Exposure to air pollution and links with cardiometabolic health in low- and middle-income countries

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TESI DOCTORAL UPF / 2019

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A la iaia Paqui i a la iaia Conxita,
tot uns exemples a seguir

Agraïments/Acknowledgements

Veig aquesta tesi com un recorregut marcat per un creixement personal i professional gràcies a un seguit de petites grans persones que, o bé em va donar una oportunitat en el seu moment, o sempre m'ha mostrat el seu suport i respecte, o ambdues. Aquest cúmul d'oportunitats encadenades fan que algú sigui on és. La meva passió per la recerca va començar amb la meva tesina final de màster a l'Institut Català d'Oncologia, sota la direcció del José Martínez Sánchez i de l'Esteve Fernández. De cada petita troballa en fan un gran descobriment, i aquesta emoció es contagia. Els admiro moltíssim i sempre els he tingut molt presents, i avui també.

La meva entrada al CREAL li dec sobretot a la Ita. Però li haig d'agrair molt més que això. Els nostres moments de teràpia i confessió han estat cabdals des de fa molts anys. Sempre tens paraules d'ànims i reconfort quan més es necessiten. La meva estada al CREAL tampoc s'entendria sense el Mark N. I feel so lucky to have worked with you. You are the responsible of my predilection for air pollution monitors and I cannot imagine having started a PhD without having worked in the field first. Als meus primers companys de batalla, a na Tània i a l'Albert, sou uns companys simplement genials. M'he rigut molt amb vosaltres. A la meva companya de pupitre plantabaixera, la Lourdes C, i al Jose, igual o més motivat que jo, que sé una mica més d'estadística gràcies a vosaltres. Als meus estimats plantabaixerus: la Marta C, la Glòria, la Judith, l'Antònia, la Montserrat. Tothom us té oblidats per dalt... però jo no! Enyoro les nostres converses i moments més esbojarrats. També tinc molt present al Pau i a l'Oren, no sé com agrair-los-hi la seva predisposició per ajudar-nos amb l'experiment de la llar de foc. I a la meva estimada Lourdes A, el que no uneix una mobile campaign no uneix res! Has estat un pilar per mi durant tota aquesta etapa, ja ho saps. Sempre tindràs un lloc allà on sigui, Melbourne inclòs ☺.

I com no... en aquests últims anys ha estat vital el caliu de la súper sala C! My favorite girl team: Debbie, the dancer, Diana, the chiringuito girl, Èrica, the gossip girl, Ángela, mi compi de seminarios, and Alba, la fiestera. You girls are amazing. I'm really proud of all of you: we're real fighters! Don't let anything or anyone make you think that you are not capable. You are. I cannot

imagine this PhD without you. Gosia, I wish you have come to sala C before! Èrica, no t'escapes. Has estat la meva companya de viatge número 1, sobretot en aquest tram final. Si estàs llegint això, dir-te que ets una campiona. Et trobaré molt a faltar allà on vagi! Només espero que segueixis enviant-me fotos del Quim per veure com es converteix en tot un homenet. Al dúo de veteranos: Alejandro y Javi. Siempre es un placer compartir conversaciones con vosotros durante la comida, sobretodo cuando somos críticos con la investigación. Os deseo todo lo mejor por Irlanda, Barcelona o allí donde vayáis! Al meu segon compi de pupitre, al Carlos, ell seria the gossip boy. Gràcies pels teus tips d'R i per reinvindicar els nostres drets de predoc, ets la canya! Tampoco me olvido de Dietmar, uno de los últimos fichajes en nuestras comidas. Siempre sabes sacar una sonrisa a cualquiera! A David R, eres un animal party y un crack! Eres como el maestro Yoda, siempre tienes un consejo que dar, y de los buenos. No dudes que David y yo te vendremos a visitar a Colorado. També agrairé sempre a totes les persones que han format part o formen part del CREAL per crear un ambient de treball tan magnífic i humà. Sempre us tindré un carinyo nostàlgic a tots i totes. Per les "rises" que m'emporto jugant a vòlei amb els ISPlayers, va ser tota una teràpia i ho trobaré a faltar! A la Ione, que també va patir amb l'últim tram final de la tesi i ho va voler compartir amb mi.

To my dear CHAI team. I feel very fortunate to have worked with such a talented group of colleagues. Sree Kanth, thanks for welcomingly so nicely in Hyderabad and to save me from the crazy traffic crossing. Also thanks to Kishore, Shatish and all the team who welcomed me and guided me in the field. To Maëlle and Margaux, the French ladies. CHAI would have not be the same without you. A l'Esther B, que fa que la burocràcia sigui menys feixuga. To my dear Carles and Otavio, who helped a lot during all the process but particularly during the last months. Carles, gràcies pel teu suport moral i estadístic, de debò. Vals molt i espero que sempre trobis la motivació que et faci brillar. Otavio, you area an amazing researcher and better person.Wish you all the best!

To Greg and Cathryn. I still remember my PhD interview talking about the Solan study, crazy. I'm very lucky to have you both, you are a very complementary supervising team. I wish you all the best and I really hope we can collaborate further in the future. Greg, te admiro como investigador y como persona. Eres increíble. He aprendido mucho contigo y te agradeceré eternamente que me abrieras las puertas de Brown y de tu casa. Tu família es adorable. Heather, Elena, Katie y Rhys también han hecho mi doctorado más entretenido y divertido. Cathryn, I would not be writing these lines if it were not for you. Thanks for always being so flexible and accessible. Thanks for gave me the opportunity to be involved in CHAI and especially for going to Hyderabad to meet the team and explore the villages.

A la Laura, la germana que mai he tingut. Al Jaume, per molt que passin els anys i ens haguem distanciat, sempre et portaré amb mi. A la Irene, que m'ha donat un suport incondicional inclòs amb un petit que no arriba als tres quilets en braços. A la Lídia, la Marta C, la Marta J i la Piñi per ser algú a qui recolçar-te en moments àlgids i baixos. To the sweet Amina, the best housemate during my stay in Brown. I hope that somehow our paths cross again.

A la meva família. A les meves àvies, que els hi dedico aquesta tesi per la seva valentía i força a la època que els hi va tocar viure, les admiro. Al avi Josep, que encara l'anyoro. Als meus tiets i tietes, en especial al tio Mixi i a la tieta Paqui. Al papurri, que li surt la sabiesa per les orelles i l'estimo amb bogeria, i a l'Eloiet, que no podria estar més orgullosa de la persona amb qui s'ha convertit. El millor germà del món. Però per sobre de tot, al David i a la mama. Sou els meus pilars de vida i aquests últims mesos heu estat el meu flotador, el meu oxigen. No sé què hagués sigut de mi sense vosaltres en aquest procés.

David, eres mi compañero de vida, mi inspiración, mi amor. Esta tesis también es tuya. Espero que la vida nos traiga más momentos alocados allí donde estemos. Contigo, me iba a la fin del mundo.

Mama, t'estimo infinit. Ets el meu referent a la vida. No saps com de recomfortants han estat els teus detalls fets amb amor de mare, des d'un simple Suchard, a escoltar-me i entendre, a venir-me a fer freges al braç per mostrar-me el teu suport incondicional. M'agradaria algún dia ser la mateixa dona i mare valenta, forta, decidida i amb conviccions que tu ets per mi.

Abstract

The aims of this thesis are: 1) to evaluate the performance of low-cost air quality monitors to monitor long-term exposure in rural areas from low- and middle-income countries; 2) to identify the determinants of personal air pollution exposure among women from a semi-rural area in Mozambique; and 3) to evaluate the associations between long-term exposure to ambient air pollution and cardiometabolic health in adults from a peri-urban area in India. We used data from: an experimental study, an observational study, and a cross-sectional epidemiologic study (CHAI). Main results: 1) the performance of low-cost monitors is not reliable yet to replace more expensive research-grade monitors; 2) kerosene-based lighting increased personal air pollution exposure in women from Mozambique; 3) long-term air pollution is associated with elevated blood pressure in women from India; and 4) we found no evidence that long-term air pollution is associated with higher blood glucose levels in peri-urban India.

Resum

Els objectius d’aquesta tesi són: 1) avaluar el rendiment dels monitors de qualitat de l’aire de baix cost per monitoritzar l’exposició a llarg termini en àrees rurals en països de renda baixa o mitjana; 2) identificar els determinants de l’exposició personal a la contaminació de l’aire en dones d’una àrea semi-rural de Moçambic; i 3) avaluar les associacions a llarg termini entre l’exposició ambiental a la contaminació de l’aire i la salut cardiometabòlica en adults d’una àrea peri-urbana de la Índia. Hem utilitzat dades provinents de: un estudi experimental, un estudi observacional i un estudi epidemiològic transversal (CHAI). Resultats principals: 1) el rendiment de monitors de baix cost encara no és prou fiable per reemplaçar a monitors més cars i establerts en recerca; 2) la il·luminació amb querosè va incrementar l’exposició personal a la contaminació de l‘aire en dones de Moçambic; 3) l’exposició a llarg termini de la contaminació de l’aire està associada a una major pressió arterial en dones de la Índia; i 4) no hem trobat evidència que la exposició a la contaminació de l’aire estigui associada a nivells més alts de glucosa en sang a la Índia peri-urbana.

Resumen

Los objetivos de esta tesis son: 1) evaluar el rendimiento de los monitores de calidad del aire de bajo coste para monitorizar la exposición a largo plazo en áreas rurales en países de renta baja o mediana; 2) identificar los determinantes de la exposición personal a la contaminación del aire en mujeres de un área semi-rural de Mozambique; y 3) evaluar las asociaciones a largo plazo entre la exposición ambiental a la contaminación del aire y la salud cardiometabólica en adultos de un área peri-urbana de la India. Hemos usado datos provenientes de: un estudio experimental, un estudio observacional y un estudio transversal (CHAI). Resultados principales: 1) el rendimiento de los monitores de bajo coste aún no es suficientemente fiable para remplazar a monitores más caros y establecidos en investigación; 2) la iluminación con queroseno incrementó la exposición personal a la contaminación del aire de mujeres de Mozambique; 3) la exposición a largo plazo de contaminación del aire está asociada a una mayor presión arterial en mujeres de la India; y 4) no hemos encontramos evidencia que la exposición a la contaminación del aire esté asociada a niveles más altos de glucosa en sangre en la India peri-urbana.

Preface

"The more you know, the more you know you don't know"
Aristotle

This thesis consists in a compilation of four original scientific articles (one published, one accepted, one submitted, one in preparation) first-authored by the PhD candidate and supervised by Dr. Gregory A Wellenius and Dr. Cathryn Tonne. The work presented started in February 2016 and has been conducted in most of its part in the Campus Mar of the Barcelona Institute for Global Health (ISGlobal). As part of the PhD, the candidate also did a one month stay in the National Institute of Nutrition in Hyderabad (Telangana, India) and a four month stay in the Department of Epidemiology at the Brown University School of Public Health (Rhode Island, USA).

According to the procedures of the PhD program in Biomedicine of the Experimental and Health Science's Department of the Pompeu Fabra University (UPF), the thesis includes: an abstract in three languages (English, Catalan, Spanish), a general introduction to the topic and state of the art, a rationale, the main and specific objectives, the methods, the results (or scientific articles), an overall discussion, and final conclusions.

This thesis provides insights into three key components in environmental epidemiology: exposure assessment, exposure determinants, and links between exposure and health. In particular, this thesis is focused on the potential of low-cost technology to assess long-term household air pollution in low- and middle-income countries, the identification of determinants in personal exposure to particles in women from a semi-rural sub-Saharan African area, and the links between ambient air pollution and cardiometabolic health in adults from a peri-urban area in South Asia.

This thesis is conducted in the framework of the CHAI project, a European-funded project aimed to investigate the cardiovascular health effects of exposure to particulate air pollution from outdoor and household sources in India. The results of this thesis are also based on data obtained from one wood-combustion experiment in

Spain and one collaborative project in Mozambique. The PhD candidate designed, coordinated, and implemented the fieldwork required for the experiment and collaborated with the fieldwork in India. For all the work presented, she formulated the research questions and performed the data management and analysis as well as the interpretation and writing of the results. The PhD candidate also disseminated results of this work in the Brown University and three international conferences (see Annexes).

Besides the PhD work, during this period the PhD candidate has taken the module "Advanced Statistical Methods in Epidemiology" offered by the London School of Hygiene and Tropical Medicine (LSHTM), has supervised two student's final projects, has co-authored two scientific articles (see Annexes), has peer-reviewed two scientific articles (see Annexes), has coordinated the ISGlobal-Campus Mar seminars and the Air Pollution and Urban Environment group meetings, has organized the 3rd ISGlobal PhD Symposium, has wrote three blog articles in the ISGlobal Health Blog (see the one related with this PhD in Annexes), and has volunteered for events aiming to bring science closer to the general public (e.g., PRBB Open Day).

Barcelona, 3rd of December 2018

Abbreviations
(by order of appearance)

HICs high-income income countries
LMICs low- and middle-income countries
DALYs disability-adjusted life-years
WHO World Health Organization
PM$_{2.5}$ particulate matter with an aerodynamic diameter of 2.5 µm or less
µg/m^3 micrograms per cubic meter
PM$_{10}$ particulate matter with an aerodynamic diameter of 10 µm or less
UFP ultrafine particles
BC black carbon
EC elemental carbon
OC organic carbon
CO carbon monoxide
LUR land-use regression model
GIS geographic information system
CVD cardiovascular disease
BP blood pressure
SBP systolic blood pressure
DBP diastolic blood pressure
mm Hg millimeters of mercury
ACC American College of Cardiology
AHA American Heart Association
JNC7 7th report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure
mmol/l millimoles per litre
T2DM Type 2 diabetes mellitus
OGTT oral glucose tolerance test
HbA$_{1c}$ glycated hemoglobin

Table of contents

1. INTRODUCTION

Humans are linked with the environment from time immemorial. Humans depend on the natural systems they live in, as much as natural systems are shaped by human actions. One of the major global environmental changes we humans have experienced is air quality deterioration or air pollution. Air pollution is one of the greatest environmental stressors threatening human health today. Air quality trends, however, are not equal across the globe. While air quality is improving in some high-income countries (HICs), it continues to worsen in **low- and middle-income countries** (LMICs) (Health Effects Institute, 2018).

Indoor air pollution in rural and peri-urban areas in LMICs is particularly dominated by the combustion of **unclean fuels** [1] for household energy or the so called **household air pollution**. Chronic exposure to household air pollution is currently hard to measure. However, the growth of low-cost air quality monitors with long-lasting batteries now may provide the opportunity to measure air pollution in rural settings for several weeks to months without intensive supervision, and could therefore potentially help to estimate chronic exposure to household air pollution more easily. Apart from conducting these measurement campaigns, it is essential to understand the patterns and sources in exposure to combustion particles to design, implement, and evaluate effective interventions to reduce exposure and associated health effects.

Air pollution is not the only health burden facing LMICs. LMICs are experiencing an emerging trend in **hypertension** and **diabetes** burdens, both projected to increase dramatically in the near future. Given the high burdens of air pollution and cardiometabolic risk factors in LMICs, even small associations between these two would have important public health implications. However, to date, most epidemiologic studies evaluating the association between air pollution and cardiometabolic health have been conducted in HICs.

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[1] Bold terms are presented in the index by words (page 265).

This introduction gives the necessary background about the main topics of this thesis within the framework of exposure science and epidemiology, and the existing evidence and knowledge gaps before this thesis started in 2016. The focus of this thesis is on LMICs, a broad concept proposed by the World Bank to classify countries according to their gross national income per capita. Although in its broader concept includes 138 countries, these can be re-classified as low-income (including Mozambique), lower-middle income (including India), and upper-middle income (including **China**).

1.1 Air pollution

According to the last Global Burden of Disease study (Gakidou et al., 2017), both **ambient air pollution** and household air pollution are leading environmental causes of death and disability worldwide. Both ambient and household air pollution burdens fall most heavily on LMICs, which face a double air pollution burden (Health Effects Institute, 2018).

a) Ambient air pollution

Ambient air pollution was responsible for 7.5% of the global deaths in 2016, equivalent to 4.1 million deaths from heart disease and stroke, lung cancer, chronic lung disease, and respiratory infections. Among these deaths occurred in 2016, 32% were in **South Asia** and 11% in India (Gakidou et al., 2017). In terms of disability-adjusted life-years (DALYs) or loss of healthy life expectancy, ambient air pollution accounted for 4.4% of all global DALYs, a loss of 106 million DALYs. China and India together contributed 50% of the total global DALYs.

According to the latest World Health Organization (WHO) air quality database, 98% of the low-middle-income population and 56% of the high-income population live in areas with unhealthy air. India has the most polluted cities in the world, including Hyderabad, the capital of the Telangana state and a city close to one of the study areas of this thesis. In Hyderabad, the annual average concentration of fine particulate matter ($PM_{2.5}$) is higher (59 µg/m^3) than in cities like New York (9 µg/m^3), Barcelona (15 µg/m^3), Hong

Kong (29 µg/m^3) or Kathmandu (49 µg/m^3) (World Health Organization, 2016).

Although global population-weighted annual $PM_{2.5}$ concentrations increased by 18% from 2010 (43 µg/m^3) to 2016 (51 µg/m^3) worldwide, some HICs (e.g., Russia, Japan, Unites States) have experienced an improvement in ambient air quality (Health Effects Institute, 2018). Some LMICs in the South Asian region (e.g., Pakistan, Bangladesh, India), on the other hand, have experienced the steepest increases in air pollution levels since 2010, reaching levels higher than 70 µg/m^3 in 2014.

b) Household air pollution

The incomplete combustion of unclean fuels (e.g., firewood, animal dung, crop wastes, charcoal, coal) to meet domestic energy needs such as cooking, heating, and lighting is known as household air pollution (**Figure 1**).

Figure 1 Exposure to household air pollution from lighting and cooking activities in Mozambique, Vietnam, and Nicaragua. a) Kerosene lamp (or *candeeiro de vidro* in Portuguese) in Manhiça, Mozambique. b) Woman making fire in Sa På, Vietnam. c) Cooking pot and stove in Matagalpa, Nicaragua.

