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| Forskningsprogram SNAP X REPROSAFE FLIPP Inriktning: Ekonomiska styrmedel Inriktning: Informationssystem och indikatorer IPP | | | |
| Projekttitel (svensk): FALKONAIR – en registerbaserad fall-kontrollstudie av långtidsexponering för luftföroreningar och hjärtinfarkt | | | |
| Projekttitel (engelsk): FALKONAIR – a register based case-control study of long-term exposure to air pollution and myocardial infarct | | | |
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Miljöforskningsnämnden

Ansökan om projektbidrag inom Naturvårdsverkets forskningsprogram

Sammanfattning på svenska strukturerad enligt följande: 1) Projektets betydelse för programmet
2) Miljörelevans och förväntad betydelse för miljöpolitiken 3) Mål och hypotes 4) Metodik och genomförande
5) Kommunikationsinsatser i relation till programmet:

1) Under de senaste 30 åren har akuta hälsoeffekter vid exponering för luftföroreningar väl dokumenterats i åtskilliga epidemiologiska studier. Däremot har endast ett fåtal studier fokuserats på hälsoeffekter av längre tids luftföroreningsexponering. Trots att konsekvenserna för folkhälsan är mer betydelsefull om man tar hänsyn till hela livet så innehåller SNAP endast ett fåtal studier av hälsoeffekter relaterat till långtidsexponering för luftföroreningar.

2) Tidigare genomförda studier av långtidsexponering för luftföroreningar har utförts i regioner med höga luftföroreningsnivåer, vilket gör riskuppskattningen för svenska förhållanden osäker. Den föreslagna studien kommer därför att bidra med väsentlig kunskap om hälsoriskerna vid långtidsexponering för luftföroreningar vid de nivåer som förekommer i vårt land, vilket är viktigt för den kvantitativa riskbedömningen, framtida revideringar av gränsvärden, vid prioriteringar av den nationella miljöpolitiken och vid utvärderingar av de svenska miljökvalitetsmålen avseende luftföroreningar. Även om riskökningen för hjärtinfarkt relaterat till luftföroreningsexponering troligen är lägre än vissa andra faktorer, så kan detta få omfattande folkhälsokonsekvenser, med hänsyn till sjukdomens höga incidens och att många människor exponeras för förhöjda luftföroreningsnivåer i städer.

3) Syftet med denna studie är att undersöka sambandet mellan långtidsexponering för luftföroreningar och hjärtinfarkt, med särskild fokus på olika aspekter av exponeringen såsom kumulativ dos, duration och olika tidsfönster, samt interaktioner med andra faktorer, såsom socioekonomi och yrke.

4) Vi kommer att använda en metod som vi tidigare utvecklat för att klassificera varje individs exponering för luftföroreningar under flera decennier tillbaka i tiden i en registerbaserad fall-kontrollstudie av hjärtinfarkt omfattande drygt 45.000 fall och över 500.000 slumpmässigt utvalda kontroller. Metoden går ut på att med hjälp av GIS koppla individernas koordinatsatta bostadsadresser till beräkningar av den geografiska spridningen av luftföroreningar under varje år sedan 60-talet i hela Stockholms län. Dessa spridningsmodeller baseras på emissionsdatabaser som innehåller information om utsläpp av kväveoxider och svaveldioxid, vilka konstruerats för 1960, 1970 och 1980. Studien kommer även att dra nytta av en ytterligare emissionsdatabas för 1990 samt spridningsberäkningar för kolmonoxid som utvecklas inom ett annat SNAP-projekt (LEAP), samt de valideringar av dessa modeller som föreslås i en annan projektansökan (EXPOSE).

5) Resultaten från studien kommer att publiceras i såväl internationella vetenskapliga tidskrifter som i nationella media, samt på SNAPs hemsida och programmets slutrapport. Särskilda ansträngningar kommer att göras för att sprida studiens slutsatser till berörda miljö- och hälsomyndigheter och statliga verk, samt andra nationella organ med intresse inom luftföroreningsområdet.

| | År 2004 | År 2005 |
|--------------------------------|---------|---------|
| Summa sökta medel per år i kr: | | |
| | 488.650 | 491.400 |

