HEI

F-1 Application for Health Effects Institute Research Agreement

All Agreements Use the Cost Reimbursement Format

_____
Number (Leave Blank)

1. Title of Application *(20 words maximum)*
Unraveling the effects of traffic on cardiometabolic and mental health from the complex network of urban exposures (THeCUE)

2. Response to RFA or RFPA Number and Title
RFA 17-1 Assessing adverse health effects of exposure to traffic-related air pollution, noise, and their interactions with socio-economic status

3. Type of Organization *(Check all that apply)*

X Private Non-Profit
__ Educational
__ Public (__ Federal, __ State, __ Local)
__ Private Profit
__ Minority Owned
__ Small Business
__ Woman Owned

4. Principal Investigator
4a. Name (Last, First, Middle) *With Signature and Date*
Basagaña, Xavier _____ July, 14th 2017
Signature and Date

4b. Mailing Address *(Organization, Street, City, State, Zip Code)*
Barcelona Institute for Global Health
Dr. Aiguader 88
Barcelona
08003
Spain

4c. Telephone Number *(Area Code, Extension)*
+34932147380
4d. Fax Number *(Area Code)*
+34932147302
4e. Email
xavier.basagana@isglobal.org

4f. Position Title
Associate Research Professor

5. Total Cost Requested First 12-Month Period *(Enter from Page F-4a)*
$511,145

7. Total Cost Requested Entire Project Period *(Enter from Page F-5a1) / Number of Years*
$999,846 / 4 Years

6. Human Subjects or Derived Materials Involved?

YES _X__ NO____

8. Applicant Institution, Congressional District, and DUNS number
Barcelona Institute for Global Health, Spain, DUNS Number: 463701134

9. Name, Title, Address, Email & Telephone Number of Individual(s) Authorized to Negotiate Agreement
Gonzalo Vicente, Managing Director
Rosselló 132, 5-2
08036 Barcelona, Spain
email: projects@isglobal.org
telephone number: +34 932279892

ISGlobal Barcelona Institute for Global Heal
14/7/17

10. Name, Title, Address, Email & Telephone Number of Individual(s) Authorized to Execute Agreement *(if different than above)*

Same as above _____

14/7/17

F-2 TABLE OF CONTENTS OF APPLICATION

Number pages consecutively at the bottom throughout the application (automatic page numbering is activated but please double check).Type the name of the Principal Investigator at the top of each page and each continuation page (see page header).

F-3 ABSTRACT OF PROJECT PLAN

PRINCIPAL INVESTIGATOR: *(Name, Title, and Institution)*
Xavier Basagaña, PhD, Barcelona Institute for Global Health (ISGlobal)

PROJECT TITLE: *(20 words maximum)*
Unraveling the effects of traffic on cardiometabolic and mental health from the complex network of urban exposures (THeCUE)

ABSTRACT OF PROJECT PLAN: *Concisely describe the application's specific aims, methodology, and long-term objectives, making reference to the scientific disciplines involved and the relationship of the project to the objectives of HEI and the Request for Applications. The abstract should be self-contained so that it can serve as a succinct and accurate description of the application when separated from it. DO NOT EXCEED ONE PAGE.*

THeCUE will use data from two well-established population-based cohorts of adults in Germany (Heinz Nixdorf Recall, HNR) and Spain (REGICOR), with detailed longitudinal data on cardiovascular health, diabetes and mental health outcomes, to conduct holistic analyses that allow unraveling the role of traffic-related air pollution on these outcomes by properly controlling for a large array of interrelated factors. Both cohorts have estimates of exposure to air pollution from different sources, which will be refined during the project by using Bayesian Maximum Entropy to combine estimates from land use regression (LUR) models and a 1-km resolution chemical transport model (CTM). Estimates of concentrations by main activity sources (traffic, industry and residential combustion), by fuel type (diesel and gasoline) and by traffic emission process (exhaust and non-exhaust) will be available. This will provide improved estimates of air pollution exposure at the residential address of participants, capturing detailed intraurban variations. In addition, information will be available on traffic-related and railway noise, green spaces, built environment, socioeconomic factors, diet and physical activity. The project will estimate the relationship between traffic-related air pollution and blood pressure, atherosclerosis, diabetes and mental health while controlling for correlated factors in longitudinal and prospective analyses. In addition, the project will evaluate the modification of the relationships by traffic noise, urban greenness, built environment, diet, physical activity and socioeconomic status. The planned analyses will provide new results not previously published, as it will analyze new outcomes, it will conduct longitudinal analyses in cases where only cross-sectional results have been published, and it will extend published longitudinal results by adding a new follow-up visit. As further extensions over previous work, apart from the improved exposure models described above, the project will use improved noise exposure assessment, derive new exposures (e.g. on greenness and built environment) and use more appropriate statistical methods, including novel tools for causal inference. In addition, having two similar cohorts for two countries will provide opportunities to analyze whether patterns of health effects are comparable in different regions. The project will touch on all the objectives of the RFA 17-1 call. Objective 1 will be covered by the improved exposure assessment, with estimates from several pollutants (including NO_2, $PM_{2.5}$, ultrafine particles (UFP), Ni, Cu, Zn, V, S, Si, Fe and K) and source-, traffic emission process-, and fuel type-specific concentrations. Objective 2 will be addressed by estimating the independent effects of traffic-related air pollution and noise, owing to the availability of traffic noise estimates, including novel predictions of indoor traffic-related noise that take into account room orientation and insulation. Objective 3 calls for the development and use of individual and community level SES indicators. Our cohorts have individual data on education, occupation and household income, and area SES indicators at the census tract level. Finally, we will address objectives 4 and 5 by accurately controlling for confounding or effect modification using detailed information on urban greenness, built environment, diet, BMI, physical activity and medication use, among others; and by disentangling the effects of different pollutants and sources. Proper control for all these factors in the statistical analyses will be obtained by using causal inference models, in particular propensity score matching and targeted learning.

F-4a BUDGET FOR FIRST 12 MONTH PERIOD

From			Through				
Personnel			Time Effort		Dollar Amount Requested *(omit cents)*		
NAME	Title or Position	Role in Project	%	Hours /Week	Salary	Fringe Benefit	Totals
Xavier Basagaña	Associate Research Professor	Principal Investigator	40%		$12,165		$12,165
Mark Nieuwenhuijsen	Research Professor	Investigator	5%		$0		$0
Payam Dadvand	Assistant Research Professor	Investigator	2.5%		$0		$0
Maria Foraster	Senior postdoc	Investigator	5%		$0		$0
To be hired	postdoc	Investigator	100%		$45,843		$45,843
To be hired	postdoc	Investigator	100%		$45,843		$45,843
TBD	Technician	GIS Technician	100%		$42,569		$42,569
TBD	Project manager	Project manager	15%		$7,859		$7,859
				Subtotals			$154,278
Consultant Costs							
Supplies (itemized) 2 Laptops + software							$3,576
Other Expenses (itemized)							
Travel (domestic only)							
Subtotal Direct Costs							$157,854
Indirect Costs - Limited to 30% of direct costs excluding equipment and subcontracts. See budget instructions. Please attach a copy of most recent approved indirect cost rate. ISGlobal indirect cost rate is 20%							$31,571
Equipment (itemized)							
Subcontractors *(Enter total from 4b)*							$321,720
Total First 12-Month Budget Costs *(Enter on Form 1 Item 5 and on Form 5a)*							$511,145

F-4b BUDGET FOR FIRST 12 MONTH PERIOD (Subcontract) IMIM

From			Through				
Personnel			Time Effort		Dollar Amount Requested *(omit cents)*		
NAME	Title or Position	Role in Project	%	Hours /Week	Salary	Fringe Benefit	Totals
Roberto Elosua	Research Professor	Investigator	10%		$0		$0,00
Jaume Marrugat	Research Professor	Investigator	5%		$0		$0,00
TBD	Data manager	Support	50%		$18,900		$18,900
TBD	Nurse	Field work	50%		$21,000		$21,000
TBD	Technician	Field work	50%		$15,000		$15,000
				Subtotals			$54,900
Consultant Costs							
Supplies (itemized)							
Other Expenses (itemized)							
Travel (domestic only)							
Subtotal Direct Costs							$54,900
Indirect Costs - Limited to 30% of direct costs excluding equipment and subcontracts. See budget instructions. Please attach a copy of most recent approved indirect cost rate. IMIM indirect cost rate is 25%							$13,725
Equipment (itemized)							
Total Subcontract Costs *(Enter on Form 4a under Subcontracts)*							**$68,625**

F-4b BUDGET FOR FIRST 12 MONTH PERIOD (Subcontract) CUE

From			Through				
Personnel			Time Effort		Dollar Amount Requested *(omit cents)*		
NAME	Title or Position	Role in Project	%	Hours /Week	Salary	Fringe Benefit	Totals
Susanne Moebus	Researcher/Epidemiologist	Co-Principal Investigator	20%	n/a	$0	$0	$0
Ester Orban	Researcher/Epidemiologist	Co-Investigator	75%	n/a	$59,454	$0	$59,454
N.N.	Biostatistician	Co-Investigator	25%	n/a	$0	$0	$0
N.N.	Data manager	Data manager	25%	n/a	$0	$0	$0
				Subtotals			$59,454
Consultant Costs							
Supplies (itemized)							
Other Expenses (itemized)							
Travel (domestic only) Kick-off meeting (1st year)							$1,200
Subtotal Direct Costs							$60,654
Indirect Costs - Limited to 30% of direct costs excluding equipment and subcontracts. See budget instructions. Please attach a copy of most recent approved indirect cost rate. CUE indirect cost rate is 22%							$13,344
Equipment (itemized)							
Total Subcontract Costs *(Enter on Form 4a under Subcontracts)*							**$73,998**

F-4b BUDGET FOR FIRST 12 MONTH PERIOD (Subcontract) BSC

From			Through				
Personnel			Time Effort		Dollar Amount Requested *(omit cents)*		
NAME	Title or Position	Role in Project	%	Hours /Week	Salary	Fringe Benefit	Totals
Maria Teresa Pay	Postdoc Researcher/ AQ modeller	Principal Investigator	67%	n/a	$43,200		$43,200
Carlos Perez	Head of Atmospheric Composition Group	Co-Investigator	2%	n/a	$1,350		$1,350
Mario Acosta	Research Engineer	Technician	100%	n/a	$64,800		$64,800
Marc Guevara	Postdoc Researcher	Co-Investigator	38%	n/a	$64,800		$24,300
				Subtotals			$133,650
Consultant Costs							
Supplies (itemized)							
Other Expenses (itemized)							
Travel (domestic only)							$240
Subtotal Direct Costs							$133,890
Indirect Costs - Limited to 30% of direct costs excluding equipment and subcontracts. See budget instructions. Please attach a copy of most recent approved indirect cost rate. BSC indirect cost rate is higher than 30%, but they apply the HEI limitation of 30%							$40,167
Equipment (itemized) 20 disks to be set in a BeeGFS filesystem with the following characteristics: WD Red Pro NAS Hard Drive, model WD40EFRX, 4 TB capacity, SATA 6Gb s interface, 5400 rpm, and 64 MB cache (210 €/disk)							$5,040
Total Subcontract Costs *(Enter on Form 4a under Subcontracts)*							$179,097

F-5a BUDGET FOR TOTAL PROJECT

BUDGET CATEGORY	1ST BUDGET PERIOD (*From page F-4a*)	ADDITIONAL YEARS SUPPORT REQUESTED			
		2ND	3RD	4TH	TOTAL
PERSONNEL (Salary and Fringe Benefits) (Applicant Organization Only)	$ 154,278	$ 65,867	$ 20,023	$ 20,023	$260,192
CONSULTANT COSTS					
SUPPLIES	$ 3,576				$ 3,576
OTHER EXPENSES		$ 2,400	$ 4,800	$ 4,800	$ 12,000
TRAVEL		$ 9,300	$ 3,000	$ 5,000	$ 17,300
SUBTOTAL DIRECT COSTS	$ 157,854	$ 77,567	$ 27,823	$ 29,823	$293,068
INDIRECT COSTS (*Note 30% Cap*) ISGlobal 20%	$ 31,571	$ 15,513	$ 5,565	$ 5,965	$ 58,614
EQUIPMENT					
SUBCONTRACTS (*From Form 5B***)**	$ 321,720	$162,114	$119,559	$ 44,772	$603,393
TOTAL COSTS	$ 511,145	$255,194	$152,947	$ 80,560	$999,846
TOTAL FOR ENTIRE PROPOSED PROJECT *(Enter on Form 1, Item 7)*					**$999,846**

Budget Justification: Total Budget

Briefly describe the specific functions of the personnel and consultants. For each year, justify any cost for which the need may not be obvious, such as equipment, foreign travel, alterations and renovations, and contractual or third party costs. For future years, justify any significant increases in any category. If a recurring annual increase in personnel costs is anticipated, give percentage. Note that an Institutional Cost Rate Agreement should be submitted once the project has been approved for funding.

Functions of personnel

The PI of the project, Xavier Basagaña (ISGlobal), will lead and coordinate the whole project. He will also coordinate the work involving the REGICOR cohort. A kick-off meeting (Barcelona), a mid-term meeting (Essen) and a final meeting (Barcelona) will be organized, complemented by at least two teleconferences/meetings with the entire team per year, to discuss the progress and the results of the project. Travel to those meetings has been budgeted. Mark Nieuwenhuijsen and Payam Dadvand will lead the acquisition of built environment and greenness variables for REGICOR, will supervise the GIS technician hired by the project and will provide their expertise in exposure assessment and environmental epidemiology throughout the project. Maria Foraster will lead the noise assessment in REGICOR, and will provide her expertise in studies disentangling the effects of traffic-related air pollution and noise. The GIS technician hired by the project will obtain and manage data from satellites and GIS databases, including air pollution and noise models. Two post-doctoral researchers will be hired by the project. They will conduct the data cleaning and harmonization, will conduct the statistical analyses for the different health outcomes and will write the scientific papers. Xavier Basagaña will write the statistical protocol and will supervise all the statistical analyses. A part-time project manager will help in coordination and preparation of all administrative and scientific reports.

Other costs

Travel includes the travel expenses of attending the kick-off (Barcelona), mid-term (Essen) and final meeting of the project (Barcelona), as well as those derived from attendance to scientific conferences (4) to present the results of the project. We are requesting fund for two computers and software for the two postdoctoral researchers. Finally, we request funding for publishing the scientific papers as Open Acces in scientific journals.

F-5b BUDGET FOR TOTAL PROJECT (Subcontract) IMIM

BUDGET CATEGORY	1ST BUDGET PERIOD (*From page F-4a*)	ADDITIONAL YEARS SUPPORT REQUESTED			
		2ND	3RD	4TH	TOTAL
PERSONNEL (Salary and Fringe Benefits) (Applicant Organization Only)	$54,900	$25,100			$80,000
CONSULTANT COSTS					
SUPPLIES					
OTHER EXPENSES					
TRAVEL	0	0	0	0	0
SUBTOTAL DIRECT COSTS	$54,900	$25,100			$80,000
INDIRECT COSTS (*Note 30% Cap*)	$13,725	$6,275			$20,000
EQUIPMENT					
SUBCONTRACTS (*From Form 5B***)**					
TOTAL COSTS	$68,625	$31,375			$100,000
TOTAL FOR ENTIRE PROPOSED PROJECT *(Enter on Form 5a under Subcontracts)*					**$100,000**

F-5b BUDGET FOR TOTAL PROJECT (Subcontract) CUE

BUDGET CATEGORY	1ST BUDGET PERIOD (*From page F-4a*)	ADDITIONAL YEARS SUPPORT REQUESTED			
		2ND	3RD	4TH	TOTAL
PERSONNEL (Salary and Fringe Benefits) (Applicant Organization Only)	$59,454	$99,090	$92,484	$29,727	$280,755
CONSULTANT COSTS					
SUPPLIES					
OTHER EXPENSES					
TRAVEL	$1,200	$1,200	$1,200	$2,400	$6,000
SUBTOTAL DIRECT COSTS	$60,654	$100,290	$93,684	$32,127	$286,755
INDIRECT COSTS (*Note 30% Cap*) CUE indirect cost rate is 22%	$13,344	$22,064	$20,610	$7,068	$63,086
EQUIPMENT					
SUBCONTRACTS (*From Form 5B***)**					
TOTAL COSTS	$73,998	$122,354	$114,294	$39,195	$349,841
TOTAL FOR ENTIRE PROPOSED PROJECT *(Enter on Form 5a under Subcontracts)*					$349,841

F-5b BUDGET FOR TOTAL PROJECT (Subcontract) BSC

BUDGET CATEGORY	1ST BUDGET PERIOD (*From page F-4a*)	ADDITIONAL YEARS SUPPORT REQUESTED			
		2ND	3RD	4TH	TOTAL
PERSONNEL (Salary and Fringe Benefits) (Applicant Organization Only)	$133,650	$4,050	$4,050	$4,050	$145,800
CONSULTANT COSTS					
SUPPLIES					
OTHER EXPENSES					
TRAVEL	$240	$2,400	$0	$240	$2,880
SUBTOTAL DIRECT COSTS	$133,890	$6,450	$4,050	$4,290	$148,680
INDIRECT COSTS (*Note 30% Cap*)	$40,167	$1,935	$1,215	$1,287	$44,604
EQUIPMENT	$5,040				
SUBCONTRACTS (*From Form 5B***)**					
TOTAL COSTS	$179,097	$8,385	$5,265	$5,577	$198,324
TOTAL FOR ENTIRE PROPOSED PROJECT *(Enter on Form 5a under Subcontracts)*					**$198,324**

Budget Justification: Subcontract Budget

Briefly describe the specific functions of the personnel and consultants. For each year, justify any cost for which the need may not be obvious, such as equipment, foreign travel, alterations and renovations, and contractual or third party costs. For future years, justify any significant increases in any category. If a recurring annual increase in personnel costs is anticipated, give percentage.

Susanne Moebus (CUE, University of Duisburg-Essen) will be the co-PI of the project and will coordinate all the work involving the HNR cohort. The two PIs will have regular teleconferences to monitor the progress of the project. The HNR team will obtain, organize and analyze their data in close cooperation and communication with the REGICOR team. The HNR team will hire a biostatistician with broad knowledge on environmental epidemiology, air pollution modeling and spatial statistics. Further, an experienced data manager from the institute will be involved in the project for data management. Susanne Moebus, Ester Orban and the biostatistician will provide their expertise in environmental epidemiology exposure assessment and biometry throughout the project. The biostatistician will be responsible for the acquisition of built environment and greenness variables for HNR. Further, the biostatistician will obtain and prepare data from satellites and GIS databases, including walkability, noise and other relevant built environment data. Ester Orban and the biostatistician will conduct the data cleaning and harmonization and the statistical analyses, and will write the scientific papers. The last 6 months of the project will be mainly devoted to the writing of the final scientific report. A first draft of the report will be written by a writing team composed by Xavier Basagaña, Susanne Moebus and one post-doctoral researcher from each center, and all the team will provide feedback on this initial draft to come up with the final report.

