FRÅGA 1

Evaluation of Strategic Research Areas (Epidemiology for Health (EpiHealth)) Self-evaluation

The self-evaluation is part of the background information for the evaluators in their assessment of the increased support to strategic research areas and the included research environments. The self-evaluation is distributed to each one of the 43 research environments included in the government’s investment in strategic research areas.

The focus of this self-evaluation is
Research Output
Strategic value for society and the business sector
Collaborations
Research and Education Integration

The following should be considered when you are carrying out the questionnaire:
The self-evaluation should be answered in consultation with co-applicant(s).
When answering the questions, the original grant application and the previously reported information provided in the annual follow-up studies should be considered.
There is limited space for your answers, use it to give as detailed and to-the-point information as possible.

Last response date for the survey is May 19, 2014

FRÅGA 2

OUT: Research output

FRÅGA 3

OUT 1a) Please fill out the proportions of different kinds of publications from the strategic research environment (numbers should correspond to the number of publications reported in the 2010-2013 follow-up studies)

<table>
<thead>
<tr>
<th></th>
<th>Number of outputs 2010</th>
<th>Number of outputs 2011</th>
<th>Number of outputs 2012</th>
<th>Number of outputs 2013</th>
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<tr>
<td>Books</td>
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<td>2</td>
<td>2</td>
<td>0</td>
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<tr>
<td>Book Chapters</td>
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<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Journal Articles</td>
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<td>659</td>
<td>803</td>
<td>819</td>
</tr>
<tr>
<td>Conference Publications</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>44</td>
<td>56</td>
<td>47</td>
<td>47</td>
</tr>
</tbody>
</table>
FRÅGA 4

OUT 1b) Please comment on the publication profile and its development over time (Out 1a) (1600 characters)

We have reported a high number of publications, reflecting the wide research activities in epidemiology that EpiHealth has coordinated. There is a growing trend of publications, and in fact EpiHealth is the leading Strategic Research Area (SRA) in Sweden according to number of publications in 2013 when a total of 819 papers were recorded in bibliometric systems (2626 papers during total period). The number of outstanding publications has also increased. This is a reflection of the increased research activities, but also influenced by collaboration within national and international consortia. Research areas of special importance are genetic studies linked to cardiovascular disease, diabetes, cancer and osteoporosis, but also gene-environment interaction studies for risk of obesity and type 2 diabetes (DM2).

A large number of publications present findings from environmental medicine, as well as social epidemiology, for example based on multi-level and life course analyses. This demonstrates the versatile nature of the the EpiHealth networks at Lund (LU) and Uppsala (UU) universities, as numerous very high profile publications have emerged either from individual research groups or through large international consortia led by members of the EpiHealth network. Many of these studies have capitalized on the large, well characterized population-based cohorts such as the Malmö Preventive Project (MPP) and the Malmö Diet Cancer (MDC) Study at LU, and ULSAM and PIVUS at UU. Among the most excellent publications many are published in these journals: Nature, Nature Genetics, PlosGenetics, JAMA, Diabetes, Circulation, Lancet, and New Engl J Med.

FRÅGA 5

OUT 2) What research results from the strategic research environment have had the most significant academic impact? Describe briefly the development and standing of the research compared to the research performed internationally. (1600 characters)

Some of the major research findings, where researchers from EpiHealth at LU and UU have been active in collaboration, include the ones describing the genetic map of risk variants for hypertension, dyslipidemia, myocardial infarction, stroke, DM2, osteoporosis and some cancers. These papers have been of the highest international standard and contributed not only to a deeper knowledge of disease etiology, but also to the definition of potential drug targets when true causal pathways (biological mechanisms) have been characterized based on causal inference (Mendelian randomization), as an analytic method. Indeed, some of the publications have led to further collaborations with scientists at centres of excellence (e.g. Harvard University), where EpiHealth has helped support short term visits for students working within those projects via the program BLUE ScY. Furthermore, a list of excellent publications related to nutritional, genetic and reproductive epidemiology have contributed to deeper understanding of the importance of diet in adult disease and the role of processes that impact early life growth and development and by consequence set disease trajectories for later life. The SIMSAM-Early life group (LU) have led much of this work. In addition, our research on social epidemiology, environmental medicine and the origins of musculoskeletal disorders have furthered understanding of the modifiable social and environmental risk factors that impact this important age-related morbidity. The new concept of “Early Vascular Ageing” has attracted international interest and also been implemented in a screening project in Malmö, with a focus on arterial stiffness and telomere biology. Another achievement is the application of metabolomics to find patterns of fatty acids behind the development of cardiovascular disease, and ultimately the link to DM2.

