Body Image and Eating Behavior in Young Adults Born Preterm

Authors: Hanna-Maria Matinolli, MHealthSci\textsuperscript{1,2}, Satu Männistö, PhD\textsuperscript{1}, Marika Sipola-Leppänen, MD, PhD\textsuperscript{1,2,3}, Marjaana Tikanmäki, MD\textsuperscript{1,2}, Kati Heinonen, PhD\textsuperscript{4}, Jari Lahti, PhD\textsuperscript{4,5}, Marius Lahti, PhD\textsuperscript{4}, Karoliina Wehkalampi, MD, PhD\textsuperscript{6}, Marjo-Riitta Järvelin, MD, PhD\textsuperscript{2,7}, Sture Andersson, MD, PhD\textsuperscript{6}, Aulikki Lano, MD, PhD\textsuperscript{6}, Timo Vartia, MD, PhD\textsuperscript{6}, Dieter Wolke, PhD\textsuperscript{8}, Johan G Eriksson, MD, DMS\textsuperscript{1,9,10}, Marja Vääräsmäki, MD, PhD\textsuperscript{1,3}, Katri Räikkönen, PhD\textsuperscript{4}, Eero Kajantie, MD, DMS\textsuperscript{1,3,6}

\textsuperscript{1}National Institute for Health and Welfare, Helsinki and Oulu, Finland; \textsuperscript{2}Institute of Health Sciences, University of Oulu, Finland; \textsuperscript{3}PEDEGO Research Unit (Research Unit for Pediatrics, Dermatology, Clinical Genetics, Obstetrics and Gynecology), Medical Research Center Oulu (MRC Oulu), Oulu University Hospital and University of Oulu, Oulu, Finland \textsuperscript{4}Institute of Behavioral Sciences, University of Helsinki, Helsinki, Finland; \textsuperscript{5}Helsinki Collegium for Advanced Studies, University of Helsinki, Helsinki, Finland. \textsuperscript{6}Children's Hospital, Helsinki University Central Hospital and University of Helsinki, Helsinki, Finland \textsuperscript{7}Imperial College, London, UK, \textsuperscript{8}Department of Psychology, University of Warwick, UK, \textsuperscript{9}Department of General Practice and Primary Health Care, University of Helsinki and Helsinki University Hospital, Helsinki, Finland, \textsuperscript{10}Folkhälsan Research Center, Helsinki, Finland

Corresponding Author: Hanna-Maria Matinolli, Chronic Disease Prevention Unit, National Institute for Health and Welfare, Po Box 57, 20521 Turku, Finland. hanna-maria.matinolli@thl.fi

Word count: abstract 239 words / manuscript 3727 words

Keywords: preterm birth, birth weight, gestational age, eating disorders, body image

BODY IMAGE AND EATING BEHAVIOR IN YOUNG ADULTS BORN PRETERM
Abstract

**Objective:** Previous studies have suggested that people born preterm have increased rates of eating disorders (ED). However, a recent study suggested lower levels of ED-related symptoms in the extreme group of adults born preterm with very low birth weight (<1500 g). We examined symptoms related to EDs in adults born early (<34 weeks of gestational age) or late (34 to <37 weeks of gestational age) preterm. **Methods:** We studied young adults (mean age 24.1 years) from two birth cohorts: ESTER (Northern Finland 1985-1989) and AYLS (Uusimaa, Finland, 1985-1986). Of the participants, 185 were born early preterm, 348 late preterm and 637 were term-born controls (N=1170). They completed 3 subscales of the Eating Disorder Inventory (EDI)-2, including Drive for Thinness (DT), Body Dissatisfaction (BD) and Bulimia (B). Group differences were examined by linear regression. **Results:** Young women born early preterm scored 4.1 points (95% CI -8.0, -0.2, p=.04) lower in summed EDI subscale scores than women born at term, when adjusted for age and cohort. This difference was observed also in DT and BD but not for B subscales. The differences persisted after adjustments for current, pre- and neonatal characteristics. We did not observe differences in EDI scores among men or women born late preterm when compared to controls. **Discussion:** Women born early preterm have significantly fewer symptoms related to eating disorders in early adulthood when compared to their peers born at term, which may protect from developing an ED.
Body Image and Eating Behavior in Young Adults Born Preterm