Roberto Elosua and Jaume Marrugat (IMIM) will lead the fieldwork of the REGICOR cohort and the standardization of the cardiovascular and cognitive phenotypes. Two technicians will be hired by IMIM to accelerate the field work in the REGICOR cohort and finish the last follow-up visit during the first year of the project. A data manager hired by IMIM will work on cleaning, harmonizing and preparing the datasets for the study.

Carlos Pérez García-Pando and Maria Teresa Pay (BSC) will implement the CTM models with source apportionment extensions for REGICOR, with the technical support of a high performance computing engineer, Mario Acosta (BSC), and will provide their expertise in air pollution modeling throughout the project. Marc Guevara (BSC) will set an update high resolution emission estimate for the socio-economical activities, essential for the source apportionment estimates using the CTM. We are requiring funds to buy 20 disks to be set in a BeeGFS filesystem with the following characteristics: WD Red Pro NAS Hard Drive, model WD40EFRX, 4 TB capacity, SATA 6Gb s interface, 5400 rpm, and 64 MB cache. Those will be used to store, share and backup the data generated with the CALIOPE system for REGICOR, which will have a size of around 40Tb.

A kick-off meeting (Barcelona), a mid-term meeting (Essen) and a final meeting (Barcelona) will be organized, complemented by at least two teleconferences/meetings with the entire team per year, to discuss the progress and the results of the project. Travel to those meetings has been budgeted.

F-6 PROJECT PLAN

The Project Plan should contain the sections listed below. Sections A, B, and C together should not exceed 4 pages. Sections D and E combined should not exceed 15 pages. Please refer to the instructions for details.

A. Specific Objectives

THeCUE (Unraveling the Effects of **T**raffic on Cardiometabolic and Mental **He**alth from the **C**omplex Network of **U**rban **E**xposures) project will use data from two well-established population-based cohorts of adults in Germany (Heinz Nixdorf Recall, HNR) and Spain (REGICOR), with detailed longitudinal data on cardiovascular health, diabetes and mental health outcomes, to conduct holistic analyses that allow unraveling the role of traffic-related air pollution on these outcomes by properly controlling for a large array of interrelated factors. Both cohorts have estimates of exposure to air pollution from different sources, which will be refined during the project by combining estimates from land use regression (LUR) models and chemical transport models (CTM). In addition, information will be available on traffic-related and railway noise, green spaces, built environment, socioeconomic factors, diet and physical activity.

We hypothesize that (1) traffic-related air pollution has an adverse effect on blood pressure, atherosclerosis, diabetes and mental health after accounting for correlated exposures and modifying factors; (2) exposure to noise, urban greenness, built environment characteristics, diet, physical activity and socioeconomic status can modify the association between pollutants and health outcomes.

To test these hypotheses, we will use causal inference methods that can control for the confounding role of a large array of correlated factors. The specific aims of the study are:

1) Obtaining more accurate estimates of traffic-related air pollution by integrating information from LUR and traffic-specific CTM models.

2) Estimating the relationship between traffic-related air pollution and
    2.1) blood pressure,
    2.2) atherosclerosis,
    2.3) diabetes,
    2.4) mental health,
   while controlling for correlated factors in a longitudinal and prospective analyses.
3) Evaluating the modification of the relationships in objective 2) by traffic noise, urban greenness, built environment, diet, physical activity and socioeconomic status.

B. Anticipated Results and Significance

Cardiovascular diseases (CVD) are important and increasing health conditions for which traffic-related air-pollution is suggested to be a contributor (Brook et al. 2010; Münzel et al 2016). For example, traffic-related air pollution has been associated with atherosclerosis (Kaufman et al. 2016) and high blood pressure (Foraster et al. 2014a,b, Fuks et al. 2011). There is emerging evidence that traffic-related air pollution can also contribute to diabetes (Eze et al. 2015) and mental health (e.g. cognitive impairment) (Tzivian et al. 2015, Tzivian et al. 2016). Given the growing prevalence of CVD, diabetes and mental health problems in the ageing population, if traffic-related air pollution has a causal contribution to these diseases then improvements in environmental health policies and land use planning can have marked effects in preventing these health problems. Such strategies could have broad social and economic impacts and it is crucial to improve the evidence to justify remediating actions.

One of the key challenges in research projects is that, in real world, traffic-related air pollution is correlated with traffic-related noise, and both of these exposures are correlated with other environmental, social and individual factors such as green space, built environment characteristics, individual and

community-level socioeconomic status (SES), air pollution exposure from other sources (e.g. industry), dietary patterns or physical activity. Traffic-related noise is particularly relevant, as it shares the source with traffic-related air pollution and has also been associated with high blood pressure (Foraster et al. 2014a,b, Fuks et al. 2011), mental health (Tzivian et al. 2015, Orban et al. 2016) and diabetes (Dzhambov 2015). However, all of the abovementioned factors have the potential to confound or modify the estimated health effects of traffic-related air pollution.

THeCUE will use data from two well-established population-based cohorts in Germany (Heinz Nixdorf Recall, HNR) and Spain (REGICOR), with well-characterized and detailed data on cardiovascular health, diabetes and mental health outcomes, to conduct holistic analyses that allow unraveling the role of traffic-related air pollution on these outcomes by properly controlling for a large array of interrelated factors. The two cohorts have previously focused on some of the associations of interest but mostly without simultaneously considering multiple exposures and potential effect modifiers. Moreover, most of the previous analyses have used a cross-sectional approach and data from longitudinal prospective studies are scarce. Here, we will refine our air pollution predictions, use improved noise exposure assessment, derive new exposures (e.g. on greenness and built environment), analyze incident health outcomes and use more appropriate statistical methods, including novel tools for causal inference. In addition, having two similar cohorts for two countries will provide opportunities to analyze whether patterns of health effects are comparable in different regions.

The project will touch on all the objectives of the RFA 17-1 call. **Objective 1** calls for having source-specific estimates of air pollution, including tailpipe and non-tailpipe, and for having improved exposure assessment. We will cover that by having estimates for several pollutants from land use regression models (LUR), including NO_2, $PM_{2.5}$ ultrafine particles (UFP), Ni, Cu, Zn, V, S, Si, Fe and K. These can represent tailpipe and non-tailpipe traffic emission, long-range transport, oil burning/industry, crustal material and biomass burning. By implementing source apportionment within chemical transport models (CTM), we will also obtain concentrations by main activity sources (e.g. traffic, industry and residential combustion), further discriminating by fuel type (diesel and gasoline) and traffic emission process (exhaust and non-exhaust) emissions (Kwok et al. 2015; Valverde et al. 2016). In addition, exposure assessment of traffic-related air pollution will be improved by integrating LUR models and traffic-specific concentrations from CTM via the Bayesian Maximum Entropy method. **Objective 2** calls for disentangling the effects of traffic-related air pollution and noise. Both of our cohorts have developed novel predictions of indoor traffic-related noise based on the individual home-outdoor predictions by taking into account room orientation and insulation (Foraster et al. 2014a). Controlling for these factors, which reduce noise levels but are not expected to reduce air pollution to the same extent, drastically decreases the correlation between pollution and noise and allows for mutual adjustment in regression models. **Objective 3** calls for the development and use of individual and community level SES indicators. Our cohorts have individual data on education, occupation and household income, and area SES indicators at the census tract level. **Objectives 4 and 5** call for an accurate control for confounding or modifying factors associated with traffic pollutants as well as for disentangling the effects of different traffic-related air pollutants. We will have new and detailed information on urban greenness (including general greenness as well as tree cover) and built environment (including walkability, accessibility to public transport and facility density), and our cohorts already have detailed data on diet, BMI, physical activity and medication use, among others. We will also be able to separate tailpipe and non-tailpipe exposure. Proper control for all these factors in the statistical analyses will be obtained by using causal inference models, in particular propensity score matching and targeted learning.

THeCUE expects to provide robust and improved evidence for the relationship between traffic-related air pollution and CVD, diabetes and mental health based on a holistic approach taking into account a large number of potential confounders and effect modifiers in two population-based cohorts in different settings and using novel statistical approaches to address causality. Including the traffic-related air pollution from a high resolution CTM will improve the estimates to answer other research questions. It will also provide

evidence for the potentials of green spaces, built environment, diet, and physical activity as measures to mitigate such effects. The project will also have the potential to estimate the independent effects of traffic-related noise on some of the health outcomes.

C. Related Previous Studies

The team includes principal investigators from the two cohorts (XB, RE, JM for REGICOR and SM for HNR). XB has led the part on estimation of air pollution and noise exposure in REGICOR, which included, for example, big campaigns to measure NO_2 in 562 sites and ultrafine particles (UFP) in 644 sites. This led to several publications, including cross-sectional studies linking air pollution exposure with atherosclerosis (Rivera et al. 2013; Perez et al. 2015) and blood pressure (Foraster et al. 2014a,b; Fuks et al. 2014), and participation on the ESCAPE consortium to estimate the effects of air pollution and noise on incidence of hypertension (Fuks et al. 2017). In addition, it led to several publications on exposure assessment, such as the development of a land use regression model for UFP (Rivera et al. 2012); monitoring of heavy metal concentrations using moss bags (Rivera et al. 2011); study of the determinants of traffic-related air pollution and traffic-related noise (Foraster et al. 2011); comparison of land use regression models with chemical transport models (Aguilera et al. 2013); evaluation of the performance of land use regression models (de Nazelle et al. 2013); statistical aspects on the use of land use regression models, including consequences of measurement error on estimation of health effects (Basagaña et al. 2012; Basagaña et al. 2013; Wang et al. 2013); evaluations of the short-term associations between traffic-related noise, particle number and traffic flow (Morelli et al. 2015); and the development of a land use regression model for traffic-related noise (Aguilera et al. 2015).
SM is PI of several large cohorts (including HNR) and her research focuses on cardiometabolic, cardiovascular and mental health and urban and environmental epidemiological topics. Exposure assessment in the HNR through different air pollution models has recently been described and compared in a publication (Hennig et al. 2016). In the HNR, previous analyses found amongst other results that exposure to PM was linked to increased levels of inflammatory markers like C-reactive protein (Hennig et al. 2014, Viehmann et al. 2015) and to atherosclerosis (Kälsch et al. 2014). An association of PM with incident type 2 diabetes was also observed (Weinmayr et al. 2015). Further, analyses of HNR data showed that long-term exposure to PM increases blood pressure chronically which is a hypothesized biologic link between air pollution and atherosclerosis (Fuks et al. 2011). Long-term $PM_{2.5}$ exposure was also clearly associated with baseline carotid intima media thickness (CIMT) in a cross-sectional analysis of the HNR (Bauer et al. 2010).
The team covers all areas of expertise needed to run the project. XB is a biostatistician with expertise on the health effects of air pollution and noise as well as on statistical topics such as multipollutant modeling and measurement error. PD is a leading expert on the health effects of green space and its interaction with air pollution. RE is an expert in cardiovascular epidemiology with a broad experience in risk functions, physical activity and the study of the genetic and epigenetic architecture of coronary heart disease. MF has broad experience in noise exposure assessment and in studying and disentangling the health effects of noise and air pollution in different European populations. JM is an expert in CV epidemiology, with broad experience in risk functions, hypertension and other CV risk factors. MJN is world-leading expert in exposure assessment and epidemiology of air pollution, noise and green space. EO has profound knowledge in urban and environmental epidemiology and studies health effects of road traffic noise, air pollution and surrounding greenness. The source apportionment modeling team includes CP, an expert on aerosol and chemistry model development who has also investigated the role of aerosol and climate on infectious disease; and MTP, who has extensive experience on air quality modeling using CMAQ and recently focused her research on source apportionment techniques. They will have the support of MG, an expert researcher on emission inventories and modeling over urban areas; and FM an experienced research support engineer in High Performance Computing.

D. Experimental Plan and Methods

Study Population

THeCUE is a project that includes two population-based cohorts, REGICOR and HNR. The *Registre Gironí del Cor* (REGICOR) study includes 7,837 participants from 12 towns that represent the geographic diversity of the Girona province in the northeast of Spain and have large contrasts in ambient air pollution (Figure 1). The study population is composed of three cohorts originally enrolled in 1994-1996, 1999-2001, and 2003-2006 (T0), with the first follow-up visit in 2007–2011 (T1, N=5,648) and the second on 2017-18 (T2, expected N~4,000). Each of the follow-up visits had a participation of around 70%. Participants were 25–79 years old at baseline.

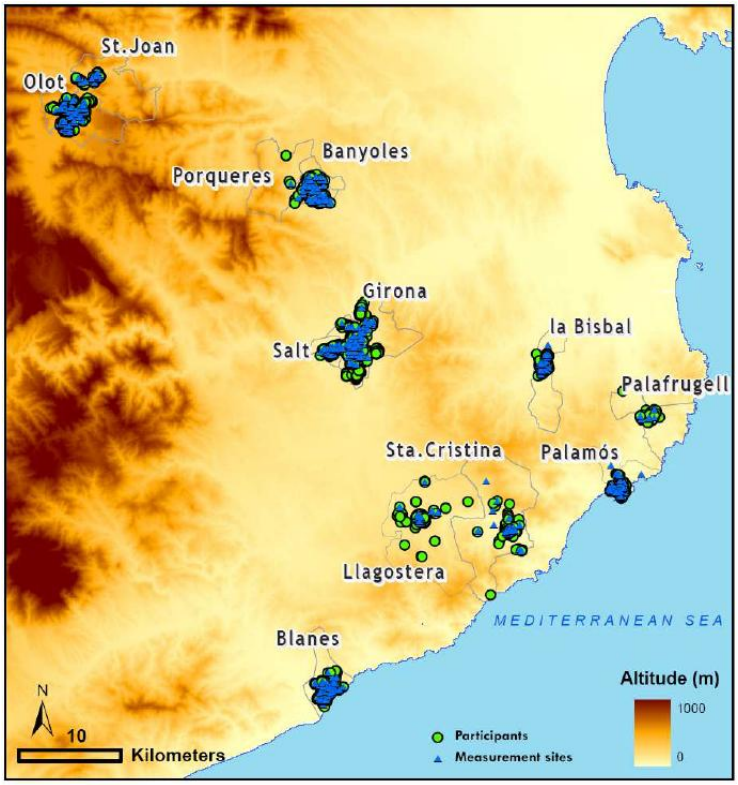

Figure 1. The REGICOR study area

The *Heinz Nixdorf Recall* (HNR) cohort includes participants from three large adjacent cities of the densely populated Ruhr Area in Germany (Figure 2). The study recruited 4,814 participants between 45 and 75 years old between 2000 and 2003 (T0), which had a first follow-up visit between 2005 and 2008 (T1, N=4,157) and a second follow-up in 2011-2015 (T2, N=3,089). Figure 3 illustrates the timeline of both cohorts.

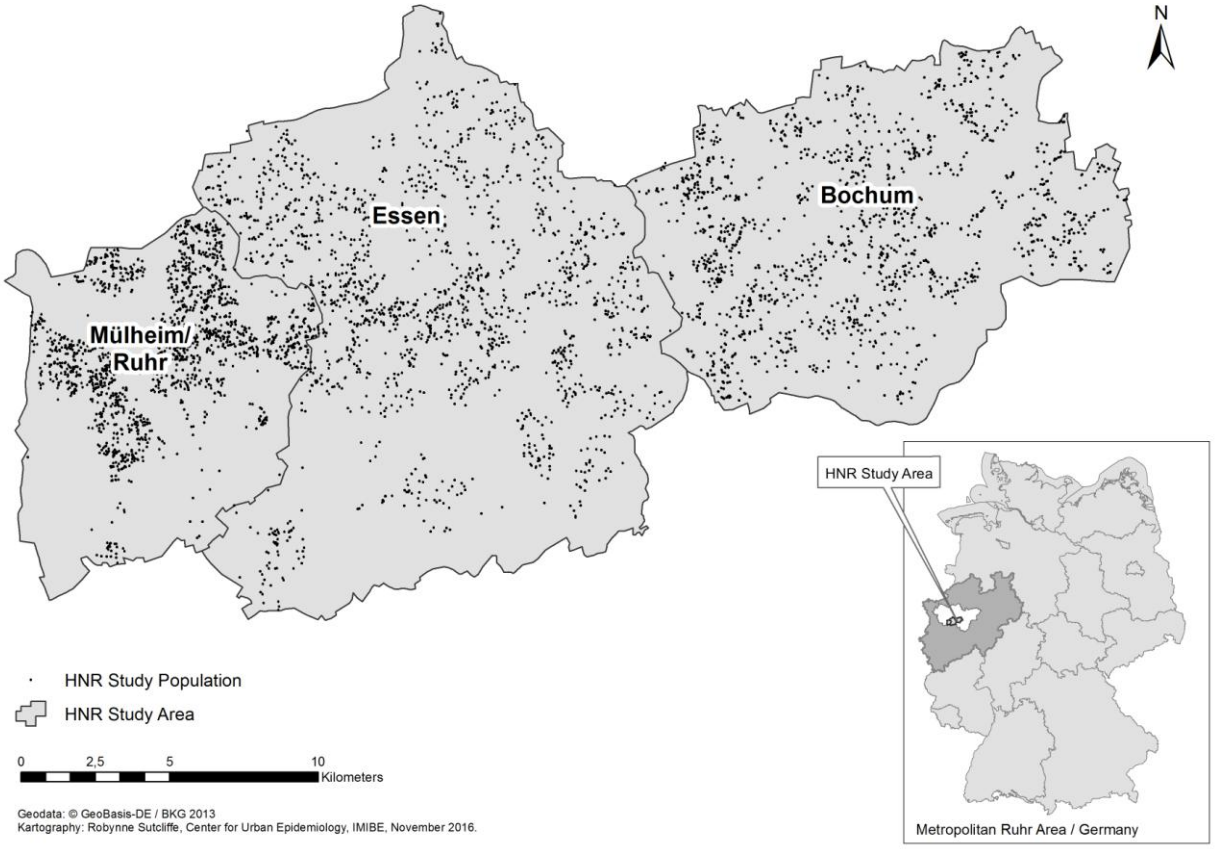

Figure 2. The Heinz Nixdorf Recall study area

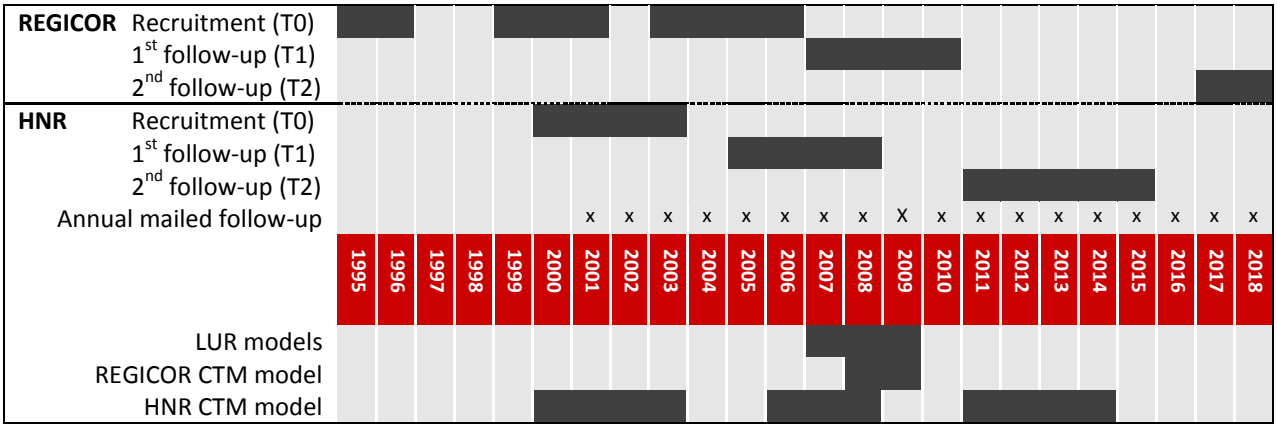

Figure 3. Timing of the cohort visits and air pollution models

Health Outcomes

The study has a focus on four health outcomes, namely blood pressure, atherosclerosis, diabetes and mental health. Several variables are available for each of those outcomes, offering the possibility to conduct several analyses. For each of the outcomes, THeCUE will define the variable/s to be used in our primary analyses, based on the following criteria: 1) the best definition available according to scientific

literature; 2) we will favor variables for which the cohorts have repeated measures, in order to conduct longitudinal analyses; 3) we will favor variables that provide new results over those already published; and 4) we will favor variables that are available in the two cohorts to be able to reproduce the same analysis in two different regions. According to these criteria, the THeCUE project will use the primary and secondary health outcomes and analyses described below. Table 1 provides an overview of the availability of data on health outcomes and covariates in the two cohorts.

