

Forskningsprogram			
SNAP <input checked="" type="checkbox"/>		REPROSAFE <input type="checkbox"/>	FLIPP <input type="checkbox"/> Inriktning: Ekonomiska styrmedel <input type="checkbox"/>
Inriktning: Informationssystem och indikatorer IPP <input type="checkbox"/>			
Projekttitel (svensk): Luftföroreningsexponering och astma i en stor europeisk kohortstudie			
Projekttitel (engelsk): Air pollution exposure and asthma in a large European cohort study			
Huvudsökande	Efternamn: Forsberg	Förnamn: Bertil	Födelseår: 1956
	Kvinna <input type="checkbox"/> Man <input checked="" type="checkbox"/>		
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Medsökande	Efternamn, förnamn, tjänst, organisation, institution: Järholm Bengt, professor, Umeå universitet, Institutionen för folkhälsa och klinisk medicin		
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Sammanfattning			
<p>Det är väl dokumenterat att luftföroreningar, särskilt partiklar och ozon, akut kan försämra personer med astma. Däremot finns stora brister i vår förståelse av luftföroreningarnas betydelse för uppkomsten av astma och för sjukdomens utveckling. SNAP saknar longitudinella studier på vuxna med möjlighet att belysa dessa samband. Stora uppföljningsstudier gällande astma blir kostsamma eftersom det krävs kliniska uppföljningar, data om en mängd riskfaktorer samt standardiserade mätningar av luftföroreningar. Det kan också vara svårt att erhålla tillräckligt tydliga exponeringskontraster, t.ex. för partikelhalten, om inte studien görs i många olika städer. Vi har fått möjlighet att ta ansvar för studierna om luftföroreningsexponeringens betydelse för uppkomst och progress av astma i den stora europeiska kohortstudien ECRHS II, där luftföroreningsdata insamlats med ett EU-anslag, men det fortsatta arbetet som delas upp mellan grupper i London, Kalifornien och Umeå återstår att finansiera.</p> <p>Eftersom astma är en vanlig och ofta kronisk sjukdom bland vuxna, är det av stor betydelse att olika luftföroreningars betydelse, samt interaktionen med andra faktorer, bättre kan beskrivas. Vår hypotes är att långtids-exponeringen för partiklar (PM2.5) är av betydelse, men att partiklarnas oxidativa kapacitet samt den kemiska sammansättningen (vissa metaller, sot, stort avgasinslag) kan ha en avgörande inverkan för riskökningen.</p> <p>Vi kommer att utnyttja data från 20 städer i 10 europeiska länder som vid kohortuppföljningen (ECRHS II) cirka 8 år efter starten (då deltagarna var 20-44 år) genomförde en särskild luftföroreningsstudie samtidigt med den medicinska uppföljningen av mer än 8000 vid starten kliniskt undersökta deltagare. Luftföroreningsstudien omfattade insamling av historiska mätvärden samt ett års standardiserad mätning av PM2.5, sot och NO2. PM2.5 filtren används för att bestämma partiklarnas sammansättning och oxidativa kapacitet. Projektet kommer därför att starta med att utforma de exponeringsdata som kommer att användas vid epidemiologiska analyser (3 arbetsmånader för en hygieniker). De epidemiologiska analyserna kommer både att avse nyinsjuknande i astma samt förändring av astmatillståndet (hos de som hade sjukdomen vid studiens början), och kommer att jämföra alternativa sätt att analysera sambanden, t.ex. nettoförändring på gruppnivå respektive incidenta fall. För de epidemiologiska analyserna söks 6 arbetsmånader vardera för en epidemiolog respektive statistiker, samt resemedel för samordning med grupperna i London och Kalifornien.</p> <p>Jämförelserna av de olika partikelvariablernas betydelse för utfallen i denna studie kommer sannolikt att vara av värde för bedömning av resultaten från flera andra studier inom SNAP.</p>			
		År 2004	År 2005
Summa sökta medel per år i kr:		576 000	432 000