In many rural areas of low-income countries, **biomass** fuel is the principal source of domestic energy so that indoor air pollution is a serious health problem. In 2016, household air pollution was responsible for 4.7% of the global deaths (equivalent to 2.6 million deaths). Of these deaths, 46% were linked to ischemic heart disease and stroke (Health Effects Institute, 2018). In terms of DALYs, exposure to household air pollution accounted for 77 million DALYs (3.2% of the global total).

Although the proportion of the worldwide population using unclean fuels has declined from over 3 billion in 1990 to about 2.4 billion in 2016 (34% of the global population), this reduction has been fastest in HICs and slowest in LMICs. The highest burdens of household air pollution are found in Asia and **sub-Saharan Africa**. When selecting countries with populations over 50 million and with at least 10% of unclean fuel use, India and China are the top leading countries with largest numbers of people exposed to household air pollution, with 43% (560 million) and 30% (416 million), respectively. Sub-Saharan African countries such as Ethiopia, Democratic Republic of the Congo, and Tanzania, however, have higher proportion of population exposed to household air pollution (>96%) (Health Effects Institute, 2018).

c) Air pollution composition and sources

Air pollution is a complex mixture of gases and particles whose sources and composition vary spatially and temporally. Air pollution sources can be either natural (e.g., volcano, wild fire, Saharan dust) or anthropogenic. In this thesis we mainly refer to anthropogenic sources. Air pollution anthropogenic sources greatly differ between HICs vs. LMICs and rural (or semi-rural) vs. urban areas. In turn, characteristics of air pollutants (e.g., particle size, shape, chemical composition) depend on the source and determine the toxicological profile of the air pollutants and therefore their potential harmful effects on health.

In urban areas from LMICs, but also in HICs, air pollution is typically dominated by traffic sources. Traffic-related pollution is mainly generated by emissions from combustion processes of motor-vehicle, but also from resuspension of road dust, tire and brake wear (Schauer et al., 2006). A simplified summary of sources differentiating rural and urban areas in LMICs is illustrated in **Figure 2**. Estimates of source-specific burdens are country-specific. In India for example, residential biomass burning was the largest individual contributor to disease burden in 2015, responsible of 267,700 deaths (Health Effects Institute, 2018). It was followed by anthropogenic dust, powerplant coal, industrial coal, open burning, and brick production.

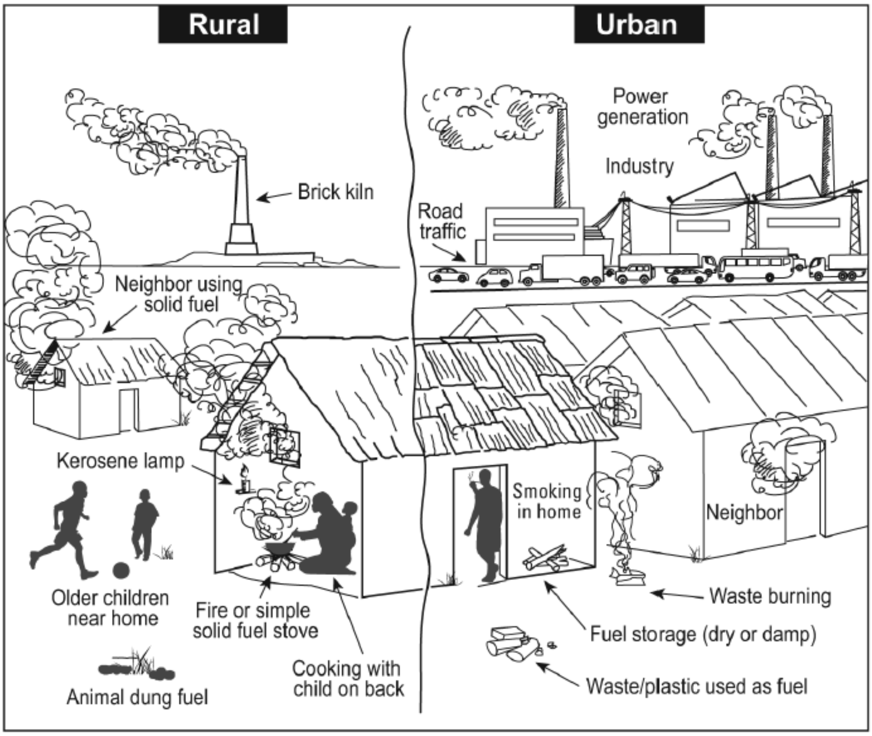

Figure 2 Comparison of air pollution sources in rural vs. urban areas in low- and middle-income countries
Source: extracted from Martin et al., 2013

In this thesis we focus on $PM_{2.5}$, black carbon and carbon monoxide as useful indicators of exposure to the mixture of particulate and gaseous products of **incomplete combustion**.

- **Fine particulate matter**

Particulate matter (also called particle pollution) denotes to the mixture of solid and liquid particles suspended in the air. Fine particulate matter ($PM_{2.5}$) is the fraction of particulate matter with an aerodynamic diameter of 2.5 µm or less, being up to 30 times smaller than human hair. Particulate matter can also contain larger size fractions (e.g., PM_{10} or particulate matter with an aerodynamic diameter of 10 µm or less) and even smaller (e.g., UFP or ultrafine particles with an aerodynamic diameter of 0.1 µm or less). Classifying particles according to their size has been extensively used in exposure science and epidemiology because it determines their transport in the atmosphere and how far the particle gets in the human respiratory system once they are inhaled. $PM_{2.5}$ for example, can travel deeply into the respiratory tract, reaching the lungs. However, as mentioned earlier, shape, density and chemical and toxic properties of the particulate material also determine the potential harmful effect of particles on health.

- **Black carbon**

Black carbon (BC) is a light-absorbing component of $PM_{2.5}$ composed of carbon. While fine particles are undifferentiated, BC is derived exclusively from incomplete combustion. BC has been often used interchangeably for elemental carbon (EC) or soot. Although they are supposed to be comparable, they have slightly different thermal, optical and chemical properties (Petzold et al., 2013). When measuring BC mass through optical absorption by collection on filters, the term BC is used. Alternatively, when measuring BC mass through thermal heating and optical absorption, the term EC is used (Bond et al., 2013). Since EC determination is complex and can be inconvenient (e.g., expensive, filter destructing), absorbance measurements of $PM_{2.5}$ filters have been used as a cheaper and easier technique to measure EC. In sites highly influenced by combustion sources such as traffic, correlation between BC/EC and **$PM_{2.5}$ absorbance** can be as high as 0.97 (Cyrys et al., 2003). EC, together with organic carbon (OC), constitutes the total particulate carbonaceous material. While EC is considered graphite-like carbon, OC is chemically combined with oxygen, hydrogen, and other elements (Petzold et al., 2013).

Although BC is a component of $PM_{2.5}$, it may serve as an additional indicator of the potential harmful effects on health when air quality is dominated by primary combustion sources, particularly when it comes to cardiovascular-related mortality and hospital admissions (Janssen et al., 2011). Additionally, BC emissions are also of concern for climate health. BC is a short-lived greenhouse pollutant that can have even stronger warming effects than carbon dioxide (Smith et al., 2009).

- **Carbon monoxide**

Carbon monoxide (CO) is a colorless, non-irritant, odorless, and tasteless gas. CO is one of the most common and widely distributed air pollutants and is involved in the formation of ozone at the ground level. Although CO can be found in urban outdoor areas due to the presence of combustion engines (including petrol- and diesel-powered motor vehicles and generators), its relevance is mainly found in indoor environments. The most important source of exposure to CO in indoor air is emissions of fuel-based cooking, lighting or heating appliances (WHO, 2010). When poorly maintained appliances are burned in confined and poorly ventilated environments, concentrations of CO can easily rise to lethal levels.

In order to address the risk of long-term exposure to CO, the WHO indoor air quality guideline establishes a value of 7 mg/m^3 (6.1 ppm) for 24-h average exposure to CO (WHO, 2010). In rural settings from LMICs, CO indoor concentrations can exceed 50 ppm from 4% to 20% of 24-h time (Klasen et al., 2015). Fuel combustion releases a complex mixture of particles and gases, varying according to the fuel type and combustion conditions. At the beginning of combustion, the pollutants released are dominated by particulate matter (elemental and organic carbon) but CO dominates towards the end. Independently of the type of fuel used, 90% of the carbon released during biomass combustion is oxidized to carbon dioxide or CO (Reid et al., 2005). Increased fire intensity also creates high concentrations of CO by limiting the oxygen entrance into the flame zone.

1.2 Air pollution exposure assessment

a) Exposure concept and classification of exposure assessment

Exposure is the contact between an agent and a target. In environmental epidemiology, the agent is a substance found in an environmental medium (e.g., water, air, soil) and the target is the surface of the human body (e.g., skin, respiratory tract) (Nieuwenhuijsen, 2015). More precisely, in air pollution epidemiology the agent (e.g., particle, gas) is found in the air and the target is the respiratory tract. The physical pathway an air pollutant takes from the source to the human is illustrated in **Figure 3**. The Figure provides a specific example of household air pollution, when the source is combustion of biomass cooking fuel, which generates emissions of products of incomplete combustion. Dispersion of the resultant combustion-related pollutants leads to environmental concentrations in air. If for example cooking occurs in an indoor kitchen, the kitchen would be considered a microenvironment or compartment where air pollutants have a relatively homogeneous concentration and where they come into contact with individuals. Thus, the concept of microenvironment is closely linked to the location of the individual. If an individual moves to another location (e.g., main living area, workplace) it would be considered a different microenvironment and therefore, potentially a different exposure (Lioy and Weisel, 2014).

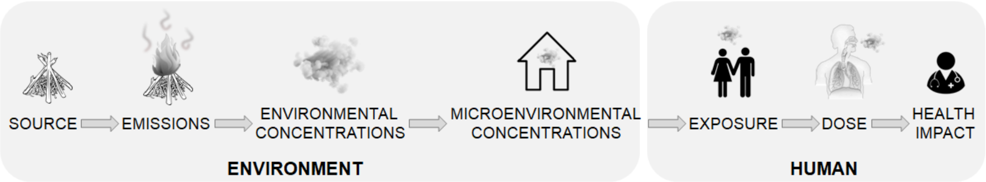

Figure 3 Exposure pathway of health-damaging air pollutants from the source (e.g., firewood) to receptor (e.g., human being). *Source: adapted from Smith, 1993 and Nieuwenhuijsen, 2015*

The intake pathway (or exposure route) is the mechanism by which the pollutant penetrates to the human body. In the case of air pollutants it is via inhalation. The dose is the amount of the inhaled pollutant that penetrates to the lungs, where it may react with body tissue and lead to a physiological change. The dose depends not only on exposure characteristics (concentration, duration, and frequency) but also on the characteristics of the pollutants (e.g., size, chemical composition) and the individuals (e.g., breathing rate, body weight).

Exposure assessment is broadly understood as the study of the distribution and determinants of the environmental agents affecting health (Nieuwenhuijsen, 2015). Although this assessment can be done in all stages presented in **Figure 3**, for air pollution epidemiologic studies it is widely accepted that exposure measurement accuracy is increased when microenvironmental concentrations are used instead of emissions. In this context, exposure assessment is specifically referring to the process of quantifying the concentration of the air pollutant (e.g., $\mu g/m^3$ in air) and the duration (e.g., hours to years) and frequency (e.g., times per day) of the contact between the individual and the air pollutant both at the microenvironmental and at the individual level.

Exposure assessment approaches to quantify the concentration or level of exposure can be classified into direct and indirect. Direct methods are those measuring the concentration using air monitoring equipment. Indirect methods are those estimating exposure using modelling techniques. Modelling exposure is optimally conducted in conjunction with direct methods in order to build and/or validate the model(s) (see more details in the following subsections). Questionnaires are also indirect methods that are widely used to quantify duration and frequency of past and present exposure as well as to obtain information on individual socio-economic characteristics (e.g., face-to-face interviews), location, and activities (e.g., time-activity diaries). They are cheap and easy to distribute, allowing the collection of relevant data for a large sample of the population. However, they are subjective tools that if not properly designed, administered, and validated can lead to high measurement error (Nieuwenhuijsen, 2015). Thanks to advances in technology, objective tools to assess patterns of exposure are growingly used. This is for example the case of smartphone-based Global Positioning System (or GPS) to track location of individuals objectively and continuously (de Nazelle et al., 2013).

- **Direct methods**

Air quality monitors can be classified as shown in **Figure 4**. Time-integrated monitors are those monitors providing average or accumulated concentrations for a specific sampling period (e.g., 24 hours). Time-resolved monitors are those monitors providing continuous concentrations for a specific time interval (e.g., every 5 min). Only time-resolved monitors can therefore provide information regarding the time when a high-polluting episode is occurring.

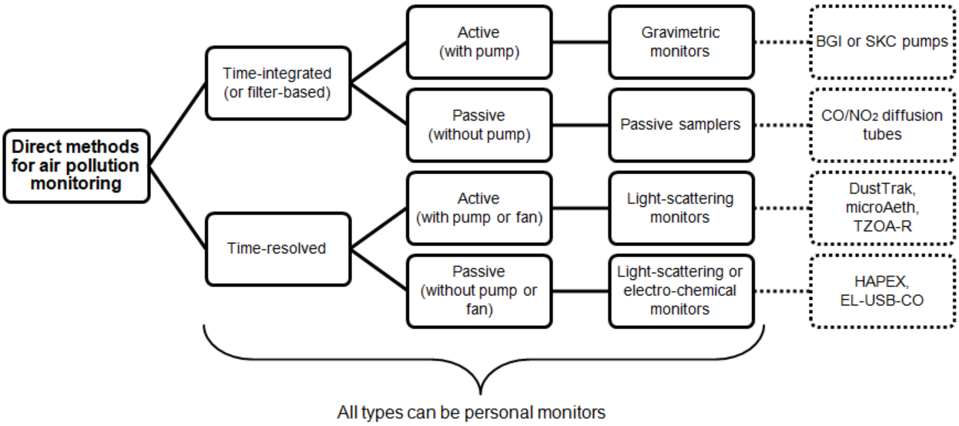

Figure 4 Possible classification of air quality monitors. Boxes with dashed lines show some examples of each type of monitors. *Source: elaborated by the author.*

Air quality monitors can have either active or passive measuring mechanisms. Active monitors are composed of a sampling pump which draws air into a collection unit. This air passes through a filter, which retains particles. The size of the particles retained in the filter will depend on cut-off size of the impactors or cyclones used. Commonly, impactors and cyclones are designed to retain $PM_{2.5}$ and PM_{10} (i.e., remove particles larger than 2.5 µm or 10 µm and collect those smaller). Exposure concentration is then determined by subtracting the weight of the filter after monitoring from the weight of the filter before monitoring and dividing this difference by the volume of air sampled. This is why they are also known as **gravimetric monitors**. Filters can be analyzed afterwards to determine the chemical composition of the aerosol sampled.

Passive monitors work by the principle of diffusion of air. Since they do not depend on a sampling pump, passive monitors do not require electricity and are cheaper and simpler to operate than active monitors. Passive monitors can be used to sample either gases or particles, but are more commonly used to sample gaseous pollutants such as nitrogen dioxide (NO_2).

The same air quality monitor can be equipped with various sensors (e.g., gas, **temperature**, and **humidity** sensors). In its broadest definition, a sensor is a device that reacts with changes in environment and sends the information to other electronics. Sensors can be grouped into those measuring gas and those measuring particles. Gas sensors operate either by electrochemical interaction with the gas or with infrared light absorption (Aleixandre and Gerboles, 2012). Particle sensors estimate the concentration of a single or different particle size ranges when a beam of infrared light is scattered after colliding with the aerosol sample. The amount of light scattered will depend on the characteristics of the particles in the aerosol (e.g., size, index of refraction, light-absorbing potential). Electrochemical sensors are sensible to meteorological fluctuations such as wind speed, temperature, and humidity, which negatively influence the chemical equilibrium of the sensor and therefore, their response to the gas (Aleixandre and Gerboles, 2012). Light-scattering sensors are generally particle counters, so they do not provide direct readings of particulate matter mass (Snyder et al., 2013). Hence, the use of monitors mounted on light-scattering sensors should be accompanied by side-by-side measurements from a **gravimetric monitor** (more cumbersome and expensive), in order to convert counts to mass or correct for bias in the mass concentration estimate based on light-scattering devices.

Air quality monitors are optimally worn by individuals to obtain exposure measurements in individual’s exact microenvironments. Personal monitors are designed to be small in size and lightweight in order to be wearable by individuals while they are doing their normal daily activities. They should be placed at the breathing zone (area immediately surrounding nose and mouth, ideally not exceeding 30 cm) to better capture the inhaled air of the individual. To do so, monitors can be either directly clipped to a backpack strap or a shirt, or carried inside a backpack or pouch but with the inlet (or where air enters) placed to the breathing zone through a tube.

Personal monitoring is generally labour-intensive for researchers (particularly if gravimetric monitors are employed) and can be burdensome for participants. This is why their use is usually restricted to small samples of individuals and so far their use has been limited if compared to microenvironmental monitoring. Microenvironmental monitoring has been the most common direct method used in exposure science and environmental epidemiology and implies the use of portable or stationary monitors. These monitors are bigger, more robust, and usually more expensive than personal monitors. While portable monitors (or hand-held) are particularly used for mobile monitoring and are commonly validated and accepted by researchers (**research-grade monitors**), stationary monitors are widely used for regulatory purposes (regulatory monitors) since they are sophisticated and well-established monitors that ensure the accuracy of measurements (Williams et al., 2014).

For decades, performance specifications of monitors such as **accuracy** and precision have been a cause of concern and debate in the air pollution community. Poor or unknown quality of data has been considered as useless as lack of data, particularly when it comes to decision-making (Snyder et al., 2013). Parameters such as accuracy (or the degree to which a measurement represent the true value), precision (or the degree of variability in a measurement), bias (or systematic deviation of measurements from the true value) (**Figure 5**), and reliability (or the degree of stability of a measurement when repeated under same conditions) have a decisive role when determining monitor’s performance.