Table 1. Availability of outcome and covariate information at the different visits.

	HNR			REGICOR		
	T0	T1	T2	T0	T1	T2
Health outcomes (in bold, main outcomes)						
Blood pressure measurements and medication	x	x	x	x	x	x
Coronary calcification	x	x				
Peripheral artery disease	x	x	x	x	x	x
Diabetes (self-reported + drug intake +blood glucose)	x	x	x	x	x	x
HBA1c	x	x	x			
Cognitive function (Verbal fluency test)		x	x		x	x
Cognitive test battery 1 (VFT, WLT, LT, CT)		x	x			
Cognitive test battery 2 (VFT, TMT, Stroop, DST, SDT, FTT)					x	x
Depression	x	x	x	x	x	x
Socioeconomic status						
Years of education	x	x	x	x	x	x
Highest educational degree	x	x	x	x	x	x
Employment status	x	x	x	x	x	x
Job category	x	x	x	x	x	x
Household income	x	x	x			
Qualifications when leaving school	x	x	x			
Contextual and neighborhood factors						
Area-level unemployment	x	x	x	x	x	
Area-level low education	x	x	x	x	x	
Neighborhood satisfaction	x	x	x			
Neighborhood social capital	x	x	x			
Neighborhood perceived safety	x	x	x			
Dietary patterns	x	x	x	x	x	x
Physical activity levels	x	x	x	x	x	x
Lifestyle						
Smoking	x	x	x	x	x	x
Alcohol	x	x	x	x	x	x
Co-morbidities	x	x	x	x	x	x
Medication intake	x	x	x	x	x	x

VFT: verbal fluency test; WLT: wordlist learning test; LT: labyrinth test; CT: clock test; TMT: trail making test; DST: digit span test; SDT: symbol digit test; FTT: finger tapping test.

Blood pressure:

For the blood pressure analyses, two main analyses will be conducted: i) Analysis on **changes in repeated measurements of systolic and diastolic blood pressure (BP) over the course of the study**; and ii) Analysis of the **incidence of hypertension**. Both analyses will be conducted using data from the three visits in each cohort, and the analyses of the two cohorts will be included in the same publication. BP was measured in a sitting position using an automated oscillometric device and a standardized protocol, according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7). Two measurements were taken, and a third one was only taken if the first and second measurement differed by more than 5 mmHg. In the analyses,

we will use the last measurement for each participant as it is the most stable measure. Hypertension was assessed according to the definition of the JNC7 as measured systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg, or current intake of blood pressure lowering medication (Chobanian et al. 2003). Intake of blood pressure lowering medication was assessed by registering all current medication. Incident hypertension will be defined as having hypertension at any of the follow-up visits among those participants free of hypertension at baseline.

Atherosclerosis:

Most of the analyses on atherosclerosis will be conducted separately by cohort, as the tools and measures available by cohort differ. Our primary analysis on atherosclerosis will be conducted in the HNR cohort, with data on **changes in coronary calcification (progression)** measured with a cardiac computed tomography (CT) at two time points. In particular, Electron beam-CT (EBCT) scans were performed utilizing a C-100 or C-150 scanner (GE Imatron, South San Francisco, CA, USA) without the use of contrast media. Imaging was prospectively triggered at 80% of the RR interval and contiguous 3 mm thick slices from the right pulmonary artery to the apex of the heart were obtained at an image acquisition time of 100 ms. A CT threshold of 4 pixels and 130 Hounsfield units (Hu) was used for the identification of a calcified lesion using the Agatston method. Thoracic aortic calcification was assessed by summation of all calcified lesions.

Secondary analyses will be done for **peripheral artery disease (PAD)**, characterized based on the ankle brachial index (ABI). Incidence will be defined as having PAD in one of the two follow-up visits among those without PAD at baseline. The PAD analysis of the two cohorts will included in the same publication. ABI was measured according to a standard protocol by investigators trained and certified in sphygmomanometry and Doppler technique. Systolic blood pressure was measured in a supine position after a 5-min rest in the brachial artery of both arms and the posterior tibial and dorsalis pedis arteries of both legs, using a continuous Doppler device. Right and left ABI were calculated as the ratio of the highest leg pressure to the highest brachial pressure in the corresponding arm, and the lowest of the two ABI ratios were categorized as low (< 0.9), normal (0.9–1.3), or high (> 1.3) for analysis (Ankle Brachial Index Collaboration 2008; McDermott et al. 2005). Those in low ABI were considered cases of peripheral artery disease, while those with high ABI were considered cases of Moenckeberg's medial calcinosis.

Type II Diabetes mellitus:

The main analysis of type II diabetes will be conducted by assessing **incidence of diabetes**. Diabetes will be defined as fulfilling at least one of the following criteria: self-reported physician diagnosis, intake of anti-diabetic drugs or random blood glucose ≥ 200 mg/dL or fasting blood glucose ≥ 126 mg/dL. Incidence will be defined as having diabetes in one of the two follow-up visits among those without diabetes at baseline. The analyses of the two cohorts will be included in the same publication. All glucose measurements were taken after at least 10 hours of fasting in REGICOR, while in HNR 70% of participants had fasting glucose.

Potential secondary analyses include analyses for known (based on self-reported physician diagnosis or intake of an antidiabetic drugs) and unknown diabetes (no self-report or medication use, but glucose values above the threshold). In the HNR cohort, additional analyses will be conducted using information on glycated haemoglobin (HbA1c), a marker of blood sugar levels over the past 2-3 months that is often used to measure treatment efficacy in diabetes patients and predicts risk of developing diabetes-related complications.

Mental health:

The main analysis on mental health will be on **changes in cognitive function**, and the results for the two cohorts will be included in the same publication. The main analysis will be done with the Verbal Fluency Test, which is available in the two cohorts for two time points, and is among the most widely used tests to study aging (Faria et al. 2015). In addition, each cohort has characterized executive functions using a

different battery of tests in two repeated occasions. A composite index will be created for each cohort by computing z-scores for each test using the mean and standard deviation at baseline, and the resulting z-scores will be averaged in each follow-up visit. This is a common practice in studies with cognitive measures to create a composite score (Gatto et al. 2014; Zhao et al. 2015). The score for HNR will be composed of the Verbal Fluency Test, the Wordlist Learning Test, the Labyrinth Test and the Clock Test. The score for REGICOR will be composed of the Verbal Fluency Test, the Trail Making Test, the Stroop Test, the Digit Span Test, the Symbol Digit Test and the Finger Tapping Test. Study participants completed these tests during the neuropsychological examination part of the interview in each visit.

In addition, we will also perform analyses on **depression**, measured using the Patient Health Questionnaire (PHQ-9), an instrument used in clinical practice with good diagnostic validity and sensitive to changes over time, combined with antidepressant medication intake obtained from the medication list reported by participants. Further, self-reported and confirmed physician diagnosis of depression will be analyzed.

Table 2 summarizes the existing studies already conducted in REGICOR and HNR and the new studies planned within the THeCUE project. Further novelties of the THeCUE analyses will be the development of new exposure models, having a more comprehensive list of correlated factors to adjust for, and using more advanced methods to account for the effect of correlated factors. These aspects are detailed below.

Table 2. Summary of published work and new planned analyses within THeCUE.

Health outcome	Published work	New work done within THeCUE
Blood pressure and hypertension	• Cross-sectional analyses[1] • Incidence analysis with 2 time points in a pooled analysis of ESCAPE centers[2]	• Incidence analysis using 3 time points, both cohorts
Atherosclerosis	• Cross-sectional analysis of coronary calcification in HNR[6] • Cross-sectional analysis on IMT[7] • Cross-sectional analysis on peripheral artery disease in REGICOR[7]	• Longitudinal change in coronary calcification in HNR. • Incidence analysis of PAD using 3 time points, both cohorts.
Diabetes	• Incidence using 2 time points, only in HNR[3] • No previous analyses in REGICOR.	• Incidence analysis using 3 time points, both cohorts • Analyses using HbA1c (HNR)
Mental health	• Cross-sectional analysis on mild cognitive impairment in HNR[4] • Analysis of effects of road traffic noise on depression[5] • No previous analyses in REGICOR.	• Longitudinal changes in cognitive tests, both cohorts. • Incidence of depression and traffic-related air pollution using 3 time points, both cohorts.

[1] Fuks et al. 2011; Foraster et al. 2014a,b; Fuks et al. 2014.
[2] Fuks et al. 2017.
[3] Weinmayr et al. 2015.
[4] Tzivian et al. 2016.
[5] Orban et al. 2016.
[6] Kälsch et al. 2014.
[7] Rivera et al. 2013; Perez et al. 2015

Air pollution

THeCUE will have two sources of information on air pollution exposure, estimates from land use regression models and estimations from chemical transport models. These two sources will be combined to obtain improved estimates.

Land Use Regression (LUR) models

Both cohorts have air pollution estimates of NO_2, NO_x, PM_{10}, $PM_{2.5}$ and $PM_{2.5}$ absorbance at residential addresses from LUR models derived in the context of the ESCAPE project (Beelen and Hoek 2010). Measurements were taken during the period 2007-2009. Data on elemental composition, namely concentrations of Ni, Cu, Zn, V, S, Si and Fe, are also available from LUR models developed in the TRANSPHORM project (de Hoogh et al 2013). Additionally, REGICOR developed its own LUR models, based on intensive measurement campaigns, for NO_2 (562 measurement sites) and UFP (644 measurement sites).

Chemical transport models (CTM)

CTMs will provide daily concentrations of PM_{10}, $PM_{2.5}$, NO_2, O_3 and a set of volatile organic compounds (VOC) on 1-km spatial resolution. In addition, they will provide source-specific (traffic, industry) contributions, and in the REGICOR study they will additionally provide fuel-type-specific (diesel, gasoline) and process-specific (exhaust and non-exhaust traffic emission) contributions using an advanced source apportionment algorithm.

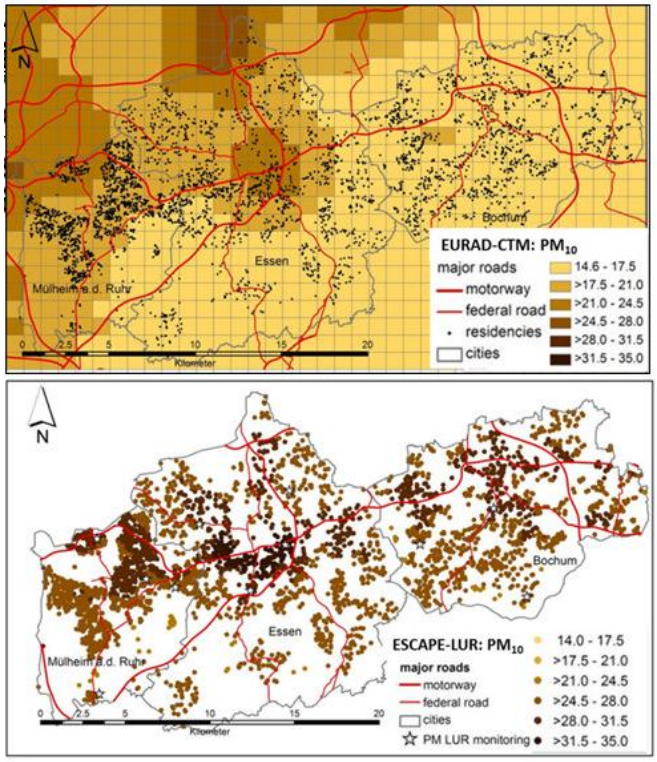

Figure 4. EURAD-CTM (A) and LUR (B) estimates of PM10 for HNR

For HNR, estimates will be based on the European Air Pollution Dispersion (EURAD) model developed by the Rhenish Institute for Environmental Research (Ebel, 2015). REGICOR will use the Community Multiscale Air Quality (CMAQ) model developed by the U.S. Environmental Protection Agency (Byun and Schere, 2006). Both CTMs have been thoroughly validated for the simulation of transport, chemical transformation, and deposition of tropospheric pollutants in the respective regions. In addition to the long-range transport, both CTMs include the formation of atmospheric gases and PM, i.e., secondary inorganic and organic aerosols from primary emitted gaseous pollutants as NO_2, sulfur dioxide (SO_2), ammonia (NH_3), and VOC. Both CMAQ and EURAD are consolidated operational air quality forecast systems in Spain (named CALIOPE system; Pay et al., 2014) and Germany (named EURAD system; Ebel et al., 2015), respectively. Table 3 summaries the main characteristics of CALIOPE and EURAD for THeCUE.

The EURAD system has three major parts: (1) the MM5 meteorological model; (2) the EURAD Emission Model, and (3) the EURAD CTM which includes the aerosol dynamics model (MADE). An additional procedure includes data assimilation on an hourly basis, using routine measurement data of monitoring sites in North Rhine-Westphalia (NRW) provided by the local environmental agency. EURAD system estimates source-specific air pollution concentrations using the brute force methodology which consist on suppressing local sources one by one. The EURAD system estimates from HNR are

already available for years 2000-2003, 2006-2008 and 2011-2014. Figure 4 displays the estimates from the LUR and EURAD-CTM estimates for the HNR study area.

Table 3. Air quality modelling system based on CTM at the two cohorts.

	EURAD system (Ebel, 2015)	CALIOPE system (Pay et al., 2014)
Cohorts	NHR	REGICOR
Chemical transport model	EURAD-CTM	CMAQv5.0.2
Meteorological model	MM5v3	WRF-ARWv3.5.1
Emission model	EURAD Emission model	HERMESv2
Anthropogenic emission	Europe (EMEP inventory) Germany (LANUV-NRW)	Europe (EMEP inventory) Spain (bottom-up)
Biogenic emission	MEGAN	MEGAN
Experience in health studies	Henning et al. (2016) Henning et al. (2014)	Akita et al. (2014) Aguilera et al. (2013)
Nesting domains (horizontal resolution)	Europe (125 km) Central Europe (25 km) North Rhine-Westphalia (5 km) Ruhr area [HNR] (1 km)	Europe (25 km) Catalonia (4 km) Girona [REGICOR] (1 km)
Tagged sources	(1) Local traffic (2) Local industry	(1) Traffic gasoline exhaust (2) Traffic diesel exhaust (3) Traffic non-exhaust (4) Industry (5) Residential combustion
Source apportionment method	brute force (zeroing out sources one by one) (Hebbinghaus et al., 2009)	integrated in the CTM (Kwok et al., 2013, 2015)
Pollutant	O_3, PM10, PM2.5 and NO2	O_3, PM10, PM2.5, PM chemical components and NO2
Period	2000-2003 and 2006-2008	2008-2009

The CALIOPE system for REGICOR will be newly developed for the project at 1-km resolution for years 2008-2009 (Aguilera et al. 2013). They will be based on the CALIOPE forecasting system, which is based on the (1) WRF meteorological model, (2) the HERMES emission model, (3) the CMAQ CTM, and the BSC-DREAM8b atmospheric mineral dust model (4). As a novelty, TheCUE project will use the Integrated Source Apportionment Method (Kwok et al., 2013, 2015) to estimate contributions of gasoline exhaust, traffic diesel exhaust, and traffic non-exhaust, industry and residential combustion. Figure 5 displays the NO_2 concentrations estimated for the REGICOR study area at 4-km horizontal resolution,

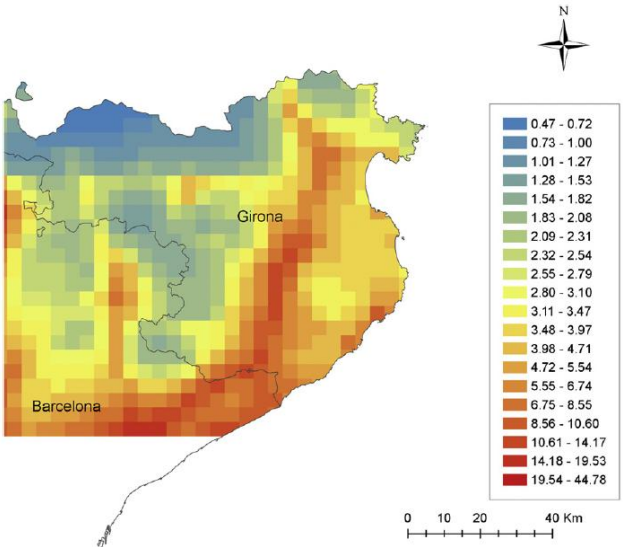

Figure 5. CALIOPE estimates of NO_2 for REGICOR. Within the project we will obtain a finer resolution.

which will be improved in the project to 1-km resolution.