**Miljöforskningsnämnden**  
**Ansökan om projektbidrag inom Naturvårdsverkets forskningsprogram**

Sökta projektmedel fördelade på kostnadslag	År 2004 (kr)	År 2005 (kr)
Personalkostnad inkl. soc. avgifter * Hygieniker 3 månader 2004	120 000	
Statistiker, fil lic Bo Segerstedt 3 månader per år	140 000	140 000
Projektledare/Lektor Bertil Forsberg 3 månader per år	160 000	160 000
Övriga omkostn exkl moms (förbrukningsmtrl, analyser, resor etc)**		
Resor för projektmöten i Stockholm	20 000	20 000
Resor för projektmöten i London	40 000	40 000
Delsumma av ovanstående poster:	480 000	360 000
Förvaltningspåslag: .....20..... %	96 000	72 000
<b>Totalsumma per år: (införs sid. 1):</b>	<b>576 000</b>	<b>432 000</b>

\*) Specificera namn, tjänst \*\*) Specificera

**Samtliga övriga miljörelaterade projekt för vilka de sökande har beviljats anslag eller söker anslag för 2004-2006. OBS Även EU-finansiering.**

Projekttitel	Finansiär	Tidsperiod	Sökt kr	Beviljat kr
Nya metoder att skatta trafikförändringars konsekvenser för avgasexponering och hälsoeffekter	CMF	2004-	Dokt tjänst	

**Miljörelaterade projekt för vilka sökande har beviljats anslag för 2000-2003  
OBS Även EU-finansiering**

Projekttitel	Finansiär	Tidsperiod	Beviljat Kr
Partiklar och akuta luftvägseffekter	Statens Energimyndighet	2000-2003	1,6 Mkr
Bättre metoder beskriva hälsopåverkan av vägtrafik	Vägverket	2002-2004	1,3 Mkr
Vägdamm och grova partiklars effekter på hälsa	Vägverket	2002-2004	658 000 kr
Hälsovinster av trängselavgifter	Naturvårdsverket	2003	300 000 kr
Miljömål för luft och biobränsleledning	Statens Energimyndighet	2003	412 000 kr
Anslag från NV, Formas, EU via andra institutioner liksom uppdrag är här ej inkluderade			

Datum och sökandes underskrift, vilken samtidigt ger Naturvårdsverket tillåtelse att publicera sökandes namn på sin webbplats:	Datum och underskrift av prefekt eller motsvarande med namnförtydligande:
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Ansökan skall bestå av detta formulär jämte högst sex sidor lång projektbeskrivning på **engelska** (strukturerad som den svenska sammanfattningen samt en redovisning av kunskapsläget). Referenser till egna publikationer ges med sifferhänvisning till CV. Andra referenser ges i löpande text. Sökandes och eventuell medsökandes CV får omfatta högst två sidor. Inga bilagor kommer att beaktas vid bedömningen. Ansökan (max 10 A4-sidor, 12 punkters teckenstorlek) skall inlämnas i **original + 15 kopior samt elektroniskt** till [ansok@naturvardsverket.se](mailto:ansok@naturvardsverket.se). Häfta ihop ansökan och använd hålat papper. Ansökan skall ha inkommit senast den 15 oktober 2003 till Naturvårdsverket, Forskningssektariatet, 106 48 STOCKHOLM.

**Miljöforskningsnämnden**  
**Ansökan om projektbidrag inom Naturvårdsverkets forskningsprogram**

## Air pollution exposure and asthma in a large European cohort study

### BACKGROUND

#### Introduction and aim

The European Community Respiratory Health Survey I (ECRHS I) was an international multi-center study focusing on asthma-like conditions, allergy and bronchial responsiveness in more than forty centers in more than 20 countries. Most participating centers were cities with at least 150 000 inhabitants. ECRHS I was conducted from 1990-1993, and was followed up by ECRHS II conducted from 2000-2003. Details about the ECRHS project are given on-line ([www.ecrhs.org](http://www.ecrhs.org)). The three Swedish centers are Umeå, Uppsala and Gothenburg. In total, 20 cities in 10 European countries participated in a special air pollution module of ECRHS II, which allow both cross-sectional and longitudinal air pollution studies. These studies are coordinated by the ECRHS II Working Group Air Pollution under the leadership of Nino Künzli. It is planned that some WG members and ECRHS centers will take care of specific epidemiological analyses. In particular it is planned that the longitudinal analyses of air pollution effects on lung function, symptoms of chronic bronchitis and asthma will be lead by WG members at University of Southern California (Nino Künzli), Kings College London (Peter Burney and Deborah Jarvis) and Umeå University (Bertil Forsberg), respectively.

