2016-05677 Malmqvist, Ebba UF-5

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Information about application

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Descriptive data

Project title (Swedish)*

Luftföroreningar inomhus och utomhus- effekter av exponering för gravida kvinnor i Afrika

Project title (English)*

Outdoor and household air pollution-exposure and effects on pregnant women in Africa

Abstract (English)*

In 2012, one in eight deaths worldwide resulted from air pollution. For Africa lack of data is a barrier to estimate effects. Satellite images indicate detrimental levels, but monitoring and high resolution outdoor air pollution modelling is lacking. Household air pollution is also a major source of exposure, more knowledge on how different cook stoves, fuels and habits affect exposure is crucial. No high quality study of the effect of outdoor and indoor air pollution on pregnant women in Africa has so far been conducted.

We will investigate consequences of air pollution in a prospective cohort of women recruited during pregnancy at public health facilities in Ethiopia. Outdoor air pollution will be assessed by high quality modelling which combines measurements with Geographical Information System tools and aerial and topographical imaging. Individual exposure will be linked to the model by residential address. Indoor exposure will be assessed by questionnaires and validated by measurements. Emission factors from different fuels and cooking methods, and particle characteristics will be assessed in our Aerosol Lab in Lund. Data on pregnancy outcomes, exposures and confounders will be compiled and epidemiological studies on the effect of outdoor and household air pollution on pregnancy complications will be done.

This study, which will increase knowledge of not only health impact but also of source characteristics, will provide important knowledge for appropriate policy making.

Popular scientific description (Swedish)*

Att luftföroreningar har en negativ inverkan på vår hälsa är knappast någon nyhet. Från epidemiologiska studier, i de delar av världen där luftföroreningar övervakas, har man gång på gång bevisat tydliga samband mellan inandade partiklar och hälsoeffekter. Det är denna typ av studier WHO grundar sina hälsogränsvärden för utomhusluften på – till exempel att halten partiklar som är mindre än 2,5 mikrometer inte bör överstiga 10 mikrogram per kubikmeter som årligt medelvärde. Dock finns det stora vita fläckar på kartan över länder där luftföroreningar mäts. Exempelvis görs i stort sett inga mätningar alls i stora delar av Afrika, och inte heller vetenskapliga studier om hälsoeffekter. Från satellitbilder över Afrika kan man gissa sig till att luftföroreningshalterna på flera ställen vida överstiger WHOs gränsvärden.

Etiopien är ett av dessa ställen, och vi åkte dit för att kontrollera detta. Våra mätningar visade att utomhusluften i Adama, Etiopiens tredje största stad, hade halter på i genomsnitt ca 100 mikrogram per kubikmeter - tio gånger högre än vad WHO förespråkar. Det har visat sig att av Etiopiens befolkning är det gravida kvinnor som är allra mest drabbade. Förutom att de konstant blir utsatta för luftföroreningarna utomhus (det är mycket liten skillnad på "utomhus" och "inomhus" i stora delar av Afrika, husen är på inga sätt täta och har sällan t ex fönsterglas) blir de också utsatta för de luftföroreningar som bildas vid matlagning. Detta är en aktivitet som utförs minst två, oftast tre gånger dagligen. 95 % av befolkningen använder kol, ved eller kodynga som bränsle och en majoritet av husen har inget separat kök utan matlagningen sker i samma rum alla sover, och lever, i. Föroreningshalterna blir enorma, vi uppmätte genomsnittliga halter på 800 mikrogram partiklar mindre än 2,5 mikrometer per kubikmeter då man lagade mat med ved.

Etiopien är också ett av länderna med högst mödradödlighet i världen, med havandeskapsförgiftning som huvudorsak. Denna graviditetskomplikation är i Etiopien orsak till 16 % av mödradödligheten och 25 % av de barn som är dödfödda är det på grund av havandeskapsförgiftning. Vi vill i denna studie titta på något ingen tidigare tittat på, nämligen hur starka sambanden mellan luftföroreningar och havandeskapsförgiftning, samt låg födelsevikt, egentligen är i Etiopien. Dessutom vill vi se om luftföroreningarna gör att kvinnorna oftare får tuberkulos.

Detta vill vi göra genom att utveckla en modell för att med stor noggrannhet kunna uppskatta faktisk exponering för alla gravida kvinnor i Adama. Det pågår en annan studie, till vilken man nu rekryterar gravida kvinnor då de besöker mödravården. Denna grupp av kvinnor, som kommer att vara ungefär 2000 personer stor, kommer vi använda. Kvinnorna får fylla i en detaljerad enkät som bland mycket annat berör var de bor, hur ofta och länge de lagar mat och vilket bränsle de använder. I vårt laboratorium i Lund vill vi mäta hur mycket föroreningspartiklar som faktiskt släpps ut varje minut då man lagar mat över öppen eld eller med en traditionell etiopisk spis med ved, kol och kodynga. Med hjälp av detaljerade satellitkartor och mätningar på flera strategiska platser under olika årstider kan vi modellera hur luftföroreningarna utomhus ser ut för kvinnorna under olika perioder av deras graviditet. När vi kombinerar detta med information om matlagningsvanor och föroreningshalter från matlagningen uppmätta i vårt laboratorium kan vi räkna ut varje kvinnas totala exponering för luftföroreningar under olika perioder av graviditeten. Från mödravårdcentralerna övervakar man varje kvinnas hälsa, och har full koll på om, och iså fall när, en kvinna utvecklar havandeskapsförgiftning eller tuberkulos. Man övervakar även det nyfödda barnets vikt. Det kommer även finnas bra data på andra riskfaktorer.

