003), knowledge and the ability to identify unused capacities (Pelkonen and Hakulinen 2002). The internal family capabilities are interaction between family members, problem-solving abilities, way of life, housing and the family's economic situation, while the external capabilities are the support received from people outside the family and the availability of social services (Pelkonen and Hakulinen 2002). It has been shown that adequate social support seems to reduce the mother's stress (Saisto et al. 2008) and to promote the child's recovery from eczema (Gustafsson et al. 2002). In this thesis the focus was to characterize mothers' personal abilities, family internal and external capabilities either as supporting or straining factors.

2.3 The parental experiences and life with an allergic child

2.3.1 Eczema

The effects of an infant's eczema on the parents and family have been described, but the ecocultural theory has not been applied to this field. A study by Elliott and Luker (1997) based on mothers' written accounts indicated that the extra work involved in caring for a young child with eczema was not solely generated by the treatment regimens but also the burden that arose from normal child care under such circumstances and the extra housework generated by the disease. These same elements are included in the conceptual framework

describing the effects of moderate and severe eczema on children and parents (Chamlin et al. 2004, Chamlin et al. 2005a). Parents face the effects of eczema on their child's symptoms, activity limitations and behaviour, on their own sleep and emotions and on the social functioning of the family as a whole (Chamlin et al. 2005a). Parental *emotional worries* include effects on their confidence in medical treatment, effects on their decisions about having other children, disappointment, frustration, helplessness, sadness and depression, guilt and self-accusation and worries about their relationship with their spouse, the child's friendships, the child's self-esteem, the costs of care, environmental and food allergens, the future and possible side-effects of the treatment (Chamlin et al. 2004, Chamlin et al. 2005a). Similar results have been found amongst caregivers and parents in terms of their experiences of children with moderate to severe eczema (Zuberbier et al. 2006). In the light of these descriptions, the findings that mothers of infants with eczema have described themselves as more depressive and hopeless and more anxious and overprotective and have characterized their infant as less frequently positive and more frequently negative than in a control group of healthy infants are not surprising. Researchers have not been able to determine, however, whether maternal hopelessness was a precursor of the infant's eczema or a result of it (Pauli-Pott et al. 1999). On the other hand, mothers of young children with eczema had been reported to have a positive, empathic attitude towards their children (Daud et al. 1993).

The severity of child's eczema is associated with the extent of *sleep disturbance* (Chamlin et al. 2005b), the amount of disruption to parental sleep (Moore et al. 2006), maternal stress (Faught et al. 2007) and maternal physical and mental health (Ho et al. 2010). As a consequence of the skin condition co-sleeping has been reported in families, which has bothered most of the parents of these children (Chamlin et al. 2005b). The younger the child, the more time the parents' sleep was disturbed. Sleep disruption correlated with measured anxiety levels in both parents and with depression scores in the mothers (Moore et al. 2006).

Maternal stress levels are related to the severity of eczema, and are equivalent to those seen in mothers of children with severe disabilities. Forty-six percent of mothers had such high stress scores that professional consultation was indicated (Faught et al. 2007). In another study the level of mental stress was no greater in mothers of school-aged children with eczema than in mothers of children with minor skin problems, and the degree of social support experienced by the families was equal (Absolon et al. 1997). These findings reveal that maternal stress is a

complex phenomenon and depends on severity of eczema, social support, the instrument used for assessment and numerous other factors.

Parents experience challenges in *contacts with health care professionals*. In the early phases of allergic disease many parents felt that their baby's condition was not taken seriously, the diagnosis was delayed and there was difficulty in receiving appropriate treatment. Parents also felt that they had to be more active than they wished in order to obtain information about the condition and its treatment (Gore et al. 2005). Cork et al. (2003) reported that less than 5% of the parents had received any explanation at baseline of the causes of eczema or any demonstration how to apply the topical treatments. Twenty-four percent of the children were not treated with any emollient cream. Parents also tended to delay initiating the treatment for 7 days after onset of a flare. Only 24% felt confident that they had managed eczema flares adequately (Zuberbier et al. 2006). A child's eczema thus affects the parents in many ways.

2.3.2 Food allergy

Mothers are responsible of feeding their children at the infant stage. One study of maternal experiences of peanut avoidance during pregnancy and lactation has revealed that mothers considered peanuts to be dangerous. Peanut avoiders believed that eating peanuts during pregnancy or lactation could be a cause of peanut allergy in their child and that peanuts represented a choking hazard for the child. The avoiders included more first-time mothers than the non-avoiders and the mean number of children in the families of avoiders was significantly less than those of non-avoiders (Turke et al. 2005).

Besides food avoidances and the implementation of elimination diets, mothers are expected to control their allergic children and educate them to cope with their food restrictions. Mothers who had lived through the experience of parenting children with food-induced anaphylaxis described themselves as "living with risk". Five themes described the essence of this experience: living with fear, worrying about their child's well-being, looking for control, relying on resources and finding life hard when it really is not. Young children were mainly supervised by their mother or another close family member and were exposed to a limited number of environments. The *risks of accidental exposure* increased and altered as the child matured, was exposed to different people and environments and had less supervision (Gillespie et al. 2007). Parents experienced different phases in their need for information: at diagnosis, at follow-up, when there was uncertainty related to the severity of the allergy and its treatment, and in the face of new events (Hu et al. 2007). Also, the role of the mother was

16

found to change as the child gets older, and the parents' use of autonomous support and emergency education increased and protection/monitoring decreased with increasing age of the child (Williams et al. 2009).

2.4 Health-related quality of life

2.4.1 The concept and measurement of health-related quality of life

Concepts

Quality of life (QOL) is a measure of individual overall satisfaction with life and a general sense of personal well-being. Four broad domains generally contribute to the overall QOL: physical, psychological, social and economic (Schipper et al. 1990). When a patient is diseased, almost all aspects of life can become health-related (Guyatt et al. 1993). Health has been defined by the World Health Organization (WHO) as a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity (WHO 2006). The term health-related quality of life (HRQOL) is a multidimensional construct that has been defined as a subjective assessment of the impact of a disease and its treatment across the physical, psychological, social and somatic domains of functioning and well-being (Revicki et al. 2000). The health component of the term refers to the QOL that exists as a result of a certain state of health (Theunissen et al. 1998). Children's quality of life measures have been developed under the concepts of health status, functional status, perception of illness, life satisfaction and quality of well-being (Eiser and Morse 2001a). A qualitative content analysis of generic HRQOL instruments for use with children and adolescents revealed that it included three domains, physical, psychological and social, but the distribution of items varied considerably (Rajmil et al. 2004). The goals of HRQOL measurement include differentiating between people who have a better and a worse HRQOL and measuring how much the HRQOL has changed (Guyatt et al. 1993). When it is possible to manage a disease but not cure it, it is important to determine how far the disease and it treatment contribute to compromising the child's HRQOL (Eiser and Morse 2001b).

Health-related quality of life instruments

The basic approaches to HRQOL measurement include generic instruments that provide a summary of HRQOL and specific instruments. All of these instruments or questionnaires are made up of questions or items included in domains which refer to the areas of behaviour that are to be measured (Guyatt et al. 1993). *Generic instruments* include health profiles and utility instruments. Health profiles attempt to measure all the important aspects of HRQOL, and

their advantages include dealing with a variety of areas and their applicability to any population, allowing broad comparisons. Consequently these generic profiles may be unresponsive to changes in specific conditions (Guyatt et al.1993). Utility instruments reflect the preferences of patients for certain treatment processes or outcomes. They incorporate preference measurements and relate given health states to death, and can thus be used in cost-utility analyses (CUA). HRQOL is summarized as a single index along a continuum from death (0) to full health (1), where the utility scores reflect both the patient's health status and the value of that health status to the patient, and they are thus useful for determining whether patients are better off is a result of a given treatment (Guyatt et al.1993). Utility instruments have also been developed for children aged from 8 to 11 years (Apajasalo et al. 1996a) and from 12 to 15 years (Apajasalo et al. 1996b). *Specific instruments* include the important aspects of HRQOL that are relevant to the patients being studied. The instruments may be specific to the disease, to a population or to a certain function or problem. In addition to the likelihood of improved responsiveness, these have the advantage of relating closely to areas routinely analysed by clinicians (Guyatt et al. 1993). This was shown in a comparison between HRQOL measured in children and teenagers with food allergic and generic Child Health Questionnaire -Child Form (CHQ -CF) and disease specific Food Allergy Quality of Life Questionnaires (FAQLQ -CF, FAQLQ -TF). The low percentage of agreement between these instruments suggested that the disease-specific questionnaire was more capable of capturing the specific aspects that impaired HRQOL in food allergy and was thus more responsive to differences over time (Flokstra-de Blok et al. 2010a).

Proxy raters of health-related quality of life

Instruments can be either administered by interviewers or self-administered. Surrogate responders or proxies are needed when patients cannot complete the measures themselves (Addington-Hall and Kalra 2001), and parent-proxy HRQOL reports can be especially useful when a child is too young or too ill to make such a report (Eiser and Morse 2001a). Even when children's responses are available, the parental perspective has an important bearing on health care decisions (Jokovic et al. 2004). The majority of QOL instruments have been developed for children above eight years, with proxy reports used to gain information about younger children. Nevertheless, children at the age of 5 years have been shown to be able to report their HRQOL reliably and validly with an age-appropriate instrument, e.g. one in which the 5-point Likert response scale was reworded to a 3-point scale (Varni et al. 2007). In another study all the children with eczema aged 9 years or more were able to complete the

Children's Dermatology Life Quality Index. Inability to read without help from their parents was the main reason for the younger children not completing the index (Ben-Gashir et al. 2004).

Several generic and disease-specific HRQOL instruments for school-aged children are available that include parallel child and parent proxy versions (Cremeens et al. 2006), but questions have been raised about the level of agreement between children's own views and those of their parents about the child's HRQOL, with suggestions that the situation may differ according to the child's age, gender and illness (Eiser and Morse 2001a). There is some evidence for greater agreement between child and parent ratings for observable forms of behaviour in physical domains and less for social and emotional dimensions (Eiser and Morse 2001a, Mulligan et al. 2009). In chronically sick children and children with deficiencies the agreement with parent proxy reports on HRQOL has varied from low to good (Annett et al. 2003, Baca et al. 2010, Ylimäinen et al. 2010; Yoo et al. 2010), while in healthy children it can vary from low to moderate (Jozefiak et al. 2008). Children with chronic diseases tend to rate their HRQOL higher than parent proxy raters (White-Koning et al. 2007, Baca et al. 2010), but parents may underestimate a child's pain (CP) (White-Koning et al. 2007). For example, the mothers on children allergic to peanuts regarded the impact of this food allergy on their children as more severe than did the children themselves (King et al. 2009), while it was found in a comparison of the teenager and parent versions of the Food Allergy Quality of Life Questionnaire (FAQLQ) that disagreement was associated with the adolescent's perceptions and characteristics (van der Velde et al. 2011). Assessments have also been made of differences in agreement between parents and physicians (Janse et al. 2005), parents and other professionals such as teachers, carers and therapists (White-Koning et al. 2008), or children, their parents and their healthy siblings (King et al. 2009, Baca et al. 2010).

Factors affecting parents' evaluations of health-related quality of life
Parents' evaluations may be influenced by the development of other children they know, their expectations and hopes for their child, additional life stresses and their own mental health (Eiser and Morse 2001b). Greater symptoms of distress in mothers have been associated with worse parent proxy reports on their children's HRQOL than their children's self-reports in cases of chronic diseases (White-Koning et al. 2007, Panepinto et al. 2010). Given that mothers tend to be more involved in child care, it is possible that they are more aware of the child's views about HRQOL than fathers, and it is typically the mothers who complete the

HRQOL instruments in 88–93% of cases (Sicherer et al. 2001, Marklund et al. 2006). There are only a few evaluations of agreement between mothers and fathers as proxy raters (Mulligan et al. 2009). The influence of parents' gender on the assessment of HRQOL in infants with eczema was examined with a disease-specific index, but no significant differences were found (Holm et al. 2006, Chernyshov 2009). It has been suggested that in repeated assessments the same parent should complete assessments at all the time points (Mulligan et al. 2009).

Upton, Lawford and Eiser (2008) concluded that differences in parent-child agreement between child health-related quality of life instruments may be consequences of each individual's beliefs about children's health and well-being. Parents may vary in their awareness, sensitivity and tolerance of children's health concerns and knowledge of these differences between parent and child reports reveals how good an estimate of the child's HRQOL a parental report is (Upton et al. 2008). The parent and child have different perspectives on the child's life, both of which are valid and constitute important information concerning the child's well-being (White-Koning et al. 2007).

2.4.2 Health-related quality of life in infants and young children with eczema

Methods

Three validated *disease-specific instruments* have been developed for measuring HRQOL in infants and young children with eczema (Table 1). The preference scores for eczema have also been evaluated on the basis of both the Childhood Impact of Atopic Dermatitis instrument and various scenarios for the severity of eczema.

Table 1. Disease-specific instruments for measuring HRQOL in infants and young children with eczema.

Authors	Instrument	Focus group	Items	Content
Lewis-Jones et al. 2001	Infant Dermatitis Quality of Life Index (IDQOL)	child < 4 y	10	infant's physical and emotional health, physical and social functioning
Chamlin et al. 2007	Childhood Atopic Dermatitis Impact Scale (CADIS)	child < 6 y parents	45	child's symptoms, activity limitations and behaviour; parental and family social function, sleep, emotions
McKenna et al. 2007	Childhood Impact of Atopic Dermatitis (CIAD)[a]	child ≤ 8 y	12	impact of AD on child, gender-specific

[a] The European version of CIAD comprises 9 items and the US version 7 items, with 6 items common to both.

These instruments differ in content, ages of the focus groups, number of items, scoring and time period. The Infant Dermatitis Quality of Life Index (IDQOL) and the Childhood Impact of Atopic Dermatitis (CIAD) focus on the infant, while the Childhood Atopic Dermatitis Impact Scale (CADIS) captures the effects of eczema on both the child and the parents, all of which limits the comparability of the results obtained with different instruments. In terms of usage, the longer the instrument is, the more accurate data it produces, as with the 45 items in CADIS, but this also limits usage in clinical practice. The period of coverage ranges from one week in IDQOL to four weeks in CADIS. CIAD have been developed separately for boys and girls.

Results

Studies which have used the *Infant Dermatitis Quality of Life Index (IDQOL)* (Lewis-Jones et al. 2001) to evaluate HRQOL are summarised in Table 2, which also includes the Dermatitis Family Index (DFI) (Lawson et al. 1998), which has often been used together with IDQOL. The mean IDQOL score in the validation study was 7.89 (SD 5.74) (n=89, children < 4 years), and a 39% improvement in HRQOL was measured in a group of children (n=24) after treatment (Lewis-Jones et al. 2001). Other studies report average scores ranging from 5.9 to 12.3, the best HRQOL, 5.9, being found in a study which included young children from primary care (Chinn et al. 2002), whereas these cross-sectional and follow-up studies mostly included infants with moderate and severe eczema from secondary care.

The highest-scoring questions, and thus most serious levels of impairment, have been reported because of itching and scratching (Lewis-Jones et al. 2001, Beattie and Lewis-Jones 2006, Gånemo et al. 2007, Park et al. 2007, Ricci et al. 2007, Ho et al. 2010), mood (Lewis-Jones et al. 2001, Gånemo et al. 2007, Ricci et al. 2007, Ho et al. 2010), the time taken to get child asleep (Beattie and Lewis-Jones 2006, Gånemo et al. 2007, Ricci et al. 2007, Ho et al. 2010), sleep disturbance (Lewis-Jones et al. 2001, Ricci et al. 2007, Ho et al. 2010), dressing and bathing (Beattie and Lewis-Jones 2006), while the lowest-scoring questions have concerned family activities (Lewis-Jones et al. 2001, Park et al. 2007) and treatment (Lewis-Jones et al. 2001). Improvements as a result of interventions have been reported in the time taken to get to sleep, difficulties at mealtimes, mood and problems with dressing (Beattie and Lewis-Jones 2006).

