Marit Saunes

Eczema in children and adolescents – epidemiology, course and impact

The Prevention of Allergy among Children
in Trondheim (PACT) study
Young-HUNT 1995-97

Thesis for the degree of Philosophiae Doctor

Trondheim, May 2012

Norwegian University of Science and Technology
Faculty of Medicine
Department of Public Health and General Practice

NTNU – Trondheim
Norwegian University of
Science and Technology

ST. OLAVS HOSPITAL
UNIVERSITETSSYKEHUSET I TRONDHEIM

NTNU
Norwegian University of Science and Technology

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ISBN 978-82-471-3545-7 (printed ver.)
ISBN 978-82-471-3546-4 (electronic ver.)
ISSN 1503-8181

Doctoral theses at NTNU, 2012:131

Printed by NTNU-trykk

Eksem hos barn og ungdom

PACT og Ung-HUNT

Atopisk eksem er en av de vanligst forekommende inflammatoriske hudlidelser i den generelle befolkning, og opp mot 25% av alle barn i den vestlige verden er rammet. Sykdommen medfører betydelig reduksjon i livskvalitet, og utgjør også en stor sosio-økonomisk belastning for barna og deres familier. Epidemiologisk studier omkring atopisk eksem er viktig for å undersøke risikofaktorer for utvikling av sykdom, samt studere effekten av spesifikke intervensjonstiltak. Atopisk eksem forårsakes av en kompleks interaksjon mellom gener (arv) og miljø, og er assosiert med andre allergiske lidelser som astma og høysnue. Den atopiske marsjen er et begrep som brukes for å beskrive den gradvise utviklingen av allergiske lidelser, eksem starter i tidlig barndom og etterfølges så av astma og høysnue noe senere. I denne avhandlingen har vi brukt data fra to store befolknings-undersøkelser i Midt-Norge, The Prevention of Allergy among Children in Trondheim (PACT) study og Ung-HUNT 1. Vi har studert forekomst, alvorlighetsgrad, arv og den atopiske marsj hos barn (PACT) og assosiasjon mellom eksem og symptomer relatert til mental helse hos ungdommer (Ung-HUNT1).

I den første studien ble et tilfeldig utvalg av 390 2-åringer tilhørende kontroll kohorten i PACT innkalt til klinisk undersøkelse. Vi fant at forekomsten av eksem i denne aldersgruppen var relativt høy, 16.5%, men mer enn to tredjedeler av barna hadde lett/mild grad av eksem. Data fra både kontroll kohorten og intervensjonskohorten i PACT ble brukt for å studere om eksem rapportert ved alder 2 år følger en maternell eller en paternell nedarvingslinje. Informasjon innhentet ved alder 6 uker ble sammenlignet med informasjon innhentet ved alder 1 år. Eksem hos både mor og far var assosiert med eksem hos barnet, og vi fant ingen holdepunkt for at arvegangen fulgte kun en av foreldrene. Eksem hos søsken var imidlertid kun assosiert med eksem når informasjonen ble rapportert ved alder 1 år.

Vi brukte data fra kontroll kohorten i PACT for å studere den atopiske marsj. Helsedata ble rapportert da barnet var 2 og 6 år. På tross av at de fleste tilfeller av eksem i en generell populasjon er milde, fant vi at barn med eksem ved alder 2 år hadde en økt risiko for å rapportere astma ved alder 6 år sammenlignet med barn uten eksem ved alder 2 år.

I den siste studien brukte vi data fra Ung-HUNT1. Vi studerte symptomer relatert til mental helse hos ungdommer med eksem. Vi sammenlignet eksem med andre kroniske plager som hodepine og nakke/skulder smerter, og fant at alle var assosiert med økt risiko for mental "distress". For ungdommer med eksem var imidlertid denne assosiasjonen sterkere for gutter enn for jenter.

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Veiledere: Roar Johnsen, Turid Lingaas Holmen, Torbjørn Øien
Finansieringskilde: Norges teknisk-naturvitenskapelige universitet, Institutt for samfunnsmedisin og St.Olavs Hospital, Hudavdelingen

Ovennevnte avhandling er funnet verdig til å forsvares offentlig for graden ph.d. i samfunnsmedisin.
Disputas finner sted i Auditoriet, Nevrosenteret Øst, St.Olavs Hospital, Trondheim fredag 4.mai 2012, kl.12.15.

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ACKOWLEDGEMENTS

This work was financed by grants from the Faculty of Medicine, Norwegian University of Science and Technology (NTNU). Part of the work is financed by St. Olavs Hospital HF, Trondheim University Hospital, Department of Dermatology.

The research project would not have been possible without the support from many people. My sincere appreciation goes to:

-My supervisor, Professor Roar Johnsen (NTNU) who without hesitation included me in the PACT project. With his immense knowledge he introduced me to the field of epidemiology and research. He patiently guided me in the right direction at times when I was at my most stubborn, and even managed to get me back on track when I was completely lost in the pre-Alps!

-My co-supervisor, Professor Turid Lingaas Holmen (HUNT Research Centre, NTNU). She provided me with the unique Young-HUNT data, willingly shared her knowledge in the field of epidemiologic research and always encouraged me.

-My co-supervisor Assistant Professor Torbjørn Øien (NTNU), for sharing his great knowledge on all matters of the PACT study. Without the endless effort he has put into PACT the last decade, this research project would not have been possible.

-All my collegues in the PACT project for excellent collaboration, inspiring discussions and good feedback. Ola Storrø for his enthusiasm and countless hours of work in the project. Ingeborg Smidesang for discussions, laughs and her bold sense of humor. Christian Kvikne Dotterud for statistical help and feed-back during the writing-process. A special thanks to bioengineer Guri Helmersen and nurse Else Bartnes for invaluable contribution in data collection, storing and management of PACT on a daily basis.

-Head of Department of Dermatology, St. Olavs Hospital HF, Kristin Ryggen. Ever since I started my training in dermatology she has kindly challenged me, gently encouraged me and always believed in me. She even made me believe I could take a PhD! For this and more I am deeply grateful.

-Department of Public Health and General Practice, Professor Jon Magnussen, for providing me with excellent working facilities during my research.

-Professor Pål Romundstad for statistical advice and for patiently helping me with both theoretical and practical answers to all kinds of research questions whenever needed.

-Professor Luigi Naldi and his staff at the Centro Studi GISED, Bergamo, Italy. He generously gave me residence, introduced me to other research colleagues and shared his

dermatologic expertise with me in a most friendly and inspiring way. A deep-felt thanks to Eugenia Caggese and her entire family for making our stay in Italy forever memorable.
-Colleagues and friends at the third floor, ISM. A special thanks to Anita Oxaas Karslen with whom I have shared not only office, but also discussions, concerns, laughs and dreams of new mountains to climb. Thanks to Kirsti Myklestad, Elisabeth Magnussen and Signe Opdahl for having open doors and open ears whenever I was in need for that.
-Colleagues at the Department of Dermatology for providing a friendly, inspiring and fun atmosphere during clinical work.
-All midwives, health visitors and assistants working at the maternal and child health centres, and the GPs in Trondheim for their enthusiasm in including participants into the PACT study.
-All parents, children and adolescents in both PACT and Young-HUNT for their invaluable contribution conscientiously filling in questionnaires.
-Finally, to my husband Per and our children Martin and Ingunn; for everything that is important in my life.

Trondheim, January 2012
Marit Saunes

LIST OF PAPERS

The thesis is based on the following papers, which will be referred to by their Roman numerals:

Paper I

Smidesang I, Saunes M, Storrø O, Øien T, Holmen TL, Johnsen R, Henriksen AH. **Atopic dermatitis among 2-year olds; High prevalence, but predominantly mild disease – The PACT study, Norway.** Pediatric Dermatology 2008; 13-18

Paper II

Saunes M, Øien T, Storrø O, Johnsen R. **Family eczema-history in 2-year-olds with eczema; a prospective, population-based study. The PACT-study, Norway.** BMC Dermatol. 2011 May 20;11:11

Paper III

Saunes M, Øien T, Dotterud CK, Romundstad PR, Storrø O, Holmen TL, Johnsen R**. Early eczema and the risk of childhood asthma; a prospective, population-based study.** Submitted.

Paper IV

Saunes M, Smidesang I, Holmen TL, Johnsen R. **Atopic dermatitis in adolescent boys is associated with greater psychological morbidity compared with girls the same age: the Young-HUNT study.** Br J Dermatol 2007; 156:283-288

ABBREVIATIONS

AD	Atopic Dermatitis
AEDS	Atopic Eczema/Dermatitis Syndrome
CI	Confidence Interval
EAACI	European Academy of Allergology and Clinical Immunology
EASI	Eczema Area and Severity Index
EDC	Epidermal Differentiation Complex
FcεR	ε Chain of the high-affinity receptor for IgE
FLG	Filaggrin
HUNT	The Nord-Trøndelag Health Studies
IgE	Immunoglobulin E
IL	Interleukin
ISAAC	International Study of Asthma and Allergy in Childhood
MD	Mental Distress
NESS	Nottingham Eczema Severity Score
OR	Odds Ratio
POEM	Patient-Oriented Eczema Measure
SCL-5	Symptom Check List 5
SCORAD	Severity Scoring of Atopic Dermatitis index
Th1	T-helper lymphocyte type 1
Th2	T-helper lymphocyte type 2
TSLP	Thymic stromal lymphopoietin
UKWP	United Kingdom Working Party
WAO	World Allergy Organization

INTRODUCTION

One of the first individuals described with symptoms resembling atopic dermatitis/eczema was emperor Augustus (63 BC-AD 14).[1] According to the historian Suetonius (70-130 AD), he suffered from "itchy dry patches of the skin, and also from seasonal respiratory symptoms". The word "eczema" comes from the Greek word "εκξεμα" meaning "to boil out".[2] Aëtius of Amida, a writer and physician who lived some 1500 years ago was the first one known to use the word. It is said to have been the name given by ancient physicians to any fiery pustule on the skin. Since then, several descriptions have been given to the skin condition we today recognize as eczema. In 1844 Ferdinand Ritter von Hebra, professor of dermatology in Vienna, described a condition with chronic, recurrent, intensely pruritic papules and nodules located to the limbs and trunk and this became synonymous to the most severe types of eczema among children and adults (prurigo ferox).[3] Another milestone in the attempt of describing atopic dermatitis/eczema came in 1892 by Ernest Henri Besnier. He described a disease featuring chronic relapsing lichenified lesions with involvement of the flexures.[4] In many European countries the term prurigo Besnier is still used to describe atopic dermatitis/eczema. The word "atopy" is derived from the Greek word "ατοπια", meaning "out of place" or "unusual". In order to emphasize the association of eczema to allergic rhinitis and asthma, Wise and Sulzberger introduced the term "atopic dermatitis" in 1933.[5] Since then, this term has been prevailing in the dermatological community.

Figure 1. Bust of emperor Augustus. From Uffizi Gallery, Florenze, Italy.

BACKGROUND

General

Epidemiology is defined as "*the study of how diseases are distributed in populations and the factors that influence or determine this distribution*".[6] A major role of epidemiology is to describe and provide clues to changes that take place over time regarding health problems presenting in the community.[7] Atopic dermatitis is one of the most common inflammatory skin diseases in the general population. It has great impact on patients and their families' quality of life and is a major socioeconomic burden.[8] Epidemiologic studies on atopic dermatitis is helpful not only in defining disease burden in a population, but also in investigating risk factors for disease and serve as a basis for the development of specific prevention strategies.

Eczema and other allergy related diseases – definitions and key concepts

The Skin

The skin comprises three layers; the subcutis, the dermis and the epidermis.

The subcutis contains subcutaneous fat as well as loosely woven connective tissue. It functions as an energy reservoir and also as insulation. In the dermis, the connective tissue is more compact and elastic. Dermis also contains sweat-glands, hair follicles and certain cells such as T-cells, dendritic cells, macrophages and mast cells.

The epidermis is the outer layer of the skin. Epidermis acts as a physical barrier against harmful irritants and organisms, and prevents water-loss from the body. It consists of a stratified squamous epithelium with no blood vessels, and a basal membrane separates it from the dermis. The main cell-type is the keratinocyte. They accumulate keratin and achieve a flat appearance as they move outward and finally rub off. Other cell-types in the epidermis are melanocytes, Langerhans cells and Merkel cells. The upper layer of the epidermis, the stratum

corneum, forms the actual barrier. Disturbance of the pH of the stratum corneum followed by changes in skin ceramides as well as alterations in expression of enzymes involved in epidermal adhesion structures can contribute to the breakdown of the epidermal barrier in patients with atopic dermatitis/eczema.[9-11] Also located in the epidermis is the protein filaggrin (FLG). This protein is essential in maintaining the skin-barrier and preventing trans-epidermal water-loss.[12, 13]

Nomenclature

Over the years, more than 20 different names have been used to describe the disease we today refer to as atopic dermatitis /atopic eczema. The disease includes several phenotypes with certain clinical characteristics in common, and the terms dermatitis/eczema are often used interchangeably. Allergen-specific immunoglobulin E (IgE) sensitization is clearly associated with atopic dermatitis. Patients with atopic dermatitis are, however, truly atopic in the sense of IgE sensitized in only about one third of the cases.[14] This led The European Academy of Allergology and Clinical Immunology (EAACI) nomenclature task force to propose a new diagnostic classification of allergic skin disorders in 2001.[15, 16] EAACI defines hypersensitivity as "*objectively reproducible symptoms or signs, initiated by exposure to a defined stimulus at a dose tolerated by normal subjects*". Allergy is "*a hypersensitivity reaction initiated by immunologic mechanisms"* and atopy is *"a personal or familial tendency to produce IgE antibodies in response to low doses of allergens, usually proteins, and as a consequence develop typical symptoms such as asthma, rhino-conjunctivitis or eczema/dermatitis*".[16] Instead of atopic dermatitis/eczema, the task force proposed the term atopic eczema/dermatitis syndrome (AEDS). In order to create a globally acceptable nomenclature for allergic diseases, the World Allergy Organization (WAO) revised the EAACI Nomenclature Position Statement in 2003.[17] This resulted in "dermatitis" as an

umbrella term for a local inflammation in the skin. In addition, the term "eczema" replaced AEDS. (Fig.2)

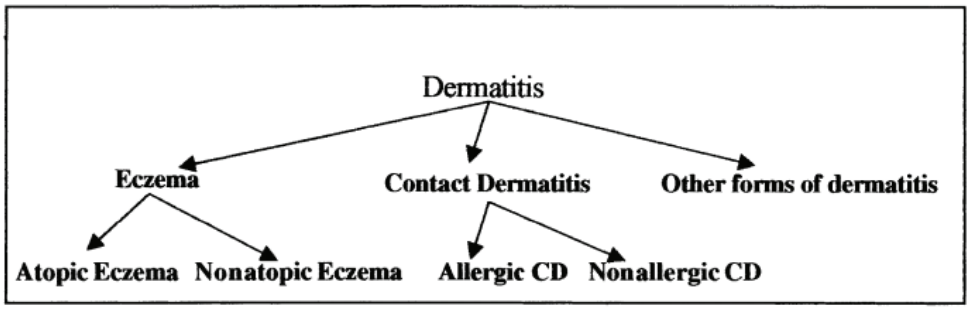

Figure 2. Nomenclature for dermatitis (Reprinted from *J Allergy Clin Immunology*, Vol 113(5), May 2004, Johansson SG et al. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003, pp832-6. Copyright (2004), with permission from Elsevier.)

When used as recommended by WAO, eczema is used when sensitization status is unknown. Atopic eczema is used when sensitization is positive.

Point of clarification

In the four papers included in this thesis, both "atopic dermatitis" and "eczema" has been used. In paper I and IV, the term atopic dermatitis is used in the WAO meaning "eczema". When referring to other studies, atopic eczema/dermatitis and eczema are used in line with how the authors have used the term.

Eczema

Epidemiology

Early epidemiologic questionnaire-based studies on eczema reported prevalence estimates in the range from 1.1% to 3.1%.[18] Studies conducted in the 1980s and 1990s revealed prevalence estimates up to 26%.[19] Also within Norway, the reported prevalence has varied between 25%-26% in the north and southwest, and 8% in Oslo.[19-21] Absences of unambiguous diagnostic criteria, use of different prevalence measurements and studies of different age-groups have, however, made comparison between studies challenging.

To attain a better global understanding of the allergic and non-allergic diseases, the International Study of Asthma and Allergy in Childhood (ISAAC) Steering Committee was established in 1991. As of today, more than 100 countries and about 2 million children have participated in this comprehensive epidemiologic study. ISAAC has conducted a systematic comparison between children 13-14 years of age and children 6-7 years of age in different countries. The first results were published in 1998.[22] Children self-reported through one-page questionnaires and the variations in prevalence of the different allergic diseases were striking throughout the world. Some of the highest prevalence of eczema was found in northern Europe (Finland, Sweden and United Kingdom). Three different phases of the ISAAC has been completed,[23, 24] and so far the findings suggest that the increase in prevalence has little to do with allergy.[23]

In a summary of studies measuring prevalence of eczema from 1990 to 2008, 48 different studies were identified, of which 23 included children under the age of 6.[25] The point prevalence varied from 1.0% in South-Africa (age 3-11)[26] to 24% in Japan (age 5-6).[27] The period prevalence varied from 1.8% in Ethiopia (age 1-5)[28] to 16.5% in the UK (age 1-5).[29] The highest cumulative incidence where found among 3 year-olds in Denmark, 44.0%.[30]

Clinical features

Eczema is a chronic, relapsing, inflammatory skin disease and the main symptoms are dry skin and pruritus.[31] In addition, there are skin lesions on typical locations such as flexures of knee and elbow, neck and face. These lesions are characterized by poorly defined erythema with edema, vesicles and oozing in the acute stage and skin thickening (lichenification) in the chronic stage. Typical location of the eczema varies with age.[32] In infancy (0-1 year), the eczema is often localized to the cheeks and the scalp in addition to the trunk and the extensor surface of the extremities. During childhood (1-4 years) the eczema can still be located on the extensor side of the extremities, but also on the flexural areas. In addition, the mouth, eyelids, neck and hands might be involved. Children from 4-16 years usually have eczema on the flexural areas, as well as on their hands and feet. Adults (over 16 years) tend to have involvement of their face, upper body, flexural areas and hands.

Etiology - Genetics

It is a well-established fact that atopic dermatitis is caused by an interaction between genes and environmental factors. The genetic component is demonstrated in twin studies, were the concordance rate for monozygotic twins are higher than among dizygotic twins.[33]

Genetic studies have identified several possible eczema loci located on chromosomes 1q21, 3q21, 3p26 and 17q25.[34-40] In addition, other loci such as 20p, 16q, 4p, 18q, 13q and 15q have been mapped and showed suggestive evidence of linkage. The region of highest linkage was identified on chromosome 1q21. Recently, a genome-wide association meta-analysis including 16 different European cohorts identified three new risk loci for atopic dermatitis.[41] In addition to linkage approaches, several candidate genes have also been of interest in studying atopic dermatitis. In the last years the gene encoding filaggrin (FLG) have been investigated in several studies.[12, 42, 43]

FLG is a large filament aggregating protein located in the granular layer of the epidermis. Its precursor is profilaggrin, and when cleaved every protein of profilaggrin forms 10-12 copies of FLG.[12] FLG is essential in building the keratin filaments into tight bundles, which lead the cells to collapse into flattened squames.[44] FLG is also essential in maintaining the skin barrier and preventing trans-epidermal water-loss. The gene encoding FLG is located on chromosome 1q21, as is a cluster of genes known as the Epidermal Differentiation Complex (EDC). Two common loss-of-function mutations in the gene encoding filaggrin, R501X and 2282del4, have been shown to be the cause of ichthyosis vulgaris. In addition, these mutations are major risk factors for the development of atopic dermatitis as well as asthma associated with atopic dermatitis and systemic allergies. The mutations are relatively common, and occur in approximately 9% of individuals of European origin.[12] Among European patients with atopic dermatitis, this mutation is identified in about 30%.[9]

When studying the family history of atopic dermatitis in an epidemiological perspective, a maternal line of inheritance is most often reported.[45-47] Later studies on family history have indicated that a paternal line of inheritance is equally related to disease development as the maternal line.[48, 49]

Etiology - Environmental factors

The increase in allergy related diseases over the past decades indicates the importance of an environmental influence. The "hygiene hypothesis" was first introduced in 1989 by a British study, hypothesizing that declining family size, improvements in household amenities and higher standards of personal cleanliness had reduced cross infections in young families, and thereby led to an increase in allergic diseases such as hayfever and eczema.[50] Findings from a German study, with increase in incidence of atopy and hayfever among children in former East-Germany, led investigators to believe that the changes were related to our Western

lifestyle.[51] Normally, microbial exposure in early life will make the immune system switch from a Th2 dominant response (present at birth) to a Th1 dominant response. Lack of this microbial environmental exposure in early life may lead the immune system to remain in a Th2 dominant, allergy-primed state. The protective effect of hygiene-related factors (such as birth order/family size, day care attendance and exposure to farm life) observed in several studies has mainly been related to allergy, hayfever and asthma.[52-60] The same risk factors that consistently are associated with asthma do not hold true for eczema.[52, 61] As the hygiene hypothesis has little to do with hygiene the way we usually define it, suggestions have been made to change the term to "the microbial deprivation hypothesis".[62] Several authors have studied the gut and differences in the composition of the intestinal microflora between allergic and non-allergic young children.[63-65] The first attempt to introduce the hygiene hypothesis into clinical practice was done by oral administration of probiotics. The aim was to prevent allergies in children.[66] Since then, several studies on probiotics and possible prevention of allergies/allergy related diseases have been conducted. Although results have been conflicting, there is some evidence to suggest that probiotics given as a supplement ante- and postnatal can reduce eczema risk in infants from high-risk families.[67] In a sub-study from PACT women received probiotics from week ≤ 36 of pregnancy and the three first postnatal months during breastfeeding. The cumulative incidence of eczema at age 2 years was significantly reduced in the offspring of those without a family history of eczema.[68]

Other environmental risk factors for eczema not directly related to the hygiene hypothesis have also been investigated, and there is some evidence of a higher risk of eczema for those living in urban compared to those living in rural areas.[69] There have also been studies showing that environmental factors, such as exposure to cat within the first year of life of those carrying FLG mutations, can alter the expression of different genes.[70] Environmental

factors easily manipulated at a population based level in order to prevent further increase in eczema prevalence have so far not been identified.[25]

Pathogenesis

During the last decade there has been a paradigmatic shift in our understanding of the mechanisms causing eczema, with a switch from a purely immunological concept to a combination of structural abnormalities and immunological dysregulation.[71] There is a close and complex relationship between the skin barrier and the immune abnormalities, and this relationship is not yet fully elucidated. The skin inflammation in ezema is characterized by an infiltration in the skin of activated CD4+ T-lymphocytes, mast cells, dendritic cells, macrophages and eosinophilic granulocytes.[72] When proteins penetrate the skin, they will be recognized by the dendritic cells. The dendritic cells migrate to the regional lymph node where they activate naïve T-cells into differentiated Th2-cells. These Th2 cells produce IL-4 and IL-13 which in turn activate B-cells into IgE-producing plasma-cells. IgE binds to the mast-cell receptor FcεR and under normal circumstances this will lead to the development of tolerance. In patients with allergies, however, re-activation of the FcεRs by antigens will trigger a cascade of intra-cellular signals leading to mast-cell deactivation. This can cause an allergic reaction either locally or systemically.[73] The cytokine thymic stromal lymphopoietin (TSLP) also have a central role in the development of allergic responses. TSLP is a potent activator of the dendritic cells leading to a Th2 polarized cytokine-profile dominated by IL-4, IL-5 and IL-13 as well as production of several potent chemokines. In addition, TSLP is an important activator of mast cells and is up-regulated in keratinocytes of atopic dermatitis skin lesions.[74] Another important subgroup of T-cells in atopic dermatitis is the Th-17 cells. Th-17 cells activate neutrophilic granulocytes and produce IL-17 and IL-22. These two interleukins are activators of the keratinocytes.

There are also other factors important for the maintenance of AD. Human skin's innate immune system produces antimicrobial peptides such as cathelicidin, human β-defensins and dermcidin. These peptides accumulate in skin affected by inflammatory diseases. In a study comparing psoriasis and AD, cathelicidin and human β-defensin2 was significantly decreased in the skin from patients with AD.[75] The up-regulation of IL-4 and IL-13 in atopic skin could account for the low expression of human β-defensin2. This down-regulation of antimicrobial peptides in atopic skin makes it more difficult to manage microbial infections such as *Staphylococcus aureus*, fungi and viruses.[76] Most patients with AD have their skin colonized with *S.aureus*. Suppression of the innate immune system, scratching with increased binding of *S.aureus* and release of *S.aureus* enterotoxins all contribute to severity of the disease, sensitization and increased inflammation.[9, 77]

IL-31 is a T-cell derived cytokine associated with itch, and is over-expressed in AD lesional skin.[78] In a murine model antibodies against IL-31 reduced scratching behavior, but did not affect the amount of skin lesions.[79]

When the foetus is *in utero*, it has a Th2 dominant lymphocyte and cytokine profile. This is of crucial importance in order for the maternal immune system to accept the foetus.[80, 81] Postnatal, probably as a consequence of stimulation by different infectious agents, the Th2 profile characteristic of the adaptive immune system changes into a Th1 profile characteristic of the innate immune system.[82] This skewing of the immune system towards a Th1 profile does not occur during the first month of life in atopic individuals, and atopic individuals will maintain immunological reactions of Th2 type as well as a Th2 cytokine profile.[83] Factors related to the Western life-style leading to reduced bacterial diversity, such as vaccination, increased use of antibiotics and fewer siblings, among others, are also thought to support the development of this Th2 dominance.[50, 51, 84, 85] This immunological "imbalance" can, however, only partly explain the complex immunology leading to allergic diseases such as

eczema. More recent studies have hypothesized that regulatory T cells and their cytokines play an important role in the protection against allergies. Microbial stimulation of dendritic cells via Toll-like receptors in the gastrointestinal mucosa or other lymphoid tissues may induce this protection.[86]

Diagnostic criteria

When studying atopic dermatitis different diagnostic criteria have been used. Brenninkmeijer el al have identified ten different criteria and evaluated the evidence concerning the validity of these different criteria (Table 1).[87]

Criteria list	Requirements (number of criteria)
Hanifin and Rajka diagnostic criteria, 1980	3 major + 3 minor (27)
Kang & Tian diagnostic criteria, 1989	1 basic + 3 minor (5)
Schultz-Larsen criteria, 1992	≥ 50 points (6)
Lillehammer criteria, 1994	Visible eczema + 4 minor (12)
U.K. diagnostic criteria, 1994	Pruritus + 3 minor (6)
ISAAC questionnaire, 1995	Score ≥ 3 (7)
Japanese Dermatology Association criteria, 1995	All 3 features (3)
Criteria of Diepgen, 1996	≥ 10 points (8)
Millennium diagnostic criteria, 1998	Allergen-specific IgE + 2 principal (4)
Danish Allergy Research Centre (DARC), 2005	3 features (3)

ISAAC, International Study of Asthma and Allergies in Childhood.

Table 1. Different diagnostic criteria for atopic dermatitis (Copyright 2008 Wiley. Used with permission from Brenninkmeijer EEA et al,Diagnostic criteria for atopic dermatitis: a systematic review. Br J Dermatol. 2008 Apr;158(4):754-65. John Wiley and Sons)

Hanifin and Rajka diagnostic criteria from 1980 are the most well-known. In order to be identified as a case the person under study is required to have three out of four major criteria, or four out of five in a more recent version, in addition to three out of 33 minor-/sub-criteria.[88, 89] Despite varying specificity the validity in two hospital-based studies showed good

outcomes.[90, 91] However, due to the long list of minor criteria, out of which some are nonspecific, the criteria are not suitable for epidemiological studies.

The United Kingdom working party (UKWP) diagnostic criteria were developed as a refinement of the Hanifin and Rajka criteria and are recommended used as a 12 month period prevalence measure.[92] This set of criteria is the one mostly validated both in hospital and community settings. In a community survey in London the UK criteria had a sensitivity of 80% and a specificity of 97%.[87, 90, 93]

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Severity outcome measures

A systematic review performed by Schmitt et al identified 20 named scales of eczema outcome measure.[94] Only three of them, SCORAD (Severity Scoring of Atopic Dermatitis index), POEM (Patient-Oriented Eczema Measure) and EASI (Eczema Area and Severity Index) had been tested sufficiently and performed adequately. NESS (Nottingham Eczema Severity Score) was found to have an adequate inter-observer reliability.

