OCCUPATION AS A RISK FACTOR FOR ASTHMA -

among young adults in Denmark

PhD Thesis

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ABBREVIATIONS

OA	Occupational asthma
BHR	Bronchial hyper responsiveness
WEA	Work exacerbated asthma
WRA	Work related asthma
JEM	Job exposure matrix
OR	Odds ratio
PR	Prevalence ratio
RAV	Risk factors for asthma among adults
ECRHS	European Community Respiratory Health Survey
HMW	High molecular weight
LMW	Low molecular weight
PAR	Population attributable fraction

CONTENTS

1. INTRODUCTION

Asthma is the most common occupational respiratory disorder in Western industrializedpopulations[1] and 15-20 % of the population burden of asthma may be attributable to occupational exposures[2;3]. The list of occupations and exposures reported to be associated with asthma is expanding and more than 250 occupational airway sensitizers have been identified as specific causes of occupational asthma (OA)[4;5].

Population-based studies have reported increased risks of asthma in farmers, painters, laboratory technicians, spray painters, bakers, other food processors, chemical processors, plastic and rubber workers, welders, agricultural workers, professional cleaners, non-professional cleaners, personal care workers, nurses, waiters and in those workers with exposure to high-molecular-weight agents, those workers using ammonia and/or bleach in health care jobs and those workers welding coated materials.[2;6-15] Professional cleaning products associated with asthma include bleaches and sprays[16;17] and, common non-professional use of household cleaning products in spray form is associated with new-onset asthma[18].

There is very little population- based research data on occupational risk factors for asthma among young adults in Denmark. Data from the Danish National Board of Industrial Injuries have indicated work related asthma (WRA) in some specific occupational groups[19]. Coverage and case ascertainment for the Danish National Board of Industrial Injuries notification system have a weakness since it relies on health care providers awareness of causality and reporting WRA, and so may underestimate the true prevalence of WRA in the general population. Community studies are likely to include workers with undiagnosed asthma and those with underlying asthma which is aggravated by work exposures, in addition to those with OA[20-29]. The European Respiratory Health Survey

(ECRHS) began as an international cross-sectional cohort study of respiratory health among adults from 28 centres in 13 countries in 1990-95. People who were included in ECRHS were recontacted and were invited to take part in the follow up survey (ECRHS II) done in 1998-2003. Since we use the ECRHS protocol in our study, I will focus on ECRHS studies and ECRHS related studies in this thesis because our results will be comparable to results from other ECRHS studies. However, other studies are considered as well.

This thesis is devoted to identifying occupational risk factors for asthma in young adults in Denmark using a population-based prevalence study approach.

1.1 DEFINING WORK RELATED ASTHMA

The realization that asthma may arise as a direct consequence of inhaled occupational agents has been the focus of particular attention over the last two or three decades, and most current knowledge has been obtained during this period [30]. However Bernardino Ramazzini (1633-1714) is credited with the earliest descriptions of occupational respiratory disease affecting bakers, handlers of old clothes, and workers dealing with flax, hemp and silk as cited in "Asthma in the Workplace"[31]. Later in the 20th century annual rates of OA from surveillance systems reported estimates from 5 cases of OA per million workers in Massachusetts in 1989-92 to 175 cases per million workers in Finland in 1990-95[30].

In longitudinal general population cohort studies of asthma published in June 1999-2007 the population attributable risk (PAR) showed a wide range of estimates (1.7%-44%), and a synthesis of previously and currently reviewed studies regarding (PAR) for occupational exposures and asthma showed a range of (7%-51%), for all studies which underscores the large remaining uncertainty regarding the magnitude of the association

between occupational exposures and asthma[3]. Some of the differences in PAR might be due to different definitions of OA.

WRA can systematically be classified as asthma caused by the workplace, OA or as asthma exacerbated by the workplace, work-exacerbated asthma (WEA). These nosological entities are identified and based on the strength of the causal relations.
In "Asthma in the Workplace" (2006) an editorial consensus definition of OA is:

Occupational asthma is a disease characterized by variable airflow limitation and/or hyper responsiveness and/or inflammation due to causes and conditions attributable to a particular occupational environment and not to stimuli encountered outside the workplace[31].

Traditionally, there is a distinguish between two types of OA based on their appearance (1): after a latency period (allergic) and (2): without a latency period (non allergic).

1. After a latency period (allergic): OA caused by most high molecular weight (HMW) and certain low molecular weight (LMW) agents for which an allergic IgE-mediated mechanism has been proven, and OA induced by specific occupational agents but the allergic mechanism is not yet fully characterized.
2. Without a latency period (non allergic): This category includes irritant-induced asthma or reactive airways dysfunction syndrome (RADS), which may occur after a single or multiple exposures to non-specific irritants at high concentrations.

WEA is used to describe the worsening of pre-existing or coincident (adult new-onset) asthma because of workplace environmental exposure.

Finally, asthma-like conditions and variants exist which are typically present at the same time as asthma-like symptoms associated with one or more objective asthmatic features (byssionosis, eosinophilic bronchitis).

In summary, WRA includes:

1. immunologic OA, characterized by a latency period before the onset of symptoms;
2. non-immunologic OA, which occurs after a single or multiple exposures to high concentrations of irritants;
3. WEA, which is pre-existing or concurrent asthma exacerbated by workplace exposures; and
4. variant syndromes[32]

Estimates of asthma in the workplace and OA come from three approaches, namely population-based studies, surveillance systems, and medico legal statistics. These approaches produce different figures because medico legal statistics are more likely to rely on objective confirmation of cases, whereas the first two identify workers with probable OA[33], thus estimates in population-based studies mainly report WRA without further confirmation of OA. However in the present study, we are not able to distinguish between immunological OA, non-immunological OA, WEA, and variant syndromes, therefore estimates reported in the present study are also mainly WRA without further confirmation of OA.

1.2 LITERATURE REVIEW OF POPULATION BASED SURVEYS PROVIDING DATA FOR ASTHMA IN RELATION TO OCCUPATIONAL EXPOSURES AMONG ADULTS

To describe occupations and occupational exposures associated with asthma, I have made a literature review to highlight data on asthma in relation to occupational exposures with focus on population studies.

I identified relevant citations through two approaches.

First, I carried out a systematic literature search in PubMed using the algorithm:

> asthma AND (occupation* OR work related OR work exacerbated) AND population based survey AND adult* NOT case reports NOT clinical asthma series

I restricted this search to English language citations with links to full text papers published from January 1900 through December 2009. There were 95 unique PubMed citations identified through this algorithm.

The following inclusion criteria were used[34-36]

i. Papers indicating in the abstract that the paper covered asthma in relation to occupational exposures
ii. Included similar research questions in introduction
iii. Study population with same characteristics as our study which is young adults
iv. Clear definition of asthma and exposures
v. Providing estimates of asthma prevalence or asthma incidence in relation to occupational exposures.
vi. Multivariate analysis including confounders

vii. Results with 95%CI .

Secondly, I scanned the reference lists from any recent review on the topic of occupational asthma, as well as the references cited in any appropriate papers identified in above citations, to identify other related studies. I included studies from health maintenance organisations, surveillances , workers compensation boards and register based studies if they were general population-based samples, comparable samples drawn from large cohorts, and systematically and prospective .

I ultimately identified 18 publications which met the inclusion criteria. Of these, five were longitudinal general population-based studies[2;22;37-39], three were case-control studies[40-42], and ten publications were cross-sectional analyses of general population based samples[6-9;43-48] (Tables 1-3).

Table 1 summarizes data on asthma incidences in relation to occupational exposures from five longitudinal analyses in four different countries and in one international study.

A large number of occupations with significant excess of asthma incidence were identified in a Finish register-based 12-year follow up study of 1.85 million people aged 25-29 in which 2,464 cases of OA were identified. The follow-up used two national registers: the Medication Reimbursement Register of the Social Insurance Institution (SII) and the Finnish Register of Occupational Disease (FROD). Individuals with clinically well-established persistent asthma and evidence of causality between specific workplace exposure and asthma, evaluated by chest physicians and notified for recognized OA to FROD, were used as cases. The risk was increased especially in agricultural work, manufacturing work, and service work[22]. The strengths of the study are the prospective design covering a very large, entire national workforce and a high predictive value of the

asthma definition. The weakness of the study is that the sensitivity of the asthma definition was lower than for the most other definitions of asthma therefore individuals with mild disease and WEA not fulfilling the SII criteria were not included. This could lead to an underestimation of the WRA fraction.

A 10-year follow-up study on adults aged 35 to 75 at baseline from northern Sweden including 271 incident cases of asthma, were investigated with a questionnaire on respiratory symptoms and occupation. The questionnaires showed increased risk of incident asthma among manual workers in industry[37]. The strength of the study was the prospective design with sufficient statistical power obtained for the bias caused by non-response could be considered to be limited. However, the weakness of the study is caused by non-response associated with low socio-economic status, and that the non-responders had a high prevalence of respiratory symptoms . This could result in a potential healthy worker effect causing a decreased effect of manual workers on the incidence of asthma. Finally the study did not validate the self-reported asthma with BHR in the reported results. This could, due to decreased specificity of the asthma diagnosis, lead to an overestimation of the association between occupation and asthma.

A 6-year follow up study of 1,426 incident asthma cases from the Chinese population aged 45-75 at baseline in Singapore, with questionnaire based information of asthma and occupation reported increased risks for adult-onset asthma following exposures to dusts and vapors. Minimal confounding by ambient air pollution, workplace smoking and coal and wood burning in home was a strength of the study. The weakness of the study was lack of information on the precise timing of exposure in relation to the start of respiratory symptoms. Therefore they were not able to differentiate between OA and WEA. Nor were

they able to determine a possible healthy worker effect because they did not have information about if workers had selected “cleaner” occupations because of the early presence of respiratory symptoms[38].

An international follow-up study of incident asthma among adults aged 20-44 at baseline during 1990-1995 to 1998-2003 (ECRHS II)[2] defined incident asthma in two principal ways: first, self-reported asthma, and second, self-reported asthma combined with a positive methacholine challenge test. Exposures was based on self-reported occupation assessed in two ways, one using a list of occupations that potentially had a high risk of asthma and the other by linking the occupations to an asthma-specific job exposure matrix (JEM) comprising 18 substances *a priori* classified as carrying high risk of asthma. Increased relative risk of new onset asthma was reported in any predefined high-risk occupation comprising baking, plastics or rubber industries, printing, chemical processing, spray painting and other painting, nursing, hairdressing, electrical processing, welding, metal works, agriculture and forestry and, cleaning and caretaking. Among major occupational groups, nurses and cleaners had the highest risks of new onset asthma. Printing, woodworking, agriculture and forestry and electrical processors had relative risks higher than 1.5[2] The relative risk of association between new onset asthma and exposure to any high risk substance was 1.58 (95% CI 1.09-2.29). In the subcategories of exposure in the JEM, HMW agents and LMW agents were associated with a higher incidence of asthma. Among the most common specific exposures, cleaning agents, reactive chemicals, and exposure to latex were associated with a higher than 1.5 relative risk[2]. The strengths of the study is that they assessed new-onset occupational asthma in a large randomly selected international population in 13 industrialized countries and they stratified the by gender when analysing any job-exposure matrix exposure. The

limitations were first, inadequate power because in some specific occupations and exposures the analyses were based on small numbers and second that the application of the JEM might result in some degree of non-differential misclassification that could result in a possible underestimation of the association between asthma and occupational exposure.

A Norwegian questionnaire based incidence study of asthma with a 11-year follow up time among adults aged 15-70 at baseline, showed an exposure prevalence of 28% with a considerable difference between men and women. They found increased asthma risk in relation to having ever been exposed to dusts or fumes (OR=1.6 (95%CI 1.01-2.5))[39]. The strength in the study was a high response rate (89%). Some of the limitations were that they could not control for selection bias due to "healthy worker effect" and they did not have exact information about time of occurrence of asthma during the follow up. Therefore there is no differentiation between OA and WEA.

Table 2 summarizes three papers reporting data from case-control studies.

In a Finnish study during 1997-2000 among adults aged 21-63, health care recruited cases and controls from the general population answered a self-administrated questionnaire about health and occupation and work environment. Asthma case status was ascertained by health care registered clinical diagnosed asthma. Male metal workers and female waiters had an increased risk of asthma-like symptoms[40]. Strengths of the study was that they took into account a change of job after appearance of respiratory symptoms and thereby reducing a potential "healthy worker effect" and they stratified the analyses by

gender. The study was limited by low precision due to small numbers of workers in many of the 25 occupational groups investigated.

A French asthma genetics study of participants on average, approximately 43 years old ascertained asthma and work environment by detailed interviewer-administrated questionnaire and reported significant associations between severe adult-onset asthma and exposure to any occupational asthmogen, HMW agents, LMW agents, including industrial cleaning agents[42]. One strength in the study is that they used a JEM to give more reliable asthmogen exposure estimates than if such estimates were based on self-reported exposure to occupational agents. The study is limited regarding the definition of asthma severity because it makes it difficult to compare with other epidemiological studies based on more non-specific asthma definitions.

In a questionnaire based case-control study of subjects aged 18-47 from Australia, exposure to any high risk exposure was associated with adult-onset asthma[41]. The study was limited by a low response rate (37%). However the non-responders did not differ in prevalence of asthma or current employment. One strength of the study is that they assessed the association between adult onset asthma and exposure at the time of onset of asthma and ,therefore including cases in the study not only having asthma in the previous 12 months. This could lead to higher fractions of WEA and thereby also higher fraction of WRA among cases included in the study.

Ten reports of cross-sectional analyses met inclusion criteria (Table 3).

A Chinese questionnaire based study of adults aged 40 to 69, showed increased risk of physician-diagnosed asthma with current wheeze in relation to occupational dust exposure[47]. The strength of the study is that it is a community-based population which are more likely to reduce the selection bias due to healthy worker effect compared to selected workers where affected workers has left the industries. One limitation was some overlap or misclassification between industrial bronchitis and asthma.

In the Spanish part of ECRHS I, questionnaire and clinical test based information about asthma and occupation among adults aged 20-44 showed that cleaners and laboratory technicians had an increased risk of BHR and asthma symptoms and/or medication[6]. A strength of the study was the use of four alternative but clearly defined and reproducible definitions of asthma, but the study was limited by lack of statistical power when examining risk in specific occupations.

Fishwick and co-workers showed based on questionnaire and clinical tests increased risk of BHR and wheeze for farmers among adults aged 20-44 [7]. The strength of the study was the use of a randomly selected adult population which reduces the selection bias and gives a more precise picture of WRA. A drawback of the study was that the predefined high risk group did not contain those workers with the highest levels of asthma which could result in a underestimation of the attributable risks.

The ECRHS I study among adults aged 20-44 based on questionnaire and clinical tests across 12 countries reported the highest risk of asthma defined as bronchial hyper

responsiveness, and reported asthma symptoms and/or medication, for farmers. The most consistent results across countries were for farmers and cleaners[8]. The strength of the study was the use of a large randomly selected adult population from different selected geographical areas. One limitation was the possible information bias indicated in the study as a positive recall of exposure among individuals with previous symptoms. A second limitation was a possible differential non-response due to a low participation rate (60%) of the people contacted.

Arif and co-workers have published two cross-sectional studies of the Third National Health and Nutrition Examination (NHANES III) data drawn from a national U.S. weighted randomised sample[43;44]. Information in these two studies among adults with mean age approximately 40, were based on questionnaire information about asthma and occupational exposures.

In the first study they analysed the risk of work-related asthma based on industry or employment considered *a priori* to carry increased risk of asthma. The main industries identified as providing risk of work related asthma and wheeze included the entertainment industry, agriculture, forestry and fishing, construction, electrical machinery, repair services, and lodging places[43].

In the second study they analysed the risk of work related asthma based on occupation *a priori* categorised to carry increased risk of asthma, in which cleaners and equipment cleaners showed the highest risks. Other major risk occupations identified were farming and agriculture, entertainment, protective services, construction, mechanics and repairs, textile, fabricators and assemblers, other transportation and material moving occupations, freight, stock and material movers, and motor vehicle operators[44]. A strength of these studies was the use of a large U.S. population. One limitation of these studies was the use

of non-validated definitions of work related asthma and another limitation was to low statistical power for several industries assessed due to few cases.

In a Spanish questionnaire based cross-sectional study of adults mean aged approximately 39, exposure to HMW agents, assessed by a JEM including expert judgement step, was associated with asthma symptoms and/or use of asthma medication[48]. The application of JEM does not introduce reporting or recall bias, but JEM have the general limitation that variations in exposure within job titles are not taken into account.

In a French study of occupational exposures and asthma in the general population 14,151 subjects aged 25-59, were investigated in 1975 with a questionnaire concerning self-reported asthma and self-reported exposure in the current or most recent job. Increased risk of "ever asthma" was found for stock clerks, personal care workers, and restaurant workers. Odds ratios $\geq$2 were found for cleaners, hairdressers, laboratory aides, bakers, textile workers, leather workers, restaurant workers, stock clerks, and child care workers for at least one of three other definitions of asthma (asthma with airflow limitations, asthma onset at/after age 14, asthma onset at/after starting of current job)[9]. The exposure in the current or most recent job was assessed by a JEM. The authors reported an adverse role for occupational asthmogen exposure for both LMW and HMW agents[9]. The strength of the study is a reduced selection bias due to healthy worker effect, because this selection bias is less important in such a large population based study. A limitation of the study was that they did not apply the expert judgement step of the JEM.

In a cross-sectional analysis of adults aged 23-25, based on questionnaire and clinical measures, from Brazil, exposures to dust, vapour, humidity, or gases and chemical

products or paints were associated with BHR and adult-onset asthma symptoms[45]. There is a possible limitation in the study since they were not able to differentiate between OA and WEA, resulting in a possible overestimation of PAR of asthma attributable to occupational exposures.