The main inputs to CTMs are anthropogenic and biogenic sources. Emission inputs to both CTMs are structured with respect to different source categories according to the Selected Nomenclature for Sources of Air Pollution (SNAP), including traffic, industry, and other source categories. At the European scale, emissions are taken from the officially-available database for the European Monitoring and Evaluation Programme (EMEP). For high resolution estimates over cohorts, the EURAD system uses the emission from LANUV-NRW, and the CALIOPE system estimates emissions for Girona with a temporal and spatial resolution of 1 h and up to 1-km resolution mainly based on a bottom-up approach based on the HERMESv2 model (Guevara et al., 2013, 2014). Emissions from vegetation in the REGICOR domain, which are critical in the formation of ozone and secondary aerosol, will be estimated by the Model of Emissions of Gas and Aerosols from Nature (MEGANv2.0.4) (Guenther et al., 2006) using temperature and solar radiation from the WRF model as input.

Combined exposures

We will integrate monitoring data and outputs from LUR and CTM models using Bayesian Maximum Entropy (BME), focusing on traffic-specific concentrations. This methodology has been applied previously by our group to provide better estimations of NO_2 in the Catalonia region (Akita et al. 2014). In the validation stage, the estimates from this geostatistical tool to combine LUR and CTM provided more accurate estimates (i.e. lower root mean square error) than the LUR or CTM models alone (Figure 6). At that time, the estimates from the CTM model were at a 4-km resolution, and within THeCUE we will obtain estimates at 1-km resolution, which provides an improved spatial respresentativeness of air pollution levels (Pay et al. 2014). The BME method categorizes data into two groups: (i) hard data, corresponding to measurements; and (ii) soft data, having an uncertainty characterized by a probability density function (PDF) of any type (e.g., Gaussian). The BME method can be viewed as a two-stage knowledge processing procedure. At the prior stage, maximum entropy theory is used to process the general knowledge base describing global characteristics of the spatial random field representing the average pollutant concentration, such as its mean trend and the covariance function, which produces a prior PDF depicting the spatial process. Then at the posterior stage, an operational Bayesian conditionalization rule is used to update this prior PDF with respect to the site-specific hard and soft data available, which produces a BME posterior PDF describing the value of the spatial process at any estimation point of interest.

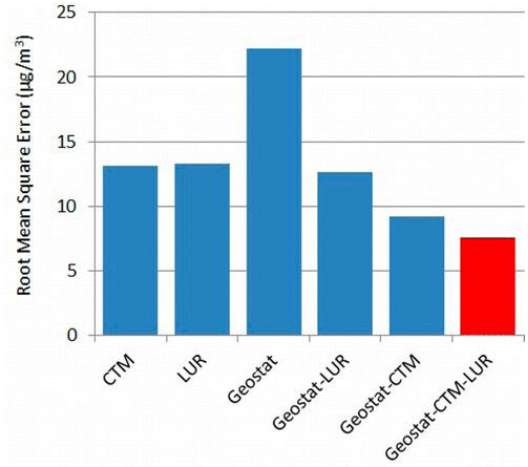

Figure 6. Improvement of BME model over CTM and LUR models alone.

In particular, we will use as secondary exposures for additional analyses the combinations of the following estimates that aim to estimate the same or similar measures:

- $PM_{2.5}$ from LUR (largely representing traffic, as shown in ESCAPE analyses) and traffic-source PM from CTM.
- $PM_{2.5}$ absorbance from LUR and traffic-source PM from CTM.
- $PM_{2.5}$ absorbance from LUR and vehicle exhaust PM from CTM.
- The sum of Cu, Fe and Zn from LUR and the non-exhaust $PM_{2.5}$ from CTM.
- K from LUR and residential combustion PM from CTM.
- The sum of Ni and V and industry PM from CTM.

Traffic Noise

Both cohorts have data on weighted day–evening–night (L_{den}) and night (L_{night}) sound pressure levels expressed in A-weighted decibels (dB) at the geocoded residential addresses according to the European Commission's Environmental Noise Directive (END) Directive 2002/49/EC of the European Parliament and Council of the European Union. In REGICOR, these estimates are available for the year 2005 from a validated and detailed model for the main city included in the analysis (Girona), which accounts for more than 70% of the participants. For the rest of towns, we will consider the estimation of traffic-related noise using the novel European CNOSSOS-EU road-traffic prediction model, and following the adaptation methods for epidemiological studies proposed by Morley et al. (2015). In such approach, model performance ranged between R^2 = 0.74 with low-resolution to R^2=0.94 with high-resolution models. At this stage, we have already confirmed the availability of all basic input data used by Morley et al. (2015) for all towns in REGICOR. In HNR, road traffic noise was assessed within the scope of the cities' Lärmkartierung and also according to END Directive 2002/49/EC of the European Parliament Council of the European Union (see figure 5 for a noise map of the HNR study area). Road traffic noise was modeled for the year 2006. In both cohorts, L_{den} and L_{night} were assigned to the geographic residences of the study participants using a geographic information system (ArcGIS) (Figure 7). Small-scale topography of the area, dimensions of buildings, noise barriers, street axis, vehicle type-specific traffic density, speed limit, and type of road surface were considered in the noise modeling processes for both cohorts.

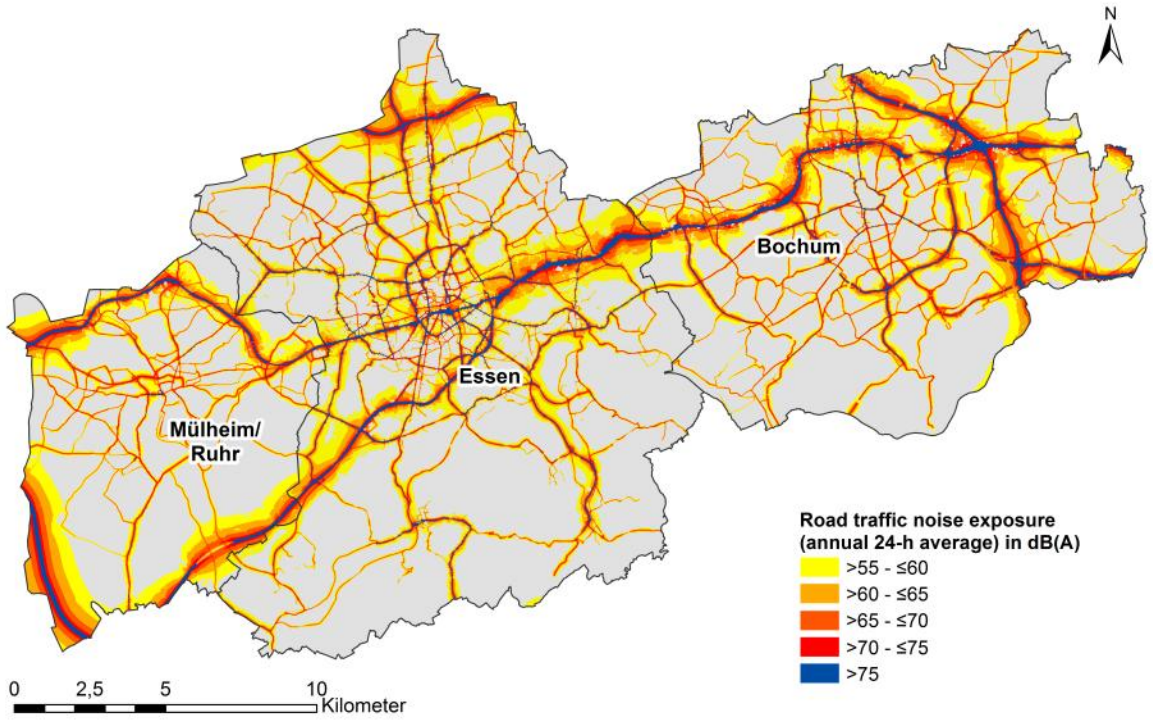

Figure 7. Road traffic noise exposure (L_{den}) in the HNR study area.

Importantly, both cohorts have derived measures of indoor traffic-related noise, which take into account noise attenuation by orientation of bedroom façade, type of windows and ventilation patterns following Foraster et al. (2014a). This is relevant because the sleeping period represents a particularly susceptible window for the effects of noise on health (WHO Regional Office for Europe 2009; Hume et al. 2012) . In

addition, our previous study showed that using the measures of indoor noise greatly alleviates the problems of collinearity between traffic-related air pollution and traffic-related noise and allows estimating the independent effects of both exposures (Foraster et al. 2014a). This approach takes advantage of the fact that several noise-reducing factors such as type of windows greatly attenuate noise levels but do not affect air pollution concentration to the same extent.

Additionally, REGICOR collected information on noise sensitivity (Weinstein 1978) and on traffic noise annoyance (Fields et al. 2001) during the night in the bedroom and due to different sources (road traffic, railway traffic, flight traffic, industrial noise, neighbors) in a face-to-face interview. In HNR, noise annoyance during day and night and due to different sources (road traffic, railway traffic, flight traffic, industrial noise, neighbors) was assessed in a self-administered questionnaire. Further, in a sub-sample noise sensitivity, hearing ability and perceived control over noise exposure was assessed.

Both cohorts also have estimates of residential railway noise (L_{den}, L_{night}) from an END-based model according to the International Organization for Standardization (ISO; Geneva, Switzerland) standard 9613. For the HNR, these data were obtained from the German Federal Railway Authority (EBA).

Green space

We will extract three different remote-sensing indices to characterize different aspects of greenness surrounding residential address of study participants. We will apply Normalized Difference Vegetation Index (NDVI) as an indicator of general greenness (i.e. photosynthetically active land cover); Vegetation Continuous Fields (VCF), as a measure of canopy cover; and Leaf Area Index (LAI), as an indicator of green leaf area per unit ground area. We will use images at 250 m × 250 m resolution obtained by the Moderate-resolution Imaging Spectroradiometer (MODIS) onboard the TERRA satellite. To maximize the contrast in exposure, we will look for MODIS images with least cloud cover obtained during the maximum vegetation period of the year for each cohort for the relevant years to each follow-up from the Data Pool website of the NASA EOSDIS Land Processes Distributed Active Archive Center. We will average each index across buffers of 300 m, 500 m, and 1000 m around residential address of each participant following the methods we have developed in our previous similar studies (e.g. Dadvand et al. 2015).

Built environment

We will derive new data on population density; building density; street connectivity (number of street intersections in a 300 meters buffer); accessibility (public transport network density); facilities (i.e. all points of interest for pedestrians as part of their daily life activities, like restaurants, shops, medical centers, schools, libraries, etc.) with facility richness index and facility density index; land use (Shannon's Evenness Index, which measures the degree of mixing of different types of land uses such as residential, commercial, entertainment, and office development); and a walkability index derived in the HELIX project, quantifying how 'walkable' around each home (300m buffer). This walkability index is based on the methods of Frank et al., 2006 and Walk Score (https://www.walkscore.com/about.shtml), and includes four components: land use Shannon's Evenness Index, facility richness, population density and connectivity index.

Individual socioeconomic status (SES)

Both cohorts have information on years of formal education, highest degree obtained, employment status and job category. Additionally, HNR has information on household income and on qualifications when leaving school.

Contextual and community factors

At area level, both cohorts have census tract level data on several SES indicators, including unemployment rate (both cohorts), percentage of low education (REGICOR), neighborhood satisfaction (HNR), neighborhood social capital (HNR) and perceived safety (HNR). In the HNR, participants also

rated satisfaction with their neighborhood and social relations, as well as trust in neighbors, helpfulness of neighbors and perceived neighborhood safety in a questionnaire handed out at the examination visits.

Diet

Both cohorts have obtained detailed information on diet through validated questionnaires and derived dietary patterns, e.g. on Mediterranean diet adherence, which is of relevance for the study as its high antioxidant potential has been suggested to modify the harmful effects of air pollution (Romieu et al. 2009).

Physical activity

Both cohorts have detailed questionnaire data on physical activity. In particular, we will use in our analyses weekly energy expenditure in leisure time, expressed in metabolic equivalents, based on the Minnesota questionnaire (Elosua et al. 1994).

Other variables

Both cohorts have a richness of detailed information on other factors, including smoking (status, intensity and history) and alcohol consumption, co-morbidities, anthropometry, psychosocial factors including stress, sleep and medication use, which can useful to consider in the different analyses.

Organization of work

The PI of the project, Xavier Basagaña (ISGlobal), will lead and coordinate the whole project. He will also coordinate the work involving the REGICOR cohort. Susanne Moebus (CUE, University of Duisburg-Essen) will be the co-PI of the project and will coordinate all the work involving the HNR cohort. The two PIs will have regular teleconferences to monitor the progress of the project. A kick-off meeting, a mid-term meeting and a final meeting will be organized, complemented by at least two teleconferences/meetings with the entire team per year, to discuss the progress and the results of the project. Roberto Elosua and Jaume Marrugat will lead the fieldwork of the REGICOR cohort and the standardization of the cardiovascular and cognitive phenotypes. Carlos Pérez García-Pando and Maria Teresa Pay will implement the CTM models with source apportionment extensions for REGICOR, with the technical support of a high performance computing engineer, and will provide their expertise in air pollution modeling throughout the project. Marc Guevara will set an update high resolution emission estimate for the socio-economical activities, essential for the source apportionment estimates using the CTM. Mark Nieuwenhuijsen and Payam Dadvand will lead the acquisition of built environment and greenness variables for REGICOR, will supervise the GIS technician hired by the project and will provide their expertise in exposure assessment and environmental epidemiology throughout the project. Maria Foraster will lead the noise assessment in REGICOR, and will provide her expertise in studies disentangling the effects of traffic-related air pollution and noise. The GIS technician hired by the project will obtain and manage data from satellites and GIS databases, including air pollution and noise models. Two post-doctoral researchers will be hired by the project. They will conduct the data cleaning and harmonization, will conduct the statistical analyses for the different health outcomes and will write the scientific papers. Xavier Basagaña will write the statistical protocol and will supervise all the statistical analyses. The HNR team will obtain, organize and analyze their data in close cooperation and communication with the REGICOR team. The HNR team will hire a biostatistician with broad knowledge on environmental epidemiology, air pollution modeling and spatial statistics. Further, an experienced data manager (not in the budget) will be involved in the project for data management. Susanne Moebus, Ester Orban and the biostatistician will provide their expertise in environmental epidemiology exposure assessment and biometry throughout the project. The biostatistician will be responsible for the acquisition of built environment and greenness variables for HNR. Further, the biostatistician will obtain and prepare data from satellites and GIS databases, including walkability, noise and other relevant built environment data. Ester Orban and the biostatistician will conduct the data cleaning and harmonization and the statistical analyses, and will write the scientific papers. The last 6 months of the project will be mainly

devoted to the writing of the scientific report. A first draft of the report will be written by a writing team composed by Xavier Basagaña, Susanne Moebus and one post-doctoral researcher from each center, and all the team will provide feedback on this initial draft to come up with the final report.

Difficulties and limitations

The project relies mostly on existing data, which minimizes the risks of not being able to conduct some parts of the study due to difficulties in data collection. In our case, a potential risk is that there are delays in data collection for the last visit in REGICOR, although this follow-up is already on-going and based on the current recruitment rate is expected to finish in the last quarter of 2018. We are requesting funds for an extra fieldwork team in order to accelerate the fieldwork. One of the limitations of the project, common to all cohort studies, is a potential bias because of lost to follow-up and missing data. To address that, we will use a combination of inverse probability weighting to address loss to follow-up and multiple imputation to account for missing data (Seaman et al. 2012). These techniques can provide corrected estimates when missingness depends on observed variables. Another of the limitations of the study is the measurement error in exposure. In order to properly account for the effect of measurement error we will implement a bootstrap strategy, as suggested by Szpiro et al. (2011).

E. Statistical Design and Analysis Plans

Statistical power

For the power calculations, we took the blood pressure analysis as a representative of the analyses for continuous outcomes, and hypertension as a representative for the analyses of incidence. For the analysis of longitudinal changes in hypertension, each single cohort has at least 88% power to detect a longitudinal change of 1 mm Hg in BP associated to an interquartile range increase in NO_2 (type I error: 5%; s.d. of change in BP: 16.7; s.d. of NO_2: 16). Those values were obtained from our available datasets.

For the incidence analysis of hypertension, we took the input data for the calculations from Fuks et al. (2017). We estimated that the REGICOR cohort has 99% power to detect an incidence rate ratio of 1.22 associated with an interquartile range increase in $PM_{2.5}$. For HNR, this was 26%. Therefore, for incidence analyses we will rely on analyses that pool both cohorts in order to have enough power. The input data to perform the calculations were: type I error: 5%; s.d. of $PM_{2.5}$: 1.6 for REGICOR and 1.1 for HNR; baseline prevalence: 36% for REGICOR and 56.9% for HNR; annual incidence: 3.6% for REGICOR and 7.1% for HNR.

Initial analyses

Initial descriptive analyses will be carried out to explore the distributions of all variables and their mutual correlations in each cohort. Figure 8 illustrates the analysis framework. Our initial analyses linking health outcomes and traffic-related air pollution will be based on generalized linear models and mixed effects models. In particular, for the incidence analyses (hypertension, diabetes, depression and peripheral artery disease) we will use Poisson regression, excluding those with the condition at baseline and using time of follow-up as an offset, to estimate incidence rate ratios. For the analyses on longitudinal changes on continuous variables (blood pressure, HbA1c, cognitive tests, coronary artery calcification) we will use linear mixed models including a random effect for participant. These models will include the interaction between exposure and age in order to estimate how the exposure affects the rate of change in the response. Linearity of the age trajectories will be examined, and polynomial terms of age will be included if needed. When data from the two centers need to be pooled, models will be adjusted for cohort as fixed effects, and potential interactions by cohort will be examined.

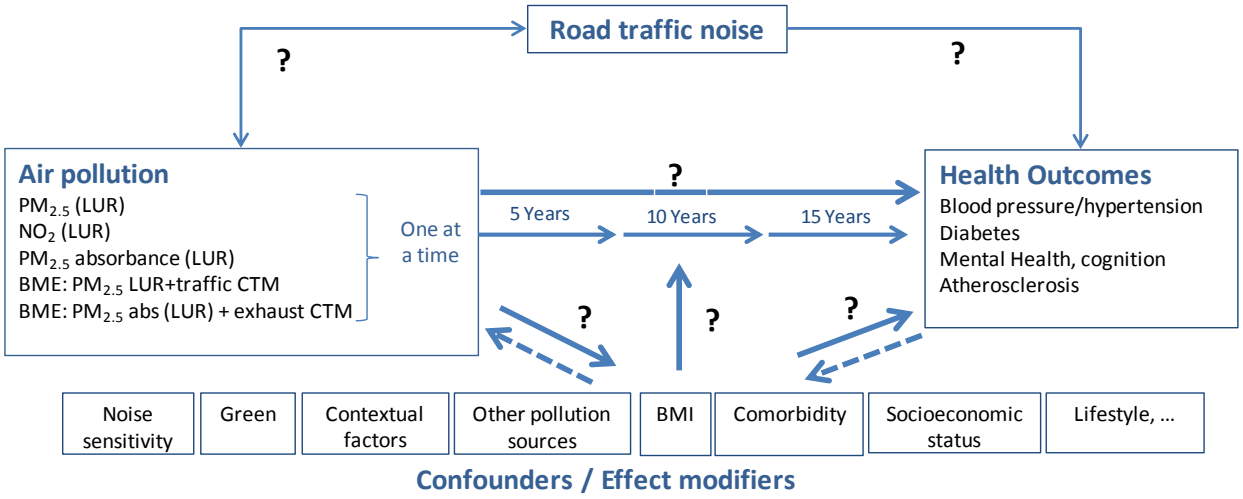

Figure 8. Statistical analysis framework.