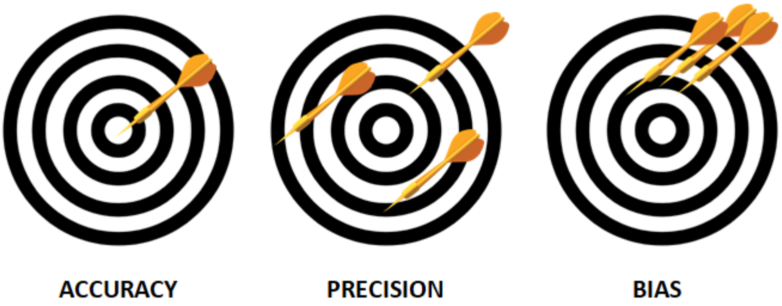

Figure 5 Graphics representing the concepts of accuracy, precision and bias. *Source: original idea extracted from the Air Sensor Guidebook of the USA Environmental Protection Agency* (Williams et al., 2014). *Dartboard icon made by Freepik from www.flaticon.com*

- **Indirect methods**

Modelling techniques are particularly useful since provide estimates of exposure in larger number of individuals and are less instrumentally demanding than personal or microenvironmental monitoring. They are particularly used for assessing long-term levels (months to years) of outdoor air pollution, although long-term indoor modelling techniques exist too. Correlation between outdoor and personal concentrations depend on the pollutant and the setting (Montagne et al., 2013), but given the high amount of time that people spend in their home and surroundings, outdoor concentrations have been generally considered a valid proxy of residential-based personal exposure.

Indirect methods used so far in epidemiological studies include: 1) proximity-based assessments (e.g., linear distance from a major road); 2) spatial interpolation (e.g., kriging); 3) land-use regression (LUR) models; 4) dispersion modelling; and 5) hybrid models (i.e., combining at least two of the abovementioned techniques) (Jerrett et al., 2005; Nieuwenhuijsen, 2015). **LUR models** have been one of the most extensively applied approaches. LUR models combine direct environmental measures of air pollution in a limited number of locations in the study area (preferably at > 40 sites) (Basagaña et al., 2012), geographic information system (GIS) data, available throughout the study area. With these, regression models to predict small-area variations in exposure based on spatially varying GIS covariates (e.g., land use, distance to source) are developed (Hoek et al., 2008). The resulting models can then be used to predict ambient exposures in any location of the study area such as the home address of individuals.

When compared to dispersion models, which are based on physical principles and emission data, LUR models have lower input demand and have been shown to perform better or similarly (Briggs et al., 2000; Hoek et al., 2008). Its use, however, has been restricted to urban areas dominated by traffic (Hoek et al., 2008; Sanchez et al., 2018). Besides, as all models, LUR models are also vulnerable to exposure measurement error. If LUR models do not account properly for all sources of variation or small number of monitoring sites is used together with a high number of potential predictors, derived health effects can suffer from bias (Basagaña et al., 2013).

b) Challenges of choosing the best exposure assessment approach

In this thesis, different air pollution exposure assessment approaches have been used. Choosing the best assessment strategy is always challenging since it depends on multiple interlinked factors. These factors can be grouped into: 1) scientific, 2) logistic, and 3) economic.

Scientific factors are those related to the research aim, which determines the time scale of the exposure (short-term vs. long-term), the type of exposure (outdoor vs. indoor vs. personal), the type of air pollutant (gas vs. particles), and the target population. Logistic factors are those related to the ease of use of monitoring equipment, participant burden, the feasibility of collecting or gathering data based on available human and material resources, and the complexity of the characteristics of the site (e.g., security, remoteness). Economic factors are those related to the budget available for the study and can determine factors such as the sample size (e.g., individuals, households, sites) and the type of the monitoring equipment (e.g., low-cost vs. research-grade).

Assessing air pollution in LMICs has additional challenges. Apart from the fact that air pollution levels can be higher and sources are often different than those in HICs, there is also high complexity and heterogeneity in cultural, seasonal, and behavioural patterns influencing exposure. Fieldwork conditions are also rougher since meteorological conditions are more extreme and there are areas without reliable sources of electricity to power monitoring equipment. Indeed, the short battery life of the majority of current monitors is one of the main challenges for long-term, continuous, and unattended sampling in all parts of the world.

c) Proliferation of low-cost sensors

Financial constraints are the main barrier to large-scale, long-term deployments for personal or microenvironmental monitoring campaigns. But rapid growth of **low-cost sensors** could shape the future of air pollution research. Sensors are commercially-available for prices as low as $10. Multiple manufacturers and start-up companies custom-built air quality monitors putting together these sensors with microprocessors to collect sensor output, convert it in human-readable data (e.g., $\mu g/m^3$ of $PM_{2.5}$) and store data internally or remotely. This in turn results in ready-to-use air quality monitors that can be much cheaper (< $600) compared to their research-grade counterparts (> $1,000).

The proliferation of low-cost sensors is seen as an opportunity for personal, indoor, and outdoor air quality assessments broadly (e.g., empowerment of citizens, educational purposes), but concerns remain about the accuracy and performance among the air pollution research community (Lewis and Edwards, 2016). Most of the manufacturers using low-cost technology release their products without a validation or with validation tests restricted to controlled laboratory environments, not representative of heterogeneous real-world environments. There are field-validation studies testing some of the emerging **low-cost monitors**, although most of these studies have been conducted in outdoor environments such that the performance of low-cost monitors in indoor environments is hard to predict. To conduct measuring campaigns on large scales and in a feasible way in terms of financial and practical grounds, we ideally need: 1) easy-to-use, 2) inexpensive, 3) accurate, and 4) portable monitors. For household air pollution studies, monitors additionally need to be robust to operate under a wide range of concentrations and temperatures. Currently there is no monitor that meets all of these criteria, highlighting the need for validation of affordable monitors to accurately assess long-term household air pollution (Clark et al., 2013).

1.3 Blood pressure and hypertension

In this thesis we link air pollution with cardiometabolic health. Chronic cardiometabolic conditions include hypertension (presented in this section) and diabetes mellitus (presented in section 1.4). Other conditions include atherosclerosis, chronic kidney disease, and obesity, among others. The metabolic syndrome is the presence of multiple cardiometabolic abnormalities that individually and interdependently increase cardiovascular disease (CVD) and diabetes morbidity and mortality (Ford, 2005). The risk factors typically used to define the metabolic syndrome are: elevated waist circumference, elevated triglycerides, reduced HDL-C (high-density lipoprotein cholesterol), elevated blood pressure (presented in this section), and elevated fasting glucose (presented in section 1.4) (Alberti et al., 2009).

a) Definition, measurement, and classification of blood pressure

Blood pressure (BP) is the pressure exerted by circulating blood on the arterial vessels due to the pumping action of the heart. Along with the cardiac cycle, BP is composed by a maximum and a minimum pressure. The maximum pressure, named systolic BP (SBP), occurs during the systole phase of the cardiac cycle (or ventricular heart muscle contraction). In contrast, the minimum pressure, named diastolic BP (DBP), occurs during the diastole phase of the cardiac cycle (or ventricular heart muscle relaxation).

Palpation of the oscillations of the blood flow (or pulse) dates back to the early Egyptians, but it was not until the 19th century that the BP measurement technique emerged as we know it today: the mercury sphygmomanometry. Although mercury sphygmomanometers are considered the gold standard when used by trained clinical staff, their use has been drastically reduced due to mercury safety concerns. This has led to the proliferation of non-mercury devices such as electronic (oscillometric) devices, which use a sensor to detect the pulse during arm cuff inflation and deflation and have led the way in clinical and public health practice (Whelton et al., 2017). In all types of devices, BP is typically expressed as millimeters of mercury (mm Hg).

Classification of BP is sensitive to international guidelines (**Table 1**). To date, the most common accepted and used diagnostic cut-off for hypertension in adults has been SBP ≥140 mm Hg and/or DBP ≥90 mm Hg (Chobanian et al., 2003). But in 2017, the American College of Cardiology (ACC) and the American Heart Association (AHA) proposed to lower the cut-offs to SBP ≥130 mm Hg and/or DBP ≥80 mm Hg based on new observational evidence (Whelton et al., 2017).

Table 1 Classification of blood pressure for adults according to the seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC7) and the 2017 guidelines from the American College of Cardiology (ACC) and the American Heart Association (AHA).

	JNC7 guidelines		**ACC/AHA guidelines**	
	SBP (mm Hg)	DBP (mm Hg)	SBP (mm Hg)	DBP (mm Hg)
Normal	<120	and < 80	<120	and < 80
Elevated	120-139	or 80-89	120-129	and < 80
Stage 1 hypertension	140-159	or 90-99	130-139	or 80-89
Stage 2 hypertension	≥160	or ≥100	≥140	or ≥90

Source: table adapted from Chobanian et al 2003 (JNC7) and Whelton et al 2017(ACC/AHA). Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure.

Since within-individual BP levels are very variable, JNC7 and ACC/AHA agree that for a proper classification of hypertension at least two BP readings should be obtained in at least two occasions. Average of BP readings obtained in a single occasion may lead to an overestimation of hypertension and it is therefore not recommended for clinical decision-making (Chobanian et al., 2003; Whelton et al., 2017).

b) Burden and prevalence of high blood pressure and hypertension

High BP is a major risk factor for CVD and chronic kidney disease. The risk of CVD progressively increases with increasing BP levels. At middle and old ages (40-69 years), every 20 mm Hg increase in SBP (or equivalently 10 mm Hg in DBP) is associated with more than a twofold risk of death from ischemic heart disease, stroke and other vascular causes (Prospective Studies Collaboration, 2002).

According to the last Global Burden of Disease study, worldwide, high BP accounts for 10.5 million deaths (representing up to 32% of total deaths) and 212 million DALYs (representing up to 20% of total DALYs) (Gakidou et al., 2017). In terms of DALYs, high BP was ranked at the second risk factor for men (only surpassed by smoking) and the first risk factor for women.

Worldwide prevalence for high BP has increased over the past four decades, going from 594 million adults in 1975 to more than one billion in 2015 (Zhou et al., 2017). This increasing trend has large regional disparities; while in the seventies prevalence was mostly present in HICs, currently is mostly present in LMICs, particularly in South Asia. Of all adults with high BP across the world, almost half (44%) live in South and East Asia; India and China are the countries with more prevalent cases in the world (18% and 20%, respectively) (Zhou et al., 2017). Indeed, the expected 60% increase in the worldwide prevalence by 2025 is mostly attributed to the rise of the prevalence in LMICs, which will increase by 80% in the coming decade and contrasts with the 24% increase in HICs (Kearney et al., 2005). In the framework of this thesis, it is also important to point out that the prevalence of hypertension among adults with diabetes can be up to 80% (Whelton et al., 2017). When both hypertension and diabetes coexist, there is a high risk of developing CVD and microvascular complications. Each 10 mm Hg decrease in SBP can reduce up to 13% microvascular complications in patients with diabetes (Adler, 2000).

Prevalence of hypertension can have a distinctive urban-rural pattern.When estimates for both HICs and LMICs are pooled together, rural areas only have a slightly less prevalence of hypertension (39%) than urban areas (40%) (Chow, 2013). However, in LMICs such as India, the prevalence of hypertension can be much higher in urban populations (33%) than rural populations (25%) (Anchala et al., 2014). In LMICs, prevalence of hypertension is generally lower in women (36%) than men (37%) (although the pattern is inverse after menopause) and women tend to have higher rates of hypertension awareness, treatment, and control than men (Chow, 2013).

c) Risk factors for hypertension

Hypertension is mainly driven by biological, sociological, and environmental risk factors. The strongest non-modifiable determinant of hypertension is age (above 50 years of age, higher BP). Most relevant risk factors of hypertension are related to lifestyle habits. Maintenance of a normal body weight, healthy dietary habits (e.g., consumption of vegetables and fruits and low-fat products), low salt intake, increased levels of physical activity, and moderation of alcohol consumption (e.g., no more than two drinks per day in men) have been shown to prevent high BP (Chobanian et al., 2003). However, social and cultural norms can limit the scope of these prevention strategies. Factors such as lack of availability of healthy food and exercise programs and patient reluctance to the health system can impede primary prevention.

Pervasive environmental factors can also affect BP: ambient **temperature** (colder temperature, higher BP), geography (higher altitude and latitude, higher BP), **noise** (louder noise, higher BP), and air pollutants (higher concentrations of pollutants, higher BP) (Brook et al., 2011).

1.4 Glucose metabolism and diabetes

a) Definition, measurement, and classification of blood glucose levels

Glucose is a simple sugar (or monosaccharide) that is used by the human body as a key source of energy. Glucose is released into the blood stream by the liver and its origin is primarily from the brake-down of ingested carbohydrates. The amount of glucose in human blood (i.e., the blood glucose level) is universally expressed in millimoles per litre (or mmol/l). The hormone in charge of regulating the blood glucose levels is insulin, which is produced by the pancreatic beta-cells (β-cells). When the β-cells detect high blood glucose levels, they produce insulin in response. When blood glucose levels are persistently high (hyperglycaemic state), β-cells are forced to produce more insulin to compensate, which could lead to **insulin resistance** (or low insulin sensitivity). Insulin sensitivity and β-cell function are therefore inversely and proportionally related (Kahn, 2001).

Diabetes was defined in 1999 by the WHO as “a metabolic disorder of multiple etiology, characterized by chronic hyperglycaemia resulting from defects in insulin secretion, insulin action or both”. Individuals with extensive β-cell destruction (attributable to an autoimmune pathologic process) require insulin for survival. These are individuals having Type 1 diabetes mellitus (Khatib et al., 2006). When β-cells cannot cope with increased insulin resistance, there is risk of developing Type 2 diabetes mellitus (T2DM) (Kahn, 2001). T2DM is more common (90-95% of all diabetes) than Type 1 and it remains asymptomatic even when pathologic and functional changes in various target tissues have started (American Diabetes Association, 2014). During this asymptomatic period, measurements of blood glucose levels are done for the detection and control of diabetes.

Table 2 Summary of cut-points and characteristics of diabetes diagnostic tests.

	Fasting blood glucose	**Oral glucose tolerance test (OGTT)**	**Glycated hemoglobin (HbA_{1c})**
Cut-points for diabetes diagnosis in adults	≥7 mmol/l	≥11.1 mmol/l	≥6.5%
Fasting required	yes, ≥8 hours	yes, ≥8 hours	no
Technique availability	widely available	widely available	may not be available
Participant burden	medium	high	low
Biological variability	high	high	low
Day-to-day variability	high	high	low
Sample stability	low	low	high
Sensitive to...	media (serum vs. plasma)	medication	ethnicity and age of participant
Cost	inexpensive	expensive	expensive

Source: table adapted from Sacks, 2011.

There are three different tests to detect high levels of blood glucose (**Table 2**). The test used in this thesis and the most extensively used for its low cost and availability is fasting blood glucose. In this test, participants are asked to fast before blood withdrawal. Blood is afterwards analyzed using standard enzymatic methods. There is no consensus on an internationally recognized cut-point to define the fasting state. While WHO defines fasting as no food or beverage consumption (other than water) for at least 10-16 hours (Khatib et al., 2006), the American Diabetes Association (ADA) defines it as “no caloric intake for at least 8 hours” (American Diabetes Association, 2014). However, participants are typically asked to fast overnight and a minimum of 8 hours fasting is generally accepted.

Other tests (to be done together with fasting blood glucose or independently) are the oral glucose tolerance test (OGTT) and glycated haemoglobin (HbA_{1c}). Glycated haemoglobin is less susceptible to biological and day-to-day variability if compared to fasting blood glucose and OGTT (**Table 2**), so is believed that it better represents long-term (3-months) average blood glucose levels. However, its accuracy has been put into question due to its susceptibility to ethnicity and age (Bansal, 2015).

In asymptomatic individuals, multiple testing is required in order to confirm the diagnosis. In symptomatic individuals, unequivocal high levels of blood glucose in a single test may be sufficient for diagnosis (Khatib et al., 2006). In epidemiologic studies interested in average population-based levels rather than diagnosis, levels from a single test may be sufficient to identify people at risk, although repeated tests are always preferable. According to WHO and ADA, an adult having a fasting blood glucose level of ≥ 7 mmol/l is considered to have diabetes.

Before the onset of diabetes, there is always the presence of a **prediabetes** state. Prediabetes is an intermediate risk state where the blood glucose levels are above normal but below the cut-point defined for diabetes. The cut-points proposed for the definition of prediabetes are not uniform. The WHO proposes that fasting blood glucose levels should be between ≥ 6.1 mmol/l and ≤ 6.9 mmol/l, while the ADA uses a lower cut-point (≥ 5.6 mmol/l).

b) Burden and prevalence of high blood glucose and diabetes

The burden of deaths from high blood glucose in 2016 was 5.6 million deaths (accounting for 17% of the total global deaths). This number includes 1.4 million diabetes deaths (26% of the total high blood glucose deaths) (Gakidou et al., 2017). Other causes of death included chronic kidney disease, ischaemic heart disease, and ischaemic stroke, among others, highlighting the large mortality burden of high blood glucose beyond diabetes. High blood glucose was also a large contributor to global morbidity, responsible of 144 million DALYs (accounting for 13% of the total global DALYs).

An estimated 422 million adults were living with diabetes in 2014, representing 8.5% of the total global population (WHO, 2016). Although the highest prevalence is found in the Eastern Mediterranean region (13.7%), most of the new cases are appearing in LMICs. South-East Asia has seen a recent dramatic increase in diabetes, with 96 million people having diabetes in this region and with India and China being the countries with more prevalent cases of diabetes in the world.

As occurs with hypertension, prevalence of diabetes also has a distinctive urban-rural pattern. Prevalence of diabetes is substantially higher in urban than rural areas. A multicenter study in India estimated that people living in urban areas had 30% higher risk of having diabetes than those living in rural areas (Anjana et al., 2011). Indeed, the number of prevalent cases in India and China is expected to grow with increasing economic development and urbanization.

c) Risk factors for diabetes

Risk factors for T2DM development are a combination of genetic and metabolic factors. Among genetic factors, ethnicity and family history of diabetes are important factors. For example, South Asians have a particular phenotype that predisposes them to higher insulin levels, greater insulin resistance, and higher prevalence of T2DM (Unnikrishnan et al., 2014). South Asians also progress from prediabetes to diabetes at younger ages than white Europeans (Sattar and Gill, 2015). Other ethnicities such as African American, Latino, and Pacific Islander are also considered high-risk.