Miljöforskningsnämnden
Ansökan om projektbidrag inom Naturvårdsverkets forskningsprogram

| Sökta projektmedel fördelade på kostnadslag | År 2004 (kr) | År 2005 (kr) |
|--|--------------|--------------|
| Personalkostnad inkl. soc. avgifter * | | |
| Lars Alfredsson (12%) Professor, PI | 92.000 | 92.000 |
| Mats Rosenlund (20%) Doktorand, Miljöinspektör | 95.000 | 95.000 |
| Melinda Cuzner (5%), Statistiker | 24.000 | 24.000 |
| Tom Bellander (5%) Docent, Miljöhygieniker | 38.000 | 38.000 |
| Övriga omkostn exkl moms (förbrukningsmtrl, analyser, resor etc)** | | |
| Resor | 10.000 | 10.000 |
| Särtryck | - | 5.000 |
| Dispersionsmodellering | 100.000 | 100.000 |
| Delsumma av ovanstående poster: | 359.000 | 364.000 |
| Förvaltningspåslag:35 % | 125.650 | 127.400 |
| Totalsumma per år: (införs sid. 1): | 488.650 | 491.400 |

*) Specificera namn, tjänst **) Specificera

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

| Projekttitel | Finansiär | Tidsperiod | Sökt kr | Beviljat kr |
|---|-----------------|------------|-----------|-------------|
| Betydelsen av miljö och levnadsvanor för uppkomst och förlopp av MS. | FAS | 2004-2005 | | 1.400.000 |
| Epidemiologic Investigation of Rheumatoid Arthritis | AFA | 2004-2005 | | 1.000.000 |
| Betydelsen av miljö och levnadsvanor för uppkomst och förlopp av reumatoid artrit; en multicenterstudie | FAS | 2004-2005 | 1.975.000 | |
| Sambandet mellan cigarettrökning och RA | Vetenskapsrådet | 2004-2005 | 535.000 | |

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

| Projekttitel | Finansiär | Tidsperiod | Beviljat Kr |
|---|-----------|------------|-------------|
| Interaktion mellan fysik aktivitet och kända riskfaktorer för kardiovaskulär sjukdom avseende risken att utveckla hjärtinfarkt. | FAS | 2003-2004 | 500.000 |
| Exponering för mineralolja, lösningsmedel och olika typer av damm och risken att utveckla RA | FAS | 2003-2004 | 542.000 |

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|--|---|
| Datum och sökandes underskrift, vilken samtidigt ger Naturvårdsverket tillåtelse att publicera sökandes namn på sin webbplats: | Datum och underskrift av prefekt eller motsvarande med namnförtydligande: |
| Lars Alfredsson, Professor | Göran Pershagen, Prefekt |

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

Project title

FALKONAIR – a register based case-control study of long-term exposure to air pollution and myocardial infarction

Lars Alfredsson, Institute of Environmental Medicine, Karolinska Institute

Mats Rosenlund, Occupational and Environmental Health, Stockholm County Council

Tom Bellander, Occupational and Environmental Health, Stockholm County Council

Melinda Cuzner, Occupational and Environmental Health, Stockholm County Council

Present state of knowledge

The effects of short-term exposure to outdoor air pollution have been well documented in numerous epidemiological studies during the last 30 years. Health effects of long-term outdoor air pollution have been less documented, even though the implications from a public health point of view may be much more substantial. Epidemiology during the last decade has shown that health effects can occur at unexpectedly low air pollution levels, resulting in reconsideration of air pollution standards in many countries. In principle, there are only three US studies of long-term effects on mortality, one Swedish study on lung cancer incidence, and recently also a Dutch mortality study (Dockery et al 1993, Pope et al 2002, Abbey et al 1991, Nyberg et al 2000, Hoek et al 2002). In the US cohort studies, the exposure classification was based on average air pollution levels from urban background monitor stations, ignoring within-city variation, while both the Swedish lung cancer study and the Dutch study estimated long-term exposure retrospectively for each subject using address data and geographic information systems (GIS). Both of the studies using individual exposure estimations included less than five thousand individuals.

The American cohort studies showed associations between long-term concentrations of ambient particles and increased cardiopulmonary and lung cancer mortality, except for one study showing no such associations using ten years of mortality data. However, a recent follow-up of that cohort showed positive associations between mortality and some of the air pollutants studied using updated mortality data through 1992 (Abbey et al 1999). The Dutch study showed high risk estimates for mortality associated with long-term exposure to traffic-related air pollution, especially for those living near a major road (Hoek et al 2002).

Despite the apparent advantages of low cost and other efficiency benefits compared to the cohort design, there are no published case-control studies on long-term ambient air pollution exposure and cardiovascular disease. Although some studies address the issue of potentially sensitive sub-groups for health effects from air pollution, there is a lack of conclusive data on possible interaction with other factors.