Denna information kombinerad med modellen och laboratoriestudierna gör att vi kan studera samband mellan luftföroreningshalterna och kvinnornas hälsa med mycket högre noggrannhet än de få studier av denna typ som hittills gjorts i Afrika, och se om och i sådana fall hur mycket luftföroreningarna bidrar till den höga mödradödligheten i Etiopien. Om det visar sig vara så är det mycket troligt att det ligger till på samma sätt i flera andra delar av Afrika och andra utvecklingsländer. Denna kunskap kan komma att vara ett mycket viktigt verktyg då det gäller att påverka myndigheter att sätta gränsvärden och lagstifta för att få bukt med utsläppsproblematiken.

Calculated project time*

2017-01-01 - 2020-12-31

Countries which the research is relevant to*	Low-income countries (unspecified) > Low-income countries (unspecified) > Low-income countries (unspecified) Africa > East Africa > Ethiopia
Collaboration countries	Ethiopia

30303. Occupational Health and Environmental Health

Research plan

Reporting of ethical considerations*

All research involving personal data has potential integrity violations for the individual. We hope that our planned research, through increased scientific knowledge, in the long run would contribute to better maternal health in LMIC.

Crucial for minimizing potential integrity violations is that data are handled properly in order to minimize the risks for identifying individual persons in the data. Data will be stored at the Department of Occupational and Environmental Medicine in Lund where long experience of handling personal data exist. All datamanagement with identifiable data will be performed on a computer with no internet access. An identifiable code key will be developed that will be stored in a secure way according to the Ethical Permission. Code key and other related data will be stored separetely. Thus, no identifiable variables or coordinates will be left in the database. All study data and management will be managed under code, accessible only to the study investigators at the respective sites and the research data management team.

The work will be conducted in line with international rules and agreements. All participants will receive care in accordance with Ethiopian guidelines (which are concordant with 2015 WHO guidelines) provided free of charge. Before inclusion and collection of data written informed consent was and will be obtained. Ethical permissions for the birth cohort exist both from the Research Ethics Review Boards at Lund University and the Institute of Science and Technology, Addis Abeba, Ethiopia. An amendment for the air pollution part has been sent in. We do not anticipate any difficulty in obtaining permission as our research team has previously had similar projects approved. The results will be presented in an aggregated form and not on an individual level.

The project includes handling of personal data

Yes

The project includes animal experiments

No

Account of experiments on humans

No

Research plan*

See following page for attachment

EFFECTS OF OUTDOOR AND HOUSEHOLD AIR POLLUTION ON PREGNANT WOMEN IN AFRICA

Purpose and aims

Air pollution is the major environmental threat to human health (GBD). Recent satellite images revealed that many places in Africa exceed WHO guidelines for outdoor air pollution, although measurements and high spatial resolution modeling is lacking. Household air pollution from cook stoves is also detrimental for health in LMIC, more knowledge on how different cooking habits can affect exposure is also crucial. Although, pregnant women and her fetus could be the most exposed and susceptible populations to air pollution, high quality studies in developing countries are lacking.

Our purpose is to investigate the effect of air pollution in regards to pregnancy complications, such as preeclampsia, tuberculosis and low birth weight, in a prospective birth cohort with high quality data on outdoor and household exposure to air pollution.

Specific aims:

1. **Model exposure to household air pollution** by combining measurements with cooking habits.
2. **Model exposure to outdoor air pollution** by combining measurements with GIS-tools and aerial and topographical images.
3. **Perform epidemiological studies** on the hypothesized association on air pollution and risk for preeclampsia, tuberculosis and low birth weight.

The results will provide important knowledge so appropriate measures can be taken for pregnant women in LMIC.

Survey of the field

Outdoor air pollution in Africa- the health threat we do not monitor or model: The exposure from outdoor air pollution is increasing in Africa due to growing urbanization, motor vehicle use, and population growth. The unregulated industrial and traffic emissions cause the air quality in African cities to rapidly deteriorate and become a key threat to health, environment, economy and quality of life for millions of Africans [1]. Satellite pictures can give a rough estimate of the problem, in fact a recent study suggests that a large part of Africans are exposed to PM (Particular Matter) levels above WHO guidelines [2]. In order to be able to conduct studies on the health effect of outdoor air pollution, air pollution models with a finer spatial resolution is crucial. Due to lack of financial and technical resources high quality air pollution exposure assessment in Sub-Saharan Africa is very scarce [3] and air quality is not monitored at all in this part of the world (see figure 1). This knowledge gap makes it hard to develop adequate policy and calculate health costs. We aim to contribute by applying cost effective, yet state-of-the art measurement and modelling tools in an area with an already up and running prospective cohort.