FRÅGA 6

STR: Strategic value for society and the business sector

Compare to question B6 in the follow-up focusing on the industrial and/or societal problems and needs that have been addressed in the research.
The EpiHealth SRA now comprises a wide range of excellent researchers in many areas of medicine, with strong focus on epidemiology and etiology of cardiovascular disease, type 2 diabetes, cancer, muscular-skeletal disorders, and dementia, just to name a few areas. This means that we have the capacity to offer excellence in research and applied epidemiology to the society and business sector. We also constantly try to increase our capability to transfer research results and knowledge to these end-users. One example from the business sector is the collaboration with Astrazeneca Ltd. Through this collaboration, EpiHealth provided epidemiological data in a joint project for evaluation of knee pain in the population (the MOA Study) to determine unmet medical needs. We also collaborate with several SME’s (OLINK, Fiomi, Athera) regarding development of proteomics and new biomarkers for cardiovascular diseases. Members of the EpiHealth Network also lead major components of two large public-private partnerships formed under the banner of the Innovative Medicines Initiative (DIRECT and SUMMIT), and in doing so make us of infrastructures organised by EpiHealth. Another example, but from the societal sector, is how expert advice from EpiHealth, based on data from the Medical Birth Register, has helped Stockholm’s County Council to revise its recommendation for induction of labor in pregnant women with extended gestational time >42 weeks. In addition, the mapping of environmental health hazards has been of importance to local county council authorities in Region Skåne. Research in health economy has influenced planning of health care needs and its utilization, as well as evaluation of cost-effectiveness of clinical methods used.

Since the mapping of cholera in London by John Snow in the 1800s, high quality epidemiological data has been recognised as a major asset for any advanced public health system. One important task is to monitor patterns and trends in the availability and quality of public health and hospital care at regional and national levels. Epidemiological surveillance of environmental health hazard has influenced the collaboration between EpiHealth researchers and technical experts. The results include better technologies for environmental surveillance that can also be translated into commercial products. The role of lifestyle and rising epidemic of obesity is a societal challenge with many implications for health and disease. Recognizing the already heavy and growing socioeconomic burden of health care, Modern medicine is moving toward the use of biomarker technologies to help stratify treatments in order to improve the cost-effectiveness of interventions and to reduce unnecessary side-effects. The interface between biomarker research and treatment application is the area of gene-environment interaction research. Researchers within the EpiHealth SRA have analysed gene-environment interactions to better understand the differing role of lifestyle in subjects with varying genotypes. This may translate into new knowledge to tailor lifestyle, for example diet and functional food, to the need of the individual ("personalized medicine"). Health economy can contribute to planning of health care and monitor its utilization for cost-effectiveness. An important aspect is to evaluate costs and savings linked to prevention. In the area of biomarker development and understanding of disease mechanisms, researchers within EpiHealth could contribute to the development of new ways to monitor diseases as well as deliver new potential targets for drug development.