The projects role and importance for the program

In this project we take advantage of an existing large register-based case-control study. An individual air pollution exposure assessment is added and forms the basis for the proposed project. The project will be highly integrated with another SNAP-project (LEAP) because the same exposure assessment technique will be used and already developed contacts with experts who developed this method will be utilized. In addition, new epidemiological expertise from the Unit of Cardiovascular Epidemiology at the Karolinska Institute and the Department of Epidemiology at Stockholm County Council will be added to SNAP and its working groups,

thus providing further integration and co-operation with national epidemiology experts. The project will thus also expand the national air pollution research capacity by including new researchers formerly not within the field. In addition, it will add to the financial support of PhD-studies. The SNAP program includes few large-scale epidemiological studies on long-term health effects, thus the proposed study will make an important contribution to this topic and the understanding of potential effects of lifelong air pollution exposure. The project will also provide important results that can be directly used for future quantitative risk assessment and in the SNAP synthesis report. It is also important to gain experience of actually applying the emission databases and dispersion models in epidemiological exposure-disease calculations, because such databases are currently being developed also in other parts of Sweden. Therefore, the project will especially interact with the other GIS-based and air pollution modeling SNAP-projects (LEAP, PASTA, GIS-tool for exposure). In general, the proposed project takes advantage of the unique possibilities provided by an established well-managed myocardial infarction (MI)-register combined with a previously developed retrospective exposure assessment using address co-ordinates, emission databases, dispersion modeling, and GIS.

Environmental relevance and expected significance for the environmental policy

Considering the high incidence of MI and that many people live in urban areas with increased air pollution levels, even a moderate excess risk would be expected to have a big impact on the public health. The proposed study will contribute to a better understanding and risk assessment for long-term air pollution exposure, especially in the low range of exposure. This is important for future regulatory decisions and priority settings in preventive public health work related to air pollution, and it may also be useful for evaluation of health benefits of regulation. Ambient air pollution levels have declined over the past decades in many countries. In Stockholm County, the ambient air pollution levels are generally low or moderate in comparison to other European or U.S. urban regions. The decreasing importance of industrial point sources has led to recent attention being focused on diffuse emission sources and motor vehicle emissions. Most studies performed to date have been carried out in regions with high air pollution levels in Europe or the U.S. Thus, little is known about potential health effects in the low range of exposure. Instead, data from the studies already performed have been used to extrapolate down to levels that are more common in less polluted areas, such as in the Nordic countries (Bellander et al 2000). This makes the risk assessment associated with lower air pollution levels uncertain. Thus, knowledge about health effects in low-dose situations is needed to validate extrapolations to the lower range of exposure on the dose-response curve.

Aims and hypothesis

The proposed study aims at investigating the association between long-term exposure to urban air pollution and the development of myocardial infarction. We will apply a methodology using historical emission data, dispersion modeling and GIS to assess individual long-term retrospective air pollution exposure, which has previously been developed and used in an epidemiological study (Nyberg et al 2000, Bellander et al 2001). Evaluation of this methods shows that this exposure assessment technique is very cost-efficient and has a high accuracy (Bellander et al 2001). We will apply this technique of exposure assessment using historical dispersion models, address coordinates, and GIS to assess individual long-term air pollution

exposure in a large register-based case-control study of myocardial infarction in Stockholm County. The study includes over 45.000 MI cases and over 500.000 controls randomly selected from the general population in Stockholm County. This will ensure a sufficient power of the study to investigate the relation between air pollution and first-time acute MI sub-divided by different factors. We will especially investigate potential interaction with factors such as socio-economic status and occupation, which is often very hard to accomplish in case-control studies of smaller size because of limited power. The study design and the long-term exposure assessment also makes it feasible to investigate the importance of different aspects of the exposure, such as intensity of exposure, duration of exposure, cumulative dose, and different time windows for individual exposure.

Material, methods and implementation

The design of the study is a population based case-control study comprising the population aged 15-79 years in Stockholm County during the period 1985-1996. Cases of MI were identified in the regional MI-register. Information on immigration and emigration was collected for the period 1968-1996 from a register at Statistics Sweden. Recurrent cases of MI have been excluded using information about previous infarctions. Controls were randomly selected for the period 1984-1996 from the study base using registers of the total population of Stockholm County each year. The sampling of controls was made stratified by gender, age (five-year age groups) and calendar year. Within each strata 1500 controls have been selected. The number of strata was built up from 13 (calendar years) \times 2 (genders) \times 13 (age groups) = 338 strata, which results in a total of 507.000 control subjects. Controls with a previous history of MI are excluded. Information about occupation and social class for cases and controls is obtained using national censuses (Folk- och bostadsräkningen) of the years 1970, 1975, 1980, 1985 and 1990. In the Swedish system for classifying socio-economic group subjects are subdivided into manual workers, non-manual employees and self-employed. The social class for cases and controls will be classified primarily from the preceding census. If the subject was not employed at that census we will use information from the next previous census back in time. Subjects without employment in the two latest censuses will be excluded. Thus, there will be good possibilities to adjust for confounding from different aspects of occupation, socio-economy and income, as well as sex and age, while other individual characteristics important for the MI-risk such as smoking (though less important for MI than for lung cancer) and BMI will not be possible to adjust for (at least on the individual level). Although we have no individual data on smoking habits in the proposed study, data on the current geographical distribution of smoking is available from e.g. a regional survey in 1997, allowing for crude control of present geographical differences at least down to the municipality level. However, the previously published studies have indicated very small effects of confounding from factors such as smoking and BMI or in some cases slightly higher adjusted estimates compared to crude. Another potential confounding factor is noise exposure. For the time being it will not be possible to adjust for noise exposure in the present study. However, the County Administration is currently developing a geographical noise map for the County of Stockholm using GIS, where the propagation of road traffic noise, aircraft noise, and railway noise will be described for the whole region. This will enable at least crude adjustments for current noise exposure, and future development of this tool could result in possibilities to further explore any interaction between air pollution and noise exposure in relation to myocardial infarction within the context of the proposed study.