Data from Canada based on questionnaire among adults aged 20-44 showed increased asthma symptoms and/or medication use in relation to past combustion smoke exposure[46]. One strength of the study was that they excluded childhood asthmatic subjects from the analysis to assess the fraction of reactivation of childhood asthma and its contribution to adult-onset, work-related asthma. They also evaluated the differences between past and current exposures associated with asthma. An important limitation in the study is the healthy worker effect as a source of bias.

Table 1: Description of longitudinal general population cohort studies of asthma published January 1900 through December 2009 in which the estimates of asthma incidence in relation to occupational exposures were provided.

Author (ref.), Year, Country	Subjects	Asthma definition	Occupational exposure	Confounders	Main results for asthma in relation to occupational exposures (95%CI)	Comments
Karjalainen ([22]), 2001, Finland	1,852,848	Documented incident asthma symptoms and at least one criteria of airway reversibility	Occupations at baseline *a priori* classified as exposed Administrative workers classified as unexposed	Age Smoking Follow up period	**Agricultural** Men, RR=2.12 (1.99-2.26) Women, RR=1.84 (1.76-1.92) **Mining** Men, RR=1.95 (1.58-2.40) **Manufacturing** Men, RR=1.56 (1.47-1.65) Women, RR=1.33 (1.27-1.39) **Service work** Men, RR=1.53 (1.42-1.66) Women, RR=1.41 (1.35-1.46)	Stratified by sex No differentiation of immunological, non-immunological, and work exacerbated asthma
Hedlund ([37]), 2006, Sweden	4,754	Physician-diagnosed asthma	Manual workers in industry and service	Age Sex Family history of asthma Smoking Occupation in which exposure to dust, gases or fumes is common	**Manual workers in industry** OR=1.7 (1.0-2.7)	Not Stratified by sex No differentiation of immunological, non-immunological, and work exacerbated asthma
LeVan ([38]), 2006, Singapore	52,325	Adult-onset physician-diagnosed asthma	Occupations at baseline *a priori* classified as exposed to I: dust, II: smoke, III: vapors	Age Gender Smoking	**Dust** OR=1.14 (1.00-1.30) **Vapor** OR=1.34 (1.15-1.56)	Not Stratified by sex No differentiation of immunological, non-immunological, and work exacerbated asthma

Kogevinas ([2]), 2007, International	6,837	A. Incident asthma symptoms or medication B. Incident asthma symptoms or medication and new bronchial hyperresponsiveness	I. Exposure to high-risk substances (at baseline and during follow up) by JEM II. Occupations *a priori* classified as exposed	Sex Age Smoking Study centre	A. **high risk occupations** RR=1.69 (1.14-2.52) A. **high-risk substances** RR=1.58 (1.09-2.29) B. **high risk occupations** RR=2.55 (1.27-5.10) B. **high-risk substances** RR=2.40 (1.25-4.60)	Stratified by sex No differentiation of immunological, non-immunological, and work exacerbated asthma
Skorge ([39]), 2009, Norway	2,401	Doctor-treated or hospitalized for asthma	"NO" "LOW" "HIGH" exposure to biological dust, mineral dust, and/or gas or fumes	Age Educational level Smoking Occupational exposures before baseline	Men **Biological dust, high exposure** OR=2.49 (0.9-7.3) Women **Gas or fumes, high exposure** OR=2.91 (0.95-8.9)	Stratified by sex No differentiation of immunological, non-immunological, and work exacerbated asthma

Table 2: Description of case-control studies published January 1900 through December 2009 in which the effect estimates of asthma in relation to occupational exposures were provided.

Author (Ref.nr.), Year, Country	Cases	Controls	Asthma definition	Occupational exposure	Confounders	Main results for asthma in relation to occupational exposures (95%CI)	Comments
Jaakkola ([40]), 2003, Finland	521	932	Asthma-like symptoms and reversibility of airways obstruction in lung function investigations	25 groups of occupations with potential exposure to asthma causing inhalants	Age Sex Smoking	**Metal workers, men** OR=4.52 (2.35-8.70) **Waiters, women** OR=3.03 (1.10-8.31)	Stratified by sex **No** differentiation of immunological, non-immunological, and work exacerbated asthma
Le Moual ([42]), 2005, France	I. 43 II. 48	228	I. Adult onset, mild II. Adult onset, severe I. + II. All adult onset asthma	Occupations at risk, defined *a priori* by a job exposure matrix	Age Sex Smoking	**Asthmogens, any** OR=4.0 (2.0-8.1) **HMW asthmogen, any** OR=3.7 (1.3-11.1) **LMW asthmogens, any** OR=4.4 (1.9-10.1) **LMW, highly reactive Chemicals** OR=4.8 (1.7-13.2) **LMW, undustrial cleaning agents** OR=7.2 (1.3-39.9) **LMW, metal sensitizers** OR=6.6 (1.5-29.5)	**Not** Stratified by sex No differentiation of immunological, non-immunological, and work exacerbated asthma

Johnson ([41]), 2006, Australia	373	4329	Adult-onset physician-diagnosed asthma	Exposures and occupations known, *a priori*, to be at risk for inducing OA	Smoking Age Sex	**Any high-risk jobs** OR=1.54 (1.19-2.01) **Any high-risk Exposure** OR=1.53 (1.17-2.00) **Either high-risk job or an exposure** OR=1.51 (1.19-1.92)	**Not** Stratified by sex **No** differentiation of immunological, non-immunological, and work exacerbated asthma

Table 3. Cross-sectional general population studies published January 1900 through December 2009 where the estimates for association between occupational exposures and asthma was derived

Author (Ref. Nr.), Year, Country	Subjects	Asthma definition	Occupational exposure	Confounders	Main results for asthma in relation to occupational exposures (95%CI)	Comments
Xu ([47]), 1993, China	3,606	Physician-diagnosed asthma with current wheeze	I. Low Moderate High Exposure to Dust Gas/fume II. High Medium Low Cumulative exposure to Dusts Gases/fumes	Age Sex Area of residence Smoking Use of coal stove for heating Education	**Dusts** OR=1.6 (1.1-2.2)	**Not** Stratified by sex **No** differentiation of immunological, non-immunological, and work exacerbated asthma
Kogevinas ([6]), 1996, Spain	A. 2,345 B. 2,345 C. 1,424 D. 1,424	A. Wheezing B. Asthma symptoms or medication C. BHR and wheeze D. BHR and asthma symptoms or medication	I. Current occupation or occupation at time of health problems, the occupation at that time, aggregated into 21 occupational sets II. An aggregated occupational group at risk defined *a priori*	Age Sex Area of residence smoking	**Cleaners (D)** OR=2.53 (1.03-6.20) **Laboratory technicians (D)**OR=9.29 (3.28-26.31)	**Not** Stratified by sex No differentiation of immunological, non-immunological, and work exacerbated asthma
Fishwick ([7]), 1997, New Zealand	A. 1,532 B. 989 C. 940	A. Wheezing B. BHR C. BHR and wheezing	I. Current occupation or occupation at time of health problems, the occupation at that time, aggregated into 21 occupational sets II. An aggregated occupational group at risk defined *a priori*	Age Sex Smoking	**Farmers (C)** OR=4.16 (1.33-13.08)	**Not** Stratified by sex **No** differentiation of immunological, non-immunological, and work exacerbated asthma

Kogevinas ([8]), 1999, International	8,420	A. Asthma symptoms or medication B. BHR and asthma symptoms or medication	I. Current occupation or occupation at time of health problems, the occupation at that time, aggregated into 30 occupational sets II. Reported exposure to dusts, vapours, gases, or fumes C. Exposure to dusts, vapours, gases, or fumes by use of JEM	Age Sex Smoking Study centre	**Farmers (B)** OR=2.62 (1.29-5.35) **Other painters (B)** OR=2.34 (1.04-5.28) **Cleaners (B)** OR=1.97 (1.33-2.92) **Agricultural (B)** OR=1.79 (1.02-3.16)	**Not** Stratified by sex **No** differentiation of immunological, non-immunological, and work exacerbated asthma
Arif ([43]), 2002, USA	5,022	Physician-diagnosed, ever	I. Occupations *a priori* classified at risk II. Industries *a priori* classified at risk	Sex Age Race Poverty income ratio Atopy smoking	**Entertainment industry** OR=5.96 (1.58-22.45)	**Not** Stratified by sex **No** differentiation of immunological, non-immunological, and work exacerbated asthma
Arif ([44]), 2003, USA	5,022	Physician-diagnosed, ever	I. Occupations *a priori* classified at risk II. Industries *a priori* classified at risk	Sex Age Smoking Atopy	**Entertainment** OR=4.35 (1.50-12.55) **Protective service** OR=9.07 (3.00-27.43) **Agriculture** OR=3.37 (1.22-9.29) **Mechanics and repairers** OR=3.08 (1.18-8.05) **Textile** OR=3.25 (1.18-8.92) **Motor vehicle operators** OR=4.21(1.79-9.90) **Equipment cleaners** OR=10.57 (1.54-72.45)	**Not** Stratified by sex **No** differentiation of immunological, non-immunological, and work exacerbated asthma

Zock ([48]), 2004, Spain	1,455	A. Asthma symptoms or use of asthma medication B. Physician-diagnosed asthma	Occupations at risk, defined *a priori* by a job exposure matrix	Sex Age Smoking	**HMW-agents (A)** PR=1.4 (1.0-2.0) **HMW-Animal derived(A)** PR=3.9 (2.0-7.7) **HMW-Flour (A)** PR=3.6 (2.2-5.8) **HMW-Mites (A)** PR=2.1 (1.1-3.9) **HMW-Enzymes(A)** PR=3.6 (2.2-5.8)	**Not** Stratified by sex **No** differentiation of immunological, non-immunological, and work exacerbated asthma
Le Moual ([9]), 2004, France	A. 14,151 B. 13,445	A. Ever asthma attack or dyspnoea with wheezing B. Adult-onset asthma during or after current job	I. Self-reported exposure to gases, dusts, and fumes II. Job-titles, coded and grouped into 29 categories III. Population-specific JEM for "dusts, gases, and fumes" IV. Asthma-specific JEM (excluding jobs with imprecise estimates, n=10,560)	Age Smoking Sex	**Stock clerks (A)** OR=1.75 (1.14-2.68) **Asthmagens, any (B)** OR=1.74 (1.17-2.60) **High molecular weight agents (B)** OR=2.09 (1.05-4.17) **Low molecular weight agents (B)** OR=1.76 (1.16-2.68)	**Not** Stratified by sex **No** differentiation of immunological, non-immunological, and work exacerbated asthma
Caldeira ([45]), 2006, Brazil	1,922	Bronchial hyperresponsiveness and adult-onset asthma symptoms	Self-reported exposure, vapours, gas, fumes or humidity	Sex Smoking Atopy Rhinitis	**Dust, vapour, humidity, or gases** Hazard ratio (HR)=2.02 (1.04-3.94) **Chemical products or paints** HR=3.69 (1.54-8.83) **More than one agent** HR=4.68 (2.40-9.94)	**Not** Stratified by sex **No** differentiation of immunological, non-immunological, and work exacerbated asthma

Demir ([46]), 2008, Canada	498	A.Current wheeze B.Asthma symptoms and/or medication C. Airway hyperresponsiveness	Current or past exposures classified as sensitizers and irritants	Sex Atopy Family history of atopy and/or asthma Parental smoking Pet in home Older sibling Attending nursery school before the age of five Lower respiratory tract infection before age of five Smoking Home environment Dietary habits Educational level	**Combustion smoke, past exposure (B)** Prevalence OR=2.38 (1.04-5.43)	**Not** Stratified by sex **No** differentiation of immunological, non-immunological, and work exacerbated asthma

1.3 POTENTIAL SUSCEPTIBILITY TO OCCUPATIONAL EXPOSURE ASSOCIATED WITH ASTHMA

Some population groups may be more susceptible for developing OA than others and the role of many risk factors involved in the onset of asthma and exacerbation remains, in part, controversial[49;50]. To describe potential susceptible groups I have included some studies on modifying effects by gender, rhinitis, atopy, growing up or childhood environment , smoking and number of siblings.

Gender

Few studies have investigated gender differences in occupational exposures associated with asthma. A study reported that women were more exposed than men to asthmagenic agents and associations of asthmagenic agents with severe asthma were stronger in women than in men[9]. Another study reported increased incidence of respiratory symptoms among female woodworkers exposed to dry wood, whereas no relations to wood dust exposure were seen for male woodworkers[51].

Rhinitis

Upper airway symptoms such as rhinitis often precede the occurrence of lower airway symptoms[31]. A longitudinal population-based study investigated the onset of asthma in patients with allergic and non-allergic rhinitis and found that rhinitis, even in the absence of atopy, is a powerful predictor of adult asthma[52]. A study investigating the risk of asthma among Finnish patients with occupational rhinitis, reported that patients with occupationally induced rhinitis had a high risk of asthma. The relative risk varied according to occupation and was highest among farmers and wood workers[53].

Atopy

Atopy has been shown to be associated with sensitisation to HMW-agents. In “Asthma in the Workplace” a Dutch study, of 393 bakery workers is cited in which a strong, statistically significant positive association between wheat flour allergen exposure and wheat flour specific sensitisation was found. These associations were found both in atopic and nonatopic workers, but the relationship was much steeper in the atopics[31].

Growing up or childhood environment

A study of Dutch farmers and agricultural industry workers reported slightly higher association between endotoxin exposure and respiratory effects such as wheezing and wheezing with shortness of breath among those with a farm childhood compared with those with no farm childhood[54], indicating farm childhood as a risk factor and not a protective factor for adult asthma symptoms when accounting for farming-job endotoxin exposure. Individuals with parental history of asthma were reported to be at high risk of occupational asthma[2]. Finally a study reported that subjects early exposed to many children at home experience more adult asthma without accounting for occupational exposures[55]

Smoking

The effect of smoking on OA appears to be dependent on the type of occupational agent. When the agents induces asthma by producing specific IgE antibodies, cigarette smoking enhances sensitisation, not when the agent induces asthma independent of IgE antibodies, non-smokers may be more frequently affected than smokers[31]

1.4 ASTHMA AND WORK RELATED ASTHMA IN DENMARK

Finally, to describe current knowledge of occupations and occupational exposures associated with the prevalence of asthma in Denmark, I have also included some population based study on asthma and WRA in Denmark including data from the Danish National Board of Industrial Injuries.

In repeated studies of development of public health in Denmark self-reported asthma prevalence in adults (age 16+) has increased from 2.9% in 1987 to 6.4 % in 2005[56]. In the Danish part of ECRHS I the asthma prevalence was 4.0% in 1994[57] and in the Danish Risk Factor for Adult Asthma study (RAV) we found an asthma prevalence of 7.0% in 2004 [58] based on the same questions defining asthma used in ECRHS I.

There is now a general consensus that there is a increasing trends in allergic disease reflecting a complex gene-environment interaction[59-61].Thus, the reason for the increased asthma prevalence may partly be explained by occupational exposures because more young adults with atopy or allergic susceptibility enters the workforce and are prone to develop OA even though occupational exposures due to inhalation has declined during the last decades.

In Denmark occupational exposure associated with asthma has until now only been studied among cleaners, farmers, bakers and wood workers but not been studied in the general population. In a Danish prospective study among 1,011 female professional cleaners in 1989-1991 cleaning seemed to be associated with an increased risk of eye, nose and throat symptoms and bronchitis. In particular, the use of sprayers was associated with an increased risk of eye, nose and throat symptoms, asthma and bronchitis[17].

A prevalence study of 210 female and 1,691 male Danish farming students found no association between occupational farming exposure and either lung symptoms or lung function[62].

An incidence study over a 20-month period of respiratory symptoms among 114 Danish baker apprentices concluded that rhinitis-and asthma-like symptoms develop commonly in Danish baker apprentices[63].

Incident respiratory symptoms associated with wood dust exposures was studied among 1,377 Danish woodworkers and the authors found that females, but not males, develop respiratory symptoms (coughing and bronchitis), and asthma, despite a relatively low wood dust level[51].

In 2008 a total of 89 cases of occupational asthma were identified in the Danish National Board of Industrial Injuries and the three most common industries where asthma was notified being manufacturing (n=66), agricultural, horticulture, forestry and fishing (n=14) and wholesale and sale and repair of motor vehicles (n=13) . During 2004-2008 the most common industries in which OA was recognized were manufacture of bread and other bakery products n=23, hairdressing saloons n=22, general public service activities n=17, farming of swine n=17, and hospital activities n=17 (personal communication with Jørgen Rasmussen at the Danish National Board of Industrial Injuries in 2009).

If a high female employment rate in Denmark is combined with a possible different pattern of occupational gender segregation and “job-task” gender segregation in gender mixed occupations with men and women dominant in different specific occupations and

men and women dominant in different specific job tasks within the same job, this could involve a hypothetically different occupational asthma risk environment for the Danish labour force and as a consequence a different pattern of occupational exposure associated with asthma in Denmark compared to other European countries.

In 2005 Denmark was the European country with the highest female employment rate, where women accounted for 47.5% of the labour force[64]. In a study of trends in the Danish work environment in 1990-2000 it was found that jobs with decreasing prevalence were clerks, cleaners, textile workers, and military personnel and jobs with increasing prevalence were academics, computer professionals, and managers. For cleaners the part-time work in this group has changed to full time work, and more hours of exposure to cleaning work for each individual. Skin contact to cleaning agents has increased among nurses[65].