The SCORAD system was developed as a consensus by the European Task Force on Atopic Dermatitis in 1993.[95] EASI is validated in several studies, all of whom are carried out in secondary/tertiary care, whilst POEM also is validated in primary care.[94]

NESS is a refinement of the Rajka and Langeland grading system proposed in 1989.[96, 97] This scoring system meets the requirements of a population research tool, such as simplicity and good validity. It also incorporates the chronicity, extent and intensity of the disease. The scoring system is, however, only validated for children 1-5 years of age.

Because outcome measures are so different in different trials, therapies evaluated in different studies are not always comparable. As a response to this, an international Delphi exercise on outcome measures for atopic dermatitis – Harmonizing Outcome Measures for Eczema (HOME) has been held.[98] Consensus was achieved for inclusion of symptoms, physician-assessed clinical signs and a measurement for long-term control of flares in the core set of

outcome domains for eczema trials. The tools used to assess these outcomes are, however, yet to be agreed upon.

Allergic diseases related to eczema

Eczema is closely related to other allergy related diseases such as food allergy, asthma and rhino-conjunctivitis. In children symptoms of eczema often precedes symptoms from the airways, and early manifestation of eczema is observed to be associated with an increased risk of asthma and rhino-conjunctivitis.[99-101] The atopic constitution starting with food allergy and proceeding to eczema, asthma and rhino-conjunctivitis is often referred to as the atopic march. Food allergies will not be covered in this thesis.

Asthma

Asthma is defined as a chronic inflammatory disorder of the airways and is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest-tightness, and coughing.[102] In children, asthma is described as "*repeated attacks of airway obstruction and intermittent symptoms of increased airway responsiveness to trigger factors such as exercise, allergen exposure and viral infections*".[103] It is a heterogenic disease, and in children 5 years and younger the symptoms are variable and non-specific.[104] Since main pathologic hallmarks cannot be assessed routinely in this age-group, a descriptive approach of recurrent episodes of chough and/or different types of wheeze has been recommended. Because there are differences in asthma presentation among children in different age-groups, both diagnostic and treatment strategies are based on age.[105] In infants (0-2 years), persistence of symptoms is a major indicator of severity. If the infant has wheezed on most days of the week during the last 3 months, a diagnosis of persistent infantile wheeze should be made. In pre-school children (3-5 years) asthma diagnosis is made if the

child has persistent symptoms during the last year. Symptoms can be virus-induced, exercise-induced or allergen-induced. School-children (6-12 years) also have persistence of symptoms during the last year as the key differentiator. In this age-group, however, allergen-induced symptoms are more common. Diagnosis of asthma in young children is only possible through long-term follow-up.

Early allergic sensitization is a major risk factor for persistent asthma.[104, 106, 107] In a large cross-sectional study performed in 8-12 year old children according to standardized methodology of Phase Two of the ISAAC the link between atopic sensitization and asthma symptoms differed strongly between different populations and increased with economic development.[108] Current wheeze attributable to atopic sensitization ranged from 0% in Ankara (Turkey) to 93.8% in Guangzhou (China). In a Norwegian study, where dispensed anti-asthmatics were used as a proxy for current asthma, the prevalence of asthma among 7-years old children was 6.5%.[109]

Management of asthma for children up to 5 years of age are given by the Global Initiative of Asthma (GINA)[102], whereas the PRACTALL consensus report also give recommendations for treatment of older children.[105]

Allergic rhinitis

Allergic rhinitis is characterized by episodes of sneezing, itching, rhinorrhea and nasal obstruction resulting from an immunologically mediated hypersensitivity reaction in the nose.[15] Conjunctivitis often accompanies the rhinitis and whenever necessary the two terms combine, as in allergic rhino-conjunctivitis. Allergic rhino-conjunctivitis is mostly IgE mediated. Classification of allergic rhinitis according to duration and severity is suggested by the World Health Organization initiative, “Allergic Rhinitis and Its Impact on Asthma”,

(ARIA).[110] Allergic rhinitis is subdivided into intermittent allergic rhinitis (less than 4 days a week or less than 4 consecutive weeks) and persistent allergic rhinitis (more than 4 days a week for more than 4 consecutive weeks), and classified as "mild" or "moderate/severe" depending on severity of symptoms and impact on social work, school and work. The prevalence of reported rhinitis-symptoms in 6-7 years old children from ISAAC phase III varies from 2.2% in Iran to 24.2% in Taiwan.[111] In a Norwegian study among 9-11 years old children the prevalence of self-reported symptoms of allergic rhinitis had increased from 16.5% in 1985 to 29.6% in 2000.[112] In a French study, reported prevalence of symptoms of allergic rhinitis among 18 months old children were 9.1 %.[113] Diagnosis of allergic rhinitis in preschool children is difficult, as symptoms resemble those of infectious rhinitis. The clinical definition of allergic rhinitis implies knowledge of immune response. Since clinical examination of large populations represents a major challenge, standardized definitions of allergic rhinitis suitable for use in an epidemiological setting are lacking.[110] This makes comparison of prevalence of allergic rhinitis in different studies difficult.

The atopic march

The natural history of atopic manifestations and the subsequent age-dependent progression of different atopic manifestations are often referred to as the atopic march.[114, 115] The majority of children with eczema appear to "grow out" of their disease, and about 60% of childhood patients are free of disease symptoms in early adolescence.[116] However, a family history of atopy, early onset of eczema, severe eczema and early sensitization are commonly held to be the main risk factors for developing asthma or allergic rhino-conjunctivitis. Some authors have argued that rather than a progressive development from atopic dermatitis to asthma, a distinct phenotype of atopic dermatitis co-existing with wheeze predisposes for asthma.[117] Others have found that in non-sensitized children eczema rather than wheeze or rhinitis

predicts subsequent sensitization.[118] The skin barrier dysfunction with the chronic skin inflammation can facilitate penetration and sensitization to allergens and thus the transition from non-atopic to atopic eczema. In this way the skin can be the entry point for further allergy related disorders, and the start of the atopic march.[9, 119] Support to the role of the barrier dysfunction and its importance in the pathogenesis of sensitization is given by the findings of an increased risk of IgE mediated peanut allergy among people with FLG mutations.[120] Several investigators have argued that a possible prevention of the atopic march can be achieved by therapies that modify eczema severity and restore the skin barrier.[115, 121, 122]

Impact of eczema

Eczema adversely affects the quality of life primarily in patients suffering from the disease, but secondarily also in people living in close relation to them, such as family, parents and siblings.[123-125] Children with eczema may have itch and disturbed sleep leading to impaired school performance and emotional stress.[126] In addition to the immediate impact, eczema may also influence carrier choice, affect close relationships, social development and maturing.[127] Several investigators have found an association between atopic dermatitis and reduced mental health.[128-130] To estimate psychological distress in populations, different instruments have been used. One of them is the Hopkins Symptom Checklist (SCL). A five-item version is validated in Norwegian, and measures mental distress along two dimensions, namely depression and anxiety.[131] The SCL-5 is suitable as a screening-instrument, and used in several health surveys conducted in Norway.[132]

AIMS

The aims of the thesis were to investigate:

1. The prevalence and severity of eczema among 2-years old children in Trondheim

2. Whether eczema in 2-years old children follow a maternal or a paternal line of inheritance

3. If eczema in 2-years old children is associated with asthma at age 6 years?

4. The association between eczema and mental distress in adolescents

MATERIAL AND METHODS

The Prevention of Allergy among Children in Trondheim (PACT) study

The Prevention of Allergy among Children in Trondheim (PACT) study was established in 2000 and conducted in primary health care as a controlled intervention study. The intervention aimed at reducing tobacco exposure, reduce indoor dampness and increase the intake of omega-3-fatty acids and oily fish, and thereby to reduce the incidence of allergic diseases among children in Trondheim. The study is a collaboration between the Municipality of Trondheim and NTNU.[133]

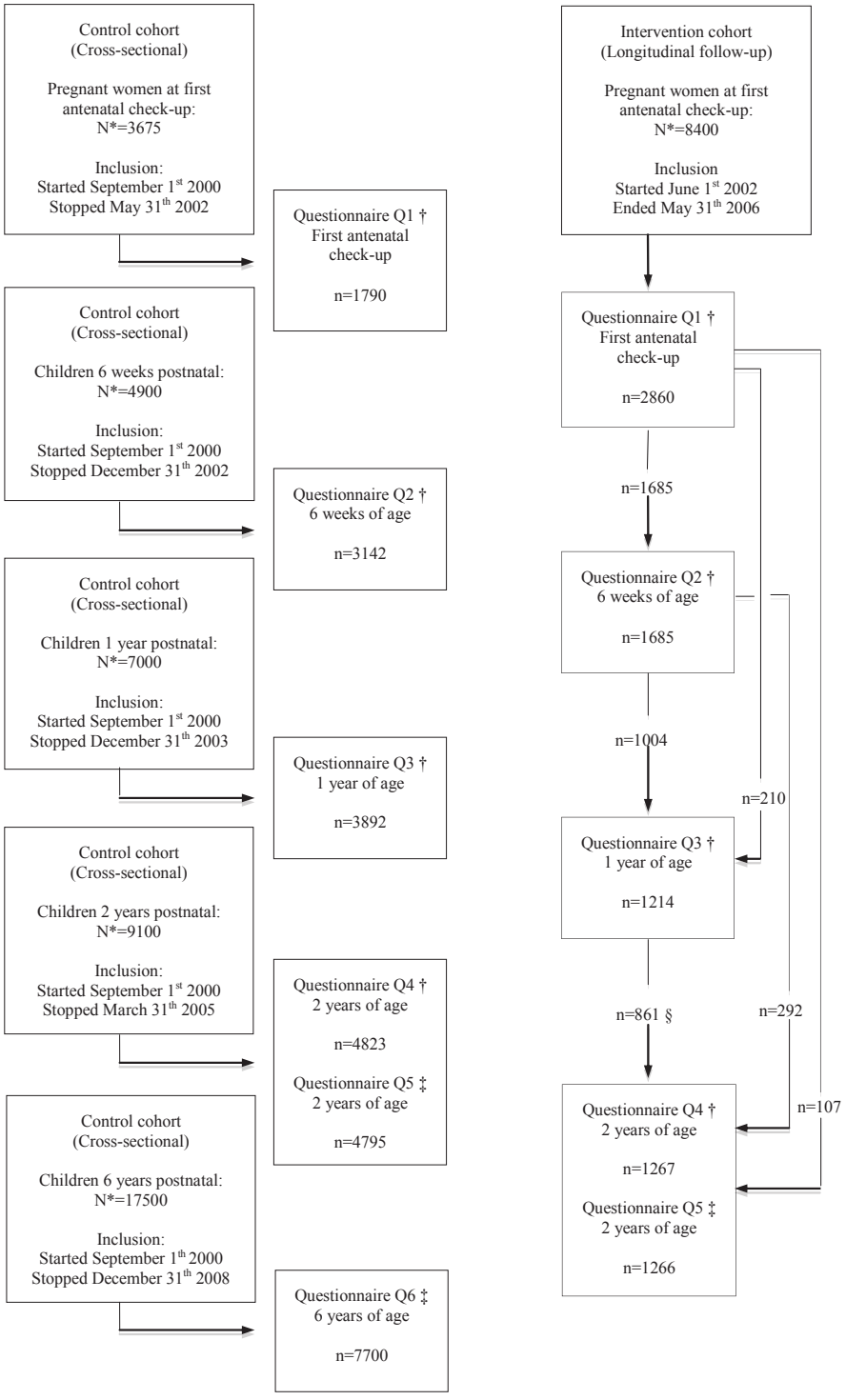
Trondheim is the largest city in central Norway, has about 170 000 inhabitants and approximately 2100 deliveries per year. In all, 32 of 35 general practices (104 GPs), all seven community-based midwives and all 20 maternity health centres in Trondheim agreed to participate. Three single practices refused to participate, and in addition four group practices withdrew from including women to the intervention cohort.

The intervention cohort included only pregnant women. The women were consecutively recruited when attending ordinary scheduled appointment with GPs or midwives. Inclusion to the intervention cohort started in July 2002 and ended in June 2006. A 6-year follow-up of the intervention cohort is still on-going, and will end December 2012 (Figure 3).

To monitor changes in lifestyle and diet habits and trends in incidence of allergy related diseases over time, a control cohort was established one years prior to the intervention cohort. The design of the control cohort is that of cross-sectional inclusion of yearly cohorts of pregnant women and children 6 weeks, 1 year, 2 years and 6 years of age. Inclusion to the control cohort started in September 2000 and ended March 2009. Inclusion to the control cohort ended when the intervention started for that actual age-group (e.g. when the first children in the intervention cohort reached 6 weeks of age, inclusion of 6 week olds to the control cohort stopped etc). In addition to the cross-sectional design of the control cohort,

children with more than one completed questionnaire could be followed prospectively. All women who had children in one of these cohorts, who received an invitation and were willing and able to complete a questionnaire in Norwegian, were included in the study.

Figure 3. Flow-chart of the PACT study.



* Total population of birth cohort in Trondheim during inclusion period
† Questionnaire on behavior and risk factors
‡ Questionnaire on health

The Young-HUNT 1 survey

The Young-HUNT Study is the youth part of The Nord-Trøndelag Health Study (HUNT). The HUNT study is a comprehensive population-based study and has been conducted three times since 1984, comprising data from questionnaires, interviews, clinical investigations and blood/urine samples. The first HUNT survey (HUNT 1) was conducted in 1984-86 and included only adults 20 years and older. In 1995-97 the HUNT 2 also included adolescents aged 13-19 years (Young-HUNT 1). In 2000-2001 a follow-up survey of students attending the last two years of high school were conducted (Young-HUNT 2). Young-HUNT 3 was part of the third wave of the HUNT 3 survey, conducted from 2006-08 and included all inhabitants of the county 13 years and older.

The primary aim of the Young-HUNT 1 study was to survey health, diseases and lifestyle among adolescents.

Nord-Trøndelag County is one of 19 Norwegian counties, located in central Norway, south of the Arctic Circle (Figure 4). The total population in 1995 was 127 000, and in 2009 130 000. The county is mostly rural but has 6 cities, the largest is Steinkjer with 20 800 inhabitants (2009).[134]

Figure 4. Norway, Nord-Trøndelag and Trondheim

Subjects included in the thesis

The PACT study

Paper I, II and III

In the yearly cross sectional control cohort, the participation rate varied from 49% to 64% for the different age groups. For the intervention cohort, 8400 pregnant women were eligible during the inclusion period. Only 2860 women were included, giving a participation rate of 34% (Figure 3).

In paper I we used information from the control cohort on child's health at 2 years obtained by January 2005 (n=4784).

In paper II we used information from 2657 children whose parents had completed both the questionnaire on exposure 6 weeks and child's health 2 years. In addition, we used data from

3087 children with information on exposure at 1 year and health at 2 years. As we only studied association, the participants were from both the intervention cohort and the control cohort.

In paper III we used the control cohort to prospectively follow 4780 children who had completed both the questionnaire on exposure and on health at age 2 years. Some 2192 (46%) answered the questionnaire on health at age 6 years. These children comprised the study population in paper III.

The Young-HUNT 1 survey

Paper IV

A total of 9917 students in junior high schools (13-16 years) and high schools (17-19 years) were invited. The participation rate was 91%. 12-year olds (n=127) and 20-year olds (n=40) were excluded, leaving 8817 students (89%) eligible for further analyses. Non-participants were mostly not in school the day of the study, did not want to participate or did not get consent from their parents (less than 1%).[135]

The Clinical Investigated Subsample

Paper I and III

From March 2001 to September 2002 a random sample of 720 pregnant women from the control cohort of PACT were invited to a sub-study, the IMPACT study. The primary aim of the IMPACT study was to investigate the intestinal microbiota composition and its impact on the immune system.[136] When their offspring reached 2 years of age, 441(61%) were eligible for follow-up. These 441 children were invited to a follow-up examination by a paediatrician or a dermatologist. The examinations were carried out from May 2003 to January 2005 and included clinical examination, skin prick test (SPT) and venous sampling. Some 390 children

(54%) met. SPT was successfully completed in 304/390 (80%), whereas venous sampling was carried out among 258/390 (66%). Allergy test (either STP or measurement of sIgE) was completed in 355/390 (91%).

Questionnaires/Data collection

The PACT study

Questionnaires on different lifestyle factors were distributed by GPs, midwives and health-workers to pregnant women and parents of children aged 6 weeks, 1 year and 2 years. At child's age 2 years and 6 years, a detailed questionnaire on child's health was completed (Appendix 1). The lifestyle questionnaire included questions on family eczema history, infections, diet habits, tobacco exposure and indoor climate. Questionnaire on health emphasized symptoms related to allergic diseases, and several of the questions were obtained from the International Study of Asthma and Allergy in Childhood (ISAAC). However, since validated questionnaires were not available for 2 year olds, the ISAAC questions were adapted from various sources to fit this actual age group.[137-140] The questionnaires were identifiable by a participant number. After completion the questionnaires were put in envelopes with prepaid postage and returned to the study office.

The Young-HUNT 1 survey

The questionnaire included questions on mental and somatic health, life-style, quality of life and detailed information on symptoms of allergy related diseases (Appendix 2). The latter were based on the ISAAC questionnaire.[141] Prior to the Young-HUNT 1 survey, a pilot study testing the questionnaire was carried out and included one sample of eight graders in junior high school (14-15 years) and one sample of student attending the second year of high school (17-18 years).

All students attending the Young-HUNT 1 completed the self-administered questionnaire during one school hour. The questionnaires were only identifiable by a bar code of the 11-digit personal number given to all Norwegians either at birth or when granted citizenship. All students put their completed questionnaire in a clean envelope and sealed it. The envelopes were collected by a project field worker.

The Clinical Investigated Subsample

Parents of children attending the subsample had completed the PACT questionnaires on lifestyle and health at child's age 2 years. In addition, they underwent a structured interview which emphasized symptoms related to allergy related diseases. Moreover, the children had a thorough inspection of the skin, and eczema diagnosis was defined according to the UKWP diagnostic criteria. The examination was carried out by two experienced physicians (IS paediatricians and MS dermatologist). To ensure agreement upon both diagnosis and severity scoring, the first 30 children were examined by both physicians. Clinical examination of the remaining children was evenly apportioned by the physicians. If the child had eczema upon examination, severity was assessed with both SCORAD and NESS.

-*UKWP diagnostic criteria*

In order to qualify as a case of atopic eczema with the UK diagnostic criteria, the child must have had an itchy skin condition in the last 12 months plus three or more of the following: i) onset below age 2 (not used in children under 4 years), ii) history of flexural involvement, iii) history of a generally dry skin, iv) personal history of other atopic disease (or history of atopic disease in first-degree relative in those under 4 years of age), v)visible flexurale dermatitis as per photographic protocol.[142] Flexural dermatitis is dermatitis located around the eyes, around the sides or front of the neck (any patch of dermatitis larger than 1 cm in diameter in an area

defined by the jaw bone above and clavicles below, and a line drawn vertically downwards from the ears with the head in an upright position looking directly forward), front of elbows (any patch of dermatitis larger than 1 cm in diameter affecting one or both elbow creases within an area marked out by the subject's palm), behind knees (any patch of dermatitis larger than 1 cm in diameter affecting one or both areas behind the knee within an area marked out by the subject's palm) and front of ankles (any patch of dermatitis larger than 1 cm in diameter affecting one or both fronts of ankles within an area marked out by the subject's palm). In addition for children under the age of 4 are cheeks (any patch of dermatitis greater than 2 cm in diameter involving **one** or **both** cheeks), forearms (at least one patch of dermatitis greater than 2 cm in diameter on **each** forearm (i.e. elbow to wrist)) and legs (at least one patch of dermatitis greater than 2 cm in diameter on **each** leg (i.e. knee to ankle)).

-*SCORAD*

The SCORAD index consists of the interpretation of A: the *extent* of the disease (according to the rule of nines; 20% of the score) B: the *intensity* composed of six items (erythema, oedema/papules, effect of scratching, oozing/crust formation, lichenification and dryness, 60% of the score. Each item has four grades, 0-3) and C: *subjective symptoms* (itch and sleeplessness, 20% of the score).[143] The score is achieved by the formula A/5+7B/2+C, and the maximum score is 103. The evaluation is performed within 7-10 minutes. Eczema is graded as mild when the score is <25, moderate when 25-50 and severe when >50. Based on training sessions, the task force later on modified the SCORAD, recommending only the objective SCORAD being used.[144] The objective SCORAD only considers the extent and intensity of the eczema. The formula is then A/5+7B/2, giving a maximum score of 83. Eczema grading is then mild when the score is <15, moderate when 25-40 and severe when >40.

-*NESS*

The following parameters are evaluated when assessing the NESS; A: clinical duration, B: intensity (measured as sleep disturbance) and C: extent of disease involvement. Each of these parameters have been given equal weighting, and graded on a five-point scale from 1 to 5. The surface area measurement is assessed by using tick boxes. Investigators record a tick in each box if more than 2 cm^2 is involved with AD. The total number of ticks is calculated by adding together the number of ticks for both the front and the back of the surface diagram. Each parameter's score (A, B and C) is added to produce the total score. Minimum score is 3 and maximum score is 15. Severity is then graded according to the final score as follows: 3-8 mild degree, 9-11 moderate degree, 12-15 severe degree.[96]

-*Skin Prick Test (SPT)*

Trained project workers performed skin prick testing according to the ISAAC procedure.[145] The following standardized extracts from Soluprick® allergens (ALK Albello, Denmark) were used: mite (Dermatophagoides pteronyssinus), mould (Cladosporium herbarum), cat and dog dander, birch, timothy (grass) and mugwort pollens, hen's egg white, codfish, hazelnut and peanut. For cow's milk fresh skimmed milk was used. In addition, two positive histamine control (Histamine 10mg/ml) and one diluents-negative control (NaCl) were applied on the volar surface of child's forearms. Before testing, the parents were told to cease child's antihistamine use and avoid the use of steroid creams on the forearms one week prior to testing.[146] The test was read after 15 minutes, and a mean diameter of at least 3 mm greater than the negative control was considered positive test.[147]

-*Specific IgE*

Sera from venous blood samples were analyzed for sIgE using assays testing for the same allergens as the SPTs. The children were offered epicutaneous anaesthesia with EMLA™ cream (AstraZeneca, Ltd, London, U.K.) prior to venous sampling attempt, which was carried out only once. The sIgE analyses were performed in the immunology laboratory at St. Olavs University Hospital, Trondheim, using Immulite® 2000 Allergen-specific IgE system (Siemens Medical Solutions Diagnostics, Deerfield, IL, U.S.A.). A sIgE ≥0.35 kUL^{-1} was considered positive.

Study variables

All variable definitions used in Paper I-IV are described in each paper, and all variables are listed in the appendices.

Variables in the PACT study

Exposure variables were collected in the questionnaires on life-style and risk factors completed by the mother/parents during pregnancy, when the child was 6 weeks, 1 year and 2 years of age. The questionnaires covered the following topics; number of siblings, parietal status, birth-weight/length, vaccination, marital status, symptoms of allergy related diseases in mother, father and sibling(s), pregnancy conditions, housing conditions, indoor dampness, semi-quantitative food frequency data for mother and child, smoking habits in parents and information on child care. Explanatory variables used in paper II were eczema in any family member, breastfeeding, keeping a dog, homeowner, age of mother at time of childbirth, smoking habits in mother and sex. In paper III the following explanatory variables were used; eczema at 2 years (from the 2-year health questionnaire), wheeze, atopy in family, smoking habits in mother, homeowner, sex and sensitization (from Clinical Investigated subsample).

Outcome variables were assessed from the questionnaires on health completed at age 2 years and 6 years. In developing these questionnaires, three requirements had to be met. First, the extent of the questionnaires should suffice estimation of the common allergy related diseases, and the use of health care services and treatment of these diseases. Second, completing the questionnaires should not take more than 30 minutes. And third, they should be designed to obtain satisfactory validity. The reliability of ten of the questions in the health questionnaire was tested, and compared to information collected from medical records.[148]

Parent-reported eczema at age 2 years (paper II) and asthma 6 years (paper III) were used as outcome variables.

Variables in the Young-HUNT 1

All exposure and outcome variables used in the Young-HUNT study (paper IV) were assessed from the questionnaire. The definition of "atopic dermatitis" in paper IV differs slightly from how we defined "atopic dermatitis" and "eczema" in the PACT study, but as in the other papers, the term is used without any knowledge of sensitization and should therefore be regarded as "eczema" according to the WAO recommendations.

The SCL-5 score was identified by 5 different questions on a four-point scale ranging from 1="not at all" to 4="extremely". The score covers two dimensions, namely depression and anxiety, and are related to the two last weeks. A total SCL-5 score of 2 or more was considered positive for mental distress.

The questions on headache and neck/shoulder pain had four response categories; "never", "seldom", "sometimes" and "often". These variables were dichotomized into "never/seldom/sometimes" and "often".

Variables in the Clinical Investigated Subsample

In the subsample, AD was diagnosed according to the UKWP diagnostic criteria. In addition, the clinicians used an 8-point visual analog scale (VAS) to make an on-site evaluation of the likelihood that the child had AD. The evaluation was based on the clinical experience of the physicians, and a score of 8 indicated that the physician was sure about the diagnosis.

Severity of AD was assessed by SCORAD and NESS. We only used the adjusted objective measures of SCORAD (score 0-83) and defined disease severity as mild when the score was <15, moderate when the score was 15-40 and severe when the score was >40. The NESS score ranges from 3-15, and AD was graded as mild moderate or severe if the score was 3-8, 9-11 and 12-15, respectively.

Sensitization was tested by SPT and/or sIgE, and the child was considered sensitized if either SPT or sIgE was positive.

Statistical analyses

In paper I, II and IV data were analyzed using SPSS for Windows version 10.0, version 13.0 and version 15.0, respectively (SPSS Inc., Chicago, IL, USA). In paper I and II, prevalence with 95% confidence intervals (CI) were estimated using STATA for Windows version 10.0 and version 11.2 (College Station, Texas, USA). In paper III, all analyses were performed using STATA for Windows version 11.2 (College Station, Texas, USA).

Paper I. Symptoms related to eczema in boys and girls were compared using the Pearson chi-squared test. All reported p-values were two-sided. Prevalence was reported with 95% confidence intervals (CI) based on binomial distribution.

Paper II. Family eczema history was categorized into 7 different categories, with no family eczema history as the reference category. Univariate associations for different categories and eczema at 2 years of age were studied using simple logistic regression. Adjusted associations

were estimated using logistic regression. Adjustments were made for confounders defined by a priori knowledge. Associations were reported as odds ratios (OR) with 95% CI for binominal distributed data.

Paper III. Baseline characteristics as well as allergy related diseases were described as prevalence with 95% CI for dichotomous variables, and mean with +/-standard deviation (SD) for continuous variables. Multivariable, logistic regression models were used to obtain adjusted associations between ever eczema at 2 years and current asthma at 6 years. Two different models were made. In one model, the explanatory variable was eczema, whereas in the other model, age of onset of eczema was used as the explanatory variable. Age of eczema onset was divided in tertiles (0-3months, 4-12 months, 13 months or older), and all other explanatory variables in model were dichotomized. The possible confounding factors were identified by a priori knowledge. Due to the large number of missing data, we used multiple imputations (MI) to assess potential impact of missing data in the regression analyses. We assumed that data were missing at random given the observed data and used chained equations (regression switching) with 50 sets of imputations to impute missing values as implemented in the STATA's ICE command. The following predictor variables reported at 2 years were included in the imputation model: eczema, age of onset eczema in tertiles, siblings, atopy in family, cat in household, symptoms of wheeze/whistling in chest, symptoms of hayfever, ever hospitalized due to any allergy related disease, homeowner, smoking mother/father and sensitization. In addition the outcome variable current asthma 6 years was included. Since reported sensitization was considered not missing at random, sensitization-data from the sub-population, where all the randomly selected participants included were tested regardless of disease symptoms or not, were used as predictor in the ICE command. A multiplicative interaction term between eczema and sensitization was also included in the predictive ICE command and tested in the final models.