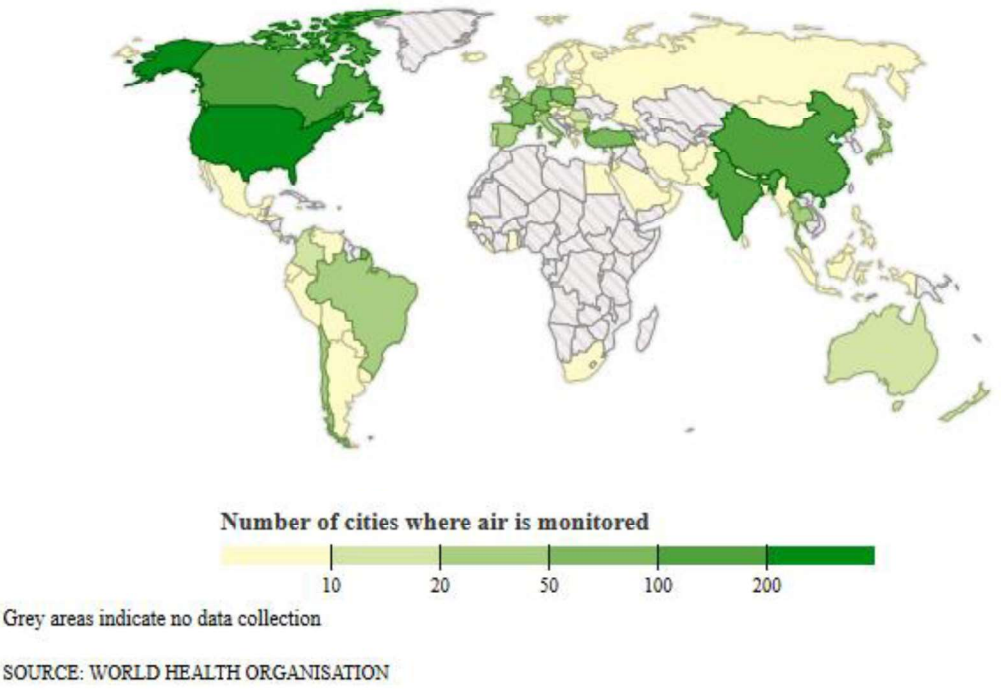

Figure 1. Map from WHO, published in The Guardian Dec 2015, showing the lack of air pollution monitoring in the area.

Household air pollution-the knowledge need of emissions by cooking habits: Globally, household air pollution is estimated to be responsible for 3.5 million premature deaths annually [4]. One in two households in the world rely on solid fuel, i.e. biomass burning for heating and cooking [5]. About 95% of the energy supply in Ethiopia comes from biomass sources [6]. In this country, the household air pollution was 2007 the estimated cause of more than 50 000 deaths and nearly 5% of the national burden of disease [6]. Still, due to lack of knowledge the effect on the pregnant women is not included in this assessment, even though cooking is mainly performed by women. During pregnancy the inhalation rates increased with 50% [7]. The few existing studies on household air pollution effects during pregnancy have crude exposure assessment without details on cooking habits (e.g. stove type or fuel used) [8]. Intervention in Sub Saharan Africa has failed and the exposed population has doubled since 1980 [5]. Yet, Sub-Saharan Africa has been identified by economists as the most promising part of the world to combat emissions from cooking [9] and hopefully this will be targeted in the future. In order for the most appropriate actions to be initiated, better knowledge is needed on emission factors related to cooking habits, fuels and stove used.

Air pollution effects -did we forget the pregnant women?: Exposure to air pollution, especially to ultra-fine particles (< 1μm), has been shown to induce oxidative stress and inflammation[10]. But we are only beginning to understand how air pollution exerts its effect on pregnant women and their fetuses. When inhaled, particles smaller than 1 μm, corresponding well to the size range of anthropogenic air pollution, can penetrate the alveolar wall into the maternal bloodstream through which particles and inflammatory mediators may reach the placenta and even the fetus [11, 12].

Despite improving population health during the last decade, Ethiopia has one of the highest rates of maternal mortality globally, with **preeclampsia** (PE) being the major cause (16%) of maternal death [13] and accountable for 25% of stillbirth and neonatal deaths. Although the cause of preeclampsia remains unknown, evidence suggests that oxidative stress disrupts vascular function in the placenta, resulting in insufficient blood perfusion and inflammation. Recent findings suggest an increased risk for preeclampsia during pregnancy due to exposure to outdoor air pollution in recent studies and meta-analysis [14, 15]. So far, to the best of our knowledge, the hypothesis that also household air pollution would affect the risk of preeclampsia has only been tested in one Indian study. This study indicated a doubled risk for preeclampsia symptoms if the woman had used solid fuels for cooking during her pregnancy, but the study had very crude exposure and outcome assessments [16].