Among metabolic factors, overweight and obesity are the strongest risk factors for T2DM. Both higher waist circumference and body mass index are associated with increased risk of T2DM. Although South Asians have lower BMI than other ethnicities, its association with high blood glucose is as strong as in any other population (Ramachandran et al., 2010). Obesity goes in hand with physical inactivity and unhealthy dietary patterns (e.g., high intake of saturated fatty acids and sugar-sweetened beverages), both important risk factors for T2DM. Other important risk factors are previous gestational diabetes, older age (prevention tests in assympomatic adults start at 45 years), and smoking (American Diabetes Association, 2014).

Emerging evidence indicates that the built and natural environment (e.g., walkability, green spaces) and environmental characteristics (e.g., air pollution, temperature, noise) can also influence T2DM (Mazidi and Speakman, 2017; Zare Sakhvidi et al., 2018; Dendup et al., 2018).

1.5 Effects of air pollution on cardiometabolic health

a) Potential biological mechanisms

The potential biological mechanisms linking air pollution exposure with cardiometabolic responses are not fully understood. However, it is well-established that the mechanisms may differ according to the particulate constituents, exposure duration (acute vs. chronic), and the underlying susceptibility of individuals (e.g., patient with heart failure).

With acute exposures (i.e., within minutes/hours after exposure), principal non-mutually exclusive pathways are autonomic imbalance favouring sympathetic activity, thrombosis (through the release of pro-coagulant proteins), and alterations in endothelial function (Münzel et al., 2016). Understanding the pathways for chronic exposures (i.e., within weeks/months after exposure) is more complex since multiple tissues can be involved and exposure can occur with other more dominant risk factors. Additionally, little is known about the effects of co-pollutant chronic exposures such as noise, which may interact additively or synergistically.

Oxidative stress is the most common pathway proposed for short- and long-term air pollution exposure in a range of different pollution scenarios (diesel exhaust, wood smoke, $PM_{2.5}$, UFP). Increase in oxidant stress can trigger endothelial injury or dysfunction and consequently alter systemic hemodynamics (leading to the development of hypertension) and increase insulin resistance (leading to the development of diabetes). Other pathways by which particulate matter and other air pollutants could lead to the development of cardiometabolic disease include impaired renal function, obesity and weight gain, and alterations in mitochondria and brown adipose tissue (Rajagopalan and Brook, 2012).

b) Evidence for particulate air pollution and high blood pressure and hypertension [1]

Before the start of this thesis in 2016, there was already a large amount of epidemiological evidence supporting that short and long-term exposure to particulate air pollution can increase BP (Brook and Rajagopalan, 2009; Liang et al., 2014; Yamamoto et al., 2014; Giorgini et al., 2016). In general, less evidence existed for long-term exposures than for short-term and almost all the existing evidence found heterogeneous results, mainly due to the different populations studied and the different methodologies used across studies.

All of the evidence regarding the effects of long-term exposure to air pollution on BP or hypertension was based on HICs, particularly North America and Europe, where annual ambient concentrations reported are generally lower ($< 20\ \mu g/m^3$) and influence of traffic-related sources is higher than in LMICs. Hence, there is a gap for people exposed to higher doses than passive smoking but lower than active smoking, typically found in LMICs due to the contribution of household air pollution (Smith and Peel, 2010).

To the best of our knowledge, there was no evidence about the effects of long-term exposure to $PM_{2.5}$ on BP in South Asia before starting this thesis. However, a systematic review covering evidence until 2012 identified nine South Asian studies assessing the link between PM_{10} and CVD, including BP (Yamamoto et al., 2014). These studies assessed the role of PM_{10} and prevalent hypertension using case-control designs (Banerjee et al., 2012; Dutta and Ray, 2013) and compared SBP and DBP levels in children from high-polluted vs. less-polluted schools (Sughis et al., 2012). Others have focused on the changes in BP after short exposure to household air pollution (Dutta et al., 2011; Baumgartner et al., 2014; Norris et al., 2016).

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[1] Search terms used for literature review are shown in Annexes (page 272).

Despite the influence of BC in cardiovascular and cardiorespiratory health, there is still limited evidence about the long-term effects of BC on high BP, as recently highlighted by a systematic review (Magalhaes et al., 2018). Existing studies conducted before this thesis started were based in the USA and only included older adults (~70 to 80 years) (Schwartz et al., 2012; Wellenius et al., 2012; Zhong et al., 2016). Although the three studies found positive and significant associations with SBP and DBP per increased concentrations in middle- or long-term BC, differences in the exposure measurement approaches used by these studies make them hard to compare.

c) Evidence for particulate air pollution and high blood glucose and diabetes [1]

Compared to high BP and hypertension, at the start of this thesis the evidence for the long-term effects of particulate air pollution on blood glucose was even more limited (Thiering and Heinrich, 2015), with few studies having evaluated this association at that time (Chuang et al., 2010; Chen et al., 2016; Liu et al., 2016; Wolf et al., 2016). Some of these studies indicated a positive association between long-term $PM_{2.5}$ and blood glucose in: 11,847 middle-aged Chinese adults (Liu et al., 2016), 1,023 Mexican American women with previous diagnosis of gestational diabetes (Chen et al., 2016), and 2,944 German adults (Wolf et al., 2016).

At the start of this thesis there were no studies including exposure to long-term BC. Only Wolf and colleagues evaluated $PM_{2.5}$ absorbance as a comparable measure of BC, without finding a strong association.

Most of the evidence at the beginning of this thesis was focused on the link between particulate air pollution and diabetes. The first study linking air pollution with diabetes prevalence in adults was an ecological Canadian study conducted 16 years ago (Lockwood, 2002). Since then, there has been a substantial increase in the number of studies assessing this potential association.

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[1] Search terms used for literature review are shown in Annexes (page 272).

Positive associations have been found for diabetes mortality, prevalence, and incidence, all generally supported by several meta-analyses (Balti et al., 2014; Janghorbani et al., 2014; Wang et al., 2014; Eze et al., 2015). The systematic review conducted by Eze and colleagues only identified studies in North America and Europe. They also listed some of the limitations of the evidence available in 2014, highlighting among other things the importance of considering risk factors such as obesity, physical activity, nutrition, and smoking when assessing the effect of air pollution on diabetes (Eze et al., 2015).

During the course of this thesis, studies assessing potential air pollution effects on cardiometabolic health have grown considerably in East Asia, mostly in China (Lin et al., 2017; Liu et al., 2017; Li et al., 2018; Qiu et al., 2018; Yang et al., 2018a, 2018c; Zhang et al., 2018; Xie et al., 2018). These studies have provided new insights on the etiologic role of long-term air pollution on BP and blood glucose in LMICs. Besides, they were conducted in settings with representation of rural areas and with comparable burdens of air pollution and cardiometabolic diseases as those found in South Asia.

2. RATIONALE

LMICs are facing four of the main drivers of morbidity and mortality worldwide, namely ambient air pollution, household air pollution, high blood pressure, and high fasting blood glucose. However, LMICs have received little attention in exposure and environmental epidemiological studies so far, leaving important research gaps in exposure science and global health.

Advances in battery technology, miniaturization, and other technological advances have brought to market a number of low-cost air quality monitors that may offer the opportunity to quickly provide air pollution data, which hold particular promise for measurements in LMIC settings, where ambient monitoring networks can be sparse and household concentrations and personal exposures significantly different from ambient concentrations. However, many questions have emerged about the potential benefits of these low-cost monitors, including their performance for long-term sampling in populations exposed to high levels of household air pollution. Accurate, easy-to-use, and affordable monitors to measure long-term household air pollution exposure are needed to move beyond currently used short-term measurements as a proxy for long-term exposure, which is of interest for many health outcomes. Evaluating the accuracy and ease of use of these monitors is also essential to design cost-effective sampling strategies in population-based studies in LMICs.

Given the substantial proportion of the population still relying on unclean fuels for household energy, it is crucial to identify specific sources or activities contributing to personal particulate exposure, especially among women, who bear a disproportionate burden of household air pollution. This information could support the design, implementation and evaluation of community-based interventions to improve health.

Very little is known whether long-term exposure to ambient air pollution is linked to higher levels of BP and fasting blood glucose in LMICs. Existing evidence is based on populations inside of HICs. Findings from these studies may have limited transportability to populations in LMICs because air pollution levels are typically outside of the range observed in HICs and influenced by a complex mixture of sources. Differences in the genetic profile, lifestyle habits, and baseline health status are also important components that could make previous findings have limited transportability to LMICs. Epidemiological studies in LMICs can therefore shed light on the exposure-response relationship in populations exposed to higher ambient concentrations.

3. OBJECTIVES, HYPOTHESES, AND CONCEPTUAL FRAMEWORK

General objectives

The overarching aims of this research are:

1) To explore the potential benefits of low-cost technology for conducting long-term monitoring campaigns in population-based studies in rural low- and middle-income areas.
2) To characterize the levels of personal and ambient particulate air pollution and to identify the sources of personal particulate air pollution in a semi-rural area in South Mozambique.
3) To evaluate the associations between long-term exposure to ambient particulate air pollution and cardiometabolic outcomes in adults from a peri-urban area in South India.

Specific objectives

1.1) To evaluate the performance of three low-cost monitors measuring indoor $PM_{2.5}$ and CO in a wood-combustion experiment in Spain and in a field-based study in India (**paper I**).

2.1) To characterize levels of ambient PM2.5, EC, and OC in a semi-rural area of Mozambique and temporal patterns of personal exposure to BC among women in the same area (**paper II**).

2.2) To identify main predictors of personal exposure to BC among women in a semi-rural area of Mozambique (**paper II**).

3.1) To evaluate associations between long-term exposure to ambient $PM_{2.5}$ and BC, systolic and diastolic blood pressure, and prevalent hypertension in adults from peri-urban India (**paper III**).

3.2) To evaluate associations between long-term exposure to ambient and personal $PM_{2.5}$ and BC, levels of fasting blood glucose, and prevalent prediabetes and diabetes in adults from peri-urban India (**paper IV**).

Hypotheses

- ✓ Low-cost technology is easy to use and provides material benefits for conducting long-term monitoring campaigns in rural low- and middle-income areas.

- ✓ Cooking-related indicators are the main determinants for personal exposure in women in semi-rural Mozambique.

- ✓ High exposure to ambient and personal air pollution is associated with poorer cardiometabolic health in adults from peri-urban India.

Conceptual framework

The conceptual framework of this thesis is illustrated in **Figure 6**.

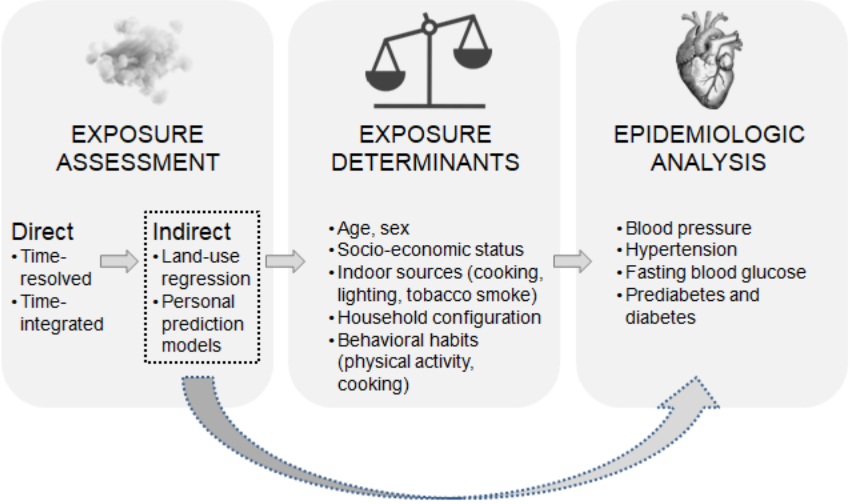


Figure 6 Conceptual framework of this thesis, covering aspects of air pollution exposure assessment, exposure determinants, and environmental epidemiology.

4. METHODS

4.1 Study areas and population

This thesis is based on two collaborative projects: the SUMA project and the CHAI project. The SUMA project is the framework for **paper II** and the CHAI project for **papers I, III and IV**.

SUMA builds on the health and demographic surveillance system (HDSS) conducted by the Manhiça Health Research Centre (Centro de Investigação em Saúde de Manhiça, CISM) since 1996 in the Manhiça district (Maputo Province), in southern Mozambique. In 2014, the HDSS area covered 500 km^2 and 95,000 inhabitants distributed in 22,000 geo-located households (Sacoor et al., 2013). In this thesis, we used cross-sectional data from a measurement campaign conducted during 2014-2015. The campaign aimed to characterize levels of ambient particulate air pollution in the HDSS area as well as levels of personal exposure to BC in women of childbearing age living in the study area. Apart from collecting air pollution data, the overarching goals of this measurement campaign were to identify determinants of personal air pollution exposure among women and to assess potential respiratory health effects.

CHAI builds on the **A**ndhra **P**radesh **C**hildren **a**nd **P**arents **S**tudy (APCAPS), a prospective cohort investigating risk factors for cardiometabolic disease over the life course conducted by investigators in India (Public Health Foundation of India, National Institute of Nutrition) and the UK (LSHTM, University of Bristol). In this thesis, we used cross-sectional data from the third follow-up of APCAPS, conducted during 2010-2012 and including around 7,000 participants residing in 28 peri-urban villages southeast of Hyderabad city (Telangana state, South India). Participants from the third follow-up of APCAPS were composed of participants originally recruited as part of the Hyderabad Nutrition Trial in 1987-1990 (and also followed-up in young adulthood in 2003-2010) and their family members (recruited for the first time in the third follow-up) (Kinra et al., 2014). CHAI (**C**ardiovascular **H**ealth effects of **A**ir pollution in Andhra Pradesh, **I**ndia) started in 2015 with the aim to characterize exposure to particulate air pollution from outdoor and household sources in the APCAPS study area and population (see more details in the next subsection).

4.2 Air pollution exposure assessment

In this thesis, different air pollution exposure assessment approaches have been used. In southern Mozambique (**paper II**), the ambient monitoring campaign consisted in collecting 24 hour background levels of $PM_{2.5}$, EC, and OC once every three days during a year (i.e. 115 days) using a gravimetric stationary monitor located at the CISM facilities. $PM_{2.5}$ concentrations were derived using **gravimetric analysis** on collected filters and EC/OC concentrations were derived from thermal-optical transmission techniques. The personal monitoring campaign consisted in collecting 24 hour time-resolved levels of BC in 202 women from the study area. A portable monitor based on Aethalometer optical absorption technology was used.

Approaches used in the framework of CHAI (**papers I, III, and IV**) are summarised in **Figure 7** and explained in more detailed elsewhere (Tonne et al., 2017). Briefly, in CHAI, an intensive monitoring campaign was conducted, collecting data at the personal, indoor, and outdoor level. Personal measurements consisted in gravimetric personal measurements in two seasons in a subsample of 349 participants. Indoor measurements consisted in 24-hour $PM_{2.5}$ measurements in two seasons in 34 households. Two **low-cost monitors** measuring $PM_{2.5}$ and CO were installed for a week in the main living area of four of these households (paper I). Outdoor measurements were conducted in the rooftops of 23 households located in 16 of the 28 villages of the study area using a gravimetric sampler. Outdoor measurements at background monitoring sites were also collected. $PM_{2.5}$ concentrations were derived using gravimetric analysis on collected filters and BC concentrations were derived from optical attenuation of the mass collected on the filters using an optical transmissometer. For epidemiological analyses, regression models to predict long-term personal and residential exposure to all APCAPS participants were developed. For details on **LUR models** development, see Sanchez *et al* (Sanchez et al., 2018) and for personal predicted models see Sanchez *et al* (Sanchez et al.).

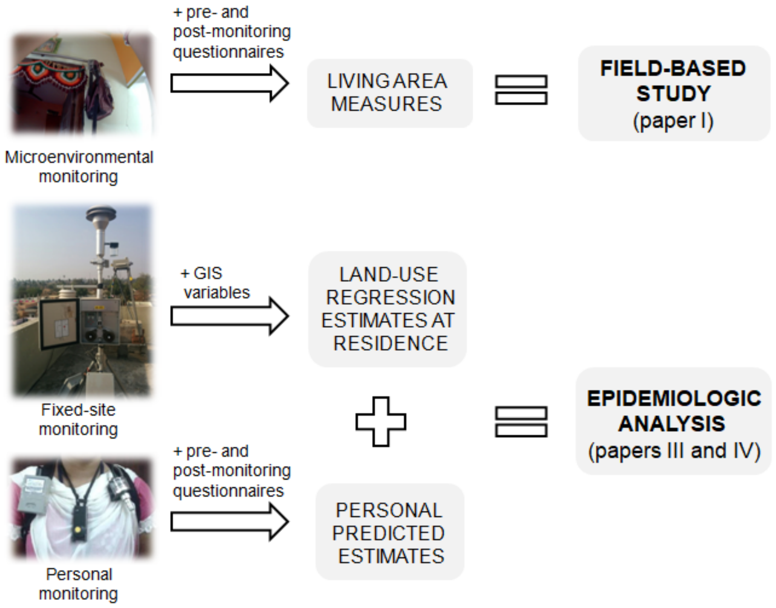


Figure 7 Exposure assessment approaches used in this thesis within the framework of the CHAI project.
Abbreviations: Geographic Information System (GIS)

5. RESULTS

This thesis is composed of the following four scientific articles:

Paper I. Performance of low-cost monitors to assess household air pollution, *published*

Paper II. Predictors of personal exposure to black carbon among women in southern semi-rural Mozambique, *submitted*

Paper III. Ambient particulate air pollution and blood pressure in peri-urban India, *accepted*

Paper IV. Particulate air pollution and blood glucose and diabetic status in peri-urban India, *in preparation*

5.1 Paper I

Curto A, Donaire-Gonzalez D, Barrera-Gómez J, Marshall JD, Nieuwenhuijsen MJ, Wellenius GA, Tonne C. Performance of low-cost monitors to assess household air pollution. Environmental Research. 2018: 163: 53-63. doi: 10.1016/j.envres.2018.01.024

5.2 Paper II

Curto A, Donaire-Gonzalez D, Manaca MN, González R, Sacoor C, Rivas I, Gascon M, Wellenius GA, Querol X, Sunyer J, Macete E, Menéndez C, Tonne C. Predictors of personal exposure to black carbon among women in southern semi-rural Mozambique. *Submitted*. Environ Int. 2019 Oct;131:104962. DOI: 10.1016/j.envint.2019.104962

5.3 Paper III

Curto A, Wellenius GA, Milà C, Sanchez M, Ranzani O, Marshall JD, Kulkarni B, Bhogadi S, Kinra S, Tonne C. Ambient particulate air pollution and blood pressure in peri-urban India. Epidemiology. 2019 Jul;30(4):492–500. DOI: 10.1097/EDE.0000000000001014

5.4 Paper IV

Curto A, Ranzani O, Milà C, Sanchez M, Marshall JD, Kulkarni B, Bhogadi S, Kinra S, Wellenius GA, Tonne C. Lack of association between particulate air pollution and blood glucose levels and diabetic status in peri-urban India. *Environ Int. 2019 Oct;131:105033. DOI: 10.1016/j.envint.2019.105033*

6. DISCUSSION

This section aims to provide an integrated discussion of the overall thesis. It therefore provides a complementary view of the aspects already addressed in each of the papers (Results section). Additionally, this section discusses the contribution and implications for exposure science and public health of this thesis along with proposals for future research ideas within these fields.