Eating Disorders (EDs) are complicated maladies that often have negative consequences on psychosocial and physical well-being throughout the life course. They include anorexia nervosa (AN), with lifetime prevalence estimated at 2.2%\(^1\) and bulimia nervosa (BN), with estimated prevalence of 2.3%\(^2\). Although the point-prevalence of manifest EDs is rather small, related symptoms such as eating disturbances and disordered body image affect a growing number of especially young women\(^3,4\). Body dissatisfaction often precedes disordered eating and manifest disorders represent an extreme of this continuum of symptoms. High levels of these symptoms predict a higher risk to develop manifest disease\(^5\). The developmental background of EDs and related symptoms is multifactorial, consisting of genetic, sociocultural, biological and psychological processes operating mainly during childhood and early adolescence\(^6,7,8\). Some studies have suggested that obstetric and perinatal factors play a role in building the future body image\(^9,10\), results are however contradictory and the methods used for describing both, the exposures and outcomes, vary depending on the study.

Preterm birth (<37 full gestational weeks), which each year complicates on average 14.9 million infants (11.1% of all livebirths)\(^11\), is listed as one potential risk factor for development of EDs\(^9,10,10,12,13,13\). The role of preterm birth is however contradictory as much of the past literature is suffering from small sample sizes and differing methodologies and definitions for both, obstetric complications and EDs. Recent meta-analysis by Krug et al, summarized six studies examining the association between obstetric complications and prematurity and EDs and found no significant association between preterm birth and AN (OR 1.17, 95% CI 0.91-1.52)\(^14\). In addition, a recent cohort study suggested lower levels of ED-related symptoms, disordered body image and eating disturbances in the small extreme of adults born preterm with very low birth weight (<1500 g)\(^15\). However a recent Swedish birth register study
with over 2 million participants found an independent association between shorter gestational age and AN in both sexes (adjusted HR per week of gestation 0.96, 95% CI 0.95, 0.98)\textsuperscript{12}.

Most preterm infants, for example more than 70\% of those in US in 2005\textsuperscript{16}, are born late preterm (34 to 36 completed weeks of gestation). The cognitive, socioeconomic and cardiometabolic risk factors in adults born preterm are present also among the late preterm population \textsuperscript{16-19}. Of the studies examining the association between early life factors and disordered eating, none have specifically assessed the role of late preterm birth in the development of eating disorders. Other perinatal factors, including maternal pregnancy disorders have also been linked to increased risk for eating disorders. In a study by Favaro et al maternal gestational diabetes and pre-eclampsia significantly increased the risk of developing anorexia nervosa\textsuperscript{10} whereas other studies have not found such a connection.

With this background, the primary aim of our study was to assess symptoms related to eating disorders in young adults born preterm, throughout the whole gestational age range. Our secondary aim was to examine whether prenatal conditions underlying preterm birth contribute to the association between preterm birth and eating disorder symptoms. We approached these aims in two population based cohort studies. We hypothesized that participants born preterm would exhibit more symptoms related to EDs.
METHODS

Participants

The 1170 participants of the study came from two separate birth cohorts in different parts of Finland. Figure 1 presents the selection of the participants.

ESTER preterm birth study (described in detail\textsuperscript{19}), is a birth cohort study of individuals born in two northernmost provinces of Finland between 1985 and 1989, aimed to explore the effects of early (<34 weeks of gestational age (GA)) and late (34-<37 weeks of GA, as defined by the American Academy of Pediatrics\textsuperscript{16}) preterm birth on health and well-being in young adult life. Exposed individuals, i.e. young adults born preterm < 37 weeks of gestation were traced through Northern Finland Birth Cohort (NFBC) 1986 or Finnish Medical Birth Registry (FMBR) and controls were randomly selected from the source population. Of the 1980 invited individuals, 779 took part in a clinical examination between years 2009-2011 at on average 22.3 (SD 1.3) years age. We now report results comprising 145 participants born early preterm, 238 participants born late preterm and 347 term-born control participants who filled in the Eating Disorder Inventory (EDI) 2-questionnaire during the clinical visit.