*The aim of this application is to have fundings for the work planned to be organized by Umeå University during the next two years (2004-2005). This work consists in 1) the derivation of an appropriate long-term measures of ambient PM<sub>2.5</sub> mass, chemical constituencies, black smoke, OH-formation, and antioxidant depletion activity of PM<sub>2.5</sub> in cooperation with the groups in California and London, and, 2) investigation of the hypothesis that ambient PM<sub>2.5</sub> mass, surrogates of traffic exposure, and redox activity of PM<sub>2.5</sub> are associated with onset of asthma and the progress of the disease.*

#### Asthma and air pollution

In time-series studies short term worsening of asthma has been associated with air pollutants, especially particulates and ozone (Holgate S et al. Air Pollution and Health. San Diego/London: Academic Press, 1999). This has been shown also in Sweden (Forsberg ref 1,6,8 in CV). However, other effects of air pollutants on asthma, *i.e.* onset of asthma and long term worsening, is far less studied. Especially for adults we are lacking data from large, well controlled and longitudinal studies representing the European air pollution scenarios.

Much of the evidence linking air pollution and asthma onset build on poorly quantified exposure data. Several studies have found asthma or asthma-like problems such as wheezing more prevalent in more polluted regions (van Niekirk et, Clin Allergy 1979:9:319-324; Heinrich et al, Environ Health Perspect 1999:107(1):1-17; Guo et al, Environ Health Perspect 1999:107:1001-1006) or close to busy streets (Edwards et al, Arch Environ Health 1994:49:223-227; Weiland et al, Ann Epidemiol 1994:4:243-247; Venn et al, Occup Environ Med 2000:57:152-158). The results from traffic exposure studies are far from consistent, and negative studies are also common. However, particle emissions are most correlated to truck traffic (diesel vehicles), and most of these studies focusing on truck traffic and children found associations with wheeze (Duhme et al, Epidemiology 1996:7:578-582; van Vliet et al, Environ Res 1997:74:122-132) and asthma or other respiratory symptoms (Ciccone et al, Occup Environ Med 1998:55:771-778; Hirsch et al, Eur Respir J 1999:14:669-677). Sensitization to pollen, but not respiratory symptoms, was related to truck traffic in Swiss adults (Wyler et al, Epidemiology 2000:11:450-456).

Some studies showed associations when measured traffic pollution indicators were used. Benzene was correlated to asthma prevalence in Dresden children (Hirsch et al, Eur Respir J

1999:14:669-677), NO<sub>2</sub> with wheeze and sensitization in children from Dusseldorf (Kramer et al, *Epidemiology* 2000:11:64-70), and, NO<sub>2</sub> and PM<sub>10</sub> with several respiratory symptoms in children from 10 Swiss communities (Braun-Fahrlander et al, *Am J Resp Crit Care Med* 1997:155:1042-1049). The prevalence of cough and irritative symptoms in adults increased with the mean NO<sub>2</sub> concentration in Sweden, while the increase in asthma was not significant (Forsberg 3). However, these studies have problems to distinguish acute effects from the long-term effects of air pollution exposure.

Very few cohort results on asthma incidence in adults exist. From the cohort study of nonsmoking adult Seventh Day Adventists in California associations have been reported between onset of (or short term worsening of) asthma and outdoor concentrations of total suspended particulates (Abbey et al, *Environ Health Perspect* 1991:94:43-50), total suspended sulphate (Abbey et al, *J Expos Anal Environ Epidemiol* 1993:1(suppl3):99-115), and, in male adolescents only, ozone (McDonnell et al, *Environ Res* 1999:80:110-121). However, there are no such studies of European populations. Although particulate matter is associated with effects on the airways, the mechanisms for the action are not well understood. The fine particulate mass, PM<sub>2.5</sub>, is usually considered more strongly associated with adverse effects than the coarse fraction. Epidemiological studies have given some indications that combustion (vehicle exhaust) related particles and the content of carbonaceous material (soot) and transition metals may be important.