1.5 SUMMARY AND CONCLUSION

Studies have shown that some jobs have increased risk of asthma such as cleaners, bakers, spray painters, health care professionals, farmers and construction workers. However these studies does not include information on occupational agents causing asthma. Highest risk of adult onset asthma is reported for grouped HMW and LMW agents. Still, information about specific exposures and differentiation between immunological, non-immunological, and work-exacerbated asthma, remain uncertain. In the study of associations between occupational exposures and asthma potential modifying factors includes gender, country or farm childhood, parental asthma, nasal allergy, number of siblings and smoking which is relevant to include in the exposure-outcome model. The aetiology for the increased prevalence of asthma in Denmark is unknown, but may partly be explained by occupational exposures. Occupational exposures associated

with asthma has until now only been studied among specific occupations such as cleaners, farmers, bakers and wood workers but has not been studied in the general population

To contribute with additional information about the relation between occupation and asthma the present study describes occupations and occupational exposure associated with the prevalence of asthma by gender within the Danish RAV-study[58]. Besides gender we also assess the modifying effects of country or farm childhood, parental asthma, nasal allergy ,number of siblings and smoking on the relation between occupational exposures and asthma.

2. AIMS OF THE STUDY

The aim of the project is

- To describe occupations and occupational exposures associated with the prevalence of asthma in Denmark by gender.
- To assess the modifying effects of country or farm childhood, parental asthma, nasal allergy ,number of siblings and smoking on the association between occupational exposures and asthma
- To describe the distribution of exposures to known or suspected occupational agents associated with the prevalence of asthma

3. HYPOTHESIS

- Chronic air-way exposures to known or suspected occupational allergens and irritants increases the risk of developing asthma (study 1).
- Cleaners in home and industrial settings are exposed to cleaning products which increases the risk of asthma (study 2 and study 3).
- Occupation as professional cleaner, health care worker, user of disinfectants, metal worker, welder and solder has increased prevalence of asthma probably caused by specific air way exposures compared with a unexposed control group (study 3)
- Country or farm childhood, parental asthma, nasal allergy and number of siblings have a modifying effect on the association between occupational exposure and asthma (study 1)

4. METHODS

4.1 DESIGN AND STUDY POPULATION

The RAV study was designed to describe risk factors for asthma in young adults. The following is a summary of the RAV-study. The RAV study protocol was based on the European Community Respiratory Health Survey (ECRHS)[66;67] using the ECRHS questionnaires, which were slightly modified by the RAV research group. Additionally we collected further information of potential occupational risk factors following the ECRHS II protocol on "Occupational Modules". Questionnaires underwent standardised translation procedures to assure comparability with results from the ECRHS, with two different persons translating from English into Danish and back translation (to English). The study was approved by the Scientific Ethical Committee in Denmark.

The RAV study population was randomly selected from the Danish Civil Registration System. In 2002-2003 a total of 10,000 individuals were contacted by mail and asked to complete the mailed slightly modified ECRHS screening questionnaire. The study population comprised randomly selected individuals from the general population, aged 20-44, standardized by sex and age, with 2,000 subjects from each of five Danish counties: Funen, Vejle, Ribe, South Jutland and North Jutland with around 1,8 million inhabitants in total. The questionnaire included items on asthma symptoms, family history, country-bred, pets, current job and industry and occupational exposures to gasses, vapours, dust and fume and also smoking history. Subjects not responding received up to two reminders.

Of the 7,271 individuals who answered the screening questionnaire three separate studies were defined, see flow chart (figure 1). These studies were termed *Asthma and occupation: A population-based study among young Danish adults, Use of home cleaning products and asthma and Occupational modules.*

Study 1- *Asthma and occupation: A population-based study among young Danish adults.*

A cross sectional study based on data reported and measured in the RAV-study[68].

The study 1 method is described in details in paper 1 (see details in paper 1).

Study 2- *Use of home cleaning products and asthma.*

An essentially population-based nested case-control study (case-non case). In 2003-2006 we contacted 2,312 subjects who responded the Phase I questionnaire and invited them to a clinical visit including a face-to-face interview and a clinical investigation (phase II). Because the RAV study was designed to evaluate risk factors for asthma, our sampling to phase II was designed to obtain all asthmatics of the study population. The invited subjects were a 20% **random sub- sample** of the initial 10,000 subjects, equally distributed by gender and age and a symptomatic group from the **complementary sub-sample** including all subjects reporting respiratory symptoms in the screening questionnaire but who had not been already selected in the random sub sample (figure 1).

The symptomatic group included all individuals reporting a positive answer to at least one of the following four questions in the phase I screening questionnaire: “Have you been woken by an attack of shortness of breath at any time in the past 12 months?”, “Are you currently taking any medication including inhalers, aerosols or tablets for asthma?”, “Have you had an attack of asthma in the last 12 months?”, or “Have you ever had asthma?” combined with an answer of older than “15 years” to the question: “How old were you when you had your first attack of asthma?”. In the clinical visit respondents who identified them selves as currently employed or self employed were asked to complete a job history including the job title/ occupation, industry and dates of employment for each job held op to ten years before the clinical visit.

All participants gave written consent and were given the opportunity to refuse participation at any time.

A total of 1,191 (52%) participated in phase II face-to-face interview.

In 2006-2007 all the persons who in the questionnaire in phase II (n=1,136) had given a job history were re-contacted by mail asking to do a telephone interview about specific occupational activities during the last 10 years (phase II, the Occupational Modules). In the 1,191 participants in phase II face-to face interview 311 participants had not given a job history (n=55), were dead, had emigrated, were impossible to trace or were ineligible/unwilling to participate (n=256). See characteristics of the 880 participants in phase II, the Occupational Modules in table 11 & 12. EpiData version 3.1 was used as the data entry program[69]. Data were entered directly during interview and were only entered once. We did not evaluate data entry errors or typing errors. Each interview lasted between 5 and 45 minutes with an average of 15 minutes and was conducted by the author and an experienced interviewer in collaboration .

By telephone-interview we used filtering questions asking if they performed seven specific activities: cleaning (professionally or at home), nursing and health care working, disinfecting, metal working, soldering or welding. If participants had a confirmative answer to the filtering question and they verified that the activity stated in filtering question lasted for more than 3 consecutive months and more than 8 hours per week preceding Phase II clinical visit, they shifted to a short supplemental questionnaire (module) about selected tasks and duration of activities for each relevant job held during up till 10 years. If the individuals performed different working tasks in any of the modules they had to complete another module. For individuals with two or more

modules, the module with the highest frequencies of exposures were selected. This gave the following groups:

Module 1: Cleaning and/or washing in the home: N=764 (492 females and 272 males)

Module 2: All types of cleaners: N=57 (51 females and 6 males)

Module 3: All types of nurses and health care workers: N=72 (71 females and 1 male)

Module 4: Disinfectants: N=192 (151 females and 41 males)

Module 5: Metal Workers: N=96 (15 females and 81 males)

Module 6: Welders: N=80 (6 females and 74 males)

Module 7: Solders: N=42 (6 females and 36 males)

No Module: N=79 (4 females and 75 males) (i.e had not performed work included in modules 1-7)

At the telephone interview in phase II, the Occupational Modules, 764 participants indicated doing or having done the cleaning and/or washing in their homes (module 1) during the follow-up period up till 10 years before clinical visit. Thirteen participants with missing values on any exposure category in module 1 were excluded.

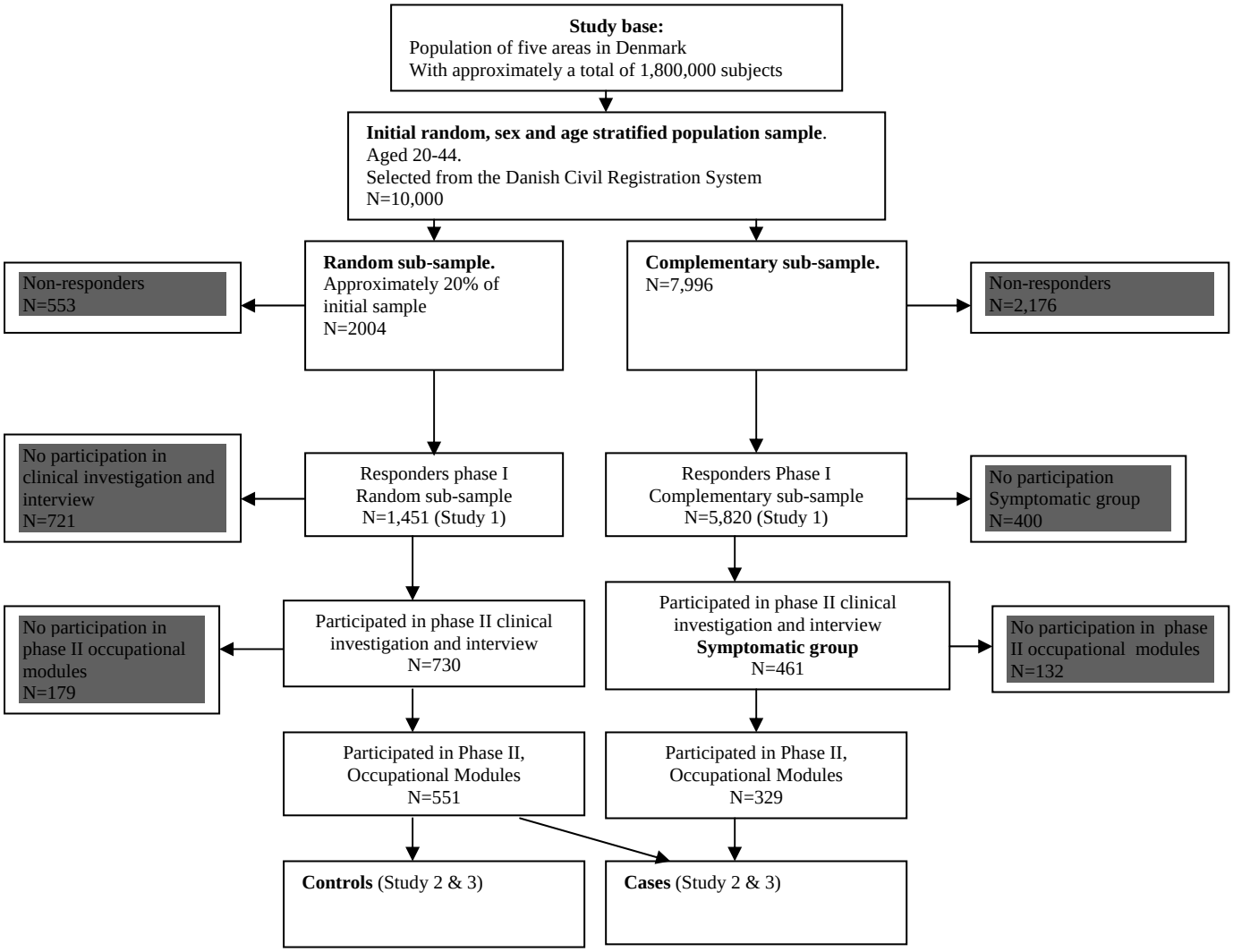
Cases was derived from both the random sample and the symptomatic group of the complementary sub-sample. Controls was derived exclusively from the random sample. Because symptoms of asthma typically show variable patterns in time[16], case-control status was determined on the basis of the presence or absence of respiratory symptoms at the time of both phase I and Phase II part of the study. Cases were defined as participants with current asthma (see 4.2 Definitions current asthma) at both phase I and Phase II and consisted of 169 participants. Controls were defined as participants who reported not

having experienced current asthma in the preceding year and did not have a history of asthma at both phase I and Phase II and consisted of 407 participants. In total the study population comprised of 576 subjects with complete information of case-control status and use of home cleaning products.

Study 3-*Occupational modules.*

A nested case-control study of cleaners, health care workers, users of disinfectants, metal workers, welders and solders within the phase II, Occupational Modules population (n=880). Cases and controls were derived as described above in study 2. In total the study population comprised 672 subjects with complete information of case-control status and confirmed work as cleaners, n=44; health care workers, n=55; users of disinfectants, n=145; metal workers, n=75; welders, n=60, and solders; n=34 and no module, n=405 (i.e had not performed work included in modules 2-7 and defines unexposed reference group)

Figure 1. Flow chart of participants in clinical investigations and occupational modules



4.2 DEFINITIONS

Information on the following variables was obtained from questionnaire response in phase I and phase II (Study 1-3)

Outcome definition

We used three definitions of asthma based on diagnosis or symptoms highly suggestive of asthma and ranging from a relatively high sensitivity to a relatively high specificity. Current wheeze (study 1) was assigned to participants with a affirmative answer to the following question: "Have you had wheezing or whistling in the chest at any time during the last 12 months when you did not have a cold?". Current asthma (study 1-3) was assigned to participants with an affirmative answer to any of the following questions: "Have you been woken by an attack of shortness of breath at any time in the last 12 months?", "Have you had an attack of asthma in the last 12 months?" and "Are you currently taking any medicine for asthma?". Doctor-diagnosed adult-onset asthma (study 1) was assigned to participants with a affirmative answer to all of the following questions: "Have you ever had asthma?", "Was it confirmed by a doctor?" and "How old were you when you had your first attack of asthma?". Having the first asthma attack after the age of 16 was chosen in the definition of doctor-diagnosed adult-onset asthma because it corresponded, for many participants in the survey, with the age of beginning work or apprenticeship in Denmark. These definitions are consistent with those used in previous analysis of the ECRHS study[2;18;66;70].

Job

The self-reported current or last held job was coded according to the Danish version of the International Labour Office system, ISCO-88 (International Standard Classification of Occupations) [71].

Occupational exposure

Two estimates of exposures were used. Coded self-reported current or most recent held job was placed among 26 categories of possible high-risk jobs. The reference group consisted of participants who worked in professional, clerical, or administrative jobs. This classification has been previously used in ECRHS[67]. Secondly, an asthma-specific job exposure matrix [15] (JEM) was used to estimate exposure to asthmagenic agents. The JEM is the basis for *a-priory* distinguishing high risk from low risk exposures. For each ISCO-88 job code, the asthma-specific job exposure matrix classifies the job as exposed or not to 18 high risk asthmagenic agents or settings. The JEM also includes the following classifications: HMW or LMW asthmagens or as mixed environments, four low risk asthmagenic agents or settings, one unlikely to be exposed to asthmagenic compounds, and one variable to identify jobs with uncertainty in the exposure estimates. The group unlikely to be exposed to asthmagenic compounds were the reference group, including jobs with no classified JEM category (see paper 1 for more details about job and JEM categories in the method section, especially about further grouping of the JEM categories in high and low risk agents).

Other suspected asthma risk factors (potential confounders or effect modifiers)

Smoking status was classified as follows: Never smokers answered “No” to the following question: ”Have you ever smoked for as long as a year?” Current smokers answered, “Yes” to both the following questions: ”Have you ever smoked for as long as a year?” and “Do you smoke now?” Ex-smokers answered “Yes” to ”Have you ever smoked for as long as a year?” and “No” to “Do you smoke now?”

Parental asthma was assigned to participants with confirmative answer to either “Did your mother ever had asthma?” or “Did your father ever had asthma?”.

Growing up environment was classified as follows: Those growing up in country

answered “yes” to “Did you grow up in the country?”. Those growing up in the country on a farm answered “yes” to both questions “Did you grow up in the country?” and “Did you live on a farm?” Those growing up in the country on a farm with animals answered yes to all the questions “Did you grow up in the country?” and “Did you live on a farm?” and “Were there animals on the farm?”

Number of siblings was defined by the question: “How many siblings do you have or did you have?

Nasal allergy was defined by the question: “Do you have nasal allergies (-e.g. hay fever)?”

Information on the following variables was obtained from clinical visit in phase II and the telephone interview in phase II, Occupational Modules (Study 2 and 3)

In phase II, Occupational Modules the following exposure estimates were used:

Module 1 (Cleaning/washing in the home) Study 2, based on telephone interview, participants were asked about the use of products for domestic cleaning and washing during the follow-up period. To create exposure variables for answering our research questions about use of cleaning products among those cleaning/washing in the home we did following. The frequency of use of 17 different products was recorded as never, less than 1 day per week, 1 to 3 days per week, or 4 to 7 days per week. To create module-based exposure variables, we dichotomised questionnaire responses according to whether respondents reported each occupational product as part of cleaning and/or washing the home in the follow-up period up till 10 years before clinical visit. As with previous analysis of ECRHS data, we dichotomised the frequency of cleaning product use (never or less than once/week vs 1–7 days/week). The frequency of cleaning product use never

or less than once a week defines unexposed participants and 1-7 days per week the exposed participants for each of the exposure variables.

General coding for module 2-7 (cleaners, health care workers, working with disinfectants, metal workers, welders and solders), in the telephone interview, participants were asked about principal working places; working tasks; use or handling of products; use of latex gloves; vapour, dust and fume exposures; use of protection devices and ventilation in the workplace during the follow-up period. The principal working places and use of protection devices and ventilation was recorded as yes or no. The frequency of working tasks, use or handling of products and latex gloves, vapour, dust and fume exposures was recorded as never, less than 1 day per week, 1 to 3 days per week, or 4 to 7 days per week. As with previous analyses of ECRHS data we dichotomised the frequency of working tasks, use or handling of products use of latex gloves, vapour, dust and fume exposures (less than once/week vs 1–7 days/week).

For comparison, we selected a population of respondents who reported in the screening survey that they had not performed the following work for at least three months preceding the Phase II clinical visit : professional cleaning, disinfecting, health care work, metal working, soldering and welding. (i.e had not performed work included in modules 2-7)

Module 2 (cleaners).

To create exposure variables for answering our research questions about use of cleaning products among cleaners we used dichotomised frequencies as described above for 17 different products.

Module 3 (health care workers)

To create exposure variables for answering our research questions about use of cleaning products among health care workers we used dichotomised frequencies as described above for 7 different products.

Module 4 (working with disinfectants)

To create exposure variables for answering our research questions about use of disinfectants at work we used dichotomised frequencies as described above for 11 different products.