The main exposures for our main analyses will be the following:

- $PM_{2.5}$ from LUR models
- NO_2 from LUR models
- $PM_{2.5}$ absorbance from LUR models
- BME combination of $PM_{2.5}$ from LUR models and the traffic source PM from CTM.
- BME combination of $PM_{2.5}$ absorbance from LUR models and the vehicle exhaust PM from CTM.

Each of these exposures will be included in the model one at a time, and the results from the different metrics will be compared.

Interrelated factors will be included in the analyses as covariates, with special attention to the effects of traffic-related noise. The pool of potential variables to be included is: traffic-related noise, railway noise, one greenness metric at a time, non-exhaust PM estimates from BME, industry PM from BME, residential combustion estimates from BME, one built environment metric at a time, individual education and job category, one community-level variable on SES at a time, diet, physical activity, smoking and alcohol. Collinearity problems will be examined by exploring variance inflation factors (VIF). If problems of extreme collinearity are encountered, precluding obtaining stable estimates, the list of interrelated factors will be reduced to alleviate those problems.

The variables considered to study effect modification will be included in the model as interaction terms. These include traffic-related noise, urban greenness, built environment, diet, physical activity and socioeconomic status. When the potential modifier has a continuous distribution, the interaction term will be built with the original continuous variable and results will be reported as the effect of the exposure at the 10^{th} and 90^{th} percentile of the modifier.

We will deal with missing data using multiple imputation. Imputations will be created using the method of chained equations following the standard recommendations to built imputation models (White et al. 2010). Ten imputed datasets will be created, and regression analyses on each imputed dataset will be combined using Rubin's rules. We will use inverse probability weighting to account for potential biases due to lost to follow up. To do that, we will build models for the probability of being lost to follow-up based on baseline characteristics, and we will use the inverse of those probabilities as weights in the analysis. Seaman et al. (2012) showed that combining inverse probability weighting and multiple imputation has good properties, and we will follow the modeling strategy outlined in that paper.

In order to account for the uncertainty in air pollution exposure prediction from models, we will apply the

bootstrap procedure proposed by Spziro et al. (2011). This method consists in repeatedly creating parametric bootstrap samples in which both the exposure and health models are refitted. The procedure allows obtaining correct confidence intervals that incorporate the uncertainty in exposure into the final estimates.

Additional analyses

As disentangling the effects of traffic-related air pollution exposure from interrelated factors is one of the main aims of the THeCUE project, in addition to the traditional models described above we will make an additional modeling effort using other techniques that may be better suited to disentangle those effects. In particular, we will use two different causal inference methods, propensity score matching and targeted learning, which can account for a large number of covariates while minimizing the unrealistic assumptions made by other models. The comparison of the results of these models with the tradional approaches described above will provide insights on potential biases of common analysis approaches.

Propensity score matching allows mimicking a randomized trial using observational data by balancing all covariates with respect to the exposure of interest (Stuart 2010). Particular attention will be given to which observations are pruned to avoid problems of bias and inefficiency, and other recommended matching methods such as coarsened exact matching will also be applied to reinforce the analysis conclusions. We will use generalizations of propensity score methods for continuous exposures (Elliot et al. 2015). Once pairs of individuals have been matched, we will conduct the following analyses:

1) For the analyses on incidence (hypertension, diabetes, depression, peripheral artery disease), a conditional Poisson regression model will be fitted on those participants free of the disease at baseline, and using time of follow-up as an offset. The indicator of matched pair will be used as strata variable.
2) For the analyses on change of a continuous outcome (blood pressure, HbA1c, cognitive tests, coronary calcification), we will conduct conditional linear regression using the change in the outcome as the response, computed as (last-first)/(elapsed_time). The indicator of matched pair will be used as strata variable.

In Targeted Learning, one properly specifies the causal parameter to be estimated, and puts no unjustified restrictions on the infinite-dimensional structure of confounding, which is estimated by a library of machine learning algorithms (SuperLearner) in combination with cross-validation (Van der Laan et al. 2014). The estimation process consists in first estimating a parametric model for the health outcome as a function of the exposure and covariates. Then, a model for the exposure-covariate relation (i. e. the propensity score) is built with the machine learning algorithms and is incorporated to improve the initial health effect estimator, to help remove some of the residual bias due to incomplete adjustment for confounding.

F. Milestones and Timeline

The project will have a duration of 42 months. The following milestone chart details the timeline of the project.

Milestone Chart

Year	Year 1				Year 2				Year 3				Year 4	
Quarter	1	2	3	4	1	2	3	4	1	2	3	4	1	2
Specific Aim 1: obtaining better estimates of traffic-related air pollution by integrating information from LUR and traffic-specific CTM models														
Task 1: Run CTM models (REGICOR)														
Task 2: Combine CTM and LUR using BME														
Task 3: Assign exposures to participants														
Specific Aim 2: estimating the relationship between traffic-related air pollution and health outcomes														
Task 4: Finish the 2nd follow up visit for REGICOR.														
Task 5: Data cleaning and harmonization														
Task 6: Create new variables (green space, noise, urban characteristics)														
Task 7: Write statistical protocol														
Task 8: Conduct statistical analyses														
Specific Aim 3: evaluate the modification of these relationships by the abovementioned potential effect modifiers														
Task 9: Conduct statistical analyses on effect modification														
Scientific papers, reports and dissemination														
Task 10: write scientific papers blood pressure – TRAP														
Task 11: write scientific papers diabetes – TRAP														
Task 12: write scientific papers mental health – TRAP														
Task 13: write scientific papers atherosclerosis – TRAP														
Task 14: write final report														
Task 15: Dissemination														

Data sharing

The estimated data from CALIOPE for TheCUE project will be around 80Tb and will be freely accessible following the World Climate Research Programme data policy on data sharing (https://www.wcrp-climate.org/WCRP-publications/2017/WCRP-data-policy.pdf). To assure this sharing, the BSC plans to buy 20 disks of 4 TB each to store the data and will give access to the data through a web server. Anonymised data from HNR will be made available for researchers according to German data protection regulations. Specific data access processes are already in place, including a formalized data access proposal and granting process. Scientific proposals to use REGICOR data should be sent to the REGICOR scientific committee for approval and they are subject to data protection regulations.

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F-7 OTHER SUPPORT

Describe current and pending grants or contracts from which each of the investigators proposed for this project are now drawing or anticipate drawing support. Identify project by title, agency, or organization supporting such work, the total level of financial support given for the project, the percentage of time (or calendar months) spent on each project, and the (projected) start and end dates. Briefly describe the contents of each. If any of these overlap, duplicate, or are being replaced or supplemented by the present application, justify and delineate the nature and extent of the scientific and budgetary overlaps or boundaries.

(1) Active Support

Xavier Basagaña

Effectiveness of plans to prevent the health effects of heat waves.
Aim: To study the short-term effects of temperature on mortality, hospital admissions and occupational injuries, and to assess the effectiveness of the preventive plans.
Funding Body: Carlos III Health Institute (Spanish Government).
Financial support: 38,115€
Role: PI
Time allocation: 15%
Period: 2015 – 2017
Overlap: None

The Human Early-Life Exposome - Novel tools for integrating early-life environmental exposures and child health across Europe (HELIX)
Aim: To measure multiple outdoor, personal and internal exposome in the INMA cohort, its association with children health and development and other 5 cohorts.
Funding body: European Commission, FP7.
Financial support: 11,292,724.89 €.
Role: Co-investigator
Time allocation: 10%
Period: 2013-2017
Overlap: None

Early-life stressors and LifeCycle health (LIFECYCLE)
Aim: Generating new integrated data on early life stressors related to socio-economic, migration, urban environment and life-style determinants, perform hypothesis-driven research on early life stressors influencing cardio-metabolic, respiratory and mental health trajectories during the full lifecycle, and the underlying epigenetic mechanisms.
Funding body: European Commission, Horizon 2020.
Financial support: 730,441 €.
Role: Co-investigator
Time allocation: 2%
Period: 2017-2021
Overlap: None

Susanne Moebus

PAnalytics - Technical and user-oriented methods to improve the quality of life.
Aim: To elaborate health-scientific connections between lifestyle and health outcomes to support the development of mobile applications.
Funding Body: Federal Ministry of Education and Research (BMBF).
Financial support: 2.374.100€
Role: Co-PI
Time allocation: 2,5%
Period: 2015 – 2019
Overlap: None

Air pollution effects on inflammation, cardiovascular risk factors and cardiovascular events – role of source-specific PM and PM components
Aim: The main objective of the ongoing project is to investigate the impact of overall PM and PM from different emission sources on inflammatory markers, cardiovascular risk factors and cardiovascular and metabolic disease in the Heinz Nixdorf Recall Study population.
Funding body: German Research Foundation (DFG)
Financial support: 137.950 €.
Role: Co-investigator
Time allocation: 10%
Period: 2015-2017
Overlap: None

Tipping points in urban meta-ecosystems: Disentangling the complex interactions of social structure, environmental and human health (URBANTIP)
Aim: To generate indicators of "urban environmental health"; to characterize individual mechanistic tipping points of major urban ecosystem types in response to typical stress combinations and rehabilitation measures and their effects on biodiversity and ecosystem services, to explore the effects of "urban environmental health" on composite ecosystem services, in particular on social effects and human health, and to identify critical threshold, i.e. resilience cutpoints, beyond which these services collapse.
Funding body: Federal Ministry of Education and Research (BMBF).
Financial support: 19.288 €.
Role: Co-PI
Time allocation: 5%
Period: 2017-2018
Overlap: None

German National Cohort Study
Aim: Nationwide cohort study, incl. 200,000 participants to investigate the causes of chronic diseases in order to improve prevention, early diagnoses and treatment of highly prevalent diseases..
Funding body: Federal Ministry of Education and Research (BMBF).
Financial support: 8.261.316€
Role: Co-PI for study centre Essen, member of the Use & Access Committee
Time allocation: 2,5%
Period: 2013-2019
Overlap: None

1000BRAINS. Study on brain ageing and related interindividual variability
Aim: To investigate the process of normal brain ageing in a group of 1000 participants of the Heinz Nixdorf Recall Study by assessing characteristic changes in structure and function of the brain due to

ageing and to distinguish them from disease-related influences.
Funding body: Helmholtz Association, Research Center Jülich, Germany
Financial support: 642.000€ (for IMIBE)
Role: PI
Time allocation: 10%
Period: 2011-2017
Overlap: None

Ester Orban

Air pollution effects on inflammation, cardiovascular risk factors and cardiovascular events – role of source-specific PM and PM components
Aim: The main objective of the ongoing project is to investigate the impact of overall PM and PM from different emission sources on inflammatory markers, cardiovascular risk factors and cardiovascular and metabolic disease in the Heinz Nixdorf Recall Study population.
Funding body: German Research Foundation (DFG)
Financial support: 137.950 €.
Role: Co-investigator
Time allocation: 25%
Period: 2015-2017
Overlap: None

Mark Nieuwenhuijsen

PASTA - Physical Activity Through Sustainable Transport Approaches
Aim: The PASTA project is an EU funded project on active transportation in 7 European cities.
Financial support: 685.839€
Period: 2013-2017
Time allocation: 10%
Overlap: none

EXPOsOMICS - Enhanced individualized exposure assessment and omic profiling for high priority environmental exposures in Europe
Aim: EXPOsOMICS is an EC funded study on the relationship between air pollution and water contaminants and OMICs data and is a ´´sister´´ project of HELIX but mainly conducted in adults.
Financial support: 1.185.108€
Period: 2012-2016 (extended by 6 months)
Time allocation: 5%
Overlap: none.

The Human Early-Life Exposome - Novel tools for integrating early-life environmental exposures and child health across Europe (HELIX)
Aim: To measure multiple outdoor, personal and internal exposome in the INMA cohort, its association with children health and development and other 5 cohorts.
Funding body: European Commission, FP7.
Financial support: 11,292,724.89 €.
Role: Co-investigator
Time allocation: 10%
Period: 2013-2017
Overlap: None

Early-life stressors and LifeCycle health (LIFECYCLE)
Aim: Generating new integrated data on early life stressors related to socio-economic, migration, urban environment and life-style determinants, perform hypothesis-driven research on early life stressors influencing cardio-metabolic, respiratory and mental health trajectories during the full lifecycle, and the underlying epigenetic mechanisms.
Funding body: European Commission, Horizon 2020.
Financial support: 730,441 €.
Role: Co-investigator
Time allocation: 5%
Period: 2017-2021
Overlap: None

BlueHealth Bluespace and health
Aim: The study evaluates the relationship between blue space and health in a large number of European countries.
Financial support: 974.437€
Period: 2016-2020
Time allocation: 10%
Overlap: none

Roberto Elosua

DNA Methylation in Myocardial Infarction: a risk biomarker and a mediator of the effects of lifestyles?
Aim: To identify differential methylation CpG sites associated with myocardial infarction.
Funding Body: Carlos III Health Institute (Spanish Government).
Financial support: 150,000€
Role: PI
Time allocation: 15%
Period: 2016 – 2018
Overlap: None

Role of micro RNAs expressed by human endothelial and vascular smooth muscle cells in myocardial infarction
Aim: To identify micro RNA associated with myocardial infarction risk.
Funding Body: BBVA Foundation (Private entity).
Financial support: 125,0005€
Role: Investigator
Time allocation: 5%
Period: 2016 – 2019
Overlap: None

Follow-up of the REGICOR population-based cohort: trends in the incidence of cardiovascular disease and in the prevalence of cardiovascular risk factors, identification of new mechanisms and predictive biomarkers of cardiovascular disease and evaluation of preventive strategies.
Aim: To perform the follow-up of the participants of the REGICOR cohort to address several objectives.
Funding Body: Catalan Government, Health Department.
Financial support: 275,205€
Role: Co-PI
Time allocation: 15%
Period: 2017 – 2019

Overlap: Follow-up of the cohort analyzed in this project.

Familiar hypercholesterolemia epidemiology, risk prediction, effectiveness and safety of lipid-lowering therapy.
Aim: To determine the effectiveness and safety of lipid-lowering therapy in patients with familiar hypercholesterolemia and to develop and validate predictive risk functions.
Funding Body: Catalan Government, Health Department.
Financial support: 5,000€
Role: Investigator
Time allocation: 2%
Period: 2017 – 2019
Overlap: None

Jaume Marrugat

Role of micro RNAs expressed by human endothelial and vascular smooth muscle cells in myocardial infarction
Aim: To identify micro RNA associated with myocardial infarction risk.
Funding Body: Carlos III Health Institute (Spanish Government).
Financial support: 175,0005€
Role: PI
Time allocation: 10%
Period: 2016 – 2018
Overlap: None

Role of micro RNAs expressed by human endothelial and vascular smooth muscle cells in myocardial infarction
Aim: To identify micro RNA associated with myocardial infarction risk.
Funding Body: BBVA Foundation (Private entity).
Financial support: 125,0005€
Role: PI
Time allocation: 10%
Period: 2016 – 2019
Overlap: None

Follow-up of the REGICOR population-based cohort: trends in the incidence of cardiovascular disease and in the prevalence of cardiovascular risk factors, identification of new mechanisms and predictive biomarkers of cardiovascular disease and evaluation of preventive strategies.
Aim: To perform the follow-up of the participants of the REGICOR cohort to address several objectives.
Funding Body: Catalan Government, Health Department.
Financial support: 275,205€
Role: Co-PI
Time allocation: 15%
Period: 2017 – 2019
Overlap: Follow-up of the cohort analyzed in this project.

Familiar hypercholesterolemia epidemiology, risk prediction, effectiveness and safety of lipid-lowering therapy.
Aim: To determine the effectiveness and safety of lipid-lowering therapy in patients with familiar hypercholesterolemia and to develop and validate predictive risk functions.
Funding Body: Catalan Government, Health Department.

Financial support: 5,000€
Role: Investigator
Time allocation: 2%
Period: 2017 – 2019
Overlap: None

Payam Dadvand

PERSIAN Birth Cohort
Aim: To study Developmental Origins of Health and Diseases (DOHaD) in Iranian population including evaluating the impact of socioenvironmental, psychological and genetic factors on pregnancy outcomes, child mental and physical health, growth, and development, and early- and late-onset chronic non-communicable diseases.
Funding body: Iranian Ministry of Health and Medical Education.
Financial support: 1,736,489.9 €.
Role: co-PI
Time allocation: 15%
Period: 2016-2021
Overlap: None

Aging lungs in European cohorts (ALEC)
Aim: To evaluate the combined effects of factors that cause poor lung function, respiratory disability and the development of COPD.
Funding body: European Commission, Horizon 2020 (PHC1).
Financial support: 5,534,095 €.
Role: co-investigator & task-leader
Time allocation: 2.5%
Period: 2016-2021
Overlap: None

Maria Teresa Pay

CAMS 84
Aim: During CAMS-84 we will progressively migrate to a common (centralised or partly distributed) processing environment based on common software. In order to achieve this, we included partner S&T who has a long experience on validation and quality control software development, including e.g. the validation tools and website developed for NORS (these tools are currently used in VAL for the NDACC observations).
Funding body: European Commission (through ECMWF)
Financial support: EUR 176,000
Role: Co-investigator
Time allocation: 17%
Period: 2015-2018
Overlap: None

REPORT: Reducció de les emissions de contaminants atmosfèrics i acústiques del Port de Barcelona i voltants, per millorar la qualitat de l'aire a Barcelona.
Aim: RePort aims at the conversion of Diesel engines to Dual-Fuel engines with Natural Gas Vehicle and a system for tracking high-technology vehicles with the aim of creating a logistics network in the Port of Barcelona and surrounding areas with an alternative fuel that will improve atmospheric and acoustic contaminant emissions and will strengthen a new industrial transport sector.