Biological activity of residual oil fly ash and Utah Valley dust has been explained by the metal content and oxidant character (Dye et al, *Am J Respir Cell Mol Biol* 1997:17:625-633; Ghio et al, *Environ Health Perspect* 2002:110 (suppl 1):89-94). Redox activity has been considered a major biological pathway to explain various effects of air pollution. However, the oxidative properties of ambient particulate matter have not yet been used to further investigate long-term effects in humans.

Abundant evidence suggest that components of diesel exhaust particles promote release of specific cytokines, chemokines, immunoglobulins, and oxidants initiating a cascade that can culminate in airway inflammation, mucus secretion, serum leakage into the airways, and bronchial smooth muscle contraction (Pandaya et al, *Environ Health Perspect* 2002:110 (suppl 1):103-112). In addition, diesel exhaust particles also seem to promote expression of the TH2 immunologic response phenotype that has been associated with allergic disease and asthma (Diaz-Sanchez et al, *Clin Immunol* 2000: 97:140-145).

## **METHODS**

### The European Community Respiratory Health Survey

Centers taking part in the ECRHS I followed a standardized protocol for sampling of subjects, assessment of symptoms, collection of risk factor information, measurement of lung function and bronchial reactivity. Blood samples were analyzed for sensitization to common environmental allergens in a single central laboratory. The study co-ordination was funded through a grant from the European Commission and each center obtained grants from local funding bodies to conduct their local studies.

Details of these methods have been published (Burney et al, *European Respir J* 1994:7: 954-960.). In each participating center, a suitable sampling frame for a population of at least 150,000 people was identified and a random sample of at least 1500 men and 1500 women aged 20 to 44 years was obtained. In stage 1 of the survey, a short postal questionnaire asking seven questions on symptoms suggestive of asthma, was sent to all those selected. In the second stage of the survey, a random sample of at least 600 persons was identified from those

who had been selected for the postal survey. They were then invited to a local clinical testing center. They underwent a questionnaire, measurement of specific and total IgE in blood, spirometry, and measurement of bronchial reactivity to methacholine. In addition people reporting asthma attacks, asthma medication or waking with shortness of breath at the postal survey were invited to the testing center to undergo these tests.

ECRHS II is a follow up study of all individuals who participated in stage 2 of ECRHS I. Firstly, a short postal questionnaire identical to that sent out in ECRHS I was sent out and all subjects were then invited to the testing center. Here they underwent a questionnaire about lifestyle and risk factors, a quality of life questionnaire, blood tests and spirometry. Centers have also performed home visits on a sub-sample of responders to assess the indoor environment, and obtain mattress dust samples for house dust mite allergen.

The collection of ECRHS II health data has been finished in 2003, and data are currently being sent to the Coordination Center in London. Among the 21 centers participating in the Air Pollution module, the proposed study include approx. 8'300 ECHRHS II respondents, corresponding to 78% of ECRHS I stage 2 participants.

#### Air pollution information

During ECRHS I air pollution was not considered. The main goal of the air pollution module in ECRHS II is to determine valid long-term mean concentrations of ambient air pollution in each of the participating centers. In total, 21 centers participated in the air pollution module of ECRHS II, representing 20 cities in 10 European countries. Apart from assembling historic data from local authorities, ECRHS II implemented an air pollution measurement study. PM<sub>2.5</sub>, it's concentrations of chemical elements and the light reflection (soot particles), were measured as the main air pollution indicators in ECRHS II.

In a final step, hydroxyl radical formation and the antioxidant depletion activity of these particles are assessed using methods developed by European partners. Borm has developed a method which determines the hydroxyl radical generating capacity of PM in an oxidant environment. Strength of the assay is that it uses little PM mass, is rapid and has been linked to biological events in cellular systems, such as DNA damage (Shi et al, *Occup Environ Med*; 60: 313-314). Kelly and colleagues have developed a complementary approach that assesses the antioxidant depleting power of PM in a reducing environment (Zielinski et al, *Am J Physiol* 1999;277:L719-26). Particular strength of this assay is that PM toxicity is examined within a biological setting, i.e. respiratory tract lining fluid and it provides a direct measure of PM oxidative potential.