For each outcome variable, a separate MI dataset was created, and resulting estimates were combined by the MIM command in STATA. To study the association between early eczema and current asthma at 6 years, logistic regression analyses were performed on the MI dataset. All results are presented as adjusted odds ratios (aOR) with 95% CI estimated for binominal distributed data. In addition to the multiple imputation approach, we also performed analyses based on individuals with complete data.

Paper IV. Prevalence of different symptoms of mental distress, mental distress and atopic dermatitis among boys and girls were reported with 95% CI. Unadjusted odds ratios between different chronic diseases and mental distress were estimated and reported as ORs with 95% CI. Variables included in the model were dichotomized. Multiplicative interaction was tested between sex and atopic dermatitis. Since the interaction term was significant, we did sex-stratified analyses. Adjusted ORs with 95% CI were estimated by using logistic regression models.

ETHICS

Parents of participating children in the PACT study signed a written consent to participate in the PACT study, and specific consent was given to allow skin prick test and venous sampling for children included in the clinical investigation subsample.

In the Young-HUNT study all participants and parents of children under 16 years of age signed a written consent to take part in the study.

The Regional Committee for Medical Research Ethics approved both PACT and Young-HUNT. The Norwegian Data Inspectorate Board approved establishment of the research registers.

The PACT study is registered in The Current Controlled Trials registration, ISRCTN28090297.

MAIN RESULTS

Review of paper I

Atopic dermatitis among 2-year olds; high prevalence, but predominantly mild disease – The PACT Study, Norway

Objective: To study the prevalence and severity of eczema among 2-years old children.

Methods: Questionnaires on health from a total population of 4783 2-years old children and clinical data from a random subsample of 390 children were used. All children were included in the control cohort of the PACT study. Eczema diagnosis was made according to reported symptoms in questionnaires. In addition, the UKWP criteria were used to assess eczema diagnosis in the random subsample. Both Severity Scoring of Atopic Dermatitis (SCORAD) and Nottingham Eczema Severity Score (NESS) measured severity outcome in the subsample.

Results: The prevalence of ever eczema in the total population was 16.5% (95% CI 15.5-17.6) when information was obtained from questionnaires. In the random subsample the corresponding prevalence was 20.6% (95% CI 16.6-24.6). When eczema in the random subsample was diagnosed according to the UKWP criteria, the prevalence was 15.9% (95% CI 12.3-19.5). More than 70% of the children diagnosed with eczema according to the UKWP criteria had mild disease.

Conclusion: We found a high prevalence of ever eczema at 2 years of age. However, more than two thirds of the cases were mild, which may imply that eczema as a risk factor for future allergy related disorders is limited.

Review of paper II

Family eczema-history in 2-year-olds with eczema; a prospective, population-based study. The PACT-study, Norway.

Objective: To prospectively study the association of reported eczema in mother, father and siblings and reported eczema in child under study.

Methods: Information on family eczema-history was obtained from questionnaires completed at age 6 weeks and 1 year. When the children turned 2 years of age, a detailed questionnaire on health/different allergy related diseases was completed. Children with data at 6 weeks and 2 years made up the 6-weeks cohort, whereas children with data at 1 year and 2 years comprised the 1-year cohort. Family eczema-history was divided into seven different groups; “eczema mother only”, “eczema father only”, “eczema sibling only”, “eczema mother and father, not sibling”, “eczema mother and sibling, not father”, “eczema father and sibling, not mother”, “eczema mother, father and sibling”. “No family history of eczema” was set as reference group.

Results: Some 13.7% and 14.2% of the girls, and 15.9% and 16.1% of the boys reported eczema at 2 years of age in the 6-week cohort (N = 2657) and in the 1-year cohort (N = 3087), respectively. Both maternal and paternal reports on eczema symptoms were significantly associated with eczema in child under study. Reporting family eczema-history at 1 year, "eczema sibling only" [adjusted odds ratio (aOR) = 3.13 (2.27-4.33)] as well as all other family-groups containing siblings with eczema were strongly associated with eczema 2 years. When family eczema-history was reported at 6 weeks, reporting of "eczema sibling only" was not associated to reported eczema at 2 years in index child [aOR = 1.31 (0.77-2.23)]. At 6 weeks of age, some 6% of children under study had had their first symptoms of eczema, while 80% of children had their first eczema-symptom by 1 year of age.

Conclusion: Both maternal and paternal history of eczema was associated with eczema in index child at 2 years of age. Having siblings with eczema strengthened the association between maternal and paternal reports of eczema with eczema in index child only when exposure was reported at 1 year. These findings indicate that results from questionnaires-based studies on family eczema-history depend on whether or not index child has yet developed eczema.

Review of paper III

Early eczema and the risk of childhood asthma; a prospective, population-based study.

Objective: To study the risk of current asthma and the co-existence of different allergy related diseases in 6 years old children with ever eczema reported at 2 years of age.

Methods: Children included in the control cohort of the PACT study were included. Questionnaires on different environmental exposures and detailed information on the child's health were answered at 2 years of age. An identical questionnaire on child's health was completed at 6 years of age. Information on sensitization was obtained from the clinical investigation of a random subsample. Sensitization was defined positive if the child either had positive skin prick test or positive sIgE. Missing data were handled by multiple imputation analyses.

Results: 2192 (46%) of included 2 years old children completed questionnaire at 6 years. The association between eczema at 2 years and current asthma at 6 years was aOR=1.80 (95% CI 1.06-3.05). Four of ten children with eczema at 6 years had onset of eczema after the age of 2 years, but co-existence of different allergy-related diseases at 6 years were higher among those with debut of eczema before 2 years of age.

Conclusion: Although most cases of early eczema in the general population are mild or moderate, they may involve an increased risk of developing asthma. Our findings support the hypothesis of an atopic march also in the general population.

Review of paper IV

Atopic dermatitis in adolescent boys is associated with greater psychological morbidity compared with girls the same age: the Young-HUNT study.

Objective: To study self-reported mental distress in adolescents with eczema compared to healthy adolescents and adolescents with other chronic complaints such as headache, neck- or shoulder-pain, asthma, allergy and rhinitis.

Methods: The young-HUNT 1 was conducted in 1995-97 as a cross-sectional survey among adolescents 13-19 years of age in Nord-Trøndelag County. All students were invited to attend. The participants completed questionnaires including information on somatic and mental health during one school hour.

Results: The participation rate was 89%. 8817 adolescents,13-19 years, (4433 boys) completed the questionnaires. The older teenagers of both sexes reported more symptoms of mental distress compared to the younger ones. Twice as many girls as boys reported eczema and except for rhinitis and allergy there was girl preponderance also in reported prevalence of other chronic complaints. Older female students with eczema reported more mental distress than younger ones. The association between headache and neck-/shoulder-pain and mental distress was significant in both sexes. The association between eczema and mental distress was stronger for boys (OR 2.1, 95% CI 1.6-2.9) than for girls (OR 1.3, 95% CI 1.1-1.6).

Conclusion: There was a strong and consistent association between mental distress and eczema, headache and neck- or shoulder-pain for both sexes. However, for adolescents with

eczema, the association between symptoms and mental distress was stronger for boys than for girls.

DISCUSSION

Methodological considerations

The underlying premise in epidemiology is that disease, illness and ill health are not randomly distributed in the human population.[7] When conducting an epidemiological study, both random as well as systematic errors may be afflictive.[149] Random errors are variability in the data that reduce the precision of our estimates, whereas systematic errors in the study design or conduction of the study may lead to lack of validity.[150, 151] Therefore, accuracy in estimation becomes an important goal.[150]

Precision/Lack of random error

Precision refers to the degree of variation in a measurement and can be increased in two different ways, either by increasing the size of the study, or by modifying the study design to obtain more precise information/measurements.[150] Tests of statistical significance (p-values) are performed in order to evaluate whether the observed value, or a more extreme value, is caused by chance or not. When the p-value is ≤0.05, the probability of the observed result being that extreme solely by chance is 5% or less. The p-value is however not as informative as the confidence intervals (CI). Confidence intervals assess the extent to which the null-hypothesis is compatible with the data and in addition provide an idea of the likely magnitude of the effect and the random variability of the point estimate.[150] The width of a confidence interval depends on the amount of random variability, the precision, inherent in the data-collection process.

Both the Young-HUNT and the PACT study are comprehensive population-based studies, and throughout this thesis we have chosen to present test of significance as confidence intervals with level of significance set to 95%. In paper IV results were relatively precise, with narrow confidence intervals. In paper II and III, however, some exposure categories included few

participants. The estimates therefore were less precise. For example; when studying different family eczema-groups in paper II, there were too few participants in some of the groups to obtain precise estimates.

Study design

A cross-sectional study includes all persons or a representative sample of all such persons at the time of ascertainment. In cross-sectional studies both exposure and disease outcome are determined simultaneously for each individual, and the objective is limited to describing the population at that time. This type of design has limitations when it comes to establishing a temporal/causal relationship between exposure and outcome. It is however useful when studying associations.

Cross-sectional data was used to study prevalence (paper I) and associations (paper IV).

In paper II and III the design was that of a prospective cohort study. We identified the population under study at the beginning of the study, and during the follow-up time identified new cases of the disease under study. A major strength of this design is the possibility to study exposure before the outcome and thereby limiting the possibility of information-/recall bias. In paper II, we used information on family eczema-history (exposure) reported at two different times (6 weeks and 1 years), to study eczema in children (outcome). We found that information on exposure (eczema in siblings) reported at 6 weeks differed from information about the same exposure reported at 1 year. This finding confirmed the importance of measuring exposure (eczema in sibling) before the outcome is known (eczema in index child under study) in order to avoid recall bias.

One limitation to the prospective design is the time aspect. If the disease under study has low incidence or takes several years to develop after exposure, the result may be a high number of non-responders/lost to follow-ups. The high number of lost to follow-up is a limitation in

paper III, where follow-up rate is only 46%. This low rate may lead to selection bias (discussed below).

Validity/Lack of systematic error

The validity of a study can be divided into two components; internal validity and external validity. Internal validity is the validity of the inferences as they pertain to the members of the source population, whereas external validity is the validity of the inferences as they pertain to the general population.[150] Internal validity is therefore a prerequisite for external validity. Several types of bias can hamper internal validity. The most important ones are selection bias, information bias, and confounding.

Internal validity

-Selection bias

Selection bias occurs when the association between exposure and disease are different for those who participate in the study and those who do not.[149]

Participation rates in epidemiologic studies have declined during the last decades, and is of concerns to epidemiologists.[152] Only 34% of eligible women were included in the intervention cohort of PACT, whereas the participation rate varied from 49% to 64% for the different age groups in the control cohort. Almost none of the participants made active withdrawal from any of the cohorts. The study is of long duration, and one can expect some degree of exhaustion among the health workers including participants to the study.[152] The low inclusion rate is as reported by the health workers, due to low inclusion activity among GPs, health visitors and midwives, and not a consequence of self-selection among parents/children. This is affirmed in a non-responder study carried out, where 391 parents consecutively visiting maternal postnatal care were asked to complete a short, anonymous questionnaire on age,

socioeconomic status, allergic diseases in the family, smoking habits and participation in PACT. Only small and minor differences were found between participants and non-participants in PACT.[133]

If both participants and health workers forgot/failed to attend, we may assume that those lost to follow-up were lost at random. In both paper II and III we did a comparison of baseline characteristics between follow-ups and lost to follow-ups. Apart from more smoking mothers and fewer homeowners among the lost to follow-ups (indicating a certain socioeconomic gradient), insignificant differences were found between the two groups. This imply that despite no self-selection among participants in PACT, there is a socio-economic gradient among follow-ups compared to the lost to follow-ups. Several other studies have confirmed that persons with higher socioeconomic status are more likely to participate in scientific studies compared to those with lower socioeconomic status.[153-155] Eczema has repeatedly been found more prevalent in higher socio-economic classes.[156-158] Our reported prevalence of eczema and other allergy related disorders might therefore be too high.

In the Young-HUNT 1, most of the non-participants were not in school the day of the survey. There is of course a possibility that the students not in school are those who suffer from the disease under study. However, if a larger number of the students had health problems, we would expect the associations found to be strengthened.

-Information bias and misclassification

In any cohort study it is important that the quality of the information obtained from the exposed is comparable and of equal quality as information obtained from the un-exposed. If this is not the case, a significant information bias and misclassification can be introduced. Misclassification is, by error, to assign a person/value into another category than what he/it should have been. Misclassification may occur in two forms; differential and non-differential.

Differential misclassification happens when either the exposure is misclassified differentially according to a person's disease status or the disease is misclassified differentially according to a person's exposure status. When having a differential misclassification, the effect we are studying can be either exaggerated or underestimated.

Non-differential misclassification results from the degree of inaccuracy that characterizes how information is obtained from any study group. When we have non-differential misclassification, the association tends to be diluted and shift the odds ratio towards 1.0. We are therefore less likely to detect an association even if there is one.

Several of the variables used in the present studies are prone to misclassification. In paper I we validated the diagnosis AD by comparing the combination of a positive answer to two ISAAC questions against the UK working party's diagnostic criteria and found the sensitivity and specificity to be 69.4% and 88.7% respectively. In other words; about 30% of those with AD are classified as false negative, whereas about 12% is classified as false positive. In using these two ISAAC questions in further studies in paper II and III, our OR estimates may be biased. However, since the misclassification is non-differential, our estimate most likely will tend to be diluted.

Differential misclassification may occur as a result of recall bias. In the PACT study, parents who have allergic symptoms or children with allergic symptoms will be more aware of the same symptoms in the child under study, and therefore may tend to respond positively to questions on allergic symptoms compared to parents without allergic symptoms in the family. In paper II, where information on exposure is reported at two different ages of index child (6 weeks and 1 year), the difference in reporting of eczema symptoms in siblings may be due to such misclassification.

Reported smoking habits may also be misclassified, as parents with asthmatic children will more likely under-report smoking. Participants in the intervention study were more aware of the study aim, and differential misclassification may have occurred (paper II).

-Confounding

A simple definition of confounding would be the mixing of effects.[150] This implies that the effect of the exposure is mixed together with the effect of another variable, leading to bias. There are three criteria for a variable to be a confounder; 1) it must be a risk factor for the disease 2) it must be associated with the exposure under study in the source population and 3) it must not be affected by the exposure or by the disease, in particular not be an intermediate step in the causal pathway between exposure and disease.

There are two principal ways of handling confounding in statistical analysis; by adjustment or by stratification.[7]

In paper II, we studied the association between different family eczema-groups and eczema in index child 2 years of age. Potential confounding factors were identified by a priori knowledge, and in this paper we adjusted for sex, current smoking mother, age of mother at time of birth, keeping a dog and breastfeeding. In addition, we regarded socio-economic status as a potential confounder. This information was, however, missing in our data, so homeowner status was used as a proxy. Since we studied different family groups, breastfeeding is not an obvious confounder. Clearly, breastfeeding is not associated with eczema in father only. However, since four of the seven family groups included siblings, and breastfeeding is associated with eczema in siblings, we decided to include this as a potential confounder in the model.

In paper III, we studied the association between ever eczema reported at 2 years of age and current asthma reported at age 6 years. The potential confounders were identified by a priori

knowledge, and in the final models, adjustments were made for sex, atopy in family, wheeze, smoking mother and sensitization. In addition, homeowner was used as a proxy for socio-economic status.

In paper IV we studied the association between atopic dermatitis (eczema) and mental distress. Due to interaction on the multiplicative level between sex and atopic dermatitis, we performed sex-stratified analyses. The stratified analyses were for headache, neck/shoulder-pain, asthma, allergy, rhinitis and being healthy. One limitation to this model is the lack of adjustment for socio-economy. This information was not available in the Young-HUNT 1 questionnaire, but could have been accounted for by merging the data with parental information on level of education. This was, however, not done.

External validity/Generalizability

External validity refers to the generalizability of the study.

The PACT study was conducted in primary health care, and the participants were included consecutively. Although the study only included approximately 34% of eligible women in the intervention cohort and varied from 49-64% for the different age-groups in the control cohort, we claim that the study is a representative sample of women and children living in Trondheim. This is supported by the formerly described non-participant study. We have also compared data from PACT with data on all pregnant women in Trondheim from the Medical Birth Registry.[159] No differences in the prevalence of smoking at the start of the pregnancy were found. There is no reason to believe that pregnant women in Trondheim differ from pregnant women in other large Norwegian cities, but this cannot be ruled out. The majority of the participants are Caucasians, and the results may not be generalized to other ethnic groups. In the Young-HUNT, the participation rate was high and invitations included the entire teenage population 13-19 years in the county. Nord-Trøndelag County has a slightly lower

level of education, income and lack of large cities compared to other Norwegian counties, but the population is stable and homogenous and considered representative for the total Norwegian population regarding industry, socio-economy, age-distribution, sex, mortality and morbidity.

Strengths of the study

The strength of the PACT study is the population based design, the inclusion of a large number of children and pregnant women from the general population, and the prospective design. A non-participant study confirms no selection bias among those included and those not included. Several of the questions used in the questionnaire have been tested regarding reliability, and questions on doctor-diagnosed asthma and symptoms of eczema showed very good/good agreement when compared to medical records.[148] The questions on eczema were validated using the UKWP diagnostic criteria (paper I).

The strength of the Young-HUNT 1 is the invitation to the entire adolescent population in Nord-Trøndelag County and the high participation rate.

Limitations of the study

Although we believe that the participants of PACT (with the limitations of socio-economy already mentioned) are representative of the general population, the low participation and follow-up rate is a limitation of the study. Self-reported data may also be a limitation, especially in the intervention cohort where the participants knew the study aim.

In the Young-HUNT 1, self-reported data may be a limitation. It is also possible that non-responders were absent from school due to more frequent illness/disease.

General discussion

Prevalence and severity of eczema in 2-years old children

Prevalence is the most common measure of disease frequency in epidemiology, and provides important information about the burden of disease in a population.[25] Prevalence can be measured as point prevalence or period prevalence. Suggestions have been made to use one-year period prevalence for comparative purposes, as this will take into consideration the relapsing nature of the disease and at the same time minimizing recall bias.[25] Prevalence of (atopic) eczema has been widely studied in 6-7 years old and 13-14 years old children through the ISAAC studies.[111] Among children 2 years of age, however, prevalence studies have been scarce.[25] In paper I we estimated the prevalence of eczema both based on reported symptoms in questionnaires and based on the UKWP criteria after clinical examination of a random subsample. In the subsample the prevalence obtained from questionnaires was 20.6% whereas the prevalence according to the U.K. criteria was 15.9%. This might reflect the fact that the prevalence measures are different; the prevalence in the questionnaire is a cumulative prevalence, whereas the prevalence according to the UKWP criteria is a one-year period prevalence. Otherwise, the reported prevalence from the questionnaire represents an over-reporting or a selection bias.

Severity outcome measures in eczema are useful for several reasons. In epidemiological studies severity of disease together with prevalence is helpful in estimating the disease burden in a community. In a systematic review of randomized controlled trials of therapeutic interventions for eczema, the investigators found that only 27% of the trials used an objective assessment of eczema severity used before.[160] In clinical practice severity grading is also a useful tool, but in order to be able to translate trial evidence into clinical practice the same outcome measures as in eczema trials should be used.[98] Also, outcome measures should be considered important both for researchers, patients and clinicians. As for diagnostic criteria,

outcome measures should also be standardized. This will help to reduce bias from selective outcome reporting, and facilitate the possibility of performing meta-analyses.[98, 161] The Harmonizing Outcome Measurements in Eczema (HOME) is yet to be agreed upon. In paper I we used both SCORAD and NESS as outcome measures. In a review article evaluating 20 different outcome measures, SCORAD was one of three measures recommended used in future studies.[94] For NESS the validity criteria were not fully met, but appeared to be acceptable until further validation studies are available. Compared to SCORAD, NESS is easy to use, and grades the severity into mild, moderate or severe. We found only 3/59 children to have severe disease when measured by NESS whereas none had severe disease according to SCORAD. This is reassuring, and strengthens our conclusion that most children in the general population have mild or moderate disease. We did, however, only investigate the children once, and the fluctuation in symptoms could therefore not be captured.

Family eczema history

Several studies on family eczema history have concluded that there seem to be a maternal line of inheritance regarding AD.[45-47, 162] Concerning allergic diseases, several factors such as maternal diet, microbial exposure and smoking have been shown to modify disease risk, some through possible epigenetic changes.[68, 163-165] Underlying mechanisms for this observation could be shared environment by mother and child such as gene-environment interactions operating *in utero,* breastfeeding, or parent-specific gene expression (genomic imprinting). Genomic imprinting implies that expression of the genetic information is modified according to whether it is passed to the child via the egg or the sperm.[48] In addition, as illustrated in Fig.5, both pre-and post-natal environment may also alter the modulation of gene expression.

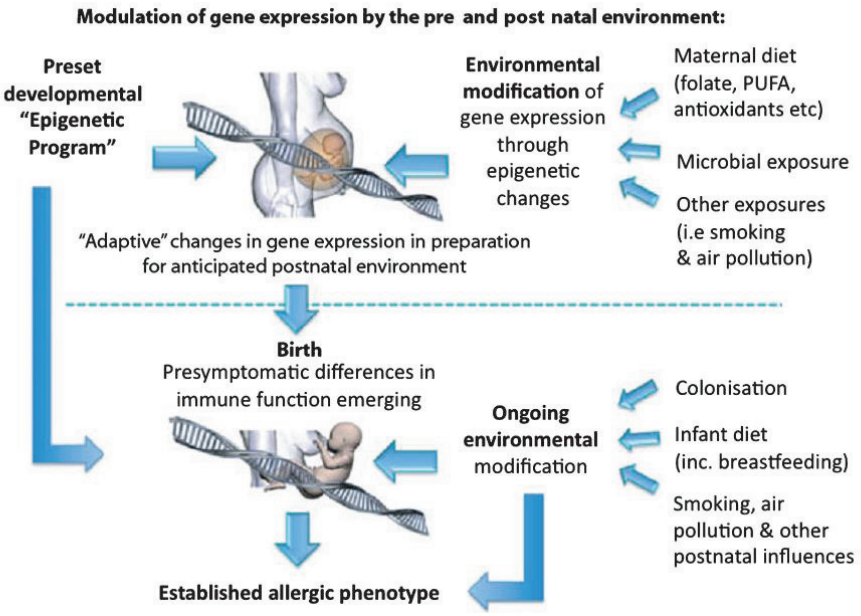


Figure 5. A range of factors in the prenatal and postnatal environment have the capacity to alter epigenetic programming and gene expression during early development. (Copyright 2010 Wiley. Used with permission from Martino DJ and Prescott SL. Silent mysteries: epigenetic paradigms could hold the key to conquering the epidemic of allergy and immune disease. Allergy 2010 Jan;65(1):7-15. John Wiley and Sons)

Disease prevention through environmental strategies that can re-programme gene expression and thereby disease phenotype and disease predisposition through epigenetic mechanisms should be addressed in future studies.[166]

In paper II we did not find support for a maternal line of inheritance, but in line with other studies found that both a paternal and a maternal history of atopy were associated with increased risk of eczema in the offspring under study.[43, 48, 61, 167] As discussed in paper II, this may be due to bias in reporting of paternal symptoms by mothers filling in the questionnaires. Another possibility is that the lack of a maternal line of inheritance might be due to different phenotypes of eczema being studied. We studied eczema, and sensitization in both parents

and offspring was unknown. In one study reporting a maternal line of inheritance, hospitalized children were included.[47] It is reasonable to assume that hospitalized children with eczema more often are sensitized and have a more severe form of eczema than those not hospitalized. However, another study found no differences regarding parental inheritance when sensitized children were compared with non-sensitized children.[61] This study was, however, performed on older children. These findings emphasize the importance of a strict disease definition in order to compare studies. Also, age of child and type of sensitization should be taken into consideration.

The atopic march

In paper III we studied the atopic march, and found an increased risk of asthma at 6 years of age among children with eczema at 2 years of age compared to children without eczema at 2 years. Whether or not there is an atopic march is debated.[117, 122] If eczema is a risk factor for subsequent asthma, the explanations could be that this is caused either by 1) a defect skin barrier function with subsequent sensitization, 2) an immunologic dysregulation, 3) shared environmental factors that predisposes for both eczema and asthma or 4) a complex combination of all these factors. Genome screens for AD and asthma have not shown any clear overlap in the chromosomal regions, indicating that susceptibility to these diseases are mediated through different genes.[168] On the other hand, association studies on FLG and eczema are strong and robust, and loss-of-function mutations in this gene confer increased risk for both eczema and eczema in combination with asthma.[12, 169] In a population-based study from the U.K., support is given to the findings of distinct phenotypes of eczema rather than a progression of related disorders.[170] However, risk of asthma was not limited to those with atopic sensitization, and the authors indicate that a possible mechanism could be priming of a Th-2 phenotype, caused by systemic effects of early eczema, which influence airway

responsiveness and has effects in later childhood. Our finding in paper III confirms that eczema is an individual risk factor for asthma regardless of sensitization. The Early Treatment of the Atopic Child (ETAC) study group is an international double-blind placebo-controlled randomized trial aiming at preventing the progression from eczema to asthma by means of administrating cetirizine.[171] At 3 years of age, asthma was delayed, and in some cases prevented, in a subgroup of patients with atopic dermatitis sensitized to grass pollen. The overall risk for eczematous children to develop asthma was, however, not reduced. Several authors have argued that restoring the skin barrier could prevent both eczema severity and progression form eczema to asthma.[115, 121, 122] If the link between eczema and asthma is causal, treatment of the eczema may lead to a reduction in incident cases of asthma.[121] The eczema treatment would include not only moisturizers containing ceramides, free fatty acids and cholesterols, but also topical treatment that reduce the skin inflammation. Thereby, both restoration of the skin barrier and treatment of the skin inflammation are taken care of. This might inhibit the systemic effects of eczema and possibly the airway responsiveness. Intervention studies are needed in order to confirm or refute this possible causation.[121]

Mental distress in adolescents with eczema

In order to manage the treatment of chronic skin diseases it is important to recognize the impact these diseases have on quality of life and mental health both in those affected by the disease and their families/caretakers. Eczema is a pruritic disease, and several investigators have showed an association between itch/pruritus and mental distress/psychosocial morbidity.[172, 173] Some have also addressed this problem among adolescents.[174] Mental health problems such as symptoms of depression and anxiety increase in prevalence throughout adolescence, and girls are more often affected than boys.[175, 176] Also, adolescents with chronic diseases have more depressive symptoms than healthy young people.[177] In paper IV we have

addressed the association between mental distress and atopic dermatitis among adolescents, and found that the association was stronger for boys than for girls.

A birth cohort from the U.K. following children up to the age of 18 years found the 12-month prevalence of eczema at age 18 years to be 16.3% in girls and 8.3% in boys. At age 4-10 and earlier, no significant difference in the prevalence among the sexes were observed. The female predominance at age 18 years was due to more girls developing non-atopic eczema, whereas more boys had outgrown their eczema.[178] Severity of eczema is correlated to serum IgE levels, and children with severe AD have increased risk of sensitization to food- and aero-allergens.[179] With this in mind, it is reasonable to hypothesize that adolescent boys may have more severe eczema than girls. Another possibility is that boys with eczema are less likely to treat their skin disease, and therefore have more itch and nuisance related to their eczema than girls.[180] Whether the eczema leads to mental distress or mental distress leads to deterioration of eczema cannot be distinguished from our study. In treating young people with eczema it is, however, important to remember the association between mental distress and eczema, and, if possible, pay extra attention to the boys.

CONCLUSIONS

1) Close to every fifth child in Trondheim have had eczema by the age of 2 years. It is one of the most common diseases of childhood, and therefore represents a challenge for health personal concerning advice given both related to treatment and prevention. Fortunately, more than two thirds of the cases had mild degree of disease.

2) A maternal line of inheritance was not confirmed in this study. Information on family eczema history should be collected as early as possible and preferably before the child develops eczema in order to avoid recall bias.

3) Despite the fact that most children with eczema have mild or moderate degree of disease, having eczema at age 2 years increased the risk of asthma at 6 years of age when comparing to those without eczema at 2 years of age. This finding confirms the hypothesis of an atopic march also in a general population.