Funding body: RIS3CAT (Catalan government)
Financial support: EUR 73,657.50
Role: Co-investigator
Time allocation: approx. 10%
Period: 2017-2018
Overlap: None

PAISA: Photochemical modelling to attribute emission sources and source regions to high particulate matter concentration in urban areas in Spain
Aim: PAISA will help to a better design national/regional air quality plans to meet the Air Quality Directive in Spain, promoting the synergies between different scientific groups (experimentalist and modellers), companies and governments.
Funding body: Programa Estatal de I+D+I Orientada a los Retos de la Socedad (Spanish government)
Financial support: EUR 118,500
Role: Principal Investigator
Time allocation: 12.5%
Period: 2016-2019
Overlap: None

Carlos Perez García

VISCA: Vineyards´ Integrated Smart Climate Application
Aim: The main objective of VISCA is making South-European wine industries resilient to climate changes, while minimizing costs and risks through an improvement of the production management (quality and quantity of final product).
Funding body: European Commission (Horizon 2020)
Financial support: EUR 295,000
Role: Co-investigator
Time allocation: 50%
Period: 2017-2020
Overlap: None

AXA Chair
Aim: This unprecedented program will improve our understanding of SDS and their variability; quantify dust effects upon weather, climate, atmospheric chemistry and ocean biogeochemistry; develop and distribute skillful SDS short- and medium-range forecasts and long-range dust predictions and projections; assess SDS impacts upon key sectors of society and economy; and promote capacity building, technology transfer, dissemination and public engagement.
Funding body: Axa Chair
Financial support: EUR 1,587,906.57
Role: Co-investigator
Time allocation: max. 40%
Period: 2016-2031
Overlap: None

Marc Guevara

REPORT: Reducció de les emissions de contaminants atmosfèrics i acústiques del Port de Barcelona i voltants, per millorar la qualitat de l'aire a Barcelona
Aim: RePort aims at the conversion of Diesel engines to Dual-Fuel engines with Natural Gas Vehicle and a system for tracking high-technology vehicles with the aim of creating a logistics network in the Port of

Barcelona and surrounding areas with an alternative fuel that will improve atmospheric and acoustic contaminant emissions and will strengthen a new industrial transport sector.
Funding body: RIS3CAT (Catalan government)
Financial support: EUR 73,657.50
Role: Co-investigator
Time allocation: 80%
Period: 2017-2018
Overlap: None

Mario Acosta

VISCA: Vineyards´ Integrated Smart Climate Application
Aim: The main objective of VISCA is making South-European wine industries resilient to climate changes, while minimizing costs and risks through an improvement of the production management (quality and quantity of final product).
Funding body: European Commission (Horizon 2020)
Financial support: EUR 295,000
Role: Co-investigator
Time allocation: 20%
Period: 2017
Overlap: None

(2) Pending Support

Xavier Basagaña

Effect of temperature and air pollution on children's cognitive function
Aim: To assess how temperature and air pollution at schools can affect cognitive function in children.
Funding Body: Carlos III Health Institute (Spanish Government).
Financial support: 114,830.21
Role: Principal investigator
Time allocation: 10%
Period: 2018-2020
Overlap: none

Citizen Science to analyze the effect of air pollution on teenagers' cognitive function
Aim: To assess how air pollution and schools can affect cognitive function of teenagers
Funding Body: RecerCaixa (La Caixa Foundation).
Financial support: 99,362.40
Role: Principal investigator
Time allocation: 10%
Period: 2018-2020
Overlap: none

Assessment of the impact of air pollution in incidence, treatment, and prognosis of acute ischemic stroke in Catalonia
Aim: To evaluate the effects of air pollution on occurrence of acute ischemic stroke, its treatment success and prognosis and its modification by urbanity and mitigation by green spaces.
Funding body: Marató TV3 Foundation.
Financial support: 173,971.3 €.
Role: Co-investigator

Time allocation: 2%
Period: 2018-2020
Overlap: None.

Ommoord
Aim: Evaluate the effects of long-term air pollution exposure on cardiovascular health
Funding body: Health Effects Institute
Financial support: 1,000,000$
Role: Senior Statistician
Time allocation: 10%
Period: 2018-2021
Overlap: Presented to the same call but using totally different data.

Traffic-related air pollution and birth weight: the roles of noise, placental function, green space, Diet, physical activity, and socioeconomic status (FRONTIER)
Aim: To estimate the effect of traffic-related air pollution and other co-exposures on fetal growth.
Funding body: Health Effects Institute
Financial support: 1,000,000$
Role: Co-investigator
Time allocation: 5%
Period: 2018-2021
Overlap: Presented to the same call but using totally different data.

Assessing adverse health effects in CHILDhood of Traffic Related Air Pollution, after accounting for correlated confounding or modifying factors (CHILDTRAP)
Aim: To estimate the effect of traffic-related air pollution and other co-exposures on children's health.
Funding body: Health Effects Institute
Financial support: 1,000,000$
Role: Co-investigator
Time allocation: 5%
Period: 2018-2021
Overlap: Presented to the same call but using totally different data.

Evaluation of Mortality Effects of Air Pollution Multipollutant Mixtures
Aim: To estimate the short-term effects of different air pollution metrics on mortality
Funding body: Health Effects Institute
Financial support: 396,000
Role: Co-investigator
Time allocation: 1%
Period: 2018-2020
Overlap: None.

Long-term exposure to air pollution and cardiovascular events in periurban India: scope for health benefits of reduced motor vehicle emissions
Aim: to quantify the relationship between air pollution and cardiovascular disease events in a setting with moderately high air pollution from a range of sources and quantify the impact of mitigating motor vehicle emissions on health.
Funding body: Health Effects Institute
Financial support: 400,000
Role: Senior Statistician
Time allocation: 2%

Period: 2018-2020
Overlap: None.

Susanne Moebus

Influence of noise on human mental disorders
Aim: To examine in detail effects of noise pollution and mental health disorders in the Heinz Nixdorf Recall cohort study.
Funding body: Environmental Protection Agency (UBA), Germany
Financial support applied for: 477.673 €.
Role: PI
Time allocation: 5%
Period: 2017-2020
Overlap: None.

Mark Nieuwenhuijsen

Participatory health impact assessment in Barcelona.
Period: 2018-2020
Financial support: 100.000€
Time allocation: 10%
Overlap: none

Roberto Elosua

Effectiveness and cost-effectiveness of LIpid-lowering treatment in priMary prevention: revIsiting TargEts and absolute risk Reduction (E-LIMITER)
Aim: To assess the effectiveness of lipid-lowering drugs in cardiovascular primary prevention.
Funding Body: European Commission (Horizon 2020)
Financial support: 1,1124,447
Role: Investigator
Time allocation: 10%
Period: 2018-2020
Overlap: none

Jaume Marrugat

Effectiveness and cost-effectiveness of LIpid-lowering treatment in priMary prevention: revIsiting TargEts and absolute risk Reduction (E-LIMITER)
Aim: To assess the effectiveness of lipid-lowering drugs in cardiovascular primary prevention.
Funding Body: European Commission (Horizon 2020)
Financial support: 1,1124,447
Role: Principal investigator
Time allocation: 20%
Period: 2018-2020
Overlap: none

Payam Dadvand

Air Pollution, Placental Oxidative Stress and Function, and Fetal Growth: a Mechanistic Approach (AirPLASM)
Aim: To evaluate the mediator role of placental oxidative stress and function in the association between maternal exposure to air pollution and fetal growth.
Funding body: Spanish Ministry of Commerce and Competitiveness.
Financial support: 115,591.3 €.
Role: PI
Time allocation: 10%
Period: 2018-2020
Overlap: None (The study is planned to be conducted in the context of an ongoing cohort in BCNatal, the same unit where FRONTIER birth cohort will be established).

Assessment of the impact of air pollution in incidence, treatment, and prognosis of acute ischemic stroke in Catalonia
Aim: To evaluate the effects of air pollution on occurrence of acute ischemic stroke, its treatment success and prognosis and its modification by urbanity and mitigation by green spaces..
Funding body: Marató TV3 Foundation.
Financial support: 173,971.3 €.
Role: Co-investigator
Time allocation: 2.5%
Period: 2018-2020
Overlap: None.

Productive green Infrastructure for post-industrial urban regeneration (proGIreg)
Aim: To demonstrate the integration of Nature Based Solutions (NBS) into business models which are economically self-sustained and multi-beneficial for the economic, ecologic and social regeneration of deprived urban areas that suffer from the consequences of de-industrialisation.
Funding body: European Commission H2020.
Financial support: 10,000,000 €.
Role: Co-investigator
Time allocation: 2.5%
Period: 2018-2023
Overlap: None.

The Impact of Urban Green Landscapes on Citizens' Health and Wellbeing (HEALTHSCAPES).
Aim: To evaluate impact of urban green infrastructure on (1) the urban environmental microbiota and its connection with commensal microbiota in children, and (2) health and wellbeing in adults and elderly by use of available cohort studies and registry data, and by providing (3) cost-benefit analysis of the impact of urban green infrastructure on health and wellbeing, and (4) by assessing the implications for planning and policymaking.
Funding body: The Research Council of Norway (BEDREHELSE).
Financial support: 1,910,174.88€.
Role: Co-investigator and work package co-leader
Time allocation: 5%
Period: 2018-2022
Overlap: None.

An ecosystem-based strategy for underpinning research and innovation about interactions between oceans and human health (OCEANIDES)
Aim: To spread and increase the understanding of Oceans and Human Health (OHH) interactions for all the stakeholders and to underpin research and innovation about this topic from a strategic and participatory perspective at European level.
Funding body: European Commission H2020.
Financial support: 2,000,000 €.
Role: Co-investigator
Time allocation: 2.5%
Period: 2018-2023
Overlap: None.

Maria Foraster

Radiofrequency electromagnetic fields, noise, and sleep problems in adolescence – INMA-Ado-Sueño Project
Aim: To study the association between radiofrequency electromagnetic fields, noise, and sleep problems in adolescents in the INMA (INfancia y MedioAmbiente) Project
Funding body: Spanish Ministry of Commerce and Competitiveness.
Financial support: 99,716 €
Role: Co-investigator
Time allocation: 2.5%
Period: 2018-2020
Overlap: None

Effect of drinking water treatment on blood pressure
Aim: To evaluate different drinking water treatments and their impact on blood pressure
Funding body: Spanish Ministry of Commerce and Competitiveness.
Financial support: 104,343 €
Role: Co-investigator
Time allocation: 2.5%
Period: 2018-2020
Overlap: None

Traffic-related air pollution and birth weight: the roles of noise, placental function, green space, diet, physical activity, and socioeconomic status (FRONTIER)
Aim: To evaluate the impact of maternal exposure to air pollution on fetal growth by disentangling the effects of co-exposures
Funding body: Health Effects Institute (RFA 17-1).
Financial support: 1,000,000$
Role: Co-investigator, WP leader: Noise
Time allocation: 5%
Period: 2018-2021
Overlap: None

Cognitive and mental health in relation to traffic related pollution in children and adolescents in five European prospective cohort studies (COMET)
Aim: To evaluate the effect of traffic-related pollution on cognition and mental health.
Funding body: Health Effects Institute (RFA 17-1).
Financial support: 1,000,000$
Role: Co-investigator
Time allocation: 5%
Period: 2018-2021
Overlap: None

Carlos Perez

CAMS 81: Global and Regional Emissions
Aim: The goal of this project is to provide gridded distributions of European and global anthropogenic emissions, as well as global natural emissions for the CAMS regional and global production chains.
Funding body: European Commission (through ECMWF)
Financial support: EUR 109,687.50
Role: Co-investigator
Time allocation: 3%-5%
Period: 2017-2020
Overlap: None

NUTRIENT: QuaNtifying the present and fUTure atmospheric deliveRy of bIoavailablE iroN to The ocean.
Aim: NUTRIENT aims to improve our understanding of the atmospheric delivery of bioavailable Fe to the ocean. The project will develop and constrain the atmospheric Fe cycle in the EC-Earth Earth System model, which will ultimately allow fully coupled simulations that account for the effect of bioavailable Fe variations upon the carbon and nitrogen cycles.
Funding body: Programa Estatal de I+D+I Orientada a los Retos de la Socedad (Spanish government)
Financial support: 335,987.96
Role: Principal investigator
Time allocation: 12.5%
Period: 2018-2020
Overlap: None

Marc Guevara

CAMS 81: Global and Regional Emissions
Aim: The goal of this project is to provide gridded distributions of European and global anthropogenic emissions, as well as global natural emissions for the CAMS regional and global production chains.
Funding body: European Commission (through ECMWF)
Financial support: EUR 109,687.50
Role: Principal investigator
Time allocation: 12.5%
Period: 2017-2020
Overlap: None

Mario Acosta

OEMES: Optimization of Earth system Models in the path to the new generation of Exascale high performance computing Systems

Aim: The aim of OEMES is to adapt ESMs to more powerful machines, becoming more parallel, scalable and robust, and to optimise for data locality on architectures with deepening and heterogeneous memory hierarchies.
Funding body: Programa Estatal de I+D+I Orientada a los Retos de la Socedad (Spanish government)
Financial support: EUR 146,414.84
Role: Principal Investigator
Time allocation: 25%
Period: 2018-2020
Overlap: None

F-8 RESOURCES AND ENVIRONMENT

FACILITIES: *Describe all the facilities to be used and, indicate their capacities, pertinent capabilities, relative proximity and extent of availability to the project. Using continuation pages if necessary include a description of the nature of any collaboration with other organizations and provide further information in the RESEARCH PLAN.*

Laboratory
N/A

Animal
N/A

Clinical
The clinical examinations in the two cohorts were conducted in collaborating health care centres.

Quality Assurance Plan
We will follow ISGlobal guidelines for data quality and data protection.

Computer
Estimates for air pollution and source apportionment at 1-km resolution for REGICOR will be calculated using the MareNostrum 4, hosted in the Barcelona Supercomputing Center, in Spain. MareNostrum 4 is one of the fastest computer in Europe, a Tier-0 PRACE system which has two distinct parts. First, the general purpose block has 48 racks with 3,456 nodes of Intel Xeon Platinum processors for a total of 165,888 cores and a central memory of 390 terabytes. Its peak power is 11.15 Petaflops with an energy consumption of 1.3 MWatt/year. Second, MareNostrum 4 is formed of clusters of three different technologies, currently being developed in the US and Japan to accelerate the arrival of the new generation of pre-exascale supercomputers: (1) IBM POWER9 processors and NVIDIA Tesla GPUs cluster (computing power over 1.5 Petaflop/s), (2) Intel Knights Hill (KNH) processors cluster (computing power in excess of 0.5 Petaflop/s) and (3) 64 bit ARMv8 processors cluster (Computing power over 0.5 Petaflop/s). MareNostrum4 has a disk storage capacity of 14 Petabytes and is connected to the Big Data infrastructures of BSC-CNS, which have a total capacity of 24.6 Petabytes.

The size of the data generated with the CALIOPE system for REGICOR will be around 40Tb. The data will be stored, shared and backuped in hard drives with the following characteristics: disks WD Red Pro NAS Hard Drive, model WD40EFRX, 4 TB capacity, SATA 6Gb s interface, 5400 rpm, and 64 MB cache. We plan to buy 20 disks (210 € each) to be set in a BeeGFS filesystem.

Other

GIS unit: The ISGlobal's GIS unit (led by MJ Nieuwenhuijsen) encompasses four fulltime and two part-time GIS technicians. Through involvement in several national and international research projects, the GIS unit has accumulated massive experience and expertise in applying geospatial analytical techniques, modeling approaches, remote-sensing and other types of spatial data, and geocoding techniques to assess individual exposures to a wide range of environmental exposures such as air pollution (e.g. applying land use regression models), noise, ultraviolet radiation, green and blue spaces, and to characterize urban built environment (e.g. walkability, land use mix, etc.). The unit relies on both free and open source softwares (e.g. QGIS, Spatialite, Postgresql/PostGIS, Geospatial Modelling Environment) as well as licensed softwares (including 6 ArcGis (ESRI) and 1 ArcInfo (ESRI) licenses with the following extensions: Network Analyst, Spatial Analyst and Geostatistical Analyst). Further to these software, the unit members have extensive experience in programming in Python, R, and STATA environments.

MAJOR EQUIPMENT: *List the most important equipment items available for this project, noting the location, and pertinent capabilities of each.*

N/A

SPONSOR PARTICIPATION ___ YES _X__ NO

If yes, on a separate page identify and explain role of any individuals employed by the EPA or industry sponsors of HEI who are involved with any aspect of the project. Also, list any resources provided by sponsors (such as facilities or animals).

F-9 BIOGRAPHICAL SKETCH

Name: **Xavier Basagaña**	Title: **Associate Research Professor**	BIRTH DATE: 01/17/1977

Education (*Begin with baccalaureate training and include postdoctoral training*)

Institution and Location	**Degree**	**Year Conferred**	**Field of Study**
Polytechnic University of Catalonia (UPC), Barcelona, Spain	Bsc	1999	Statistics
Polytechnic University of Catalonia (UPC), Barcelona, Spain	Msc	2003	Statistical Sciences
Harvard University, Cambridge, MA, USA	Ph. D.	2008	Biostatistics

RESEARCH AND/OR PROFESSIONAL EXPERIENCE

Xavier Basagaña started working as a statistician in the Respiratory and Environmental Research Unit of the Municipal Institute of Medical Research (IMIM) in Barcelona in 1999. During the five years he worked in the institution, he was involved in several national and international projects investigating the health effects of air pollution and other environmental exposures. His main activities were writing analysis protocols, conducting statistical analyses, contributing to study design, and writing scientific papers. He obtained a training grant from the Health Ministry in Spain that covered two of the five years he spent at IMIM.

In 2003, he obtained a "La Caixa" grant to pursue his graduate studies in the U.S. and enrolled at the Harvard School of Public Health, where he obtained his PhD in Biostatistics. His research at Harvard was on statistical tools for the design of longitudinal observational studies. During his time at Harvard, he served as teaching assistant in several graduate courses in Statistics and obtained a Teaching Assistant award.
In 2008, he joined the Centre for Research in Environmental Epidemiology (CREAL) as Assistant Research Professor. He is currently Associate Research Professor at the Barcelona Institute for Global Health (ISGlobal). His research is divided in two main blocks: epidemiologic research and statistical methodology. His epidemiologic research has explored the health effects of two main exposures: air pollution and extreme temperatures. He has been principal investigator in several national and European projects (REGICOR-Air, TRI-TABS, APHEKOM, MED-Particles, MED-HISS, TEMPERATURE, DECHM) and participated in other coordinated European projects such as ESCAPE, where he was member of the statistical group, or HELIX (exposome project) and MeDALL, where he is coordinating the statistical analyses.