In order to obtain a more differentiated image of the prevailing pollution patterns, measurement of NO<sub>2</sub> with passive samplers was included. The NO<sub>2</sub> tubes were exposed for 14 days during the PM<sub>2.5</sub> measuring period. In most centers a subsample were visited at home and indoor and outdoor NO<sub>2</sub> was measured over a two week period using passive samplers. In addition, all participants provided information within a questionnaire on traffic density and perceived air quality at their place of residence (Oglesby et al, *Am J Epidemiol* 2000;152:75-83).

#### *Characterization of long-term particle exposure*

The location of choice for the PM<sub>2.5</sub> sampler was an official air monitoring station, the advantage being simultaneous measurements of other pollutants from other equipment at the same site. We obtained descriptive data, including pictures and maps about sampling sites. In addition, historic air pollution data was collected (see [www.ecrhs.org/reports](http://www.ecrhs.org/reports)). PM<sub>2.5</sub> sampling was conducted over a 24 and 48 hour period on weekdays and weekends, respectively. Each month, six filter samples were generated, and were distributed over a two-weeks period. From

these samples a monthly mean was calculated. Annual mean concentrations hence are the mean of the 12 monthly mean concentrations (based on 72 filters or 84 days of measurement). All centers were equipped with a PM<sub>2.5</sub>-sampler from BGI ([www.bgiusa.com](http://www.bgiusa.com)). The equipment contained an EPA-WINS impactor designed to sample particles with a 50% cut-off size of 2.5 µm aerodynamic diameter. The pump was equipped with a microprocessor-controlled timing and mass flow adjustment system. A calibrator was used for regular air flow controls. All pre- and post-weighing of Teflon filters was conducted in one central laboratory. Methods and winter results are published in Hazenkamp et al (J Air W Manage Assoc 2003;53(5):617-28.).

#### *Particle pollution information besides PM<sub>2.5</sub>*

The elemental composition of 1926 PM<sub>2.5</sub> filters sampled in the framework of the ECRHS II study has been analyzed by energy-dispersive X-ray fluorescence spectrometry (ED-XRF). The used methodology has been developed for the European multi centre study EXPOLIS (Jantunen et al, J Exp Analys Environ Epidemiol 1998;8:495-518). Details are given in <http://www.ecrhs.org/reports/wp7report.pdf>. We have data for the following elements: Na, Mg, Al, Si, P, S, Cl, K, Ca, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, As, Se, Br, Zr, Cd, Sn, I, Pb, Bi. With regard to the epidemiological analyses, contents of transition metals will be of specific interest, as they are assumed to play an important role for the oxidative properties of particles.

Since elemental carbon is the dominant light absorbing substance in the atmosphere (Forsberg 5), measuring light absorption or reflectance of particulate matter, collected on filter media, is an alternative way to estimate elemental carbon (EC) concentrations (“soot”) in the atmosphere. The focus on traffic related air pollution makes EC a desirable indicator. Reflectometry was applied in ECRHS II following the procedure from the ULTRA study based on ISO 9835.

The respective measurements are soon available. In the first step of our work, we will investigate the effect of the measurement location such as local traffic on the various features of PM<sub>2.5</sub> to a priori rank the appropriateness of considering annual and seasonal means as surrogates of long-term exposure. In particular, little is known about spatial and temporal patterns of our novel oxidative properties. This step will lead to long-term mean exposures reflecting urban background, urban traffic, and oxidative activity.

#### Epidemiological analyses

Asthma is characterized by chronic inflammation and oxidant/antioxidant imbalance. The sources of the increased oxidative stress derive from the increased burden of inhaled oxidants, and from the increased amounts of reactive oxygen species (ROS) generated by several inflammatory, immune and various structural cells of the airways. We argue that redox-activity of particulate matter may be a more relevant characteristic of PM exposure than what is captured by the mass concentration in ambient air. To investigate the association between new onset of asthma and exposure to air pollution, the following approach will be applied.