We have developed contacts and projects with both global enterprises such as Astrazeneca Ltd, and with smaller biotech companies, functional food designers and other SMEs. This has been based on joint projects and also the fact that experienced researchers from EpiHealth held part-time positions at Astrazeneca Ltd. (G Engström, LU, and Lars Johansson, UU). In Lund, contacts with the AntiDiabetic Food Centre and biotech companies have contributed to the developments of nutritional epidemiology, exemplified by the joint symposia and seminars that EpiHealth organized. Another task is to deliver new data on the pathogenesis of common disorders in order to find and dissect new causal biological mechanisms for establishing potential drug targets. As many observational findings in conventional epidemiology are spurious and prone to bias, new approaches in molecular epidemiology exploit advanced genetic methods to dissect these causal pathways by use of methods called causal inference modelling (Mendelian randomization). In fact, several excellent publications from EpiHealth in high-ranking journals have used the novel approaches to highlight causal biological pathways, which provide excellent targets for the pharmaceutical industry and biotech SMEs. One example is the pathway linking the biomarker proneurotensin, involved in metabolic and endocrine mechanisms, and its genetic regulators, to various disease outcomes in women (Melander O, et al, JAMA 2012). Another example is that researchers are closely collaborating with academically derived SME’s to find new biomarkers for cardio-metabolic diseases. Some of these biomarkers, including mapping of the gut microbiome, are analyzed in collaboration with private laboratories, for example in Germany.
FRÅGA 10

STR 6) Exemplify how industrial and societal needs have been identified and how it has influenced the choice of research problems addressed. (1600 characters)

We have developed EpiHealth primarily as a unique academic research network, but because industry and society represent "end users" of the epidemiological data and inferences we generate, we have focused on also establishing a strong and functional interface with these entities. Major societal issues that we tackle include the rising tide of obesity, caused by adverse lifestyle, and its adverse health consequences. As food quality and dietary patterns, as well as lack of exercise, are important determinants of obesity and DM2 against a background of genetic susceptibility, we developed nutritional-genetic epidemiology. Other societal challenges addressed by EpiHealth include the environmental changes leading to pollution and adverse health impacts (environmental epidemiology). The challenge from demographic change, including an ageing workforce, is addressed in a cluster of projects, conducted in close collaboration with industry and the public sector. EpiHealth has coordinated the formation of a national advocacy platform to promote "Sustainable work as a Resource for Health, Innovation and Growth" (H2020). We have been heavily involved in high-lighting the adverse impact of climate change on the heat stress for manual workers in already hot climates. This is a cross-disciplinary theme at the Pufendorf institute (LU). Epidemiologists and aerosol technologists work together on health effects from exposure to small particles and climate change. We also focused on the importance of early life factors for programming of adult health in a life course perspective. Finally, EpiHealth (P Nilsson) has participated in national committees to propose new laws in 2014 (Westerberg committee) to facilitate epidemiological research built on registers and biobanks. Similar advice was given when the so called LifeGene law was passed in 2013 (L Lind).

FRÅGA 11

COL: Collaborations

Collaboration with co-applicant(s) universities/research institutes

FRÅGA 12

COL 7) What is the long term plan for the collaboration between host-university and co-applicant(s) regarding the strategic research environment? (1600 characters)

LU and UU work together for the development not only of EpiHealth but also for other strategic research areas (EXODIAB, eSSENCE). This is based on a long-term agreement that the two oldest universities of present-day Sweden should continue the development for excellence in science and its applications. This bold ambition is based on both formal contracts and a number of less formal contacts and research collaborations. Within EpiHealth this is very obvious as many of our activities link the two universities, most pronounced as manifested in our EpiHealth Cohort screening project, now reaching almost 15,000 screened middle-aged subjects for phenotyping, biobanking and advanced molecular epidemiology when resources from SciLife are used. In addition, the Meta-Health project, led from UU, is a national project of great importance to link a number of national cohorts for the study of risk factors of rare diseases when high numbers of screened subjects is important. Meta-Health is financed by another Swedish Research Council-funded national infrastructure, the Biobanking and Molecular Resource Infrastructure of Sweden (BBMRI.se), with which EpiHealth actively collaborates (www.bbmri.se), both on a national and a local level. The Director of EpiHealth is also responsible for the hub of BBMRI.se at LU, linking Faculties of Medicine and the Faculty of Engineering. Thus, a long-term strategy is to strengthen the ties between LU and UU benefiting the research that EpiHealth is involved in, besides other priority areas in medicine and technology, i.e. the life sciences. This will be supported by BBMRI.se for advanced used of biobank technologies, where representatives from LU and UU will play important roles during the next period 2016-2018, and by "Svensk Nationell Dataljänst (SND.se) where our cohorts are listed and put on display, showing meta-data.
When EpiHealth started in 2010 the administrative routines had to be developed to facilitate the collaboration between LU and UU. These routines included how reports were written from UU and the research finances summarized from both LU and UU for the annual reports to the funding agencies, written, finalized and submitted from LU and the Director of EpiHealth. Another important routine was the compilation of publications, including full papers, book chapters and symposia proceedings, to be sent from UU to LU on an annual basis. A list of available cohorts (some with biobanks) for joint epidemiological research was developed, including both population-based and patient-based cohorts, and put on both the EpiHealth and the SND web-sites (36 cohorts).