Module 5 (metal workers)

To create exposure variables for answering our research questions about use of metal products and vapour, dust and fume exposures among metal workers we used dichotomised frequencies as described above for 5 different products and 11 different vapour, dust and fume exposures

Module 6 (welders)

To create exposure variables for answering our research questions about welders we used dichotomised frequencies as described above for 8 different welding methods and 6 different welding materials

Module 7 (solders)

To create exposure variables for answering our research questions about solders we used dichotomised frequencies as described above for 5 different soldering methods

Potential confounders

A priori county, gender, age and smoking was used as potential confounders in study 1 in analysis other than those stratified by sex were age, smoking and county was used a priory as confounders as previously used in ECRHS[2] and because these factors are known to be important risk factors for asthma and asthma symptoms and expected to be associated with the exposures of interest.

These variables were selected before the final analyses. In study 1 a classical (Mantel-Haenszel) method- based on stratification was used to estimate the confounding effects

of age, sex, smoking, county, parental asthma, growing up environment, number of siblings and nasal allergy in study 1. We controlled for each of these in turn to see if there were any change in effect estimates. We also controlled for the main a priori confounders (age, sex, smoking, county) together with those additionally potential confounders (parental asthma, environment when growing up, number of siblings and nasal allergy)for these in turn to see whether there were any appreciable change in the effect estimate. Since all potential confounders considered except sex changed effect estimates with less than 10 % in study 1 only unadjusted estimates stratified by gender are given in study 2 & 3. This strategy is chosen in order to maximise number of participants and increase power.

4.3 STATISTICAL ANALYSIS

All analyses were performed using Stata version SE 10.1 (Stata Corporation, College Station, Texas, USA). Subjects for whom values were missing were excluded from the analyses. As significance level $p<0.05$ was used.

For study 1, Prevalence Ratios (PR) [72] between occupational exposures and asthma in the three categories were calculated with log-binomial regression models stratified by sex and for the total study population. The PRs and 95% Confidence Intervals (95% CI) were adjusted for age, sex, smoking, and county in analyses other than those stratified by sex, which was adjusted for age, smoking, and county. In a stratified analysis we assessed prevalence ratios by sex, smoking status, nasal allergy, parental asthma status, country-bred and number of siblings and tested differences in prevalence ratios between categories by introduction of an interaction term in a Poisson regression model with robust estimation of error.

Analyses using the job-exposure matrix, were repeated after exclusion of jobs with uncertain exposure estimates.

Making multiple comparisons vastly increases the probability of obtaining significant association by chance. Therefore a way of taking this in account is the Bonferroni correction in which the significance is set as the originally chosen divided by the number of parallel comparisons. In study 1 the number of jobs compared was 26 giving a "real" significance level of 0.05 /26 =0.0019. On the other hand the problem can be addressed more qualititatively looking at the distribution of risk estimates.

For study 2, in a nested case-control design, associations between case control status and use of 17 different home cleaning products were estimated by means of the crude OR with 95% CI using unconditional logistic regression analysis separate for each sex.

For study 3, in a nested case-control design for each module, crude associations between case control status and different exposures were estimated by unconditional logistic regression analysis and presented as OR with 95% CI to compare the risk of asthma among participants in each exposure to that of participants not included in any of the modules 2-7.

A separate analysis of the odds-ratios for the products was made exclusively within the part of the population included in the random sample. This was done to elude a possible effect of the increased number of cases included. However in the random sample only 13 male and 41 female cases fulfilled the criteria. Therefore none of the products included at least 5 cases and a comparison of odds ratios could not be made.

5. RESULTS

The main and detailed results of study 1, *Asthma and occupation: A population-based study among young Danish adults* are described in the attached paper 1.

The following is a summary of results for current asthma and occupational groups and occupational exposure groups with more than 10 participants in total.

A total of 6,327 participants with complete information on the main outcome variables and exposure variables were eligible for the occupational analysis. Table 4 summarizes the descriptive statistics for the participants stratified by sex.

Table 4. Characteristics of the study population by gender

	Men (n= 2,937)	Women (n= 3,390)
Age, years (mean (SD*))	33.1 (6.9)	32.8 (7.0)
Age group, years (%)		
20-24	14.9	16.2
25-29	18.4	19.3
30-34	21.2	21.0
35-39	22.4	21.8
40-44	23.1	21.7
County (%)		
Funen	20.7	20.7
Vejle	20.6	20.1
Ribe	18.7	18.7
Southern Jutland	19.8	20.5
Northern Jutland	20.2	20.0
Smoking (%)		
Never smokers	50.9	49.8
Ex-smokers	20.1	22.1
Current smokers	29.0	28.1
Definitions of asthma (%)		
Current wheeze	14.4	12.9
Current asthma	8.0	9.4
Doctor diagnosed adult-onset asthma	2.9	4.8
Nasal allergy** (%)	22.5	23.2
Parental asthma (%)	13.1	17.9
Number of siblings (%)		
0	4.5	4.8
1	35.4	36.6
2	28.7	29.9
3	15.2	15.2
4 or more	9.9	10.3
Don't know/missing	6.3	3.2
Growing up environment		
In country (%)	38.5	36.7
In country on farm (%)	19.3	18.4
In country on farm with animals (%)	18.3	17.7

*SD, standard deviation **Data missing for 39 participants

Job and current asthma

A statistically significant increased PR of current asthma was found for female cleaners and caretakers and male printing workers (Table 5). A more than two-fold increased PR, albeit non-significantly, was found for male bakery workers and female electrical processors and drivers. A small but borderline significant increased PR was observed for female medical and pharmacy group other than nurses. Potentially interesting categories such as hairdressers, welders, plastics and rubber workers, and paper workers had too small numbers of asthma cases, therefore adjusted prevalence ratios could not be calculated.

Table 5. Prevalence ratios (PR) with 95% Confidence Interval (95%CI) for associations between occupational groups with more than 10 participants in total and current asthma by gender adjusted for county, age, and smoking status.

	Men		Women	
Occupational group	Number	PR (95%CI)	Number	PR (95%CI)
Legislators, managers, administrators (reference)	1,204	1.00	1,924	1.00
Cleaners and caretakers	45	1.20 (0.51-2.82)	124	**2.17 (1.47-3.21)**
Nurses	4	NE	158	0.97 (0.56-1.66)
Other medical and pharmacy	56	0.78 (0.29-2.07)	577	1.25 (0.95-1.65)
Agriculture and forestry	166	0.80 (0.45-1.43)	63	1.24 (0.61-2.52)
Wood workers	142	1.07 (0.61-1.86)	6	1.61 (0.27-9.64)
Bakery workers	16	2.23 (0.77-6.44)	4	NE
Food and tobacco processing	70	1.22 (0.59-2.53)	83	1.41 (0.78-2.56)
Chemical and physical science technicians	3	NE	15	0.78 (0.11-5.29)
Metal making and treating	99	1.26 (0.70-2.28)	6	NE
Other metal workers	221	0.85 (0.51-1.42)	16	1.46 (0.38-5.57)
Electrical processors	106	0.74 (0.35 -1.57)	6	2.20 (0.37-13.11)
Painters	22	1.70 (0.59-4.90)	28	0.39 (0.06-2.71)
Textile, leather and fur workers	4	NE	13	0.93 (0.14-6.08)
Printing workers	16	**3.37 (1.41-8.06)**	3	NE
Construction and mining	192	0.79 (0.45-1.39)	24	0.53 (0.08-3.63)
Drivers	128	0.74 (0.37-1.48)	12	2.25 (0.63-8.12)
Remainder transport and storage	70	0.70 (0.26-1.84)	27	0.83 (0.21-3.19)
Remainder blue-collar	203	0.63(0.34-1.16)	132	0.99(0.55-1.78)
Not classifiable	128	0.79(0.41-1.52)	116	1.17(0.67-2.05)

JEM and current asthma

Exposure to HMW agents assessed by the JEM was associated with current asthma in men PR=1.59 (95%CI 1.10-2.51), while PR for women was borderline significant (Table 6). Findings were consistent for several specific agents within this category, in particular flour, plants and mites. Exposure to LMW agents was less clearly associated with current asthma, although the nested category of cleaning agents was related to current asthma in women but not in men. A significantly increased PR of current asthma was associated with exposure to possible irritants among women. This increased PR was not seen in men.

Table 6. Prevalence ratios (PR) with 95% Confidence Interval (95% CI) for Associations between occupational exposure groups with more than 10 participants in total and current asthma by gender adjusted for county, age, and smoking status

	Men		Women	
Exposures grouped according to Asthma-specific Job Exposure Matrix*	Number	PR (95%CI)	Number	PR (95%CI)
Not exposed (reference)	1,498	1.00	2,174	1.00
High risk asthma agents	482	1.14 (0.82-1.59)	827	1.21 (0.95-1.54)
HMW agents	153	**1.59 (1.01-2.51)**	709	1.25 (0.97-1.61)
Flour	17	3.29 (1.38-7.80)	4	NE
Mites	1	**9.10 (5.50-15.04)**	20	**3.55 (1.76-7.14)**
Enzymes	16	2.58 (0.89-7.42)	4	NE
Bioaerosols	71	1.44 (0.73-2.86)	23	1.53 (0.53-4.45)
LMW agents	272	1.08 (0.71-1.65)	553	1.22 (0.92-1.61)
Cleaning agents	40	0.60 (0.15-2.34)	438	**1.40 (1.04-1.87)**
Mixed environments	235	1.09 (0.69-1.72)	77	1.18 (0.60-2.31)
Accidental peak exposures	45	1.37 (0.59-3.18)	5	NE
Low asthma risk agents	957	0.94 (0.71-1.25)	389	1.30 (0.95-1.77)
Possible irritants	418	0.91 (0.62-1.33)	146	**1.68 (1.10-2.55)**
Low risk antigens	450	1.04 (0.73-1.48)	347	1.31 (0.95-1.81)

NE, not estimable due to small numbers of cases
*According to published matrix [15]
Subjects, can be categorised in more than one exposure category, therefore, numbers exceed 100%

The main jobs identified for women exposed to possible irritants were cleaners and caretakers (71%) food and tobacco processing (9%) and construction and mining (16%).

After exclusion of job with uncertain estimates according to the JEM (n=1.771) there were no major changes in the effect estimates between the three asthma definitions and the JEM categories.

Current asthma PRs were slightly more increased for high and low risk asthma agents, and the current asthma PR for HMW changed from significantly increased to borderline significant (PR=1.67, 95%CI; 0.95-2.92) in men.

When analysing potential confounders, sex was found to be the main potential confounder. All other potential confounders considered showed very little inference in the causal pathway.
Figures 1 and 2 in paper 1 show the PRs for current asthma due to any JEM high- or any low- risk asthma agent exposures in the workplace in separate groups defined by potential effect modifiers, including gender. Figure 1 in paper 1 shows that the PRs for current asthma related to any high-risk asthma agent exposure was significantly lower for never smokers (p=0.048 for interaction) than for ex-smokers or current smokers. No significantly differences were observed for gender, nasal allergy, parental asthma or country and farm childhood. When dichotomising the number of siblings (0-2 siblings vs. 3 or more), a significant interaction (p=0.04) was found between having three or more siblings and exposure to high-risk asthma agents in the relationship with current asthma.
Figure 2 in paper 1 shows that the PRs for current asthma related to low-risk asthma agent exposure were significantly higher for those growing in country on a farm and those growing up on a farm with animals (p=0.027 and p=0.041 respectively for interaction) compared with those with no farming or country childhood. No significant differences were observed for gender, nasal allergy, smoking status or parental asthma. When dichotomising the number of siblings (0-2 siblings vs. 3 or more), a significant interaction (p=0.0023) was found between having three or more siblings and exposure to low-risk asthma agents in the relationship with current asthma.

The following results of study 2 & study 3 are original chapters. The main outcome variable is current asthma in relation to different occupational exposure categories since the current asthma definition is consistent with those used in previous analysis of the ECRHS data[8;12]. In addition, as showed in study 1 (se paper supplementary Tables 1-4) the results using the other two asthma definitions gave very similar PRs as to those using current asthma in the relation to different exposure categories. Therefore current wheeze and doctor diagnosed adult-onset asthma were omitted as outcome variables.

STUDY 2. *Use of home cleaning products and asthma*

The mean age of the study population was 35.2 years, similar for cases and controls (Table 7). Women maked up 62 % of the study population doing the cleaning and/or washing in the home. Approximately 30 % had current asthma. The proportion of current smokers was similar for cases and controls.

The frequency of use varied largely between the different cleaning products (Table 8). The majority of products were not significantly associated with current asthma and the majority of ORs were below 1. Significant positive association was observed for ammonia unadjusted but the association disappeared in the analyses stratified by sex (Table 9 and 10).

Table 7. Demographic characteristics of 576 participants using 17 different home cleaning products

	Cases	Controls
Number	169	407
Age, years, mean (SD)	33.60 (7.02)	35.85 (6.63)
(range)	(20.96-46.40)	(21.60-46.82)
Female	120 (71%)	236 (58%)
Male	49 (29%)	171 (42%)
Current smoker	42 (25%)	114 (28%)
Ex-smoker	31 (18%)	75 (18%)
Never-smoker	96 (57%)	218 (54%)
County		
Vejle	41 (24%)	85 (21%)
Funen	34 (20%)	77 (19%)
Southern Jutland	40 (24%)	64 (16%)
Ribe	27 (16%)	103 (25%)
Northern Jutland	27 (16%)	78 (19%)

Table 8. Association (unadjusted odds ratios and 95% confidence intervals) between the use of cleaning products at home at least weekly and current asthma (n=576)

Cleaning Product	Use >= 1 d/wk among 576 participants n (%)	OR* (95% CI) associated with use of cleaning product
Washing powders	515 (89)	0.99 (0.55-1.77)
Liquid multi-use cleaning products	485 (84)	0.82 (0.51-1.32)
Polishes, waxes	14 (2.4)	1.84 (0.63-5.37)
Bleach	48 (8.3)	0.89 (0.46-1.72)
Ammonia	11 (1.9)	**4.35 (1.26-15.07)**
Decalcifiers, acids	95 (16)	0.84 (0.51-1.37)
Solvents, stain removers	33 (5.7)	0.90 (0.41-1.97)
Other cleaning products	146 (25)	1.36 (0.91-2.03)
Furniture sprays	4 (0.7)	NE
Glass cleaning sprays	205 (36)	1.23 (0.85-1.79)
Sprays for carpets rugs or curtains	1 (0.2)	NE
Sprays for mopping the floor	1 (0.2)	NE
Oven sprays	1 (0.2)	NE
Ironing sprays	0 (0.0)	NE
Air freshening sprays	46 (8.0)	0.94 (0.48-1.84)
Other sprays	16 (2.8)	0.80 (0.25-2.51)
Use perfumed or scented cleaning products	424 (74)	0.73 (0.49-1.09)

*The reference category consisted of participants that used the cleaning product under study never or less than once a week
NE, not estimable due to small numbers of cases

Table 9. Association (unadjusted odds ratios and 95% confidence intervals) between the use of cleaning products at home at least weekly and current asthma among females (n=356)

Cleaning Product	Use >= 1 d/wk among 356 female participants n (%)	OR* (95% CI) associated with use of cleaning product
Washing powders	348 (98)	3.64 (0.44-29.91)
Liquid multi-use cleaning products	315 (88)	0.87 (0.44-1.71)
Polishes, waxes	4 (1.1)	1.98 (0.28-14.25)
Bleach	33 (9.3)	0.84 (0.39-1.83)
Ammonia	8 (2.2)	3.38 (0.79-14.38)
Decalcifiers, acids	59 (17)	0.76 (0.41-1.41)
Solvents, stain removers	27 (7.6)	0.67 (0.27-1.63)
Other cleaning products	110 (31)	1.12 (0.70-1.79)
Furniture sprays	3 (0.8)	NE
Glass cleaning sprays	157 (44)	1.11 (0.71-1.73)
Sprays for carpets rugs or curtains	0 (0.0)	NE
Sprays for mopping the floor	1 (0.3)	NE
Oven sprays	1 (0.3)	NE
Ironing sprays	0 (0.0)	NE
Air freshening sprays	33 (9.3)	1.14 (0.54-2.40)
Other sprays	12 (3.4)	0.98 (0.29-3.33)
Use perfumed or scented cleaning products	274 (77)	0.60 (0.36-1.00)

*The reference category consisted of participants that used the cleaning product under study never or less than once a week
NE, not estimable due to small numbers of cases

Table 10. Association (unadjusted odds ratios and 95% confidence intervals) between the use of cleaning products at home at least weekly and current asthma among males (n=220)

Cleaning Product	Use >= 1 d/wk among 220 male participants n (%)	OR* (95% CI) associated with use of cleaning product
Washing powders	167 (76)	0.50 (0.25-1.00)
Liquid multi-use cleaning products	170 (77)	0.58 (0.28-1.18)
Polishes, waxes	10 (4.5)	2.44 (0.66-9.03)
Bleach	15 (6.8)	0.86 (0.23-3.19)
Ammonia	3 (1.4)	7.23 (0.64-81.52)
Decalcifiers, acids	36 (16)	0.99 (0.42-2.35)
Solvents, stain removers	6 (2.7)	1.77 (0.31-10.00)
Other cleaning products	36 (16)	1.69 (0.76-3.73)
Furniture sprays	1 (0.4)	NE
Glass cleaning sprays	48 (22)	1.05 (0.48-2.24)
Sprays for carpets rugs or curtains	1 (0.4)	NE
Sprays for mopping the floor	0 (0.0)	NE
Oven sprays	0 (0.0)	NE
Ironing sprays	0 (0.0)	NE
Air freshening sprays	13 (5.9)	0.27 (0.03-2.17)
Other sprays	4 (1.8)	NE
Use perfumed or scented cleaning products	150 (68)	0.84 (0.43-1.65)

*The reference category consisted of participants that used the cleaning product under study never or less than once a week
NE, not estimable due to small numbers of cases

STUDY 3. *Occupational modules*

The mean age of participants in phase II modules 1-7 was very similar to that of the non-participants (Table 11). Also the percentage of women, number of cases and number of not fulfilling case/control definition among participants was very similar to that of the non-participants.