HRQOL improvements have ranged from 33 to 75% after consultation with a paediatric dermatology team (Beattie and Lewis-Jones 2006), an educational programme consisting of six weekly meetings (Ricci et al. 2009), treatment with a new emollient (Grimalt et al. 2007, Msika et al. 2008) or a new probiotic (Gerasimov et al. 2010). By contrast, no significant changes were measured in the case control studies after a single consultation with a primary care nurse (Chinn et al. 2002), wet wrap therapy (Beattie and Lewis-Jones 2004), an educational programme through a two hour workshop (Grillo et al. 2006) or interaction with an AD educator for 15 minutes (Shaw et al. 2008). The level of care provided by a practitioner nurse in terms of improvement in the eczema and in the IDQOL score was comparable with that provided by a dermatologist, but the parents were more satisfied in the former case (Schuttelaar et al. 2010). It can be concluded on this basis that single sessions were not adequate to allow the caregiver or parent to receive all the information for making significant improvements in the infant's skin condition.

Table 2. Summary of studies that have used the Infant Dermatitis Quality of Life Index (IDQOL) or Dermatitis Family Impact (DFI)

Authors	Type of study	N	Age, years M, range	Follow-up weeks	IDQOL (I) Base	IDQOL (I) Change %	IDQOL (C) Base	IDQOL (C) Change %	DFI (I) Base	DFI (I) Change %	DFI (C) Base	DFI (C) Change %
Cross-sectional studies												
Balkrishnan et al. 2003[a]	explanatory analysis	49	4.7 0.5–12						9.7			
Beattie and Lewis-Jones 2006	1) evaluation of the usefulness of the IDQOL and DFI	203	19.8 mo 1–53 mo		8.47				8.47			
Gånemo et al. 2007		28	2–4		8.6				10.3			
Park et al. 2007		101	3.9 0–6		11.5				10.1			
Ricci et al. 2007	case (AD) control (healthy) study	65	2 0.25–4		10.2		3.3		11		7.4	
Ho et al. 2010[b]		104	6.4 0–16		6.20 8.68 12.0 15.5				49% normal, 27% low, 18% mod., 6% high			
Intervention studies												
Chinn et al. 2002	case-control intervention by a primary care nurse	115	2.12 0.5–4	12	5.9	–8		+12	4.6	+2		+7
Thomas et al. 2002[c]	randomized controlled trial of a potent topical corticosteroid (I) compared with a mild preparation (C)	207	5 and 6 1–15	18					4.1/ 2.9	–0.6[c]	4.9/2.5	–0.5[c]
Balkrishnan et al. 2003[a]	before and after dermatologist visit	35	0.5–12	4					10	–43		
Beattie and Lewis-Jones 2004	intervention study, wet wrap therapy (I) vs. hydrocortisone (C) for AD	19	1.77/1.44 0.3–3	3	10.8	–42	12.3	–66	11.2	–40	13	–62

24

Study	Design / intervention	N	Age	n	V1	%	V2	%	V3	%	V4	%
Beattie and Lewis-Jones 2006[d]	2) before/after intervention by a dermatology team	50	12 mo / 4–39 mo	10	9.74	–38						
Grillo et al. 2006	longitudinal, randomized controlled study, educational intervention	61	4.3 / 0.3 –13	12	11	–37	8.62	–38	11.09	–32	10.86	–27
Grimalt et al. 2007	randomized, controlled intervention with a new emollient	162	<12 mo / 6.07/5.8 mo	6	6.32	–43	7.2	–48	5.3	–56	6.42	–45
Msika et al. 2008[e]	multicentre, randomized study to demonstrate the corticosteroid sparing effect of a new emollient	86	16 mo / 4 – 48 mo	3		–38–75				–56–88		
Shaw et al. 2008	randomized, controlled, intervention by an AD educator	71	4.62 / 6.34	4, 12	8.88	–31	8.05	–27				
Kubota et al. 2009	pilot study of sequential application of topical corticosteroids and topical tacrolimus	28	7.1 / 2–15	12	6.40	–57						
Ricci et al. 2009	intervention	30	1.5 / 0.4–5	6	6.85	–36			8.8	–50		
Gerasimov et al. 2010	randomized, double-blind, placebo controlled trial of a new probiotic preparation (I)	90	25.6 / 24.1 mo / 0.2–3	8	11.2	–33	12.1	–19	12.2	–35	12.6	–24
Schuttelaar et al. 2010	level of care achieved by nurse practitioners (NP) as compared with that achieved by dermatologists (DE)	80	≤4 / 4–16	48	10.7	–46	11.6	–56	8.0	–59	9.2	–47%

I = intervention group, C = control group.
[a] A slightly US-modified version of the DFI, ADFIS; [b] Results of IDQOL and CDLQI (Children's Dermatitis Life Quality Index, > 4 years) and DFI are reported as a single figure categorized according to the severity of the family impact; 0–5 normal, 5–10 low impact, 11–20 moderate impact and >20 high impact; [c] 33 subjects from hospital and 174 from the community; DFI change as a mean value of the hospital and community sample; [d] Age is presented as a median; [e] Five groups.

The Childhood Atopic Dermatitis Impact Scale (CADIS) (Chamlin et al. 2005a) has been shown to differentiate patients at each severity level as measured by the SCORAD index and to provide an accurate measure of change in patients whose disease improves (Chamlin et al. 2007). The average total CADIS scores were 80.75 (SD 21.32) in children with mild eczema, 99.61 (SD 28.55) in those with moderate eczema and 135.51 (SD 23.10) in those with severe eczema (Chamlin et al. 2007) higher scores meaning stronger impact and thus worse HRQOL.

Some new instruments have been developed shortening longer ones. The *Childhood Impact of Atopic Dermatitis* (CIAD) scale, for instance, was derived from the Parent's Index of Quality of Life-Atopic Dermatitis (PIQoL-AD) (McKenna et al. 2007), intended as a valuation survey for parents of children with AD and members of the general population that estimated preference weights for each of 16 health states, as required for the calculation of quality-adjusted life years (QALY). The values assigned to these health states ranged from 0.356 to 0.84 on a continuum from zero (death) to one (perfect health) (Stevens et al. 2005).

Another study of preference weights employed case scenarios for 5 levels of AD severity (mild, mild to moderate, moderate, moderate to severe and severe) generated by combining the characteristics of a global investigator assessment with scores for the Eczema Area and Severity Index (EASI) scores. The aims were to elicit preference weights for the levels of severity of eczema using a visual analogue scale and to ascertain whether parents of children with eczema assign different preferences to the health state scenarios than parents who do not have a child with eczema. The mean preference scores for mild, mild to moderate, moderate, moderate to severe and severe eczema were 91, 84, 73, 61 and 49, respectively, on a scale of 100 (=1) (perfect health) to 0 (death). The score for asthma was 58 and that for the use of spectacles 87. Parents perceived that the negative effect of eczema increased with disease severity, and the parents of children with eczema gave slightly higher preferences than the others (Friedman et al. 2004). The preference weights reported in these two studies of childhood eczema were of the same order.

2.4.3 Health-related quality of life in families and parents of infants and young children with eczema

Methods

The first *generic instrument* for the description of the effect of chronic childhood disease on the family was the *Impact on Family scale* published by Stein and Riessman (1980). This has also been used in the context of eczema. Three *disease-specific instruments* have been

developed and used for measuring the HRQOL of families and parents of children with eczema (Table 3). In contrast to the others, the German instrument proposed by von Rüden et al. (1999) provides a profile.

Table 3. Disease specific instruments for measuring family and parent HRQOL.

Authors	HRQOL instrument	Focus group	Items	Content
Lawson et al. 1998	Dermatitis Family Impact questionnaire (DFI)	parents	10	impact of AD on family and parents
von Rüden et al. 1999	Quality of life in parents of children with atopic dermatitis (QLPCAD) [a]	child, parents	26	five subscales: psychosomatic wellbeing, effects on social life, confidence in medical treatment, emotional coping, and acceptance of the disease
McKenna et al. 2005	Parent's Index of Quality of Life-Atopic Dermatitis (PIQoL-AD)	parents of children < 8 years	28	needs-based: life gains its quality from the ability and capacity of the individual to satisfy his or her needs

[a] In German: Eine Krankheitsspezifische Fragebogen zur erfassung der lebensqualität von eltern neurodermitiskranker kinder.

It is typical of all of these instruments that the age of the children varies widely, although they all are designed to measure parents' and families' HRQOL. DFI includes ten items, which, contrary to those in QLPCAD are not further divided into subscales. The philosophical basis of PIQoL-AD, as a needs-based instrument, differs from that of the other instruments, which measure impact. DFI is the earliest and most widely used, while QLPCAD has mainly been used in German-speaking countries.

Results

Generic the *Impact on Family* scale consists of 24 items and four dimensions that measure the family's financial situation, social interactions within and outside the home, subjective distress felt by the parent and the positive sense of mastery which may emerge from coping with the associated stress (Stein and Riessman 1980). In one Australian study, children (aged 4.5 years) with moderate to severe eczema had higher scores than those with diabetes (Su et al. 1997). By contrast, a German study using a modified version of the instrument recorded low levels of family strain (Warschburger et al. 2004).

A summary of studies using the *Dermatitis Family Impact questionnaire* (DFI) in families of infants and young children with eczema is presented in Table 2. Since the majority of the

children had been recruited from secondary care, they represent young children with moderate to severe eczema, with the exception of two studies where the scores ranged from 2.5 to 4.6 in families of children from primary care (Chinn et al. 2002, Thomas et al. 2002). In cross-sectional studies the score has ranged from 8.47 to 11, which may be interpreted as indicating a minor family impact (6–10 low alteration, 11–20 moderate alteration) (Ricci et al. 2007). The other studies can be classified as before/after designs applied to the same children, where the score ranged from 8.8 to 10 with improvements of 43–88% in family QOL, and case-control studies, in which the score ranged from 5.3 to 12.2 with an improvement of 33–59% in the intervention group and from 6.42 to 13 with an improvement of 24–62% in the control group of children with eczema. The improvements in DFI were due to an episode of specialist care (Bahlkrishnan et al. 2003a), consultation with a paediatric dermatology team (Beattie and Lewis-Jones 2006) and use of a new emollient preparation (Msika et al. 2009). Programmes that aim to improve HRQOL in families may nevertheless cause negative effects, as was shown in one study, where differences were measured after a single educational programme for severe eczema. Compliance required more family time and effort and also increased the financial burden (Grillo et al. 2006). Three distinct parent characteristics have been associated with a higher family impact, namely self-formed opinions about the severity of the child's condition, worries about payments for medical care and intensive use of supplementary non-medical services (Balkrishnan et al. 2003b). The HRQOL of a family measured by DFI was related to the severity of eczema in the case of school-aged children, with one unit increase in the objective SCORAD causing a 0.23–0.25 unit increase in DFI (Ben-Gashir et al. 2002).

The highest impairments in questions included in DFI have been reported in parental sleep disturbance, tiredness and exhaustion (Lawson et al. 1998, Lewis-Jones et al. 2001, Beattie and Lewis-Jones 2006, Gånemo et al. 2007, Ricci et al. 2007), emotional distress (Lawson et al. 1998, Lewis-Jones et al. 2001, Beattie and Lewis-Jones 2006), costs (Gånemo et al. 2007, Ricci et al. 2007) and treatment (Lawson et al. 1998, Gånemo et al. 2007), while the lowest-scoring questions have been family leisure activities (Lewis-Jones et al. 2001) and shopping (Lewis-Jones et al. 2001, Ben-Gashir et al. 2003, Gånemo et al. 2007).

The *Quality of life in parents of children with atopic dermatitis* questionnaire (QLPCAD) has been developed in the context of a Berlin public health study (von Rüden et al. 1999). This questionnaire has been used in German studies in which parents' HRQOL improved after a 12-month follow-up period (Staab et al. 2002, Staab et al. 2006). Both of these studies used

the Berlin model, an educational programme for the parents of children with eczema aimed at improving their self-management skills with regard to their child's disease and achieving a positively impact on the family's QOL. The programme included six group sessions arranged to consider medical, nutritional and psychological issues under the direction of a team of dermatologists, paediatricians, psychologists and dieticians (Wenninger et al. 2000).

The *Parents Index of Quality of Life in Atopic Dermatitis* (PIQoL-AD) is a needs-based instrument (McKenna et al. 2005) which has been used in two trials comparing the impact of emollients, pimecrolimus and topical corticosteroids with the usual care involving emollients, topical corticosteroids and a vehicle cream. Both trials were randomized and double-blinded. The first trial involved patients aged between 3 months and 2 years and the second children aged 2 to 17 years. HRQOL assessments were conducted at baseline and after 6 weeks, 6 months and 12 months. The PIQoL-AD scores showed a greater improvement in the parents' HRQOL for pimecrolimus than with the usual care at all time points. The instrument was able to show improvements in HRQOL (Whalley et al. 2002, McKenna et al. 2006).

The only instrument which has been used in multiple studies has been the IDQOL, whereas the use of QLPCAD has been restricted mainly to Germany and the use of PIQoL-AD has been limited as yet.

2.4.4 Health-related quality of life in children with food allergy and their families

The HRQOL of children with food allergy and their families has been measured using both generic (Table 4) and disease-specific instruments (Table 5). Families with food allergy children have been recruited from private allergy practices, hospital out-patient departments or allergy networks, thus representing the most severely allergic cases. The focus has been on school-aged children and their HRQOL, and in most cases parents have completed the measures on behalf of their children and the results are reported as if they applied to all ages. One consequence of this is that the most prevalent food allergy in these studies has been allergy to peanuts and the anaphylaxis that may occur.

2.4.4.1 Health-related quality of life measurement with generic instruments

Methods

The generic HRQOL instruments that have been used in food allergy studies are the Children's Health Questionnaire (CHQ-PF) (Landgraf et al. 1999) and the Paediatric QoL

Inventory 4.0 (PedsQL[TM]) (Varni et al. 2003). The CHQ-PF was designed for parents of children from five to 18 years of age and includes questions on the child's HRQOL and the parents' and family's HRQOL (Landgraf et al. 1999). The child form was first used for food allergy by Flokstra-de Blok and colleagues (2010a).

Table 4. Summary of studies using generic HRQOL instruments for evaluating children with food allergy and their families.

Authors	HRQOL instruments	Age, y M (range)	Rater	Comparison groups
Primeau et al. 2000	Children's Health Questionnaire, parent form (CHQ-PF)[a]	6.4 (0–17)	parent	peanut allergy vs. reumatological disease
Sicherer et al. 2001	Children's Health Questionnaire, parent form (CHQ-PF50)[a]	10.8 (5–18)	parent	food allergy vs. population norms
Marklund et al. 2006	Children's Health Questionnaire, parent form (CHQ-PF28)[a]	12.5 (8–19)	parent	FHS with asthma, eczema and/or rhino conjunctivitis vs. FHS
Östblom et al. 2008b.	Children's Health Questionnaire, parent form (CHQ-PF28)[a]	9	parent	food allergy vs. allergic disease vs. healthy age-mates
King et al. 2009 [c]	Paediatric QoL Inventory 4.0 (PedsQL[TM]) [b,c]	10 (8–12)	parent child sibling	peanut allergy
Flokstra-de Blok et al. 2010a	Children's Health Questionnaire, child form (CHQ-CF87)[a]	10.2 (8–12)	child	food allergy vs. general population

FHS = food hypersensitivity
[a] Landgraf et al. 1999. [b] Varni et al. 2003, self-report forms for children and proxy report forms for parents; [c] Also includes measurement of HRQOL with a disease-specific instrument.

Results

These studies using the CHQ-PF have shown that food allergy impairs the child's general HRQOL and the parents' HRQOL and disrupts family activities (Marklund et al.2006, Östblom et al. 2008b) as compared with healthy age-mates (Östblom et al. 2008b) or population norms (Sicherer et al. 2001). Families of children with peanut allergy have more disruption in their activities and impairment of familial-social interactions than do families of children with rheumatological disease, which is due to their children's risk of death (Primeau et al. 2000). Boys had lower scores on general health and physical functioning and girls on mental health (Marklund et al. 2006). The children with food allergy themselves, however, evaluated their emotional and behavioural capabilities as being better than those of healthy

children (Flokstra-be Blok et al. 2010a). Children with food allergy may even have better capabilities in some of the domains measured.

Food allergy associated asthma, atopic dermatitis or rhino conjunctivitis may cause a further significant reduction in perceived general health and thus deterioration in the child's HRQOL (Sicherer et al. 2001, Marklund et al. 2006). The more food allergies a child has the lower will be the HRQOL (Sicherer et al. 2001). On the other hand, children from a population-based cohort reported by their parents to have FHS had significantly lower scores on many of the subscales of the CHQ than did children with asthma, eczema or rhinitis, and thus had a poorer HRQOL (Östblom et al. 2008b).