Evidence is accumulating that poorer growth during the fetal period, often estimated by low **birth weight**, is an important risk factor for mortality and adverse health later in life (also referred to as the 'fetal programming' or 'Barker hypotheses) [17]. Low birth weight has been associated with maternal exposure to traffic related air pollution during pregnancy [18]. Also household air pollution has a strong evidence of effect on birth weight [8] but as for previous outcomes exposure assessments needs to be improved.

Tuberculosis (TB) is estimated to be the leading infectious cause of mortality in the world. There is an estimated 9.0 million incident cases and 1.5 million deaths every year [19], the majority of which occur in low-income countries. Pregnancy is a susceptible period for developing TB. Several respirable risk factors including smoking (active and passive) and air pollution from biomass has been suggested to increase the risk of TB because of their potential negative impact on the airway defense mechanism [20]. There is however, limited evidence on the association of exposure to household air pollution and tuberculosis. Reviews have highlighted the need of high quality studies to clarify the association and if such an association exist to magnify the problem [20, 21]. The main concern with previous studies have been that they rely on crude exposure assessment and that the diagnoses of tuberculosis haven't been based on bacteriological results or standardized criteria [21].

In this multidisciplinary project we will assess exposure to air pollution from both household cooking and outdoor sources. The methods developed could be used in a wider framework but will here be used in epidemiological studies using a well characterized cohort of pregnant women in Adama, Ethiopia. The knowledge gained in this project could have great implication for preventative actions in order to protect health especially for pregnant women and her future children.

Methods

Study setting: This project is conducted in an uptake area with around 600 000 inhabitants in and around the city of Adama (also called Nazret), Ethiopia. Originally, the Pan-African highway connecting Djibouti and Addis Ababa ran through Adama, but a new multi lane stretch of the highway has been built around the city to shorten travel time (Figure 2). However, choosing this stretch instead of the road through the city costs a fee, resulting in most vehicles-especially the older ones- takes the route through Adama. This makes the city a busy and polluted transportation center.

Security situation in collaboration country: The study setting, Adama, is an area deemed fit to travel to by The Swedish Ministry of Foreign Affairs.

Figure 2. Map of Adama (courtesy of Google) showing with a red arrow the new toll road and with blue arrow the old road. The study site can be great example of policy if health costs associated with old road are greater than toll on new road.

Outdoor air pollution- applying high quality modelling tools and assessing exposure

Land use regression (LUR) is a well validated air pollution modelling tool used in European and North American epidemiological studies to assess exposure [22, 23]. One previous study demonstrated that LUR was a valid and cost-effective approach for air pollution modelling also in an African setting [3]. Briefly, the basis of developing a LUR-model is to collect a large number of digitalized geographical variables, such as road networks and land use, surrounding each of the measuring sites and to include these into Geographical Information Systems [GIS]. The collected variables should previously be known to have an impact on the pollutant of interest. LUR is a statistical approach to model air pollution, by trying to explain the variation in measured levels between different sites based on differences in geographical variables, hereafter referred to as predictor variables. Levels of pollution may then be

predicted for any location, such as individual homes, using the parameter estimates derived from LUR-model. The LUR procedure is further described in the ESCAPE exposure manual:(http://www.escapeproject.eu/manuals/ESCAPE_Exposure-manualv9.pdf.

In this study we will at 40 systematically selected locations measure nitrogen dioxide (NO_2) during 48h at each location using passive samplers at a height of 3 meter. The locations will be selected to represent street, urban and regional background sites. The collected samples will be stored in an icebox and transported to Umeå University for analysis. The geographical variables will be collected from the following sources; traffic data from Open Street Map and Google Earth, land use data (collected as near sampling period as possible) from Landsat-5 ™ (30m) satellite images (http://usgs.gov) and the multispectral RapidEye image (5m-pixel size, 5 spectral bands (www.blackbridge.com). The land cover classes will be inspected visually and verified using Google Earth. As elevation can affect pollutant concentrations we will also use elevation at sampling sites from STRM 90m from the digital elevation model (http://cgiar-csi.org). We will use ArcGIS (ESRI, Redlands, CA, USA) for spatial analyses and SPSS (IBM) and SAS for statistical analyses. Validation will be done by cross-validation and against measurements at residential addresses.

This approach will result in an air pollution model with the fine spatial resolution needed for high quality epidemiological studies.