Current asthma percentages among cleaners (33%) was higher compared to the reference group (23%), and current asthma percentages among nurses and health care workers (15%), metal

workers (19%), welders (16%) and solders (17%) was low compared to the reference group (23%), (Table 12).

Occupation as professional cleaner, health care worker, user of disinfectants, metal worker, welder and solder showed no increased risk of asthma compared with the reference group neither in the total group, nor after stratification by gender, (Table 13)

Table 11. Characteristics of participants in phase II modules 1-7, non-participants in modules 1-7, and participants in phase II face-to-face interview

Characteristics	Participants in modules 1-7, n=880	Non-participants in modules 1-7, n=311	Participants in phase II face-to-face interview, n=1,191
Women, n (%)	500 (57%)	170 (55%)	670 (56%)
Age, yr, mean (SD)	34.8 (7.0)	33.5 (7.4)	34.5 (7.1)
Cases, n (%)	197 (22%)	75 (24%)	272 (23%)
Controls, n (%)	475 (54%)	152 (49%)	627 (53%)
Not fulfilling case/control definition, n (%)	208 (24%)	84 (27%)	292 (24%)

Table 12. Characteristics of the participants in phase II occupational modules 2-7

Characteristics	No module, reference, n=527	Module 2, all types of cleaners, n=57	Module 3, all types of nurses and health care workers, n=72	Module 4, disinfectants, n=192	Module 5, metal workers, n=96	Module 6, welders, n=80	Module 7, solders, n=42
Women (%)	287 (54%)	51 (89%)	71 (99%)	151 (79%)	15 (16%)	6 (7%)	6 (14%)
Age, yr, mean (SD)	35.4 (6.9)	30.6 (7.5)	35.4 (7.4)	34.1 (7.2)	34 (6.7)	34.7 (6.4)	33.7 (6.6)
Cases	120 (23%)	19 (33.3%)	11 (15.3%)	46 (24%)	18 (19%)	13 (16%)	7 (17%)
Controls	285 (54%)	25 (43.9%)	44 (61.1%)	99 (52%)	57 (59%)	46 (58%)	27 (64%)
Not fulfilling case/control definition	122 (23%)	13 (22.8%)	17 (23.6%)	47 (24%)	21 (22%)	21 (26%)	8 (19%)

Table 13. Characteristics of participants fulfilling case control status, crude OR with 95% CI for current asthma and module 2-7 in total and stratified by gender

Module	Males Cases, n	Males Controls, n	OR (95%CI)	Females Cases, n	Females Controls, n	OR (95%CI)	Total Cases, n	Total Controls, n	OR (95%CI)
No module	48	150	Ref	72	135	Ref	120	285	Ref
Module 2	3	1	9.3 (0.9-92)	16	24	1.2 (0.6-2.5)	19	25	1.2 (0.6-2.5)
Module 3	0	1	NE	11	43	0.5 (0.2-1.0)	11	44	0.6 (0.3-1.2)
Module 4	10	20	1.6 (0.7-3.6)	36	79	0.8 (0.5-1.4)	46	99	1.1 (0.7-1.7)
Module 5	14	51	0.9 (0.4-1.7)	4	6	1.2 (0.3-4.6)	18	57	0.7 (0.4-1.3)
Module 6	10	44	0.7 (0.3-1.5)	3	2	2.8 (0.4-17)	13	46	0.7 (0.3-1.3)
Module 7	5	23	0.7 (0.2-1.9)	2	4	0.9 (0.2-5.2)	7	27	0.6 (0.3-1.5)

Professional cleaners

In the professional cleaning group the percentage of women was high 89% compared to the reference group 54%, (Table 12) .

Professional cleaning was an activity performed in 11 different ISCO categories, one category unclassifiable and one missing values category. Professional cleaning was most common in the category helpers and cleaners in offices and hotels (68%), (data not shown).

In the following analysis we have excluded males and included 40 women with information of case/control status as the final study population. We only report OR for the 5 products where the number of asthma cases were equal to or more than 5. The OR for current asthma among women employed as professional cleaner was (1.2; 95% CI 0.6-2.5) compared to the reference group, (Table 13).

The most common used products was liquid multi-use cleaning product, decalcifers, glass cleaning sprays and perfumed or scented cleaning products (Table 14).

For the exposures liquid multi-use cleaning product, decalcifers, other cleaning products, glass cleaning sprays and perfumed or scented cleaning products the OR was above unity but were not significantly associated with current asthma. Most of the associations could not be estimated due to low numbers of cases.

Table 14. Crude OR and 95% CI for current asthma for use of different cleaning products in female cleaners if number of asthma cases is > 5. <1 denotes using the product less than 1 day per week, while >1 denotes using it one day or more per week.

Cleaning product (day week^{-1})	Cases	Controls	Current asthma Crude OR (95% CI)
No module (reference)	72	135	1 (reference)
Liquid multi-use cleaning products			
<1	0	0	NE
≥1	16	24	1.2 (0.6-2.5)
Decalcifers, acids			
<1	2	4	NE
≥1	8	11	1.4 (0.5-3.5)
Other cleaning products			
<1	1	0	NE
≥1	5	2	4.7 (0.9-24.8)
Glass cleaning sprays			
<1	0	0	NE
≥1	8	8	1.9 (0.7-5.2)
Use of perfumed or scented cleaning products			
<1	0	0	NE
≥1	9	10	1.7 (0.7-4.3)

These products did not include five cases: Washing powders, polishes and waxes, bleach, ammonia solvents, and stain removers, furniture sprays, sprays for carpets, rugs, or curtains, sprays for mopping the floor, oven sprays, ironing sprays, air freshening sprays, Other sprays

Health care workers

In the health care workers group the percentage of women was very high 99% compared to the reference group 54%, (Table 12) .

Health care work was an activity performed in 9 different ISCO categories, one category unclassifiable job and one missing values category. Health care workers was most common in the category institution-based personal care workers (58%) and in the category nursing associate professionals (24%) , (data not shown).

In the following analysis we have excluded males and included 45 women with information of case/control status as the final study population. We only report OR for the 2 products where the number of asthma cases were equal to or more than 5. The OR for current asthma among women

employed as health care worker was (0.5; 95% CI 0.2-1.0) compared to the reference group, (Table 13).

The most commonly used products was washing powders and liquid multi-use cleaning product, (Table 15). For the exposures washing powders and liquid multi-use cleaning product the OR were below unity but not significantly associated with current asthma. Most of the associations could not be estimated due to low numbers of cases.

Table 15. Crude OR and 95% CI for current asthma for use of different cleaning products in female health care workers if number of asthma cases is > 5. <1 denotes using the product less than 1 day per week, while ≥1 denotes using it one day or more per week

Cleaning product (day week^{-1})	Cases	Controls	Current asthma Crude OR (95% CI)
No module (reference)	72	135	1 (reference)
Washing powders			
<1	0	3	NE
≥1	5	16	0.6 (0.2-1.7)
Liquid multi-use cleaning products			
<1	0	5	NE
≥1	7	22	0.6 (0.2-1.5)

These products did not include five cases: Washing powders, bleach ammonia, solvents and stain removers, any cleaning products in spray-form, other cleaning products

Users of disinfectants

In the users of disinfectants group the percentage of women was high 79% compared to the reference group 54%, (Table 12) .

Use of disinfectants was an activity performed in 60 different ISCO categories, one category unclassifiable job, one full-time student category and one missing values category. Use of disinfectants was most common in the categories institution-based personal care workers (20%), nursing associate professionals (9%), Cooks (6%) and preprimary education teaching associate (6%), (data not shown).

In the following analysis we have excluded males and included 115 women with information of case/control status as the final study population. We only report OR for the 2 disinfectant products where the number of asthma cases were equal to or more than 5. The OR for current asthma among women users of disinfectants was (0.8; 95% CI 0.5-1.4) compared to the reference group, (Table 13).

The most common used products was alcohol and the category "Don't know the active compound", (Table 16). For alcohol and the category "Don't know the active compound" the OR was below unity but not significantly associated with current asthma. Most of the associations could not be estimated due to low numbers of cases.

Table 16. Crude OR and 95% CI for current asthma for use of different disinfectant products in female users of disinfectant products if number of asthma cases is ≥ 5. <1 denotes using the disinfectant product less than 1 day per week, while ≥1 denotes using it one day or more per week

Disinfectant product (day week^{-1})	Cases	Controls	Current asthma Crude OR (95% CI)
No module (reference)	72	135	1 (reference)
Alcohol			
<1	2	4	NE
≥1	24	52	0.9 (0.5-1.5)
Don't know the active compound			
<1	2	3	NE
≥1	14	28	0.9 (0.5-1.9)

These disinfectant products did not include five cases: Formaldehyde, glutaraldehyde, bleach, chlorine, chloroamine-T, ammonia, quaternary ammonium compounds, ethylene oxide, halamid other product

Metal workers

In the metal workers group the percentage of women was very low 16% compared to the reference group 54%, (Table 12) .

Metal work was an activity performed in 27 different ISCO categories, one category unclassifiable job, one full-time student category and one missing values category. Metal work was most common in machine-tool setters and setter-operators (15%), blacksmiths and hammer-

smiths (11%), motor vehicle mechanics and fitters (9%) and Tool-makers and related workers (7%), (data not shown).

In the following analysis we have excluded women and included 66 men with information of case/control status as the final study population. We only report OR for the 4 metal products and 6 vapour, dust and fume exposures where the number of asthma cases were equal to or more than 5. The OR for current asthma among male metal workers was (0.9; 95% CI 0.4-1.7) compared to the reference group, (Table 13).

The most common used products were ferrous (iron, steel), aluminium, hard metal (tungsten, cobalt, beryllium) and Others. The most common vapour, dust or fume exposures were metal dusts and fumes, water-based metal working fluids, oil-based metal working fluids, welding fumes, organic solvents (degreasing) and oil and greases. (Table 17). None of the used metal products and vapour, dust and fume exposures was significantly associated with current asthma. The majority of the estimates were below unity. Most of the associations could not be estimated due to low numbers of cases.

Table 17. Crude OR and 95% CI for current asthma for use of different metal products and vapour, dust and fume exposures among male metal workers if number of asthma cases is ≥ 5. <1 denotes using the product or being exposed to vapour, dust and fume exposure less than 1 day per week, while ≥1 denotes using it or being exposed one day or more per week

Metal products and vapour, dust and fume exposures (day week^{-1})	Cases	Controls	Current asthma Crude OR (95% CI)
No module (reference)	48	150	1 (reference)
Metal products			
Ferrous (iron, steel)	2	4	NE
<1	11	43	0.8 (0.4-1.7)
≥1			
Aluminium			
<1	3	11	NE
≥1	8	24	1.0 (0.4-2.5)
Hard metal (tungsten, cobalt, beryllium)			
<1	0	2	NE
≥1	7	10	2.2 (0.8-6.0)
Others			
<1	0	0	NE
≥1	7	12	1.8 (0.7-4.9)
Vapour, dust and fume exposures			
Metal dusts and fumes			
<1	1	2	NE
≥1	10	43	0.7 (0.3-1.6)
Water-based metal working fluids			
<1	1	6	NE
≥1	10	32	1.0 (0.4-2.1)
Oil-based metal working fluids			
<1	1	3	NE
≥1	8	38	0.7 (0.3-1.5)
Welding fumes			
<1	0	6	NE
≥1	8	35	0.7 (0.3-1.6)
Organic solvents (degreasing)			
<1	1	11	NE
≥1	5	24	0.6 (0.2-1.8)
Oil and greases			
<1	2	8	NE
≥1	10	36	0.9 (0.4-1.9)

These metal products and vapour, dust and fume exposures did not include five cases: other non-ferrous (copper), moulding dusts and fumes, acid fumes (plating), soldering fumes, other degreasing agents, (water-based) and paints.

Welding

In the welding group the percentage of women was very low 7% compared to the reference group 54%, (Table 12) .

Welding was an activity performed in 26 different ISCO categories, one category unclassifiable job and one missing values category. Welding was most common in blacksmiths and hammer-smiths (15%), motor vehicle mechanics and fitters (13%), plumbers and pipe fitters (8%) and tool-makers (6%). Welders and flame cutters only comprised 1%, results not shown.

In the following analysis we have excluded women and included 54 men with information of case/control status as the final study population. We only report OR for the 2 welding methods and 2 welding materials where the number of asthma cases were equal to or more than 5 The OR for current asthma among male welders was (0.7; 95% CI 0.3-1.5) compared to the reference group, (Table 13). The most common used welding methods were MAG/MIG (metal active/inert gas welding) and by hand. The most common welding materials were stainless steel and mild steel (ferrous alloy, for ship construction), (Table 18).

None of the welding methods or welding materials was significantly associated with current asthma. All the estimates of OR´s were below unity. Most of the associations could not be estimated due to low numbers of cases.

Table 18. Crude OR and 95% CI for current asthma for welding methods and welding in different materials among male welders if number of asthma cases is ≥ 5. <1 denotes using the welding method or welding in different materials less than 1 day per week, while ≥1 denotes welding method or welding in different materials one day or more per week

Welding methods and welding in different materials (day week^{-1})	Cases	Controls	Current asthma Crude OR (95% CI)
No module (reference)	48	150	1 (reference)
Methods			
MAG/MIG (metal active/inert gas welding)			
<1	2	5	NE
≥1	5	26	0.6 (0.2-1.6)
By hand			
<1	1	7	NE
≥1	9	35	0.8 (0.4-1.8)
Materials			
Stainless steel			
<1	1	1	NE
≥1	5	19	0.8 (0.3-2.3)
Mild steel (ferrous alloy, for ship construction)			
<1	1	3	NE
≥1	5	21	0.7 (0.3-2.1)

These welding methods and welding materials did not include five cases: MMA (manual metal arc welding), TIG (tungsten inert gas welding), SAW (submerged arc welding), FCW (flux cored arcwelding), other, operating a fully automated welding machine, galvanised iron or steel, aluminium, painted metal, other

Soldering

In the soldering group the percentage of women were very low 14% compared to the reference group 54%, (Table 12).

Soldering was an activity performed in 20 different ISCO categories and one missing values category. Soldering was most common in motor vehicle mechanics and fitters (14%), building and related electricians (12%) and electronic-equipment assemblers (7%), (data not shown) . In the following analysis we have excluded women and included 28 men with information of case/control status as the final study population. We only report OR for the soldering methods where the number of asthma cases were equal to or more than 5. The OR for current asthma

among male solderes was (0.7; 95% CI 0.2-1.9) compared to the reference group, (Table 13). The most common used soldering methods were soft soldering (electric resistance) and by hand , (Table 19).

Table 19. Crude OR and 95% CI for current asthma for different soldering methods among male solders if number of asthma cases is ≥5. <1 denotes using the soldering method less than 1 day per week, while ≥1 denotes soldering method one day or more per week

Soldering methods (day week^{-1})	Cases	Controls	Current asthma Crude OR (95% CI)
No module (reference)	48	150	1 (reference)
Soft soldering (electric resistance)			
<1	2	5	NE
≥1	3	10	NE
By hand			
<1	2	7	NE
≥1	3	16	NE

These soldering methods did not include five cases: brazing (hard or silver soldering), soft soldering (electric resistance), other, by hand, operating a fully automated soldering machine

6. DISCUSSION

OCCUPATION AND EXPOSURE

This population-based study among young adults in Denmark showed a consistently increased PR of current asthma in female cleaners and caretakers, male printing workers, and for men exposed to high molecular weight agents. Workplace exposure to irritants and other airborne contaminants showed increased PR for asthma in women. Very similar results were found for current wheeze and doctor-diagnosed adult-onset asthma.

Women are more exposed to JEM high risk asthma agents in the present survey than men but less exposed to JEM low asthma risk agents. The associations seem different in men (significant association for HMW in general) and women (significant association for industrial cleaning agents) consistent with exposures observed by job. This could probably be explained by gender differences in job exposures in job choice or in suscebtibility[9;51;73;74]. We cannot estimate the effect of susceptibility in our study. Therefore, further research is needed to elucidate whether these findings reflects true susceptibility gender differences as proposed by Jacobsen [51] or they are due to gender specific occupational exposures differences in asthma findings and occupation.

Ammonia use in home cleaning was significantly associated with current asthma. There were no results significantly associated with current asthma in occupation as professional cleaner, health care worker, user of disinfectants, metal worker, welder and solder in the occupational modules. The majorities of the estimated ORs were below unity for specific air way exposures and asthma in the occupational modules and most of the associations could not be estimated due to low numbers of cases.

Use of ammonia cleaning product in home settings may be a risk factor for adult current asthma. This result is partly consistent with those of ECRHS occupational modules, where increased risk of asthma was found for health care workers using ammonia and/or bleach at work and those using household cleaning sprays. We were not able to show any increased risk of current asthma among those working with metals including welding in metals as shown in ECRHS occupational modules among those welding in painted metals and those welding with manual metal arc technique[13;14;18].

A high risk of (occupational) asthma in cleaners has been noted in other populations as well [2;6;8]. In cleaners, chemicals, such as bleach, ammonia-containing compounds and disinfectants including glutaraldehyde and formaldehyde, have been identified as specific causes of respiratory disorders including asthma. Increased risks of asthma have also been related to specific job tasks, such as mopping the floor, cleaning windows, mirror and ovens, and washing dishes[75]. Some studies have identified specific professional cleaning products associated with asthma, including bleach and sprays [16;17]. Still, it remains unclear how much asthma is related to specific sensitisation to certain chemicals or other agents and how much of the asthma among cleaners is associated to inflammation in the airways induced by exposure to a mixture of irritant chemicals and other compounds[75].