*Outcome definition and analyses:* In most cohort studies the incidence and remission of symptoms has been reported without appropriate consideration of the effect of measurement error at baseline and follow up, as previously described (Järholm ref 4 in CV). Measurement error is more likely to occur when subjective markers of disease are utilized and when the course of disease is variable.

The following measures will be used to study air pollution effects on the asthma morbidity:

- the change in prevalence of asthma between the centers during the study period
- the change in symptoms and use of pharmaceuticals in persons with asthma in the ECRHS I survey. (e.g. worsening and remission)
- The number of new cases of asthma (i.e persons who reported asthma in ECRHS II but not in ECRHS I).

The incidence rate for asthma onset in adults is about 2 per 1000 person-years, i.e. about 160 new cases will occur among those participating in ECRHS II. If it assumed that the incidence rate among those living in the 4 cities with the highest concentrations is doubled compared with the 4 centers with the lowest exposure, theoretically the power of the study would be around 90 %. However, due to measurement errors of asthma the true power could probably be somewhat lower. The power to detect differences in the progress of the disease and use of pharmaceuticals would likely be higher.

Associations of asthma outcome and worsening and the pollution measures will be tested. Possible confounding and effect modification will be controlled for in the analysis. The extensive amount of information in ECRHS I and ECRHS II makes it possible to conduct multivariate analyses with adjustments for a variety of suitable and potentially influential covariates, which have been measured both cross-sectionally as baseline information and/or in the cohort follow-up. The list of covariates includes both, markers of health conditions as well as of other relevant exposures, and fixed as well as time-varying factors. We will include the use hierarchical linear mixed models to assess effects at both the subject and community level. Predictors can be individual-specific, time-specific, or community-specific.

*Exposure assignment:* ECRHS follows the paradigm of the semi-individual approach where pollutants measured at one location are assigned to those living in the community. The power of this design is particularly driven by the ratio of the between-community versus the within-community variability of exposure. Thus, we will first analyze the data using PM<sub>2.5</sub> mass concentration and sulfur (S) on PM<sub>2.5</sub> as exposure surrogates. Annual and winter means will be used as separate surrogates as they may reflect differences in toxicity (Hazenkamp et al, 2003). These PM<sub>2.5</sub> measures show little within-community variability, but an exceptional range across the 21 ECRHS centers, which is larger than in any other air pollution cohort study published so far. This is an important strength of ECRHS II.

Second, we will use other surrogates of PM<sub>2.5</sub> such as markers of traffic (BS, Pb) and the oxidative properties of the PM<sub>2.5</sub> as described in above. ECRHS II is the first large-scale epidemiologic study with information about the OH-formation rate of ambient PM<sub>2.5</sub> and measured antioxidant depletion rates for ascorbate, ureate, and glutathione.

Third, we will make use of the availability of NO<sub>2</sub> at home outdoor monitored in several centers. The departure of the central monitor NO<sub>2</sub> level from the 'true' population mean value can be estimated. Linear regression models will be used to assess the influence the location characteristics on the measured levels of other pollutants.

### Short CV for Bertil Forsberg

Senior lecturer Bertil Forsberg, Dept of Public Health and Clinical Medicine, Umeå University, holds a MSc in environmental health and a PhD in epidemiology and public health (1997). He is presently involved in several studies on exposure to air pollution, weather and morbidity and mortality in Swedish and international projects such as EU-funded *APHEA-2*, *APHEIS*, *ECRHS* and *PHEWE*. Current Swedish projects lead by Forsberg are funded by The National Road Administration, The Swedish National Energy Administration, The Swedish EPA and The National Institute for Public Health. These projects are focussing on quantification of dose-response relations and methods for health impact assessment. Bertil Forsberg is a national (National Institute for Public Health) international (WHO) consultant and expert on air pollution and health. He is a member of EU Airnet Working Group on epidemiology and secretary of The Swedish association of Occupational and Environmental medicine. In 2001 he was first author to a book on outdoor air and health (Forsberg B & Bylin G, Uteboken) produced by the Swedish EPA and National Institute for Public Health.