NO_2 which can be sampled easily and cost effectively is commonly used as a proxy for traffic related air pollution exposure in high income countries. It is not known how well it correlates with emissions from old, heavy vehicles with neither particle filters nor catalytic converters. Therefore, and for obtaining more information about the characteristics of outdoor air pollution, supplementary mass concentration measurements will be conducted at 20 of the 40 locations. The measurements will be conducted during both dry and rainy seasons using a DustTrak DX. This optical instrument gives time resolved mass concentrations of PM10 (particles smaller than 10 µm), PM2.5 (particles smaller than 2.5 µm) and PM1 (particles smaller than 1 µm), as well as the possibility to simultaneously sample on a filter for calibration purposes. This will provide us with the possibility to evaluate how good NO_2 measurements are as a proxy for traffic related air pollution, something which has not been done with such an old vehicle fleet as the Ethiopian. We will also collect particles for chemical characterization, and for the opportunity to conduct toxicological studies (not included in this application) using a BGI900 High Volume sampler. This device samples 1 m^3 of air per minute, and collects airborne particles smaller than 10 µm and smaller than 2.5 µm on a polyurethane foam substrate [19]. A technique based on extracting the collected particles in pure methanol (MeOH extraction protocol), will be used. We have previously used this method successfully for diesel exhaust particles, candle soot and welding fume, and the extraction method has also been used in the EU project *Respiratory Allergy and Inflammation due to Ambient Particles*. After extraction, the particle-MeOH solution is dried and the chemical properties of the dried collected particles will be analyzed for constituents who are of health relevance using Inductively Coupled Plasma Mass Spectrometry (ICP-MS) for elemental – including metal - composition, gas chromatography-mass spectrometry (GC-MS) for polyaromatic hydrocarbons (PAH) and OC-EC for analysis of organic carbon and soot. Particle shape will be investigated using Sweeping Electron Microscopy.

This approach will allow us to test our model assumptions in an African setting

Individual exposure will be based on residential addresses collected in the questionnaires, which will be digitalized using a Geographical Positioning System (GPS). For a subsample we will test and verify this approach by determining GPS coordinates by home visits.

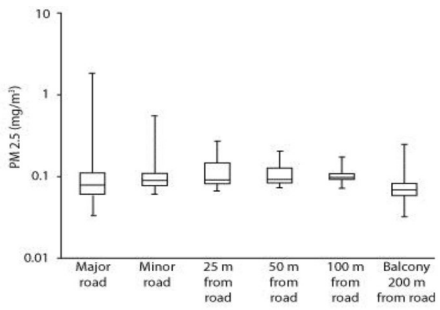

Figure 3. Boxplots showing the high outdoor PM2.5 mass concentrations at the study site (please note logarithmic axis) as measured by DustTrak DRX8534. The boxes denote the quartiles, horizontal lines the medians and whiskers maximum and minimum concentrations. Although the maximum value decreases with distance from main road, there is no decrease in medians. Even at a balcony on the 3rd floor 200 m from the road, the PM2.5 concentrations are still very high (on average 73 µg/m³, as compared to the WHO health limit value of 10 µg/m³).

Preliminary results and significance: A pilot study conducted by Malmqvist and Isaxon in Oct 2015, indicated pollution levels with peak orders of magnitude higher than WHO guidelines (Figure 3). The pilot study was done using mass concentration instruments without the possibility to calibrate with parallel filter measurements (DustTrak DRX8534 and SidePak AM510), meaning that results are approximate only. The measurements suggested in this proposal will generate more reliable data, which, through the network with co-applicant Dr. Taye Balcha who works at Ministry of Health as Head of Office of the State Minister, can be used to influence governmental bodies to design appropriate policies which incorporate exposure and health.

Household air pollution-assessing exposure and increasing the knowledge of emissions by cooking habits

In the cohort questionnaire there are several questions on household air pollution based on e.g. cooking fuels, methods and exposure times. In the Aerosol laboratory at Lund University we will use three main types of Ethiopian fuels: wood, charcoal and cow dung, in both an Ethiopian traditional stove and an open fireplace, to generate aerosols in a well-characterized, representative, and reproducible way. By measuring mass- and number concentrations with state-of-the-art instruments (Tapered Oscillating Micro Balance (TEOM) for time resolved mass concentrations and Scanning Mobility Particle Sizer (SMPS) for time- and size resolved number concentrations) we will assess number and mass of particles emitted per unit time. These emission factors will be used together with answers from the questionnaire to calculate each woman's indoor exposure. The particles generated in the lab will also be collected with the BGI900, for the possibility to make detailed chemical analysis. All aerosol technical equipment mentioned is already in place at Lund University. The emission factors this will generate will be used together with answers from the cohort questionnaire to calculate each woman's indoor exposure.

Preliminary results and significance: Our pilot study indicates the severity of the exposure and that different cooking habits have different emission factors (Table 1). The results will make it possible to provide new and valuable knowledge of emissions related to LMIC's cooking habits, fuels and stoves. This knowledge can be used to combat emissions by implementing different habits and/or cleaner stoves and/or promoting cleaner fuels.

Table 1. Average and peak number concentration of particles < 300 nm and PM2.5 mass concentration measured in the breathing zone of women cooking in two homes. Cooking (with wood) took place just outside of the entrance of home 1, which was 3x5 m, and cooking (with charcoal) occurred in the corner of a 3x5 m room with one of the walls being a bast mat in home 2, which was of the same size as home 1. The difference in exposure suggests that there is a difference in emission factors between the two fuels and/or between the two cooking methods. There are reasons to believe that cow dung, which have lower energy density causes even highet emissions.