4) Eczema as well as other chronic complaints was associated with mental distress among adolescents 13-19 years. The association between eczema and mental distress was, however, stronger for boys than girls.

Uniform diagnostic criteria and outcome measure are of crucial importance in future studies of eczema.

FUTURE PERSPECTIVES

The PACT study is comprehensive, and unique in its kind in Norway. One of the main points in further research will be to investigate if the intervention has led to a decrease in incident cases of allergy related disorders at 6 years. Two sub-studies have been conducted within the frames of the PACT study, the IMPACT study and the ProPACT study. These sub-studies have collected biological material, and a large biobank has been stored. Collaboration with the Norwegian University of Life Sciences in Ås has already been established, and further studies on gut microbiota composition and microbial composition/cytokine profile in breast-milk will be conducted.

Collaboration with the Instituto di Ricerche Farmacologiche Mario Negri, Milan, Italy, has also been established. Together with Institut National de la Santé et de la Recherche Médicale (INSERM) Paris, France, they conduct the project "The Hygiene Hypothesis: Revisiting the Concept by Integrating Epidemiology and Mechanistic Studies". This project is granted funding by the European Research Council. Since the Italian arm of this study use questionnaires very similar to the questionnaires used in the PACT, pooling of data is possible. Direct and indirect markers related to the hygiene hypothesis will be explored in both PACT and the Italian dataset. This work has started.

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PAPER I

Smidesang I, Saunes M, Storrø O, Øien T, Holmen TL, Johnsen R, Henriksen AH

Atopic Dermatitis Among 2-Year Olds; High Prevalence, but Predominantly Mild Disease – The PACT Study, Norway. Pediatr Dermatol. 2008 Jan-Feb;25(1):13-8

Is not included due to copyright

PAPER II

Saunes M, Øien T, Storrø O, Johnsen R.

Family eczema-history in 2-year olds with eczema; a prospective, population-based study. The PACT-study, Norway. BMC Dermatology 2011,**11**:11

Saunes et al. BMC Dermatology 2011, 11:11
http://www.biomedcentral.com/1471-5945/11/11

BMC Dermatology

RESEARCH ARTICLE Open Access

Family eczema-history in 2-year olds with eczema; a prospective, population-based study. The PACT-study, Norway

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Abstract

Background: A maternal line of inheritance regarding eczema has been described in several studies, whereas others find associations to both a maternal as well as a paternal line of inheritance. When studying family history of eczema symptoms, cohort studies including siblings are rare. Time point for assessing family eczema-history could be of importance when studying the associations between family eczema-history and children with eczema, as parents with unaffected children may not recall mild symptoms in other siblings or their own disease history. We therefore aimed to study the associations between reported eczema in mother, father and siblings and reported eczema in index child where information on family history was collected at two different ages of index child.

Methods: Parents/children participating in The Prevention of Allergy among Children in Trondheim (PACT) study were given questionnaires on reported eczema symptoms in mother, father and siblings at 6 weeks and 1 year. When index child was 2 years of age, a detailed questionnaire on different health issues with emphasize on different allergy related disorders were filled in.

Results: Both maternal and paternal reports on eczema were significantly associated with eczema in index child. Reporting family eczema-history at 1 year (N = 3087), "eczema sibling only" [adjusted odds ratio (aOR) = 3.13 (2.27-4.33)] as well as all other family-groups containing siblings with eczema were strongly associated with eczema 2 years. When family eczema-history was reported at 6 weeks (N = 2657), reporting of "eczema sibling only" was not associated to reported eczema at 2 years in index child [aOR = 1.31 (0.77-2.23)].

Conclusions: Having sibling(s) with eczema strengthened the associations between maternal and paternal reports on eczema with eczema in index child only when exposure was reported at 1 year. These findings indicate that results from questionnaires-based studies of family eczema-history depend on whether or not index child has yet developed eczema.

Trial registration: ISRCTN: ISRCTN28090297

Background

Atopic eczema is a complex disease caused by a mainly unknown interaction between genetic and environmental factors [1]. The genetic component of the disease has been demonstrated in twin studies [2], and several studies have emphasized the association of atopy in the mother with the development of atopic eczema in the child whereas the evidence for association to an atopic father has been somewhat weaker [3-6]. In the last years, however, other studies have concluded that the association with both paternal as well as maternal atopy is important in the development of allergic disease in the offspring [7-10] Several candidate genes linked to the development of eczema have been identified [11], but so far only mutations in the gene encoding filaggrin (FLG) have been widely replicated [12].

When family eczema-history is studied, several investigators have studied the protective effect of having a high

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number of siblings on the development of allergic diseases [13,14]. However, few prospective studies from the general population have addressed the association between allergy related disorders in older siblings and the child under study [4,15].

When studying diseases in the general population, self-reported questionnaires are often used. One of the flaws with such information could be recall bias concerning how well adults remember both their own childhood diseases as well as diseases in children with mild symptoms [16-18].

The aim of this prospective study was therefore to investigate the associations between reported eczema in mother, father and siblings and reported eczema in index child at 2 years of age where family eczema-history as well as exposure was collected at two different ages of the index child.

Methods

The Prevention of Allergy among Children in Trondheim (PACT) study is a large population- based prospective study on allergy related disorders conducted in Trondheim, central Norway. Trondheim has approximately 165 000 inhabitants and 2100 deliveries pr year.

From September 2000 all pregnant women as well as children 6 weeks, 1 year, and 2 years of age visiting their general practitioner or community based midwife were consecutively invited to attend the study. Women/parents were eligible to participate if they were able to complete a questionnaire in Norwegian. Recruitment of 6 weeks old, 1 year and 2 years old children closed June 30th 2006. The PACT-study is described in further detail elsewhere [19].

-Study design

Family eczema-history and exposure variables was assessed from questionnaires when the child was 6 weeks old (Q2) and 1 year old (Q3) [19]. When the child was approximately 2 years of age, the parents answered a questionnaire on the child's health (Q5). The questionnaires Q2 and Q3 included questions on different allergic diseases in parents/siblings (including family eczema-history) as well as on indoor climate, infections, medication, vaccines, day-care, exposure to nicotine, pets, breastfeeding and diet. Q5 included questions on different health issues in index child with emphasize on allergy related disorders. The latter questions were adopted from the International Study of Asthma and Allergies in Childhood (ISAAC) protocol and modified to fit the actual age group [20].

By March 2009 some 2657 parents (54.6%) had completed Q2 as well as the child's health-questionnaire at the age of 2 years (Q5), and these are included in the 6 weeks cohort. The 1 year cohort comprises 3087 parents (60%) who had completed Q3 together with Q5 (table 1).

These two cohorts (6 weeks, N = 2657 and 1 year, N = 3087) were used to prospectively study reported family eczema-history and association to eczema in index child reported at 2 year.

-Study variables

-*The outcome variable* studied was ever eczema reported at the age of 2 years (Q5). The index child was defined as having eczema if both questions "Has your child *ever* had eczema?" and "Has your child *ever* had an itchy rash which was coming and going for at least 6 months?" were answered positively [21].

Family eczema-history and exposure variables were assessed in Q2 and Q3.

-Family eczema- history

Eczema in mother, father or sibling was defined as "yes" if any one of the questions "have you, the child's father or any of your joint children ever had eczema" or "have you, the child's father or any of your joint children had eczema or used medication against eczema during the last 12 months" were ticked "yes" for mother, father or sibling.

The reporting of family eczema history was then categorized into the seven different family eczema groups possible; "mother only", "father only", "sibling only", "mother and father", "mother and sibling", "father and sibling", "mother, father and sibling".

-Exposure variables

The term "breastfeeding now" was used regardless of whether or not solid food or formulas was given to the child in addition to breast milk.

"Current smoking mother" was regarded as "yes" when the question "do you smoke now?" was answered positively.

Maternal and paternal level of education was not accounted for in the original questionnaire. Thus, home-owner status from the questionnaire was used as a proxy for socioeconomic status.

"Dampness" was defined "yes" when the sum of 8 different questions concerning damp/mould at home was 3 or more.

-Ethics

All parents signed a written consent form to participate in the PACT study. The study was approved by the Regional Committee for Medical Research Ethics and the Norwegian data Inspectorate Board (Ref 120-2000) (Ref 2003/953-3 KBE/-).

-Statistics

Univariate associations between eczema in index child and different family eczema-groups as well as the

Table 1 Characteristics of the two study populations with exposure reported at 6 weeks and 1 year

		Exposure reported at 6 weeks, N = 2657			Exposure reported at 1 year, N = 3087		
Reported exposure [a]		n	%	(95% CI)	n	%	95% CI
Gender	Male	1333	50.2	(48.3-52.1)	1529	49.5	(47.8-51.3)
Homeowner	Yes	2242	84.4	(82.9-85.7)	2680	86.8	(85.6-88.0)
Cat	Yes	239	9.0	(7.9-10.1)	266	8.6	(7.7-9.7)
Dog	Yes	247	9.3	(8.2-10.5)	249	8.1	(7.1-9.1)
Bird	Yes	63	2.4	(1.8-3.0)	70	2.3	(1.8-2.9)
Dampness	Yes	105	4.0	(3.2-4.8)	117	3.8	(3.1-4.5)
Maternal current smoking	Yes	189	7.1	(6.2-8.2)	453	14.7	(13.4-16.0)
Paternal current smoking	Yes	399	15.0	(13.7-16.4)	499	16.2	(14.9-17.5)
Premature birth, < 37 weeks	Yes	75	2.8	(2.2-3.5)	75	2.4	(1.9-3.0)
Birth-weight	<2500gr	74	2.8	(2.2-3.5)	105	3.4	(2.8-4.1)
	2500-3999gr	1937	72.9	(71.2-74.6)	2196	71.1	(69.5-72.7)
	≥4000gr	623	23.4	(21.8-25.1)	691	22.4	(20.9-23.9)
Breastfeeding now	Yes	2481	93.4	(92.4-94.3)	1114	36.1	(34.4-37.8)
Number of siblings	0	1172	44.1	(42.2-46.0)	1343	43.5	(41.7-45.3)
	1	920	34.6	(32.8-36.5)	1033	33.5	(31.8-35.2)
	2 or more	533	20.1	(18.6-21.6)	711	23.0	(21.6-24.6)
Any kind of infection, child	Yes	903	34.0	(32.2-35.8)	2983	96.6	(95.9-97.2)
Antibiotics ever, child	Yes	58	2.2	(1.7-2.8)	706	22.9	(21.4-24.4)
	mean	**range**	**SD**		**mean**	**range**	**SD**
Maternal age	30.1	17-48	4.49		29.98	17-48	4.46

[a] Number of missing varies

different exposure variables were analysed using simple logistic regression.

Associations adjusted for potential confounders were obtained by logistic regression models. Maternal age was used as a linear variable in the regression analysis. All other explanatory variables were either dichotomized or categorized. Dummy variables were made when the independent variables contained more than two categories. Family eczema-groups were also categorized, and those with no family history of eczema (mother, father or sibling) were set as reference group.

The logistic regression models were adjusted for confounding factors identified by *a priori* knowledge to the problem being studied. In the final multivariable regression analysis, adjustments were made for gender, homeowner, current smoking mother, breastfeeding, keeping a dog and age of mother at the time of birth.

A separate model was made for older siblings with and without eczema. In addition to adjustment for the *a priori* defined confounding factors, adjustment was made for eczema mother and eczema father. Interaction between eczema mother and eczema father was tested.

In the multivariable analysis the number of missing varied for each variable under study, but never exceeded 9%.

Unadjusted and adjusted associations are presented as odds ratios (OR, aOR). 95% confidence intervals (CI) were estimated for binominal distributed data.

Statistical Package for Social Science version 15.0 (SPSS inc., Chicago; IL, USA.) and STATA version 11.2 for Windows (STATA Corporation, College Station, TX, USA) were used for the analyses.

Results

Some 13.7% and 14.2% of the girls, and 15.9% and 16.1% of the boys reported eczema at 2 years of age in the 6-week cohort (N = 2657) and in the 1-year cohort (N = 3087), respectively.

When exposure was reported at 6 weeks, only some 6% of the index children with eczema had had their first symptoms of eczema, whereas the corresponding number was about 80% among those who reported exposure at 1 year.

Some 77% of children in the 6-week cohort also attended the 1-year cohort. Between 6 weeks and 1 year, some 9.6% of these parents changed their answer from "no" to "yes" regarding whether or not the index child had a sibling with eczema or not. Among those with eczema in index child reported at 2 years, some 28.5% changed their answer from "no" to "yes" from 6 weeks to 1 year, as opposed to some 6.4% among those without eczema in index child 2 years (data not shown).

In univariate analyses, keeping a dog was the only statistically significant environmental factor associated with reported eczema at 2 years of age in both cohorts.

When reporting family history at 6 weeks, the association between eczema in index child at 2 years and different eczema- groups containing only one or both of the parents, both "eczema mother only" and eczema father only" were statistically significant in the univariate analyses [(OR, 1.61; 95% CI 1.18-2.21), (OR, 1.69; 95% CI 1.16-2.46)] (table 2). When adding reporting of eczema in a sibling to eczema in one or both of the parents, we found "eczema mother and sibling, not father" and "eczema mother, father and sibling" to be significantly associated with eczema in the index child at 2 years [(OR, 3.41; 95% CI 1.91-6.10) and (OR, 3.15; 95% CI 1.42-7.02)].

Corresponding univariate analyses of different family history eczema-groups reported at 1-year showed no differences in associations with eczema in index child at 2 years for any of the groups containing one or both of the parents without a sibling compared to 6 weeks. For all groups including eczema in siblings there were a consistent and highly significantly association with eczema at 2 year in the index child (table 2).

In the adjusted model, we found a significant association between "eczema mother only" and "eczema father only" reported at 6 weeks and eczema in the index child at 2 years [(aOR, 1.57; 95% CI 1.13-2.18), (aOR, 1.73; 95% CI 1.18-2.55)] (table 3). No association was found with "eczema sibling only" (aOR, 1.31; 95% CI 0.77-2.23).

When adapting the same model on reported eczema in mother, father and sibling at 1 year, we found a significant association with eczema at 2 years in all groups but "eczema mother and father" (Table 3). As opposed to the family eczema-history reported at 6 weeks, a significant association was observed for "eczema sibling only" (aOR, 3.13; 95% CI 2.27-4.33). Adding eczema in sibling to either of the eczema parent groups significantly strengthened the associations in the 1 year cohort; "eczema mother and sibling, not father" (aOR, 4.48; 95% CI 2.96-6.78), "eczema father and sibling, not mother" (aOR, 5.43; 95% CI 3.27-9.02).

In the model testing association between siblings with and without eczema and association to eczema in index child 2 years, we found a significant association for siblings with eczema in the 1 year cohort only (aOR, 2.18; 95% CI 1.63-2.92). No interaction between eczema mother and father was found in either of the cohorts (p for interaction = 0.48 at 6 weeks, p for interaction = 0.10 at 1 year) (data not shown).

Table 3 Adjusted association between different family eczema-groups and eczema 2 years [a,b]

	Reported at 6 weeks		Reported at 1 year	
	aOR	(95% CI)	aOR	(95% CI)
Eczema mother only	1.57	(1.14-2.18)	1.62	(1.17-2.24)
Eczema father only	1.73	(1.18-2.55)	1.98	(1.35-2.90)
Eczema mother and father, not sibling	1.83	(0.97-3.42)	1.73	(0.91-3.28)
Eczema sibling only	1.31	(0.77-2.23)	3.13	(2.27-4.33)
Eczema mother and sibling, not father	2.59	(1.34-5.00)	4.48	(2.96-6.78)
Eczema father and sibling, not mother	2.14	(0.99-4.63)	5.43	(3.27-9.02)
Eczema mother, father and sibling	3.78	(1.66-8.63)	6.25	(3.09-12.65)

[a]) No family eczema is the reference point for all other family eczema-groups
[b]) Model adjusted for gender, homeowner, current smoking mother, breastfeeding, keeping a dog and age of mother at time of birth.

Table 2 Univariate association between different family eczema-groups and eczema 2 years

	Proportion of children with eczema 2 years	OR (95% CI)		Proportion of children with eczema 2 years	OR (95% CI)
Reported 6 weeks			Reported at 1 year		
No family eczema [a]	12.5% (217/1738)	1.0	No family eczema [a]	10.7% (201/1885)	1.0
Eczema mother only	18.7% (61/326)	1.61 (1.18-2.21)	Eczema mother only	16.7% (59/354)	1.68 (1.22-2.30)
Eczema father only	19.4% (39/201)	1.69 (1.16-2.46)	Eczema father only	18.1% (39/215)	1.86 (1.27-2.71)
Eczema mother and father, not sibling(s)	19.7% (13/66)	1.72 (0.92-3.21)	Eczema mother and father, not sibling(s)	16.0% (12/75)	1.60 (0.85-3.01)
Eczema sibling(s) only	16.9% (22/130)	1.43 (0.88-2.31)	Eczema sibling(s) only	25.5% (67/263)	2.86 (2.09-3.92)
Eczema mother and sibling (s), not father	24.1% (19/79)	3.41 (1.91-6.10)	Eczema mother and sibling (s), not father	33.9% (42/124)	4.29 (2.88-6.40)
Eczema father and sibling (s), not mother	23.1% (9/39)	2.10 (0.99-4.49)	Eczema father and sibling (s), not mother	37.5% (27/72)	5.03 (3.05-8.28)
Eczema mother, father and sibling(s)	31.0% (9/29)	3.15 (1.42-7.02)	Eczema mother, father and sibling(s)	40.0% (14/35)	5.59 (2.80-11.16)

[a] No family eczema is the reference point for all other family eczema-groups

Discussion

In this large population based study with reports of family eczema-history at two different points of time, we found that having either parent with eczema was significantly associated with reported eczema at the age of 2 years. The associations were consistent when reported at 6-weeks as well as 1 year. Having one or several siblings with eczema, with or without either of the parents with eczema reported at 1 year, was also strongly associated with reported eczema at 2 years and significantly stronger for siblings only.

We have data on exposure reported at 6 weeks and 1 year. Although the reporting of exposure was at two different points of time, the two cohorts are comparable. Some 77% of those who answered Q2 (6 weeks) also answered Q3 (1 year) as well as Q5 (2 years). The two cohorts are generated from the same geographic area (the city of Trondheim), during the same time-period, and by the same midwifes and GPs.

Although eczema is a relatively prevalent disease among children in the western world, most children have mild degree of disease, making the diagnosis and differentiating between different phenotypes of the disease as well as mild cases challenging [21-23]. We found the prevalence of reported eczema 2 years to about 15% both among those who reported the family eczema history at 6-week and those who reported at 1 year, indicating a high reliability of the questions. Any misclassification of eczema cases might therefore be non-differential, and if so may have diluted the associations.

Several studies describe a maternal line of inheritance concerning eczema [5,6,22]. This maternal line of inheritance has led investigators to hypothesize that environmental influences operating *in utero* or in early infancy may be essential in determining disease expression [24]. In this study eczema in the index child was significantly associated with eczema in mothers as well as fathers. This finding is in accordance with several others [8,9,25] and not supportive to the hypothesis of paternal genomic imprinting. However, parental recall bias should be taken into consideration also here. Any one parent who followed the child was asked to participate in the PACT-study. One limitation in this study is the fact that we don't know which parent filled in the questionnaire. Since many of the women were included during pregnancy and during their child's first year of living, we assume that mothers most likely have accepted to participate in the study when visiting her GP or midwife. It is therefore most likely that mothers have filled in the questionnaires. In both cohorts more boys than girls reported eczema at age 2 years. Despite this, more mothers than fathers reported to have ever eczema. When studying recall bias in parental questioning, a German group found that mothers tended to report more atopic diseases in a second questionnaire than in the first, whilst fathers were influenced by their child's development of atopic disease [16]. In families without childhood eczema the sensitivity for mothers reporting paternal eczema was lower than in families with at least one child with eczema. The specificity was about the same [26]. Although effect size is small in a population setting, filaggrin haploinsufficiency is a highly penetrant trait, and associated with increased eczema severity [27]. It is therefore likely that severe eczema in any one of the parents represent a greater risk of eczema in the offspring. It seems also likely, that mothers more often would report a positive paternal history of eczema if the disease was severe or persisted into adulthood. The latter is supported by a Swedish study, who found that recall of childhood eczema history among adults was influenced by several factors such as high prevalence of eczema after the age of 15, more visits to the physician after the age of 15, more hand eczema and more sick-leave due to eczema [17]. Since mothers most likely have filled in our questionnaires, an overestimation of the association between paternal eczema and eczema in index child is possible. This might be due either to more severe eczema in fathers or increased awareness due to development of eczema in one of the children. Both could explain the lack of a maternal line of inheritance in this study.

When family history of eczema is studied, allergy related disorders in siblings are seldom accounted for in the risk analysis. We found that, although having any one parent with eczema was associated with eczema in index child at 2 years, having one or several siblings with eczema together with mother and/or father with eczema was strongly associated with eczema in index child 2 years when reports were collected at 1 year. This association was also seen when eczema was reported only in sibling(s). There are different interpretations of these findings. One possible explanation could be that this is a reflection of a parental genetic disposition with incomplete penetrance [4]. Mutations in the gene encoding filaggrin (FLG) have been identified as a strong predisposing factors for eczema [28] and especially severe phenotypes of the disease [29], but other candidate genes are also under investigation [11]. Different environmental factors can alter the expression of different genes, as have been showed with the exposure to cat within the first year of life in those who carry mutations of FLG [30]. Other environmental factors such as early colonisation from maternal microbial flora as well as shared environment among siblings with the same genetic predisposition may act in a similar way and explain the "eczema-sibling-effect" in this study.

The "eczema-sibling-effect" was not significant when reported at 6 weeks. Awareness of disease in first child with mild disease might be absent until same kinds of symptoms as e.g. dry skin is observed in second child. Also, in mild cases of eczema a significant proportion of the children are disease free by the age of 3 years [31]. In this study, some 28.5% of parents with eczema in index child at 2 years changed their answer from "no" when reported at 6 weeks to "yes" when reported at 1 year regarding the question on whether or not siblings had eczema, as opposed to 6.4% among those without eczema in index child. These findings could be interpreted as an increase in awareness since some 80% of index children had developed symptoms on eczema at age 1 year. Another interpretation is that some of the older siblings have not yet been diagnosed with eczema. This is however less likely, since a majority of children with eczema starts with their disease during their first year of life [31].

In a German study of children 9-11 years old having two first degree relatives with the same atopic disease was highly associated with eczema [4]. Diepgen & Blettner found a stronger correlation between siblings than between siblings and parents for all atopic diseases, also atopic dermatitis [5]. Eczema in an older sibling was also found to be an independent risk factor for eczema among 4-years old in Sweden [9].

When only some 60% of those finishing the questionnaires on exposure were answering the questionnaires on health, one could argue that the data are prone to self-selection. In both cohorts the lost-to-follow-up group contained more current smoking mothers and fewer homeowners, indicating a lower socio-economic status (data not shown). However, other exposure data, including reported family eczema-history did not differ among those who followed up and those who did not.

Another limitation of the study was the reporting eczema in parents and siblings without a clinical verification. The question "have you, the child's father or any of your joint children ever had eczema" is a core ISAAC questions, but is most often used in combination with a question on rash located in typical places or diagnosis verified by a doctor. To the best of our knowledge, the question has not been validated in an adult population. However, the almost similar phrasing "have you ever had childhood eczema" was validated among adults in a Swedish population. The sensitivity and specificity of this question was 89.9% and 70.7%, respectively [32], and an overestimation of the reported prevalence of childhood eczema among adults is therefore likely. Regarding the use of this question among children (siblings), we have validated this in a former publication [21]. This question alone, without a question identifying rash on typical location, gave a sensitivity of 96.8% and a specificity of 68.0% when validated against the UK Working Party Criteria. Adding a question of rash on typical locations decreased the sensitivity whereas the specificity increased. This gives reason to believe, that there might be an overestimation of reported eczema among the siblings, since other forms of dermatitis in young children, such as seborrhoeic dermatitis as well as nappy dermatitis might have been included. However, in case of such a misclassification, there is no reason to believe that this has changed from 6 weeks to 1 year, and could therefore not explain the differences in reporting of eczema in siblings in the two cohorts.

The strengths of this study are the large number of unselected participants as well as the prospective design. The consistency of reported eczema indicates a high reliability of the questions and the prevalence of reported eczema is well in line with the prevalence found in the PACT endpoint-study [21]. In addition, the focus is on eczema-groups only, since other studies have showed that parental eczema may be a better marker for eczema in the offspring than other parental atopic diseases [8,33].

Conclusions

We found that reporting having a sibling with eczema at 1 year was significantly associated with reported eczema at 2 years. Eczema in mother as well as eczema in father was both associated with eczema 2 years. When family eczema-history was reported when index child was 1 years of age, the associations with eczema 2 years were significantly stronger for both parents if sibling(s) of the index child had eczema, and association was significantly stronger for sibling(s) reported at 1 year compared to 6 weeks. However, although siblings had eczema, the shared environment by mother and child did not result in any difference between maternal and paternal associations to eczema 2 years in index child.

The finding of different associations when family-eczema history was reported at 6 weeks compared to when family eczema-history was reported at 1 year indicate bias in information gathering and has important implications on comparability of studies measuring the effect of older sibling disease on index child`s risk of eczema.

Acknowledgements

The authors would like to thank all parents, children, general practitioners and midwifes for participating in the study. A special thank to bioengineer Guri Helmersen and nurse Else Bartnes for their invaluable contribution in the PACT-study.

Funding for the PACT study was obtained from the Norwegian Department of Health and Social affairs 1997-2003, and the control cohort was funded by AstraZeneca Norway AS 2000-2001. A university scholarship from the Norwegian University of Science and Technology (NTNU) is funding MS from 2008-2012. A university scholarship from NTNU and a scholarship from Norwegian Research Council 1999-2003 funded TØ and OS. Grants were

obtained from the Norwegian Medical Association and SINTEF Unimed 1999. A scholarship from Nidarosfondet funded TØ in 2007.

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Authors' contributions
MS participated in the design of the study, performed statistical analysis and drafted the manuscript. TØ, OS and RJ conceived the study, participated in its design and co-ordination and helped draft the manuscript.
All authors read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

Received: 17 December 2010 Accepted: 20 May 2011
Published: 20 May 2011

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Pre-publication history
The pre-publication history for this paper can be accessed here:
http://www.biomedcentral.com/1471-5945/11/11/prepub

doi:10.1186/1471-5945-11-11
Cite this article as: Saunes *et al.*: Family eczema-history in 2-year olds with eczema; a prospective, population-based study. The PACT-study, Norway. *BMC Dermatology* 2011 **11**:11.

PAPER III

Saunes M, Øien T, Dotterud CK, Romundstad PR, Storrø O Holmen TL, Johnsen R.

Early eczema and the risk of childhood asthma; a prospective, population-based study.

Submitted

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PAPER IV

Saunes M, Smidesang I, Holmen TL, Johnsen R.

Atopic dermatitis in adolescent boys is associated with greater psychological morbidity compared with girls of the same age: the Young-HUNT study. Br J Dermatol. 2007 Feb;156(2):282-8

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APPENDIX I

PACT questionnaires

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Barneallergistudien i Trondheim

Spørreskjema om livsstilsfaktorer ved 6 ukers alder

Skriv tydelige tall og kryss. Bruk **svart** eller **blå** penn.

Utfylt dato (dd.mm.åå) ☐☐.☐☐.☐☐

Spørsmål om barnet

1. Er barnet tvilling ? ☐ Ja ☐ Nei **Hvis tvilling**, svar på alle spørsmålene for tvilling I, deretter svar på spørsmål 1-6 og 47-51 for tvilling II på eget skjema.