Arvo Ylppö Longitudinal Study (AYLS) is part of an extensive bi-national multicenter follow-up study conducted in Bavaria, Germany and Uusimaa, Finland\textsuperscript{20,21}. The study includes 2193 individuals born between 14.3.1985 and 15.3.1986 in the province of Uusimaa in Southern Finland. The original study cohort comprises 1) 1535 infants born alive and admitted to neonatal wards of the birth hospitals or transferred to the Neonatal Intensive Care Unit of the Children’s Hospital, University of Helsinki and Helsinki University Hospital within ten days of birth and 2) 658 controls without evidence of neonatal illness and born after every second admitted infant in one of the three largest
maternity hospitals. When reaching adulthood, the individuals were invited to participate in a follow-up. Clinical examination took place in Helsinki between years 2009-2012. Of the 1136 (51.8% of the original cohort) individuals who participated at the average age of 25.2 (SD 0.6) years, we collected comprehensive data on maternal pregnancy and peri- and neonatal period from hospital records, available for 899 participants. Of the 899 participants we included in this study those who filled in the EDI-2 questionnaire and were born early (n=40) or late (n=110) preterm; those who filled in EDI-2, were born at term and belonged to the original control group (n=290) served as controls.

Both studies were approved by the Coordinating Ethics Committee at Helsinki and Uusimaa Hospital District. All participants gave written informed consent in accordance with the Declaration of Helsinki.

Gestational age

Gestational age of the participants from both cohorts was confirmed as accurately as possible from medical records as described in\(^2\). Length of gestation was determined by ultrasonography for 719, and based on last menstrual period for 449; for 2 participants, the gestational age was determined according to clinical decision in birth hospital.

Eating disorders

To assess the symptoms commonly associated with anorexia nervosa (AN) and bulimia (BN) we used 3 subscales of the Eating Disorder Inventory (EDI)-2, developed for measurement of behavioral and psychological symptoms in AN and BN\(^2\). These subscales, Drive for Thinness (DT, 7 items, Cronbach’s \(\alpha\) for reliability in women 0.87, \(\alpha\) for men 0.81), Body Dissatisfaction (BD, 8 items, \(\alpha\) for women 0.90, \(\alpha\) for men 0.85) and Bulimia (B, 7 items, \(\alpha\) for women 0.89, \(\alpha\) for men 0.82), assess the attitudes towards weight, body shape and eating. Participants rated their response to each item on a
6-point Likert scale (ranging from ‘always’ to ‘never’). We added the scores of the subscales together to form the EDI sum score (22 items in total, α for women 0.93, α for men 0.90). Higher scores are indicative of more ED-related symptoms.

Covariates

As potential confounders, maternal gestational disorders, including maternal gestational diabetes, hypertension (gestational or chronic) and preeclampsia (including superimposed) were defined by reviewing diagnoses from original hospital records and confirming them according to current criteria. We calculated the birth weight SD score according to Finnish birth weight standards and defined small for gestational age (SGA) as -2 SD less than mean for sex and length of gestation. Maternal smoking during pregnancy (yes/no), maternal pre-pregnancy body mass index (BMI; kg/m²) and primiparousness came from hospital records. Further confounder was educational attainment of the higher educated parent to indicate the childhood socio economic status (dummy coded, with separate category for missing data). We also adjusted for subject’s current BMI as calculated from the height and weight measured during the clinical visit and smoking (daily smoking, yes/no) as self-reported by questionnaire.

Sensitivity analyses

We reran all the analyses separately by excluding the participants with major mental or physical impairments (self-reported, n=17, including cerebral palsy, mental disabilities and several physical disabilities) due to their possible effect on the development of body image and eating behavior. To take the strong correlation between mood disorders and disordered eating into account in our analyses, we excluded participants who were at risk for mild-moderate depression, as indicated by Beck Depression Inventory of 10 points or more. Additionally we took the association between
pubertal development\textsuperscript{28} and eating disorders into account by rerunning the analyses by adjusting for age at first menstrual period in women and age at voice break in men (self-reported by questionnaire). We also ran the analyses by replacing the current BMI with body fat percentage, which was available for 1147 (98\%) participants, assessed by segmental multifrequency bioelectrical impedance (InBody 3.0, Biospace Co., Seoul, Korea)\textsuperscript{19}.