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## Short CV for Bengt Järholm

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**Academic degrees:** Master of engineering (technical physics) 1970. Doctor of medicine 1981. Certified in occupational medicine in 1981. Certified in occupational and environmental medicine in 1992.

**Appointments:** Assoc. prof of occup. med. university of Göteborg in 1984. Different positions as medical doctor at the department of Occupational Medicine, Sahlgren's University hospital Göteborg (1980-1989) and chief physician 1989-1996. Professor and consultant Umeå University since 5 Feb 1996. Head of department since 1999.

Principal tutor for training of nine graduate students to the completion of their dissertation. Former vice president of the Swedish Association of Epidemiology (one year), former president of Swedish association of Occupational and Environmental medicine (8 years). Participated in the IARC evaluation of carcinogens. Been a member of committees for evaluating the risks with electromagnetic fields, member of the Swedish committee for scientific basis of threshold limit values. During 1995 been the project leader of an evaluation of Swedish work environment on behalf of National Board of Occupational Health and Safety, Council for research on work life and National institute for working life. Previous member of committees for grants (MISTRA, SNV and RALF), at present member of board of Swedish council for working life and social research (FAS) and chairman of a grant committee. Published about 150 papers in refereed journals.

### Selection of scientific publications of relevance for this project

1. Torén K, Brisman J, Järholm B. Asthma and asthma-like symptoms in adults assessed by questionnaires. *Chest* 1993;104:601-608.
2. Brisman J, Järholm B. Occurrence of self-reported asthma in Swedish bakers - a retrospective study. *Scand J Work Environ Health*, 1995;21:487-93.
3. Plaschke P, Jansson C, Norrman E, Björnsson E, Lundbäck B, Lindholm N, Rosenhall L, Järholm B, Boman G. Skin prick tests and specific IgE in adults from three different areas of Sweden. *Allergy, Eur J Allergy Clin Immunol* 1996;51:461-472.
4. Järholm B, Brisman J, Torén K. The association between epidemiological measures of the occurrence of asthma. *Int J Tuberc Lung Dis*, 1998;2:1029-1036.
5. Brisman J, Järholm B. Bakery work, atopy and the incidence of hay fever and rhinitis. *Eur Respir J*, 1999;13:502-507.
6. Plaschke P, Janson C, Balder B, Löwhagen O, Järholm B. Adult asthmatics sensitised to cats and dogs: Symptoms, severity and bronchial hyperresponsiveness in patients with furred animals at home and patients without these animals. *Allergy* 1999; 54:843-850.
7. Plaschke P, Janson C, Norrman E, Björnsson E, Ellbjär S, Järholm B. Association between atopic sensitization and asthma and bronchial hyperresponsiveness in Swedish adults: pets and not mites are the most important allergens. *J Allergy Clin Immunology* 1999;103:58-65.
8. Torén K, Järholm B, Brisman J, Hagberg S, Hermansson BA, Lillienberg L. Adult-onset asthma and occupational exposure. *Scand J Work Environ Health* 1999;25:430-435.
9. Brisman J, Järholm B, Lillienberg L. Exposure-response relations for self-reported asthma and rhinitis in bakers. *Occup Environ Med*, 2000;57:335-340.
10. Plaschke P, Janson C, Norrman C, Björnsson E, Ellbjär S, Järholm B. Onset and remission of allergic rhinitis and asthma and the relationship with atopic sensitization and smoking. *Am Rev Crit Care Med*. *Am-J-Respir-Crit-Care-Med*. 2000; 162: 920-4
11. C.-G. Bornehag, G. Blomquist, F. Gyntelberg, B. Järholm, P. Malmberg, L. Nordvall, A. Nielsen, G. Pershagen, J. Sundell. Dampness in Buildings and Health. *Indoor Air* 2001;11:72-86.
12. Brisman J, Lillienberg L, Belin L, Åhman M, Järholm B. Sensitisation to occupational allergens in baker's asthma and rhinitis – a case referent study. *Int Arch Occup Environ Health* 2003;76:167-170.
13. Boman C, Forsberg B, Järholm B. Adverse health effects from ambient air pollution in relation to residential wood combustion in modern society. *Scand J Work Environ Health* 2003;29:251-260