Site	Fuel	Cook-stove	Number concentration ± Std [#/cm³]	Peak number concentration [#/cm³]	PM2.5 ± Std [µg/m³]	Peak PM2.5 [µg/m³]
Home 1	Wood	None	$2.58 \cdot 10^6 \pm 2.6 \cdot 10^6$	$9.84 \cdot 10^6$	1.00 ± 3.26	$60 \cdot 10^3$
Home 2	Charcoal	Traditional	$2.68 \cdot 10^5 \pm 2.01 \cdot 10^5$	$1.39 \cdot 10^6$	0.53 ± 0.66	$6.3 \cdot 10^3$

Air pollution effects on the pregnant women

Study participants: Participants are recruited and followed up at antenatal care (ANC) clinics at two public health centers and at the Adama regional hospital. Around 8 000 women register annually for ANC at these facilities. Inclusion of study participants started in November 2015, until at least 2 000 pregnant women have been included (as of March 31 2016, 705 women have been included). Trained health facility staff will perform all study investigations, with weekly monitoring by study investigators and the research data management team.

Study design: At inclusion, structured information on socio-demographic conditions, education, occupation and poverty indicators are collected; as well as medical history (in particular for obstetric, gynecological and TB details). Detailed information on aspects of household cooking and ventilation is also included for exposure assessment. Physical and obstetric examination is performed. Apart from the study procedures and investigations, participants receive care according to current Ethiopian ANC guidelines. Participants will be followed one month after inclusion, and then at two-monthly intervals. TB testing will be ongoing until one year after delivery. In case of suspected active TB bacteriological testing will be done according to the study protocol. If diseases or complications of pregnancy are suspected, testing is performed according to Ethiopian guidelines for pregnancy care.

Outcomes: **Preeclampsia** is defined as: 2 readings of blood pressure ≥140/90 mm Hg at least 4 hours apart, and proteinuria, ≥300mg in 24 hours, or 2 readings of at least +2 on dipstick analysis of midstream or catheter urine specimens if no 24-hour urine collection was available [24]. We will also investigate **birth weight** defined as weight below 2500g, the 5th percentile, -2 standard deviations and as a continuous variable. Birth weight is measured at delivery or shortly after for home deliveries. Women are tested for latent **Tuberculosis (TB)** at inclusion during pregnancy and at 9 months post-partum in case of previous negative results (using Quantiferon TB-Gold Plus, an interferon-gamma release assay). In addition, testing for active TB is performed continuously during the study period.

Confounders: The abundance of data collected during antenatal visits allows us to adjust for all a priori confounders' i.e. medical history, maternal age, parity, pre-pregnancy BMI, smoking, poverty indicators and maternal education.

Statistical analyses: The effect of outdoor and indoor air pollution will be investigated on preeclampsia and low birth weight using logistic regression. Birth weight deviation (with adjustment for gestational age) as a continuous variable will be assessed with linear regression. Tuberculosis will be investigated using survival and logistic analyses. Relevant confounders such as parity, maternal age, socioeconomic status, medical history are included in the cohort (collected at maternal care visits) and adjusted for.

Statistical power: A number of graphs of statistical power have been the basis for planning the project, although such calculations are marred by assumptions of varying certainty. The statistical power in any study depends on a range of circumstances. Here, contrasts of air pollution exposure and exposure measurement error are among the most important. We have used a very conservative approach in the power calculations below (contrasts of air pollution exposure will according to pilot study be much larger). Random-effect meta-analysis combined odds ratio associated with a 10-μg/m3 increase in PM2.5 was 1.62 (95%confidence interval, 1.28-2.00) for **preeclampsia** [15]. If we assume that 650 women are defined as the

high exposed group then we will be able to detect true relative risks of 1.5 or higher in high exposed subjects relative to lower exposed subjects with a power of 80% (alpha 0.005). Low **birth weight** risk; pooled odds ratios for low birth weight 1.22 (1.07-1.39) per 10 μg/m^3 PM2.5[25]. If we assume that 650 women are defined as the high exposed group then we will be able to detect true relative risks of 1.2 or higher in high exposed subjects relative to lower exposed subjects with a power of 80% (alpha 0.005). **Tuberculosis** cases are more likely to be exposed to IAP than healthy controls (pooled OR 1.30; 95% CI, 1.04-1.62; P = 0.02)[21]. If we assume that 650 women are defined as the high exposed group then we will be able to detect true relative risks of 1.2 or higher in high exposed subjects relative to lower exposed subjects with a power of 80% (alpha 0.005).

Ethical considerations and data security: All research involving personal data has potential integrity violations for the individual. We hope that our planned research, through increased scientific knowledge, in the long run would contribute to better maternal health in LMIC. Crucial for minimizing potential integrity violations is that data are handled properly in order to minimize the risks for identifying individual persons in the data. Data based on above mentioned variables will be stored at the Department of Occupational and Environmental Medicine in Lund. An identifiable code key will be developed that will be stored in a secure way according to the Ethical Permission. Thus, no identifiable variables or coordinates will be left in the database. Only involved researchers will be allowed to access the database. In addition the database will have a password. The work will be conducted in line with international rules and agreements. The results would be presented in an aggregated form and data would be handled with appropriate high confidentiality in order to avoid integrity violations. Ethical permissions for the birth cohort exist both from Ethiopia and Sweden. An amendment for the air pollution part has been sent in. We do not anticipate any difficulty in obtaining permission as our research team has previously had similar projects approved.