**Statistical methods**

As we found a statistically significant interaction between the effects of sex and gestational age (p for interaction < .001) on EDI-2 scores, we conducted the analyses separately for men and women. We compared descriptive characteristics between preterm and control participants using t-test for continuous and chi-squared test for categorical variables. Linear regression was used to compare differences between preterm and term born groups. Mean imputations were carried out for 39 women and 16 men with missing data on one EDI item and three women and five men with missing data on two EDI items. A two-tailed P-value < 0.05 was considered statistically significant throughout the analyses. All statistical analyses were performed with SPSS for Windows, Version 22.0.
RESULTS

Demographic characteristics of study participants

Characteristics of the study groups are presented in Table 1. Participants of the preterm groups in both cohorts were more often twins or SGA. They were also more likely to be born from pre-eclamptic pregnancy. Additionally preterm participants were slightly younger than controls.

We first assessed group differences in each cohort separately. This is shown in Supplementary Table S1. As the differences between the preterm groups and controls were similar in both cohorts (p for interaction >.05), we report the results pooled, separately for both sexes (interaction for sex p<.001).

Eating Disorder Inventory-2

The correlations between the three subscale scores were 0.71 and 0.65 (in women and men, respectively) between body dissatisfaction and drive for thinness; 0.41 and 0.35 between body dissatisfaction and bulimia; and 0.58 and 0.55 between drive for thinness and bulimia. Mean scores of the preterm and term born groups, separately for both sexes, are presented in Table 2. When compared to control women born at term, women born early preterm at <34 weeks of GA scored lower in summed EDI scores (mean difference 4.1 points (95% CI -8.0,-0.2, p=.04) adjusted for age and cohort) (Table 3). The difference remained similar after further adjustments for socioeconomic status and peri-and neonatal characteristics and further increased when adjusted in addition for the current characteristics of the participant (mean difference -5.3 (95% CI -8.9, -1.7, p=.004). We did not observe a statistically significant difference between women born late preterm and controls or men born preterm and controls in any of the adjusted models.
When adjusted for age and cohort women born early preterm scored 1.8 points lower in Drive for thinness-subscale (95% CI -3.4 to -0.2, p=.03) when compared to control women. The difference remained similar when controlled for covariates. There were no differences between women born late preterm and controls or men born preterm and controls in unadjusted or adjusted models.

Also in the body dissatisfaction-subscale women born early preterm scored 2.3 points lower (95% CI -4.1 to -0.4, p=.02) when compared to control women when adjusted for age and cohort. The difference remained similar after adjustments. There were no differences between women born late preterm and controls or men born preterm and controls in unadjusted and adjusted models.

There were no differences in bulimia subscale scores among women born preterm and controls or between preterm born men and controls in any of the adjusted models.

**Fetal growth, multiple pregnancies and maternal pregnancy disorders**

There were no statistically significant differences in EDI sum scores between participants born small for gestational age (SGA) and average for gestational age (AGA) when adjusted for age, cohort and gestational age. Further adjustments did not change the result. We found no differences between those born from multiple pregnancies and singletons either. Men exposed to maternal gestational diabetes scored 6.9 points (95% CI 1.6 to 12.3, p=.01) higher and maternal gestational hypertension 3.1 (-0.1, 6.2, p=.06) higher in EDI sum score when compared to those not exposed when adjusted for age, cohort and gestational age. The differences attenuated after adjustments for other prenatal covariates and current lifestyle of the participant. We found no difference between the EDI sum scores in women exposed to maternal pregnancy disorders and those not exposed.

**Sensitivity analyses**
The exclusion of participants with major mental or physical impairments did not have an effect on our results in EDI sum scores or any of the subscale scores alone. As the prevalence of depression is high in the population suffering from eating disorders we excluded participants with BDI score greater than 10 (controls n=112 / early preterm n=29 / late preterm n=54) or missing BDI from the analyses. Within men the results remained similar. Within women the difference between preterm groups and controls in EDI sum scores as well as in subscale scores separately was strengthened and became statistically significant also in the late preterm group. When adjusted for age and cohort, only women born early preterm scored -6.9 (-11.1 to -2.8, p=.001) points lower and women born late preterm -3.9 (-7.1 to -0.6, p=.019) lower when compared to controls. When further adjusted for all covariates in full model early preterm born women scored -8.3 (-12.2 to -4.5, p<.001) points lower and late preterm -3.2 (-6.1 to -0.2, p=.03) points lower when compared to controls. The results were similar in drive for thinness- and body dissatisfaction-subscapes.