We also wanted to develop effective and fair systems for the leadership structure of EpiHealth, with a representation of each university reflecting the proportion of funding agreed in the first application (LU 60%; UU 40%). This had the consequence that one additional seat for a UU representative was decided in 2012 to increase the balance within the Steering Committee (Board) of EpiHealth. This new representative was S Sandler, Dean of the Faculty of Medicine at UU, thus strengthening the links between the two universities also for administrative aspects.

Finally, we have organized annual meetings for researchers, as well as annual advanced courses in statistics and epidemiology every second year at LU and in between at UU, respectively. This had the implications that researchers from one university travelled to the other, for increased contact and mutual exchange, thus strengthening the EpiHealth joint structure.

We have collaborated mostly with EXODIAB for diabetes epidemiology, register use, and gene-environment interactions in the etiology of DM2. This collaboration is formalized in the way that we have an exchange of representatives in the Boards of EXODIAB and EpiHealth. Furthermore we collaborate with eSSENCE at LU for development of technical equipment used for surveillance of the fetus during deliveries, and with MULTIPARK for epidemiology of Parkinson’s disease and dementia. Of utmost importance is the collaboration with SciLife for advanced molecular epidemiology.
FRÅGA 19

Collaboration Case Study

We have chosen a case study format. This to create the possibility for you to focus on one successful (“best practice”) project that includes collaboration as an example of when it has served the purpose of conducting research of high international quality with relevance for society or the business sector.

You can describe your case in a separate document to be uploaded below.
One excellent research area where EpiHealth has made a significant contribution is Nutrition- and Genetic Epidemiology (NGE). This project aims to understand how food intake is shaped by external factors, to what degree and how genes interact with the diet to modify disease risk, and to understand the role of gut and oral microbiome in this process. It aims for better understanding of the “healthy diet” concept, and development of new functional food products in close contact with biotech SMEs and the food industry, with the ultimate goal to offer the public better and healthier products.

<table>
<thead>
<tr>
<th>Name of project</th>
<th>Project period</th>
<th>Short description (500 characters)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>2010-2020</td>
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</tr>
</tbody>
</table>

**FRÅGA 20**

**COL 12) Choose one of your research projects that include collaboration with one or several non-academic organizations or companies to illustrate how collaboration a) has improved the research quality and b) has improved the prerequisites for society and the business sector to utilise the research.**

Please enter the name of the chosen project and the project period in the table. Also give a short description of the project (500 characters).

<table>
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</tr>
</tbody>
</table>

**FRÅGA 21**

**Please enter collaboration partners (maximum 2) and verified contact information.**

<table>
<thead>
<tr>
<th>Name of organisation</th>
<th>Name of contact person</th>
<th>Verified contact information, including e-mail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partner 1 Antidiabetic Food Center</td>
<td>Inger Björck</td>
<td><a href="mailto:inger.bjorck@appliednutrition.lth.se">inger.bjorck@appliednutrition.lth.se</a></td>
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<td>Partner 2 GATCBiotech</td>
<td>Peter Pohl</td>
<td><a href="mailto:customservice@gatc-biotech.com">customservice@gatc-biotech.com</a></td>
</tr>
</tbody>
</table>
We have integrated our research in the undergraduate training of medical students by providing formal teaching in medical statistics and epidemiology using research projects as examples, but also by providing tutors for papers or short reports. Many of these papers are later published. More recently we have supported the Faculty of Medicine at LU to revise the curriculum for improving standards of undergraduate teaching in medical statistics and epidemiology, to be presented in 2014.