Based on a detailed regional emission database from 1993 and detailed information on changes in traffic and other historical land-use variations from 1960, emission databases for

air pollution have been reconstructed for the years 1960, 1970, and 1980. These databases describe emissions of nitrogen oxides (NO_x, NO₂) and sulfur dioxide (SO₂) from traffic-related line sources (currently covering over 90% of the estimated emission from road traffic), different point sources (district heating facilities, industries, etc), area sources (diffuse emission sources, e.g. air traffic and merchant vessels), and grid sources (population-density related sources, e.g. local heating, work machines). An additional database is currently being developed for 1990 in another SNAP-project (LEAP). These emission databases, describing the air pollution from different sources, provide information for dispersion calculations to obtain annual mean levels of NO_x, NO₂, and SO₂ everywhere within Stockholm County, with a resolution of up to 100×100 meters (Gaussian model used). Calibration of the models have been performed to minimize deviation when compared to available measured levels of NO₂ and SO₂ for the corresponding period. In addition, because the air pollution levels in the city may vary considerably depending on local traffic conditions and distance to the ground of the dwelling, a street canyon contribution is added for main streets in the city center. Modeled annual NO₂ levels based on a 1995 edition of the emission database correlated well (r=0.96) with measured levels in 16 locations throughout the County (Johansson et al 1999). The dispersion calculations will be further validated by independent air pollution measurement data, as described in a separate application for funding from SNAP ("EXPOSE"). In an ongoing SNAP-project, also dispersion models for carbon monoxide (CO) is being developed. Thus, it will be possible to evaluate if CO is a better indicator for primary emissions from traffic than NO₂, since, contrary to NO₂, there is no atmospheric transformation of CO. There may also be a direct cardiovascular effect from CO, although the ambient levels are low. In order to link the individual addresses to the air pollution dispersion models, the geographical co-ordinates for each subject's home address during 1980, 1985, and 1990 have been collected. These co-ordinates will then be linked to air pollution data from these dispersion models, as described before (Nyberg et al 2000, Bellander et al 2001).

The data collection of cases and controls and all other register data (except air pollution data) have been approved by an ethical committee at the Karolinska Institute (Dnr KS 99-106). An application for expanding the data also with air pollution data will be sent in soon.

Dissemination of results

The results from the study will be presented at national and international scientific conferences and will be published in international scientific journals in the field of environmental medicine. The results will also be presented in Swedish reports aimed at public agencies and the general public. In particular, the knowledge gained from the project will be published on the SNAP website and the results will be included in the final synthesis report of the program.

Time plan

The work will be performed during 2004-2005, and all reporting and dissemination of results will be finished before the end of 2005. Most of the data collection has already been performed and the next major task will be to link the address co-ordinates to dispersion models based on historical emission data, and finally to perform the epidemiological analysis of exposure-disease associations, which will mostly be done during 2004.

References

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Project group – CV:s

Lars Alfredsson, professor in Epidemiology at the Karolinska Institute. PhD in Epidemiology 1983. Mainly carried out research with the aim of identifying causes of cardiovascular diseases and musculoskeletal diseases, and also in the field of pharmaco-epidemiology. Author of more than 160 published scientific articles.

In addition to the applicant, the project group consists of:

Mats Rosenlund, BSc, MPH, Environmental Health Officer, Occupational and Environmental Health, Stockholm County Council.

Tom Bellander, PhD, Environmental Hygienist, Occupational and Environmental Health, Stockholm County Council.

Melinda Cuzner, MSc, Statistician, Occupational and Environmental Health, Stockholm County Council.