Adding the self-reported age of first menstrual period (available for 599 (97%) women) or self-reported age of breaking of the voice (available for 497 (89%) men) to the full model did not change our results nor did replacing of current BMI by body fat percentage in the full adjusted model.
DISCUSSION

We found that young women born early preterm have lower levels of symptoms related to eating disorders than women born at term or women born late preterm. Within men, we found no difference in levels of these symptoms between the preterm and term born groups. While the results of some of the previous studies have suggested that individuals born preterm have an increased risk for EDs, the results of our study indicate that especially young women born at the lowest range of gestational age actually have healthier body image when compared to term born peers. In our study young women born early preterm scored lower on EDI sum score and subscales measuring body dissatisfaction and drive for thinness. The early preterm born group however did not differ significantly from the term group on a subscale measuring symptoms related to bulimia.

A recent study by our group showed that adult women born preterm with very low birth weight (VLBW, <1500g) showed lower levels of ED-related symptoms than their peers born at term. Our study now confirms that this finding extends to the larger group of women born early preterm, who had 4 points lower EDI sum score than controls, and to nondepressed women born late preterm, whose EDI scores were 4 points lower. For comparison, the difference previously shown between VLBW and term women was 8 points. Furthermore, while we found no difference among men, in the previous study a difference of 2 EDI points between VLBW men and controls became statistically significant when adjusted for covariates.

Our results are in marked contrast with some of the previous studies identifying shorter gestational age as one potential predisposing attribute in the development of an eating disorder. A recent Swedish birth register study with over 2 million participants found an independent association between shorter gestational age and AN in both sexes. That study identified AN cases from national
hospital impatient and outpatient and death registers and used extensive adjustments for main maternal, perinatal and socioeconomical confounding providing strong evidence on the role of low gestational age at birth in the development of eating disorders. Reasons for these differences are not clear. It is possible that altered body image and eating behaviour have a smaller role in the etiology of AN and other EDs in individuals born preterm than in the general population.

Previous studies assessing the association between preterm birth and eating disorders have linked preterm birth to AN but have failed to show an association between preterm birth and BN. Interestingly we found young women born early preterm scoring lower on subscales measuring drive for thinness and body dissatisfaction which are important in assessing body attitudes and behavior concerning weight and shape and thus relate closely AN. Further we did not find a difference between preterm and term born women in bulimia subscale which measures the tendency to bulimic type eating disorder. These findings suggest that young women born early preterm have less symptoms related to AN, but may not differ in symptoms related to BN when compared to term born peers.

When looking at our results in light of past literature it needs however to be taken in account that there are extensive methodological differences between the studies examining the association between pre- and postnatal factors and EDs. A few of the studies have focused on ED symptomatology assessed by self-report questionnaires as an outcome whereas most studies have focused on clinical diagnoses of EDs. Some of the past studies have used population-based case control designs, whereas others have used cohort designs. These differences make it hard to draw meaningful conclusions. In a recent meta-analysis assessing the association between pre- and postnatal factors and EDs only 6 of 14 studies included in a systematic review were included in meta-analysis and there was still extensive variability in the studies included.
Potential explanation for the protective effect of preterm birth could be parent-child relationship which also has a role to play in the development of eating disorders. Parents of preterm infants are characterized by a more protective and supportive parenting style, which could probably add a protective effect against the development of symptoms related to EDs. However eating problems, for example hypersensitivity and behavioural problems related to eating are frequent among children born early preterm and have therefore been suggested to model one possible pathway in the association between preterm birth and later eating disorders. For example a large cohort study including 11,211 participants found infant feeding problems to be an independent predictor for later eating disorders (OR 2.1, 95% CI 1.32 to 3.7). Our study population included a relatively low number of those born most immature among whom the eating difficulties are most frequent so we probably would not have been able to observe the resulting effect of eating problems in our data.

Past studies have proposed that hypoxic-induced damage, caused by obstetric complications or placental dysfunction and resulting in impairments in neurodevelopment, might in part underlie eating disorders, especially anorexia nervosa. We adjusted for the confounding effect of these factors, as indicated by maternal smoking during pregnancy and maternal pregnancy disorders such as gestational diabetes and gestational hypertension. This did not change our results. When assessing the effect of maternal gestational disorders on later eating disorders we however found that men born from pregnancies complicated by gestational diabetes scored higher on EDI. The number of participants in this analysis was however small so further conclusions from this finding should be drawn with caution. We had no data on maternal eating disorders that could predispose to preterm birth and eating disorder symptoms in the offspring; adjustment for maternal BMI as a proxy did not, however, change the results. Puberty hormones present one growing line of interest in the study of the etiology of eating disorders. Pubertal status and timing seem to be positively related to the incidence of
most eating disorder phenotypes in girls. Preterm birth on the other hand is associated with earlier puberty which could present one potential pathway of increased risk for eating disorders. We observed no differences in our results when the timing of puberty was added as a covariate in our analyses, suggesting that the timing of puberty is unlikely to play a major role in mediating the associations we found.