2. Barnets fødselsvekt ? ☐☐☐☐ gram og fødselslengde ? ☐☐ cm

3. Hvor mange søsken har barnet ?
(ta med fellesbarn og særkullsbarn, **ikke** fosterbarn og adoptivbarn)
Ingen søsken : ☐ (kryss)
Antall søsken : ☐ brødre ☐ søstre

4. Når ble barnet født i forhold til beregnet ultralydtermin ? (ett kryss)
Tidligere enn 2 uker før beregnet ultralydtermin ☐
Mellom 3 uker før og 2 uker etter beregnet ultralydtermin ☐
Senere enn 2 uker etter beregnet ultralydtermin ☐

5. Har barnet blitt vaksinert ? ☐ Ja ☐ Nei
Hvis ja, hvilken vaksine ? ☐ BCG ☐ Hepatitt ☐ Andre _____

6. Har barnet hatt noen av sykdommene nedenfor ?

	Ja	Nei	Hvis ja, antall ganger	Er noen av sykdommene behandlet med penicillin/antibiotika ? Ja	Nei	Vet ikke	Hvis ja, hvor mange behandlinger
Forkjølelse	☐	☐	☐	☐	☐	☐	☐
Ørebetennelse	☐	☐	☐	☐	☐	☐	☐
Bronkitt	☐	☐	☐	☐	☐	☐	☐
RS-virusinfeksjon	☐	☐	☐	☐	☐	☐	☐
Falsk krupp	☐	☐	☐	☐	☐	☐	☐
Lungebetennelse	☐	☐	☐	☐	☐	☐	☐
Urinveisinfeksjon	☐	☐	☐	☐	☐	☐	☐
Mage-tarminfeksjon	☐	☐	☐	☐	☐	☐	☐

7. Foreldrenes sivilstatus: ☐ Gift ☐ Samboer ☐ Enslig ☐ Annet

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Spørsmål om foreldre og søsken

8. Har mor, far eller noen av barna **noen gang** hatt astma, eksem eller allergi i øyne/nese ?

☐ Ja ☐ Nei

Hvis nei, gå til spørsmål 14.
Hvis ja, kryss av for de familiemedlemmer det gjelder (flere kryss) :

	Astma	Eksem	Allergi i øyne/nese
Mor	☐	☐	☐
Far	☐	☐	☐
Fellesbarn	☐	☐	☐
Dine særkullsbarn	☐	☐	☐
Barnefarens særkullsbarn	☐	☐	☐

9. Har, eller har mor, far eller fellesbarn **noen gang** hatt astmasykdom ? ☐ Ja ☐ Nei

Hvis nei, gå til spørsmål 11.
Hvis ja, angi alder i dag, når astmasykdommen startet, om sykdommen fortsatt er til stede, og når den eventuelt sluttet.

	Alder i dag	Startalder astma	Har fortsatt astma (kryss)	Sluttalder astma
Mor	☐☐ år	☐☐ år	☐	☐☐ år
Far	☐☐ år	☐☐ år	☐	☐☐ år
Fellesbarn 1	☐☐ år	☐☐ år	☐	☐☐ år
Fellesbarn 2	☐☐ år	☐☐ år	☐	☐☐ år
Fellesbarn 3	☐☐ år	☐☐ år	☐	☐☐ år

10. Har, eller har mor, far eller fellesbarn hatt astmaplager eller brukt astmamedisiner de **siste 12 måneder** ?

☐ Ja ☐ Nei

Hvis ja, kryss av for de det gjelder :

	Hyppighet av astmaplager siste 12 måneder				Brukt astmamedisin siste 12 måneder	
	Daglig	Ukentlig	Månedlig	Sjeldnere enn månedlig	Ja	Nei
Mor	☐	☐	☐	☐	☐	☐
Far	☐	☐	☐	☐	☐	☐
Fellesbarn 1	☐	☐	☐	☐	☐	☐
Fellesbarn 2	☐	☐	☐	☐	☐	☐
Fellesbarn 3	☐	☐	☐	☐	☐	☐

11. Har, eller har mor,far eller fellesbarn hatt eksemplager, eller brukt eksemmedisin de **siste 12 måneder** ?

☐ Ja ☐ Nei

Hvis ja, kryss av for de det gjelder :

	Hyppighet av eksemplager siste 12 måneder				Brukt eksemmedisin siste 12 måneder ?	
	Daglig	Ukentlig	Månedlig	Sjeldnere enn månedlig	Ja	Nei
Mor	☐	☐	☐	☐	☐	☐
Far	☐	☐	☐	☐	☐	☐
Fellesbarn 1	☐	☐	☐	☐	☐	☐
Fellesbarn 2	☐	☐	☐	☐	☐	☐
Fellesbarn 3	☐	☐	☐	☐	☐	☐

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12. Har, eller har mor, far eller fellsbarn hatt allergi i øyne/nese, eller brukt allergimedisiner ?

☐ Ja ☐ Nei

Hvis nei, gå til spørsmål 14.
Hvis ja, kryss av (flere kryss) for de det gielder :

	Allergi mot				Brukt allergimedisin siste 12 måneder ?	
	Pollen	Dyrehår	Husstøv/ midd	Andre	Ja	Nei
Mor	☐	☐	☐	☐	☐	☐
Far	☐	☐	☐	☐	☐	☐
Fellesbarn 1	☐	☐	☐	☐	☐	☐
Fellesbarn 2	☐	☐	☐	☐	☐	☐
Fellesbarn 3	☐	☐	☐	☐	☐	☐

13. Hvis mor, far eller fellsbarn har allergi i øyne/nese, hvordan er det påvist ?
Kryss av for de det gielder :

	Allergi påvist ved blodprøve ?			Allergi påvist ved prikk(hud)-testing ?		
	Ja	Nei	Vet ikke	Ja	Nei	Vet ikke
Mor	☐	☐	☐	☐	☐	☐
Far	☐	☐	☐	☐	☐	☐
Fellesbarn 1	☐	☐	☐	☐	☐	☐
Fellesbarn 2	☐	☐	☐	☐	☐	☐
Fellesbarn 3	☐	☐	☐	☐	☐	☐

14. Kryss av om mor hadde noen av følgende plager i siste svangerskap. Oppgi i hvilken periode, og om mulig navn på medisiner som ble brukt.

	Plager i siste svangerskap ?	Periode i svangerskapet (flere kryss) 0-3 mnd	4-6 mnd	7-9 mnd	Medisinnavn
Svangerskapsblødning	☐	☐	☐	☐	_____
Svangerskapsforgiftning	☐	☐	☐	☐	_____
Forhøyet blodtrykk	☐	☐	☐	☐	_____
Svangerskapsdiabetes	☐	☐	☐	☐	_____
Diabetes, insulinbehandlet	☐	☐	☐	☐	_____
Diabetes, tablettbehandlet	☐	☐	☐	☐	_____
Soppinfeksjon i skjeden	☐	☐	☐	☐	_____
Skjedekatarr/uvanlig utflod	☐	☐	☐	☐	_____
Forkjølelse	☐	☐	☐	☐	_____
Influensa	☐	☐	☐	☐	_____
Bronkitt	☐	☐	☐	☐	_____
Lungebetennelse	☐	☐	☐	☐	_____
Astma	☐	☐	☐	☐	_____
Eksem	☐	☐	☐	☐	_____
Allergi i øyne /nese	☐	☐	☐	☐	_____
Andre plager	☐				
Ingen plager	☐				

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Spørsmål om bolig / innemiljø nå

15. I hvilken type bolig bor **barnet** ? (ett kryss)

- Enebolig/våningshus uten sokkel/kjeller ☐
- Enebolig/våningshus med sokkel/kjeller ☐
- Sokkelleilighet i enebolig ☐
- Tomannsbolig, firemannsbolig ☐
- Rekkehus/kjedehus ☐
- Terrassehus ☐
- Boligblokk/bygård ☐
- Annen bolig ☐

16. Boligens byggeår ? (årstall) ☐☐☐☐

Hvilket år flyttet du inn i boligen ? ☐☐☐☐

17. Eier du/dere boligen ?

- Ja, som selveiere ☐
- Ja, i borettslag ☐
- Nei ☐

18. Boligens boareal (cirka) ? ☐☐☐ m^2

19. Hvor mange personer bor det for tiden i boligen ? ☐☐

20. Hvor ofte vaskes boligen ? ☐☐ ganger per måned

Hvor ofte støvsuges boligen ? ☐☐ ganger per måned

21. Har boligen sentralstøvsuger ? ☐ Ja ☐ Nei

22. Hvor mange timer oppholder **barnet** seg i gjennomsnitt i boligen ?

I boligen ☐☐ timer per døgn

I eget soverom ☐☐ timer per døgn

23. Hvilke av følgende husdyr oppholder seg i boligen ? (flere kryss)

- Hund ☐
- Katt ☐
- Andre pelsdyr (marsvin, kanin o.l.) ☐
- Fugl ☐
- Andre dyr ☐
- Ingen dyr ☐

24. Bor **barnet** på gårdsbruk ? ☐ Ja ☐ Nei

Hvis ja, hvilke husdyr er det på gården ? (flere kryss)

- Kyr ☐
- Gris ☐
- Sau ☐
- Hest ☐
- Fjørfe ☐
- Andre husdyr ☐
- Ingen husdyr ☐

25. Hvilke energikilder brukes til oppvarming av boligen ? (flere kryss)

- Elektristitet ☐
- Vedfyring ☐
- Olje ☐
- Fjernvarme ☐
- Annet ☐

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26. Har, eller har boligen hatt noen av følgende problemer ?
(besvar alle spørsmål)

	Ja	Nei	**Hvis ja**, er problemet utbedret ? Ja, utbedret	Nei, ikke utbedret
Mugglukt eller kjellerlukt	☐	☐	☐	☐
Aviser og pappesker blir ved lagring 'fuktige'	☐	☐	☐	☐
Dugg på vinduer (utenom ved dusjing, fosskoking og sterk kulde)	☐	☐	☐	☐
Fuktflekker på vegg eller tak (fuktflekker som skyldes mindre søl med vann regnes ikke med her)	☐	☐	☐	☐
Vannlekkasjer fra sanitærinstallasjoner (rør, kraner, dusj, vask o.l.)	☐	☐	☐	☐
Vannlekkasjer fra yttertak	☐	☐	☐	☐
Vannlekkasjer fra grunnen/oversvømmelse	☐	☐	☐	☐
Blærer, bobler i eller misfarging av gulvbelegg	☐	☐	☐	☐
Ingen problemer	☐			

27. Hvilke av følgende ventilasjonsutstyr er installert i boligen ?

	Ja	Nei
A. Egen avtrekksvifte over komfyr	☐	☐
B. Egen avtrekksvifte i ventil i yttervegg på våtrom	☐	☐
C. Ventiler i yttervegg/vinduskarm eller luftevindu	☐	☐
D. Sentral avtrekksventilasjon (sentral vifte som gir avtrekk fra bad, toalett og kjøkken)	☐	☐
E. Ventilasjonsanlegg (sentral vifte som gir avtrekk fra bad, toalett og kjøkken, og en sentral vifte som gir tilførsel av luft til oppholdsrom og soverom)	☐	☐

Hvis ja på D eller E - Omtrent hvor mange **timer per døgn** er det for tiden i bruk : ☐☐ Skriv 0 hvis ikke i bruk

- Omtrent hvor mange **ganger per år** skiftes filter : ☐☐ Skriv 0 hvis ingen

28. Hvor ofte gjennomluftes boligen for tiden ved å åpne vindu eller dører i minimum 3-5 minutter ?
(ett kryss)

- Aldri ☐
- Sjeldnere enn 1 gang om dagen ☐
- 1 gang om dagen ☐
- 2 ganger daglig ☐
- 3 eller flere ganger daglig ☐

29. Hvilke av følgende aktiviteter foregår **daglig i boligen uten** at elektrisk avtrekksvifte/ventilasjon benyttes ? (flere kryss)

- Tørking av tøy ☐
- Koking av mat ☐
- Bruk av tørkeskap/tørketrommel ☐
- Dusjing (mer enn 5 minutter) ☐
- Bruk av luftfukter ☐
- Ingen aktiviteter ☐

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30. I hvilken etasje av bygningen er **barnets** soverom ? (ett kryss)

Sokkel	☐
Kjeller	☐
1. etasje	☐
2. etasje eller høyere	☐

31. Sover **barnet** for tiden med åpent vindu ?

☐ Ja ☐ Nei

32. Hva slags dyne eller pute bruker **barnet** nå ?

	Dyne	Pute
Syntetiske fibre	☐	☐
Dun	☐	☐
Annet	☐	☐
Bruker ikke dyne eller pute	☐	☐

33. Hvor gammel er **barnets** nåværende dyne, pute og madrass ?

	Alder, (under 1 år skriv 0)
Dyne	☐☐ år
Pute	☐☐ år
Madrass	☐☐ år

34. Hvor ofte vaskes sengetøyet til **barnet** ? ☐☐ ganger per måned

Hvor ofte rengjøres madrassen til **barnet** ? ☐☐ ganger per **år**

35. Tørkes sengetøyet i tørketrommel ?

☐ Ja ☐ Nei

36. Hvor mange våtrom og andre rom har **vinylgulv med gulvvarme** ? (Skriv 0 hvis ingen)

Våtrom (bad, vaskerom, WC)	☐ antall rom
Andre rom	☐ antall rom

37. Hvilke materialer er brukt **på gulv** i soverommet, og i oppholdsrommet **barnet** bruker mest ? (flere kryss)

	Gulv i barnets soverom	Gulv i barnets mest brukte oppholdsrom
Heldekkende tepper	☐	☐
Vinyl (PVC-plast)	☐	☐
Furu tregulv	☐	☐
Parkett/andre harde materialer	☐	☐
Annet	☐	☐

38. Hvilke overflater har **veggene i** soverommet og i oppholdsrommet **barnet** bruker mest ?

(flere kryss)	Vegg i barnets soverom	Vegg i barnets mest brukte oppholdsrom
Ubehandlet/lutet trepanel	☐	☐
Malt/lakkert trepanel	☐	☐
Annen malt/lakkert overflate	☐	☐
Annen overflate	☐	☐

39. Har det blitt gjort noen av følgende endringer i boligen **siste 12 måneder** ?

	Ja	Nei
Nytt furu trepanel eller furu gulv	☐	☐
Nytt vinyl gulv (PVC-plast)	☐	☐
Liming av tapet, strie, gulvbelegg etc.	☐	☐
Maling, lakkering	☐	☐
Andre endringer	☐	☐

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Spørsmål om kosthold

I svangerskapet og i ammeperioden

40. Hvor ofte i gjennomsnitt spiste mor torsk, sei eller annen mager fisk til middag ?

	I svanger-skapet	I amme-perioden
Aldri	☐	☐
Sjeldnere enn 1 gang i uken	☐	☐
1 gang i uken	☐	☐
2 ganger i uken	☐	☐
3 ganger i uken	☐	☐
4 ganger i uken eller oftere	☐	☐

41. Hvor ofte i gjennomsnitt spiste mor uer, kveite, laks, ørret, sild, makrell eller annen fet fisk til middag ?

	I svanger-skapet	I amme-perioden
Aldri	☐	☐
Sjeldnere enn 1 gang i uken	☐	☐
1 gang i uken	☐	☐
2 ganger i uken	☐	☐
3 ganger i uken	☐	☐
4 ganger i uken eller oftere	☐	☐

42. Hvor ofte i gjennomsnitt tok mor tran eller fiskeoljekapsler ?

	I svanger-skapet	I amme-perioden
Aldri	☐	☐
Sjeldnere enn 1 gang i uken	☐	☐
1 gang i uken	☐	☐
2 ganger i uken	☐	☐
3 ganger i uken	☐	☐
4 ganger i uken eller oftere	☐	☐

43. Hvor mange brødskiver i gjennomsnitt spiste mor der pålegget bestod av fet fisk (sild, sardiner, makrell, laks ol.) ?

	I svanger-skapet	I amme-perioden
Aldri	☐	☐
Mindre enn 1 skive i uken	☐	☐
1-2 skiver i uken	☐	☐
3-6 skiver i uken	☐	☐
1-2 skiver i daglig	☐	☐
3-4 skiver i daglig	☐	☐
5 eller flere skiver i daglig	☐	☐

44. Hvor ofte spiste mor i gjennomsnitt grønnsaker til middag eller som egen rett (her menes rå eller kokte grønnsaker) ?

	I svanger-skapet	I amme-perioden
Aldri	☐	☐
Sjelden	☐	☐
Omtrent 1 gang i uken	☐	☐
2-3 ganger i uken	☐	☐
4-5 ganger i uken	☐	☐
Omtrent daglig	☐	☐

45. Hva slags type fett ble brukt til matlaging (ikke på brødet) i mors husholdning ?
(flere kryss)

	I svanger-skapet	I amme-perioden
Meierismør	☐	☐
Hard margarin	☐	☐
Bløt (soft) margarin	☐	☐
Smør/margarin blanding	☐	☐
Soyaolje	☐	☐
Olivenolje	☐	☐

46. Har mor i ammeperioden spist noen av følgende matemner ?

	Ofte (minst ukentlig)	Av og til (noen ganger i måneden)	En gang	Aldri
Kumelk	☐	☐	☐	☐
Egg	☐	☐	☐	☐
Fisk	☐	☐	☐	☐
Skalldyr	☐	☐	☐	☐
Nøtter	☐	☐	☐	☐
Erter/belgfrukter	☐	☐	☐	☐

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Spørsmål om barnets ernæring

47. Har barnet fått morsmelk ?
☐ Ja ☐ Nei

48. Får barnet morsmelk fremdeles ?
☐ Ja ☐ Nei
Hvis nei, hvor gammelt var barnet da det sluttet med morsmelk ?
☐☐ måneder

49. Får barnet tran ?
☐ Ja ☐ Nei

50. Får barnet annet vitamintilskudd ?
(for eksempel Biovit, Sanasol)
☐ Ja ☐ Nei

51. Får barnet morsmelkerstatning ?
☐ Ja ☐ Nei

Hvis ja, hvilken type ?
Collett ☐
NAN ☐
Nutramigen ☐
Soyamelk ☐
Annet ☐

Hvis ja, hvor gammelt var barnet da det startet med morsmelkerstatning ?
☐☐ måneder

Spørsmål om røykevaner

52. Røykte du eller ektefelle/ samboer ved svangerskapets start ?

	Nei, røykte ikke	Ja, røykte ukentlig	Ja, røykte daglig
Du	☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig
Ektefelle/samboer	☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig

53. Røyker du eller ektefelle/ samboer nå ?

	Nei, røyker ikke	Ja, røyker ukentlig	Ja, røyker daglig
Du	☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig
Ektefelle/samboer	☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig

54. Røykes det **innendørs** hjemme ?

Nei, det røykes ikke innendørs	Ja, det røykes ukentlig innendørs	Ja, det røykes daglig innendørs
☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig

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Barneallergistudien i Trondheim

Spørreskjema om livsstilsfaktorer ved 1 års alder

Skriv tydelige tall og kryss. Bruk **svart** eller **blå** penn.

Utfyllt dato (dd.mm.åå) ☐☐.☐☐.☐☐

Spørsmål om barnet

1. Er barnet tvilling ? ☐ Ja ☐ Nei **Hvis tvilling**, svar på alle spørsmålene for tvilling I, deretter svar på spørsmål 1-6 og 47-57 for tvilling II på eget skjema.

2. Barnets fødselsvekt ? ☐☐☐☐ gram og fødselslengde ? ☐☐ cm

3. Hvor mange søsken har barnet ?
(ta med fellesbarn og særkullsbarn, **ikke** fosterbarn og adoptivbarn)
Ingen søsken : ☐ (kryss)
Antall søsken : ☐ brødre ☐ søstre

4. Når ble barnet født i forhold til beregnet ultralydtermin ? (ett kryss)
Tidligere enn 2 uker før beregnet ultralydtermin ☐
Mellom 3 uker før og 2 uker etter beregnet ultralydtermin ☐
Senere enn 2 uker etter beregnet ultralydtermin ☐

5. Har barnet blitt vaksinert ? ☐ Ja ☐ Nei

6. Har barnet hatt noen av sykdommene nedenfor ?

	Ja	Nei	Hvis ja, antall ganger	Er noen av sykdommene behandlet med penicillin/antibiotika ? Ja	Nei	Vet ikke	Hvis ja, hvor mange behandlinger
Forkjølelse	☐	☐	☐	☐	☐	☐	☐
Ørebetennelse	☐	☐	☐	☐	☐	☐	☐
Bronkitt	☐	☐	☐	☐	☐	☐	☐
RS-virusinfeksjon	☐	☐	☐	☐	☐	☐	☐
Falsk krupp	☐	☐	☐	☐	☐	☐	☐
Lungebetennelse	☐	☐	☐	☐	☐	☐	☐
Urinveisinfeksjon	☐	☐	☐	☐	☐	☐	☐
Mage-tarminfeksjon	☐	☐	☐	☐	☐	☐	☐

7. Foreldrenes sivilstatus: ☐ Gift ☐ Samboer ☐ Enslig ☐ Annet

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Spørsmål om foreldre og søsken

8. Har mor, far eller noen av barna **noen gang** hatt astma, eksem eller allergi i øyne/nese ?

☐ Ja ☐ Nei

Hvis nei, gå til spørsmål 14.
Hvis ja, kryss av for de familiemedlemmer det gjelder (flere kryss) :

	Astma	Eksem	Allergi i øyne/nese
Mor	☐	☐	☐
Far	☐	☐	☐
Fellesbarn	☐	☐	☐
Dine særkullsbarn	☐	☐	☐
Barnefarens særkullsbarn	☐	☐	☐

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9. Har, eller har mor, far eller fellesbarn **noen gang** hatt astmasykdom ? ☐ Ja ☐ Nei

Hvis nei, gå til spørsmål 11.
Hvis ja, angi alder i dag, når astmasykdommen startet, om sykdommen fortsatt er til stede, og når den eventuelt sluttet.

	Alder i dag	Startalder astma	Har fortsatt astma (kryss)	Sluttalder astma
Mor	☐☐ år	☐☐ år	☐	☐☐ år
Far	☐☐ år	☐☐ år	☐	☐☐ år
Fellesbarn 1	☐☐ år	☐☐ år	☐	☐☐ år
Fellesbarn 2	☐☐ år	☐☐ år	☐	☐☐ år
Fellesbarn 3	☐☐ år	☐☐ år	☐	☐☐ år

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10. Har, eller har mor, far eller fellesbarn hatt astmaplager eller brukt astmamedisiner de **siste 12 måneder** ? ☐ Ja ☐ Nei

Hvis ja, kryss av for de det gjelder :

	Hyppighet av astmaplager siste 12 måneder				Brukt astmamedisin siste 12 måneder	
	Daglig	Ukentlig	Månedlig	Sjeldnere enn månedlig	Ja	Nei
Mor	☐	☐	☐	☐	☐	☐
Far	☐	☐	☐	☐	☐	☐
Fellesbarn 1	☐	☐	☐	☐	☐	☐
Fellesbarn 2	☐	☐	☐	☐	☐	☐
Fellesbarn 3	☐	☐	☐	☐	☐	☐

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11. Har, eller har mor,far eller fellesbarn hatt eksemplager, eller brukt eksemmedisin de **siste 12 måneder** ? ☐ Ja ☐ Nei

Hvis ja, kryss av for de det gjelder :

	Hyppighet av eksemplager siste 12 måneder				Brukt eksemmedisin siste 12 måneder ?	
	Daglig	Ukentlig	Månedlig	Sjeldnere enn månedlig	Ja	Nei
Mor	☐	☐	☐	☐	☐	☐
Far	☐	☐	☐	☐	☐	☐
Fellesbarn 1	☐	☐	☐	☐	☐	☐
Fellesbarn 2	☐	☐	☐	☐	☐	☐
Fellesbarn 3	☐	☐	☐	☐	☐	☐

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12. Har, eller har mor, far eller fellesbarn hatt allergi i øyne/nese, eller brukt allergimedisiner ?

☐ Ja ☐ Nei

Hvis nei, gå til spørsmål 14.
Hvis ja, kryss av (flere kryss) for de det gjelder :

	Allergi mot				Brukt allergimedisin siste 12 måneder ?	
	Pollen	Dyrehår	Husstøv/ midd	Andre	Ja	Nei
Mor	☐	☐	☐	☐	☐	☐
Far	☐	☐	☐	☐	☐	☐
Fellesbarn 1	☐	☐	☐	☐	☐	☐
Fellesbarn 2	☐	☐	☐	☐	☐	☐
Fellesbarn 3	☐	☐	☐	☐	☐	☐

13. Hvis mor, far eller fellesbarn har allergi i øyne/nese, hvordan er det påvist ?
Kryss av for de det gjelder :

	Allergi påvist ved blodprøve ?			Allergi påvist ved prikk(hud)-testing ?		
	Ja	Nei	Vet ikke	Ja	Nei	Vet ikke
Mor	☐	☐	☐	☐	☐	☐
Far	☐	☐	☐	☐	☐	☐
Fellesbarn 1	☐	☐	☐	☐	☐	☐
Fellesbarn 2	☐	☐	☐	☐	☐	☐
Fellesbarn 3	☐	☐	☐	☐	☐	☐

14. Kryss av om mor hadde noen av følgende plager i siste svangerskap. Oppgi i hvilken periode, og om mulig navn på medisiner som ble brukt.