2.4.4.2 Health-related quality of life measurement with disease-specific instruments

Methods

Disease-specific HRQOL instruments include a heterogeneous group of validated (Cohen et al. 2004, Flokstra de Blok et al. 2009, DunnGalvin et al. 2010) and unvalidated (Avery et al. 2003, Bollinger et al. 2006, LeBovidge et al. 2006, Williams et al. 2009) instruments (Table 5), that vary greatly in content and age range. The differences between considering the child's HRQOL or that of the parents or family are sometimes subsumed under a single measure and infrequently separated, but the forms are intended for the parents to complete. The instruments have indeed been completed by a parent, except for the *Quality of life questionnaire for children with peanut allergy* and *the Food Allergy Quality of Life Questionnaire - Child Form* (FAQLQ -CF) which is the first disease-specific questionnaire intended for self-completion by children with food allergy aged 8–12 years. The validation study showed that it discriminated well between children who reported more than two food allergies and those who reported two or less (Flokstra-de Blok et al. 2009).

Results

Children with peanut allergy have a poorer QOL than children with insulin-dependent diabetes mellitus. They were more afraid of accidentally eating peanuts than diabetics were of having a hypoglycaemia. The results were based on a study using two disease-specific questionnaires, the first designed especially for that purpose and the second adapted from the *Vespid Allergy QOL questionnaire* for individuals with anaphylactic sensitivity to wasp stings (Avery et al. 2003). They also have poorer emotional and psychological HRQOL than in

healthy normative data, and the mother's QOL was better if the child had been prescribed an auto-injector (Cummings et al. 2010).

A study by Cohen et al. (2004) revealed numerous HRQL domains included in the *Food Allergy Quality of Life - Parental Burden questionnaire* (FAQL-PB) which were affected in families with food allergic children. Family social activities were affected, especially social activities that involved food, leaving the children in the care of others or the children being near others who were eating. The time required for meal preparation is affected, and precautions are necessary when leaving home. The parents were concerned about their children's health and nutrition, and worried that they might not be on hand to help in the event of a reaction. Emotional issues included anxiety about reactions, frustration in dealing with others, sadness and worry that their child might not overcome the allergy and have a normal upbringing (Cohen et al. 2004).

Independent risk factors for low parental HRQOL in the case of 2–7-year-old Chinese children were three or more foods avoided, current food avoidance, current flexural dermatitis and adverse food reactions caused by peanuts, egg and cow's milk (Leung et al. 2009). In another study impaired caregiver HRQOL was more likely among children allergic to milk or wheat (0–17 years, 53% <5 years) (Springston et al. 2010), who were most frequently troubled by items assessing social interaction and limitations. The risk of being extremely troubled was significantly higher among caregivers whose children had had an emergency department visit in the past year on account of food allergy or had multiple food allergies when measured using the FAQL-PB (Springston et al. 2010). The findings that the parents' and child's HRQOL findings are significantly affected by multiple food allergies relative to peanut allergy alone, or that they are affected by emergency department visits were not verified in a study which used parents', siblings' and children's evaluations in the context of generic and disease-specific QOL instruments (King et al. 2009). In another study using the *Food Allergy Parent Questionnaire*, higher scores on parental anxiety and distress were associated with a younger child, a greater number of food allergies and a history of anaphylactic reaction (LeBovidge et al. 2006). When using the *Food Allergy Impact Scale* the same family activities were affected, including meal preparation, social activities and parent stress levels. The child's going to play at a friend's home or going to birthday parties or sleepovers could be affected as well (Bollinger et al. 2006). It can be concluded from these findings that a child's food allergy affects the parents and family in many ways, but more

research is needed with respect to factors that contribute to the HRQOL in connection with food allergy at different ages.

Table 5. Summary of studies using disease-specific instruments to evaluate children with food allergy and their families.

Authors	HRQOL instrument	Age y M(range)	Rater	Content
Avery et al. 2003	Vespid Allergy Quality of Life Questionnaire [a] & Quality of life questionnaire for children with peanut allergy [b]	9 (7–12)	child child	– QOL of individuals with anaphylactic sensitivity to wasp stings/in this case to peanuts – how often things happen
King et al. 2009[e]	Quality of Life questionnaire for children with peanut allergy [c]	10 (8–12)	parent child sibling	"
Cohen et al. 2004	Food Allergy Quality of Life – Parental Burden (FAQL-PB)[b]	6.2 (0.16–17)	parent	– to measure the effect of food allergy on HRQOL of parents of children with FA
Leung et al. 2009	Food Allergy Quality of Life – Parental Burden (FAQL-PB)[d] Chinese	4.2 (2–7)	parent	"
Springston et al. 2010	Food Allergy Quality of Life – Parental Burden (FAQL-PB)[d]	0–17	parent	"
Cummings et al. 2010	Food Allergy Quality of Life – Parental Burden (FAQL-PB)[d] & Quality of Life questionnaire for children with peanut allergy[ce]	6–16	parent child	"
Williams et al. 2009	Parenting Children with Food Allergy (PCFA)[b]	8	parent	– to evaluate specific parenting practices related to caring for a child with FA
LeBovidge et al. 2006	The Food Allergy Parent Questionnaire[b]	6.3 (0-18)	parent	– parental adjustment to and coping with children's food allergy
LeBovidge et al. 2008	Food Allergy Quality of Life – Parental Burden (FAQL-PB)[d] & Family Coping with Food Allergy Questionnaire (FCFAQ)	6.4 (5-7)	parent	– parental perceived competence in supporting a family coping with FA
Bollinger et al. 2006	Food Allergy Impact Scale[b]	0.7–17	parent	– caregiver's perception of the impact of the child's FA on meal preparation, family social activities, caregiver–supervised child social activities, autonomous child social activities, school activities, family relations, caregiver stress and free time and employment and finance.
Flokstra-deBlok et al. 2009	Food Allergy Quality of Life Questionnaire – Child Form (FAQLQ-CF)[b]	8–12	child	– impact on shopping/labelling, food preparing, eating in general, eating out, social activities, emotions, holidays and medication
DunnGalvin et al. 2008 & 2010	Food Allergy Quality of Life Questionnaire – Parent Form (FAQLQ-PF)	0–12	parent	– general emotional impact, food anxiety, social and dietary limitations
van der Velde et al. 2010	Food Allergy Independent Measure – Child Form (FAIM-CF)	8–12	child	– perceived expectation of patients of the chance of accidental exposure and the perception of what will happen following accidental exposure

FA = Food allergy
[a] Oude Elberink et al. 2002; [b] developed for this study or an initial development and validation study; [c] Avery et al. 2003; [d]Cohen et al. 2004; [e] also measurement of HRQOL with a generic instrument.

2.5 Economic evaluation

2.5.1 Concept and measurement

In general economic evaluation is defined as the comparative analysis of alternative courses of action in terms of both their costs and consequences. The basic task is to identify, measure, value and compare the costs and consequences of the alternatives being considered. When there is no comparison of alternatives, the programme is described as an outcome description. When only cost is examined, it is described in the literature as the cost of illness or burden of illness. If both the outcomes and costs of a single service or programme are described, the evaluation is a cost-outcome description. When two or more alternatives are compared, but the costs and consequences of each are not examined, the terms are either efficacy and effectiveness evaluation or cost analysis. All these are partial evaluations, as a full economic evaluation should include both. Analyses in which costs are related to a single, common effect that may differ in magnitude between the alternative programmes are referred to as cost-effectiveness analyses (CEA). The results may be stated as cost per unit effect. CEA cannot be performed unless the alternatives have a common effect. In cost-utility analyses (CUA) the term utility refers to the preferences of individuals or of society as a whole. The generic outcome as expressed in QALY, arrived at in each case by adjusting the length of time affected through the health outcome by the utility value of the resulting health status on a scale of 0 to 1. CEA results are typically expressed in terms of the cost per healthy year, and CUA results as cost per QALY gained by undertaking one programme instead of another. Both CEA and CUA are techniques for constrained maximization, where a decision-maker is considering how best to allocate an existing budget. Analyses that measure both the costs and the consequences of alternatives in monetary units are called cost-benefit analyses (CBA)(Drummond et al. 2005).

The existing literature on economic evaluation in health care classifies costs and benefits as direct, indirect and intangible, although the terms are not used consistently in all studies. Direct costs and benefits denote the resources consumed or saved by the programme as compared with an alternative programme. Indirect costs have been used to denote the amount of patients' time consumed, and are considered synonymous with productivity gains and losses. Intangible costs and benefits denote those consequences that are difficult to measure and value, such as the value of improved health, or pain and suffering. The latter are not costs and these items are not strictly intangible as they are often measured and valued employing

the utility or willingness to pay approach (Drummond et al. 2005). The approach in this thesis is a cost of illness analysis including direct and indirect costs.

2.5.2 Cost of eczema

Interest in the costs of illness has increased since 2000, especially in the USA and Germany. Because of the differences in health care provision and financing systems, variations in patients' disease severity and the costs entailed, large variations can be found in the estimated treatment costs associated with eczema from one country to another. Most of these studies have used retrospective data covering a year. Frequently used data acquisition methods have been clinical examinations, questionnaires, interviews, physicians or insurance databases. A summary of cost-of-illness studies of childhood eczema that include direct and indirect costs and costing studies that include direct costs is presented in Table 6. In the review by Mancini et al. (2008), which gives examples of the direct and indirect costs of eczema, the direct costs are taken to include professional fees, hospitalization, diagnostic and laboratory testing, medications, transportation, dietary and environmental changes, special clothing and co-payments. Indirect costs include pain and suffering, school performance and absence, work performance and absence and career choice.

To summarize, the costs have been counted from the perspective of society (6 studies), the family and patient (9 studies), a third party payer (5 studies), the state (one study) and the health care provider (2 studies). The focus of the study determines which cost components should be included. The annual costs of childhood eczema to society range from 725 USD (~578 EUR in 1997[1]) to 1468 EUR (~1551 USD in 2001[1]) (Fivenson et al. 2002, Ehlken et al. 2005). The highest value observed has been 8646 DM (~4421 EUR in 2000[2]) (Rathjen et al. 2000). Two studies gave the cost estimates to society as 79 GBP (~96 EUR in 1996[1]) and 71 USD (~60 EUR in 1999[1]) in primary care, the first including only young children (Emerson et al. 2001, Verboom et al. 2002). The proportion of the total costs met by the family has usually 35-45% (range 11–60%), the average family costs being between 28.94 GBP (~35 EUR in 1996[1]) (Emerson et al. 2001) and 1254 EUR (Ricci et al. 2006). In one study the median cost for families was 0 because over 50% of the parents of children under the age of 2 years had no expenditure at all. In the United Kingdom, patients in that age group do not pay for prescriptions and health care (Herd et al. 1996).

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[1] Historic Exchange Rates, 2011.
[2] European Commission. Eurostat. 1 EUR=1.95583 DM.

Only a few studies have compared the severity of eczema with the total costs in children (Su et al. 1997; Ricci et al. 2006). Here the costs to society have been 1142 AUD (~723 EUR in 1997[1]) in cases of mild eczema, 3624 AUD (~2294 EUR in 1997[1]) in moderate eczema and 6099 AUD (~3860 EUR in 1997[1]) in severe eczema (Su et al. 1997). Average family costs have varied according to severity, from 480 AUD (~304 EUR in 1997[1]) to 694 EUR (~1119 AUD in 2006[2]) in mild eczema, from 1712 AUD (~1084 EUR in 1997[1]) to 1172 EUR (~1890 AUD in 2006[2]) in moderate eczema and from 2545 AUD (~1610 EUR in 1997[1]) to 1809 EUR (~2918 AUD in 2006[2]) in severe eczema (Su et al. 1997, Ricci et al. 2006). The average annual costs have doubled in children with moderate eczema and tripled in children with severe eczema relative to children with mild eczema (Ricci et al. 2006). The accumulation of 85% of the total costs was found to be caused by 20% of the children in a German birth cohort study (Weinmann et al. 2003).

In studies across ages the highest costs of eczema have been borne by prescriptions, clothing and laundry, over-the-counter preparations, hospital in-patient and out-patient care, medical visits and time off work (Herd et al. 1996, Rathjen et al. 2000, Fivenson et al. 2002, Ehlken et al. 2005, Barbeau et al. 2006). The three most often reported cost components in the case of families with children have been hospitalization, changes in the home environment, medical consultations, time off work, over-the-counter medicines, medications & moisturizing (Su et al. 1997, Emerson et al. 2001, Fivenson et al. 2002, Ricci et al. 2006). Income losses for parents of affected children have been reported to range from 150 to 1290 AUD (94 to 816 EUR in 1997[1]) from mild to severe eczema, and from 365 USD (~291 EUR in 1997[1]) to 280 USD (~223 EUR in 1997[1]) in 0–4 years and 4–16 years old children (Su et al. 1997, Fivenson et al. 2002). The use of alternative medicine has also been included in some studies. (Su et al.1997, Emerson et al.2001, Ricci et al. 2006, Witt et al. 2009). Potential strategies have been proposed for reducing the costs of eczema, including appropriate resource utilization, early therapeutic intervention, education of the patient, parent or physician, dietary modification and environmental modification (Mancini et al. 2008). A significant cost reduction was achieved, for example, as a result of a parental training programme (Staab et al. 2002), and a decrease occurred in monthly out-of-pocket costs, from 43 USD (~31 EUR in 2007[2]) to 27 USD (~20 EUR in 2007[2]) (Boguniewicz et al. 2007). Also, no patient required additional visits to a physician apart from the regular examinations (Boguniewicz et al. 2007).

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[1] Historic Exchange Rates, 2011.
[2] European Commission. Eurostat.

Table 6. Summary of cost of illness and costing studies including infants and young children with eczema.

Authors	Perspective	N	Ages	Duration y	Currency	Costs included	Annual mean total cost (original currency) per child to				society (total, EUR)
							family	third party payer	health care, state or community	society (total)	
Cost of illness studies											
Herd et al. 1996 *UK*	patient health care society	155	19: 0–2 y 58: 2–15 y 69: 16≤ y	0.2	GBP 1996	– treatment – GP consultations – hospital consultations – income loss – clothing and laundry – other expenses	153 0: 0–2 y 2.95: 2–15 y 39.7: >16 y		97 110: 0–2 y 64: 2–15 y 36: >16 y	250	303
Su et al. 1997 [a] *Australia*	family community	48	4.5 y 0.3–15y	1	AUD 1996	– medications – health professional visits – hospital admission – income loss – employment – hours a day spent on treatment	480 mild 1712 moderate 2545 severe		662 mild 1912 moderate 3554 severe	1142 mild 3624 moderate 6099 severe	723 mild 2294 moderate 3860 severe
Rathjen et al. 2000. *Germany*	family society	204	children	0.5	DM 2000	– consultations – medications – home environmental changes – food preparations – alternative medicine – income loss	5187			8646	4421
Emerson et al. 2001 *UK*	state family	290	1–5 y	1	GBP 1996	State: consultation costs – prescribing costs Family: environment changes – over-the-counter costs – transport costs – private specialist – alternative medicine – income loss	28.94		50.65	79.59	96
Ellis et al. 2002 *USA*	third party payer	35404 private 89381 Medicaid	insured population	1	USD 1997	– inpatient – outpatient service – prescription drug		580 private 1250 Medicaid Children < 16 y: 450 private 740 Medicaid			

Study	Perspective	N	Age		Currency Year	Cost categories	Costs
Fivenson et al. 2002 *USA*	society	298	17.22 y; 19.5% <4 y; 44.6% 4–16 y; 36% adult ≥16	1	1997 USD	Direct: in- and outpatient costs – emergency – medications, laboratory, phototherapy Out-of-pocket expenses – practitioner visits – visit co pays, medications – household items, child care Productivity loss	Child < 4 y 725 / All 609; 578
Ehlken et al. 2005 *Germany*	third party payer patient society	193	23 y; 1–71 y; 32: 1–6 y 35: 7–17 y 81: >17y	1	EUR 2001	– physician visits, diagnosis – medications – hospitalization – rehabilitation – nutrition preparations – household expenses – absenteeism	526: 1–6 y / 438: 7–17 y; 766: 1–6 y / 509: 7–17 y; 176 1–6 y; 1468 1–6 y / 947 7–17 y / 1–71 y / 811 mild / 1239 moderate / 1993 severe; 1468 1–6 y / 947 7–17 y
Barbeau et al. 2006 *CANADA*	society patient	54 adults and 22 children	0.5 to 84 y	1	CAD 2001	– over-the-counter treatment – household expenses – healthcare practitioner visits – other medical services – hospitalization – absenteeism	53 mild / 138 moderate / 145 severe; 232 mild / 316 moderate / 1097 severe; 282 mild / 454 moderate / 1242 severe; 203 mild / 327 moderate / 895 severe
Ricci et al. 2006 *Italy*	family	33	2.8; 1–9 y	1	EUR 2006	– consultations – medications – special food – alternative therapies – home care – absenteeism	1254 / 694 mild / 1172 moderate / 1809 severe
Costing studies							
Paller et al. 2002 *USA*	patient	429	29% <2 y; 42 % 3–7 y; 2 % 8–15 y	postal survey	USD 2002	– over-the-counter products – prescriptions	–OCT products 72% <20 –prescriptions 41% <10 44% 11–40 14% >41
Staab et al. 2002 *Germany*	third party payer	145	Intervention 72; 2.7 y and control 73 / 3.4 y	0.5	EUR 2002	– consultations – medications	–baseline 6 mo cost 269 –after intervention 177 – cost reduction 119 / 65

37

Study	Perspective	Sample		Duration	Currency year	Cost components	Mean cost (EUR)
Verboom et al. 2002 *Netherlands*	health care provider	2809 population	26	11 mo	USD 1999	– GP visits – medication – laboratory tests – specialist	71 186 referred to a specialist
Weinmann et al. 2003 *Germany*	third party payer	91 birth cohort		8	USD 1996	– inpatient services – physician visits – physician telephone contacts – hospital outpatient services – drugs, appliances and devices – diagnosis	219 per disease year 164 mild 417 moderate 911 severe
Suh et al. 2007 [e] *USA*	third party payer	cohort study	8174: 0–20 y	12	USD 2005	– medical services – prescription costs	– 173 < 20 y – incremental cost of atopic manifestation 393 < 20 y

EUR = Euro; In the last column cost to society currencies are changed to Euro values by using either European Comission's Eurostat or Historic exchange rates.
[a] Family and community costs included; [b] Monthly costs included, postal survey; [c] Cost of treatment during the previous 6 months, at baseline and after a year were compared; [d] Medications include antihistamine, moisturizing, topical steroids and detergents; [e] Cohort study.