International and national collaboration:

The project is conducted in collaboration with Ethiopian researchers from the Armauer Hansen Research Institute (AHRI), Addis Ababa, and representatives of the Federal Ministry of Health and the Oromia Regional Health Bureau. This specific project already has a funded PhD student led by Co-applicant Ass. Prof. Isaxon (conducted through collaboration between AHRI and Lund University funded by SIDA). We further aim to strengthen the Ethiopian capacity to perform high quality air pollution epidemiological studies by research training and communication projects. We also have close international collaboration with Prof. Kiros Berhane and Prof. Jonathan Samet from University of Southern California. In their project Geo Health Hub for Eastern Africa (funded by Fogarty and NIH) they will work on interdisciplinary research and training in environmental and occupational health for East Africa with a special focus on air pollution. Our main areas of collaborations will be in air pollution modelling and research training.

Significance

So far there is a knowledge gap on the air pollution effects on pregnant women, especially in Africa. The main knowledge gap has been in assessing exposure as high spatial outdoor air pollution modelling and household emission factors are lacking.

We aim to contribute by applying cost effective, yet state-of-the art measurement and modelling tools on an up and running prospective cohort of pregnant women. This

multidisciplinary project will strengthen research of high quality by combining expertise from several areas, infectious medicine, obstetrics, epidemiology, environmental health and aerosol technology in a joint effort to evaluate environmental health risk with such details so proper actions can be taken. Since one of our co-applicants works at the Ministry of Health in Ethiopia we have the resources to disseminate our results locally. In addition we already are partly funded by SIDA with an Ethiopian PhD-student who will disseminate this knowledge at Addis Ababa University. Furthermore, we are collaborating with researchers from University of Southern California in their East African project so our models will be applied also in Uganda, Kenya and Rwanda to assess air pollution effects on children's respiratory functions (http://geohealthhub.org/). Well-designed African studies that increase knowledge on not only the health impact but also on the attributed sources could contribute by raising awareness and lead to better policies and actions.

Work plan and contingency plan

Figure 4, work plan with main tasks and responsible researchers.

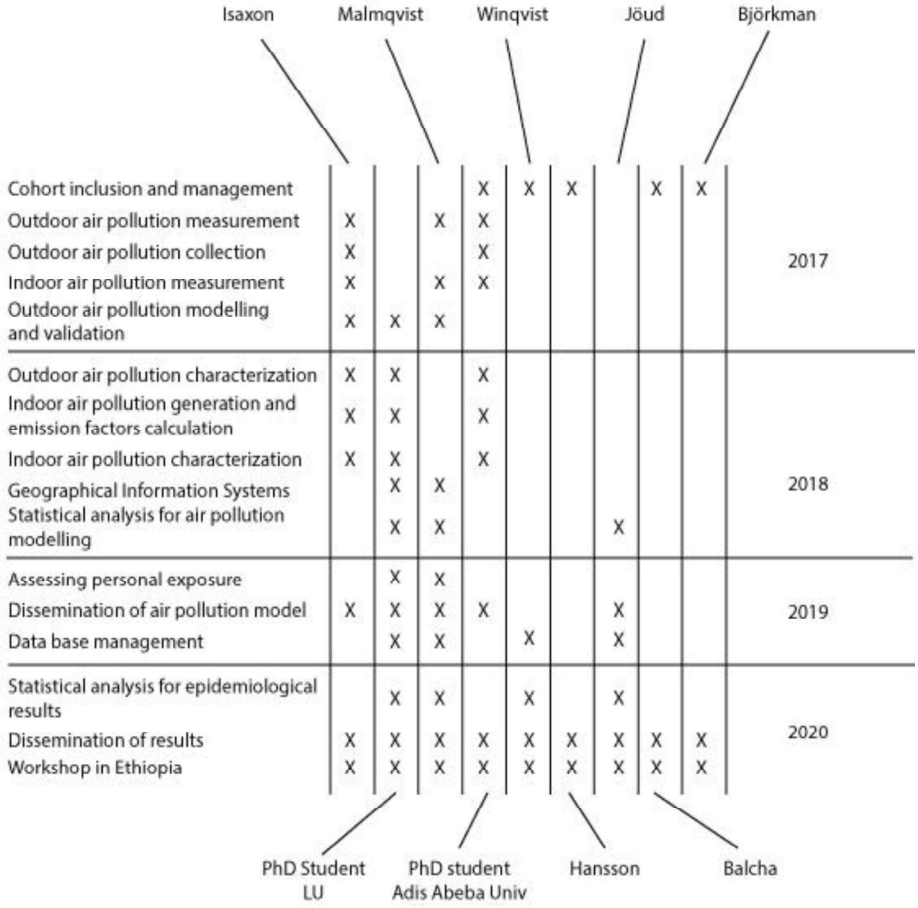

Table 2, main identifiable risks and contingency plan.