6.1 Main findings and contribution to the current knowledge

Overall, this thesis advances the frontier of air pollution epidemiology in several ways. First, it addresses one of the priorities in household air pollution research: the search for affordable and accurate air quality monitors able to capture the wide range of indoor concentrations typically found in LMICs. Second, this thesis fills an important gap in exposure science, which is the characterization of ambient and personal exposure to air pollution in sub-Saharan Africa, where the availability of air pollution data has been so far scarce. This characterization has in turn provided evidence regarding the relative contribution of modifiable sources linked to personal exposure. Finally, this thesis sheds light on the important scientific question of the relationship between particle exposure and cardiometabolic health in areas not dominated by traffic sources, which have received far less attention than traffic-dominated areas. All together, this thesis goes a step further in understanding the measurement, determinants, and effects of air pollution on cardiometabolic health.

a) Air pollution measurement and determinants: contribution of papers I and II

Papers I and II used direct methods to assess microenvironmental and personal air pollution exposures, respectively. **Paper I** was the first to evaluate the performance of three low-cost monitors under semi-controlled and real-world indoor conditions. **Paper II** was the first to characterize personal time-resolved exposure to BC in sub-Saharan African women.

The performance of the low-cost monitors of **paper I** was found to be unsatisfactory in terms of high rates of failure or malfunction. Rates of data logging failure are usually under-reported even though they provide very helpful information for researchers aiming to start new measurement campaigns. Indeed, the importance of developing more transparent data communication practices in low-cost sensing studies has been already highlighted (Clements et al., 2017). The failure rates among the low-cost monitors measuring particulate matter (HAPEX and TZOA-R) were possibly due to manufacturing defects given by their early design stage. The CO monitor we tested (EL-USB-CO), however, is a more established low-cost monitor in the literature and still had high rates of malfunction. Frequent calibration during sampling has been proposed as one of the solutions to prevent this malfunction (Piedrahita, 2017). However, under the desired scenario of unattended sampling, frequent calibration would require intensive supervision by the field staff. In some other cases, the reasons why a monitor fails remain unknown, limiting the confidence in low-cost monitors for population-based studies.

The households in India selected for the field-based study in **paper I** used clean energy as a primary source for cooking, thus limiting our ability to measure wide ranges of exposure. When low-cost sensors are exposed to high indoor air pollution levels, they can fail to provide quantitative information after saturation (observed at 5 mg/m^3) (Patel et al., 2017). In **paper II**, we also found saturation or clogging issues with the research-grade personal BC monitor used (i.e., microAeth). In this case, the monitor kept providing quantitative data, although likely with an underestimation of the true value. Saturation issues can be sometimes solved by reducing the flow rates, but in the case of our study, the flow rate was set at the minimum (i.e., 50 ml/min).

In **paper II**, temporal patterns of BC were evaluated for the first time in sub-Saharan Africa, providing further understanding of the personal BC levels among women during the day. As shown in **Figure 8**, in European areas influenced by traffic (e.g., Barcelona), the peaks of personal exposure are commonly determined by traffic rush hours (8-9 am) (Nieuwenhuijsen et al., 2015). In semi-rural sub-Saharan Africa, we found that peaks were determined by fuel-based lighting activities starting in the evening (6-7 pm). Indeed, the use of kerosene lamps for lighting was identified as the major source contributing to high personal BC average and peak levels. Although we hypothesized that cooking-related indicators were likely to be the greatest determinants for personal exposure in this population, the study sample was quite homogenous in regards to the type of cooking fuel. We acknowledge that this finding may not be applicable to other areas in sub-Saharan Africa with higher access to electricity, but it is still applicable to the 57% of the rural and semi-rural areas from sub-Saharan Africa and 76% from Mozambique where there is no access to electricity (World Bank, 2016).

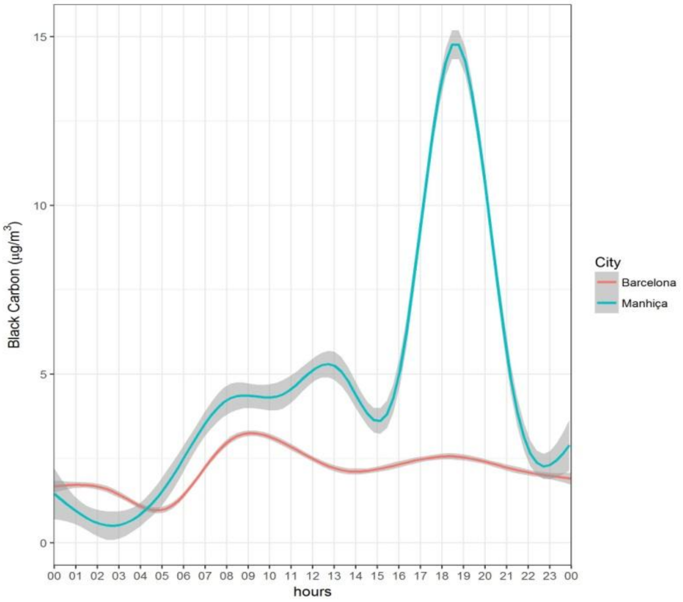


Figure 8 Daily temporal patterns of personal black carbon exposure in Barcelona (Spain) and Manhiça (Mozambique). Lines represent the smoothed daily means of all personal measurements combined and grey shadow represents the 95% Confidence Interval.

b) Cardiometabolic health effects: contribution of papers III and IV

Papers III and IV were the first to evaluate the associations between long-term exposure to ambient particulate air pollution and cardiometabolic outcomes in South Asia. This research therefore expands the current evidence to a region that has been underinvestigated so far (Yang et al., 2018b) and has higher air pollution levels than other HICs. In **paper III**, long-term exposure to ambient $PM_{2.5}$ was associated with high BP and prevalent hypertension in women, with stronger associations for SBP than for DBP. This association was found to be independent of the type of fuel used for cooking, highlighting the independent contribution that ambient and household air pollution can have on cardiovascular health. In **paper IV**, we found no evidence that ambient $PM_{2.5}$ and BC are associated with blood glucose or prevalence of prediabetes/diabetes in this population.

Areas with high levels of ambient air pollution tend to have higher risk of stroke and heart failure than those with lower levels (Shah et al., 2013; Yang et al., 2014). As discussed earlier in Introduction and Results (see pages 32 and 164-165), previous evidence in areas covering high air pollution ranges has focused on East Asia, with the majority of contributions coming from China. However, not all regional differences are due to air pollution levels. When areas with similar air pollution levels are compared, differences in health estimates can remain. This was the case of our comparisons between $PM_{2.5}$-BP associations in our study vs. Chinese studies, discussed in **paper III** (see pages 164-165). We hypothesized that the higher magnitude of our $PM_{2.5}$-SBP association in women may partly reflect the high rates of undiagnosed and untreated hypertension in our study population, perhaps due to comparatively lower income and socioeconomic status and lower access to health care systems than the Chinese areas studied.

Apart from income and socioeconomic factors, regional differences may be driven by other risk factors for hypertension such as genetic susceptibility, lifestyle habits, and co-pollutant exposures such as noise (Yang et al., 2018b). In the light of our null associations between air pollution and blood glucose levels and prevalence of prediabetes/diabetes in **paper IV**, it is interesting to explore the potential shape of the $PM_{2.5}$-diabetes exposure-response relationship. A recent study has characterized an integrated concentration-response function using worldwide existing evidence linking long-term $PM_{2.5}$ with incidence of diabetes (Bowe et al., 2018), observing a non-linear exposure-response relationship (**Figure 9**). Although the risk of diabetes increased substantially above 6.2 $\mu g/m^3$ of $PM_{2.5}$ (set as the reference), it exhibited a more moderate increase at concentrations of $PM_{2.5}$ above 10 µg/m^3 and reached a plateau at 13 µg/m^3 (**Figure 9**).

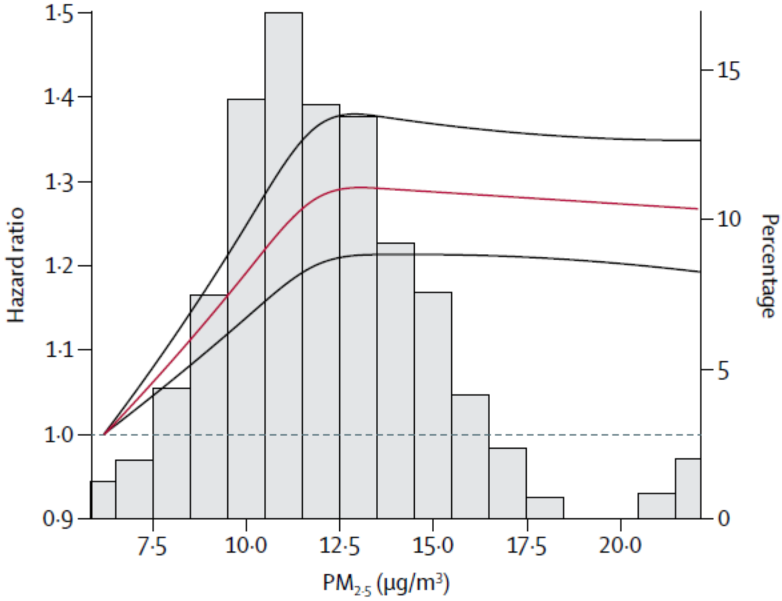


Figure 9 Integrated exposure-response function for ambient $PM_{2.5}$ and risk of diabetes. Red line is representing the hazard ratio and black lines the 95% confidence intervals. In the background, the histogram with the distribution of $PM_{2.5}$ exposure is presented. *Source: original plot extracted from Bowe et al., 2018*

From this study, it becomes apparent the exposure gap in $PM_{2.5}$ concentrations > 17.5 µg/m^3. Indeed, the concentrations observed in the highest range of concentrations were derived from active smoking studies due to the lack of studies reporting > 20 µg/m^3. Hence, our research helps to shed some light in $PM_{2.5}$ concentrations in a range where there is a lot of uncertainty. If this non-linear concentration-response function is confirmed in future longitudinal studies, it would have very relevant implications for policy, environmental economics, engineering, and epidemiology (Marshall et al., 2015).

6.2 Strengths and limitations

The main strength and differentiating content of this thesis is the research settings: rural Mozambique and India, both LMICs that have received relatively little attention in environmental epidemiologic literature despite their high air pollution burdens. Assessment of the effect of air pollution on health in LMICs is labour-intensive because it requires extensive data collection campaigns due to the lack of air pollution data and a paucity of disease surveillance data. Within the framework of the HDSS in Manhiça and the APCAPS in Hyderabad, solutions to the logistical complexities of data collection have been overcome through the experience of the teams in the field, as well as their positive working relationship with local community members, who have facilitated participation.

The main limitation of this thesis is the cross-sectional design used in epidemiologic analyses. This could have affected the causal sequence assumed. We assume that exposure preceded the outcome, but it could have been the other way around (reverse causation). Diseased participants could have moved to villages near to primary roads to facilitate access to Hyderabad city, where more primary health care services are available. Although some of the previous longitudinal studies have supported an increased risk between long-term air pollution and incident hypertension (Chen et al., 2014; Zhang et al., 2016; Fuks et al., 2016; Zhang et al., 2018) and diabetes (Coogan et al., 2012; Hansen et al., 2016; Requia et al., 2017; Qiu et al., 2018; Bowe et al., 2018), none of these was conducted in South Asia. Other strengths and limitations of this thesis are discussed in the following subsections.

a) Paper I

The main limitation of **paper I** was the limited external validity of results. The measurement procedures to collect and analyse data were systematic and likely reproducible: we uploaded the raw data from the experiment to a public repository and made accessible the codes to read the output data. However, the validity of our results is highly dependent on factors such as the amount of humidity in the wood, the quality of the wood, the wind speed during ventilated hours, and the temperature and humidity reached during fire hours. Environmental conditions in rural areas from LMICs could be more extreme (e.g., high humidity levels during cooking activities or the monsoon) and heterogeneous (e.g., multiple cooking fuels used) than in the semi-controlled experiment. Therefore, the failure and malfunction rates in these real-world environments could be even higher than the ones observed in the experiment.

b) Paper II

Paper II was affected by measurement error due to the saturation issues encountered among the most exposed women. This implies that the true personal exposure concentrations of these women were even higher than the ones reported. We decided to keep these women in analysis to prevent selection bias that could have resulted if highly exposed women who were more likely to perform specific activities (e.g., cooking) were excluded. Participants were women of childbearing age randomly selected from the HDSS, and all who were invited agreed to participate reducing the influence of selection bias. Another potential source of bias in this study was information bias. Face-to-face interviews aimed at collecting socio-demographic information and activities conducted during monitoring could be affected by recall bias and social desirability bias. For example, women more concerned about the wood smoke effects could better recall the time of cooking events than those who were not.

c) Papers III and IV

In **papers III and IV**, it is important to point out that 32% of APCAPS members invited in the third follow-up did not accept to participate. Nonetheless, the household survey administered to almost all village residents allowed us to confirm that the demographic characteristics between adult study participants and adults from the general population in the villages were comparable (see page 189), reducing the potential selection bias. We therefore expect the epidemiological findings to be transportable to populations in South Asia and elsewhere at a similar stage of development as the APCAPS villages.

Our epidemiologic analyses are based on the rationale that sex-stratified are more informative than sex-adjusted results because of the large differences in time-activities and the distribution of confounders between men and women, as we found in **paper III**. Due to the sparse data problems found in **paper IV**, we could not perform sex-stratified analyses for the association between ambient air pollution and blood glucose and prevalence of prediabetes/diabetes. When considering estimates of personal air pollution exposure in **paper IV**, we did sex-stratified analyses since the personal prediction models were developed separately for each sex. Although we observed differences by sex, these results were strongly affected by unmeasured confounding. We did not have sufficiently detailed data needed to adjust for the influence of individual characteristics correlated with personal exposure and predictive of cardiometabolic health (e.g., occupation-related physical activity).

A limitation of our epidemiologic analyses was the lack of control for potentially relevant co-pollutant exposures, which could have increased our residual confounding. In the case of BP associations, it is possible that airborne lead could have affected our observed associations, since it is a well-known environmental determinant of elevated BP (Lipfert et al., 2003). Apart from petrol-motored vehicles that still use lead, exposure to airborne lead in LMICs may come from lead mining, smelting, battery factories, and cottage industries (Tong et al., 2000). In our study population, it may be the case that associations between particulate air pollution and BP among those households living closer to a brick kiln industry, already linked with airborne lead emissions in South Asia (Ishaq et al., 2010), could have been confounded by collinearity with airborne lead. Another relevant environmental exposure for both hypertension and diabetes is **noise** (Münzel et al., 2017; Zare Sakhvidi et al., 2018). In our study area, two villages could be affected by aircraft noise coming from the international airport in Hyderabad and other few villages close to primary roads could be affected by traffic-related noise. Since the closest distance from a household to these sources was relatively large (closest proximity was 5.7 km for the airport and 1.6 km for the primary road), we do not think noise would have had a major impact in our estimates, although we do not have data to support our hypothesis (e.g., traffic intensity). Residual confounding was also possible due to the potential misclassification of relevant covariates such as smoking, diet, and physical activity. All were derived from questionnaires, which, as opposed to objective measures, are prone to different sources of information bias. However, the dietary and physical activity questionnaires used were specifically designed for our study population and showed very reasonable validity (Bowen et al., 2012; Matsuzaki et al., 2015).

- **Exposure assessment**

The use of LUR models and personal prediction models to characterize residential and personal exposure in a peri-urban area in a LMIC is a major exposure assessment improvement. Previous studies conducted in East Asia have commonly used proximity of residence to fixed-site monitoring stations and estimates derived solely from poor resolution satellite-based imagery to conduct epidemiologic analyses (Chuang et al., 2010; Dong et al., 2013; Chen et al., 2015; Lin et al., 2017; Liu et al., 2016, 2017; Qiu et al., 2018; Yang et al., 2018a; Zhang et al., 2018). Both methods are built under the assumption that each individual in the same spatial unit (e.g., 10 km × 10 km) is equally exposed to air pollution and therefore it is not reflecting the variability of air pollutants within the same spatial unit. In contrast, LUR models assess long-term air pollution at a finer spatial scale and help to reduce exposure misclassification (Nieuwenhuijsen, 2015). However, LUR models can also be affected by some degree of exposure misclassification because their performance is sensitive to the ratio of number of sites and predictor variables used and derived estimates may not correlate to long-term average personal exposure. We acknowledge that we had few number of sites (n=23) in relation to the number of predictors (n>150). Although the number of sites was comparable to previous studies (Sanchez et al., 2018), the variance explained in our models could have overestimated (Basagaña et al., 2012).