**Strengths and limitations**

Body image disturbance is a core feature of eating disorders. In our study we used the EDI-2 subscales that assess body dissatisfaction, drive for thinness and bulimic-type eating behavior. EDI-2 has been shown to be a valid measure for assessing the eating disorder risk both in women and men although it has been mainly validated in women. EDI-2 has been shown to identify only half of clinical ED cases, however it still has a very high overall accuracy in detecting individuals at risk. There are no published data that would enable us to directly quantify the difference we observed in the EDI-2 scores in terms of risk of manifest EDs. The strengths of our study include this widely validated measure and large body of data generalizable to the wider community. One of the main strengths is also our data that includes the whole range of preterm births.

An important possible limitation of our study is participation bias. In the Ester study, a previously published detailed non-participant analysis did not raise any concern of such bias; neither did the non-participant analyses in both cohorts which we now report on (Supplementary Tables S2 and S3). Due to different cohort designs there were differences in the proportions of preterm and term born groups. To take this difference in account all analyses were adjusted for the recruitment cohort. Our results are based on internal comparisons between the preterm and term groups. The low participation
rate would only be expected to introduce bias if the reasons for non-participation were different between these groups. This is unlikely but cannot be excluded.

A risk of residual confounding also remains a possibility, although we performed a wide range of adjustments for all the main confounders. We were not able to detect possible maternal eating disorders that might influence offsprings eating behavior.

**CONCLUSIONS**

Women born early preterm have significantly fewer symptoms related to eating disorder in early adulthood when compared to their peers born at term. Other risk factors being equal, this suggests a lower risk for developing EDs.
References


Figure captions:

Figure 1.

Flowchart of the study participants*

Footnote: *Design and recruitment of the Ester cohort is described in detail in 19 and design and perinatal characteristics of the AYLS cohort in 20.
Acknowledgements/Disclosure of Conflicts

The ESTER study was supported by grants from the Academy of Finland (SALVE program for 2009–2012 and grants 127437, 129306, 130326, 134791 and 263924 to EK), the Emil Aaltonen Foundation, European Commission (Framework 5 award QLG1-CT-2000-001643; to MRJ), the Finnish Foundation for Pediatric Research, the Finnish Government Special Subsidiary for Health Sciences (evo), Finnish Medical Society: Duodecim, the Jalmari and Rauha Ahokas Foundation, the Juho Vainio Foundation, the Novo Nordisk Foundation, the Signe and Ane Gyllenberg Foundation, the Sigrid Jusélius Foundation, the Jenny and Antti Wihuri Foundation and the Yrjö Jahnsson Foundation. In addition, NFBC1986 received financial support from the Academy of Finland (grants 175617, 173454, 24300269, 24300217); EU FP7- ENV-2008-1-226534; USA/NIH/NHLBI 1-R01-HL087679-01; RFP-RM-06-008; NorFA (50847); Thule Institute (50925); Oulu University Hospital, Oulu, Finland (24301140); University of Oulu, Finland (24000692, 24500283).

The AYLS Study childhood follow-up was financially supported by the Bundesministerium für Forschung und Technik (Federal Government of Germany, Ministry of Science and Technology) program grants PKE 4 and JUG 14 (FKZ’s 0706224, 0706564, and 01EP9504) to Drs Klaus Riegel, Dieter Wolke, and Barbara Ohrt. Adulthood follow-up was financially supported by the Academy of Finland program grants (to Drs Eriksson, Raikkonen and Kajantie). The work by Aulikki Lano was supported by Foundation of Pediatric Research. The work by Dr Heinonen and Dr. J. Lahti was supported by Academy of Finland post-doctoral grant. Dr Eriksson was supported also by grant from Samfundet Folkhälsan and Dr Andersson from Päivikki and Sakari Sohlberg Foundation and Finska Läkaresällskapet.