Our findings of increased prevalence of asthma related to use of cleaning agents raise the question whether it is primary causation or provocation of asthma symptoms in people with pre-existing asthma caused be these agents. We are not able to answer this question because the study is cross-sectional and we mainly report work related asthma with no distinction between immunological or non-immonulogical phenotypes of asthma. However, the increased PRs of current wheeze and current asthma for cleaners and caretakers were similar in those with and without nasal allergy (i.e possible atopy). This may suggest an irritant rather than sensitisation mechanism of LMW exposures.

Moreover, positive association between asthma prevalence and HMW agents exposure is consistent with results from other population based prevalence and incidence studies using a asthma specific job exposure matrix[2;9].

We found that exposure to LMW agents was less clearly associated with asthma, although the nested category of cleaning agents was related to asthma in women but not in men. These results are partly consistent with those of the ECRHS study and the French Pollution Atmosphérique et Affections Respiratoires Chroniques (PAARC) survey, where a risk of asthma was found for subjects exposed to industrial cleaning agents and reactive chemicals[2;9]. Industrial cleaning agents could be considered as LMW according to the JEM but some of them also as irritants[2].

Workplace exposures to irritants (not high peak-exposure) showed an increased PR for asthma in women. Evidence is growing for the importance of repeated moderate exposures to irritants in the development of asthma[76;77] and evidence is accumulating about the effects of irritant exposures on occurrence of asthma through studies in specific occupations such as cleaning or pulp and paper industries[2;78]. Recent population based studies suggest a greater relative risk of asthma in occupations with low-to-moderate respiratory irritant exposure, and that these exposures are common[78]. Additional studies are needed to determine the airway effects of such exposures.

Growing up in country and having siblings

In the unexposed persons a protective effect on asthma of farming childhood and having more than one sibling was seen in our material[79]. However, a subsequent occupational exposure to high and low risk asthma agents seems to counteract this effect, which can explain the elevated prevalence ratio in occupationally exposed persons growing up in farms as well as having more than on sibling.

Other studies support this result. A study of Dutch farmers and agricultural industrial workers showed slightly steeper association between endotoxin exposure and respiratory effects such as wheezing and wheezing with shortness of breath among those with a farm childhood compared with those with no farm childhood[54]. In the ECRHS it was found that participants exposed in childhood to many children at home or in day care experienced more asthma in adulthood[55]

LIMITATIONS

Cross-sectional data analysis

In general, a cross-sectional study design provides good estimates of the prevalence of different conditions and exposures. However the cross-sectional design is generally a weak design as the associations investigated may go in both directions. In the present study, this will be a problem when examining occupational exposures on the one hand and asthma on the other hand. The state of asthma may be a consequence of occupational exposures and asthma may itself contribute to changes in occupational exposures because individuals with asthma may change work environment because of the asthma condition (i.e. healthy worker effect). In the case of OA, cross-sectional studies are particularly liable to underestimate rates because of the healthy worker effect bias referred to above[31].

Our cross-sectional study can lead to either over- or underestimation of the prevalence both regarding outcome and exposure, because we are not able to distinguish between WRA, WEA, and OA and thereby the direction of the association between asthma and exposure.

We were not able to confirm elevated PRs for established high-risk occupations and exposures such as farmers, painters, laboratory technicians, plastic and rubber workers, welders and exposures to latex, highly reactive chemicals and textiles[6-8]. Nevertheless, non-significant associations for male spray painters (PR=3.2; 95%CI 0.7-15) and bakery workers (PR=2.2; 95%CI 0.8-6.4) are

consistent with other reports. This can be explained by a lack of statistical power for some job groups and occupational exposures. Alternatively, a lower than expected prevalence of asthma in these risk occupations may reflect either possible differences in occupational risk factors or selection tendencies into different occupations in Denmark compared with other European countries[64;65] or the fact that the job title does not cover exposure since the JEM shows flour as a risk factor.

Misclassification of asthma

Discrepancies with previous findings could also be due to asthma misclassification since our diagnoses were based on self-reported respiratory symptoms and/or medication. We have validated our definition of the symptomatic sample to ascertain that this method was a relevant method for identifying asthmatics[80]. As a substitute for a "gold standard" for asthma, we used self-reported "physician-diagnosed asthma" in phase II which yielded a Youden´s index (sensitivity added specificity minus 1) of 0.64.

We did not include validation of asthma diagnosis with bronchial hyper-responsiveness or atopy status by skin prick test. This could lead to an under estimation of associations between differing occupational exposures and asthma. However, the ECRHS definition of asthma symptoms or medication has been validated against bronchial responsiveness[8], indicating that such underestimation, if present, would be minimal. Additionally a cross-sectional design is unable to establish whether atopy and/or bronchial hyperresponsiveness measured precede or follow the first clinical manifestations of asthma. Moreover, our results were fairly consistent using the three definitions of asthma (ranging from relatively sensitive to relatively specific). Therefore we believe that a possible underestimation in our study is minimal.

Nevertheless, we believe that a validation by clinical outcome data would strengthen the documentation of our reported results especially when defining different phenotypes of asthma and nasal allergy.

Misclassification of occupational exposure

In study 2-3 we relied on recall of occupations and occupational exposures in the 10 preceding years which potential introduce bias and therefore a potential over- or underestimation of the associations between asthma and exposure. We think that 10 years is a short time span and that young adults in general are able to remember sufficient details about their jobs in the last 10 years. Combined with that, we believe it is unlikely that that participants in certain jobs were more likely to participate in the study, we think that recall bias is of minor importance. Different exposures and awareness of symptoms in different social classes may also be a factor leading to over or under estimation of possible associations between symptoms.

We believe that the participant's general knowledge about occupational asthma and its causes are low and therefore it is unlikely that participants in certain jobs are more likely to report or become diagnosed with asthma than those in other jobs and the application of JEM reduce reporting or recall bias, thus minimizing potential overestimation of the prevalence of asthma in relation to occupational exposure.

Use of asthma specific job exposure matrix

The JEM have the limitations that exposure variations within job titles are not taken into account and it does not identify asthma risks associated with unknown agents[15;48]. Another limitation in our study was that we applied the JEM without the recommended expert reviewing step, which could lead to lack of incorporating country specific exposure risks and lack of improvement of specificity in estimates for jobs with uncertain exposures. In our main results only minor changes were seen

after exclusion of jobs with imprecise estimates of exposures and in the ECRHS [7], the odds ratios did not change considerable after the expert review step. Therefore we find that the use of the JEM without the expert reviewing step in our study is still useful.

ECRHS Occupational modules

Using the ECRHS occupational module categories, we were able to assess exposures and tasks across a range of occupations but our analyses are limited by a very small number of participants with current asthma and with each specific work-related task and product.

The description of occupational tasks and use of different products may not adequately reflect the potential range of home cleaning exposures and workplace exposures. Nonetheless, by assessing the risk of current asthma within the module categories it can better characterise occupational risk categories than job title and JEM categories alone[14]

We did not make any attempt to estimate a trend in a dose-response analysis for different cleaning agent exposure levels and we have no measures of lung function before and after cleaning activities. Therefore, further longitudinal studies are needed to get more insight into these important questions to strengthens our results.

Non-response and healthy worker effect

The response rates in this study were fair in phase I (73%) and in phase II (52%), however it could have biased the results away from the null. Nevertheless, I believe that potential bias is non-differential with respect to the primary aim of the survey namely risk factors for adult asthma in general and not occupational risk factors in particular. Therefore, it is unlikely that participants in certain jobs were more likely to participate in the study. The findings of higher asthma rates among the youngest and among females may partly be due to differences in participation rates of participants in phase II or ascribed either to genuine differences in asthma prevalence between

genders or to information bias because of gender differences in symptoms reported. The presence of information bias can not be ruled out. To reduce this potential bias we have taken sex into consideration in our analysis.

In study 1 we examined the effect of current job or last held job and not job at the time of worsening respiratory symptoms, which could lead to healthy worker effect i.e. over-representation of participants who are more resistant to occupational exposures and an underestimation of associations between asthma and occupational exposures[6;7].

Statistical considerations

The size of the study was based on power calculations where we intended to conduct clinical investigations in a population consisting of 1,004 exposed to JEM high risk asthma agents and 4,847 unexposed. The asthma prevalence was set to more than 7 % among exposed. Setting significance at 5% this yielded a power of 80% to show OR=1,45 and a power of 90% to show OR=1.53 in a case control analysis. We did not perform power calculations for the multivariate scenario. The Bonferroni p-value significance level in study 1 was 0.05 /26 =0.0019. Therefore with the significance level of 0.05 in our multiple comparison scenario with many observations based on very low "n" we can not rule out type I & II errors (i.e. could lead to false-positive or false-negative results) in many of the estimates. However in the major JEM groups we judge this to be of minor importance and therefore we interpret these results as valid.

We included a priori gender, age, county, and smoking as potential confounders in our regression model in study 1, we further tested other potential confounders by including them in the model one by one. Except for gender, we did not find significant differences between crude estimates and adjusted estimates for neither the a priori confounders nor for the other potential confounders. Still our results may be distorted by residual confounding, random sampling error, selection bias, and information bias.

In study 3 we restricted our analysis to participants recruited as random sample only but the impact on results could not be estimated because the number of cases was very low in the modules and none of the products included at least 5 cases.

Asthma reporting and compensation systems in Denmark

In 2007 a total of 102 cases of occupational asthma was identified in the Danish National Board of Industrial Injuries[81]. A crude estimation in our data showed a mean asthma incidence rate of 3.3 per 1000 person-years in 2003 [58]. Using a population attributable risk at 15% of asthma due to occupation we estimate 1341 new cases/year of occupational asthma among the employed population in Denmark in 2007.This suggests that occupational asthma is considerably under reported in the reporting and compensation systems in Denmark.

Closing remarks

This population based cross sectional study has some weaknesses in the estimation of the effect of occupational exposures and asthma as the associations investigated may go in both directions. Participants come from many different occupations and the numbers involved in a possible risk occupation will be only a minor part. However, the population size makes it possible at least in the larger groups to detect relevant increased risks. The nested case-control design can due to the higher proportion cases have comparable strength but more specific knowledge about specific exposures relevant to asthma should be specifically addressed in other studies.

Despite the weaknesses of a retrospective design, we think we can get some information about occupational exposures and asthma based on the large population-based material and the validated exposure assessment methods and at least it can be used to generate hypotheses and compare with similar material in ECRHS.

7. CONCLUSIONS

The associations between occupational exposures and asthma seem different in men and women. This could probably be explained by gender differences in job exposures or in job choice. However we can not rule out a possible difference in susceptibility due to gender.

Our data indicate a consistent increased prevalence ratio of asthma in female cleaners and caretakers and in men with workplace exposure to HMW agents.

Use of ammonia cleaning products in home setting might be a risk factor for adult asthma .

Those who grew up on a farm and/or had more siblings showed increased risk of asthma associated with occupational exposures.

However the cross-sectional design is generally a weak design as the associations investigated may go in both directions

8. FUTURE STUDIES

Further research including follow-up studies with recording of respiratory health effects and detailed exposure assessment are needed to confirm our results and to elucidate whether these findings is true susceptibility gender differences or gender specific occupational exposures differences in asthma findings and occupation.

In future studies it would be necessary to increase the number of participants in risk occupations and among those with potential asthmagenic exposures in order to raise the power to detect occupational exposures with an impact on work related asthma.

We did not perform the expert evaluating step using the JEM. This should be done in order to improve the exposure assessment in future studies within our material.

Further research aiming for identification of work related exposures could lead to elimination of these risk factors for adult asthma and thereby help prevent new cases of work related asthma and since occupational exposures are common this suggests a relevant public health issue.

9. SUMMARY

Rationale: Certain occupations and occupational exposures have been associated with asthma in European and other industrialised countries. Occupational risk factors for asthma have rarely been studied in Denmark

Objectives:

- To describe occupations and occupational exposures associated with the prevalence of asthma in Denmark by gender.
- To assess the modifying effects of country or farm childhood, parental asthma, nasal allergy and number of siblings on the association between occupational exposures and asthma.
- To describe the distribution of exposures to known or suspected occupational agents associated with the prevalence of asthma

Methods: In a population-based cross-sectional study among Danish men and women aged 20 to 44 (phase I), 7,271 persons (73% response rate) answered a screening questionnaire including asthma symptoms, occupation smoking status, parental asthma, country or farm childhood, number of siblings and nasal allergy. Asthma was defined as: current wheeze, current asthma, and doctor-diagnosed adult-onset asthma. Current or last held job was coded according to ISCO-88 and linked to an asthma specific job exposure matrix. Associations between asthma and occupational exposures were evaluated using log-binomial regression analysis, stratified by gender and adjusted for county, age and smoking status. In a stratified analysis we assessed prevalence ratios (PR) by gender, smoking status, nasal allergy, parental asthma, country or farm childhood and number of siblings in separate models.

In a second phase (phase II) of the study in 2003-2006 we contacted 2,312 responders from phase I and invited them to a clinical visit including a face-to-face interview and a clinical investigation. 1,191 participated (52%).

In 2006-2007 all the persons who in the questionnaire in phase II (n=1,136) had given a job history were re-contacted by mail asking to do a telephone interview about specific occupational activities during the last 10 years. A series of job-specific questionnaires for selected occupations or exposures (homemakers, cleaners, nurses, metal workers, and specific exposures related to welding, soldering and disinfectants) were used;. Interview by telephone were conducted for 880 persons (77%) answered the interview about specific occupational activities, including 672 persons with complete information about asthma and one or more selected occupations or exposures. Asthma in phase II was defined as an attack of asthma or nocturnal shortness of breath in the last year, current asthma medication, or both.

In each group of responders to the modules, associations between exposures and asthma were evaluated in a nested case-control design, using unconditional logistic regression analysis.

Results: In phase I, occupation as a cleaner or caretaker was associated with an increased prevalence of current asthma and current wheeze compared to non-manual workers. These associations were most pronounced in females than in males (PR 2.17; 95%CI 1.47-3.21 and PR 1.50; 95%CI 1.02-2.18, respectively) and not modified by nasal allergy. Exposure to high molecular weight agents was associated with an increased prevalence of current asthma in males where an increased prevalence of current asthma was found among women exposed to industrial cleaning agents when compared to a category unlikely to be exposed to any asthmagenic compounds. Workplace exposure to irritants showed an increased PR for current asthma in women. Those who grew up on a farm or had more siblings showed increased current asthma PRs associated with occupational exposures.

In phase II, use of ammonia in home cleaning setting was associated with current asthma (OR=4,35, 95%CI 1.26-15.07). .

Conclusions: The associations between occupational exposures and asthma seem different in men and women in part probably explained by gender differences in job exposures, in job choice or in susceptibility.

Our data indicate a consistently increased risk of asthma in female cleaners and caretakers and in men with workplace exposure to high molecular weight agents.

Use of ammonia cleaning products in home settings might be a risk factor for adult asthma.

Those who grew up on a farm and/or had more siblings showed increased risk of asthma associated with occupational exposures.

However the cross-sectional design is generally a weak design as the associations investigated may go in both directions

10. SUMMARY IN DANISH

Rationale: Visse erhverv og erhvervsmæssig eksponering har været forbundet med astma i Europa og andre industrialiserede lande. Erhvervsmæssige risikofaktorer for astma er sjældent blevet undersøgt i Danmark

Formål:

o At beskrive erhverv og erhvervsmæssig eksponering i forbindelse med forekomsten af astma i Danmark efter køn.

o At vurdere betydningen af opvækst på landet, forældre astma, nasal allergi og antallet af søskende i forholdet mellem erhvervsmæssig eksponering og astma.

o At beskrive fordelingen af kendte eller mistænkte erhvervsmæssige agens i forbindelse med forekomsten af astma.

Metoder: I en populationsbaseret tværsnitsundersøgelse blandt danske mænd og kvinder i alderen 20 til 44 (fase I), besvarede 7,271 personer (73% responsrate) et spørgeskema om astma, erhverv, rygestatus, forældre astma, opvækst på landet, antal søskende og nasal allergi. Astma blev defineret som: Aktuel hvæsen, aktuel astma, og lægediagnosticeret voksendebut astma. Det aktuelle eller seneste job blev kodet efter ISCO-88 og knyttet til en astma specifik job eksponerings matrix. Associationer mellem astma og erhvervsmæssige eksponeringer blev vurderet ved hjælp af log-binomial regressionsanalyse, stratificeret efter køn og justeret for amt, alder og rygestatus. I en stratificeret analyse vurderedes køn, rygestatus, nasal allergi, forældre astma, opvækst på gård og antallet af søskende i forskellige modeller.

I anden fase (fase II) af undersøgelsen i 2003-2006 kontaktede vi 2,312 deltagere, som havde svaret på spørgeskemaet i fase I og inviterede dem til en klinisk undersøgelse, herunder et interview og en klinisk undersøgelse. 1,191 deltog (52%).

I 2006-2007 blev deltagere fra fase II med de seneste op til 10 års erhvervsmæssig oplysninger (n

=1,136) igen kontaktet per brev, med henblik på at lave et telefoninterview om særlige erhvervsmæssige aktiviteter med brug af job-specifikke spørgeskemaer for udvalgte erhverv, hjemmegående, rengøringspersonale, sygeplejersker, metalarbejdere, og særlige eksponeringer i forbindelse med svejsning, lodning og brug af desinfektionsmidler. I alt 880 personer svarede telefoninterview om særlige erhvervsmæssige aktiviteter, heraf 672 med fuldstændige oplysninger om astma og en eller flere udvalgte erhverv eller eksponeringer.
Astma i fase II blev defineret som et anfald af astma eller natlige åndenød i det sidste år, nuværende astmamedicinbrug, eller begge dele.
I et case-kontrol-design (case-non-case) blev relationen mellem eksponeringer og astma evalueret med logistisk regressionsanalyse.