As in all modelling approaches focusing on ambient air pollution as a proxy of personal exposure, the LUR models did not capture the contribution of indoor sources to personal exposure nor the infiltration from the outdoor sources to the indoor environment, where people spent most of their time. In traffic dominated areas in HICs, is likely that BC, a combustion specific indicator, is less affected by indoor sources than outdoor sources, that’s why correlations between ambient and personal concentrations can be higher for BC (20-44%) than for $PM_{2.5}$ (0-0.08%) in these areas (Montagne et al., 2013). However, this may not be the case for LMICs, where indoor environments are highly affected by household combustion sources. This is the case in our study area, where previous work showed that ambient concentrations were not predictive of personal. Personal concentrations can therefore unmask other relevant sources of exposure, such as indoor sources.

- **Outcome assessment**

Our BP assessment consisted in three repeated readings in a single visit using an oscillometric device and following standard procedures. To reduce misclassification of hypertensive participants, taking readings in at least two occasions is recommended to obtain more precise average BP levels. Since this misclassification could have happened in both directions (either classifying undiagnosed hypertensive participants as non hypertensive or classifying non hypertensive participants as hypertensive), misclassification is non-differential and possibly produced bias towards the null (Rothman et al., 2008).

Our blood glucose level assessment consisted in 8-h fasting blood glucose in a single blood extraction. Similarly than with BP, a second blood sample would have reduced our outcome misclassification, although as mentioned earlier in Introduction (page 25), levels from a single test may be sufficient to identify people at risk in epidemiologic studies.

The cut-points for the classification of hypertension, prediabetes, and diabetes are arbitrary. We used the most updated guidelines, which are the 2017 ACC/AHA guidelines for hypertension and the 2014 ADA guidelines for prediabetes and diabetes. These guidelines use lower cut-points than the equivalent WHO guidelines. Given the strong underlying risk of South Asians for cardiometabolic diseases, we found convenient to apply lower cut-points even if it would represent overestimating the prevalent cases if compared to the WHO cut-points. In terms of clinical practice, however, the use for the ACC/AHA guidelines has been discouraged in India because it would suppose a collapse of the health systems given the significant amount of new patients that would be identified (140% relative increase in the hypertension prevalence compared to the 43% in the USA) (Venkateshmurthy et al., 2018).

6.3 Implications for public health and policy making

This thesis has important implications in terms of indoor air pollution and air pollution epidemiologic research. First, our study populations in Mozambique and India were exposed to ambient $PM_{2.5}$ levels exceeding those recommended by international guidelines, particularly in the case of India, where all participants were exposed to higher annual average $PM_{2.5}$ levels than the WHO guideline and the US Environmental Protection Agency air quality standards. Poor air quality is considered a major determinant of health and in these countries is affecting likewise urban and rural populations. Hence, policies aimed at mitigating air pollution levels should be addressed equally in urban, rural and peri-urban areas.

Second, our research highlights the role of kerosene, previously regarded as a “modern” fuel by the WHO (WHO, 2010), as unclean lighting fuel. Liquid unclean fuels such as kerosene are often ignored when the so-called term “solid fuels” is used to refer to the mixture of unclean household fuels burned to meet energy demands. The search for more inclusive standard terms is encouraged. Our findings also highlights the need to replace fuel-based lighting to other cleaner alternatives to reduce the adverse climate and human health impacts of combustion particles in populations with very low levels of access to household energy. Interventions and educational campaigns aimed to implement cost-effective lighting alternative sources would also have additional safety and health benefits. The use of kerosene lamps for lighting is also linked with burns and fires (lamps are easily spilled), poisoning by accidental ingestion among children (kerosene is a transparent liquid often sold with plastic bottles, easily confused with water) and poor visual health (light emitted is dull and flickers) (Lam et al., 2012; Mills, 2016). Furthermore, these interventions would be relatively more feasible to implement and have less adoption barriers than interventions focused on improved cookstoves. Improved cookstoves are more energy-demanding and tend to have more impact on socio-cultural factors (e.g., inability to cook traditional dishes, limited size of improved cookstoves for large pots and meals) (Debbi et al., 2014) than some of the alternatives proposed to replace kerosene lamps (e.g., solar-powered lamps).

Third, the magnitude of the association between ambient levels of $PM_{2.5}$ and SBP found in women suggests that women can have higher risk of death due to CVD than men in this population, since it has been shown that even small increases in BP can result in higher risk of death due to CVD (Chobanian et al., 2003; Stamler et al., 1993). Given the high burdens of ambient air pollution and CVD in India, both projected to increase, air pollution abatement policies should be a key target for health policy to ease this exposure burden and decelerate the cardiovascular epidemic facing India.

6.4 Implications for future research

Development of low-cost sensors for measuring air pollutants is a fast-growing area of research. While much has been invested in the development of air quality sensors and monitors, improvement of their responsiveness at high levels of indoor concentrations and temperature requires further work. Further evaluations should be conducted in the field and include several weeks of continuous sampling to test the stability and durability of the monitors. To improve external validity, future studies should also include larger sample size of households, preferably covering settings with different climate and energy-related behaviours to capture a wide range of environmental conditions.

To prevent measurement error, future studies in rural or semi-rural areas would benefit from strategies to avoid filter saturation when using filter-based air quality monitors. During this thesis, a new upgraded version of the microAeth used in Mozambique was released. According to manufacturer, this newest model (MA350, AethLabs, San Francisco, CA, USA) has an automatic filter tape advance system which allows for 3-12 months of continuous measurements without the need to replace the filter manually in a daily basis. Although this monitor is prohibitively expensive ($10,000), this filter tape advance system could be soon applied to more affordable monitors and would therefore provide a solution to the saturation issues in environments with high concentrations. To prevent information bias from questionnaires, future studies should seek for more objective tools to assess exposure determinants. To better quantify and compare the contribution of air pollution sources between men and women, it is recommended that further investigations monitor men living in the same household than women as well as other household members from a wide range of ages.

Additional epidemiologic evidence is needed in LMICs, ideally from studies using longitudinal designs. Further investigations should overcome some of the limitations in the field that still remain. First, and in the light of our null health associations for ambient BC, further studies are needed aimed to explore source apportionment and composition or toxicity of particles in areas not dominated by traffic. Second, BP measurement should be repeated in a second occasion out of the clinic to control for the “white-coat” effect (when BP is higher in the clinic/office than in other locations such as at home of the participant) (Whelton et al., 2017). To do so, the use of a 24-h ambulatory BP device would be recommended to reduce this source of misclassification and provide more accurate average BP levels. Although fasting blood glucose is sufficient for the diagnosis of diabetes, the use of additional tests such as the OGTT and HbA1c would strengthen future studies. Third, future studies in peri-urban areas should take into account the spatial patterning of villages (or other spatial units) within the area. Clustering within spatial units is likely to be present, meaning that participants in the same spatial unit are likely to be more similar to each other than to participants in a different spatial unit. In the framework of CHAI/APCAPS, the 28 peri-urban villages had the particularity to be distributed at different distances from Hyderabad city (from 29 to 66 km), which created distinctive spatial clusters in terms of socioeconomic, lifestyle, and ambient air pollution. Fourth, efforts in predicting long-term personal air pollution exposure should be maintained since better capture location and activities of individuals than estimates based on residential levels. Such efforts should be guided by the collection of a wide range of multiple co-exposures (e.g., noise, built environment, temperature) and the refinement in variables related to household air pollution (e.g., historical data to quantify cumulative exposure) and important risk factors for hypertension and diabetes (e.g., physical activity, diet). Fifth, future studies should confirm if the effects of outdoor and indoor air pollution on cardiometabolic health in LMICs are independent or synergistic.

7. CONCLUSIONS

1) The performance of low-cost monitors measuring $PM_{2.5}$ and CO is yet not reliable enough to replace more expensive and established research-grade monitors.

2) People living in semi-rural Mozambique are exposed to high levels of ambient EC and personal BC.

3) Kerosene-based lighting is an important contributor to personal exposure to combustion particles in women from semi-rural Mozambique.

4) Long-term residential levels of $PM_{2.5}$ can contribute to elevated blood pressure in women residing in peri-urban India.

5) There was no clear evidence that increased levels of particulate air pollution were associated with blood glucose levels and prevalence of prediabetes/diabetes in peri-urban India.

References

Adler, A.I. (2000). Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study. BMJ *321*, 412–419.

Alberti, K.G.M.M., Eckel, R.H., Grundy, S.M., Zimmet, P.Z., Cleeman, J.I., Donato, K.A., Fruchart, J.-C., James, W.P.T., Loria, C.M., and Smith, S.C. (2009). Harmonizing the Metabolic Syndrome: A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation *120*, 1640–1645.

Aleixandre, M., and Gerboles, M. (2012). Review of small commercial sensors for indicative monitoring of ambient gas. Chem. Eng. Trans. 169–174.

American Diabetes Association (2014). Diagnosis and Classification of Diabetes Mellitus. Diabetes Care *37*, S81–S90.

Anchala, R., Kannuri, N.K., Pant, H., Khan, H., Franco, O.H., Di Angelantonio, E., and Prabhakaran, D. (2014). Hypertension in India: a systematic review and meta-analysis of prevalence, awareness, and control of hypertension. J. Hypertens. *32*, 1170–1177.

Anjana, R.M., Pradeepa, R., Deepa, M., Datta, M., Sudha, V., Unnikrishnan, R., Bhansali, A., Joshi, S.R., Joshi, P.P., et al., on behalf of the ICMR–INDIAB Collaborative Study Group (2011). Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: Phase I results of the Indian Council of Medical Research–INdia DIABetes (ICMR–INDIAB) study. Diabetologia *54*, 3022–3027.

Balti, E.V., Echouffo-Tcheugui, J.B., Yako, Y.Y., and Kengne, A.P. (2014). Air pollution and risk of type 2 diabetes mellitus: A systematic review and meta-analysis. Diabetes Res. Clin. Pract. *106*, 161–172.

Banerjee, M., Siddique, S., Mukherjee, S., Roychoudhury, S., Das, P., Ray, M.R., and Lahiri, T. (2012). Hematological, immunological, and cardiovascular changes in individuals residing in a polluted city of India: A study in Delhi. Int. J. Hyg. Environ. Health *215*, 306–311.

Bansal, N. (2015). Prediabetes diagnosis and treatment: A review. World J. Diabetes *6*, 296.

Basagaña, X., Rivera, M., Aguilera, I., Agis, D., Bouso, L., Elosua, R., Foraster, M., de Nazelle, A., Nieuwenhuijsen, M., Vila, J., et al. (2012). Effect of the number of measurement sites on land use regression models in estimating local air pollution. Atmos. Environ. *54*, 634–642.

Basagaña, X., Aguilera, I., Rivera, M., Agis, D., Foraster, M., Marrugat, J., Elosua, R., and Künzli, N. (2013). Measurement Error in Epidemiologic Studies of Air Pollution Based on Land-Use Regression Models. Am. J. Epidemiol. *178*, 1342–1346.

Baumgartner, J., Zhang, Y., Schauer, J.J., Huang, W., Wang, Y., and Ezzati, M. (2014). Highway proximity and black carbon from cookstoves as a risk factor for higher blood pressure in rural China. Proc. Natl. Acad. Sci. *111*, 13229–13234.

Bond, T.C., Doherty, S.J., Fahey, D.W., Forster, P.M., Berntsen, T., DeAngelo, B.J., Flanner, M.G., Ghan, S., Kärcher, B., Koch, D., et al. (2013). Bounding the role of black carbon in the climate system: A scientific assessment: BLACK CARBON IN THE CLIMATE SYSTEM. J. Geophys. Res. Atmospheres *118*, 5380–5552.

Bowe, B., Xie, Y., Li, T., Yan, Y., Xian, H., and Al-Aly, Z. (2018). The 2016 global and national burden of diabetes mellitus attributable to PM 2·5 air pollution. Lancet Planet. Health *2*, e301–e312.

Bowen, L., Bharathi, A.V., Kinra, S., Destavola, B., Ness, A., and Ebrahim, S. (2012). Development and evaluation of a semi-quantitative food frequency questionnaire for use in urban and rural India. Asia Pac. J. Clin. Nutr. *21*, 355–360.

Briggs, D.J., de Hoogh, C., Gulliver, J., Wills, J., Elliott, P., Kingham, S., and Smallbone, K. (2000). A regression-based method for mapping traffic-related air pollution: application and testing in four contrasting urban environments. Sci. Total Environ. *253*, 151–167.

Brook, R.D., and Rajagopalan, S. (2009). Particulate matter, air pollution, and blood pressure. J. Am. Soc. Hypertens. *3*, 332–350.

Brook, R.D., Weder, A.B., and Rajagopalan, S. (2011). “Environmental Hypertensionology” The Effects of Environmental Factors on Blood Pressure in Clinical Practice and Research: Effects of Environmental Factors on BP. J. Clin. Hypertens. *13*, 836–842.

Chen, H., Burnett, R.T., Kwong, J.C., Villeneuve, P.J., Goldberg, M.S., Brook, R.D., van Donkelaar, A., Jerrett, M., Martin, R.V., Kopp, A., et al. (2014). Spatial Association Between Ambient Fine Particulate Matter and Incident Hypertension. Circulation *129*, 562–569.

Chen, S.-Y., Wu, C.-F., Lee, J.-H., Hoffmann, B., Peters, A., Brunekreef, B., Chu, D.-C., and Chan, C.-C. (2015). Associations between Long-Term Air Pollutant Exposures and Blood Pressure in Elderly Residents of Taipei City: A Cross-Sectional Study. Environ. Health Perspect.

Chen, Z., Salam, M.T., Toledo-Corral, C., Watanabe, R.M., Xiang, A.H., Buchanan, T.A., Habre, R., Bastain, T.M., Lurmann, F., Wilson, J.P., et al. (2016). Ambient Air Pollutants Have Adverse Effects on Insulin and Glucose Homeostasis in Mexican Americans. Diabetes Care *39*, 547–554.

Chobanian, A.V., Bakris, G.L., Black, H.R., Cushman, W.C., Green, L.A., Izzo, J.L., Jones, D.W., Materson, B.J., Oparil, S., Wright, J.T., et al. (2003). Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension *42*, 1206–1252.

Chow, C.K. (2013). Prevalence, Awareness, Treatment, and Control of Hypertension in Rural and Urban Communities in High-, Middle-, and Low-Income Countries. JAMA *310*, 959.

Chuang, K.-J., Yan, Y.-H., and Cheng, T.-J. (2010). Effect of Air Pollution on Blood Pressure, Blood Lipids, and Blood Sugar: A Population-Based Approach: J. Occup. Environ. Med. *52*, 258–262.

Clark, M.L., Peel, J.L., Balakrishnan, K., Breysse, P.N., Chillrud, S.N., Naeher, L.P., Rodes, C.E., Vette, A.F., and Balbus, J.M. (2013). Health and Household Air Pollution from Solid Fuel Use: The Need for Improved Exposure Assessment. Environ. Health Perspect.

Clements, A.L., Griswold, W.G., Rs, A., Johnston, J.E., Herting, M.M., Thorson, J., Collier-Oxandale, A., and Hannigan, M. (2017). Low-Cost Air Quality Monitoring Tools: From Research to Practice (A Workshop Summary). Sensors *17*, 2478.

Coogan, P.F., White, L.F., Jerrett, M., Brook, R.D., Su, J.G., Seto, E., Burnett, R., Palmer, J.R., and Rosenberg, L. (2012). Air Pollution and Incidence of Hypertension and Diabetes Mellitus in Black Women Living in Los Angeles. Circulation *125*, 767–772.

Cyrys, J., Heinrich, J., Hoek, G., Meliefste, K., Lewné, M., Gehring, U., Bellander, T., Fischer, P., van Vliet, P., Brauer, M., et al. (2003). Comparison between different traffic-related particle indicators: elemental carbon (EC), PM2.5 mass, and absorbance. J. Expo. Anal. Environ. Epidemiol. *13*, 134–143.

Debbi, S., Elisa, P., Nigel, B., Dan, P., and Eva, R. (2014). Factors Influencing Household Uptake of Improved Solid Fuel Stoves in Low- and Middle-Income Countries: A Qualitative Systematic Review. Int. J. Environ. Res. Public. Health *11*, 8228–8250.

Dendup, T., Feng, X., Clingan, S., and Astell-Burt, T. (2018). Environmental Risk Factors for Developing Type 2 Diabetes Mellitus: A Systematic Review. Int. J. Environ. Res. Public. Health *15*, 78.

Dong, G.-H., Qian, Z., Xaverius, P.K., Trevathan, E., Maalouf, S., Parker, J., Yang, L., Liu, M.-M., Wang, D., Ren, W.-H., et al. (2013). Association Between Long-Term Air Pollution and Increased Blood Pressure and Hypertension in China. Hypertension *61*, 578–584.

Dutta, A., and Ray, M.R. (2013). Increased cardiovascular risk due to systemic inflammatory changes and enhanced oxidative stress in urban Indian women. Air Qual. Atmosphere Health *6*, 501–508.

Dutta, A., Mukherjee, B., Das, D., Banerjee, A., and Ray, M.R. (2011). Hypertension with elevated levels of oxidized low-density lipoprotein and anticardiolipin antibody in the circulation of premenopausal Indian women chronically exposed to biomass smoke during cooking: Biomass smoke and oxidized LDL. Indoor Air *21*, 165–176.

Eze, I.C., Hemkens, L.G., Bucher, H.C., Hoffmann, B., Schindler, C., Künzli, N., Schikowski, T., and Probst-Hensch, N.M. (2015). Association between Ambient Air Pollution and Diabetes Mellitus in Europe and North America: Systematic Review and Meta-Analysis. Environ. Health Perspect.

Ford, E.S. (2005). Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. Diabetes Care *28,* 1769–1778.

Fuks, K.B., Weinmayr, G., Basagaña, X., Gruzieva, O., Hampel, R., Oftedal, B., Sørensen, M., Wolf, K., Aamodt, G., Aasvang, G.M., et al. (2016). Long-term exposure to ambient air pollution and traffic noise and incident hypertension in seven cohorts of the European study of cohorts for air pollution effects (ESCAPE). Eur. Heart J. ehw413.