2.5.3 Cost of food allergy

Costing from the perspective of society as a whole is a challenging task in the case of food allergy. One framework for analysing the economic impact identified six categories of stakeholders who may be economically affected by food allergy: consumers, carers and proxy carers, health services, the food industry, employers and regulators (Miles et al. 2005). To date the economic impact of food allergy on society has been considered only in one study, in which the direct medical costs and indirect costs associated with food allergy and anaphylaxis were estimated from health care databases (Patel et al. 2011). Annual direct medical costs were estimated to be 225 million USD (~166 million EUR in 2007[2]) per year, with office visits accounting for 52% of the costs, emergency department visits for 20%, in-patient hospital care for 11% and out-patient care for 4%. Children under the age of 18 years accounted for 46% of the total in-patient costs, 31% of the costs of emergency department visits, 67% of the office visit costs and 97% of the total costs of out-patient department visits. Indirect costs were morbidity–related, i.e. they concerned the number of days of sick leave. Direct medical costs per patient were 4719 USD (~3494 EUR in 2007[2]) for in-patient care, 553 USD (~409 EUR in 2007[2]) for emergency department visits, 193 USD (~142 EUR in 2007[2]) for visits to a physician's office and 280 USD (~207 EUR in 2007[2]) for visits to an out-patient department (Patel et al. 2011).

Decision analysis has served as a means for estimating the economic impact of managing CMA from the perspective of health care insurers (Sladgevicius & Guest 2010a, Sladgevicius & Guest 2010b), publicly funded health care systems (Guest & Nagy 2009, Sladkevicius et al. 2010) and parents of CMA infants (Sladgevicius & Guest 2010a). A summary of these models is presented in Table 7. They highlight national differences in health care provision and insurance. The CMA cost to public health care ranged from 1150 AUD (~687 EUR in 2007[2]) over six months (Guest & Nagy 2009) to 1381 GBP (~2024 EUR in 2006/2007[2]) over 12 months (Sladkevicius et al. 2010). The main cost items were visits to a clinician or general practitioner (44–50% of costs) and nutrition preparations (38–87% of costs). When the chosen perspective was that of the health care insurer, the costs were 202 EUR (Sladgevicius and Guest 2010a) and 2567 EUR (Sladgevicius and Guest 2010b). In these models costs accrued from visits to a general practitioner or paediatrician (Sladgevicius and Guest 2010a, Sladgevicius and Guest 2010b). In South Africa patients pay the major share of the costs

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[2] European Commission. Eurostat.

themselves, including nutrition preparations. The nutrition preparation used depends on whether the child is treated in the private or public sector. The mothers of affected infants saw a dietician as part of a clinical visit to a paediatric gastroenterologist in 15% of cases and to a paediatric immunologist or allergist in 40% of cases (Guest and Nagy 2009). It was estimated in the Netherlands that 83% of breast-feeding mothers and 50% of bottle-feeding mothers would be referred to a dietician (Sladgevicius and Guest 2010b).

Table7. Decision analysis models of resource use and budget impact in connection with cow's milk allergy.

Authors	Perspective	Period	Cost per child	National budget impact in millions
Guest & Nagy 2009[a] *Australia*	public health care	6 months following referral to a specialist	1150 AUD	6.5 million AUD (6150 infants)
Sladkevicius et al. 2010[b] *UK*	national health service	12 months following initial presentation to a GP	1381 GBP	25.6 million GBP (18350 infants)
Sladgevicius & Guest 2010a *South-Africa*	public and private health care insurers, family	12 months following initial presentation to a paediatrician	Private sector: insurer 202 EUR patient 3634 EUR Public sector: insurer 89 EUR patient 2076 EUR	1.8 million EUR for insurers and 40.8 million EUR for patients (18270 infants)
Sladgevicius & Guest 2010b[c] *Netherlands*	health care insurer	up to 1 year of age following initial visit to a physician	2567 EUR	11.28 million EUR (4382 infants)

[a] Australian dollar 2006/2007, 1150 AUD~687 EUR in 2007[1], national cost drivers for all infants irrespective of symptoms were clinical nutrition preparations 62–65% and visits to a clinician 28%;
[b] British Pound 2006/2007, 1381 GBP~2024 EUR in 2006/2007[2], 25.6 million GBP~17.5 million EUR in 2006/2007[2]; [c] Euro 2007/2008.

It has been also shown by modelling that the adoption of new reimbursement guidelines for CMA may lead to increased health care resource use, parents' costs and costs to society as a consequence of absenteeism (Guest and Valovirta 2008), which highlights the importance of economic evaluations between new and old practices in cases of food allergy, particularly before implementation of new health policies. Epidemiological studies are also needed concerning resource use and the prevalence of allergic diseases. The incidence of food allergy testing, including skin prick testing, IgE and open food challenges, by the age of 4 years was 18% in an unselected Finnish population (Pyrhönen et al. 2011).

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[1] Historic Exchange Rates, 2011.
[2] European Commission. Eurostat.

The family perspective has been included in clinical studies describing the cost of eczema and related food allergy. Su et al. (1997) evaluated the financial cost of childhood eczema, including diet, to families in Australia and arrived at annual dietary costs of 0 AUD in cases of mild eczema, 81 AUD (~51 EUR in 1997[1]) in moderate eczema and 360 AUD (~227 EUR in 1997[1]) in severe eczema. The data were collected by means of a questionnaire covering 12 months, but no details were given about these costs (Su et al. 1997). An Italian study focused on eczema (Ricci et al. 2006) inquired about the use of food products by means of a questionnaire which asked for information on the name of the product, the cost and the quantity used in one month, and concluded that these food products accounted for 10% (117 EUR) and 25% (452 EUR) of family costs in cases of moderate and severe dermatitis, respectively. 30% of all children used food products, mainly formulas for CMA children, implying an increase of 684 EUR relative to standard dietary costs and 56% of total annual costs. Dietary costs were 506 DM (~259 EUR in 2000[2]) in a German study (Rathjen et al. 2000). From the perspective of a third party payer, the risk of a child with eczema developing food allergy was 1.8%, with an additional cost of 257 USD (~191 EUR in 2005[2]) resulting from out-patient visits and prescriptions (Suh et al. 2007). The whole picture of costs related to food allergy is fragmented, and more research is needed.

[1] Historic Exchange Rates, 2011.
[2] European Commission. Eurostat.

3 AIMS OF THE STUDY

The aim of this work was to evaluate the whole burden to the family due to an infant's food allergy and eczema during the first 24 months of age.

The specific aims were:

1. to characterize the family activities related to food allergy and eczema from the mother's perspective at the infant's ages of 12 and 24 months (I)

2. to identify mothers' perceptions of supporting or straining factors in motherhood, particularly in relation to a child's food allergy and eczema at the infant's ages of 12 and 24 months (II)

3. to evaluate HRQOL in infants with eczema and factors contributing to this at ages of 6, 12 and 24 months (III), and

4. to determine the costs to the family and to society as a whole arising from allergic diseases during the first 24 months of life (IV).

4 SUBJECTS AND METHODS

4.1 Study design for the main study

The data were collected in connection with an on-going study. A total of 256 pregnant women from risk families with allergic disease in the mother, father or sibling of the unborn child were recruited from April 2002 to November 2005 to participate in a prospective, parallel-group, combined dietary counselling and probiotics intervention study (NCT0016700; section 3, http://www.clinicaltrials.gov) (Piirainen et al. 2006, Laitinen et al. 2009). The exclusion criteria were any other chronic diseases in the mother except for allergy. The overall aims were to optimize maternal dietary intake and metabolism, to advance maternal health and to reduce the risk of disease in the child. Study visits took place three times during pregnancy and at 1, 6, 12, 24, 48 and 72 months post partum. At the first visit the mothers were randomized into three groups: dietary counselling with probiotic capsules, dietary counselling with a placebo, and controls. Clinical evaluations were performed to identify factors related to the onset of allergy and the infant's growth and dietary intake. Symptoms or signs of atopic disease were assessed at all the visits. The children were classified as healthy if they had no signs of food allergy, eczema, rhino conjunctivitis, wheezing or any other chronic disease.

4.1.2 Study design for each paper

Papers I and II: Descriptive qualitative interviews of mothers of infants with food allergy and eczema and of healthy infants at 12 and 24 months of age.

*Paper III: C*ross-sectional parental evaluation by questionnaire of infant HRQOL at the ages 6, 12 and 24 months.

Paper IV: Nested case-control cost of illness study due to infant's allergic disease (FA, eczema, asthma).

4.2 Subjects

The mothers and their infants referred to in papers I–IV were followed up from birth to 24 months between 2002 and 2007 (Figure 1).

Papers I and II: The material consisted of interviews both with mothers of 12-month-old healthy infants and with mothers of infants with eczema and/or FA of the same age, and repeat interviews with the mothers of allergic infants when they reached 24 months of age. Mothers fulfilling the criteria at the infant's visit for examination by a physician at the age of 12 months was asked for permission to perform this interview. The mothers who agreed were contacted and interviewed (Figure 1).

Paper III: Parents who consented to complete the HRQOL instrument appropriately was included (Figure 1). The HRQOL of the infants was evaluated at the ages of 6, 12 and 24 months. The presence of eczema and the severity of eczema were determined using SCORAD assessments.
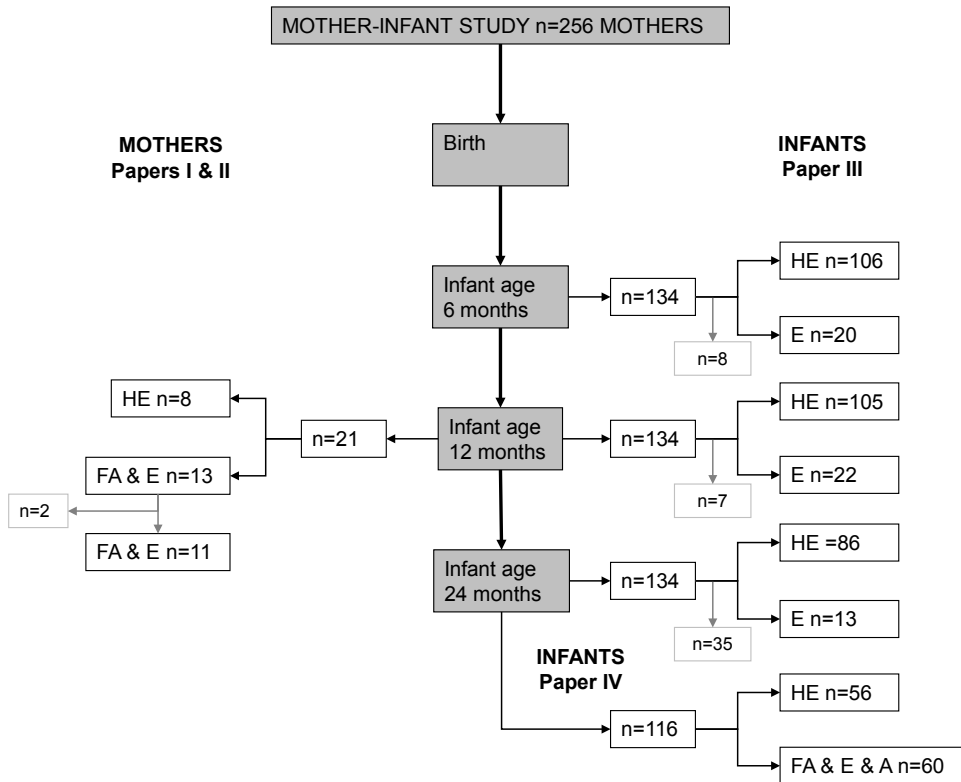

Figure 1. Study design and subjects (HE=healthy, FA & E=food allergy, eczema, E=atopic dermatitis/ eczema, FA & E & A= food allergy, eczema, asthma).

Paper IV: Data for the evaluation of allergy costs were obtained for all the infants who developed an allergic disease by the age of 24 months and for the healthy ones who did not (Figure 1). The criteria for the evaluation of allergy costs were a diagnosis of eczema (=AD), FA, i.e. cow's milk allergy, and/or an allergy to wheat, recurrent wheezing leading to a special reimbursement for asthma medication and a questionnaire completed by the parents concerning the child's diseases and medications between the ages of 12 and 24 months. An age and sex-matched group of healthy infants with no diagnosed allergic disease were monitored in the same prospective manner.

4.3 Methods

4.3.1 Diagnosis of allergic diseases

Eczema (=AD) was diagnosed according to the criteria of Hanifin and Rajka (1980), which requires the presence of 3 out of 4 major criteria which are defined as pruritus, typical morphological features and distribution, chronic dermatitis and an atopic history. The severity of AD was determined using SCORAD assessment (European Task Force on Atopic Dermatitis 1993) and classified as mild (SCORAD < 15), moderate (15 < SCORAD < 40) or severe (SCORAD > 40) (Kunz et al. 1997) at the ages of 6, 12 and 24 months.