Resultater: I fase I, fandtes rengøringserhvervet forbundet med en øget forekomst af astma og hvæsen sammenlignet med ikke-manuelle arbejdere. Disse relationer var mest udtalt hos kvinder (PR henholdsvis 2.17, 95% CI 1.47-3.21 og PR 1.50, 95% CI 1.02-2.18) og ikke ændret ved nasal allergi. Eksponering for højmolekylære stoffer var forbundet med en øget forekomst af aktuel astma hos mænd og en øget forekomst af aktuel astma blev fundet blandt kvinder udsat for industrielle rengøringsmidler i forhold til en kategori, som ikke forventedes at være udsat for nogle astmagene agens. Eksponering på arbejdspladsen for irritanter viste en øget PR for aktuel astma hos kvinder. De, der voksede op på en gård eller havde flere søskende viste øget aktuel astma forbundet med erhvervsmæssig eksponering.
I fase II, var brug af ammoniak i hjemmet ved rengøring forbundet med astma (OR = 4.35, 95%CI 1.26-15).
Konklusioner: Associationerne mellem erhvervsmæssig eksponering og astma synes forskellig hos mænd og kvinder. Dette kan måske forklares med kønsforskelle i eksponeringer, job valg eller sårbarhed.

Vores data indikerer en konsistent øget risiko for astma hos kvindelige rengøringsassistenter og blandt mænd med eksponering for højmolekylære stoffer på arbejdspladsen.

Brug af rengøringsmidlet ammoniak i hjemmet kan være en risikofaktor for voksen astma.

At vokse op på en gård og/eller med flere søskende øger risikoen for astma efter erhvervsmæssig eksponering.

Men tværsnitsdesignet er generelt et svagt design til at belyse hvilket tidsmæssig årsagsforløb, der er mellem erhvervseksponeringer og astma.

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12. APPENDIX

RAV Face-to-face interview questionnaire (selected questions used in this study)

RAV Occupational modules. Telephone interview questionnaire

Paper 1 *Asthma and occupation: A population-based study among young Danish adults* (submitted)

RAV FACE-TO-FACE INTERVIEW QUESTIONNAIRE

(SELECTED QUESTIONS USED IN THIS STUDY)

	M	F
Deltagerens køn	☐	☐

Deltagerens fødselsdato ☐☐ ☐☐ ☐☐
DAG MÅNED ÅR

JEG VIL STILLE DIG NOGLE SPØRGSMÅL. I BEGYNDELSEN VIL DE FLESTE OMHANDLE
DIN VEJRTRÆKNING. HVOR DET ER MULIGT, VIL JEG BEDE DIG SVARE "JA" ELLER "NEJ".

Hvæsen og trykken for brystet

	NEJ	JA
1. Har du haft pibende eller hvæsende vejrtrækning på noget tidspunkt i de seneste ***12 måneder***?	☐	☐

HVIS "NEJ" GÅ TIL SPØRGSMÅL 2, HVIS "JA":

	NEJ	JA
1.1 Har du på nogen måde haft åndenød samtidig med pibende eller hvæsende vejrtrækning?	☐	☐
1.2 Har du haft denne pibende eller hvæsende vejrtrækning ***uden***	NEJ	JA

at være forkølet? ☐ ☐

2. Er du vågnet med en fornemmelse af trykken for brystet på noget tidspunkt i de seneste ***12 måneder***? NEJ JA ☐ ☐

Åndenød

3. Har du haft et anfald af åndenød i løbet af dagen, når du var i hvile på noget tidspunkt i de seneste ***12 måneder***? NEJ JA ☐ ☐

4. Har du haft anfald af åndenød, som kom ***efter*** svær anstrengelse på noget tidspunkt i de seneste ***12 måneder***? NEJ JA ☐ ☐

5. Er du blevet vækket af et anfald af åndenød på noget tidspunkt i de seneste ***12 måneder***? NEJ JA ☐ ☐

HVIS "NEJ" GÅ TIL SPØRGSMÅL 6, HVIS "JA":

5.1 Er du blevet vækket af et anfald af åndenød i de seneste **3 måneder?** NEJ JA ☐ ☐

HVIS "NEJ" GÅ TIL SPØRGSMÅL 6, HVIS "JA":

5.1.1 Er du ***i gennemsnit*** blevet vækket af et anfald af åndenød ***Mindst en gang om ugen*** i ***de seneste 3 måneder?*** NEJ JA ☐ ☐

HVIS ”NEJ” GÅ TIL SPØRGSMÅL 6, HVIS ”JA”:

5.1.1.1 Hvor mange gange om ugen er du ***i gennemsnit*** blevet vækket af åndenød i de ***seneste 3 måneder?*** ANTAL ☐☐

Astma

NEJ JA

14. Har du nogensinde haft astma? ☐ ☐

HVIS “NEJ” GÅ TIL SPØRGSMÅL 15, HVIS “JA”:

NEJ JA

14.1 Er dette bekræftet af en læge? ☐ ☐

ALDER

14.2 Hvor gammel var du, da du havde dit første astmaanfald? ☐☐

ALDER

14.3 Hvor gammel var du, da du havde dit seneste astmaanfald? ☐☐

NEJ JA

14.5 Har du haft et astmaanfald i de seneste ***12 måneder***? ☐ ☐

Uddannelse og erhverv

Nu vil jeg gerne stille dig nogle spørgsmål om, hvilke typer jobs du har haft.

Jeg er interesseret i hvert af de jobs, du har haft i mere end 3 måneder i træk. Disse jobs kan være udenfor hjemmet eller i hjemmet, fuld tid eller deltid, lønnet eller ulønnet, inklusive selvstændig virksomhed, for eksempel i en familievirksomhed.

Vær venlig kun at medtage deltidsjobs, hvis du havde udført dem i mere end 8 timer om ugen.

39. Er du for øjeblikket: SÆT KUN ET KRYDS

a) ansat (inklusive militærtjeneste)?	1	☐
b) selvstændig?	2	☐
c) arbejdsløs, arbejdssøgende?	3	☐
e) arbejder ikke på grund af dårligt helbred?	4	☐
f) fuldtids hjemmegående?	5	☐
g) fuldtids studerende?	6	☐
h) pensioneret?	7	☐
i) andet?	8	☐

HVIS ANSAT ELLER SELVSTÆNDIG ELLER FULDTIDS HJEMMEGÅENDE GÅ TIL SPØRGSMÅL 41

	NEJ	JA
40. Har du været ansat i noget job i tre måneder i træk eller mere?	☐	☐

HVIS "JA", GÅ NU TIL ERHVERVSSKEMAET

Deltagernummer | | | | | |

41. Hvis du havde mere end et job i samme firma, eller hvis du udførte flere jobs samtidig, vil vi gerne tale om dem hver for sig. Begynd venligst med dit nuværende eller seneste job.

JOB	41.1 Hvad er (var) titlen på dit nuværende (seneste) job? FAG	41.2 Hvad producerede firmaet, selskabet eller organisationen, eller hvilke services tilbød det? BRANCHE	41.3 Hvilken måned og hvilket år begyndte du i dette job? MÅNED ÅR	41.4 Hvilken måned og hvilket år ophørte du med dette job? MÅNED ÅR
JOB 1				
JOB 2				
JOB 3				

JOB 4				
JOB 5				
JOB 6				
JOB 7				
JOB 8				
JOB 9				
JOB 10				

ÅR

Rygning

NEJ JA

92. Har du nogensinde røget i op til et år? ☐ ☐

['JA' betyder mindst 20 pakker cigaretter eller 360 gram tobak i gennem hele livet,

eller mindst én cigaret om dagen eller én cigar om ugen i et år)

NEJ JA

92.2 Ryger du **nu**, d.v.s. indenfor den seneste måned? ☐ ☐

92.3 Er du holdt op med at ryge, eller har du skåret forbruget ned? ☐ ☐

Occupational modules. Telephone interview questionnaire

Vejledning til jobmoduler

Baggrund

Der er 7 forskellige moduler. Om en forsøgsperson skal deltage i et modul eller ikke deltage i et modul afhænger af svaret på et ”Screeningsspørgsmål”. Der er 7 screeningsspørgsmål som skal spørges til forsøgsdeltagere ved et telefoninterview.

Screeningsspørgsmål

Stil alle screeningsspørgsmålene først, før der skiftes til modulerne.
Alle screeningsspørgsmålene refererer til en aktivitet som har varet i mere end 3 på hinanden følgende måneder i mindst 8 timer ugentligt de seneste 10 år indtil den kliniske undersøgelse.
Hvis en forsøgsperson svare bekræftende på et sreeningsspørgsmål, skal det verificeres at aktiviteten varede i mere end 3 på hinanden følgende måneder.

1. Rengøring og/eller vask i hjemmet: Rengøring i hjemmet (gulv, tæpper, møbler, badeværelse, vinduer; og/eller tøjvask.
2. Alle typer af rengøringsassistenter; inkluderende hjemmerengøringsassistenter (rengøringskone), rengøringsassistenter på skoler, kontorer, i offentlige bygninger,…….
3. Ansatte i social- og sundhedsvæsenet herunder alle typer sygeplejersker, inkluderende hjemmesygeplejersker, hjemmehjælpere, sygehjælpere, social og sundhedshjælpere, social

og sundhedsassistenter, tandplejere, jordemødre, anæstesiassistenter, assistenter i almen praksis.

4. Desinfektionsmidler er kemiske blandinger som benyttes til at nedbryde bakterier og andre mikroorganismer. Desinfektionsmidler bruges i forskellige faggrupper som landmænd og andre landbrugsmedhjælpere, laboratoriearbejdere, industri- og butiksslagtere, rengøringsassistenter, sygeplejersker og andre sundhedsplejearbejdere. Kontrollering af kakerlakker med pesticider er IKKE desinfektion.
5. Alle "metalarbejdere".

   Eksempler: maskinarbejdere, højovnsarbejdere, industrirobotoperatører (produktion og reparation), instrumentproduktion, galvanisering.
6. Svejsning hjemme: refererer ikke til jobmatrice og kan derfor være en aktivitet med kortere varighed end 3 måneder.

   Svejsning hjemme er sædvanligvis en bibeskæftigelse som for eksempel reparation af gamle biler.
7. Lodning i hjemmet: refererer ikke til jobmatrice og kan derfor være en aktivitet med kortere varighed end 3 måneder.

   Lodning hjemme er sædvanligvis en bibeskæftigelse for eksempel elektronikarbejde som hobby.

Generel vejledning til modulerne

- Første spørgsmål: se på spørgsmål 41 i hovedinterviewskema
- Hvis der er flere jobs til modulet følges rækkefølgen i matricen (seneste job først og herefter arbejdes nedefter i matricen)
- Første spørgsmål i hvert modul: Registrer et jobnummer

- Sidste spørgsmål i hvert modul: Mærk tilegnet hvert af de pågældende jobs 1-10
- Frekvenskategorisering betragtes alle som et gennemsnitlig antal dage i ugen, indtil sidste undersøgelse.

Aldrig	som der står
<1 dag/uge	f.eks. en gang hver 14. dag, lejlighedsvis, 1 gang om måneden
1-3 dage/uge	f.eks. halvdelen af mine arbejdsdage
4-7 dage/uge	f.eks grundlæggende alle (arbejds-) dage

Der vælges altid en af disse 4 mulige svarkategorier, afkryds aldrig to svarmuligheder.

Det samme gælder for modul 3.5, modul 3.7, modul 4.4, modul 6.2 og modul 7.2.

Modul 1: RENGØRING/VASK I HJEMMET

1.1 Vedrørende rengøring/vask i hjemmet skal dette modul kun sammenkædes med et job i matricen når det drejer sig om en stuepige, oldfrue, ung pige i huset, medhjælpende hustru. Hvis dette ikke er tilfældet, angiv et 0

1.3 Støve af ELLER fejning ELLER støvsugning ELLER tæppebankning

1.4 Flydende universalrengøringsmidler; ikke til tallerkner eller tøjvask

1.5 Strygningssprays : **ikke** dampstrygning

1.6 Ethvert parfumeret eller duftende rengøringsmiddel , enten i pulver, flydende eller på sprayform.

Modul 2: RENGØRINGSASSISTENTER

2.2 Hvis ”somme tider” rengøring af kontorer, registrer et negativt svar

Mere end en svarmulighed:

2.3 Støve af ELLER fejning ELLER støvsugning ELLER tæppebankning

Fabrikker, industriel rengøring

2.5 Strygningssprays : **ikke** dampstrygning

2.6 Ethvert parfumeret eller duftende rengøringsmiddel , enten i pulver, flydende eller på sprayform.

Modul 3: ANSATTE I SOCIAL- OG SUNDHEDSVÆSENET

3.2 Mere end en svarmulighed

3.8 Flydende universalrengøringsmiddel; ikke til tallerkner eller tøjvask

Modul 4: DESINFEKTIONSMIDLER

4.3 Sanitær: toiletter, brusebade, vaskerum

4.6 Hvis deltageren ikke husker den aktive komponent, spørg efter mærke og udfyld så detaljeret som muligt (f.eks. ”HYPOCHLORAN, GUL FLASKE, FLYDENDE”)

modul 5: METALARBEJDERE

5.6 Vejledning m. tegninger fra Arbejdstilsynet vedrørende ventilation

5.7 Vejledning m. tegninger fra Arbejdstilsynet vedrørende åndedrætsværn

Modul 6: SVEJSNING

6.1 Ved svejsning hjemme, kodes med 0

6.7 Vejledning m. tegninger fra Arbejdstilsynet vedrørende ventilation

6.8 Vejledning m. tegninger fra Arbejdstilsynet vedrørende åndedrætsværn

Modul 7: LODNING

7.1 Ved loddearbejde hjemme, kodes med 0

7.2 Vejledning m. tegninger fra Arbejdstilsynet vedrørende ventilation

7.3 Vejledning m. tegninger fra Arbejdstilsynet vedrørende åndedrætsværn

Kodevejledning

Generelt

JA	1
NEJ	2
Irrelevant	8
Ikke kendt/ikke besvaret	9

Spørgsmål om frekvenser

ALDRIG	1
<1 dag/uge	2
1-3 dage/uge	3
4-7 dage/uge	4

Første spørgsmål i hvert modul

Et jobnummer (1-10) , eller 0 for modulerne 1, 6 og 7

Sidste spørgsmål i hvert modul

NEJ 1

JA, forskellige arbejdsopgaver 2

JA, ens arbejdsopgaver 3

10 variable (JOB1, JOB2,…..JOB10) NEJ (1) JA (2)

Modul 1

1.1: kodes med 0 hvis modulet ikke refererer til et job i matricen

Modul 2

2.2: Mere end en svarmulighed; hvert svar nej/ja

Modul 3

3.2 Mere end en svarmulighed; hvert svar nej/ja

3.5 og 3.7

INGEN 1

1-2 2

3-5 3

6-10 4

Mere end 10 5

Modul 4

4.4:

<1 time per dag 1

1-4 timer per dag 2

>4 timer per dag 3

4.6: to felter til fri tekst om navnet på desinfektionsmiddel

Modul 6

6.1 mærk med 0 hvis modulet refererer til svejsning hjemme

6.2:

<1 time per dag 1

1-4 timer per dag 2

>4 timer per dag 3

Modul 7

7.1: mærk med 0 hvis modulet refererer til loddearbejde hjemme

7.2:

<1 time per dag 1

1-4 timer per dag 2

>4 timer per dag 3

JOBMODULER

(efter spørgsmål 44 i hovedinterviewet)

i. Har du været den person som gjorde rent og/eller vaskede i dit hjem?

Ja → udfør modul 1

Nej

ii. Har du arbejdet som rengøringsassistent?

Ja → udfør modul 2

Nej

iii. Har du været ansat i social- og sundhedsvæsenet?

Vi er interesseret i alle typer af sygeplejersker, inklusiv jordemødre, tandplejere, medicinsk teknikerarbejde, hjemmehjælpere, sygehjælpere, social og sundhedshjælpere, social og sundhedsassistenter .

Ja → udfør modul 3

Nej

iv. Har du brugt desinfektionsmidler på arbejde?

Ja → udfør modul 4

Nej

v. Har du arbejdet i et job som medførte produktion, forarbejdning eller håndtering af metal eller metalemner?

Ja → udfør modul 5

Nej

vi. Har du udført svejsning, på arbejde eller hjemme?

Ja → udfør modul 6

Nej

vii. Har du udført loddearbejde på arbejde eller hjemme?