Gakidou, E., Afshin, A., Abajobir, A.A., Abate, K.H., Abbafati, C., Abbas, K.M., Abd-Allah, F., Abdulle, A.M., Abera, S.F., Aboyans, V., et al. (2017). Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet *390*, 1345–1422.

Giorgini, P., Di Giosia, P., Grassi, D., Rubenfire, M., Brook, R.D., and Ferri, C. (2016). Air Pollution Exposure and Blood Pressure: An Updated Review of the Literature. Curr. Pharm. Des. *22*, 28–51.

Hansen, A.B., Ravnskjær, L., Loft, S., Andersen, K.K., Bräuner, E.V., Baastrup, R., Yao, C., Ketzel, M., Becker, T., Brandt, J., et al. (2016). Long-term exposure to fine particulate matter and incidence of diabetes in the Danish Nurse Cohort. Environ. Int. *91*, 243–250.

Health Effects Institute (2018). State of Global Air 2018 (Boston, MA).

Hoek, G., Beelen, R., de Hoogh, K., Vienneau, D., Gulliver, J., Fischer, P., and Briggs, D. (2008). A review of land-use regression models to assess spatial variation of outdoor air pollution. Atmos. Environ. *42*, 7561–7578.

Ishaq, M., Khan, M.A., Jan, F.A., and Ahmad, I. (2010). Heavy metals in brick kiln located area using atomic absorption spectrophotometer: a case study from the city of Peshawar, Pakistan. Environ. Monit. Assess. *166*, 409–420.

Janghorbani, M., Momeni, F., and Mansourian, M. (2014). Systematic review and metaanalysis of air pollution exposure and risk of diabetes. Eur. J. Epidemiol. *29*, 231–242.

Janssen, N.A.H., Hoek, G., Simic-Lawson, M., Fischer, P., van Bree, L., ten Brink, H., Keuken, M., Atkinson, R.W., Anderson, H.R., Brunekreef, B., et al. (2011). Black Carbon as an Additional Indicator of the Adverse Health Effects of Airborne Particles Compared with PM10 and PM2.5. Environ. Health Perspect. *119*, 1691–1699.

Jerrett, M., Arain, A., Kanaroglou, P., Beckerman, B., Potoglou, D., Sahsuvaroglu, T., Morrison, J., and Giovis, C. (2005). A review and evaluation of intraurban air pollution exposure models. J. Expo. Sci. Environ. Epidemiol. *15*, 185–204.

Kahn, S.E. (2001). The Importance of β-Cell Failure in the Development and Progression of Type 2 Diabetes. J. Clin. Endocrinol. Metab. *86*, 4047–4058.

Kearney, P.M., Whelton, M., Reynolds, K., Muntner, P., Whelton, P.K., and He, J. (2005). Global burden of hypertension: analysis of worldwide data. The Lancet *365*, 217–223.

Khatib, O.M.N., World Health Organization, and Regional Office for the Eastern Mediterranean (2006). Guidelines for the prevention, management and care of diabetes mellitus (Cairo: World Health Organization, Regional Office for the Eastern Mediterranean).

Kinra, S., Radha Krishna, K., Kuper, H., Rameshwar Sarma, K., Prabhakaran, P., Gupta, V., Walia, G.K., Bhogadi, S., Kulkarni, B., Kumar, A., et al. (2014). Cohort Profile: Andhra Pradesh Children and Parents Study (APCAPS). Int. J. Epidemiol. *43*, 1417–1424.

Klasen, E.M., Wills, B., Naithani, N., Gilman, R.H., Tielsch, J.M., Chiang, M., Khatry, S., Breysse, P.N., Menya, D., Apaka, C., et al. (2015). Low correlation between household carbon monoxide and particulate matter concentrations from biomass-related pollution in three resource-poor settings. Environ. Res. *142*, 424–431.

Lam, N.L., Smith, K.R., Gauthier, A., and Bates, M.N. (2012). Kerosene: A Review of Household Uses and their Hazards in Low- and Middle-Income Countries. J. Toxicol. Environ. Health Part B *15*, 396–432.

Lewis, A., and Edwards, P. (2016). Validate personal air-pollution sensors. Nature *535*, 29–31.

Li, W., Dorans, K.S., Wilker, E.H., Rice, M.B., Kloog, I., Schwartz, J.D., Koutrakis, P., Coull, B.A., Gold, D.R., Meigs, J.B., et al. (2018). Ambient air pollution, adipokines, and glucose homeostasis: The Framingham Heart Study. Environ. Int. *111*, 14–22.

Liang, R., Zhang, B., Zhao, X., Ruan, Y., Lian, H., and Fan, Z. (2014). Effect of exposure to PM2.5 on blood pressure: a systematic review and meta-analysis. J. Hypertens. *32*, 2130–2141.

Lin, H., Guo, Y., Zheng, Y., Di, Q., Liu, T., Xiao, J., Li, X., Zeng, W., Cummings-Vaughn, L.A., Howard, S.W., et al. (2017). Long-Term Effects of Ambient PM $_{2.5}$ on Hypertension and Blood Pressure and Attributable Risk Among Older Chinese AdultsNovelty and Significance. Hypertension *69*, 806–812.

Lioy, P., and Weisel, C. (2014). Exposure Science Research Design. In Exposure Science, (Elsevier), pp. 51–69.

Lipfert, F.W., Perry, H.M., Miller, J.P., Baty, J.D., Wyzga, R.E., and Carmody, S.E. (2003). Air pollution, blood pressure, and their long-term associations with mortality. Inhal. Toxicol. *15*, 493–512.

Liu, C., Yang, C., Zhao, Y., Ma, Z., Bi, J., Liu, Y., Meng, X., Wang, Y., Cai, J., Kan, H., et al. (2016). Associations between long-term exposure to ambient particulate air pollution and type 2 diabetes prevalence, blood glucose and glycosylated hemoglobin levels in China. Environ. Int. *92–93*, 416–421.

Liu, C., Chen, R., Zhao, Y., Ma, Z., Bi, J., Liu, Y., Meng, X., Wang, Y., Chen, X., Li, W., et al. (2017). Associations between ambient fine particulate air pollution and hypertension: A nationwide cross-sectional study in China. Sci. Total Environ. *584–585*, 869–874.

Lockwood, A.H. (2002). Diabetes and Air Pollution. Diabetes Care *25*, 1487–1488.

Magalhaes, S., Baumgartner, J., and Weichenthal, S. (2018). Impacts of exposure to black carbon, elemental carbon, and ultrafine particles from indoor and outdoor sources on blood pressure in adults: A review of epidemiological evidence. Environ. Res. *161*, 345–353.

Marshall, J.D., Apte, J.S., Coggins, J.S., and Goodkind, A.L. (2015). Blue Skies Bluer? Environ. Sci. Technol. *49*, 13929–13936.

Martin, W.J., Glass, R.I., Araj, H., Balbus, J., Collins, F.S., Curtis, S., Diette, G.B., Elwood, W.N., Falk, H., Hibberd, P.L., et al. (2013). Household Air Pollution in Low- and Middle-Income Countries: Health Risks and Research Priorities. PLoS Med. *10*, e1001455.

Matsuzaki, M., Sullivan, R., Ekelund, U., Krishna, K.R., Kulkarni, B., Collier, T., Ben-Shlomo, Y., Kinra, S., and Kuper, H. (2015). Development and evaluation of the Andhra Pradesh Children and Parent Study Physical Activity Questionnaire (APCAPS-PAQ): a cross-sectional study. BMC Public Health *16*.

Mazidi, M., and Speakman, J.R. (2017). Ambient particulate air pollution (PM2.5) is associated with the ratio of type 2 diabetes to obesity. Sci. Rep. *7*.

Mills, E. (2016). Identifying and reducing the health and safety impacts of fuel-based lighting. Energy Sustain. Dev. *30*, 39–50.

Montagne, D., Hoek, G., Nieuwenhuijsen, M., Lanki, T., Pennanen, A., Portella, M., Meliefste, K., Eeftens, M., Yli-Tuomi, T., Cirach, M., et al. (2013). Agreement of Land Use Regression Models with Personal Exposure Measurements of Particulate Matter and Nitrogen Oxides Air Pollution. Environ. Sci. Technol. *47*, 8523-31.

Münzel, T., Sørensen, M., Gori, T., Schmidt, F.P., Rao, X., Brook, F.R., Chen, L.C., Brook, R.D., and Rajagopalan, S. (2016). Environmental stressors and cardio-metabolic disease: part II–mechanistic insights. Eur. Heart J. ehw294.

Münzel, T., Center for Cardiology, University Medical Center Mainz, Mainz, Germany, Sørensen, M., and Danish Cancer Society Research Center, Copenhagen, Denmark (2017). Noise Pollution and Arterial Hypertension. Eur. Cardiol. Rev. *12*, 26.

de Nazelle, A., Seto, E., Donaire-Gonzalez, D., Mendez, M., Matamala, J., Nieuwenhuijsen, M.J., and Jerrett, M. (2013). Improving estimates of air pollution exposure through ubiquitous sensing technologies. Environ. Pollut. *176*, 92–99.

Nieuwenhuijsen, M.J. (2015). Exposure assessment in environmental epidemiology (Oxford; New York: Oxford University Press).

Nieuwenhuijsen, M.J., Donaire-Gonzalez, D., Rivas, I., de Castro, M., Cirach, M., Hoek, G., Seto, E., Jerrett, M., and Sunyer, J. (2015). Variability in and Agreement between Modeled and Personal Continuously Measured Black Carbon Levels Using Novel Smartphone and Sensor Technologies. Environ. Sci. Technol. *49*, 2977–2982.

Norris, C., Goldberg, M.S., Marshall, J.D., Valois, M.-F., Pradeep, T., Narayanswamy, M., Jain, G., Sethuraman, K., and Baumgartner, J. (2016). A panel study of the acute effects of personal exposure to household air pollution on ambulatory blood pressure in rural Indian women. Environ. Res. *147*, 331–342.

Patel, S., Li, J., Pandey, A., Pervez, S., Chakrabarty, R.K., and Biswas, P. (2017). Spatio-temporal measurement of indoor particulate matter concentrations using a wireless network of low-cost sensors in households using solid fuels. Environ. Res. *152*, 59–65.

Petzold, A., Ogren, J.A., Fiebig, M., Laj, P., Li, S.-M., Baltensperger, U., Holzer-Popp, T., Kinne, S., Pappalardo, G., Sugimoto, N., et al. (2013). Recommendations for reporting "black carbon" measurements. Atmospheric Chem. Phys. *13*, 8365–8379.

Piedrahita, R.A. (2017). On the Assessment of Air Pollution and Behavior within a Cookstove Intervention Study in Northern Ghana and Development of Improved Measurement Techniques.

Prospective Studies Collaboration. (2002). Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. The Lancet *360*, 1903–1913.

Qiu, H., Schooling, C.M., Sun, S., Tsang, H., Yang, Y., Lee, R.S., Wong, C.-M., and Tian, L. (2018). Long-term exposure to fine particulate matter air pollution and type 2 diabetes mellitus in elderly: A cohort study in Hong Kong. Environ. Int. *113*, 350–356.

Rajagopalan, S., and Brook, R.D. (2012). Air Pollution and Type 2 Diabetes: Mechanistic Insights. Diabetes *61*, 3037–3045.

Ramachandran, A., Das, A., Joshi, S., Yajnik, C., Shah, S., and Prasanna Kumar, K. (2010). Current Status of Diabetes in India and Need for Novel Therapeutic Agents.

Reid, J.S., Koppmann, R., Eck, T.F., and Eleuterio, D.P. (2005). A review of biomass burning emissions part II: intensive physical properties of biomass burning particles. Atmospheric Chem. Phys. *5*, 799–825.

Requia, W.J., Adams, M.D., and Koutrakis, P. (2017). Association of PM2.5 with diabetes, asthma, and high blood pressure incidence in Canada: A spatiotemporal analysis of the impacts of the energy generation and fuel sales. Sci. Total Environ. *584–585*, 1077–1083.

Rothman, K.J., Greenland, S., and Lash, T.L. (2008). Modern epidemiology (Philadelphia Baltimore New York: Wolters Kluwer Health, Lippincott Williams & Wilkins).

Sacks, D.B. (2011). A1C Versus Glucose Testing: A Comparison. Diabetes Care *34*, 518–523.

Sacoor, C., Nhacolo, A., Nhalungo, D., Aponte, J.J., Bassat, Q., Augusto, O., Mandomando, I., Sacarlal, J., Lauchande, N., Sigauque, B., et al. (2013). Profile: Manhica Health Research Centre (Manhica HDSS). Int. J. Epidemiol. *42*, 1309–1318.

Sanchez, M., Ambros, A., Milà, C., Salmon, M., Balakrishnan, K., Sambandam, S., Sreekanth, V., Marshall, J.D., and Tonne, C. (2018). Development of land-use regression models for fine particles and black carbon in peri-urban South India. Sci. Total Environ. *634*, 77–86.

Sanchez, M., Milà, C., Sreekanth, V., Balakrishnan, K., Sambandam, S., Nieuwenhuijsen, M., Kinra, S., Marshall, J.D., and Tonne, C. Personal exposure to particulate matter in peri-urban India: predictors and association with ambient concentration at residence. *Under Review*.

Sattar, N., and Gill, J.M.R. (2015). Type 2 diabetes in migrant south Asians: mechanisms, mitigation, and management. Lancet Diabetes Endocrinol. *3*, 1004–1016.

Schauer, J.J., Lough, G.C., Shafer, M.M., Christensen, W.F., Arndt, M.F., DeMinter, J.T., and Park, J.-S. (2006). Characterization of metals emitted from motor vehicles. Res. Rep. Health Eff. Inst. 1-76-88.

Schwartz, J., Alexeeff, S.E., Mordukhovich, I., Gryparis, A., Vokonas, P., Suh, H., and Coull, B.A. (2012). Association between long-term exposure to traffic particles and blood pressure in the Veterans Administration Normative Aging Study. Occup. Environ. Med. *69*, 422–427.

Shah, A.S., Langrish, J.P., Nair, H., McAllister, D.A., Hunter, A.L., Donaldson, K., Newby, D.E., and Mills, N.L. (2013). Global association of air pollution and heart failure: a systematic review and meta-analysis. The Lancet *382*, 1039–1048.

Smith, K.R. (1993). Fuel Combustion, Air Pollution Exposure, and Health: The Situation in Developing Countries. Annu. Rev. Energy Environ. *18*, 529–566.

Smith, K.R., and Peel, J.L. (2010). Mind the Gap. Environ. Health Perspect. *118*, 1643–1645.

Smith, K.R., Jerrett, M., Anderson, H.R., Burnett, R.T., Stone, V., Derwent, R., Atkinson, R.W., Cohen, A., Shonkoff, S.B., Krewski, D., et al. (2009). Public health benefits of strategies to reduce greenhouse-gas emissions: health implications of short-lived greenhouse pollutants. The Lancet *374*, 2091–2103.

Snyder, E.G., Watkins, T.H., Solomon, P.A., Thoma, E.D., Williams, R.W., Hagler, G.S.W., Shelow, D., Hindin, D.A., Kilaru, V.J., and Preuss, P.W. (2013). The Changing Paradigm of Air Pollution Monitoring. Environ. Sci. Technol. *47*, 11369–11377.

Stamler, J., Stamler, R., and Neaton, J.D. (1993). Blood pressure, systolic and diastolic, and cardiovascular risks. US population data. Arch. Intern. Med. *153*, 598–615.

Sughis, M., Nawrot, T.S., Ihsan-ul-Haque, S., Amjad, A., and Nemery, B. (2012). Blood pressure and particulate air pollution in schoolchildren of Lahore, Pakistan. BMC Public Health *12*.

Thiering, E., and Heinrich, J. (2015). Epidemiology of air pollution and diabetes. Trends Endocrinol. Metab. *26*, 384–394.

Tong, S., von Schirnding, Y.E., and Prapamontol, T. (2000). Environmental lead exposure: a public health problem of global dimensions. Bull. World Health Organ. *78*, 1068–1077.

Tonne, C., Salmon, M., Sanchez, M., Sreekanth, V., Bhogadi, S., Sambandam, S., Balakrishnan, K., Kinra, S., and Marshall, J.D. (2017). Integrated assessment of exposure to PM 2.5 in South India and its relation with cardiovascular risk: Design of the CHAI observational cohort study. Int. J. Hyg. Environ. Health.

Unnikrishnan, R., Anjana, R.M., and Mohan, V. (2014). Diabetes in South Asians: Is the Phenotype Different? Diabetes *63*, 53–55.

Venkateshmurthy, N.S., Geldsetzer, P., Jaacks, L.M., and Prabhakaran, D. (2018). Implications of the New American College of Cardiology Guidelines for Hypertension Prevalence in India. JAMA Intern. Med. *178*, 1416.

Wang, B., Xu, D., Jing, Z., Liu, D., Yan, S., and Wang, Y. (2014). MECHANISMS IN ENDOCRINOLOGY: Effect of long-term exposure to air pollution on type 2 diabetes mellitus risk: a systemic review and meta-analysis of cohort studies. Eur. J. Endocrinol. *171*, R173–R182.

Wellenius, G.A., Wilhelm-Benartzi, C.S., Wilker, E.H., Coull, B.A., Suh, H.H., Koutrakis, P., and Lipsitz, L.A. (2012). Ambient Particulate Matter and the Response to Orthostatic Challenge in the Elderly: The Maintenance of Balance, Independent Living, Intellect, and Zest in the Elderly (MOBILIZE) of Boston Study. Hypertension *59*, 558–563.

Whelton, P.K., Carey, R.M., Aronow, W.S., Casey, D.E., Collins, K.J., Dennison Himmelfarb, C., DePalma, S.M., Gidding, S., Jamerson, K.A., Jones, D.W., et al. (2017). 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/ PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. J. Am. Coll. Cardiol.

Williams, R., Vasu Kilaru, E., Snyder, A., Kaufman, T., Dye, A., Rutter, A., Russell, A., and Hafner, H. (2014). Air Sensor Guidebook (Washington, DC: U.S. Environmental Protection Agency).