Cow's milk and wheat allergies were verified by means of either open or double-blind placebo-controlled challenges (Isolauri and Turjanmaa 1996). Physician's diagnosed asthma was defined as a qualification for a special reimbursement for asthma medication costs. This reimbursement requires at least four attacks of wheezing with respiratory distress within a year or three attacks in a year together with a positive asthma predictive index (Castro-Rodriquez et al. 2000, Kela 2012). Infants were considered healthy if they had no diagnosed allergic disease.
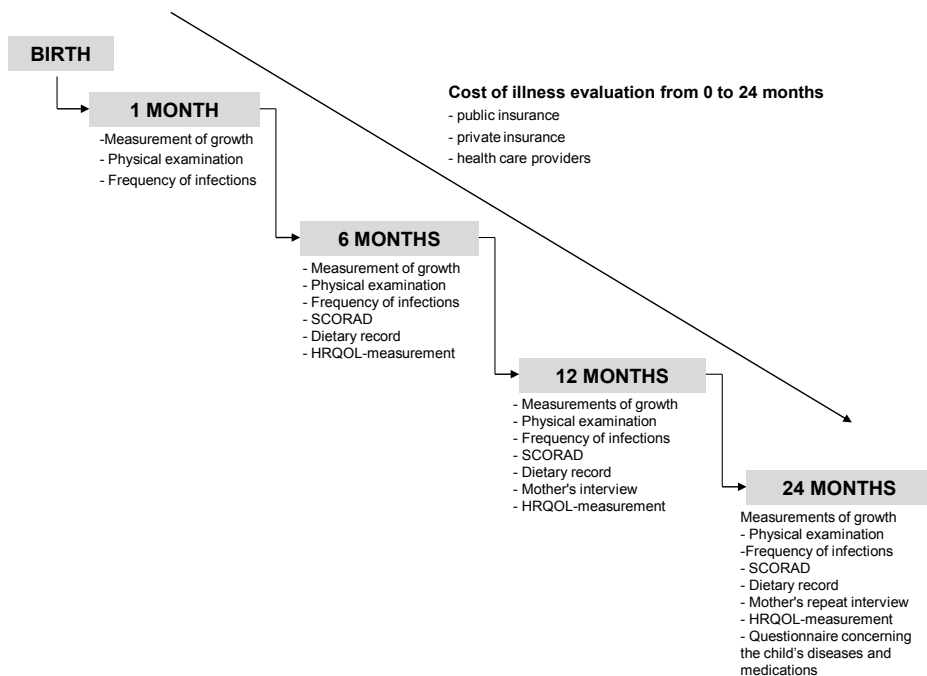
BIRTH

1 MONTH
-Measurement of growth
- Physical examination
- Frequency of infections

Cost of illness evaluation from 0 to 24 months
- public insurance
- private insurance
- health care providers

6 MONTHS
- Measurement of growth
- Physical examination
- Frequency of infections
- SCORAD
- Dietary record
- HRQOL-measurement

12 MONTHS
- Measurements of growth
- Physical examination
- Frequency of infections
- SCORAD
- Dietary record
- Mother's interview
- HRQOL-measurement

24 MONTHS
Measurements of growth
- Physical examination
-Frequency of infections
- SCORAD
- Dietary record
- Mother's repeat interview
- HRQOL-measurement
- Questionnaire concerning the child's diseases and medications

Figure 2. Summary of data collection methods.

4.3.2 Qualitative interviews

The method was "purposive sampling", which aimed to find as large a number and variety of cases as possible (Polit and Beck 2008). Semi-structured interviews were used with the mothers (I, II).

The interviews reported in paper I were concerned with the appearance of allergic symptoms, the diagnosis of food allergy and eczema and daily family life in the light of the infant's allergic disease. The mothers in paper II were asked to describe supporting and straining factors and to assess the effect of the infant's food allergy or eczema as one or other of these. The questions posed were: "*How would you evaluate (on the traditional school grading scale) your resources at the present moment? Explain why. What factors strain your resources as a mother most just now? What factors help you to manage?*" The focus was on the facts and stories recounted by the mothers about their life situations.

The taped interviews were transcribed verbatim and subjected to deductive (I, II) content analysis, focusing on their manifest textual content (Graneheim and Lundman 2004). The meaning units that conformed to the initial aims of the research were reduced to condensed meaning units (I, II) (Strauss and Corbin 1998, Graneheim and Lundman 2004). In paper I ecocultural theory (Gallimore et al. 1989) served as a framework through which the data were approached. The analysis began with listening to the interviews twice and reading the transcriptions to gain an insight as to whether there were any recognizable family themes. In the second phase the unit of analysis was an activity, a caring activity or task related to the infant's food allergy and eczema that was performed. The family activities involved in the child's allergic disease were identified on the basis of the mother's descriptions. They were further grouped into two subcategories: treatment activities and examining and diagnosing activities. These were further related to the categories of daily activities and occasional activities depending on their frequencies, and were united by the leading family theme.

In paper II the condensed meaning units were divided into two broad categories representing supporting and straining factors. This analytical process was guided and connections were made by means of the supporting and straining factors, with reference to the empowerment model for family nursing regarding the mother's personal abilities and the family's internal and external capabilities (Pelkonen 1994, Pelkonen and Hakulinen 2002). The categories were first constructed according to each mother's own description of the factors that gave her

support and those that caused strain. Comparisons were made within these two categories in terms of similarities and differences, using the chosen model to guide this organization of the data. The interviews with the mothers of 12-month-old healthy infants and those of infants with food allergy and eczema at the ages of 12 and 24 months were analysed separately. The meaning units in the interviews with the mothers of infants with food allergy and eczema that described the infant's allergy as a supporting or straining factor were analysed separately for each age group.

4.3.3 Health-related quality of life measurement

The HRQOL of the infants with eczema was measured when they were aged 6, 12 and 24 months using the Infant Dermatitis Quality of Life (IDQOL) index form, filled in by the parents (Lewis-Jones et al. 2001) (III). This questionnaire had been translated and used before on one occasion in Finland (Skarp 2005). The questions evaluate eczema-related difficulties such as itching and scratching, mood, difficulties with sleep, play, family activities, mealtimes, eczema treatment, dressing and bathing. The scoring of each question ranges from 0 to 3, with a total index score ranging from 0 to 30, the latter figure indicating the poorest QOL. A total score of 0–5 was considered to reflect a normal QOL, 6–10 a minor alteration in QOL, 11–20 a moderate alteration and >20 a marked alteration (Ricci et al. 2007). The IDQOL index also included a separately scored question in which parents were asked to evaluate the severity of eczema in their child, ranging from none to extremely severe (scored 0 to 4).

Prior to the study the IDQOL index was evaluated in infants aged 6–12 months who had been referred to hospital on account of eczema with suspected food allergy or food allergy with gastrointestinal symptoms. The index was found to be easy and quick to complete, but the evaluation confirmed the need for a separate questionnaire for infants with no eczema. A modified index questionnaire was thus formulated and tested prior the study (III) to the HRQOL of healthy infants, as no comparable validated index was available for healthy infants in this age group. The first four questions on the IDQOL index form, concerning itching and scratching, mood, difficulties in getting to sleep and sleep disturbance, remained the same, but the question on the treatment of eczema was excluded and the word "eczema" was changed to "state of health" in the other questions. An additional open question concerning the infant's overall state of health, and consequently a separate open question asking about the health of the child, was added to evaluate the possible impact of random life

events such as acute illnesses, teething and deviations from daily routines, including exceptional events in the infant's daily life, on the scoring of the index.

4.3.4 Costing

Data were obtained from the national public insurance organization, private insurance companies, health care providers and the parents. Cost included direct costs (use of primary care and hospital care services, private services, examinations and treatment, medications, formulas for infants with cow's milk allergy, dietary costs, disability allowances) and indirect costs (time off work, travel, the time spent by parents).

The data obtained from the Social Insurance Institution included costs related to use of the services of a private specialist, examination and treatment charges, medications, formulas for infants with cow's milk allergy, disability allowances and travel costs in connection with public and private sector services. These same costs were also inquired about from private insurance companies in the case of infants who were insured privately. The health care providers were asked about the use of primary and secondary care services.

The parents' travelling times and times taken to reach sources of primary care, hospital care, private services and pharmaceutical services were estimated by counting the number of visits and multiplying these by the unit costs (Hujanen et al. 2008).

The parents' time off work due to the infant's allergy was ascertained in the questionnaire concerning the child's diseases and medications. Since the mothers were on a maternity allowance for the first 9–12 months of the infant's life, the questionnaire concerning the child's diseases and medications covered the second year. The questionnaire was administered when the child was aged 24 months and included questions about the type and amount of infections, prescriptions and the amounts of medication used, the use of over-the-counter medicines, emollients and cortisone or nutrition preparations and working days lost due to the child's allergy. Under the age of 12 months these were traced from the data collected at the visits arranged at ages of 1, 6 and 12 months.

The dietary costs were evaluated from the infants' 3-day food records, including one weekend day, with household measures, at infant ages of 6, 12 and 24 months. The mothers were given personal and written instructions on recording, and the records were reviewed for completeness and accuracy by a nutritionist with the aid of a portion picture booklet. Missing

portion sizes and food descriptions were added after discussions with the mothers. Daily amounts of food were saved using the Micro-Nutrica® computer program (version 2.5, Research Centre of the Social Insurance Institution, Turku, Finland) and further transferred to Excel for cost calculation. Food prices were obtained from local supermarkets and the prices of vitamins, minerals and food supplements from the University Pharmacy. The baseline for food-related costs was set at the age of four months, when solid foods were introduced into the child's diet. When estimating dietary costs up to the 24 months, the average daily costs (EUR/d) were multiplied by the number of days in the period concerned and the product multiplied by the differences in daily costs between follow up points. Incremental dietary costs were obtained by deducting the mean annual dietary costs for the healthy infants in their first and second years from those of the allergic infants.

All prices were adjusted to the 2006 price level by reference to the cost-of-living index (Tilastokeskus 2011). Unit prices, including those of blood tests and skin prick tests, were obtained from a standard price list (Hujanen et al. 2008). Costs were allocated separately to the various payers: the family, the state and local authority, public insurance or private insurance.

4.3.5 Statistics (III–IV)

A qualitative approach was adopted in papers I–II, so that no statistical methods were applied.

To evaluate the use of the IDQOL and modified index for healthy infants in paper III, the first four questions of the index, which were the same in both questionnaires, were first compared with all the questions as means of explaining the total index score separately in both groups by linear regression analysis. Comparisons of the differences between infants with eczema and healthy infants indices were tested with the independent samples t-test. The values were logarithmically transformed (ln+1) and p-values ($p < 0.05$) were used to evaluate their significance. Fisher's exact test was used to assess differences between groups. Differences in the evaluations of infants with AD and all the HRQOL measurements at each time point were analysed with Friedman's test.

In paper IV the costs quoted in the tables include means, medians, standard deviations (SD) and ranges. Percentages were calculated from the mean values. Differences between groups were tested with the non-parametric Kruskal-Wallis test, and the Chi-Square test was used to test the difference in the number of infections between the children with and without an

allergic disease. The results were presented in the text as medians with the mean in brackets, because costs are naturally bounded by zero and have no upper bound (Drummond et al. 2005). The statistical analyses were carried out using SPSS for Windows (versions 14.0 and 17.0; SPSS Inc., Chicago, IL, USA).

4.4 Ethics

The study complies with the Declaration of Helsinki as revised in 2000. The research plan and written informed consent forms were approved separately for the evaluation of costs and HRQOL and for the interviews by the Ethical Committee of the Hospital District of South-West Finland. The researcher fully explained the potential risks and benefits at the beginning of each interview (I, II), as mentioned in the advice on the ethics of qualitative research published by Orb et al. (2001).

5 RESULTS

5.1 Characteristics of the mothers and infants

Detailed descriptions of mothers interviewed (I–II) and their infants are presented in Table 8.

Table 8. Characteristics of the mothers and their infants.

	Child age		
	12 months		24 months
	Healthy	Allergic	Allergic
Interviews, N=32, (n)	8	13	11
Interviewed at home (%)	100	92	92
Mothers			
Age (years, range)	34 (28–41)	33 (28–41)	33 (28–36)
Allergic (pollen, cat, dog, asthma) (%)	75	69	73
On maternity leave (%)	87	54	27
Married or living in common-law marriage (%)	100	92	91
With two allergic children (%)	13	38	46
Infants			
Boys/girls (n/n)	6/2	9/4	7/4
Age (mo) (mean, range)	13.1 (12–14)	13.7 (12–15)	27.2.(24–29)
Eczema (Atopic dermatitis) (%) [a]	0	61.5	27.3
Severity of dermatitis, mild/moderate (%) [b]	0	50/50	–/100
Cow's milk allergy (%) [c]	0	61.5	72.7
Allergy to wheat, oats, barley (%)	0	23	36.4

[a] Diagnosis of atopic dermatitis based on the criteria of Hanifin and Rajka (1980); [b] SCORAD <15 (mild), 15<SCORAD<40 (moderate) (Kunz et al. 1997); [c] Diagnosis based on clinical symptoms related to cow's milk or double-blind placebo-controlled cow's milk challenge (Isolauri and Turjanmaa 1996).

HRQOL measurements were included for 134 infants (boys 53%) whose parents completed the IDQOL index either two or three times (III). There were 106 healthy infants and 28 infants who developed eczema during the 24 months follow-up (III). The groups were similar in terms of birth weight and height (p=0.076, p=0.22) and the number of children in the family (p=0.98), but there were significantly more boys among the infants with eczema at the ages of 6 (45.5% vs. 90%, p=0.0001), 12 (44.8% vs. 77.3%, p=0.009) and 24 months (43.7% vs. 76.9%, p=0.036). The severity of eczema was mild in 62–70% of the infants with eczema (III).

In paper IV 116 infants were followed up for 24 months, 60 of these having allergic disease and 56 being healthy. The allergic diseases and their combinations in the infants are presented in Table 9. There were no statistically significant differences in the number of respiratory or gastrointestinal infections between these two groups.

Table 9. Numbers of infants with allergic diseases and their combinations

	Allergic
Boys/girls (n/n)	36/24
Atopic dermatitis (n)	35
Eczema[a] and food allergy (n)	15
Atopic dermatitis, food allergy and asthma (n)	3
Food allergy (n)	4
Food allergy and asthma (n)	1
Asthma (n)	2
Total	60

5.2 Family activities related to food allergy and eczema (I)

The mothers considered their child's allergy to be mainly a practical matter, which meant that the disease caused certain necessary actions in a family. These were referred to as family activities of daily routines, according to the ecocultural theory (Gallimore et al. 1989). Activities involved in the examining, diagnosis and treatment of the child's allergy contributed to the leading family theme: "Living an ordinary family life" (I). Embedded in this leading theme is the assumption that the parents arranged the activity settings for the daily routines to enable optimal child development despite the food allergy and eczema. This leading family theme could be described in terms of the following quotes,

 "If the diet is under control and he gets only food that suits him, then life is more or less the same as in any other family with children".

Activities were divided into daily and occasional ones according to their frequency. Daily activities were performed on a daily basis or several times a week, while occasional activities were accomplished on a weekly or monthly basis. The daily activities consisted of the major treatment activities presented in Figure 3. The occasional activities were categorized into examining and diagnosing activities and treatment activities (Figure 3).
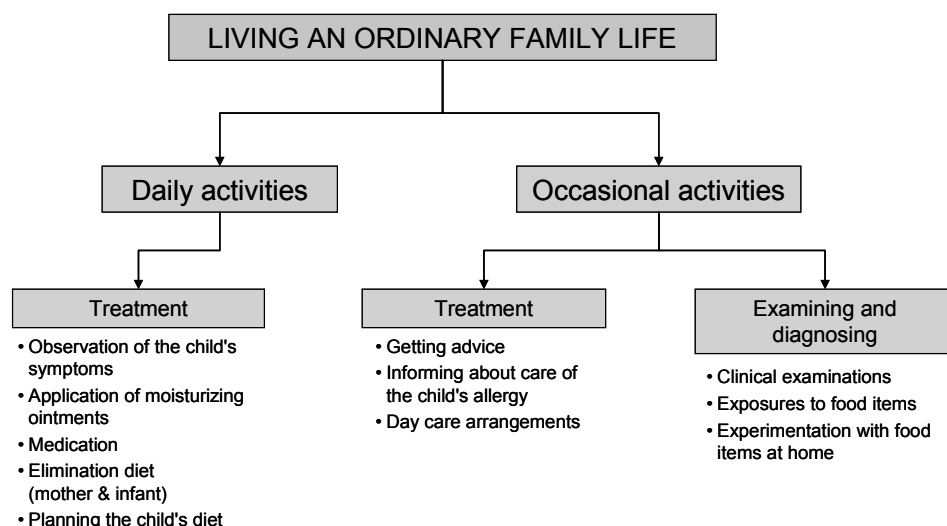
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        ┌─────────────────────────────────────┐
        │   LIVING AN ORDINARY FAMILY LIFE    │
        └─────────────────────────────────────┘
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Daily activities	Occasional activities

Treatment	Treatment	Examining and diagnosing
• Observation of the child's symptoms • Application of moisturizing ointments • Medication • Elimination diet (mother & infant) • Planning the child's diet	• Getting advice • Informing about care of the child's allergy • Day care arrangements	• Clinical examinations • Exposures to food items • Experimentation with food items at home

Figure 3. Family activities in the treatment of food allergy and eczema.

Clinical examinations included taking the infant for blood tests, skin prick tests and other medical check-ups. Exposure to food items included nutritionally essential food items if these exposures were started in out-patient clinics where it was possible to check on the appearance of early symptoms and possible severe reactions. Experimentation with other nutritionally non-essential food items in the infant's diet was done at home by parents.