Ja → udfør modul 7

Nej

Modul 1: Rengøring/vask i hjemmet

Undersøgelsescenter

Deltagerens fødselsdato

DAG		MÅNED		ÅR	

1.1 Hvilket jobnummer i erhvervsskemaet refererer dette modul til (kun hvis det referer til et job som stuepige, oldfrue, ung pige i huse eller medhjælpende hustru). Hvis aktiviteten ikke refererer til et af de nævnte jobs i erhvervsskemaet markeres med et 0

1.2 Hvor mange dage om ugen udførte du følgende opgaver?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Rengøring af huset				
Tøjvask i hånden				
Tøjvask med maskine				
Madlavning				

1.3 Hvor mange dage om ugen udførte du følgende rengøringsopgaver?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Støve af, fejning, støvsugning, tæppebankning				
Gulvvask, vådrengøring, aftørring med fugtig klud				
Rengøring af toiletkumme				
Polering, voksning , vaskning med shampoo				
Rengøring af vinduer eller spejle				
Rengøring af køkken (ikke opvask)				

1.4 Hvor mange dage om ugen brugte du følgende rengøringsmidler?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Vaskepulvere (detergenter)				
Flydende universalrengøringsmiddel				
Polermiddel, voks (gulve, møbler)				
Blegemiddel (eksempler)				
Ammoniak (eksempler)				
Afkalkningsmiddel, ætsende middel (flydende)				
Opløsningsmiddel, pletfjernere				
Andre rengøringsmidler				

1.5 Hvor mange dage om ugen brugte du følgende sprays?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Møbelrensningssprays				
Sprays til glas (vinduer, spejle)				
Sprays til gulvtæpper, uldne tæpper, eller gardiner				
Sprays til gulvvask				
Ovnsprays				
Strygningssprays				
Luftfrisker på sprayform				
Andre sprays				

1.5 Hvor mange dage om ugen brugte du parfumeret eller duftende rengøringsmidler?

a) aldrig	1	
b) < 1 dag/uge	2	
c) 1-3 dage/uge	3	
d) 4-7 dage/uge	4	

1.6 Har du været den person som gjorde rent og/eller vaskede i dit hjem i andre tidsperioder?

Nej → *returner til første side i modulet*

Ja, med væsentlige forskellige arbejdsopgaver→ udfør et modul 1 yderligere

Ja, med lignende arbejdsopgaver		
Vær venlig at angive jobnummer (-re) fra matricen :		

MODUL 2: RENGØRINGSASSISTENTER

Undersøgelsescenter

Deltagerens fødselsdato

DAG		MÅNED		ÅR	

2.1 *Hvilket jobnummer i matricen refererer dette modul til ?*

2.2 Hvad/ hvor gjorde du rent? Nævn dine vigtigste arbejdssteder.

	Ja	Nej
Private hjem		
Skoler		
Kontorer		
Sygehuse, apoteker		
Butikker		
Cafeer, restauranter		
Køkkener		
Fabrikker (produktionsområder)		
Udendørs		

2.3 Hvor mange dage om ugen udførte du følgende rengøringsopgaver?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Støve af, fejning, støvsugning, tæppebankning				
Gulvvask, vådrengøring, aftørring med fugtig klud				
Rengøring af toiletkumme				
Polering, voksning , vaskning med shampoo				
Rengøring af vinduer eller spejle				
Rengøring af køkken				
Tøjvask med hænder				
Tøjvask med maskine				
Industriel rengøring (*regelmæssig vedligehold, rengøring af forarbejdningsmaskiner, daglig sprayning af sigter, rengøring af sækkelærredmaskine med trykluft*				
Rengøring med trykluft				
Rengøring med højtryksspuling				
Rengøring med lavtryksspuling				

2.4 Hvor mange dage om ugen brugte du følgende rengøringsmidler?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Vaskepulvere (detergenter)				
Flydende universalrengøringsmiddel				
Polermiddel, voks (gulve, møbler)				
Blegemiddel (eksempler)				
Ammoniak (eksempler)				
Afkalkningsmiddel, ætsende middel (flydende kalkfjernere)				
Opløsningsmiddel, Pletfjernere(eksempler)				
Andre rengøringsmidler				

2.5 Hvor mange dage om ugen brugte du følgende sprays?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Møbelrensningssprays				
Sprays til glas (vinduer, spejle)				
Sprays til gulvtæpper, uldne tæpper, eller gardiner				
Sprays til gulvvask				
Ovnsprays				
Strygningssprays				
Luftfrisker på sprayform				

Andre sprays				

2.6 Hvor mange dage om ugen brugte du parfumeret eller duftende rengøringsmidler?

a) aldrig	1	
b) < 1 dag/uge	2	
c) 1-3 dage/uge	3	
d) 4-7 dage/uge	4	

2.7 Hvor mange dage om ugen brugte du åndedrætsværn eller anden beskyttelse af luftvejene under dit rengøringsarbejde?

a) aldrig	1	
b) < 1 dag/uge	2	
c) 1-3 dage/uge	3	
d) 4-7 dage/uge	4	

2.8 Har du været rengøringsassistent i andre tidsperioder?

Nej → *returner til første side i modulet*

Ja, med væsentlige forskellige arbejdsopgaver→ udfør et modul 2 yderligere

Ja, med lignende arbejdsopgaver

Vær venlig at angive jobnummer (-re) fra matricen :		

MODUL 3: ANSATTE I SOCIAL- OG SUNDHEDSVÆSENET

Undersøgelsescenter

Deltagerens fødselsdato

DAG		MÅNED		ÅR	

3.1 *Hvilket jobnummer i matricen refererer dette modul til ?*

3.2 Hvad var dit job? Identificer dit vigtigste arbejde.

	Ja	Nej
Sygeplejerske hos privat praktiserende læge		
Sygeplejerske hos privat praktiserende kirurg		
Klinisk sygeplejerske på sygehus		
Sygehjælper på sygehus		
Anæstesisygeplejerske		
Tekniker på sygehus		
Hjemmesygeplejerske i private hjem		
Sygeplejerske i beskyttede boliger eller på plejehjem		
Jordemoder		
Sygeplejerske på fødeafdeling		

Tandplejer eller tandklinikassistent		
Hjemmehjælper		
Social og sundhedsassistent		
Social og sundhedshjælper		
Andre		

3.3 Hvor mange dage om ugen udførte du følgende arbejdsopgaver?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Assistance hos almen praktiserende læge				
Arbejde på ambulatorie				
Arbejde som uddannet førstehjælpsarbejder				
Arbejde på skadestue				
Arbejde på intensiv afdeling				
Arbejde på operationsstue				
Arbejde i endoskopiambulatorie				
Arbejde på onkologisk afdeling				
Arbejde på røngen/-nuklearafdeling				
Forberedelse af medicin				
Medicingivning				
Laboratoriearbejde				
Desinfektion				

3.4 Hvor mange dage om ugen brugte du pudrede latex (naturgummi) handsker?

a) aldrig	1	
b) < 1 dag/uge	2	
c) 1-3 dage/uge	3	
d) 4-7 dage/uge	4	

3.5 Hvor mange par pudrede latex hansker brugte du om dagen?

a) ingen	1	
b) 1-2	2	
c) 3-5	3	
d) 6-10	4	
e) mere end 10	5	

3.6 Hvor mange dage om ugen brugte du ikke-pudrede latexhandsker?

a) aldrig	1	
b) < 1 dag/uge	2	
c) 1-3 dage/uge	3	
d) 4-7 dage/uge	4	

3.7 Hvor mange par ikke-pudrede latexhandsker brugte du om dagen?

a) ingen	1	
b) 1-2	2	

c) 3-5 3 ☐

d) 6-10 4 ☐

e) mere end 10 5 ☐

3.8 Hvor mange dage om ugen brugte du pudrede latex fri (ikke gummi) handsker?

a) aldrig 1 ☐

b) < 1 dag/uge 2 ☐

c) 1-3 dage/uge 3 ☐

d) 4-7 dage/uge 4 ☐

3.9 Hvor mange par pudrede latex fri (ikke gummi) handsker brugte du om dagen?

a) ingen 1 ☐

b) 1-2 2 ☐

c) 3-5 3 ☐

d) 6-10 4 ☐

e) mere end 10 5 ☐

3.10 Hvor mange dage om ugen brugte du ikke-pudrede latex fri (ikke gummi) handsker?

a) aldrig 1 ☐

b) < 1 dag/uge 2 ☐

c) 1-3 dage/uge 3 ☐

d) 4-7 dage/uge 4 ☐

3.11 Hvor mange par ikke-pudrede latex fri (ikke gummi) handsker brugte du om dagen?

a) ingen	1	
b) 1-2	2	
c) 3-5	3	
d) 6-10	4	
e) mere end 10	5	

3.12 Hvor mange dage om ugen brugte du følgende rengøringsmidler på dit arbejde?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Vaskepulvere (detergenter)				
Flydende universalrengøringsmiddel				
Blegemiddel (eksempler)				
Ammoniak (eksempler)				
Opløsningsmiddel, pletfjernere(eksempler)				
Ethvert rengøringsmiddel på sprayform				
Andre rengøringsmidler				

3.13 Har du været ansat i social- og sundhedsvæsenet

(Vi er interesseret i alle typer af sygeplejersker, inklusiv jordemødre, tandplejere, medicinsk teknikerarbejde, hjemmehjælpere, sygehjælpere, social og sundhedshjælpere, social og sundhedsassistenter)

i andre tidsperioder?

Nej → *returner til første side af modulerne*

Ja, med væsentlige forskellige arbejdsopgaver→ udfør et modul 3 yderligere

Ja, med lignende arbejdsopgaver		
Vær venlig at angive jobnummer (-re) fra matricen :		

MODUL 4: DESINFEKTIONSMIDLER

Undersøgelsescenter

Deltagerens fødselsdato

DAG	MÅNED	ÅR

4.1 *Hvilket jobnummer i matricen refererer dette modul til ?*

4.2 Hvor mange dage om ugen udførte du følgende arbejdsopgaver med desinfektionsmidler?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Tilberedelse/blanding af desinfektionsmidler				
Fyldning af beholdere før brug				
Desinfektion				
Rengøring af udstyr efter brug				

4.3 Hvor mange dage om ugen desinficerede du følgende?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Sanitære lokaler (toiletter, baderum)				
køkkener				

Medicinske instrumenter				
Laboratorieudstyr				
Industrimaskiner				
Kølehuse				
Dyrestalde				
Drivhuse				
Landbrugsjord				
Slagtehuse				
Slagtebutikker				
Andre fødevarebutikker				
Butikker				
Andre steder				

4.4 På dage hvor du desinficerede, hvor mange timer per dag i gennemsnit brugte du da desinfektionsmidler?

a) <1 time/dag 1 ☐

b) 1-4 timer/dag 2 ☐

c) >4 timer/dag 3 ☐

4.5 Hvor mange dage om ugen brugte du følgende desinfektionsmetoder?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Spray				
Manuel skylning				

Vaske med maskine				
Rengøring af overflader med svamp eller klud				
Rengøring eller skuring af gulv				
Andre metoder(højtryksspuling/lavtryksspuling)				

4.6 Hvor mange dage om ugen brugte du følgende rengøringsmidler?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Formaldehyd				
Glutaraldehyd				
Blegemiddel, klorin (eksempler)				
Chloroamin-T				
Alkohol (ethanol, methanol)				
Ammoniak				
Kvartinære ammoniumforbindelser				
Ethylenoxid				
Halamid				
Hvis du ikke kender den aktive komponent, udfyld med mærke nedenfor:				

Andre produkter				

4.7 Hvilke af følgende åndedrætsværn benyttede du under dit arbejde med desinfektionsmidler?

	Ja	Nej
Ansigtsmaske		
Ansigtsmaske med filter		
Friskluftforsynet åndedrætsværn		
Andre (eks. Skærm mod stænk)		

4.8 Har du brugt desinfektionsmidler i andre tidsperioder?

Nej → *returner til første side af modulerne*

Ja, med væsentlige forskellige arbejdsopgaver→ udfør et modul 4 yderligere

Ja, med lignende arbejdsopgaver		
Vær venlig at angive jobnummer (-re) fra matricen :		

Modul 5: Metalarbejdere

Undersøgelsescenter

Deltagerens fødselsdato

DAG		MÅNED		ÅR	

5.1 *Hvilket jobnummer i matricen refererer dette modul til ?*

5.2 Hvor mange dage om ugen udførte du følgende arbejdsopgaver?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Metalsmeltning				
Valseværksarbejde				
Metalsmeltning og genopvarmning				
Metalstøbning				
Metalformning og borekernefremstilling				
Metaludglødning, afhærdning og hærdning				
Metaltrækning og ekstrudering				
Metalbeklædning/galvanisering				
Metalovertræk/spraymaling				

Metal efterbehandling/rengøring				
Grovsmedning /smedepresseoperatør				
Værktøjsfremstilling				
Maskinopsætter				
Metalværktøjsbetjening				
Metalslibning og polering				
Maskinjustering og samling				
Fremstilling af præcisionsintrumenter				
Automekanikerarbejde				

5.3 Hvor mange dage om ugen udførte du følgende arbejdsopgaver?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Håndarbejde				
Betjening af maskiner tæt ved processen				
Betjening af fuldautomatisk maskine				

5.4 Hvor mange dage om ugen arbejdede du med følgende metaller

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge

Ferro (jern, stål)				
Aluminium				
Andre ikke ferro (kobber)				
Hård metal (tungsten, cobolt,beryllium)				
Andre				

5.5 Hvor mange dage om ugen forekom følgende udsættelser under dine arbejdsopgaver?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Metalstøv og røg				
Støbestøv og røg				
Syrerøg (beklædning)				
Vandbaserede smøremidler				
Oliebaserede smøremidler				
Svejserøg				
Lodderøg				
Organiske opløsningmidler (affedtningsmidler)				
Andre affedtningsmidler(vandbaserede)				
Maling				
Olie og fedt				

5.6 Hvilke af følgende typer ventilation blev brugt ved dit arbejdssted?

	Ja	Nej
Mekanisk ventilation		
Punktudsugning, fast udsugningsrør		
Punktudsugning, flytbart udsugningsrør		
Punktudsugning, udsugningsrør ved spids af værktøj		

5.7 Hvilke af følgende åndedrætsværn benyttede du under dit arbejde med metaller?

	Ja	Nej
Ansigtsmaske		
Ansigtsmaske med filter		
Friskluftforsynet åndedrætsværn		
Andre		

5.8 Har du arbejdet som metalarbejder i andre tidsperioder?

Nej → *returner til første side af modulerne*

Ja, med væsentlige forskellige arbejdsopgaver→ udfør et modul 5 yderligere

Ja, med lignende arbejdsopgaver		
Vær venlig at angive jobnummer (-re) fra matricen :		

MODUL 6: SVEJSNING

Undersøgelsescenter

Deltagerens fødselsdato

DAG	MÅNED	ÅR

6.1 *Hvilket jobnummer i matricen refererer dette modul til ?*

Hvis det referer til svejsning hjemme angives et 0

6.2 Hvis du udførte svejsning i hvor mange timer i gennemsnit per dag svejsede du da?

a) <1 time/dag 1

b) 1-4 timer/dag 2

c) >4 timer/dag 3

6.3 Hvor mange dage om ugen brugte du følgende svejsemetoder?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Elektrodesvejsning (**MMA** (**M**anual **M**etal **A**rc), svejsning med beklædte elektroder)				
MAG/MIG (metal-aktiv-gas/metal-				

inert-gas)				
TIG (tungsten-inert-gas)				
Pulversvejsning (**SAW** (**S**ubmerged **A**rc **W**elding))				
Rørtrådsvejsning (**FCA** (**F**lux **C**ored **A**rc), beskyttelsesgassvejsning med pulverfyldt rørtråd)				
Andre(Modstandssvejsning (punktsvejsning, sømsvejsning, projektionssvejsning, boltesvejsning), plasmasvejsning, lasersvejsning)				

6.4 Hvor mange dage om ugen svejsede du?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Manuelt				
Ved betjening af automatisk svejsemaskine				

6.5 Hvor mange dage om ugen svejsede du i følgende materialer?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Rustfrit stål				

Blødt stål				
Galvaniseret jern eller stål				
Aluminium				
Malet metal				
Andre				

6.6 Hvor mange dage om ugen svejsede du på følgende steder?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Lukkede rum (lastrum, indeni en tank eller lastbil)				
Værksteder				
Skibsværfter, men ikke i lukkede rum				
Udendørs				

6.7 Hvilke af følgende typer ventilation blev brugt ved dit arbejdssted?

	Ja	Nej
Mekanisk almenventilation		
Punktudsugning, fast udsugningsrør		
Punktudsugning, flytbart udsugningsrør		
Punktudsugning, udsugningsrør ved spids af værktøj		

6.8 Hvilke af følgende åndedrætsværn benyttede du under dit svejsearbejde?

	Ja	Nej

Ansigtsmaske		
Ansigtsmaske med filter		
Friskluftforsynet åndedrætsværn		
Andre		

6.9 Har du udført svejsning i andre tidsperioder?

Nej → *returner til første side af modulerne*

Ja, med væsentlige forskellige arbejdsopgaver→ udfør et modul 6 yderligere

Ja, med lignende arbejdsopgaver		
Vær venlig at angive jobnummer (-re) fra matricen :		

MODUL 7: LODNING

Undersøgelsescenter

Deltagerens fødselsdato

DAG		MÅNED		ÅR	

7.1 *Hvilket jobnummer i matricen refererer dette modul til ?*

Hvis det referer til lodning hjemme angives et 0

7.2 Hvis du udførte lodning i hvor mange timer i gennemsnit per dag loddede du da?

a) <1 time/dag	1	
b) 1-4 timer/dag	2	
c) >4 timer/dag	3	

7.3 Hvor mange dage om ugen brugte du følgende lodningsmetoder?

	aldrig	<1 dag/uge	1-3 dage/uge	4-7 dage/uge
Slaglodning (hård eller sølvlodning)				
Blødlodning				
Andre				

7.4 Hvor mange dage om ugen udførte du lodning?

	aldrig	<1	1-3	4-7

		dag/uge	dage/uge	dage/uge
Manuelt				
Ved betjening af fuldautomatisk lodningsmaskine				

7.5 Hvilke af følgende typer ventilation blev brugt ved dit arbejdssted?

	Ja	Nej
Mekanisk almenventilation		
Punktudsugning, fast udsugningsrør		
Punktudsugning, flytbart udsugningsrør		
Punktudsugning, udsugningsrør ved spids af værktøj		

7.6 Hvilke af følgende åndedrætsværn benyttede du under dit svejsearbejde?

	Ja	Nej
Ansigtsmaske		
Ansigtsmaske med filter		
Friskluftforsynet åndedrætsværn		
Andre		

7.7 Har du udført lodning i andre tidsperioder?

Nej → *returner til første side af modulerne*

Ja, med væsentlige forskellige arbejdsopgaver→ udfør et modul 7 yderligere

Ja, med lignende arbejdsopgaver		
Vær venlig at angive jobnummer (-rer) fra matricen :		

PAPER 1

Asthma and occupation: A population-based study among young Danish adults (submitted)