	Plager i siste svangerskap ?	Periode i svangerskapet (flere kryss) 0-3 mnd	4-6 mnd	7-9 mnd	Medisinnavn
Svangerskapsblødning	☐	☐	☐	☐	_____
Svangerskapsforgiftning	☐	☐	☐	☐	_____
Forhøyet blodtrykk	☐	☐	☐	☐	_____
Svangerskapsdiabetes	☐	☐	☐	☐	_____
Diabetes, insulinbehandlet	☐	☐	☐	☐	_____
Diabetes, tablettbehandlet	☐	☐	☐	☐	_____
Soppinfeksjon i skjeden	☐	☐	☐	☐	_____
Skjedekatarr/uvanlig utflod	☐	☐	☐	☐	_____
Forkjølelse	☐	☐	☐	☐	_____
Influensa	☐	☐	☐	☐	_____
Bronkitt	☐	☐	☐	☐	_____
Lungebetennelse	☐	☐	☐	☐	_____
Astma	☐	☐	☐	☐	_____
Eksem	☐	☐	☐	☐	_____
Allergi i øyne /nese	☐	☐	☐	☐	_____
Andre plager	☐				
Ingen plager	☐				

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Spørsmål om bolig / innemiljø nå

15. I hvilken type bolig bor **barnet** ? (ett kryss)

- Enebolig/våningshus uten sokkel/kjeller ☐
- Enebolig/våningshus med sokkel/kjeller ☐
- Sokkelleilighet i enebolig ☐
- Tomannsbolig, firemannsbolig ☐
- Rekkehus/kjedehus ☐
- Terrassehus ☐
- Boligblokk/bygård ☐
- Annen bolig ☐

16. Boligens byggeår ? (årstall) ☐☐☐☐

Hvor lenge har barnet bodd i boligen ? ☐ år ☐☐ måneder

17. Eier du/dere boligen ?

- Ja, som selveiere ☐
- Ja, i borettslag ☐
- Nei ☐

18. Boligens boareal (cirka) ? ☐☐☐ m^2

19. Hvor mange personer bor det for tiden i boligen ? ☐☐

20. Hvor ofte vaskes boligen ? ☐☐ ganger per måned

Hvor ofte støvsuges boligen ? ☐☐ ganger per måned

21. Har boligen sentralstøvsuger ? ☐ Ja ☐ Nei

22. Hvor mange timer oppholder **barnet** seg i gjennomsnitt i boligen ?

I boligen ☐☐ timer per døgn

I eget soverom ☐☐ timer per døgn

23. Hvilke av følgende husdyr oppholder seg i boligen ? (flere kryss)

- Hund ☐
- Katt ☐
- Andre pelsdyr (marsvin, kanin o.l.) ☐
- Fugl ☐
- Andre dyr ☐
- Ingen dyr ☐

24. Bor **barnet** på gårdsbruk ☐ Ja ☐ Nei

Hvis ja, hvilke husdyr er det på gården ? (flere kryss)

- Kyr ☐
- Gris ☐
- Sau ☐
- Hest ☐
- Fjørfe ☐
- Andre husdyr ☐
- Ingen husdyr ☐

25. Hvilke energikilder brukes til oppvarming av boligen ? (flere kryss)

- Elektristitet ☐
- Vedfyring ☐
- Olje ☐
- Fjernvarme ☐
- Annet ☐

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26. Har, eller har boligen hatt noen av følgende problemer ?
(besvar alle spørsmål)

	Ja	Nei	**Hvis ja**, er problemet utbedret ? Ja, utbedret	Nei, ikke utbedret
Mugglukt eller kjellerlukt	☐	☐	☐	☐
Aviser og pappesker blir ved lagring 'fuktige'	☐	☐	☐	☐
Dugg på vinduer (utenom ved dusjing, fosskoking og sterk kulde)	☐	☐	☐	☐
Fuktflekker på vegg eller tak (fuktflekker som skyldes mindre søl med vann regnes ikke med her)	☐	☐	☐	☐
Vannlekkasjer fra sanitærinstallasjoner (rør, kraner, dusj, vask o.l.)	☐	☐	☐	☐
Vannlekkasjer fra yttertak	☐	☐	☐	☐
Vannlekkasjer fra grunnen/oversvømmelse	☐	☐	☐	☐
Blærer, bobler i eller misfarging av gulvbelegg	☐	☐	☐	☐
Ingen problemer	☐			

27. Hvilke av følgende ventilasjonsutstyr er installert i boligen ?

	Ja	Nei
A. Egen avtrekksvifte over komfyr	☐	☐
B. Egen avtrekksvifte i ventil i yttervegg på våtrom	☐	☐
C. Ventiler i yttervegg/vinduskarm eller luftevindu	☐	☐
D. Sentral avtrekksventilasjon (sentral vifte som gir avtrekk fra bad, toalett og kjøkken)	☐	☐
E. Ventilasjonsanlegg (sentral vifte som gir avtrekk fra bad, toalett og kjøkken, og en sentral vifte som gir tilførsel av luft til oppholdsrom og soverom)	☐	☐

Hvis ja på D eller E - Omtrent hvor mange **timer per døgn** er det for tiden i bruk : ☐☐ Skriv 0 hvis ikke i bruk

- Omtrent hvor mange **ganger per år** skiftes filter : ☐☐ Skriv 0 hvis ingen

28. Hvor ofte gjennomluftes boligen for tiden ved å åpne vindu eller dører i minimum 3-5 minutter ?
(ett kryss)

- Aldri ☐
- Sjeldnere enn 1 gang om dagen ☐
- 1 gang om dagen ☐
- 2 ganger daglig ☐
- 3 eller flere ganger daglig ☐

29. Hvilke av følgende aktiviteter foregår **daglig i boligen uten** at elektrisk avtrekksvifte/ventilasjon benyttes ? (flere kryss)

- Tørking av tøy ☐
- Koking av mat ☐
- Bruk av tørkeskap/tørketrommel ☐
- Dusjing (mer enn 5 minutter) ☐
- Bruk av luftfukter ☐
- Ingen aktiviteter ☐

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30. I hvilken etasje av bygningen er **barnets** soverom ? (ett kryss)

Sokkel	☐
Kjeller	☐
1. etasje	☐
2. etasje eller høyere	☐

31. Sover **barnet** for tiden med åpent vindu ?

☐ Ja ☐ Nei

32. Hva slags dyne eller pute bruker **barnet** nå ?

	Dyne	Pute
Syntetiske fibre	☐	☐
Dun	☐	☐
Annet	☐	☐
Bruker ikke dyne eller pute	☐	☐

33. Hvor gammel er **barnets** nåværende dyne, pute og madrass ?

Alder, (under 1 år skriv 0)

Dyne	☐☐	år
Pute	☐☐	år
Madrass	☐☐	år

34. Hvor ofte vaskes sengetøyet til **barnet** ? ☐☐ ganger per måned

Hvor ofte rengjøres madrassen til **barnet** ? ☐☐ ganger per **år**

35. Tørkes sengetøyet i tørketrommel ?

☐ Ja ☐ Nei

36. Hvor mange våtrom og andre rom har **vinylgulv med gulvvarme** ? (Skriv 0 hvis ingen)

Våtrom (bad, vaskerom, WC)	☐	antall rom
Andre rom	☐	antall rom

37. Hvilke materialer er brukt **på gulv** i soverommet, og i oppholdsrommet **barnet** bruker mest ? (flere kryss)

	Gulv i barnets soverom	Gulv i barnets mest brukte oppholdsrom
Heldekkende tepper	☐	☐
Vinyl (PVC-plast)	☐	☐
Furu tregulv	☐	☐
Parkett/andre harde materialer	☐	☐
Annet	☐	☐

38. Hvilke overflater har **veggene i** soverommet og i oppholdsrommet **barnet** bruker mest ? (flere kryss)

	Vegg i barnets soverom	Vegg i barnets mest brukte oppholdsrom
Ubehandlet/lutet trepanel	☐	☐
Malt/lakkert trepanel	☐	☐
Annen malt/lakkert overflate	☐	☐
Annen overflate	☐	☐

39. Har det blitt gjort noen av følgende endringer i boligen **siste 12 måneder** ?

	Ja	Nei
Nytt furu trepanel eller furu gulv	☐	☐
Nytt vinyl gulv (PVC-plast)	☐	☐
Liming av tapet, strie, gulvbelegg etc.	☐	☐
Maling, lakkering	☐	☐
Andre endringer	☐	☐

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Spørsmål om kosthold

I svangerskapet og i ammeperioden

40. Hvor ofte i gjennomsnitt spiste mor torsk, sei eller annen mager fisk til middag ?

	I svanger-skapet	I amme-perioden
Aldri	☐	☐
Sjeldnere enn 1 gang i uken	☐	☐
1 gang i uken	☐	☐
2 ganger i uken	☐	☐
3 ganger i uken	☐	☐
4 ganger i uken eller oftere	☐	☐

41. Hvor ofte i gjennomsnitt spiste mor uer, kveite, laks, ørret, sild, makrell eller annen fet fisk til middag ?

	I svanger-skapet	I amme-perioden
Aldri	☐	☐
Sjeldnere enn 1 gang i uken	☐	☐
1 gang i uken	☐	☐
2 ganger i uken	☐	☐
3 ganger i uken	☐	☐
4 ganger i uken eller oftere	☐	☐

42. Hvor ofte i gjennomsnitt tok mor tran eller fiskeoljekapsler ?

	I svanger-skapet	I amme-perioden
Aldri	☐	☐
Sjeldnere enn 1 gang i uken	☐	☐
1 gang i uken	☐	☐
2 ganger i uken	☐	☐
3 ganger i uken	☐	☐
4 ganger i uken eller oftere	☐	☐

43. Hvor mange brødskiver i gjennomsnitt spiste mor der pålegget bestod av fet fisk (sild, sardiner, makrell, laks ol.) ?

	I svanger-skapet	I amme-perioden
Aldri	☐	☐
Mindre enn 1 skive i uken	☐	☐
1-2 skiver i uken	☐	☐
3-6 skiver i uken	☐	☐
1-2 skiver i daglig	☐	☐
3-4 skiver i daglig	☐	☐
5 eller flere skiver i daglig	☐	☐

44. Hvor ofte spiste mor i gjennomsnitt grønnsaker til middag eller som egen rett (her menes rå eller kokte grønnsaker) ?

	I svanger-skapet	I amme-perioden
Aldri	☐	☐
Sjelden	☐	☐
Omtrent 1 gang i uken	☐	☐
2-3 ganger i uken	☐	☐
4-5 ganger i uken	☐	☐
Omtrent daglig	☐	☐

45. Hva slags type fett ble brukt til matlaging (ikke på brødet) i mors husholdning ?

(flere kryss)

	I svanger-skapet	I amme-perioden
Meierismør	☐	☐
Hard margarin	☐	☐
Bløt (soft) margarin	☐	☐
Smør/margarin blanding	☐	☐
Soyaolje	☐	☐
Olivenolje	☐	☐

46. Har mor under ammeperioden spist noen av følgende matemner ?

	Ofte (minst ukentlig)	Av og til (noen ganger i måneden)	En gang	Aldri
Kumelk	☐	☐	☐	☐
Egg	☐	☐	☐	☐
Fisk	☐	☐	☐	☐
Skalldyr	☐	☐	☐	☐
Nøtter	☐	☐	☐	☐
Erter/belgfrukter	☐	☐	☐	☐

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Spørsmål om barnets ernæring

47. Har barnet fått morsmelk ?
☐ Ja ☐ Nei

Hvis ja, har barnet eventuelt sluttet med morsmelk ?
☐ Ja ☐ Nei

Hvis ja, hvor gammelt var barnet da det eventuelt sluttet med morsmelk ?
☐☐ måneder

48. Har barnet noen gang fått tran ?
☐ Ja ☐ Nei

Hvis ja, hvor gammelt var barnet da det fikk tran første gang ?
☐☐ måneder

Har barnet sluttet med tran ?
☐ Ja ☐ Nei

Hvis ja, hvor gammelt var barnet da det eventuelt sluttet med tran ?
☐☐ måneder

49. Får barnet annet vitamintilskudd ?
(for eksempel Biovit, Sanasol)
☐ Ja ☐ Nei

50. Får barnet morsmelkerstatning ?
☐ Ja ☐ Nei

Hvis ja, hvilken type ?
- Collett ☐
- NA ☐
- Nutramigen ☐
- Soyamelk ☐
- Annet ☐

Hvis ja, hvor gammelt var barnet da det startet med morsmelkerstatning ?
☐☐ måneder

51. Hvor gammelt var barnet da det startet med følgende matslag ?

	Alder i måneder	(kryss) Ikke fått
Risgrøt	☐☐	☐
Maisgrøt	☐☐	☐
Hvetegrøt	☐☐	☐
Brødskive	☐☐	☐
Kokte grønnsaker	☐☐	☐
Rå grønnsaker	☐☐	☐
Frukt	☐☐	☐
Middagsmat på glass	☐☐	☐
Middagsmat hjemmelaget	☐☐	☐
Fisk	☐☐	☐
Melk	☐☐	☐
Egg	☐☐	☐

52. Hvor ofte i gjennomsnitt spiser barnet torsk, sei eller annen mager fisk til middag ? (ett kryss)
- Aldri ☐
- Sjeldnere enn 1 gang i uken ☐
- 1 gang i uken ☐
- 2 ganger i uken ☐
- 3 ganger i uken ☐
- 4 ganger i uken eller oftere ☐

53. Hvor ofte i gjennomsnitt spiser barnet uer, kveite, laks, ørret, sild, makrell eller annen fet fisk til middag ? (ett kryss)
- Aldri ☐
- Sjeldnere enn 1 gang i uken ☐
- 1 gang i uken ☐
- 2 ganger i uken ☐
- 3 ganger i uken ☐
- 4 ganger i uken eller oftere ☐

54. Hvor ofte i gjennomsnitt tar barnet tran eller fiskeoljekapsler ? (ett kryss)

- Aldri ☐
- Sjeldnere enn 1 gang i uken ☐
- 1 gang i uken ☐
- 2 ganger i uken ☐
- 3 ganger i uken ☐
- 4 ganger i uken eller oftere ☐

55. Hvor mange brødskiver i gjennomsnitt spiser barnet der pålegget består av fet fisk (sild, sardiner, makrell, laks ol.) ? (ett kryss)

- Aldri ☐
- Mindre enn 1 skive i uken ☐
- 1-2 skiver i uken ☐
- 3-6 skiver i uken ☐
- 1-2 skiver daglig ☐
- 3-4 skiver daglig ☐
- 5 eller flere skiver daglig ☐

56. Hvor ofte spiser barnet i gjennomsnitt grønnsaker til middag eller som egen rett ?

	Rå grønnsaker	Kokte grønnsaker
Aldri	☐	☐
Sjelden	☐	☐
Omtrent 1 gang i uken	☐	☐
2-3 ganger i uken	☐	☐
4-5 ganger i uken	☐	☐
Omtrent daglig	☐	☐

57. Hva slags type fett brukes til matlaging i din husholdning og på brødet til barnet ? (flere kryss)

	I husholdningen	På brødet til barnet
Meierismør	☐	☐
Hard margarin	☐	☐
Bløt (soft) margarin	☐	☐
Smør/margarin blanding	☐	☐
Soyaolje	☐	☐
Olivenolje	☐	☐

Spørsmål om røykevaner

58. Røykte du eller ektefelle/samboer ved svangerskapets start ?

	Nei, røykte ikke	Ja, røykte ukentlig	Ja, røykte daglig
Du	☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig
Ektefelle/samboer	☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig

59. Røyker du eller ektefelle/samboer nå ?

	Nei, røyker ikke	Ja, røyker ukentlig	Ja, røyker daglig
Du	☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig
Ektefelle/samboer	☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig

60. Røykes det **innendørs** hjemme ?

Nei, det røykes ikke innendørs	Ja, det røykes ukentlig innendørs	Ja, det røykes daglig innendørs
☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig

61. Ble det røykt innendørs hjemme etter barnets første leveår ?

Nei, det ble ikke røykt innendørs	Ja, det røykes ukentlig innendørs	Ja, det røykes daglig innendørs
☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig

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Barneallergistudien i Trondheim

Spørreskjema om livsstilsfaktorer ved 2 års alder

Skriv tydelige tall og kryss. Bruk **svart** eller **blå** penn.

Utfylt dato (dd.mm.åå) ☐☐.☐☐.☐☐

Spørsmål om barnet

1. Er barnet tvilling ? ☐ Ja ☐ Nei **Hvis tvilling**, svar på alle spørsmålene for tvilling I, deretter svar på spørsmål 1-6 og 40-50 for tvilling II på eget skjema.

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2. Barnets fødselsvekt ? ☐☐☐☐ gram og fødselslengde ? ☐☐ cm

---

3. Hvor mange søsken har barnet ?
(ta med fellesbarn og særkullsbarn, **ikke** fosterbarn og adoptivbarn)

Ingen søsken : ☐ (kryss)
Antall søsken : ☐ brødre ☐ søstre

---

4. Når ble barnet født i forhold til beregnet ultralydtermin ? (ett kryss)

Tidligere enn 2 uker før beregnet ultralydtermin ☐
Mellom 3 uker før og 2 uker etter beregnet ultralydtermin ☐
Senere enn 2 uker etter beregnet ultralydtermin ☐

---

5. Har barnet blitt vaksinert ? ☐ Ja ☐ Nei

---

6. Har barnet hatt noen av sykdommene nedenfor ?

	Ja	Nei	Hvis ja, antall ganger	Er noen av sykdommene behandlet med penicillin/antibiotika ? Ja	Nei	Vet ikke	Hvis ja, hvor mange behandlinger
Forkjølelse	☐	☐	☐☐	☐	☐	☐	☐☐
Ørebetennelse	☐	☐	☐☐	☐	☐	☐	☐☐
Bronkitt	☐	☐	☐☐	☐	☐	☐	☐☐
RS-virusinfeksjon	☐	☐	☐☐	☐	☐	☐	☐☐
Falsk krupp	☐	☐	☐☐	☐	☐	☐	☐☐
Lungebetennelse	☐	☐	☐☐	☐	☐	☐	☐☐
Urinveisinfeksjon	☐	☐	☐☐	☐	☐	☐	☐☐
Mage-tarminfeksjon	☐	☐	☐☐	☐	☐	☐	☐☐

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7. Foreldrenes sivilstatus: ☐ Gift ☐ Samboer ☐ Enslig ☐ Annet

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Spørsmål om foreldre og søsken

8. Har mor, far eller noen av barna **noen gang** hatt astma, eksem eller allergi i øyne/nese ? ☐ Ja ☐ Nei

Hvis nei, gå til spørsmål 14.
Hvis ja, kryss av for de familiemedlemmer det gjelder (flere kryss) :

	Astma	Eksem	Allergi i øyne/nese
Mor	☐	☐	☐
Far	☐	☐	☐
Fellesbarn	☐	☐	☐
Dine særkullsbarn	☐	☐	☐
Barnefarens særkullsbarn	☐	☐	☐

9. Har, eller har mor, far eller fellesbarn **noen gang** hatt astmasykdom ? ☐ Ja ☐ Nei

Hvis nei, gå til spørsmål 11.
Hvis ja, angi alder i dag, når astmasykdommen startet, om sykdommen fortsatt er til stede, og når den eventuelt sluttet.

	Alder i dag	Startalder astma	Har fortsatt astma (kryss)	Sluttalder astma
Mor	☐☐ år	☐☐ år	☐	☐☐ år
Far	☐☐ år	☐☐ år	☐	☐☐ år
Fellesbarn 1	☐☐ år	☐☐ år	☐	☐☐ år
Fellesbarn 2	☐☐ år	☐☐ år	☐	☐☐ år
Fellesbarn 3	☐☐ år	☐☐ år	☐	☐☐ år

10. Har, eller har mor, far eller fellesbarn hatt astmaplager eller brukt astmamedisiner de **siste 12 måneder** ? ☐ Ja ☐ Nei

Hvis ja, kryss av for de det gjelder :

	Hyppighet av astmaplager siste 12 måneder				Brukt astmamedisin siste 12 måneder	
	Daglig	Ukentlig	Månedlig	Sjeldnere enn månedlig	Ja	Nei
Mor	☐	☐	☐	☐	☐	☐
Far	☐	☐	☐	☐	☐	☐
Fellesbarn 1	☐	☐	☐	☐	☐	☐
Fellesbarn 2	☐	☐	☐	☐	☐	☐
Fellesbarn 3	☐	☐	☐	☐	☐	☐

11. Har, eller har mor,far eller fellesbarn hatt eksemplager, eller brukt eksemmedisin de **siste 12 måneder** ? ☐ Ja ☐ Nei

Hvis ja, kryss av for de det gjelder :

	Hyppighet av eksemplager siste 12 måneder				Brukt eksemmedisin siste 12 måneder ?	
	Daglig	Ukentlig	Månedlig	Sjeldnere enn månedlig	Ja	Nei
Mor	☐	☐	☐	☐	☐	☐
Far	☐	☐	☐	☐	☐	☐
Fellesbarn 1	☐	☐	☐	☐	☐	☐
Fellesbarn 2	☐	☐	☐	☐	☐	☐
Fellesbarn 3	☐	☐	☐	☐	☐	☐

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12. Har, eller har mor, far eller fellesbarn hatt allergi i øyne/nese, eller brukt allergimedisiner ?

☐ Ja ☐ Nei

Hvis nei, gå til spørsmål 14.
Hvis ja, kryss av (flere kryss) for de det gjelder :

	Allergi mot				Brukt allergimedisin siste 12 måneder ?	
	Pollen	Dyrehår	Husstøv/ midd	Andre	Ja	Nei
Mor	☐	☐	☐	☐	☐	☐
Far	☐	☐	☐	☐	☐	☐
Fellesbarn 1	☐	☐	☐	☐	☐	☐
Fellesbarn 2	☐	☐	☐	☐	☐	☐
Fellesbarn 3	☐	☐	☐	☐	☐	☐

13. Hvis mor, far eller fellesbarn har allergi i øyne/nese, hvordan er det påvist ?
Kryss av for de det gjelder :

	Allergi påvist ved blodprøve ?			Allergi påvist ved prikk(hud)-testing ?		
	Ja	Nei	Vet ikke	Ja	Nei	Vet ikke
Mor	☐	☐	☐	☐	☐	☐
Far	☐	☐	☐	☐	☐	☐
Fellesbarn 1	☐	☐	☐	☐	☐	☐
Fellesbarn 2	☐	☐	☐	☐	☐	☐
Fellesbarn 3	☐	☐	☐	☐	☐	☐

14. Kryss av om mor hadde noen av følgende plager i siste svangerskap. Oppgi i hvilken periode, og om mulig navn på medisiner som ble brukt.

	Plager i siste svangerskap ?	Periode i svangerskapet (flere kryss) 0-3 mnd	4-6 mnd	7-9 mnd	Medisinnavn
Svangerskapsblødning	☐	☐	☐	☐	_____
Svangerskapsforgiftning	☐	☐	☐	☐	_____
Forhøyet blodtrykk	☐	☐	☐	☐	_____
Svangerskapsdiabetes	☐	☐	☐	☐	_____
Diabetes, insulinbehandlet	☐	☐	☐	☐	_____
Diabetes, tablettbehandlet	☐	☐	☐	☐	_____
Soppinfeksjon i skjeden	☐	☐	☐	☐	_____
Skjedekatarr/uvanlig utflod	☐	☐	☐	☐	_____
Forkjølelse	☐	☐	☐	☐	_____
Influensa	☐	☐	☐	☐	_____
Bronkitt	☐	☐	☐	☐	_____
Lungebetennelse	☐	☐	☐	☐	_____
Astma	☐	☐	☐	☐	_____
Eksem	☐	☐	☐	☐	_____
Allergi i øyne /nese	☐	☐	☐	☐	_____
Andre plager	☐				
Ingen plager	☐				

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Spørsmål om bolig / innemiljø nå

15. I hvilken type bolig bor **barnet** ? (ett kryss)

- Enebolig/våningshus uten sokkel/kjeller ☐
- Enebolig/våningshus med sokkel/kjeller ☐
- Sokkelleilighet i enebolig ☐
- Tomannsbolig, firemannsbolig ☐
- Rekkehus/kjedehus ☐
- Terrassehus ☐
- Boligblokk/bygård ☐
- Annen bolig ☐

16. Boligens byggeår ? (årstall) ☐☐☐☐

Hvor lenge har barnet bodd i boligen ? ☐ år ☐☐ måneder

17. Eier du/dere boligen ?

- Ja, som selveiere ☐
- Ja, i borettslag ☐
- Nei ☐

18. Boligens boareal (cirka) ? ☐☐☐ m^2

19. Hvor mange personer bor det for tiden i boligen ? ☐☐

20. Hvor ofte vaskes boligen ? ☐☐ ganger per måned

Hvor ofte støvsuges boligen ? ☐☐ ganger per måned

21. Har boligen sentralstøvsuger ? ☐ Ja ☐ Nei

22. Hvor mange timer oppholder **barnet** seg i gjennomsnitt i boligen ?

I boligen ☐☐ timer per døgn

I eget soverom ☐☐ timer per døgn

23. Hvilke av følgende husdyr oppholder seg i boligen ? (flere kryss)

- Hund ☐
- Katt ☐
- Andre pelsdyr (marsvin, kanin o.l.) ☐
- Fugl ☐
- Andre dyr ☐
- Ingen dyr ☐

24. Bor **barnet** på gårdsbruk ☐ Ja ☐ Nei

Hvis ja, hvilke husdyr er det på gården ? (flere kryss)

- Kyr ☐
- Gris ☐
- Sau ☐
- Hest ☐
- Fjørfe ☐
- Andre husdyr ☐
- Ingen husdyr ☐

25. Hvilke energikilder brukes til oppvarming av boligen ? (flere kryss)

- Elektristitet ☐
- Vedfyring ☐
- Olje ☐
- Fjernvarme ☐
- Annet ☐

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26. Har, eller har boligen hatt noen av følgende problemer ?
(besvar alle spørsmål)

	Ja	Nei	**Hvis ja**, er problemet utbedret ? Ja, utbedret	Nei, ikke utbedret
Mugglukt eller kjellerlukt	☐	☐	☐	☐
Aviser og pappesker blir ved lagring 'fuktige'	☐	☐	☐	☐
Dugg på vinduer (utenom ved dusjing, fosskoking og sterk kulde)	☐	☐	☐	☐
Fuktflekker på vegg eller tak (fuktflekker som skyldes mindre søl med vann regnes ikke med her)	☐	☐	☐	☐
Vannlekkasjer fra sanitærinstallasjoner (rør, kraner, dusj, vask o.l.)	☐	☐	☐	☐
Vannlekkasjer fra yttertak	☐	☐	☐	☐
Vannlekkasjer fra grunnen/oversvømmelse	☐	☐	☐	☐
Blærer, bobler i eller misfarging av gulvbelegg	☐	☐	☐	☐
Ingen problemer	☐			

27. Hvilke av følgende ventilasjonsutstyr er installert i boligen ?

	Ja	Nei
A. Egen avtrekksvifte over komfyr	☐	☐
B. Egen avtrekksvifte i ventil i yttervegg på våtrom	☐	☐
C. Ventiler i yttervegg/vinduskarm eller luftevindu	☐	☐
D. Sentral avtrekksventilasjon (sentral vifte som gir avtrekk fra bad, toalett og kjøkken)	☐	☐
E. Ventilasjonsanlegg (sentral vifte som gir avtrekk fra bad, toalett og kjøkken, og en sentral vifte som gir tilførsel av luft til oppholdsrom og soverom)	☐	☐

Hvis ja på D eller E - Omtrent hvor mange **timer per døgn** er det for tiden i bruk : ☐☐ Skriv 0 hvis ikke i bruk

- Omtrent hvor mange **ganger per år** skiftes filter : ☐☐ Skriv 0 hvis ingen

28. Hvor ofte gjennomluftes boligen for tiden ved å åpne vindu eller dører i minimum 3-5 minutter ?
(ett kryss)

- Aldri ☐
- Sjeldnere enn 1 gang om dagen ☐
- 1 gang om dagen ☐
- 2 ganger daglig ☐
- 3 eller flere ganger daglig ☐

29. Hvilke av følgende aktiviteter foregår **daglig i boligen uten** at elektrisk avtrekksvifte/ventilasjon benyttes ? (flere kryss)

- Tørking av tøy ☐
- Koking av mat ☐
- Bruk av tørkeskap/tørketrommel ☐
- Dusjing (mer enn 5 minutter) ☐
- Bruk av luftfukter ☐
- Ingen aktiviteter ☐

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30. I hvilken etasje av bygningen er **barnets** soverom ? (ett kryss)

- Sokkel ☐
- Kjeller ☐
- 1. etasje ☐
- 2. etasje eller høyere ☐

31. Sover **barnet** for tiden med åpent vindu ?

☐ Ja ☐ Nei

32. Hva slags dyne eller pute bruker **barnet** nå ?

	Dyne	Pute
Syntetiske fibre	☐	☐
Dun	☐	☐
Annet	☐	☐
Bruker ikke dyne eller pute	☐	☐

33. Hvor gammel er **barnets** nåværende dyne, pute og madrass ?

Alder, (under 1 år skriv 0)

- Dyne ☐☐ år
- Pute ☐☐ år
- Madrass ☐☐ år

34. Hvor ofte vaskes sengetøyet til **barnet** ? ☐☐ ganger per måned

Hvor ofte rengjøres madrassen til **barnet** ? ☐☐ ganger per **år**

35. Tørkes sengetøyet i tørketrommel ?

☐ Ja ☐ Nei

36. Hvor mange våtrom og andre rom har **vinylgulv med gulvvarme** ? (Skriv 0 hvis ingen)

- Våtrom (bad, vaskerom, WC) ☐ antall rom
- Andre rom ☐ antall rom

37. Hvilke materialer er brukt **på gulv** i soverommet, og i oppholdsrommet **barnet** bruker mest ? (flere kryss)

	Gulv i barnets soverom	Gulv i barnets mest brukte oppholdsrom
Heldekkende tepper	☐	☐
Vinyl (PVC-plast)	☐	☐
Furu tregulv	☐	☐
Parkett/andre harde materialer	☐	☐
Annet	☐	☐

38. Hvilke overflater har **veggene i** soverommet og i oppholdsrommet **barnet** bruker mest ? (flere kryss)

	Vegg i barnets soverom	Vegg i barnets mest brukte oppholdsrom
Ubehandlet/lutet trepanel	☐	☐
Malt/lakkert trepanel	☐	☐
Annen malt/lakkert overflate	☐	☐
Annen overflate	☐	☐

39. Har det blitt gjort noen av følgende endringer i boligen **siste 12 måneder** ?

	Ja	Nei
Nytt furu trepanel eller furu gulv	☐	☐
Nytt vinyl gulv (PVC-plast)	☐	☐
Liming av tapet, strie, gulvbelegg etc.	☐	☐
Maling, lakkering	☐	☐
Andre endringer	☐	☐

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Spørsmål om barnets ernæring

40. Har barnet fått morsmelk ?

☐ Ja ☐ Nei

Hvis ja, har barnet eventuelt sluttet med morsmelk ?

☐ Ja ☐ Nei

Hvis ja, hvor gammelt var barnet da det eventuelt sluttet med morsmelk ?

☐☐ år ☐☐ måneder

41. Har barnet noen gang fått tran ?

☐ Ja ☐ Nei

Hvis ja, hvor gammelt var barnet da det fikk tran første gang ?

☐☐ år ☐☐ måneder

Har barnet sluttet med tran ?