His methodological research covers several areas, including longitudinal study design, missing data, measurement error, spatial analysis and the analysis of correlated data. Of particular interest for this proposal is his study on the effects of measurement error in epidemiological studies using air pollution predictions from land use regression (LUR) models and his work on analysis of correlated data.
He is Adjunct Professor and member of the direction committee of the Master of Public Health Program of Pompeu Fabra University, where he teaches Epidemiology and Statistics. He is a member of the Expert Committee of the Observatory of Climate Change and Health of the Spanish government, and is a member of the working group on Climate Change Adaptation of the Catalan government. He is member of the editorial board of the journal *Epidemiology* and he is the statistical editor of the journal *Respiration.*

Overall, he is co-author of more than 130 peer-reviewed scientific papers in epidemiologic and statistical journals, 83% published in journals on the 1st quartile of their subject and 58% in the 1st decile. He has a Scopus h-index of 31.

Selected publications (out of 146):

1. Sunyer J, Suades-González E, García-Esteban R, Rivas I, Pujol J, Alvarez-Pedrerol M, Forns J, Querol X, **Basagaña X**. Traffic-related Air Pollution and Attention in Primary School Children: Short-term Association. Epidemiology. 2017;28(2):181-189.
2. de Keijzer C, Agis D, Ambrós A, Arévalo G, Baldasano JM, Bande S, Barrera-Gómez J, Benach J, Cirach M, Dadvand P, Ghigo S, Martinez-Solanas È, Nieuwenhuijsen M, Cadum E, **Basagaña X**; MED-HISS Study group. The association of air pollution and greenness with mortality and life expectancy in Spain: A small-area study. Environ Int. 2017;99:170-176.
3. **Basagaña X**, Esnaola M, Rivas I, Amato F, Alvarez-Pedrerol M, Forns J, López-Vicente M, Pujol J, Nieuwenhuijsen M, Querol X, Sunyer J. Neurodevelopmental Deceleration by Urban Fine Particles from Different Emission Sources: A Longitudinal Observational Study. Environ Health Perspect. 2016 Oct;124(10):1630-1636.
4. Schifano P, Asta F, Dadvand P, Davoli M, **Basagana X***, Michelozzi P*. Heat and air pollution exposure as triggers of delivery: A survival analysis of population-based pregnancy cohorts in Rome and Barcelona. Environ Int. 2016;88:153-159. [* joint authorship]
5. Barrera-Gómez J, **Basagaña X**. Models with transformed variables: interpretation and software. Epidemiology. 2015;26(2):e16-7.
6. Robinson OJ, **Basagaña X**, Agier L, de Castro M, Hernandez-Ferrer C, Gonzalez JR, Grimalt JO, Nieuwenhuijsen MJ, Sunyer J, Slama R, Vrijheid M. The Pregnancy Exposome: multiple environmental exposures in the INMA-Sabadell Birth Cohort. Environ Sci Technol 2015; 49(17):10632-41.
7. **Basagaña X**, Jacquemin B, Karanasiou A, Ostro B, Querol X, Agis D, Alessandrini E, Alguacil J, Artinano B, Catrambone M, de la Rosa JD, Diaz J, Faustini A, Ferrari S, Forastiere F, Katsouyanni K, Linares C, Perrino C, Ranzi A, Ricciardelli I, Samoli E, Zauli-Sajani S, Sunyer J, Stafoggia M. Short-term effects of particulate matter constituents on daily hospitalizations and mortality in five South-European cities: Results from the MED-PARTICLES project. Environ Int 2015; 75: 151-8
8. Foraster M, Kunzli N, Aguilera I, Rivera M, Agis D, Vila J, Bouso L, Deltell A, Marrugat J, Ramos R, Sunyer J, Elosua R, **Basagaña X**. High Blood Pressure and Long-Term Exposure to Indoor Noise and Air Pollution from Road Traffic. Environ Health Perspect 2014; 122(11): 1193-200.
9. **Basagaña X**, Aguilera I, Rivera M, Agis D, Foraster M, Marrugat J, Elosua R, Künzli N. Measurement Error in Epidemiologic Studies of Air Pollution Based on Land-Use Regression Models. Am J Epidemiol 2013;178(8):1342-6.
10. Barrera-Gomez J, Spiegelman D, **Basagaña X**. Optimal combination of number of participants and number of repeated measurements in longitudinal studies with time-varying exposure. Stat Med 2013;32(27): 4748-62
11. **Basagaña X**, Barrera-Gomez J, Benet M, Anto JM, Garcia-Aymerich J. A framework for multiple imputation in cluster analysis. Am J Epidemiol 2013; 177(7): 718-25.
12. **Basagaña X**, Rivera M, Aguilera I, Agis D, Bouso L, Elosua R, Foraster M, de Nazelle A, Nieuwenhuijsen M, Vila J, Kuenzli N. Effect of the number of measurement sites on land use regression models in estimating local air pollution. Atmos Environ 2012; 54: 634-42.
13. **Basagaña X**, Liao X, Spiegelman D. Power and sample size calculations for longitudinal studies estimating a main effect of a time-varying exposure. Stat Methods Med Res 2011; 20(5): 471-87.

F-9 BIOGRAPHICAL SKETCH

NAME Mario César Acosta Cobos	Postdoctoral Researcher	**BIRTH DATE** *(Month, Day, Year)* 12/18/1985

Education (*Begin with baccalaureate training and include postdoctoral training*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Cordoba (Spain)	Bsc	2008	Computer Scientist
University of Granada (Spain)	Msc	2010	Computer Scientist
University of Granada (Spain)	PhD	2015	High performance computing and Computational Fluid Dynamics

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: *Concluding with present position, list in chronological order previous employment, experience, and honors. List, in chronological order, the titles and complete references to recent representative publications, especially those most pertinent to this application.*

During his PhD, Dr Acosta contributed greatly to HPC applied to ESMs and therefore developed expertise in this field. The general knowledge acquired was to improve the computational efficiency of existing computational dynamic fluids models to address the study of circulation, transport and mixing of water components, obtaining the results in an efficient way. This expertise includes wide knowledge in numerical models (governing equations, numerical algorithms and computational implementation) and how to adapt them efficiently to actual and new HPC resources. He has moved to BSC two years ago. He is leading the performance team inside the department, being the supervisor of one PhD student and one master student, who are developing theses in the HPC topic. Only during the last year, Dr Acosta has collaborated in the submission of five peer-reviewed papers (two accepted), five oral communications, four posters in international conferences and four technical memoranda, all within the framework of five H2020 and FP7 projects. He has also several formal collaborations with international institutions, the Centre Européen de Recherche et de Formation Avancée en Calcul Scientifique (CERFACS, OASIS developers), and the ECMWF (IFS developers), where Acosta did a post-doctoral visit (Severo Ochoa mobility grant) of two months in 2017. During his career, the applicant has participated in 9 national and international projects. He is author of 4 peer-reviewed articles in international journals. He presented his work at 11 congresses and workshops, and reviewed some manuscripts for peer-review journals. He is part of the group of experts of European eXtreme Data and Computing Initiative: Weather, Climatology and Solid Earth Sciences (EXDCI/WCES). The group is responsible of the reviewing of deliverables related to Earth Sciences, produced by the coordination and support action EXDCI project, to coordinate the development and implementation of a common strategy for the European HPC Ecosystem.

List in chronological order previous employment

2015 – Present	Postdoctoral Researcher
2015 – 2015	Postdoctoral Researcher
2011 – 2015	FPU grant (Research Fellow), PhD Student
2010 – 2011	Junior Researcher

Publications

1. Oriol Tinto, **Mario Acosta**, et al. 2017. Optimizing domain decomposition in an ocean model: the case of NEMO Procedia Computer Science. Elsevier. 108-2017, pp.776-785.
2. Xavier Yerpes; **Mario Acosta** et al. 2017. SIMULATION-BASED PERFORMANCE ANALYSIS OF EC-EARTH 3.2.0 USING DIMEMAS Technical memorandum - Barcelona Supercomputing Center - Public Wiki.
3. Oriol Tinto, Mario Acosta, (…) et al. 2017. Detecting, analyzing and optimizing MPI communication bottlenecks in Earth System models Journal of Computational Science.
4. Neven Fuckar; (…) **Mario Acosta**. 2016. Record Low Northern Hemisphere Sea Ice Extent in March 2015 Bulletin of the American Meteorological Society. 97-12.
5. **Mario Acosta**; et al. 2016. PERFORMANCE ANALYSIS OF EC-EARTH3.2: COUPLING Technical memorandum - Barcelona Supercomputing Center - Public Wiki.
6. Xavier Yerpes; **Mario Acosta** et al. 2016. SCALABILITY AND PERFORMANCE ANALYSIS OF EC-EARTH 3.2.0 USING A NEW METRIC APPROACH (PART II) Technical memorandum - Barcelona Supercomputing Center - Public Wiki.
7. Xavier Yerpes; **Mario Acosta** et al. 2016. SCALABILITY AND PERFORMANCE ANALYSIS OF EC - EARTH 3.2.0 USING A NEW METRIC APPROACH (PAR T I) Technical memorandum - Barcelona Supercomputing Center - Public Wiki.
8. Mancia Anguita; Mario Acosta, et al. (/2). 2015. Scalable parallel implementation for 3D semi-implicit hydrodynamic models of shallow waters Journal of Environmental Modelling & Software. Elsevier Journals. 64, pp.241-261. ISSN 1364-8152.
9. **Mario Acosta**; et al. (/1). 2014. Evaluation of a nested-grid implementation for 3D finite-difference semi-implicit hydrodynamic models Journal of Environmental Modelling & Software. Elsevier Journals. 64, pp.241-261. ISSN 1364-8152.
10. **Mario Acosta**; et al. (/1). A hybrid parallel implementation of a 3D hydrodynamic numerical model optimized and adapted to the architecture Journal of Parallel Computing. Elsevier Journals. (In review)
11. Domingo Manubens-Gil; (…) Mario Acosta et al. Autosubmit: a versatile tool for managing Earth system models on HPC platforms Future Generation Computer Systems.
12. **Mario Acosta**; Mancia Anguita; Javier Fernández-Baldomero. (/ 1). Conjugate gradient preconditioners in parallel water hydrodynamic software with implicit treatment of surface gravity waves Journal of Parallel Computing. Elsevier Journals. (In review)
13. **Mario Acosta** et al. 2012. Tecnología RFID: Teoría y Aplicaciones Periféricos Avanzados. Grupo Editorial Garceta. ISBN 978-84-1545-203-4.
14. Teresa López; **Mario Acosta**; Elena Sanchez. 2012. Influencia de los Mecanismos de Suspensión de Sedimentos Inducidos por la Acción del Oleaje en el Clima Lumínico Influencia de los Mecanismos de Suspensión de Sedimentos Inducidos por la Acción del Oleaje en el Clima Lumínico. ISBN 978-84-1545-203-4.

F-9 BIOGRAPHICAL SKETCH

Name: **Payam Dadvand**	Title: **MD, PhD**	BIRTH DATE: **05/01/1977**

Education (*Begin with baccalaureate training and include postdoctoral training*)

Institution and Location	Degree	Year Conferred	Field of Study
Isfahan University of Medical sciences, Iran	Medical Doctor (MD)	2002	Medicine
Newcastle University, UK	PhD in epidemiology	2009	Epidemiology

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: Payam Dadvand is a medical doctor by training and has a PhD in environmental epidemiology. For the last decade he has conducted pioneering studies on the impacts of both environmental stressors (e.g. air pollution) and environmental mitigation measures (e.g. green spaces) on maternal and child health applying his expertise in using remote sensing data, GIS-based spatial analytical methods, and spatiotemporal modelling approaches. He has led one of the largest ever-reported studies on the impact maternal air pollution exposure on fetal growth including ~3 million births across the North & South America, Europe, Asia, and Oceania and has been the first to report on **1)** the association between air pollution and preterm premature membrane rupture in pregnant women (2014); **2)** the impact of Saharan dust episodes on pregnancy outcomes (2011); **3)** the effect of different sources of particulate air pollution on preeclampsia (2104); **4)** the mitigation effect of green space on personal exposure to air pollution in pregnant women (2012); and **5)** air pollution levels in schools (2015); **6)** the impact of greenness exposure on cognitive development in primary schoolchildren (2015), and **7)** the impact of ambient temperature on maternal vaginal bacterial colonisation during pregnancy (2011).

List in chronological order previous employment, experience, and honors

2014 – Present **Assistant research professor**, Centre for Research in Environmental Epidemiology. (CREAL-ISGlobal)
2013 – 2014 Research fellow, Center for Research in Environmental Epidemiology (CREAL).
2009 – 2012 Postdoctoral researcher, Center for Research in Environmental Epidemiology. (CREAL)
2002 – 2004 General practitioner Isfahan, Iran

Honours and Awards

1. *Rebecca James Baker Award* for *"scientific excellence, integrity, compassion, resourcefulness, and patience in cross-cultural research for the improvement of public health"* awarded by the International Society for Environmental Epidemiology (ISEE) at the 24th Annual ISEE congress, Columbia, South Carolina, US, 2012.
2. *Outstanding Abstract by a New Investigator* awarded by the International Society for Environmental Epidemiology (ISEE) at the 24th Annual ISEE congress, Columbia, South Carolina, US, 2012.
3. *Ramón y Cajal fellowship* (2014-2018) awarded by the Spanish Ministry of Economy and Finance (I was **ranked one** in the field of "clinical medicine and epidemiology" in Spain.)
4. *Juan de la Cierva post-doctoral fellowship* (2012-2015) awarded by the Spanish Ministry of Science and Innovation.
5. *International Research Scholarship (IRS)* (2005-2008) awarded by Newcastle University for three years to carry out PhD there.
6. One paper as Issue Highlight in Proceedings of the National Academy of Sciences of the United States

of America and Two papers as Science Selection by Environmental Health Perspectives.

List, in chronological order, the titles and complete references to recent representative publications.

Mohammadyan M, Alizadeh-Larimi A, Etemadinejad S, Latif MT, Heibati B, Yetilmezsoy K, Abdul-Wahab SA, **Dadvand P**. Particulate Air Pollution at Schools: Indoor-Outdoor Relationship and Determinants of Indoor Concentrations. *Aerosol and Air Quality Research*. 2016; doi: 10.4209/aaqr.2016.03.0128

Dadvand P, Rivas I, Basagaña X, Alvarez-Pedrerol M, Su J, De Castro Pascual M, Amato F, Jerret M, Querol X, Sunyer J, Nieuwenhuijsen MJ. The association between greenness and traffic-related air pollution at schools. *Science of the Total Environment.* 2015; 523:59-63.

Dadvand P, Ostro B, Figueras F, Foraster M, Basagaña X, Valentín A, Martinez D, Beelen R, Cirach M, Hoek G, Jerrett M, Brunekreef B, Nieuwenhuijsen MJ. Residential proximity to major roads and term low birth weight: the roles of air pollution, heat, noise, and road-adjacent trees. *Epidemiology*, 25(4), 5,18-25, 2014

Dadvand P, Basagaña X, Figueras F, Martinez D, Beelen R, Cirach M, de Nazelle A, Hoek G, Ostro B, Nieuwenhuijsen MJ. Air Pollution and Preterm Premature Rupture of Membranes: A Spatiotemporal Analysis. *American Journal of Epidemiology*, 15;179(2):200-7, 2014

Pedersen M, Stayner L, Slama R, Sørensen M, Figueras F, Nieuwenhuijsen MJ, Raaschou-Nielsen O, **Dadvand P.** Ambient Air Pollution and Pregnancy-Induced Hypertensive Disorders: A Systematic Review and Meta-Analysis. *Hypertension* 64(3):494-500, 2014

Dadvand P, Nieuwenhuijsen MJ, Agustí A, de Batlle j, Benet M, Beelen R, Cirach M, Martinez D, Hoek G, Basagaña X, Ferrer A, Ferrer JJ, Rodriguez-Roisin R, Sauleda J, Guerra S, Anto JM, Garcia-Aymerich J. Air Pollution and Biomarkers of Systemic Inflammation and Tissue Repair in COPD Patients. *European Respiratory Journal*. 2014; 44(3):603-13.

Dadvand P, Wright J, Martinez D, Basagaña X, McEachan RR, Cirach M, Gidlow CJ, de Hoogh K, Grazuleviciene R, Nieuwenhuijsen M. Inequality, Green Spaces, and Pregnant Women: Roles of Ethnicity, Individual, and Neighbourhood Socioeconomic Status. *Environment International*, 2014; 71:101–108.

Dadvand P, Parker J, Bell ML, Bonzini M, Brauer M, Darrow L, Gehring U, Glinianaia SV, Gouveia N, Ha E, Leem JH, van den Hooven EH, Jalaludin B, Jesdale BM, Lepeule J, Morello-Frosch R, Morgan G, Pesatori AC, Pierik FH, Pless-Mulloli T, Rich DQ, Sathyanarayana S, Seo J, Slama R, Strickland M, Tamburic L, Wartenberg D, Nieuwenhuijsen M, Woodruff TJ. Maternal Exposure to Particulate Air Pollution and Fetal Growth; A Multi-Country Evaluation of Effect and Heterogeneity. *Environmental Health Perspectives*. 2013. 121:367–373.

Dadvand P, Ostro B, Amato F, Figueras F, Minguillón MC, Martinez D, Basagaña X, Querol X, Nieuwenhuijsen MJ. Particulate Air Pollution and Preeclampsia: A Source-based Analysis. *Occupational and Environmental Medicine*. 2014; 71(8):570-7.

Dadvand P, Figueras F, Basagaña X, Beelen R, Martinez D, Cirach M, Schembari A, Hoek G, Brunekreef B, Nieuwenhuijsen MJ. Ambient Air Pollution and Preeclampsia: a Spatiotemporal Analysis. *Environmental Health Perspectives* 121(11-12):1365-71, 2013.

Dadvand P, Sunyer J, Basagaña X, Ballester F, Lertxundi A, Fernández-Somoano A, Estarlich M, García-Esteban R, Mendez MA, Nieuwenhuijsen MJ. Surrounding greenness and pregnancy outcomes in four Spanish birth cohorts. Environmental Health Perspectives 120(10), 1481-7, 2012

Dadvand P, de Nazelle A, Triguero-Mas M, Schembari A, Cirach M, Amoly E, Figueras F, Basagaña X, Ostro B, Nieuwenhuijsen M. Surrounding Greenness and Exposure to Air Pollution During Pregnancy: An Analysis of Personal Monitoring Data. *Environmental Health Perspectives*. 120(9) 1286- 90, 2012

F-9 BIOGRAPHICAL SKETCH

Name Roberto Elosua	**Title** Doctor	**BIRTH DATE** *(Month, Day, Year)* 04/07/1964

Education (*Begin with baccalaureate training and include postdoctoral training*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Universidad de Navarra	Medicine & Surgery	1988	Medicine & Surgery
Universitat Autònoma de Barcelona	Medicine & Surgery	1997	Medicine & Surgery

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: *Concluding with present position, list in chronological order previous employment, experience, and honors. List, in chronological order, the titles and complete references to recent representative publications, especially those most pertinent to this application.*

2014 – act.	Consultant 1	IMIM-PSMAR
2008 – act.	Leader Group Cardiovascular Epidemiology & Genetics	IMIM-PSMAR
2008 – act.	Research accreditation (AGAUR)	IMIM-PSMAR
1996-2008	Investigator	Fundació IMIM
1995-1996	Fellow	Hosp. Sta Creu i St. Pau

PUBLICATIONS (selected from a total of 301):

1.- Molina L, Sarmiento M, Peñafiel J, Donaire-González D, Garcia-Aymerich J, Gómez-Pérez MA, Ble M, Ruiz-Bustillo S, Francés A, Schröder H, Marrugat J, **Elosua R**[*], Validation of the Regicor Short Physical Activity Questionnaire for the Adult Population, PLoS ONE 2017; 12(1): e0168148. (FI: 3.057).