Main identifiable risks	Contingency plan
Failure to obtain ethical permission	Risk is low (prior ethical approvals)/Review ethical approval
Failure to develop adequate model for outdoor air pollution	Measure traffic counts on also minor roads and apply to model
Failure to distinguish air pollution and covariate effects	Evaluate effects in smaller areas where the covariate effects are smaller
Failure to find any association between exposure and outcomes	No risks are also important for public health and will be communicated
Failure to obtain permission from Ethiopian customs to bring the High volume sampler	Collect smaller samples will be collected using traditional portable pumps, which will be sufficient for chemical characterization.
Analysis shows that NO_2 is not a valid proxy for traffic emissions in developing countries.	Base the model on mass concentration measurements. Model resolution would be lower, but accurate.

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Relevance for development research*

This study, which will increase knowledge of not only health impact but also of source characteristics, will provide important knowledge for appropriate policy making.

Significance for, and communication with the Swedish foreign aid institutions: This project addresses several aspects of the 17 international Sustainable Development Goals, as air pollution are linked to both the natural science perspective of clean and affordable energy and climate change and health risks for women and child to the medical perspective of Good health and well-being. It is also in line with two (nr 3 and 4) of the six goals in the Swedish government foreign aid political platform (Skr 2013/14:131), especially the sub goal of improved survival and healthier life for women and children. We will in this context shed light upon the situation in Sub-Saharan Africa by presenting results from our study in a report specifically targeted at foreign aid. Isaxon was last year active at Almedalen (Sweden's biggest political meeting place"), and our plan is to contribute with a seminar on maternal health in developing countries in 2019, to further influence Swedish politicians to focus foreign aid at this highly susceptible group. The release of a report to foreign aid institutions, as well as relevant results will also be communicated through press releases from Lund University. This method of communicating important results has been used before, especially by Ass Prof Isaxon and Dr. Malmqvist. Their PhD theses gained a lot of attention in media, and several interviews were conducted resulting, amongst other things, in a lot of research communication to the public. Below we will go in more details on how each part of this project have relevance for developmental research.

Outdoor air pollution

Increasing urbanization brings an emerging type of air pollution mainly from traffic. The effect of this added exposure needs to be evaluated but so far Africa has been neglected when it comes to air pollutant monitoring and modelling. We aim to contribute by developing and sharing cost effective, yet state-of-the art, measurement and modelling tools which can be used in any developing country setting.

Cooperation within the scientific society: We will work in close collaboration with Prof. Kiros Berhane and Prof. Jonathan Samet from University of Southern California and their project Geo Health Hub for Eastern Africa (funded by Fogarty and National Institute of Health (NIH)). Our main areas of collaborations will be in air pollution modelling and research training allowing us to test the air quality models in several other low and middle income countries in the future.

Household air pollution

Sub-Saharan Africa has been identified by economists as the most promising part of the world to combat emissions from cooking. In order for appropriate actions to be taken, better knowledge of emission factors and particle characteristics related to cooking habits, fuels and stove needs urgently to be communicated. This knowledge is one of the outcomes of our project and will be disseminated during 2018 and 2019 at international conferences and in scientific journals but also presented in a report (web-based and in paper) using accessible language and semi-quantitative infographics which will be spread to relevant NGO's (non-governmental organizations) and international stakeholders such as WHO and UNEP. By communicating this knowledge we will provide NGO's with information needed to do interventions (e.g. provide simple stoves with lower emission factors) and public information events. We will of course, as experts, contribute to such events, if needed. We will also share our exposure assessment tools, such as questions on cooking habits through CoLab. CoLab is an initiative funded by Gates Foundation with the purpose of harmonizing large datasets across studies. All possible entries in CoLab concerning outdoor and indoor air pollution in both low level and high level income countries have been developed by Isaxon and Malmqvist.

Air pollution effects on pregnant women

Significance for, and communication with, the Ethiopian public: This multidisciplinary project aims to identify risk factors during pregnancy that could have large implication for the health of the woman and her child. So far there is a knowledge gap on the air pollution effect on women during their susceptible pregnancy period in low income countries. Due to the public health relevance of the project it is of uttermost concern that results are presented in a comprehensive way yet acknowledging any uncertainties.

Communication with Ethiopian government: Since one of our co-applicants works at the Ministry of Health in Ethiopia we have the unique resources to disseminate our results to governmental bodies and other stakeholders in Ethiopia. An aim is that information communicated to governmental stakeholders during the workshop will result in additional meetings with local politicians, during which we can discuss information from the study together, hopefully resulting in that they are confident enough to do lobbying for improved national air pollution health guidelines.

Workshop in Ethiopia: An open workshop in Ethiopia will be arranged in 2019, where we will present our results and demonstrate our measurement and modelling tools and how the strategy can be applied in any low income county. To this workshop we will invite local stakeholders, health workers at antenatal care clinics and public health centers, governmental employees and students, but also other research groups including the Geo Health Hub that aims to do similar studies in other countries.

I am the project leader of an ongoing project grant in Development research, subject to disbursements from the Swedish Research Council up to and including 2016