For research students an annual course for “Advanced epidemiology” has been organized, with international speakers, alternating between LU and UU, but also an annual conference for tutors and PhD students together at Örenäs Castle close to Lund. Students are also encouraged to participate with abstracts and presentations at the many symposia organized by EpiHealth, as a way to give academic feedback on their findings.

Members of EpiHealth are active in the so called SPSS courses provided for PhD-students where basic training is given in the way statistical analyses are carried out with a tutor. These courses are given four times annually at LU. At UU other courses in basic epidemiology and genetic epidemiology are given on a regular basis as part of the PhD training program.

A fruitful collaboration between EpiHealth and other networks (META-Lund and SIMSAM) has led to the development of a research-oriented PhD school at LU with a focus on environmental health hazards. This has been well attended and successful.

The newly started research school for gerontology, geriatrics and healthy ageing called The Swedish National Graduate School for Competitive Science on Ageing and Health (SWEAH) is officially supported by EpiHealth. It is funded by the Swedish Research Council and with its leadership located at LU. There will also be arranged an international course (ISSA) in August 2014.
Applied epidemiology, along with biostatistics and bioinformatics, is an integrated part of both industrial and societal needs. EpiHealth serves these needs by recruiting and developing expertise in three main areas: basic epidemiology (gene-environment interactions), clinical epidemiology (patient centered research, health economy, population spread of infections) and building of infrastructures (biobanks, biostatistics, registers). A number of PhD students linked to EpiHealth have published their theses in these areas (listed in our annual reports), and thereby provide both new knowledge and scientifically trained experts for the industry (i.e. for planning of study designs, development of drug targets, functional food) and society (i.e. for health surveillance, register applications, and health economy).

Research-based knowledge is visible through the very high number of excellent publications and offered to the industry and society. This knowledge is translated into practice when public health problems are addressed or programs developed for reproductive health, i.e. for safeguarding healthy pregnancies and deliveries.

In addition, Master of Public Health programs, where EpiHealth is active, include a wide range of epidemiological aspects, for example when dealing with the distribution of risk factors and health surveillance. Students will later be able to work at societal institutions or in international organizations (Sida, WHO) for global health tasks.

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**FRÅGA 25**

**INT 14)** Explore to what extent the educational programs associated with the strategic research environment provide the industry and society with qualified personnel and research based knowledge. (1600 characters)

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**FRÅGA 26**

**INT 15)** Explain to what extent you use international recruitment of students (including research training of PhD students and post-docs) to achieve the goals for the strategic research environment? (1600 characters)

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**FRÅGA 27**

**OTHER**
In essence we have kept to our primary strategic plan to develop EpiHealth, as outlined in the 2009 application. We launched our EpiHealth screening cohort (45-75 years) in Uppsala (2011) and Malmö (2012) following recruitment of staff and setting up the screening centers, rented by EpiHealth. This forms the first steps to accomplish a large national population-based cohort, with a potential for collaboration with the corresponding LifeGene cohort (0-45 years).

We have also recruited a number of senior scientists for positions paid fully or partly by EpiHealth. One such example is a new Professor in Medical Epidemiology at LU (G Engström) that was announced in early 2011 for recruitment but not appointed until end of 2012 because of formal reasons in the evaluation process. Two other professors in epidemiological methods (J Björck, LU) and genetic epidemiology (E Ingelsson, UU) have strengthened the academic infrastructure of EpiHealth during the project period, as well as one senior lecturer in reproductive epidemiology (K Källén, LU). Our ambition is to fund and recruit candidates for even more academic positions. Our financial resources are, however, limited and this has caused us to move at a slower pace than planned for, even if we have tried our best to use resources in a very effective way.