Differences in activities between infants with food allergy and eczema and healthy infants
Activities were also detected in some of the families of healthy infants. The symptoms experienced by healthy infants were mild and occasional during the first 12 months of age. *Treatment activities* that were identified were *application of moisturizing ointments* and an *elimination diet for an infant*. When eczema in an allergic infant became exacerbated, the application of moisturizing had to be done 1 to 3 times a day, while in healthy infants with dry skin this was done once or twice a week or only during the wintertime. The elimination diet during breastfeeding and infancy was considered an important daily activity in families of infants with food allergy. This was not detected in families of healthy infants as such, but mainly consisted of a decision to eliminate single food items from the infant's diet just in case of symptoms. Some mothers of healthy infants introduced those food items that were usually believed to cause allergic symptoms into the infant's diet later. The occasional *examining and diagnosing activities*, including *clinical examinations, exposures to food items* and *experimentation with food items at home*, and *treatment activities*, including *informing other people about caring for an allergic child, asking for advice* and *day care arrangements* were

not detected as such in healthy infants. All of these activities thus meant an extra workload for the parents of infants with food allergy and eczema by comparison with parents of healthy infants.

5.3 Mothers' resources for caring for infants with food allergy and eczema (II)

A mother's resources are needed for the daily and occasional activities involved in caring for an allergic or healthy infant. The mothers' answers to the question "*How would you evaluate (on the traditional school grading scale) your resources at the present moment?* are presented in Figure 4. The school grading scale was classified as follows; unsatisfactory (6.0–6.9), satisfactory (7.0–7.9), good (8.0–8.9) and excellent (≥9). Nearly half of the mothers with an infant with food allergy and eczema (46%) evaluated their resources as either unsatisfactory or satisfactory more frequently than did the mothers of healthy infants (13%) at the child age of 12 months (Figure 4). One year later 20% (2/10) of the mothers of these allergic infants evaluated their resources as unsatisfactory or satisfactory still more frequently than at the infant's age of 12 months (Figure 5).
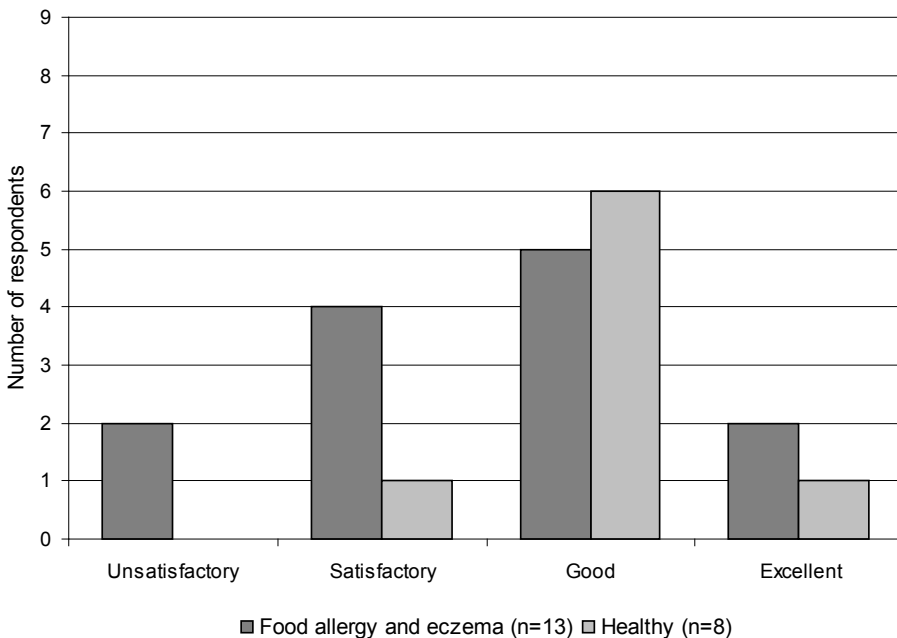
Figure 4. Mother's evaluations of their current resources for caring for an infant with food allergy and eczema or healthy infant at the age of 12 months.
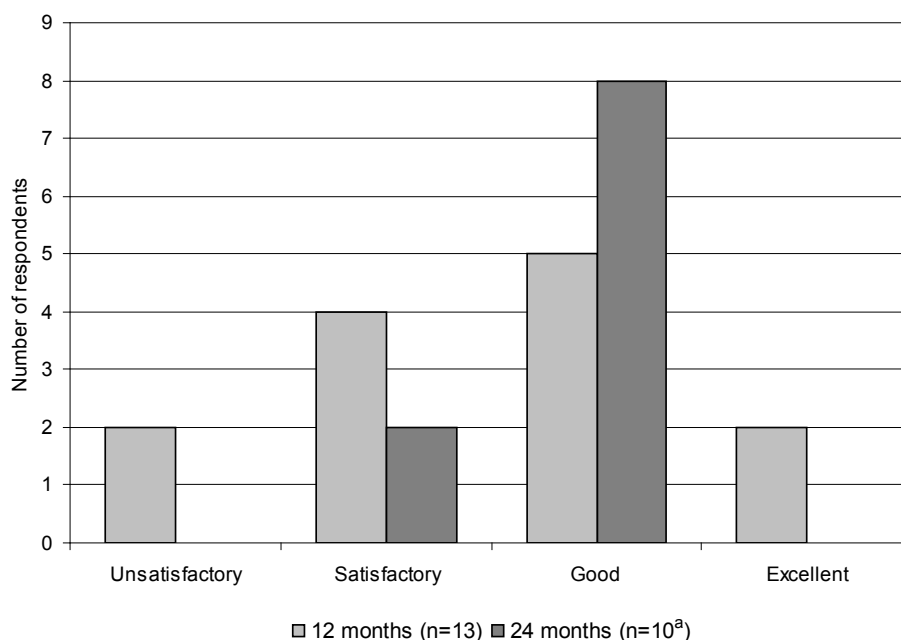
Figure 5. Evaluations by mothers of infants with food allergy and eczema of their current resources for caring infant at the age of 12 and 24 months.
[a] Evaluation by one mother was not available at 24 months.

At the age 12 months an infant's food allergy and eczema places an unspecified mental burden on the mother, together with specific problems related to food allergy or eczema (Figure 6). The mental burdens were partly everyday worries about the infant. Food allergy and the introduction of new foods into the infant's diet arose as significant topics in the interviews. Trying new foods aroused the hope of finding them suitable, and if they, too, caused symptoms and had to be avoided the disappointment was enormous. The mothers reported that it was especially depressing when this pattern went on and on. The mothers had to weigh up the severity of the symptoms against the advantage of adding a new food to the rather limited diet.

Skin problems related to eczema in infants caused unexpected reactions, and it was often hard to find the cause, which bothered the mothers. The continuous waking in the night and the resulting tiredness bothered the mothers. The infants continued to wake up in the night at the age of 24 months because of itching.

For the mothers the food allergy and eczema was not merely a straining factor but also a source of support. Specific supporting factors related to food allergy and eczema in 12 months old infant were the mother's own experience and knowledge of allergy and hopes for an improvement in the infant's allergic condition. Internal capabilities included a stable skin situation for the child and the achievement of allergen-free surroundings, while the external capabilities experienced included support from friends, grandparents and the mothers of other allergic children.

As the infants advanced from 12 to 24 months of age the situation changed (Figure 6). The causes of the mother's strain factors were still the food allergy and skin symptoms in eczema. The infant's diet usually included a wider variety of foodstuffs by this time, but if it had remained the same over the year without any significant change, this, too, tended to affect the mother negatively, in that her hope of some improvement in the situation had vanished.
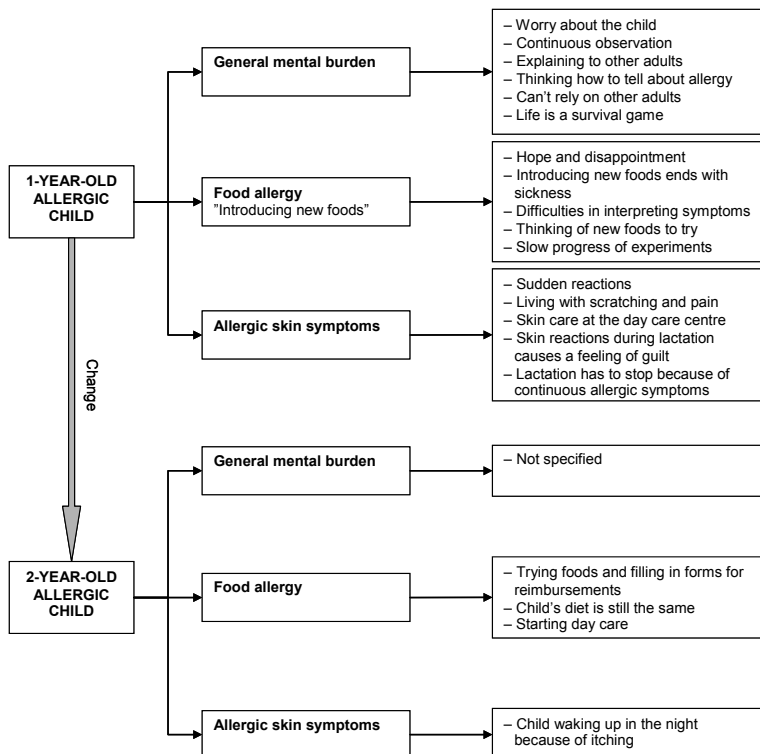
Figure 6. Infant's food allergy and eczema as straining factors for mothers.

At this time the supporting factors (II) were mainly personal psychological abilities, which were a hope for a better future, experience and knowledge of allergy, and the experience that life includes something other than the infant's allergy, e.g. through going back to work as an external capability attached to the family. By the time the child was 24 months of age the mother had learned to live with the allergic disease.

Maternity plays a significant role in life of women, it is full with contradictions, which are common to all either you have a healthy infant or an infant with chronic disease. The same capabilities could be regarded as supporting or straining depending on their extent and situation (Article II, Figure 1).

5.4 Infants health-related quality of life (III)

The total mean score on the IDQOL index was 4.15 (SD 2.96), 3.89 (SD 3.62) and 3.23 (SD 2.71) in infants with eczema at the ages of 6, 12 and 24 months. The total score was within the normal range (score 0–5) in 65%, 81.8% and 84.6% of the infants, respectively. No change in HRQOL with time was detected when the infants with eczema for whom all three QOL measurements were available and evaluated (n=13, p=0.40) (III, Figure 2).

The modified index scores for the healthy infants were 2.11 (SD 1.96), 2.05 (SD 2.12) and 2.50 (SD 2.94) at 6, 12 and 24 months, respectively (III, Figure 2). The total score was within the normal range (score 0–5) in 93.4%, 93.3% and 92% of the infants at the three time points, respectively.

The sum of the four questions that were the same in the IDQOL index and the modified index was found to differ statistically significantly between the infants with eczema and the healthy infants at 6 months of age (p=0.009, 95% CI –0.64 to –0.09) and 12 months (p=0.02, 95% CI –0.55 to –0.05), but not at 24 months (p=0.08, 95% CI –0.55 to 0.05).

The HRQOL of the infants with eczema was impaired by itching and scratching at all three points in time, by sleep disturbances at the ages of 6 and 12 months and by difficulties with the treatment at the age of 6 months. Problems in getting the infant to sleep were reported at all the time points (Figure 7). Difficulty in getting the infant to sleep was reported at all stages and disturbed sleep at 6 and 12 months in healthy infants. A detailed description of all the questions included in the IDQOL can be found in paper III, Figure 3.
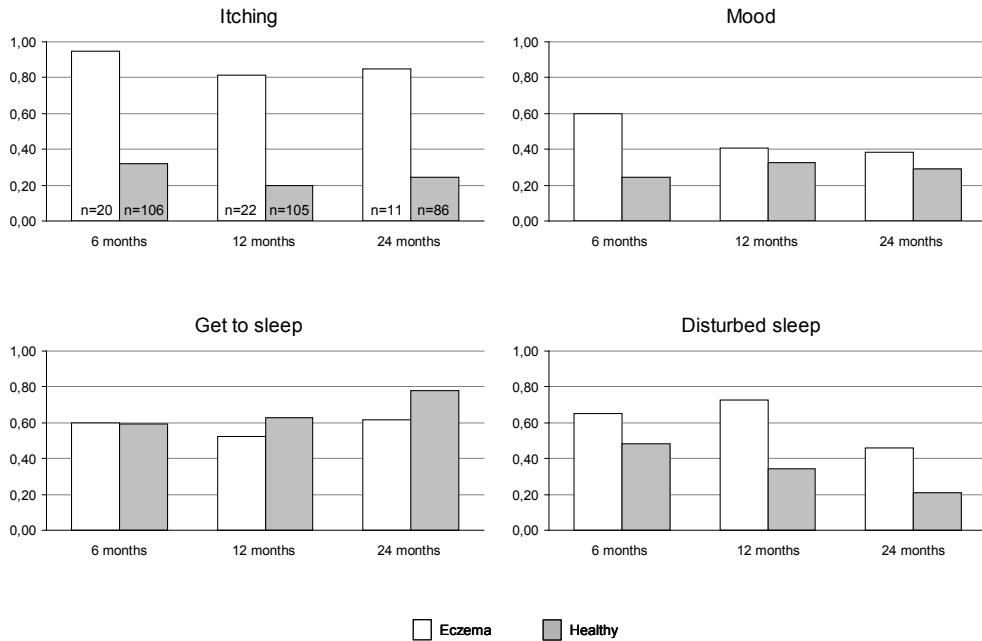
Figure 7. Mean scores on the first four questions in the index for the children with eczema (n=20, n=22, n=11) and the healthy children (n=106, n=105, n=86) at the ages of 6, 12 and 24 months.

The parents reported in the separate open question concerning the child's overall state of health that factors such as tooth eruptions, birthdays, family vacations and recent acute sickness had detracted from the HRQOL, but there were no significant differences between the infants with eczema and the healthy infants (III) (6 months, p=0.74; 12 months p=0.74; 24 months, p=1).

5.5 Cost of allergic diseases (IV)

Costs

The costs incurred to family and society by the healthy infants due to the exclusion of allergies was a median of 10 EUR (mean 50 EUR) over 24 months (Table 10). These costs were caused by the use of emollients, travel, hospital out-patient care and primary care.

The median cost in the cases of eczema was 275 EUR (mean 425 EUR), with 56% of this occurring in the first year (IV, Table 2). The largest cost components were primary care consultations, emollients, travel costs and time costs. Topical corticosteroids combined with antimicrobials accounted for 49.5% of the total costs of the treatment of eczema during the

two-year period, while the percentages for topical calcineurin inhibitors, antihistamines, other medications and topical steroids alone were 20.2%, 13.8%, 8.8% and 7.7 %, respectively.

FA caused a median cost of 3182 EUR (mean 4348 EUR) during the first two years, with 41% of this occurring in the first year (IV, Table 2). The highest costs arose from hospital out-patient care, including food challenges, formulas for infants with cow's milk allergy, disability allowances and travel costs. Medications were needed to treat eczema and food-related anaphylaxis. Topical calcineurin inhibitors comprised 38.5% of the treatment costs during the two-year period, topical steroids combined with antimicrobial substances 22.8%, topical steroids alone 20.7%, antihistamines 11.7% and other medications 6.2% in those infants who had food allergy and eczema. The diet of the infants with food allergy was a median of 47 EUR (mean 115 EUR) more expensive than that of the healthy children in the two-year period. The additional cost of the diet of the infants with food allergy relative to the healthy infants was a median of 778 EUR (mean 2041 EUR) when reimbursed formulas for infants with cow's milk allergy were included.

The median cost of asthma was 1408 EUR (mean 1858 EUR), of which 78% occurred in the second year (Table 10). The proportions accounted for by bronchodilators and asthma control medications were 15% and 85% of the medication costs, respectively. Individual differences in this group of infants were large, and the costs mainly arose from cases requiring hospital care, disability allowances and medications. A more detailed description of the cost in the first and second years can be found in paper IV. The cost components are presented in Figure 8.

Table 10. Costs of allergic diseases during the first 24 months. Modified from paper IV.