☐ Ja ☐ Nei

Hvis ja, hvor gammelt var barnet da det eventuelt sluttet med tran ?

☐☐ år ☐☐ måneder

42. Får barnet annet vitamintilskudd ? (for eksempel Biovit, Sanasol)

☐ Ja ☐ Nei

43. Har barnet fått morsmelkerstatning ?

☐ Ja ☐ Nei

Hvis ja, hvilken type ?

- Collett ☐
- NA ☐
- Nutramigen ☐
- Soyamelk ☐
- Annet ☐

Hvis ja, hvor gammelt var barnet da det startet med morsmelkerstatning ?

☐☐ måneder

44. Hvor gammelt var barnet da det startet med følgende matslag ?

	Alder i måneder	(kryss) Ikke fått
Kokte grønnsaker	☐☐	☐
Rå grønnsaker	☐☐	☐
Frukt	☐☐	☐
Fisk	☐☐	☐
Melk	☐☐	☐
Egg	☐☐	☐

45. Hvor ofte i gjennomsnitt spiser barnet torsk, sei eller annen mager fisk til middag ? (ett kryss)

- Aldri ☐
- Sjeldnere enn 1 gang i uken ☐
- 1 gang i uken ☐
- 2 ganger i uken ☐
- 3 ganger i uken ☐
- 4 ganger i uken eller oftere ☐

46. Hvor ofte i gjennomsnitt spiser barnet uer, kveite, laks, ørret, sild, makrell eller annen fet fisk til middag ? (ett kryss)

- Aldri ☐
- Sjeldnere enn 1 gang i uken ☐
- 1 gang i uken ☐
- 2 ganger i uken ☐
- 3 ganger i uken ☐
- 4 ganger i uken eller oftere ☐

47. Hvor ofte i gjennomsnitt tar barnet tran eller fiskeoljekapsler ? (ett kryss)

- Aldri ☐
- Sjeldnere enn 1 gang i uken ☐
- 1 gang i uken ☐
- 2 ganger i uken ☐
- 3 ganger i uken ☐
- 4 ganger i uken eller oftere ☐

48. Hvor mange brødskiver i gjennomsnitt spiser barnet der pålegget består av fet fisk (sild, sardiner, makrell, laks ol.) ? (ett kryss)

- Aldri ☐
- Mindre enn 1 skive i uken ☐
- 1-2 skiver i uken ☐
- 3-6 skiver i uken ☐
- 1-2 skiver daglig ☐
- 3-4 skiver daglig ☐
- 5 eller flere skiver daglig ☐

49 Hvor ofte spiser barnet i gjennomsnitt grønnsaker til middag eller som egen rett ?

	Rå grønnsaker	Kokte grønnsaker
Aldri	☐	☐
Sjelden	☐	☐
Omtrent 1 gang i uken	☐	☐
2-3 ganger i uken	☐	☐
4-5 ganger i uken	☐	☐
Omtrent daglig	☐	☐

50. Hva slags type fett brukes til matlaging i din husholdning og på brødet til barnet ? (flere kryss)

	I husholdningen	På brødet til barnet
Meierismør	☐	☐
Hard margarin	☐	☐
Bløt (soft) margarin	☐	☐
Smør/margarin blanding	☐	☐
Soyaolje	☐	☐
Olivenolje	☐	☐

Spørsmål om røykevaner

51. Røykte du eller ektefelle/samboer ved svangerskapets start ?

	Nei, røykte ikke	Ja, røykte ukentlig	Ja, røykte daglig
Du	☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig
Ektefelle/samboer	☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig

52. Røyker du eller ektefelle/samboer nå ?

	Nei, røyker ikke	Ja, røyker ukentlig	Ja, røyker daglig
Du	☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig
Ektefelle/samboer	☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig

53. Røykes det **innendørs** hjemme ?

Nei, det røykes ikke innendørs	Ja, det røykes ukentlig innendørs	Ja, det røykes daglig innendørs
☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig

54. Ble det røykt innendørs hjemme etter barnets første leveår ?

Nei, det ble ikke røykt innendørs	Ja, det røykes ukentlig innendørs	Ja, det røykes daglig innendørs
☐	☐☐ sigaretter ukentlig	☐☐ sigaretter daglig

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Barnepass

55. Har barnet hatt daglig tilsyn av andre enn mor eller far **siden fødselen** ?

☐ Ja ☐ Nei

Hvis ja, oppgi hvem som har hatt tilsyn med barnet, start, slutt og varighet av tilsynet ?

	Barnets alder ved start med tilsynet	Barnets alder ved slutt med tilsynet	Tilsynets varighet
Dagmamma o.l. hjemme	☐☐ måneder	☐☐ måneder	☐☐ timer pr. uke
Dagmamma o.l. utenfor hjemmet	☐☐ måneder	☐☐ måneder	☐☐ timer pr. uke
Familiebarnehage	☐☐ måneder	☐☐ måneder	☐☐ timer pr. uke
Barnepark	☐☐ måneder	☐☐ måneder	☐☐ timer pr. uke
Barnehage	☐☐ måneder	☐☐ måneder	☐☐ timer pr. uke

56. Hva slags tilsyn har barnet nå ?
(flere kryss)

- Mor eller far hjemme ☐
- Dagmamma o.l. hjemme ☐
- Dagmamma o.l. utenfor hjemmet ☐
- Familiebarnehage ☐
- Barnepark ☐
- Barnehage ☐
- Annet ☐

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Barneallergistudien i Trondheim

Spørreskjema om barnets helse ved 2 eller 6 års alder

Skriv tydelige tall og kryss. Bruk **svart** eller **blå** penn.

Utfylt dato (dd.mm.åå) ☐☐.☐☐.☐☐

1. Har barnet **noen gang** hatt pustevansker ?

   ☐ Ja ☐ Nei ☐ Vet ikke

2. Har barnet **noen gang** hatt episoder med piping i brystet ?

   ☐ Ja ☐ Nei ☐ Vet ikke

3. Har barnet **noen gang** hatt episoder med surkling eller tetthet i brystet ?

   ☐ Ja ☐ Nei ☐ Vet ikke

4. Har barnet **noen gang** hatt tørr hoste om natten unntatt ved forkjølelse eller andre luftveisinfeksjoner ?

   ☐ Ja ☐ Nei ☐ Vet ikke

5. Har barnet **noen gang** hatt episoder med hvesing eller tung pust ?

   ☐ Ja ☐ Nei ☐ Vet ikke

Hvis du har svart "Ja" på **minst ett** av spørsmålene over så fortsetter du med spørsmål 6.
Hvis du har svart "Nei" på **alle** spørsmålene ovenfor, gå til spørsmål 18.

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6. Har barnet **noen gang** hatt anfall av piping, surkling eller tetthet i brystet i ro, når han/hun ikke er forkjølet ?

   ☐ Ja ☐ Nei ☐ Vet ikke

7. Har barnet hatt piping, surkling eller tetthet i brystet de **siste 12 måneder** ? (ett kryss)

   ☐ Ja, nesten daglig
   ☐ Ja, 1-3 ganger pr. uke
   ☐ Ja, 1-3 ganger pr. måned
   ☐ Ja, sjeldnere enn 1 gang pr. måned
   ☐ Nei

---

8. **I de siste 12 månedene** : Har barnet ditt vanligvis virket tett i brystet eller hostet opp slim :

Ved forkjølelse ?	☐ Ja	☐ Nei	☐ Vet ikke
Når han/hun ikke var forkjølet ?	☐ Ja	☐ Nei	☐ Vet ikke
Er barnet ditt tett i brystet eller hoster opp slim på de fleste dager (4 eller flere dager i uken, så lenge som 3 måneder i året) ?	☐ Ja	☐ Nei	☐ Vet ikke

forts. på baksiden

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9. **I de siste 12 månedene** : Har barnet ditt hatt tung pust, tetthet eller piping i brystet :

	Ja	Nei	Vet ikke
Under eller etter fysisk aktivitet ?	☐	☐	☐
Når han/hun **ikke** har vært fysisk aktiv ?	☐	☐	☐

10. **I de siste 12 månedene** : Har barnet ditt hatt tung pust, tetthet eller piping i brystet når :

	Ja	Nei	Vet ikke
Han/hun var forkjølet eller hadde influensa ?	☐	☐	☐
Han/hun **ikke** var forkjølet eller hadde influensa ?	☐	☐	☐

11. Har barnet ditt **noen gang** våknet opp med :

	Ja	Nei	Vet ikke
Pustevansker ?	☐	☐	☐
Tetthet i brystet ?	☐	☐	☐

12. Forårsaker noe av det følgende piping, surkling eller tetthet i brystet ? (besvar alle spørsmål)

	Ja	Nei
Nyklippet gress, blomster, eller trær	☐	☐
Kontakt med dyr	☐	☐
Re senger eller husrengjøring	☐	☐
Løp eller annen aktivitet	☐	☐
Kulde	☐	☐
Annet	☐	☐

13. Har barnet **noen gang** fått stilt diagnosen astma av lege ?

☐ Ja ☐ Nei

Hvis nei, gå til spørsmål 18.

Hvis ja, hvor gammel var barnet første gang det hadde astma ?

☐☐ år ☐☐ måneder

14. Har barnet fremdeles astma ?

☐ Ja ☐ Nei

15. Hvis barnet ikke lenger har astma, hvor gammelt var barnet da astmaen forsvant ?

☐☐ år ☐☐ måneder

16. Har barnet **noen gang** fått behandling av lege eller vært innlagt i sykehus for astma ?

☐ Ja ☐ Nei

17. Har barnet i løpet av de **siste 12 måneder** brukt tabletter, inhalasjonsmedisiner eller annen behandling for piping, tetthet i brystet eller astma ?

☐ Ja ☐ Nei ☐ Vet ikke

Hvis ja, gjør rede for medisinene barnet bruker :
(Med fast medisin mener vi medisin som brukes hver dag minst to måneder i året)

	Ved behov	Fast medisin	Før, under eller etter anstrengelse
Acculate	☐	☐	☐
Airomir	☐	☐	☐
Atrovent	☐	☐	☐
Bambec	☐	☐	☐
Becotide	☐	☐	☐
Berotec	☐	☐	☐
Bricanyl	☐	☐	☐
Flunitec	☐	☐	☐
Flutide	☐	☐	☐
Lomudal	☐	☐	☐
Oxis	☐	☐	☐
Pulmicort	☐	☐	☐
Salbuvent	☐	☐	☐
Serevent	☐	☐	☐
Seretide	☐	☐	☐
Singulair	☐	☐	☐
Ventoline	☐	☐	☐

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18. Har barnet **noen gang** hatt tett nese, eller hatt rennende nese uten å være forkjølet ?

☐ Ja ☐ Nei ☐ Vet ikke

Hvis ja, når har eller har barnet hatt tett nese eller rennende nese uten å være forkjølet ? (flere kryss)

☐ Vår ☐ Sommer ☐ Høst ☐ Vinter

19. Har barnet hatt tett nese eller rennende nese uten å være forkjølet **siste 12 måneder** ?

☐ Ja ☐ Nei ☐ Vet ikke

20. Har barnet **noen gang** hatt høysnue, neseallergi eller allergisk øyekatarr ?

☐ Ja ☐ Nei ☐ Vet ikke

Hvis ja, hvor gammelt var barnet første gang det hadde høysnue, neseallergi eller allergisk øyekatarr ?

☐☐ år ☐☐ måneder

21. Har barnet **noen gang** hatt eksem ?

☐ Ja ☐ Nei ☐ Vet ikke

Hvis ja, hvor gammelt var barnet første gang det hadde eksem ?

☐☐ år ☐☐ måneder

22. Har barnet **noen gang** hatt kløende utslett som har kommet og gått i minst 6 måneder ?

☐ Ja ☐ Nei ☐ Vet ikke

23. Har barnet i løpet av de **siste 12 månder** brukt noen medisiner, salver, kremer, tabletter eller naturmedisiner mot eksem ?

☐ Ja ☐ Nei ☐ Vet ikke

24. Har barnet i løpet av de **siste 12 måneder** brukt allergimedisiner ?

☐ Ja ☐ Nei ☐ Vet ikke

25. Er barnet allergitestet med hudtest/prikktest eller blodprøve ?

☐ Ja ☐ Nei ☐ Vet ikke

Hvis ja, hvilken allergi ble påvist ? (flere kryss)

Pollen ☐
Dyrehår ☐
Husstøv ☐
Annen ☐
Vet ikke ☐

26. Har barnet **noen gang** fått behandling av lege eller vært innlagt i sykehus for :
(besvar alle spørsmål)

	Ja	Nei
Høysnue, neseallergi eller allergisk øyekatarr ?	☐	☐
Eksem ?	☐	☐
Elveblest (urtikaria) ?	☐	☐

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27. Har barnet hatt noen av sykdommene nedenfor ? (besvar alle spørsmål)

	Ja	Nei	Hvis ja, antall ganger	Er noen av sykdommene behandlet med penicillin/antibiotika ? Ja	Nei	Vet ikke	Hvis ja, hvor mange behandlinger
Forkjølelse	☐	☐	☐☐	☐	☐	☐	☐☐
Ørebetennelse	☐	☐	☐☐	☐	☐	☐	☐☐
Bronkitt	☐	☐	☐☐	☐	☐	☐	☐☐
RS-virusinfeksjon	☐	☐	☐☐	☐	☐	☐	☐☐
Falsk krupp	☐	☐	☐☐	☐	☐	☐	☐☐
Lungebetennelse	☐	☐	☐☐	☐	☐	☐	☐☐
Urinveisinfeksjon	☐	☐	☐☐	☐	☐	☐	☐☐
Mage-tarminfeksjon	☐	☐	☐☐	☐	☐	☐	☐☐

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28. Opplysninger om sykehusinnleggelser :

Siste innleggelse - dato ? (dd.mm.åå) ☐☐.☐☐.☐☐

Siste innleggelse - hvor ? _____

Barnets fastlege : _____

Legesenter : _____

APPENDIX II

Young-HUNT questionnaires

(Questions 115-125 only for students attending second year of high school)

VIDEREGÅENDE SKOLE

FOLKEHELSA
Statens Institutt for Folkehelse
Samfunnsmedisinsk
forskningssenter,
Verdal

ung-hunt

Helseundersøkelsen i Nord-Trøndelag

Nå er det *din tur* til å delta i den store helseundersøkelsen i Nord-Trøndelag (***hunt***)!

Vi håper du har lest igjennom informasjonen du fikk med hjem om ung-hunt og bestemt deg for å være med!

Les nå først gjennom samtykkeerklæringen som ligger i spørreskjemaet. Sjekk at det er ditt navn som står der! Kryss av for om du vil delta eller ikke, og undertegn. Lever denne lappen til læreren. Alle lappene legges i en konvolutt som klistres igjen.

Navnet ditt skal IKKE være med på spørreskjemaet!

Fyll så ut spørreskjemaet. Sett et kryss i rutene ☒ *du synes passer for deg. Svar så godt du kan! Spørsmål du ikke ønsker å svare på, kan du hoppe over. Når du er ferdig, legger du spørreskjemaet i den konvolutten du har fått, klistrer igjen og leverer konvolutten til læreren. Lever også spørreskjemaet selv om du ikke ble helt ferdig.*

Alle svarene dine blir behandlet med taushetsplikt!

Ingen på skolen får se svarene dine.

Hvis du ønsker å snakke med noen om undersøkelsen, kan du ta kontakt med ***ung-hunt***-sykepleieren på skolen din eller ringe Folkehelsa i Verdal (se baksiden).

Lykke til og tusen takk!

FOR ELEVER I VIDEREGÅENDE SKOLE

Disse spørsmålene står bare i spørreskjemaet for dere som går i videregående skole.

115. **Har du i løpet av det siste året ofte følt at du har presset deg, eller stadig drevet deg selv framover ?**

Ja ☐ *Nei* ☐ *Vet ikke* ☐

116. **Føler du deg under tidspress, også når det gjelder daglige gjøremål ?**

* *Alltid, eller nesten alltid* ..... ☐
* *Noen ganger* ..... ☐
* *Aldri* ..... ☐

117. **Har du hatt tanker om å ta ditt eget liv ?** *Ja* ☐ *Nei* ☐

118. **Har du noen gang prøvd hasj, marihuana eller lign. ?** *Ja* ☐ *Nei* ☐

119. **Har du noen gang brukt anabole steroider eller andre dopingmidler ?** *Ja* ☐ *Nei* ☐

120. Hvis ja, **hvor gammel var du første gang ?** _____år

121. **Har du noen gang hatt samleie ?** *Ja* ☐ *Nei* ☐

122. **For JENTER: Har du noen gang vært gravid uten at du ønsket det ?**

Ja ☐ *Nei* ☐

123. **For GUTTER: Har en jente noen gang blitt gravid med deg uten at det var meningen ?**

Ja ☐ *Nei* ☐ *Vet ikke* ☐

For BÅDE gutter og jenter:

Hvis ja:

124. **Hvor gammel var du da dette skjedde ?** _____år

125. **Ble det utført abort ?** *Ja* ☐ *Nei* ☐ *Vet ikke* ☐

KOMMENTARER

Hvis du har tid, kan du gjerne skrive litt om det du synes er viktig, men som det ikke er spurt etter i spørreskjemaet. Hvordan synes du det er å være ung i dag? Er det noe du mener kan bli bedre når det gjelder helse og trivsel for dere som er unge?

Vennlig hilsen

FOLKEHELSA
Statens Institutt for Folkehelse
Samfunnsmedisinsk forskningssenter, Verdal

Turid Lingaas Holmen
overlege, prosjektleder
Folkehelsa, Verdal
Tlf. 74 07 71 44

Kjell Terje Gundersen
høgskoledosent,
prosjektansvarlig ved
Høgskolen i Nord-Trøndelag
Levanger

Dato for utfylling av skjema: ____/ ___19 ___

1. Er du gutt eller jente ? *Gutt* ☐ *Jente* ☐

2. Hvilken klasse går du i ?

	Allmennfaglig	Yrkesfaglig
* *1. videregående*	☐	☐
* *2. videregående*	☐	☐
* *3. videregående*	☐	☐
* *Folkehøgskole*	☐	

3. Hvilke planer for videre utdanning har du ? (Sett ett eller flere kryss)

* *Ingen* ..... ☐
* *Høgskole eller universitet mindre enn 4 år* ..... ☐
* *Høgskole eller universitet i 4 år eller mer* ..... ☐
* *Annen yrkesutdanning* ..... ☐
* *Vet ikke* ..... ☐

OM DER DU BOR

4. Hvilken type bolig (hus) bor du i ? (Sett bare ett kryss)

* *Enebolig/villa* ..... ☐
* *Blokk/terasseleilighet* ..... ☐
* *Gardsbruk* ..... ☐
* *Rekkehus/2-4 mannsbolig* ..... ☐
* *Annen bolig* ..... ☐

5. Hvem bor du sammen med nå ? (Her kan du sette ett eller flere kryss)

* *Mor* ..... ☐
* *Far* ..... ☐
* *1-2 søsken* ..... ☐
* *3 eller flere søsken* ..... ☐
* *Mors nye mann eller samboer* ... ☐
* *Fars nye kone eller samboer* ... ☐
* *Ektefelle/samboer/venner* ..... ☐
* *Alene/på hybel* ..... ☐
* *Fosterforeldre* ..... ☐
* *Andre* ..... ☐

6. Er det heldekkende tepper (teppegulv) hjemme hos deg:

- i stua ?	*Ja* ☐	*Nei* ☐
- på soverommet ditt ?	*Ja* ☐	*Nei* ☐

7. Er det katt i boligen (hjemme hos deg) ? *Ja* ☐ *Nei* ☐

8. Er det hund i boligen (hjemme hos deg) ? *Ja* ☐ *Nei* ☐

9. Er det andre pelskledde dyr i boligen (hjemme hos deg)? *Ja* ☐ *Nei* ☐

OM HELSA DI

10. Hvordan er helsa di nå ? (Sett ett kryss for det som passer for deg)

* Dårlig ..... ☐		* God ..... ☐	
* Ikke helt god ..... ☐		* Svært god ..... ☐	

11. Er du funksjonshemmet på noen av disse måtene ?
(Sett ett kryss på hver linje)

	Nei	Litt	Middels	Mye
* Er bevegelseshemmet	☐	☐	☐	☐
* Har nedsatt syn	☐	☐	☐	☐
* Har nedsatt hørsel	☐	☐	☐	☐
* Hemmet pga. kroppslig sykdom	☐	☐	☐	☐
* Hemmet pga. psykiske plager	☐	☐	☐	☐

12. Har du hatt noen av disse plagene i løpet av de siste 12 månedene ?
(Sett ett kryss på hver linje)

	Aldri	Sjelden	Av og til	Ofte
A Hodepine (uten kjent medisinsk årsak)	☐	☐	☐	☐
B Nakke og skuldersmerter	☐	☐	☐	☐
C Ledd og muskelsmerter	☐	☐	☐	☐
D Magesmerter (uten kjent medisinsk årsak)	☐	☐	☐	☐
E Kvalme	☐	☐	☐	☐
F Treg mage	☐	☐	☐	☐
G Diare, magesyke	☐	☐	☐	☐
H Hjertebank	☐	☐	☐	☐
I Bronkitt eller lungebetennelse	☐	☐	☐	☐
J Ørebetennelse	☐	☐	☐	☐
K Bihulebetennelse	☐	☐	☐	☐

13. Hvis du har svart «aldri» på alle plagene nevnt ovenfor: Har du hatt noen av disse plagene ofte tidligere (dvs. før de siste 12 månedene) **?**

Ja ☐ Nei ☐

Hvis ja: **Hvilke plager (se ovenfor) var det ?** (Skriv navn eller bokstavene ovenfor som passer)

OM LUFTVEISPLAGER

14. Har du noen gang hatt tung pust eller piping/surkling/tetthet i brystet ?

Ja ☐ *Nei* ☐

HVIS DU HAR SVART «NEI»: GÅ TIL SPØRSMÅL **19**

15. Har du hatt tung pust eller piping/surkling/tetthet i brystet i løpet av de siste 12 månedene ?

Ja ☐ *Nei* ☐

HVIS DU HAR SVART «NEI»: GÅ TIL SPØRSMÅL **19**

16. Hvor mange anfall med tung pust eller piping/surkling/tetthet i brystet har du hatt i løpet av de siste 12 månedene ?

Ingen ☐ *1 til 3* ☐ *4 til 12* ☐ *Mer enn 12* ☐

17. Hvor ofte i gjennomsnitt har søvnen din blitt forstyrret p.g.a. tung pust eller piping/surkling/tetthet i brystet de siste 12 månedene?

Aldri våknet ☐ *Mindre enn en natt pr. uke* ☐ *En eller flere netter pr. uke* ☐

18. Har piping/surkling/tetthet i brystet eller tung pust vært så alvorlig de siste 12 månedene at du har hatt problemer med å snakke, slik at du bare har kunnet si ett eller to ord mellom hver pust ?

Ja ☐ *Nei* ☐

****

19. Har du noen gang hatt astma ? *Ja* ☐ *Nei* ☐

Hvis ja:
Har lege sagt du har hatt astma ? *Ja* ☐ *Nei* ☐

20. **Har du i løpet av de siste 12 månedene hatt tung pust eller piping/surkling/tetthet i brystet under eller etter fysisk trening, aktiv lek eller mosjonering ?**

Ja ☐ *Nei* ☐

21. **Har du i løpet av de siste 12 månedene hatt tørr hoste om natten uten å være forkjølet eller ha annen luftveisinfeksjon ?**

Ja ☐ *Nei* ☐

OM UTSLETT

22. **Har du noen gang hatt kløende utslett som har kommet og gått i minst 6 måneder ?** *Ja* ☐ *Nei* ☐

HVIS DU HAR SVART «NEI»: GÅ TIL SPØRSMÅL **27**

23. **Har du noen gang hatt dette kløende utslettet i løpet av de siste 12 månedene ?** *Ja* ☐ *Nei* ☐

HVIS DU HAR SVART «NEI»: GÅ TIL SPØRSMÅL **27**

24. **Har dette kløende utslettet noen gang sittet på noen av de følgende stedene: albuebøyene** (på innsiden), **bak knærne, foran på anklene, under baken eller rundt hals, ører eller øyne ?**

Ja ☐ *Nei* ☐

25. **Har dette utslettet vært helt borte noen gang i løpet av de siste 12 månedene ?** *Ja* ☐ *Nei* ☐

26. **I løpet av de siste 12 månedene, hvor ofte i gjennomsnitt har du blitt holdt våken om natten på grunn av dette kløende utslettet ?**

* *Ingen ganger de siste 12 månedene* ..... ☐
* *Mindre enn en natt per uke* ..... ☐
* *En eller flere netter per uke* ..... ☐

****

27. **Har du noen gang hatt eksem ?** *Ja* ☐ *Nei* ☐

OM NESEPLAGER

Alle spørsmålene er om problemer som oppstår når du IKKE er forkjølet eller har influensa.

28. Har du noen gang hatt problemer med nysing eller tett eller rennende nese når du IKKE har vært forkjølet eller har hatt influensa ?

Ja ☐ *Nei* ☐

HVIS DU HAR SVART «NEI»: GÅ TIL SPØRSMÅL **33**

29. I løpet av de siste 12 månedene, har du da hatt problemer med nysing, rennende eller tett nese uten å ha vært forkjølet eller å ha hatt influensa?