EpiHealth is a growing strategic research area and very proud of its recruitment of young brilliant researchers and many PhD students, as well as some senior researchers. It is still keeping its gender balance. In fact, in 2013 there was a perfect gender balance in the EpiHealth network (108 women and 108 men in total). This is influenced by the fact that many women are active in epidemiology and especially in our two new focus areas for excellence in epidemiology, nutritional epidemiology and reproductive epidemiology. The present Director (P Nilsson) and vice Director (M Orho-Melander) share responsibilities and both represent EpiHealth at various meetings and symposia, thus demonstrating the equity we aim for. EpiHealth has also been able to show diversity in the recruitment of young researchers from different countries, and ethnic groups, as well as foreign students coming to do joint research for a few months, or even longer periods. Especially the Department of Work- and Environmental Medicine at LU has started several projects in Third World countries for collaboration on societal needs where skilful epidemiological studies can make a difference. Furthermore, another facet of EpiHealth is the “Global Health” research group in Malmö, offering collaborative projects and also a Master of Public Health course where modern principles of community epidemiology are taught. The new “Boston, Lund, Umeå Education in Science opportunity” (“BLUE ScY”) program (P Franks) links LU with Umeå and Harvard universities to increase rotation of research students between the universities. This will increase the supply of competence.


Our long-term strategy is also built on the reform of programs for undergraduate students at LU, for example in the areas of “Medical statistics” and “Medical epidemiology” (J Björck, J Merlo). These reforms will update and modernize the curriculum needed in order to increase the interest from talented young students to develop skills and research projects in epidemiology (reports, full papers, PhD theses) linked to different topics within the EpiHealth structure. Similar revisions are taking place at UU. Another aim for the future is the organization of annual conferences (retreats) for tutors and their PhD students at the Örenäs Castle in Skåne, where lectures and group sessions, including feedback on students’ papers is given. This is planned for the third time in 2014. Because of these activities and strategic plan for the future we are confident that EpiHealth will expand and further recruit young talented researchers, keeping equity and diversity as important goals. Our fruitful contacts with academic excellence centers and universities abroad (Cambridge, Harvard, Leiden, Oxford, Paris, Stanford, Broad Institute, Boston, George Institute, Sidney, and NIH in Washington D.C.) all contribute to this bold ambition.
The funding was needed to start the EpiHealth cohort, now with almost 15,000 screened subjects (45-75 years). The procedures include phenotyping and biobanking, with the potential to use the SciLife infrastructure for high-throughput molecular technologies. The cohort, and its cognitive tests, was also important in procuring a 3-year structural grant (15 mill SEK) from the Swedish Research Council for research in vascular dementia in 2013 (S Elmståhl). It is also possible to use the rich cohort data for validation studies of findings in other contemporary population-based cohorts (SCAPIS). A new epidemiological study started in 2013, aiming to analyse trans-generational influences on risk of chronic disease conditions, in the “Malmö Offspring Study” (MOS), supported by EpiHealth, where advanced phenotyping is combined with gene-environmental interaction analyses (diet-gene-microbiota). MOS has been supported by a 5-year grant from the Swedish Research Council and is currently used to bring many competent researchers in epidemiology together. Of strategic importance is also that the funding helped to build academic infrastructures at both LU and UU.

We constantly try to envisage future needs of epidemiological research according to industrial and societal needs. One problem for the pharmaceutical industry is the lack of new drugs under development, especially relevant for cardiovascular disease. Our ambition is to use available population-based cohorts, advanced methods, and causal inference (Mendelian randomization), to identify true mechanism leading to disease and thereby potential drug targets. This is of great importance because the exploration of non-causal pathways for interventions might prove to be ineffective and very costly, as recently illustrated by the costly failures to test HDL cholesterol elevating drugs for prevention of myocardial infarction in several large-scale randomized studies.

A societal need now and in the future is: (a) to better understand the role of lifestyle and susceptibility genes for unhealthy diet in order to better prevent the rising tide of obesity and risk of type 2 diabetes. EpiHealth contributes to a better understanding of the gene-environmental interactions leading to these conditions. This can lead to development of new functional food products. Another societal need that will increase in importance is (b) the negative influences from environmental hazards. This is met by advanced mapping of pollution in defined geographical areas, where we work together with technical experts and authorities for better community planning. A third area is (c) to map and characterize risk factors acting in early life, by use of reproductive epidemiology surveillance. In fact, EpiHealth has been instrumental to create and develop a local network at LU named “Centre of Excellence for Reproduction and Perinatal Sciences” (CERPS), in collaboration with representatives from the clinical sciences and SIMSAM-Lund, supported by the Swedish Research Council.

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