Costs (€) per child	From birth to two years			
	Mean	SD	Median	Range
HEALTHY CHILDREN (n = 56)[a]				
Primary care consultations	6	18	0	0–62
Hospital out-patient care	11	45	0	0–197
Private specialists & examinations	3	14	0	0–68
Emollients	11	26	4	0–177
Medications	3	8	0	0–48
Travel expenses	9	15	3	0–84
Time costs	6	14	0	0–51
Total	**50**	**118**	**10**	**0–619**
CHILDREN WITH ECZEMA (n = 35)[a]				
Primary care consultations	73	28	62	62–124
Hospital out-patient care	136	243	0	0–830
Private consultations & examinations	24	45	0	0–165
Emollients	66	90	40	0–456
Medications	15	29	0	0–148
Travel expenses	56	47	40	6–169
Time costs	56	32	51	26–128
Total	**425**	**364**	**275**	**94–1306**
CHILDREN WITH FOOD ALLERGY (n = 23)				
Primary care consultations	67	37	62	0–186
Hospital out-patient care	925	636	983	0–2465
Private specialists & examinations	181	365	0	0–1383
Emollients	110	124	73	0–435
Medications	64	92	26	0–290
Diet, incremental cost	116	564	47	−783–2078
Infant formulas	1925	2668	731	0–8254
Disability allowance	626	660	714	0–2205
Travelling costs	252	104	245	81–439
Time costs	197	90	179	77–410
Total (excluding diet)	**4348**	**3225**	**3182**	**628–11195**
Total (including diet)	**4445**	**3292**	**3214**	**628–11560**
CHILDREN WITH ASTHMA (n = 6)				
Primary care consultations	21	32	0	0–62
Hospital outpatient care	359	637	0	0–1568
Hospital in-patient care	260	637	0	0–1560
Private specialists & examinations	111	109	69	0–306
Medications	283	264	201	46–788
Disability allowance	415	725	0	0–1776
Travelling costs	119	131	57	20–362
Time costs	90	79	64	26–230
Time off work	169	415	0	0-1016
TOTAL	**1858**	**2024**	**1408**	**163–5408**

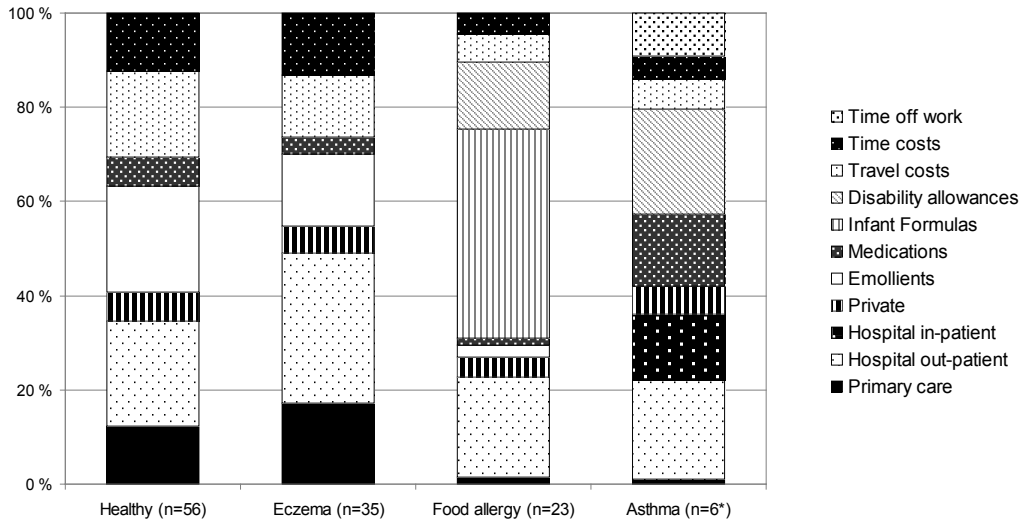[a] Healthy children and children with eczema cannot receive disability allowance.

Figure 8. Cost components of allergic diseases during the 24 months.

Cost per payer

Costs per payer are presented in Figure 9. The median costs to the family were 0 EUR (mean 27 EUR) in the healthy cases, 131 EUR (mean 183 EUR) in eczema, 525 EUR (mean 529 EUR) in food allergy and 235 EUR (mean 300 EUR) in asthma (Figure 9), and those covered by the state and local authorities were 0 EUR (mean 15 EUR) in the healthy cases, 62 EUR (mean 194 EUR) in eczema, 934 EUR (mean 898 EUR) in food allergy and 62 EUR (mean 629 EUR) in asthma. The series included 32% infants who had no private insurance, and a further 16.4% (n=14) for whom no data were available. The proportion of the total costs that was covered by private insurance was lowest in those who had the highest costs. Comparison of the costs per payer between the disease groups showed that when infants had private insurance cover this paid for 9.3% of the costs for the healthy infants, 8.3% for those with eczema and 7.6% for those with food allergy.
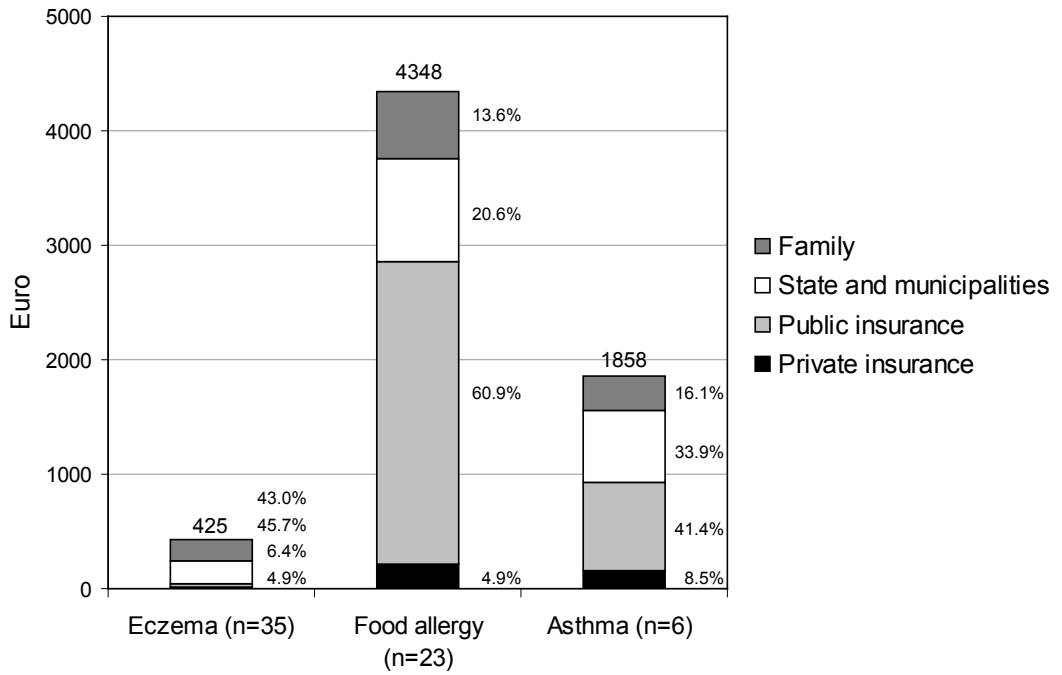
Figure 9. Costs of allergic diseases in early childhood per payer during the 24 months.

6 DISCUSSION

6.1 Family activities related to food allergy and eczema

Ecocultural theory (Gallimore et al. 1989) proposes that family life has a thematic character. The main finding in this study was the guiding family theme in caring for an infant with food allergy and eczema: "living an ordinary family life". The goal of caring for the child was revealed as being to create as natural and normal a childhood as possible and thus to allow the child to develop in the same way as in a family without chronic disease. Similar themes can also be found in earlier studies, e.g. "a sense of ordinariness" (Prout et al. 1999), or as a feature of parents' narratives about their child's allergy (Lauritzen 2004). Parents and their children with moderate asthma did not only manage the disease, but tried to maintain their sense of ordinariness, largely by means of medicines (Prout et al. 1999). In a study describing 'lay voices' on children's allergic conditions, parents' narratives about their children's illness led to the identification of three main storylines. The first was that of a child who had been ill but was now healthy again, the second depicted the child as healthy but with episodes of illness, and the third regarded the child as having a chronic health problem but still able to live in the manner of a healthy child given the right conditions (Lauritzen 2004). Although the ecocultural approach was not applied in these studies, the same kind of interpretation by the parents was reported.

The ecocultural approach has been employed mainly for studying children with developmental disabilities (Kellegrew 2000, Schneider et al. 2006), although it has been stated that it is applicable to all children in all families (Gallimore et al. 1989). Families of developmentally delayed children are engaged in trying to make the children more normal, whereas families with non-delayed children are trying to make a normally developing child less normal (Gallimore et al. 1989). On the basis of the present findings this statement seems to apply to families of allergic infants as well.

This leading theme was maintained through daily and occasional activities. The daily activities related to eczema consisted of treatment activities and the occasional examining and diagnosing activities. All other activities except the *application of moisturizing ointments* are important parts of living in a family with food allergic infants. By comparison with families of healthy infants, the distinction is clear, in that planning of the child's diet and experimentation with food items at home are necessary because they belong to the period of

introducing food items into the infant's diet during the first 12 months, although this is not necessarily planned in advance or systematic. For the parents, the infant's eczema was mainly a practical problem of a chronic disease that caused extra activities and work, similarly as described by Elliott and Luker (1997). Earlier studies have shown that a child's eczema may cause time-consuming treatments (Chamlin et al. 2004). Eczema is usually mild at the age of 24 months (Smidesang et al. 2008), which may explain why ordinary life with such infants was easier to maintain despite the allergy. Likewise, food allergy may significantly affect the preparation of the family's meals and the family's social activities, including children playing at friends' homes, birthday parties and sleepovers (Bollinger et al. 2006), and disruptions in family activities (Primeau et al. 2000, Marklund et al. 2006, Östblom et al. 2008b). Social activities were planned carefully in advance in these families of food allergic infants. The children were in any case so young that such activities played a minor part in their lives by comparison with school-aged children (Bollinger et al. 2006).

According to the ecocultural theory, families must sometimes respond in various ways to conflicting circumstances in order to create and sustain activities of daily routines, a situation referred to as the family accommodation process (Gallimore et al. 1993b). In previous reports on families with allergic children it was certain phases characterized by information needs, e.g. at diagnosis or at follow-up visits, that left a measure of uncertainty about the child's allergy and about the occurrence of new events that could be interpreted as situations where families might need to re-accommodate to daily life in a new and meaningful way (Hu et al. 2007). They experienced uncertainty regarding the appropriate balance between keeping their children safe from accidental food exposure and not jeopardizing the child's growth, nutritional status or social development (Hu et al. 2007). Health care professionals, especially dietitians counseling parents of food allergic infants and young children could target counseling into these situations where changes in diet or treatment are needed. The information could be given by using ecocultural approach and tailored to family's existing daily activities of caring for an infant with food allergy and eczema by using the results of this study.

In general, the perspective describing the impact of eczema (Su et al. 1997, Lawson et al. 1998, von Rüden et al. 1999, Chamlin et al. 2004) and food allergy (Cohen et al. 2004, Bolliger et al. 2006, DunnGalvin et al. 2010) on parents and families has prevailed. In health care the aim is to support positive normal life and not emphasizing the impact of disease. It is

natural that families may act as they are expected to behave by telling about the difficulties with treatment and disease when they meet health care professionals.

6.2 Mothers' resources for caring for infants with food allergy and eczema

The mothers' evaluations of their resources for caring for infants with food allergy and eczema and healthy infants are important. In the present material the mothers' own evaluations of their current resources revealed that 46% (6/13) felt these to be either unsatisfactory or satisfactory, as compared with 13% (1/8) of the mothers of healthy infants aged 12 months. A year afterwards there was a shift towards better resources. This difference highlights the challenge of caring for an infant with food allergy and eczema. As eczema is most often diagnosed during the first 12 months of life, this can affect the mother's resources.

Various situations related to an infant's allergy were identified that challenged the mothers. Food allergy in an infant at the age of 12 months strained the mother when new foods had to be introduced into the diet, as this process can be delayed by food allergy and the mother will often be unable to follow the suggested guidelines. Although the mothers interviewed here had learned to live with the allergy problem by the time the child reached the age of 24 months, their burden continued to be a serious one if the situation remained stable, with continuing symptoms and delayed introduction of new foods into the diet. Counseling by dietitian in the cases of food allergy support significantly these mothers and several appointments may be needed. This counselling may significantly alleviate itching if eczema is a symptom of food allergy. It is known that food allergens provoke eczema in 35% of patients (Greenhawt 2010).

Eczema, which caused the child to wake up in the night because of itching, also meant a strain for the mothers at the infant's ages of 12 and 24 months. Chamlin and colleagues (2004) categorized the effects of a child's eczema on the parents into four domains: physical health, emotional health, physical functioning and social functioning. Physical health and emotional health were consistent with the general mental burden recognised here, including all the problems described and with the same elements such as exhaustion/tiredness, sleep deprivation, disappointment, frustration and guilt. Employed mothers have been shown previously to develop feelings of guilt in situations which they interpret as implying a failure to meet up to their responsibilities (Elvin-Nowak 1999). During breastfeeding, however, mothers experienced feelings of guilt and personal responsibility for having caused the allergic symptoms in the child. A child's sleep problems when suffering from eczema have

been reported to affect maternal sleep (Moore et al. 2006), stress (Faught et al. 2007), mental health (Ho et al. 2010) and depression (Moore et al. 2006).

The supporting and straining factors formulated for the mothers of both the allergic and healthy infants in this series included the same basic elements. The profile of motherhood was constructed from dichotomies between factors such as children. The husband and the mother's work pointed to both supporting and strain factors, where a feeling of strength can revert to strain due to a sudden occurrence. These findings support those reported in earlier studies in which mothers were happy with their baby but tired by the time the child was aged 8 months (Symon et al. 2003). The mothers who suffered more stress felt much more tired and had less personal time and more work-related problems (Symon et al. 2003), and the same work-related features were to be seen in the present results among the mothers who had returned to work. Maternity thus includes conflicting situations.

The supporting and straining factors for the mothers were classified in the present case from the empowerment perspective, although the same basic elements existed as in this earlier study with regard to parenting. The concept of empowerment, which belongs to the chosen model, was adopted to describe the mothers' situations, where it was regarded as both an individual, personal process and a social process (Siitonen 1999). The outcome was that the mothers were aware of their strengths, competences and capabilities and were able to maintain their own sense of power under the changing circumstances. Empowerment can be influenced by several factors, such as the mother's values, beliefs, will and motivation, and the experience and social support received from her spouse, friends, health care professionals and other mothers (Gibson 1995). The mothers described these in the interviews as sources of support, but mothers of infants with food allergy and eczema emphasized that this enabled them to understand such an infant and sharing life with him or her. Social support has been shown to play role in a child's recovery from allergy (Gustafsson et al. 2002), but mothers have felt less socially supported than mothers of healthy children (Daud et al. 1993). Most of the supporting factors were related to a mother's personal abilities, such as experience and knowledge of allergy and the hope of recovery from allergy and a better future. Dietary counselling which aims for the successful introduction of new foods, find nutritionally comparable alternative choices to elimination diets and ensure nutritionally balanced diet may support mothers as well. Mothers obtain knowledge that is targeted to infant's current situation. These mothers living in straining situations need to be recognized and supported.

6.3 Infants' health-related quality of life

This study characterized the changes in HRQOL in infants with eczema and specified the factors that impaired the HRQOL during the first 24 months, indicating focal points for improvements in the care provided. It may be seen from the results that although the participating infants with mild or moderate eczema had a normal HRQOL on average as measured by the IDQOL index, their HRQOL was significantly impaired at the ages of 6 and 12 months compared with that of healthy infants. The situation was worst at the age of 6 months, with an improvement towards 24 months.

The HRQOL in infants with eczema was better here than in earlier studies performed using the same IDQOL index (Lewis-Jones et al. 2001, Chinn et al. 2002, Grillo et al. 2006). There are also studies where it has ranged from 5.6 to 6.85, indicating quite a low impact at baseline (Chinn et al. 2002, Grimalt et al. 2007, Kubota et al. 2009, Ho et al. 2010) and an improvement by 36–57%, resulting in a normal HRQOL (Grimalt et al. 2007, Kubota et al. 2009, Ricci et al. 2009). This also means that an improvement in HRQOL is achievable by simple means, including consultation (Beattie and Lewis-Jones 2006), parental education (Ricci et al. 2009) and new treatment options (Grimalt et al. 2007, Msika et al. 2008, Gerasimov et al. 2010). The good HRQOL found in the present infants was largely because the majority had mild dermatitis, as is typical of this age group (Smidesang et al. 2008). Previous studies had concerned children with moderate or severe eczema, often recruited from hospital in-patient or out-patient clinics or a dermatologist's practice. Also, the present children were participating in a intervention project, which enabled early detection of their symptoms and initiation of treatment by means of regular contacts at the early stages. Effective guidance of the parents regarding the care of their children has been shown previously to play an important role in reducing the severity of eczema (Grillo et al. 2006).