Ja ☐ *Nei* ☐

HVIS DU HAR SVART «NEI»: GÅ TIL SPØRSMÅL **33**

30. I løpet av de siste 12 månedene, har disse neseproblemene vært ledsaget av kløende, rennende øyne ? *Ja* ☐ *Nei* ☐

31. I hvilke av de siste 12 månedene har du hatt neseproblemene ?
(Sett ett kryss for hver måned som passer)

* *Januar* .... ☐	* *Mai* ..... ☐	* *September* ..... ☐
* *Februar* .... ☐	* *Juni* ..... ☐	* *Oktober* ..... ☐
* *Mars* ..... ☐	* *Juli* ..... ☐	* *November* ..... ☐
* *April* ..... ☐	* *August* ..... ☐	* *Desember* ..... ☐

32. I løpet av de siste 12 månedene, hvor mye har disse neseproblemene virket inn på din daglige aktivitet ?

Ikke i det hele tatt ☐ *Litt* ☐ *Mye* ☐ *Veldig mye* ☐

****

33. Har du noen gang hatt høysnue eller neseallergi ? *Ja* ☐ *Nei* ☐

OM ALLERGI

34. Er du allergisk ? *Ja* ☐ *Nei* ☐ *Vet ikke* ☐

HVIS DU HAR SVART «NEI»: GÅ TIL SPØRSMÅL **37**

35. Hva kjenner du selv at du er allergisk for ? Kryss av for hva slags plager du har for hver ting. (Sett ett eller flere kryss for hver linje)

	Ingen plager	Nese-plager	Øye-plager	Eksem-plager	Mage-plager	Astma/ puste-plager	Annet
* Hund	☐	☐	☐	☐	☐	☐	☐
* Katt	☐	☐	☐	☐	☐	☐	☐
* Andre dyr .	☐	☐	☐	☐	☐	☐	☐
* Gress/trær	☐	☐	☐	☐	☐	☐	☐
* Husstøv ...	☐	☐	☐	☐	☐	☐	☐
* Mat	☐	☐	☐	☐	☐	☐	☐
* Røyk	☐	☐	☐	☐	☐	☐	☐
* Annet	☐	☐	☐	☐	☐	☐	☐

36. Har du tatt allergitest hos lege (blodprøve, hudtest) **?**

Ja ☐ *Nei* ☐

OM MEDISINER

37. Bruker du noen av disse medisinene eller kosttilskuddene ?
Tenk på hva du bruker medisinene for. (Sett ett kryss for hver linje)

	Aldri	Av og til	Nesten daglig
* Smertestillende medisin	☐	☐	☐
* Migrenemedisin	☐	☐	☐
* Sovemedisin	☐	☐	☐
* Nervemedisin	☐	☐	☐
* Beroligende medisin	☐	☐	☐
* Astmamedisin	☐	☐	☐
* Allergimedisin	☐	☐	☐
* Eksemsalve	☐	☐	☐
* Avføringstabletter	☐	☐	☐
* Jerntabletter	☐	☐	☐
* Vitamintilskudd	☐	☐	☐
* Tran	☐	☐	☐
* Homøopatmedisin, naturmedisin	☐	☐	☐
* Annet	☐	☐	☐

*Hvis annet, hva*_____

OM ANDRE SYKDOMMER

38. Har lege sagt at du har:

	Ja	Nei
* Epilepsi	☐	☐
* Diabetes (sukkersyke)	☐	☐
* Migrene	☐	☐

39. Har du noen andre sykdommer som har vart over 3 måneder ?

Ja ☐ Nei ☐

Hvilke(n) ?_____

OM TOBAKK

40. Røyker noen hjemme hos deg ? (Sett ett eller flere kryss)

* Nei, ingen ☐
* Ja, mor ... ☐
* Ja, far ..... ☐
* Ja, søsken ..... ☐
* Ja, andre ..... ☐

41. Har du prøvd å røyke ? (minst en sigarett) Ja ☐ Nei ☐

HVIS DU HAR SVART «NEI»: GÅ TIL SPØRSMÅL **45**

42. Røyker du selv ?
(Sett ett kryss og oppgi evt. antall sigaretter. En pakke tobakk er ca. 50 sigaretter)

- ☐ Ja, jeg røyker ca _____ sigaretter daglig
- ☐ Ja, jeg røyker av og til, men ikke daglig
- ☐ Nei, ikke nå, men tidligere røykte jeg av og til
- ☐ Nei, ikke nå lenger, men tidligere røykte jeg ca _____ sigaretter daglig
- ☐ Nei, jeg røyker ikke

HVIS DU HAR SVART «NEI, JEG RØYKER IKKE»: GÅ TIL SPØRSMÅL **45**

43. Hvor gammel var du da du begynte å røyke ? _____år

44. Hvor mange år tilsammen har du røykt daglig ? _____år

45. **Blir du noen gang sjenert av røyklukt :**

	Aldri	Av og til	Ofte
- på skolen ?	☐	☐	☐
- hjemme ?	☐	☐	☐

46. **Bruker du eller har du brukt snus, skrå eller lignende ?**

Nei, aldri ☐ *Ja, men jeg har sluttet* ☐ *Ja, av og til* ☐ *Ja, hver dag* ☐

HVIS DU HAR SVART «NEI, ALDRI»:GÅ TIL SPØRSMÅL **50**

47. **Hvor gammel var du da du begynte med snus/skrå ?** _____*år*

48. **Hvor mange år til sammen har du brukt snus/skrå ?** _____*år*

49. **Hvor mange esker/poser snus/skrå bruker/brukte du i uka ?** _____*antall*

OM IDRETT OG MOSJON

50. Utenom skoletida: **Hvor mange dager i uka driver du idrett, eller mosjonerer du så mye at du blir andpusten og/eller svett?**
(Sett bare ett kryss)

* *Hver dag* ..... ☐	* *Ikke hver uke, men minst en dag hver 14.dag* . ☐
* *4-6 dager i uka* .. ☐	* *Ikke hver 14.dag, men minst en dag i måneden* ☐
* *2-3 dager i uka* ... ☐	* *Sjeldnere enn en dag i måneden* ..... ☐
* *1 dag uka* ..... ☐	* *Aldri* ..... ☐

51. Utenom skoletida: **Til sammen hvor mange timer i uka driver du idrett eller mosjonerer du så mye at du blir andpusten og/eller svett?**
(Sett bare ett kryss)

* *Ingen* ..... ☐	* *Omtrent 2-3 timer* ..... ☐
* *Omtrent ½ time* .. ☐	* *Omtrent 4-6 timer* ..... ☐
* *Omtrent 1 time* ... ☐	* *7 timer eller mer* ..... ☐

52. **Bruker du astma-medisin før mosjon, trening eller idrettskonkurranser?**
Ja ☐ *Nei* ☐

53. Driver du aktiv idrett ?

Ja ☐ *Nei, men jeg drev med aktiv idrett før* ☐ *Nei* ☐

HVIS DU HAR SVART «NEI» (aldri drevet aktiv idrett): GÅ TIL SPØRSMÅL **59**

54. Hvis du har sluttet: **Hvor gammel var du da du sluttet med aktiv idrett ? __*år***

55. Hvilke(n) idrett(er) er/var du med i ? (Sett ett eller flere kryss)

A Ski (langrenn, skiskyting) ..... ☐
B Ski (slalåm, hopp) ..... ☐
C Fotball ..... ☐
D Riding ..... ☐
E Skøyter, ishockey ..... ☐
F Håndball, basket, volleyball ..... ☐
G Kampidrett, boksing ..... ☐
H Bodybuilding ..... ☐
I Sykling ..... ☐
J Styrkeløft/vektløfting ..... ☐
K Friidrett/løp/orientering . ☐
L Svømming ..... ☐
M Gymnastikk/turn ..... ☐
N Annet, ... ☐
Hva ? _____

56. Deltar du i idrettskonkurranser, kamper ? (Sett ett kryss)

Ja ☐ *Nei, men jeg deltok før* ☐ *Nei* ☐

HVIS DU HAR SVART «NEI» (aldri deltatt i konkurranser, kamper): GÅ TIL SPØRSMÅL **59**

57. På hvilket nivå deltok/deltar du i idrettskonkurranser ? (Angi høyeste nivå)

* *Lokalt nivå* (klubbmesterskap, serier etc.) ..... ☐
* *Kretsnivå* ..... ☐
* *Nasjonalt nivå* (landsstevne, Norgesmesterskap) ..... ☐

58. I hvilke(n) idrett(er) er/var dette ? (Skriv inntil 3 idretter du er/ var mest med på)

Jeg er/har vært mest aktiv i.....og har hold på med dette i .....år

Jeg er/har vært nest mest aktiv i .....og har holdt på med dette i .....år

Jeg er/har vært 3. mest aktiv i .....og har holdt på med dette i.....år

HVORDAN DU HAR DET

59. Når du tenker på hvordan du har det for tida, er du stort sett fornøyd eller er du stort sett misfornøyd ? (Sett bare ett kryss)

- * Svært fornøyd ..... ☐
- * Meget fornøyd ..... ☐
- * Ganske fornøyd ..... ☐
- * Både og ..... ☐
- * Nokså misfornøyd ..... ☐
- * Meget misfornøyd ..... ☐
- * Svært misfornøyd ..... ☐

60. Føler du deg stort sett sterk og opplagt eller trøtt og sliten ? (Sett bare ett kryss)

- * Meget sterk og opplagt . ☐
- * Sterk og opplagt ..... ☐
- * Ganske sterk og opplagt. ☐
- * Både og ..... ☐
- * Ganske trøtt og sliten ... ☐
- * Trøtt og sliten ..... ☐
- * Svært trøtt og sliten ..... ☐

61. Er du vanligvis glad eller nedstemt (trist) ? (Sett bare ett kryss)

- * Svært nedstemt (trist) .... ☐
- * Nedstemt (trist) ..... ☐
- * Nokså nedstemt (trist) .. ☐
- * Både og ..... ☐
- * Nokså glad ..... ☐
- * Glad ..... ☐
- * Svært glad ..... ☐

62. Hva slags oppfatning har du av deg selv ? Kryss av for hver av setningene under ettersom du er enig eller uenig i at de passer for deg. (Ett kryss for hver linje)

	Svært enig	Enig	Uenig	Svært uenig
* Jeg har en positiv holdning til meg selv	☐	☐	☐	☐
* Jeg føler meg virkelig ubrukelig til tider	☐	☐	☐	☐
* Jeg føler at jeg ikke har mye å være stolt av ...	☐	☐	☐	☐
* Jeg føler at jeg er en verdifull person, i hvert fall på lik linje med andre	☐	☐	☐	☐

63. Har du i løpet at den siste måneden:

	Nesten hver natt	Ofte	Av og til	Aldri
* hatt vanskelig for å sovne inn ?	☐	☐	☐	☐
* våknet for tidlig og ikke sovnet igjen ?.	☐	☐	☐	☐

64. Spørsmålene nedenfor dreier seg om hvordan du vanligvis opptrer, føler og handler. Kryss av det som passer best, enten Ja eller Nei for hver linje.

	Ja	Nei
* *Er du forholdsvis livlig ?*	☐	☐
* *Ville du bli oppskaket av å se et barn eller dyr lide ?*	☐	☐
* *Liker du å treffe nye mennesker ?*	☐	☐
* *Blir dine følelser lett såret ?*	☐	☐
* *Hender det ofte at du «går trøtt»?*	☐	☐
* *Liker du å spille andre et puss som av og til kan såre dem ?*	☐	☐
* *Er du ofte bekymret ?*	☐	☐
* *Er gode manérer og renslighet viktig for deg ?*	☐	☐
* *Bekymrer du deg for at fryktelige ting kan skje ?*	☐	☐
* *Tar du vanligvis selv det første skrittet for å få nye venner?*	☐	☐
* *Er du for det meste stille når du er sammen med andre ?*	☐	☐
* *Liker du å komme til avtaler i god tid ?*	☐	☐
* *Har du ofte følt deg trøtt og giddeslaus uten grunn ?*	☐	☐
* *Er det mange mennesker som forsøker å unngå deg ?*	☐	☐
* *Klarer du å holde fart i et selskap ?*	☐	☐
* *Bekymrer du deg for lenge etter en pinlig opplevelse ?*	☐	☐
* *Liker du å ha masse liv og røre rundt deg ?*	☐	☐
* *Forteller folk deg en masse løgner ?*	☐	☐

65. Nedenfor er en liste over noen problemer eller plager. Har du vært plaget av noe av dette <u>de siste 14 dagene</u> ? (Sett ett kryss for hver linje)

	Ikke plaget	Litt plaget	Ganske plaget	Veldig plaget
* *Vært stadig redd og engstelig*	☐	☐	☐	☐
* *Følt deg anspent eller urolig*	☐	☐	☐	☐
* *Følt håpløshet når du tenker på framtida*	☐	☐	☐	☐
* *Følt deg nedfor eller trist*	☐	☐	☐	☐
* *Bekymret deg for mye om forskjellige ting*	☐	☐	☐	☐

66. Har du i løpet av <u>den siste måneden</u> vært plaget av nervøsitet (irritabel, urolig, anspent eller rastløs) ?

Nesten hele tida ☐ *Ofte* ☐ *Av og til* ☐ *Aldri* ☐

OM FRITIDA

67. Tenk tilbake på den siste uka, altså de 7 siste dagene. Hvis du gjorde noe som står på lista nedenfor, omtrent hvor mange ganger gjorde du det ? (Sett ett kryss for hvert punkt med stjerne)

	Ingen gang	En gang	To eller tre ganger	Fire eller flere
* *Besøkte noen du kjente*	☐	☐	☐	☐
* *Fikk besøk*	☐	☐	☐	☐
* *Leste en bok du likte*	☐	☐	☐	☐
* *Hørte på musikk eller spilte et instrument lengre enn et kvarter av gangen*	☐	☐	☐	☐
* *Var ute mer enn 2 timer av gangen med kamerater eller venninner*	☐	☐	☐	☐
* *Var på møte eller trening i en forening eller et lag*	☐	☐	☐	☐
* *Drev med en annen hobby*	☐	☐	☐	☐
* *Så på TV eller video*	☐	☐	☐	☐
* *Gjorde lekser eller hjemmearbeid lengre enn en time*	☐	☐	☐	☐

68. Hvor mange lag eller foreninger er du med i ? (f.eks. idrettslag, speiderforening, musikk-korps el.)

Ingen ☐ *En* ☐ *To eller flere* ☐

OM VENNER

69. Har du hatt noen som du har regnet som din beste venn gjennom mesteparten av skoletiden ? *Ja* ☐ *Nei* ☐

70. Hender det at du føler deg ensom ? (Sett ett kryss)

* *Svært ofte* ..... ☐
* *Ofte* ..... ☐
* *Av og til* ..... ☐
* *Sjelden* ..... ☐
* *Svært sjelden eller aldri* ..... ☐

71. Er dine foreldre separert eller skilt, eller har de noen gang flyttet fra hverandre for mer enn ett år ? (Sett ett kryss og evt. alderen din)

* *Nei* ..... ☐

* *Ja, de flyttet fra hverandre eller ble separert da jeg var _____år, men flyttet senere sammen igjen* ..... ☐

* *Ja, de ble skilt eller flyttet fra hverandre for godt da jeg var _____år* ..... ☐

72. Hvis du har søsken, hvor godt forhold føler du at du har til søsteren eller broren din ? Hvis du har flere søsken, tenk på den du har det beste forholdet til. (Sett ett kryss)

* *Mye dårligere enn vanlig* ..... ☐
* *Dårligere enn vanlig* ..... ☐
* *Som vanlig* ..... ☐
* *Bedre enn vanlig* ..... ☐
* *Mye bedre enn vanlig* .... ☐
* *Har ikke søsken* ..... ☐

73. Omtrent hvor mange nære venner har du ? Regn med de du kan snakke fortrolig med og som kan gi deg god hjelp når du trenger det. Regn ikke med de du bor sammen med, men regn med andre slektninger. (Sett ett kryss)

* *Ingen* ..... ☐
* *En* ..... ☐
* *2 eller flere* ..... ☐
* *4 eller flere* ..... ☐

74. Har du fast kjæreste ? *Ja* ☐ *Nei* ☐

75. Føler du at du har mange nok venner ? *Ja* ☐ *Nei* ☐

OM SKOLEN

76. Hender noe av dette deg på skolen, eller har det hendt før? (Sett ett kryss for hvert punkt med stjerne)

	Aldri	En gang i blant	Ofte	Svært ofte
* *Har vanskelig for å konsentrere deg i timen*	☐	☐	☐	☐
* *Synes gym eller formingstimene er morsomme*	☐	☐	☐	☐
* *Synes andre timer er morsomme*	☐	☐	☐	☐
* *Krangler med læreren*	☐	☐	☐	☐
* *Gleder deg til å gå skolen*	☐	☐	☐	☐
* *Skulker*	☐	☐	☐	☐
* *Forstår når lærerne underviser*	☐	☐	☐	☐
* *Har det morsomt i friminuttene*	☐	☐	☐	☐
* *Er fornøyd med resultatene på prøver*	☐	☐	☐	☐
* *Kommer i slåsskamp*	☐	☐	☐	☐
* *Blir mobbet av andre elever*	☐	☐	☐	☐
* *Får skjenn av læreren*	☐	☐	☐	☐
* *Klarer ikke å være rolig i timene*	☐	☐	☐	☐
* *Kjeder deg, eller mistrives*	☐	☐	☐	☐

OM KOSTHOLD OG SPISEVANER

77. Hvor ofte spiser du til vanlig disse måltidene? (Sett ett kryss for hver linje)

	Hver dag	4-6 dg i uka	1-3 dg i uka	Sjeldnere eller aldri
* *Frokost*	☐	☐	☐	☐
* *Formiddagsmat/ nistepakke*	☐	☐	☐	☐
* *Varm middag*	☐	☐	☐	☐

78. Prøver du å slanke deg ?

Nei, vekten min er passe ☐ *Nei, men jeg trenger å slanke meg* ☐ *Ja* ☐

79. Hvor ofte hender det at du ikke spiser matpakken selv om du har den med ? (Sett ett kryss)

* *Hver skoledag* ..... ☐
* *4-6 dager i uka* ..... ☐
* *1-3 dager i uka* ..... ☐
* *Sjeldnere eller aldri* ..... ☐
* *Har aldri med matpakke* .. ☐

80. Hvor ofte drikker du eller spiser du noe av dette ?
(Sett ett kryss for hver linje)

	Mer enn 1 gang pr. dag	En gang pr. dag	Hver uke, men ikke hver dag	Sjeldnere	Aldri
* *Cola, brus eller andre leskedrikker*	☐	☐	☐	☐	☐
* *Lettmelk/skummet melk*	☐	☐	☐	☐	☐
* *Helmelk*	☐	☐	☐	☐	☐
* *Kaffe*	☐	☐	☐	☐	☐
* *Potetgull o.l*	☐	☐	☐	☐	☐
* *Sukkertøy, sjokolade, andre søtsaker*	☐	☐	☐	☐	☐
* *Pommes frites, hamburger, pølser*.....	☐	☐	☐	☐	☐
* *Grovt brød/knekkebrød*	☐	☐	☐	☐	☐
* *Meierismør*	☐	☐	☐	☐	☐
* *Margarin*	☐	☐	☐	☐	☐
* *Frukt*	☐	☐	☐	☐	☐
* *Grønnsaker*	☐	☐	☐	☐	☐

81. Vil du si om deg selv at du er: (Sett ett kryss)

* *Svært tykk* ..... ☐
* *Litt tykk* ..... ☐
* *Omtrent som andre* ..... ☐
* *Heller tynn* ..... ☐
* *Svært tynn* ..... ☐

82. **Nedenfor er en liste over ting som gjelder spisevaner.** Kryss av for hva som passer deg. (Sett ett kryss for hvert punkt med stjerne)

	Aldri	Sjelden	Ofte	Alltid
* *Når jeg først har begynt å spise, kan det være vanskelig å stoppe*	☐	☐	☐	☐
* *Jeg bruker for mye tid til å tenke på mat*	☐	☐	☐	☐
* *Jeg føler at maten kontrollerer livet mitt*	☐	☐	☐	☐
* *Når jeg spiser, skjærer jeg maten opp i små biter*	☐	☐	☐	☐
* *Jeg bruker lengre tid enn andre på et måltid*	☐	☐	☐	☐
* *Eldre mennesker synes at jeg er for tynn*	☐	☐	☐	☐
* *Jeg føler at andre presser meg til å spise*	☐	☐	☐	☐

OM ALKOHOL

83. **Har du noen gang prøvd å drikke alkohol ? (Dvs. alkoholholdig øl, vin , brennevin eller hjemmebrent)**

Ja ☐ *Nei* ☐ *Vet ikke* ☐

HVIS DU HAR SVART «NEI», GÅ TIL SPØRSMÅL **87**

84. **Har du noen gang drukket så mye alkohol at du har vært beruset (full) ?** (Sett ett kryss)

* *Nei, aldri* ..... ☐
* *Ja, en gang* ..... ☐
* *Ja, 2-3 ganger* ... ☐
* *Ja, 4-10 ganger* ..... ☐
* *Ja, mer enn 10 ganger* ..... ☐

85. **Omtrent hvor mye øl, vin eller brennevin drikker du vanligvis i løpet av <u>to uker</u> ?** Regn ikke med alkoholfritt øl. Sett **0** hvis du **ikke drikker**.

Øl _____ *antall ½ flasker* *Brennevin* _____ *antall glass(ca ½ dl)*

Vin _____ *antall glass (ca 1 dl)* *Hjemmebrent* _____ *antall glass(ca ½ dl)*

86. På hvilke ukedager drikker du som oftest alkoholholdige drikker?
(Sett ett eller flere kryss)

* *Drikker ikke* ..... ☐
* *Fredager* . ☐
* *Lørdager* . ☐
* *Andre dager i uken* ..... ☐

****

87. Har du noen gang sett at noen av dine foreldre har vært beruset?
(Sett ett kryss)

* *Aldri* ..... ☐
* *Noen få ganger* .. ☐
* *Noen ganger i året* ..... ☐
* *Noen ganger i måneden* ..... ☐
* *Noen ganger i uka* ..... ☐

LESE- OG SKRIVEVANSKER

88. Hvor ofte føler du at din lese- og skriveferdighet er utilstrekkelig for de oppgavene du skal gjøre på skolen og /eller i fritiden?

	Aldri	Nesten aldri	Noen ganger	Ofte	Alltid
* *Lesing*	☐	☐	☐	☐	☐
* *Skriving*	☐	☐	☐	☐	☐

89. Har du hatt spesielle lese- eller skriveproblemer de siste 12 månedene ?

	Store problemer	Noen problemer	Ingen problemer
* *Lesing*	☐	☐	☐
* *Skriving*	☐	☐	☐

90. Får du hjelp for lese- eller skriveproblemer nå? *Ja* ☐ *Nei* ☐

91. Har du hatt lese- eller skriveproblemer tidligere, men ikke de siste 12 månedene ? *Ja* ☐ *Nei* ☐

Hvis ja, ***fikk du hjelp den gangen?*** *Ja* ☐ *Nei* ☐

92. **Har du noen form for talevansker?** *Ja* ☐ *Nei* ☐

Hvis ja: **hvilke:**

* *Stamming* ..... ☐
* *Uttalevansker* ..... ☐
* *Stemmevansker* ..... ☐
* *Vansker med å uttrykke meg* .... ☐

OM HELSETJENESTEN

93. **Har du i løpet av de siste 12 månedene vært hos:** (Ett kryss på hver linje)

	Ja	Nei
* *Allmennpraktiserende lege* (lege utenom sykehus)	☐	☐
* *Lege på sykehus* (uten at du var innlagt)	☐	☐
* *Psykolog*	☐	☐
* *Fysioterapeut*	☐	☐
* *Kiropraktor*	☐	☐
* *Homøopat*	☐	☐
* *Annen behandler* (naturmedisiner,fotsoneterapeut, håndspålegger, «healer», «synsk», e.l.)	☐	☐

94. **Har du noen gang vært innlagt på sykehus** (utenom da du ble født)**?**

Nei, aldri ☐ *Ja, en gang* ☐ *Ja, mer enn en gang* ☐

Hvis ja: **Har du vært innlagt på sykehus i løpet av de siste 12 månedene?**

Ja ☐ *Nei* ☐

95. **Hvor ofte har du vært hos skolehelsetjenesten de siste 12 månedene?**

Ingen ganger ☐ *1 -3 ganger* ☐ *Mer enn 3 ganger* ☐

96. **Har du selv noen gang tatt kontakt med skolehelsetjenesten?**

Ja ☐ *Nei* ☐

97. **Ønsker du deg mer kontakt med skolehelsetjenesten enn det du har hatt?**

Ja ☐ *Nei* ☐

98. Hvor ofte har du vært borte fra skolen p.g.a. sykdom de siste 12 månedene ?

Mindre enn en uke ☐ *1-2 uker* ☐ *Mer enn 2 uker* ☐

OM UTVIKLING

Du er nå i en alder da kroppen din kan ha begynt å forandre seg og bli mer og mer lik kroppen til en voksen. Her er det noen spørsmål om kroppslige forandringer som skjer med ungdommer i din alder.

99. Når man er tenåring, er det perioder da man vokser raskt. Har du merket at kroppen din har vokst fort (blitt høyere) ? (Sett ett kryss)

* *Nei, den har ikke begynt å vokse* ..... ☐
* *Ja, den har såvidt begynt å vokse raskt* ..... ☐
* *Ja, den har helt tydelig begynt å vokse* ..... ☐
* *Ja, det virker som om jeg er ferdig med å vokse raskt* ..... ☐

100. Og hva med hår på kroppen (under armene og i skrittet) ? Vil du si at håret på kroppen din har: (Sett ett kryss)

* *Ikke begynt å vokse enda* ..... ☐
* *Såvidt begynt å vokse* ..... ☐
* *Helt tydelig begynt å vokse* ..... ☐
* *Det virker som om håret på kroppen er utvokst* ..... ☐

101. Når du ser på deg selv nå, mener du at du er/var tidligere eller senere fysisk moden enn andre på din alder ? (Sett ett kryss)

* *Mye tidligere* ..... ☐
* *Noe tidligere* ..... ☐
* *Lite grann tidligere* ..... ☐
* *Akkurat som andre* ..... ☐
* *Lite grann senere* ..... ☐
* *Noe senere* ..... ☐
* *Mye senere* ..... ☐

SPØRSMÅL BARE FOR JENTER

102. Har du begynt å få bryster? (Sett ett kryss)

* *Nei, har ikke begynt ennå* ☐
* *Ja, har såvidt begynt* ..... ☐
* *Ja, har helt tydelig begynt* ..... ☐
* *Det virker som om brystene er fullt utviklet* ☐

103. Har du fått menstruasjon («mensen»)? *Ja* ☐ *Nei* ☐

HVIS DU HAR SVART «NEI»: GÅ TIL SPØRSMÅL **106**

104. Hvor gammel var du da du fikk din første menstruasjon?

Jeg var .....år og .....måneder.

105. Har du noen gang etter en blødning vært blødningsfri i flere måneder (uten å ha vært gravid)? (Sett ett kryss)

* *Ja, 2-5 mnd* ..... ☐
* *Ja, 6-12 mnd* ..... ☐
* *Ja, mer enn 1 år* ..... ☐
* *Nei, aldri* ..... ☐

****

106. Har du noen gang fått behandling av lege for:

	Ja	Nei
* *Underlivsbetennelse (eggstokkbetennelse, eggleder betennelse)?*	☐	☐
* *Utflod*	☐	☐
* *Menstruasjonssmerter*	☐	☐

107. Har du noen gang brukt p-piller eller minipiller? *Ja* ☐ *Nei* ☐

HVIS DU HAR SVART «NEI»: GÅ TIL SISTE SIDE

108. Hvor gammel var du første gang du brukte p-piller? _____år

109. Hvor lenge har du brukt p-piller i alt? _____år

110. Bruker du p-piller nå? *Ja* ☐ *Nei* ☐

SPØRSMÅL BARE FOR GUTTER

112. Har du begynt å komme i stemmeskiftet? (Sett ett kryss)

* *Nei, har ikke begynt ennå* ☐
* *Ja, har såvidt begynt* ☐
* *Ja, har helt tydelig begynt* ☐
* *Det virker som om stemmeskiftet er ferdig* ☐

113. Har du begynt å få bart eller skjegg? (Sett ett kryss)

* *Nei, har ikke begynt ennå* ☐
* *Ja, har såvidt begynt* ☐
* *Ja, har helt tydelig begynt* ☐
* *Ja, har fått en god del skjeggvekst* ☐

114. Har du vært behandlet hos lege for: (Sett ett kryss for hver linje).

	Ja	Nei
* *Trang forhud*	☐	☐
* *Utflod fra urinrøret*	☐	☐
* *Betennelse i forhuden eller pungen* (testiklene)	☐	☐

Dissertations at the Faculty of Medicine, NTNU

1977

1. Knut Joachim Berg: EFFECT OF ACETYLSALICYLIC ACID ON RENAL FUNCTION
2. Karl Erik Viken and Arne Ødegaard: STUDIES ON HUMAN MONOCYTES CULTURED *IN VITRO*

1978

3. Karel Bjørn Cyvin: CONGENITAL DISLOCATION OF THE HIP JOINT.
4. Alf O. Brubakk: METHODS FOR STUDYING FLOW DYNAMICS IN THE LEFT VENTRICLE AND THE AORTA IN MAN.

1979

5. Geirmund Unsgaard: CYTOSTATIC AND IMMUNOREGULATORY ABILITIES OF HUMAN BLOOD MONOCYTES CULTURED IN VITRO

1980

6. Størker Jørstad: URAEMIC TOXINS
7. Arne Olav Jenssen: SOME RHEOLOGICAL, CHEMICAL AND STRUCTURAL PROPERTIES OF MUCOID SPUTUM FROM PATIENTS WITH CHRONIC OBSTRUCTIVE BRONCHITIS

1981

8. Jens Hammerstrøm: CYTOSTATIC AND CYTOLYTIC ACTIVITY OF HUMAN MONOCYTES AND EFFUSION MACROPHAGES AGAINST TUMOR CELLS *IN VITRO*

1983

9. Tore Syversen: EFFECTS OF METHYLMERCURY ON RAT BRAIN PROTEIN.
10. Torbjørn Iversen: SQUAMOUS CELL CARCINOMA OF THE VULVA.

1984

11. Tor-Erik Widerøe: ASPECTS OF CONTINUOUS AMBULATORY PERITONEAL DIALYSIS.
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1985

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1986

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1988

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1998

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1999

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2000

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159. xxxxxxxxx (blind number)
160. Christina Vogt Isaksen: PRENATAL ULTRASOUND AND POSTMORTEM FINDINGS – A TEN YEAR CORRELATIVE STUDY OF FETUSES AND INFANTS WITH DEVELOPMENTAL ANOMALIES.
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178. Alexander Wahba: THE INFLUENCE OF CARDIOPULMONARY BYPASS ON PLATELET FUNCTION AND BLOOD COAGULATION – DETERMINANTS AND CLINICAL CONSEQUENSES
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