Wolf, K., Popp, A., Schneider, A., Breitner, S., Hampel, R., Rathmann, W., Herder, C., Roden, M., Koenig, W., Meisinger, C., et al. (2016). Association Between Long-term Exposure to Air Pollution and Biomarkers Related to Insulin Resistance, Subclinical Inflammation, and Adipokines. Diabetes *65*, 3314–3326.

World Bank (2016). Access to electricity: 1990-2016. Available at: https://data.worldbank.org/indicator/EG.ELC.ACCS.ZS [Accessed Dec 18, 2018]

World Health Organization (WHO). (2010). WHO guidelines for indoor air quality: selected pollutants (Copenhagen: WHO). Availabe at: http://www.euro.who.int/__data/assets/pdf_file/0009/128169/e94535.pdf [Accessed Dec 18, 2018]

World Health Organization (WHO). (2016). Global Urban Ambient Air Pollution map (update 2016). Available at: https://www.who.int/airpollution/data/cities-2016/en/ [Accessed Dec 18, 2018]

World Health Organization (WHO). (2016). Global report on diabetes (Geneva, Switzerland: World Health Organization). Available at: https://www.who.int/diabetes/global-report/en/ [Accessed Dec 18, 2018]

Xie, X., Wang, Y., Yang, Y., Xu, J., Zhang, Y., Tang, W., Guo, T., Wang, Q., Shen, H., Zhang, Y., et al. (2018). Long-Term Effects of Ambient Particulate Matter (With an Aerodynamic Diameter ≤2.5 μm) on Hypertension and Blood Pressure and Attributable Risk Among Reproductive-Age Adults in China. J. Am. Heart Assoc. *7*.

Yamamoto, S.S., Phalkey, R., and Malik, A.A. (2014). A systematic review of air pollution as a risk factor for cardiovascular disease in South Asia: Limited evidence from India and Pakistan. Int. J. Hyg. Environ. Health *217*, 133–144.

Yang, B.-Y., Qian, Z. (Min), Li, S., Chen, G., Bloom, M.S., Elliott, M., Syberg, K.W., Heinrich, J., Markevych, I., Wang, S.-Q., et al. (2018a). Ambient air pollution in relation to diabetes and glucose-homoeostasis markers in China: a cross-sectional study with findings from the 33 Communities Chinese Health Study. Lancet Planet. Health *2*, e64–e73.

Yang, B.-Y., Qian, Z., Howard, S.W., Vaughn, M.G., Fan, S.-J., Liu, K.-K., and Dong, G.-H. (2018b). Global association between ambient air pollution and blood pressure: A systematic review and meta-analysis. Environ. Pollut. *235*, 576–588.

Yang, W.-S., Wang, X., Deng, Q., Fan, W.-Y., and Wang, W.-Y. (2014). An evidence-based appraisal of global association between air pollution and risk of stroke. Int. J. Cardiol. *175*, 307–313.

Yang, Y., Guo, Y., Qian, Z. (Min), Ruan, Z., Zheng, Y., Woodward, A., Ai, S., Howard, S.W., Vaughn, M.G., Ma, W., et al. (2018c). Ambient fine particulate pollution associated with diabetes mellitus among the elderly aged 50 years and older in China. Environ. Pollut. *243*, 815–823.

Zare Sakhvidi, M.J., Zare Sakhvidi, F., Mehrparvar, A.H., Foraster, M., and Dadvand, P. (2018). Association between noise exposure and diabetes: A systematic review and meta-analysis. Environ. Res. *166*, 647–657.

Zhang, Z., Laden, F., Forman, J.P., and Hart, J.E. (2016). Long-Term Exposure to Particulate Matter and Self-Reported Hypertension: A Prospective Analysis in the Nurses' Health Study. Environ. Health Perspect. *124*.

Zhang, Z., Guo, C., Lau, A.K., Chan, T.-C., Chuang, Y.C., Lin, C., Jiang, W.K., Yeoh, E., Tam, T., Woo, K.S., et al. (2018). Long-

Term Exposure to Fine Particulate Matter, Blood Pressure, and Incident Hypertension in Taiwanese Adults. Environ Health Perspect *126*.

Zhong, J., Cayir, A., Trevisi, L., Sanchez-Guerra, M., Lin, X., Peng, C., Bind, M.-A., Prada, D., Laue, H., Brennan, K.J.M., et al. (2016). Traffic-Related Air Pollution, Blood Pressure, and Adaptive Response of Mitochondrial AbundanceCLINICAL PERSPECTIVE. Circulation *133*, 378–387.

Zhou, B., Bentham, J., Di Cesare, M., Bixby, H., Danaei, G., Cowan, M.J., Paciorek, C.J., Singh, G., Hajifathalian, K., Bennett, J.E., et al. (2017). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants. The Lancet *389*, 37–55.

Index by words

Annexes

Presentations during the course of this thesis

1. (2016). Poster & Oral Presentation: Low-cost sensors to estimate long-term exposure to household air pollution. 26th Annual International Society of Exposure Science (**ISES**) Conference, Utrecht, Netherlands. Main Audience: Researcher
2. (2016). Poster Presentation: Low-cost sensors to estimate long-term exposure to household air pollution. 3rd PhD ISGlobal **Symposium**. Barcelona, Spain. Main Audience: Researcher, Competitive?: Yes. Awardee of the best poster presentation.
3. (2017). Poster & Oral Presentation: Personal exposure to black carbon among women in semi-rural Mozambique. 27th Annual International Society of Exposure Science (**ISES**) Conference, Durham, United States. Main Audience: Researcher
4. (2017). Oral Presentation: Household air pollution and cardiovascular health in India. **Rin4'** PhD student competition (doctoral students from the Pompeu Fabra University give a four-minute oral presentation of their research to a general audience), Barcelona, Spain. Main Audience: General Public, Competitive?: Yes
5. (2018). Oral Presentation: Residential ambient air pollution and blood pressure in peri-urban villages near Hyderabad, India. Seminar series of the Center for Environmental Health and Technology (CEHT), **Brown** School of Public Health, Providence, United States. Main Audience: Researcher
6. (2018). Oral presentation: Residential ambient particulate air pollution and blood pressure in periurban India. The Joint Annual Meeting of the International Society of Exposure Science (**ISES**) and the International Society for Environmental Epidemiology (**ISEE**), Ottawa, Canada. Main Audience: Researcher
7. (2018). Oral presentation: Residential ambient particulate air pollution and blood pressure in periurban India. 5th PhD ISGlobal **Symposium**. Barcelona, Spain. Main Audience: Researcher, Competitive?: Yes

Papers co-authored during the course of this thesis

Apart from the original papers included in the present thesis, the PhD candidate has been involved in two other papers on personal monitoring assessment.

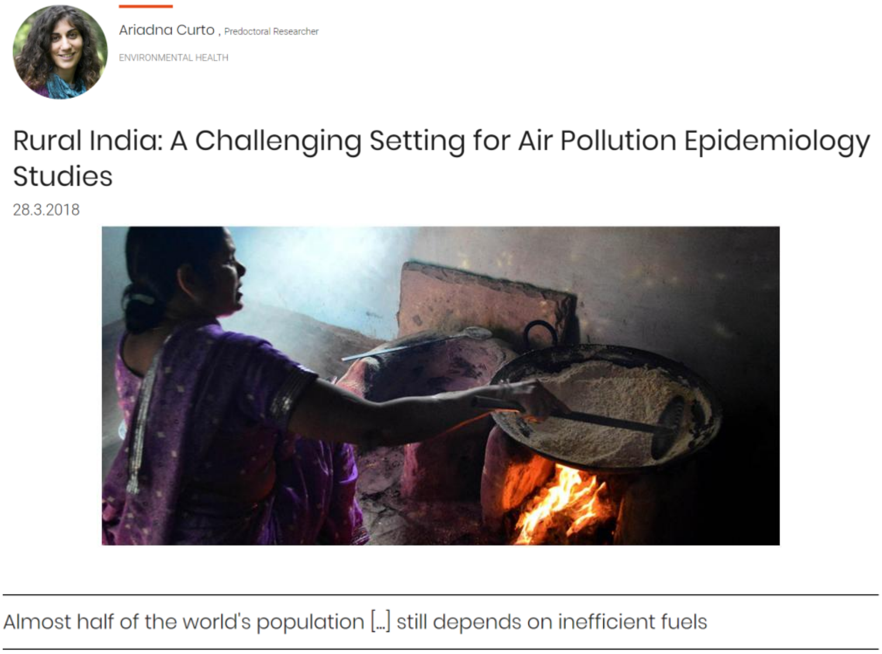
1. David Donaire-Gonzalez, Antònia Valentín, Erik van Nunen, **Ariadna Curto**, Albert Rodriguez, Mario Fernandez-Nieto, Alessio Naccarati, Sonia Tarallo, Ming-Yi Tsai, Nicole Probst-Hensch, Roel Vermeulen, Gerard Hoek, Paolo Vineis, John Gulliver, Mark Nieuwenhuijsen. **ExpoApp: an integrated system to assess multiple personal environmental exposures**. *Under Review*.
2. David Donaire-Gonzalez, **Ariadna Curto**, Antònia Valentín, Sandra Andrusaityte, Xavier Basagaña, Maribel Casas, Leda Chatzi, Jeroen de Bont, Montserrat de Castro, Audrius Dedele, Berit Granum, Regina Grazuleviciene, Mariza Kampouri, Sarah Lyon-Caen, Cyntia B. Manzano-Salgado, Gunn Marit Aasvang, Rosemary McEachan, Carin Helena Meinhard-Kjellstad , Eirini Michalaki, Pau Pañella, Inga Petraviciene, Per E. Schwarze, Rémy Slama, Oliver Robinson, Ibon Tamayo-Uria, Marina Vafeiadi, Dagmar Waiblinger, John Wright, Martine Vrijheid, Mark J Nieuwenhuijsen. **Personal assessment of the external exposome during pregnancy and childhood in Europe**. *Under Review.*

Journal review activities during the course of this thesis

2018/2 - 2018/5 Reviewer, Environmental Pollution
Number of Works Reviewed / Refereed: 1

2017/11 - 2018/1 Reviewer, Sensors
Number of Works Reviewed / Refereed: 1

One of the contributions to the ISGlobal Health Blog



Ariadna Curto , Predoctoral Researcher

ENVIRONMENTAL HEALTH

Rural India: A Challenging Setting for Air Pollution Epidemiology Studies

28.3.2018

Almost half of the world's population [...] still depends on inefficient fuels

Most people living in urban areas in high income countries associate air pollution with road traffic or possibly industry. However, **lack of access to clean household energy is also an important contributor to air pollution exposure**. **Almost half of the world's population** (about 3 billion people) **still depends on inefficient fuels** for cooking, lighting, and household heating.

In such homes, an everyday task such as cooking with fuels like wood, coal, crop waste and cow dung becomes a source of high exposure to polluting particles, especially in women, who are the primary cook. The particles do not stay within the house. They travel beyond the walls making **household air pollution**, together with local industries and road traffic, **a major source of outdoor air pollution**.

The **CHAI study** (Cardiovascular Health effects of Air pollution in Andhra Pradesh, India) was developed to **look at air pollution from outdoor and household sources in an integrated way** in rural South India and link air

CHAI
Cardiovascular Health effects
of Air pollution in Telangana, India

pollution exposures to markers of cardiovascular disease.
Accurately measuring exposure to air pollution in settings like rural India is a challenge. Environments are very dusty, access to electricity is unreliable, and high temperature and humidity make measurements challenging. Temperatures reached in summer (>40ºC), for example, were a strain for the field workers and participants as well as a problem for the air pollution monitoring equipment. During a particularly hot week, we painted the black boxes protecting the sampling equipment white so they would not absorb so much heat and keep working.

Lack of access to clean household energy is also an important contributor to air pollution exposure

Many health studies are interested in the effects of several years or a lifetime of exposure to household air pollution; however, this is currently nearly impossible to measure. The growth of **low-cost air quality monitors with long-lasting batteries** now provide the **opportunity to measure air pollution in rural settings for several weeks to months** without intensive supervision.

As a PhD, I tested two potentially useful low-cost monitors (<500€) able to measure fine particulate matter and carbon monoxide and deployed them for one week in households participating in CHAI. In this real-world (compared to laboratory) environment, the monitors were very sensitive to environmental changes and often malfunctioned. In light of our results, recently published in *Environmental Research*, we concluded that the low-cost monitors we tested were **not yet ready to measure chronic exposures for epidemiological studies in these challenging settings**. However, the technology is rapidly advancing and we can expect low-cost monitors to help get closer to the goal of unattended, long-term monitoring in the future.

Women were found to spend on average 13 hours of their daytime at home [...] compared to just 9 hours for men

In one of the first publications from CHAI, postdoctoral researcher Margaux Sanchez analyzed the **daily mobility patterns** of study participants. **Women were found to spend on average 13 hours of their daytime at home or within 50 meters of the home, compared to just 9 hours for men**. I am now exploring whether these sex differences in mobility and time-activity patterns are also reflected in the association between outdoor air pollution at the home and blood pressure.

> CHAI is providing evidence of the need to reduce air pollution exposure at multiple levels

This association could imply a large burden of hypertension due to air pollution in India given the pervasiveness of high exposure to air pollution.

CHAI is providing evidence of the **need to reduce air pollution exposure at multiple levels** including ambient air pollution, household air pollution from cooking with biomass fuel, and exposures in occupational settings. These issues relate to several of the United Nations Sustainable Development Goals, including reducing illness from air pollution (Goal 3) and universal access to affordable, clean, and sustainable energy (Goal 7).

Search terms

Evidence for particulate air pollution and high blood pressure and hypertension

In Pubmed:

("Blood Pressure"[Mesh] OR "Hypertension"[Mesh]) AND "Developing Countries"[Mesh] AND ("Air Pollution"[Mesh] OR "Particulate Matter"[Mesh])

("Blood Pressure"[All Fields] OR "Hypertension"[All Fields]) AND ("Developing Countries"[All Fields] OR "low-income"[All Fields] OR "poor"[All Fields]) AND ("Air Pollution"[All Fields] OR "Particulate Matter"[All Fields] OR "black carbon"[All Fields] OR "air quality"[All Fields])

("Blood Pressure"[All Fields] OR "Hypertension"[All Fields]) AND (“south asia” OR “Afghanistan” OR “Bangladesh” OR “Bhutan” OR “India” OR “Maldives” OR “Nepal” OR “Pakistan” OR “Sri Lanka”) AND ("Air Pollution"[All Fields] OR "Particulate Matter"[All Fields] OR "black carbon"[All Fields] OR "air quality"[All Fields])

In Google Scholar:

(air pollution OR particulate matter OR PM2.5) AND developing countries AND (blood pressure OR hypertension)

(air pollution OR particulate matter OR PM2.5 OR black carbon) AND (developing countries OR low-income OR poor) AND (blood pressure OR hypertension)

(air pollution OR particulate matter OR PM2.5 OR black carbon) AND (south asia OR Afghanistan OR Bangladesh OR Bhutan OR India OR Maldives OR Nepal OR Pakistan OR Sri Lanka) AND (blood pressure OR hypertension)

Evidence for particulate air pollution and high blood pressure and hypertension

In Pubmed:

("Insulin"[All Fields] OR "insulin resistance"[All Fields] OR "diabetes"[All Fields] OR "type 2 diabetes"[All Fields] OR "HOMA-IR"[All Fields] OR "glucose"[All Fields] OR "glucose metabolism"[All Fields] OR "glucose regulation"[All Fields] OR "glucose homeostasis"[All Fields]) AND ("Developing Countries"[All Fields] OR "low-income"[All Fields] OR "poor"[All Fields]) AND ("Air Pollution"[All Fields] OR "Particulate Matter"[All Fields] OR "black carbon"[All Fields] OR "air quality"[All Fields] OR "Ambient Air Pollution"[All Fields])

("Insulin"[All Fields] OR "insulin resistance"[All Fields] OR "diabetes"[All Fields] OR "type 2 diabetes"[All Fields] OR "HOMA-IR"[All Fields] OR "glucose"[All Fields] OR "glucose metabolism"[All Fields] OR "glucose regulation"[All Fields] OR "glucose homeostasis"[All Fields]) AND ("Air Pollution"[All Fields] OR "Particulate Matter"[All Fields] OR "black carbon"[All Fields] OR "air quality"[All Fields] OR "Ambient Air Pollution"[All Fields])

(“Insulin Resistance”[Mesh] OR insulin resistan*[tiab] OR insulin sensitivity[tiab] OR (resistan*[tiab] AND insulin*[tiab]) OR metabolic syndr*[tiab]) AND ("Air Pollution"[All Fields] OR "Particulate Matter"[All Fields] OR "black carbon"[All Fields] OR "air quality"[All Fields] OR "Ambient Air Pollution"[All Fields]) AND "humans"[MeSH Terms]

(“Insulin Resistance”[Mesh] OR insulin resistan*[tiab] OR insulin sensitivity[tiab] OR (resistan*[tiab] AND insulin*[tiab]) OR metabolic syndr*[tiab] OR glucose*[tiab] OR diabetes*[tiab] NOT “gestational diabetes”) AND ("Air Pollution"[All Fields] OR "Particulate Matter"[All Fields] OR "black carbon"[All Fields] OR "air quality"[All Fields] OR "Ambient Air Pollution"[All Fields]) AND "humans"[MeSH Terms]

In Google Scholar:

(air pollution OR air pollutants OR particulate matter OR PM10 OR PM2.5 OR black carbon) AND (type 2 diabetes OR diabetes mellitus OR insulin OR glucose)

(air pollution OR air pollutants OR particulate matter OR PM10 OR PM2.5) AND (developing countries OR low-income OR poor) AND (type 2 diabetes OR diabetes mellitus OR insulin OR glucose)

(air pollution OR air pollutants OR particulate matter OR PM10 OR PM2.5) AND south asia OR Afghanistan OR Bangladesh OR Bhutan OR India OR Maldives OR Nepal OR Pakistan OR Sri Lanka) AND (type 2 diabetes OR diabetes mellitus OR insulin OR glucose)

(air pollution OR air pollutants OR particulate matter OR PM10 OR PM2.5 OR black carbon) AND (developing countries OR low-income OR poor) AND (type 2 diabetes OR diabetes mellitus OR insulin OR glucose OR insulin resistance OR metabolic)