This deterioration in HRQOL was a result of itching and scratching, sleep disturbances, the treatment and difficulties in getting the child to sleep, the last-mentioned being a problem for the healthy children as well. The results support earlier findings that itching and scratching (Lewis-Jones et al. 2001, Beattie and Lewis-Jones 2006, Gånemo et al. 2007, Park et al. 2007, Ricci et al. 2007, Ho et al. 2010) and sleep disturbance (Lewis-Jones et al. 2001, Ricci et al. 2007, Ho et al. 2010) are specific features impairing the HRQOL. There are many cross-sectional and short-term follow-up studies from 3 to 12 weeks among these. Difficulties with the treatment were scored high at 6 months, suggesting that the parents of young children may

need simple treatment regimens and additional, effective support in managing their infant's eczema. The greatest improvements in response to treatment have been in problems encountered at mealtimes and the time taken to get the child to sleep (Beattie and Lewis-Jones 2006), which were not seen in our follow-up. Problems with getting the child to sleep have often been reported in children with eczema (Beattie and Lewis-Jones 2006, Gånemo et al. 2007, Ricci et al. 2007, Ho et al. 2010). Our findings nevertheless indicate that the time taken to get children to sleep at the ages of 6, 12 and 24 months may reflect more their age-related development, irrespective of eczema.

In infancy the parents evaluate the HRQOL on behalf of their children and the results of the HRQOL measurements are based on their experiences. When the DFI has been used together with the IDQOL index the improvements in the child's and parent's HRQOL have been of about the same magnitude. This may be due to the fact that both are a parent's evaluations and objective measures are needed to verify the real improvements. Both the infants with eczema and the healthy children had had recent acute infections, but the HRQOL was good despite these, and it is accepted that infections are part of life at this age. Although the time span for IDQOL covers the previous week, parents felt that infections may affect their infants' HRQOL for weeks. This raises a challenge for measuring HRQOL in infants and young children. The HRQOL measured with IDQOL –index was however an easy way to measure infant's well-being and changes as a result of treatment in clinical practice.

6.4 Costs of allergic diseases

This cost of illness study included direct and indirect costs caused by food allergy, eczema and asthma. Food allergy was the most expensive allergic disease, the highest costs being those arising from hospital out-patient visits, including consultations with a physician and food challenges. The results are supported by a previously presented model for the diagnosis and treatment of food allergy (Guest and Valovirta 2008). The second major cost category was treatment by means of an elimination diet and hydrolysed infant formulas. Sladkevicius and Guest used decision analysis modelling to evaluate the economic impact of managing cow's milk allergy during the first year (Sladkevicius and Guest 2010a, Sladkevicius and Guest 2010b, Sladkevicius et al. 2010), quoting an estimated cost of 2567 EUR per patient in the Netherlands (Sladkevicius and Guest 2010b) and 1381 GBP (~2024 EUR in 2006/2007[2]) in the UK (Sladkevicius et al. 2010), where 72% and 38% of this was due to extensively

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[2] European Commission. Eurostat.

hydrolyzed formulas, while the expected costs in South Africa were 3836 EUR in the private sector and 2166 EUR in the public sector (Sladkevicius and Guest 2010b). In the UK model visits to a general practitioner were the bigger cost driver, accounting for 44% (Sladkevicius and Guest 2010b). The time span in these reports was only 6 or 12 months, whereas here the infants were followed up for the first 24 months of life and thus the impact of diagnoses related costs remain less significant along time.

The family perspective was included in the South African model, where families paid a major part of the annual costs accrued, 3624 EUR in the private sector and 2076 EUR in the public sector (Sladcevicius & Guest 2010a). In our study the figure was 13%. The South African families paid for the nutrition preparations themselves, which accounted for 25–28% in Finland. Other studies have reported the annual dietary costs for families as being 81 AUD (~51 EUR in1997[1]) in the case of moderate eczema and 360 AUD (~227 EUR in 1997[1]) for severe eczema (Su et al. 1997) and have stated the annual cost of food products to be 684 EUR (Ricci et al. 2006), which approaches our result of a median of 778 EUR (mean 2041 EUR) over a two-year period. The dietary costs quoted in earlier studies have been based on crude measures compared with the dietary records and social insurance institution databases used here. Other studies also included pre-school and school-aged children (Su et al. 1997, Ricci et al. 2006).

The median societal cost of eczema was 275 EUR (mean 425 EUR) over 24 months, which represents a medium level by comparison with previously quoted annual costs of 79.59 GBP (96 EUR in 1996[1]) (Emerson et al. 2001) and 1468 EUR (Ehlken et al. 2005). The main cost categories here were primary care consultations, emollients and parents' travel and time costs. These same factors, prescriptions, over-the-counter preparations, hospital in- and outpatient care, primary care consultations, i.e. medical visits, and time off work have generally made up a significant proportion of the costs (Herd et al. 1996, Rathjen et al. 2000, Fivenson et al. 2002, Ehlken et al. 2005, Barbeau et al. 2006). Clothing and laundry and home environmental changes were not investigated here, although in other cultures they have been an important cost driver (Su et al. 1997). In one study 50% of the infants under the age of two years had no expenditure, so that the median cost was 0 GBP (Herd et al. 1996). The use of emollients was not asked about until after the age of 12 months, and instead was traced from the diaries and public and private insurance claims, so that their use may be underestimated.

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[1] Historic Exchange Rates, 2011.

Some studies have reported the cost of eczema in early childhood together with the part borne by the family (Herd et al. 1996, Su et al. 1997, Rathjen et al. 2000, Emerson et al. 2001, Ehlken et al. 2005, Ricci et al. 2006). The proportions of the estimated costs paid by the family have varied from 36% to 53%, which were close to the figures presented here (Su et al. 1997, Rathjen et al. 2000, Emerson et al. 2001, Ehlken et al. 2005, Ricci et al. 2006). Parents were asked about time off work on account of their infant's asthma, but as only one family reported having been off work for about two days, this factor was included. Elsewhere it has accounted for almost 50% of the total burden on the parents of young children (Fivenson et al. 2002), but only 5% of the costs in another connection (Emerson et al. 2001), where this aspect was included in a parents' questionnaire, as in the present case.

The prognosis for childhood eczema has been shown to be usually good, and the majority of children have mild eczema (Gustafsson et al. 2000, Smidesang et al. 2008,). Studies in which children were recruited from hospital out-patient care represent the costs of moderate to severe eczema and may give a distorted impression of the cost level if the results are extrapolated to produce national estimates (Rathjen et al. 2000).

The median cost of asthma, 1408 EUR, is comparable with the annual cost of 1386 CAD (900 EUR) to society reported earlier for children under the age of four years (Ungar and Coyte 2001), and again the main sources of expenditure were the same as reported previously: hospital admissions and medications (Ungar and Coyte 2001, Weinmann et al. 2003). Hospital in-patient care has been shown to be more expensive for younger children than for older ones (Valovirta et al. 2002).

The median was chosen to describe the costs at the group level, as the mean was affected by resource use in infants with severe disease, but in any case a significant proportion of the costs are often attributable to children with severe disease. Weinmann and colleagues (2003) reported that 20% of children with asthma incurred 76% of the health care costs and 20% of those with atopic eczema incurred 85% of the costs. There exist great variations in estimated costs ranging from 628 to 11 195 EUR in food allergy and 94 to 1306 EUR in eczema because of severity of disease and food products used.

6.5 Material and methodological aspects

The on-going prospective mother-infant study was ideal for data collection purposes, even though participation was voluntary and the participating mothers were from families with a

70

risk of allergy development in an infant. Firstly, many infants were not sensitized in the course of the mother-infant study and had no allergy-related symptoms, so that they could be included as healthy infants. Secondly, the mothers were asked by familiar nurses for their consent to be interviewed, and the nurses could provide the interviewer with the information needed to contact the mothers, a procedure that was repeated at second interview. The mothers were thus not constrained to be interviewed. Thirdly, triangulation was used in the costing study, which was easier to accomplish in the context of the on-going follow-up. As a compromise of the design chosen population examined were not randomly chosen.

Qualitative studies

Interviewing was chosen as the method for papers I and II in order to gain reliable information on the mothers' experiences. The researcher met all the families in similar life situations, which made it easier to distinguish the impact of an infant's allergy on the mother and on family life in general relative to life in a family with healthy infants when the interviews were carried out upon the infant reaching the ages of 12 and 24 months. A child's physical and psychological development inevitably presents challenges for the mother, and the age similarity of the children in the present series made the group of mothers homogeneous. In earlier studies the children's ages have varied (Chamlin et al. 2004). The interviews took place at home in most cases, which gave the researcher an opportunity to meet the mothers and their children in their natural surroundings. Eleven mothers were interviewed twice, at infant age of 12 and 24 months, which adds to the reliability of the results.

The data analysis began with transcription of the interview followed by listening to the tapes. This active listening enabled the researcher to focus on what the mothers had said. The transcribed interviews were analysed with Excel, which enabled the researcher to move back and forth between the meaning units and condensed meaning units on the screen, and to check that she had kept in touch with the original data. The trustworthiness of the findings was kept in mind throughout the study from the selection of participants and data acquisition and analysis to the writing of each paper (Lincoln and Guba 1984, Graneheim and Lundman 2004, Elo and Kyngäs 2008). The results presented in paper I were based on the mothers' perceptions of the extra care required, which were interpreted as implying family activities. The mothers were in these cases the main people taking care of their young children, and their stories were considered reliable.

In paper II the researcher posed extra questions that were equivalent to the essential ones but worded differently in order to verify the reliability of the responses, because mothers can understand questions about supporting and straining factors as applying either to everyday life or to the child's allergy. The categories were first constructed according to each mother's own description of the factors that gave her support and those that caused strain, and then matched with the model. The researcher tried to be objective in this process of categorization, and the findings were read through by an experienced nurse who had seen the families and had a long experience of allergic diseases.

The mothers interviewed were those who had expressed their willingness to participate. Some mothers had also had previous experience of allergy treatment in connection with older siblings and their own allergy, so that an allergy as such was not a new thing for them. These factors may explain why the findings were positive. Due to these facts and the small sample size, the generalizability of the results should be approached with caution, as the sample may not be representative.

Infant's health-related quality of life
The IDQOL index was chosen because it has been validated and designed to cover HRQOL in the age group concerned here. The only options available for the measurement of infant HRQOL during the planning of this study were generic, the Warwick Child Health and Morbidity Profile (Spencer and Coe 1996), Quality of Well Being (Bradlyn et al. 1993), TNO-AZL Preschool Children Quality of Life (Fekkes et al. 2000) and disease-specific IDQOL (Lewis-Jones et al. 2001). If a questionnaire in a different language is used, a simple translation is unlikely to be adequate. To be fully confident of an instrument's validity in a new language or culture, a complete repetition of the validation process is required. This applied here to the translated IDQOL index, which had been tested before in Finland (Skarp 2005). Separate assessments and a regression analysis were performed to confirm that it could be used in the present circumstances to assess healthy infants and to compare the two groups. The first four questions in the index already explained 73–76% of the total scores (III).

The measurement of HRQOL in the infants with eczema was affected by remission of eczema (Illi et al. 2004), and consequently the sample with all three HRQOL measurements for the same subjects remained small. Nevertheless, no differences in longitudinal HRQOL were found. It is particularly significant that the HRQOL was measured here in all the children over the first 2 years of life, with little age variation. The growing number of missing index values

from 12 to 24 months, at the same time as a tendency for remission of eczema is seen, might be due the lack of motivation to fill in questionnaires when the child is healthy. Furthermore, an increased number of mothers have started working again by the time their infant reaches the age of 24 months, which may lead to difficulties in arranging the assessment visits. One weakness in this study may be that the DFI was not used, as the researchers chose an alternative approach in which the mothers were interviewed. The questionnaire may not be usable as such in the Finnish culture, although it has been used in one Finnish study to date (Skarp 2005).

Costing

The fact that our data were obtained from families with a risk of contracting infant allergy means that the series may be self-selected. The costs are nevertheless related to the illness per se and the selection of the families during pregnancy does not alter the cost figures obtained. These figures may represent underestimates, as telephone calls to the health services were not included, nor was the extra time required for parents to prepare special food or the effects of differences in diet at ages from four to six months. The regular follow-ups were aimed at early diagnosis and treatment, and the changes made by the researchers to some of the children's treatment paths may have distorted the costs in this instance.

6.6 Future prospects

According to ecocultural theory, activity settings provide opportunities for children to learn and develop through modelling, joint participation, task engagement and various forms of social learning in goal-directed interactions (Gallimore et al. 1989). In this light an interesting topic for future studies would be to find out what children with food allergy and eczema really learn from these diagnosis and treatment activities and whether they learn health-promoting practices (Christensen 2004). If food allergy significantly limits food variety in the diet in early childhood, it inevitably changes taste preferences. This may further cause selective eating in school-aged children. This can be approached by using ecocultural approach.

Straining situations for mothers were revealed, as also were factors that supported mothers. Further research is needed to determine whether support for mothers based on the identification of straining situations is possible, and whether the identified supporting factors promote mother's empowerment in the long run.

Due to the changing nature of eczema in later years, the HRQOL in toddlers remains a subject for future study, especially as it would require a discussion of the differences in HRQOL and impairing factors between healthy and allergic children of the same age. Eczema and food allergy often occur simultaneously and the questionnaires could be adjusted to include both, so that they could possibly be used to evaluate HRQOL in a broader context.

In the future obtained preference weights for different levels of eczema severity and measured severity with standardized severity score for example SCORAD seems a step forward in the estimating of QALY as a basis for cost-effectiveness evaluation in the management of eczema.

7 CONCLUSIONS

This study aimed to evaluate the whole burden to family followed by infant's food allergy and eczema during the first 24 months of age including mother's perspective. The family activities related to food allergy and eczema from the mother's perspective at the infant ages of 12 and 24 months were characterized through guiding family theme: "Living an ordinary family life". The theme was seen to be attainable through daily and occasional activities involved in the management of the infant's food allergy and eczema such a way that it disturbed family life as little as possible. Advantage may be taken of such themes and activities in the treatment of allergic disease, especially at points where new or altered treatment regimens are recommended. When the themes that help to organize family life and give meanings to decisions are considered, parents may approve new treatment regimens better, and this may further enhance compliance.

Mothers' perceptions of the supporting or straining factors in motherhood generally and in relation to infant's food allergy and eczema at the infant age of 12 and 24 months were identified. Straining situations related to allergy were when food allergy delayed the entering of new foods into the child's diet, so that the variety of foods in the diet was limited compared with that of age-mates, or where itching and scratching because of eczema constantly disturbed the mother's sleep. These mothers should be identified by health care professionals and supported.

The HRQOL of infants with mild to moderate eczema was good, but poorer at 6 and 12 months than that of healthy infants, mainly due to itching and scratching, the treatment regimens and sleep disturbances. The findings indicate that simple treatment regimens targeting itching in particular are likely to contribute most to the HRQOL of infants with eczema in this age group. Problems in getting the child to sleep, however, seemed to be related more to age than to the disease.

Estimates of the costs related to eczema, food allergy and asthma during the first two years of life identified food allergy as the most expensive allergic disease. The median cost to the family during the 24 months was 131 EUR (2006) in cases of eczema and 525 EUR (2006) in food allergy. The median total costs to society were 275 EUR (2006) (range 94–1306 EUR) for eczema and 3183 EUR (range 628–11 196 EUR) for food allergy. There were great variations in costs caused by severity of the disease and infant formulas used.

The ecocultural theory integrates the findings into the overall picture of family life. The families with an infant with food allergy and eczema were trying to live a normal life. but with an occasional need to accommodate their daily routines to the realities of the child's food allergy and eczema, including treatment and management routines. Food allergy and eczema presents special challenges for a mother's resources in certain identifiable straining situations, and mothers may be empowered by means of supporting factors, which can be considered a positive force stemming from outside the family. Within the family fathers and siblings have an important role to provide support to the mothers. Society has a significant role in balancing the costs to the family through public insurance and promoting equity with families with healthy infants.

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Isokyrö, June, 2012

Soili Alanne

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