2.- NCD Risk Factor Collaboration (NCD-RisC) (...,**Elosua R**, Marrugat J, Porta M,...). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants. Lancet 2017; 389(10064): 37-55. (FI: 44.002).

3.- Marcelino-Rodríguez I, Oliva-García J, Alemán-Sánchez JJ, Almeida-González D, Dominguez-Coello S, Brito-Diaz B, Gannar F, Rodríguez-Pérez MC, **Elosua R**, Cabrera de León A[*]. Lipid and inflammatory biomarker profiles in early insulin resistance. Acta Diabetol 2016; 53(6): 905-913. (FI: 3.074)

4.- Baena-Diez JM, Peñafiel J, Subirana I, Ramos R, **Elosua R**, Marin-Ibañez A, Guembe MJ, Rigo F, Tormo-Díaz MJ, Moreno-Iribas C, Cabré JJ, Segura A, García-Lareo M, Gómez de la Cámara A, Lapetra J, Quesada M, Marrugat J, Medrano MJ, Berjón J, Frontera G, Gavrila D, Barricarte A, Basora J, García J, Pavone NC, Lora-Pablos D, Mayoral E, Franch J, Mata M, Frances A, Grau M[*], on behalf of the FRESCO Investigators. Risk of Cause-Specific Death in Individuals With Diabetes: A Competing Risks Analysis. Diabetes Care 2016; 39(11): 1987-1995. (FI: 8.934).

5.- Ehret GB, (...), **Elosua R**, (...), Newton-Cheh C[*], Munroe PB[*], Wellcome Trust Case Control Consortium. The genetics of blood pressure regulation and its target organs from association studies in 342,415 individuals. Nat Genet 2016; 48(10): 1171-1184. (FI: 31.616).

6.- Soriano C*, Giralt E, Mola M, Vivanco R, Ois A, Rodríguez-Campello A, Cuadrado E, Sayols-Baixeras S, **Elosua R**, Roquer J, Jiménez-Conde J*. Ischemic stroke patients are biologically older than their chronological age. Aging (Albany NY) 2016; 8(11): 2655-2666. (FI: 3.979).

7.- **Elosua R***, Lluís-Ganella C, Subirana I, Havulinna A, Läll K, Lucas G, Sayols-Baixeras S, Pietilä A, Alver M, Cabrera de León A, Sentí M, Siscovick D, Melander O, Fischer K, Salomaa V, Marrugat J Cardiovascular Risk Factors and Ischemic Heart Disease: Is the Confluence of Risk Factors Greater than the Parts? A Genetic Approach. Circ Cardiovasc Genet 2016; 9(3): 279-286. (FI: 3.719).

8.- Zhou B, Lu Y, Hajifathalian K, Bentham J, Di Cesare M, Danaei G, Bixby H, Cowan MJ, Ali MK, Taddei C, Lo WC, Reis-Santos B, Stevens GA, Riley LM, Miranda JJ, Bjerregaard P, Rivera JA, Fouad HM, Ma G, Mbanya CN, McGarvey ST, Mohan V, Onat A, Pilav A, Ramachandran A, Ben Romdhane H, Paciorek CJ, Bennett JE, Ezzati M*, NCD Risk Factor Collaboration (NCD-RisC) (...,**Elosua R**, Porta M,...). Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants. Lancet 2016; 387(10027): 1513-1530. (FI: 44.002).

9.- Soriano C, Jiménez-Conde J*, Giralt E, Mola M, Vivanco R, Ois A, Rodríguez-Campello A, Cuadrado E, Sayols-Baixeras S, **Elosua R**, Roquer J, on behalf of the GENESTROKE Consortium. Epigenome-wide association study identifies TXNIP gene associated with Type 2 diabetes mellitus and sustained hyperglycemia. Hum Mol Genet 2016; 25(3): 609-619. (FI: 5.985).

10.- Nikpay M, (...), **Elosua R,** (...),Farrall M*, for the CARDIoGRAMplusC4D Consortium. A comprehensive 1000 Genomes-based genome-wide association meta-analysis of coronary artery disease. Nat Genet 2015; 47(10): 1121-1130. (FI: 31.616).

11.- Pérez-Grau L*, Wolf K, Hennig F, Pennell J, Basagaña X, Aguilera I, Agis D, Beelen R, Brunekreef B, Cyrys J, Fuks K, Adam M, Baldassare D, Cirach M, **Elosua R**, Dratva J, Hampel R, Koenig W, Marrugat J, de Faire U, Pershagen G, Probst-Mensch NM, de Nazelle A, Nieuwenhuijsen M, Rathmann W, Rivera M, Seissler J, Schindler C, Thiery J, Hoffmann R, Peters A, Künzli N. Air Pollution and Atherosclerosis: A Cross-Sectional Analysis of Four European Cohort Studies in the ESCAPE Study. Environ Health Perspect 2015; 123(6): 597-605. (FI: 8.443).

12.- Stitziel NO, (...), **Elosua R**, (...), Kathiresan S*, The Myocardial Infarction Genetics Consortium Investigators. Inactivating Mutations in NPC1L1 and Protection from Coronary Heart Disease. New Engl J Med 2014; 371(22): 2072-2082. (FI: 55.873).

13.- Foraster M*, Künzli N, Aguilera I, Rivera M, Agis D, Vila JS, Bouso L, Deltell A, Marrugat J, Ramos R, Sunyer J, **Elosua R**, Basagaña X. High Blood Pressure and Long-Term Exposure to Indoor Noise and Air Pollution from Road Traffic. Environ Health Perspect 2014; 122(11): 1193-1200. (FI: 7.977).

14.- Fuks K*, (...), **Elosua R**, (...), Tsai MY, Turunen AW, Peters A, Hoffmann R. Arterial Blood Pressure and Long-Term Exposure to Traffic-Related Air Pollution: An Analysis in the European Study of Cohorts for Air Pollution Effects (ESCAPE). Environ Health Perspect 2014; 122(9): 896-905. (FI: 7.977).

15.- Rivera M*, Basagaña X, Aguilera I, Foraster M, Agis D, de Groot E, Pérez-Grau L, Méndez MA, Bouso L, Targa J, Ramos R, Sala J, Marrugat J, **Elosua R**, Künzli N. Association between Long-Term Exposure to Traffic-Related Air Pollution and Subclinical Atherosclerosis: The REGICOR Study. Environ Health Perspect 2013; 121(2): 223-230. (FI: 7.029).

F-9 BIOGRAPHICAL SKETCH

NAME: MARIA FORASTER	TITLE: PHD	BIRTH DATE *(Month, Day, Year)* 02/27/1984

Education (*Begin with baccalaureate training and include postdoctoral training*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Barcelona, Spain	Master in	2008	Pharmaceutical
University Pompeu Fabra, Spain	Master Public	2009	Public Health
University Pompeu Fabra, Spain	PhD in	2013	Epidemiology
Swiss Tropical and Public Health Institute,	Postdoctoral	2017	Epidemiology

RESEARCH AND/OR PROFESSIONAL EXPERIENCE:

Maria Foraster holds a Master in Pharmacy, a Master in Public Health and a PhD in Epidemiology. She is interested in understanding the impact of transportation noise and urban co-exposures on the life-course. Her PhD at CREAL (2009-2013) focused on the evaluation of the long-term effects of noise and air pollution on cardiovascular diseases and on disentangling their health effects. In parallel to her thesis within the Spanish REGICOR cohort (Girona's Heart Registry), she led analyses for the ESCAPE project (European Study of Cohorts for Air Pollution Effects), participated in the European Noise and Health Network, and supervised and performed noise and air pollution exposure assessment and epidemiology analyses in a Tri-national European study (Tri-TABS). After her PhD, she was involved in the ERC funded project on children's brain development and air pollution (BREATHE). She planned the indoor-outdoor noise exposure assessment in schools and contributed to studying the effects of air pollution and traffic noise on children's neurodevelopment. In 2014 she started working as Postdoctoral researcher at the Swiss Tropical and Public Health Institute, Switzerland. There she has been involved in project supervision, analyses, publication and grant writing related to noise exposure assessment and noise epidemiology (SiRENE and SIAS projects, SAPALDIA and SNC cohorts). She has focused on the effects of transportation noise on sleep, cardiometabolic diseases, arterial stiffness, and lifestyles, considering co-exposures (air pollution and green space). Among others, she has also served as adviser for the upcoming World Health Organization Environmental Noise Guidelines and Air Pollution Guidelines (2014-2016). Recently, she obtained a Spanish Ministry Fellowship for returning postdoctoral scientists to work at the Barcelona Institute for Global Health, Spain.

List in chronological order of previous employment, until present

2017-	Senior Postdoctoral researcher, Barcelona Institute for Global Health (ISGlobal) (Former CREAL)
2014-2017	Postdoctoral researcher, Swiss Tropical and Public Health Institute, Basel (SwissTPH), Switzerland
2013-2014	Scientific collaborator, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain
2009-2013	PhD candidate, Centre for Research in Environmental Epidemiology (CREAL), Spain
2008-2009	Research assistant, Centre for Research in Environmental Epidemiology (CREAL), Spain
2008	Hospital pharmacy trainee, Université Livre de Bruxelles, Hôpital St Pièrre, Belgium.
2002-2007	Pharmacy assistant, community pharmacy, Spain

Honors and Awards

1. Outstanding Presentation Award, International Congress on Noise as a Public Health Problem (ICBEN), Zürich, Switzerland, 18-22 June 2017.
2. Juan de la Cierva Postdoctoral Fellowship, Spanish Ministry of Science and Innovation (2017-2018)
3. International Institute of Noise Control Engineering (I-INCE) Young Scientist Award, 41st

INTERNOISE conference, NY, USA, 19-22 Aug. 2012.

4. European Network on Noise and Health Young Researcher Exchange Program Grant (2010) to SwissTPH, Switzerland.
5. Instituto de Salud Carlos III PhD fellowship, Spanish Ministry of Science and Innovation (2009-2013).

List, in chronological order, the titles and complete references to recent representative publications.

Foraster, M., Eze, I.C., Schaffner, E., Vienneau, D., Héritier, H., Endes, S., et al. 2017. Exposure to road, railway, and aircraft noise and arterial stiffness in the SAPALDIA study: annual average noise levels and temporal noise characteristics. Environ. Health Perspect. (In Press).

Héritier H.*; Vienneau D.*; **Foraster M.**, Eze I.C., Schaffner E., Thiesse L., et al. *Equal contribution. 2017. Transportation noise exposure and cardiovascular mortality: a nationwide cohort study from Switzerland. Eur J Epidemiol 32:307–315.

Eze I.C., **Foraster M.**, Schaffner E., Vienneau D., Héritier H., Rudzik F., et al. 2017. Long-term exposure to transportation noise and air pollution in relation to incident diabetes in the SAPALDIA study. Int J Epidemiol.

Foraster, M., Eze, I.C., Vienneau, D., Brink, M., Cajochen, C., Caviezel, S., et al, 2016. Long-term transportation noise annoyance is associated with subsequent lower levels of physical activity. Environ Int 91, 341–349.

Fuks, K.B., Weinmayr, G., Basagaña, X., Gruzieva, O., Hampel, R., Oftedal, B., (…) **Foraster, M.**, et al. 2017. 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. 38, 983–990.

Morelli, X., **Foraster, M.**, Aguilera, I., Basagana, X., Corradi, E., Deltell, A., et al. 2015. Short-term associations between traffic-related noise, particle number and traffic flow in three European cities. Atmospheric Environment 103, 25–33.

Aguilera, I., **Foraster, M.**, Basagaña, X., Corradi, E., Deltell, A., Morelli, X., et al., 2015. Application of land use regression modelling to assess the spatial distribution of road traffic noise in three European cities. J Expo Sci Environ Epidemiol. 25, 97–105

Foraster, M., Basagaña, X., Aguilera, I., Rivera, M., Agis, D., Bouso, L., et al. 2014a. Association of long-term exposure to traffic-related air pollution with blood pressure and hypertension in an adult population-based cohort in Spain (the REGICOR study). Environ. Health Perspect. 122, 404–411.

Foraster, M., Künzli, N., Aguilera, I., Rivera, M., Agis, D., Vila, J., et al. 2014b. High blood pressure and long-term exposure to indoor noise and air pollution from road traffic. Environ. Health Perspect. 122, 1193–1200.

Fuks, K.B., Weinmayr, G., **Foraster, M.**, Dratva, J., Hampel, R., Houthuijs, D., et al. 2014. Arterial Blood Pressure and Long-Term Exposure to Traffic-Related Air Pollution: An Analysis in the European Study of Cohorts for Air Pollution Effects (ESCAPE). Environ. Health Perspect. 122, 896–905.

Rivera, M., Basagaña, X., Aguilera, I., **Foraster, M.**, Agis, D., de Groot, E., et al. 2013. Association between Long-Term Exposure to Traffic-Related Air Pollution and Subclinical Atherosclerosis: The REGICOR Study. Environ. Health Perspect. 121, 223–230.

Foraster, M., 2013. Is it traffic-related air pollution or road traffic noise, or both? Key questions not yet settled! Int J Public Health 58, 647–648.

Foraster, M., Deltell, A., Basagaña, X., Medina-Ramón, M., Aguilera, I., Bouso, L., et al. 2011. Local determinants of road traffic noise levels versus determinants of air pollution levels in a Mediterranean city. Environ. Res. 111, 177–183.

F-9 BIOGRAPHICAL SKETCH

NAME	TITLE	BIRTH DATE *(Month, Day, Year)*
Marc Guevara Vilardell	PhD	12/29/1986

Education (*Begin with baccalaureate training and include postdoctoral training*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Polytechnic University of Catalonia, Spain	Bsc	2010	Industrial Engineering
Polytechnic University of Catalonia, Spain	PhD	2014	Environmental Engineering

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: *Concluding with present position, list in chronological order previous employment, experience, and honors. List, in chronological order, the titles and complete references to recent representative publications, especially those most pertinent to this application.*

Dr. Marc Guevara is a postdoc researcher with 7 years' experience in the areas of Atmospheric Emissions and Air Quality. His main expertise includes geographic information systems (GIS), development of emission inventories, emission scenarios and emission models suitable for input to atmospheric models, high resolution air quality modeling and environmental impact assessment. In 2010 he was enrolled as research support engineer at the Earth Sciences Department of the Barcelona Supercomputing Center, and in 2015 he moved to the emission modeling postdoc researcher position. He is co-chair of the Emissions Working Group under the Forum for Air Quality Modelling in Europe (FAIRMODE) since 2015. He has coordinated the development and implementation of an air quality forecast system for the Secretariat of Environment of Mexico City (2015-2016) and he is currently coordinating the assessement of the impact of the 2011-2020 Programme to Improve Air Quality in the Valley of Mexico City. He is currently involved in an European Regional Development Fund Project (Report) and has participated in the FP7 Framework programme (APPRAISAL), as well as in several national technology transfer projects related with air quality impact assessment. He has coauthored 12 papers in international scientific journals, 1 book chapter and 8 communications to international conferences. He is currently co-directing a PhD student and he has acted as a reviewer of several international journals.

CURRENT POSITION
01/2015– Postdoctoral Researcher
Earth Sciences Department, Barcelona Supercomputing Center (BSC), Spain

PREVIOUS POSITION
2010-2014 Research Support Engineer
Earth Sciences Department, Barcelona Supercomputing Center (BSC), Spain

RECENT PUBLICATIONS

1. **Guevara, M.**, C. Tena, A. Soret, K. Serradell, D. Guzmán, A. Retama, P. Camacho, M. Jaimes-Palomera and A. Mediavilla, 2017. An emission processing system for air quality modelling in the Mexico City metropolitan area: Evaluation and comparison of the MOBILE6.2-Mexico and MOVES-Mexico traffic emissions. Science of The Total Environment, 584-585, 882-900
2. **Guevara, M.,** Lopez-Aparicio, S., Cuvelier, C., Tarrason, L., Clappier, A., Thunis, P. (2017). A benchmarking tool to screen and compare bottom-up and top-down atmospheric emission inventories. Air Quality, Atmosphere & Health, 10, 627-642,
3. Thunis, P., Degraeuwe, B., Cuvelier, K., **Guevara, M.**, Tarrason, L., Clappier, A., 2016. A novel approach to screen and compare emission inventories, Air Quality Atmosphere & Health, 9.
4. Borrego, C., Monteiro, A., Martins, H., Ferreira, J., Fernandes, A.P., Rafael, S., Miranda, A.I., **Guevara, M.**, Baldasano, J.M., 2015. Air quality plan for ozone: an urgent need for North Portugal. Air Quality Atmosphere & Health. doi: 10.1007/s11869-015-0352-5.
5. **Guevara, M.**, Soret, A., Arévalo, G., Martínez, F., Baldasano, J.M., 2014. Implementation of plume rise and its impacts on emissions and air quality modelling, Atmospheric Environment, 99, 618-629.
6. Soret, A., **Guevara, M.**, Baldasano, J.M., 2014. The potential impacts of electric vehicles on air quality in the urban areas of Barcelona and Madrid (Spain), Atmospheric Environment, 99, 51-63.
7. **Guevara, M.**, Pay, M.T., Martínez, F., Soret, A., Denier van der Gon, H.A.C., Baldasano, J.M., 2014. Inter-comparison between HERMESv2.0 and TNO-MACC-II emission data using the CALIOPE air quality system (Spain), Atmospheric Environment, 98, 134-145.
8. Pay, M.T., Martínez, F., **Guevara, M.**, Baldasano, J.M., 2014. Air quality forecasts at kilometer scale grid over Spanish complex terrains. Geoscientific Model Development, 7, 1979-1999.
9. Baldasano, J.M., Soret, A., **Guevara, M.**, Martínez, F., Gassó, S., 2014. Integrated assessment of air pollution using observations and modelling in Santa Cruz de Tenerife (Canary Islands). Science of the Total Environment, 473–474, 576-588
10. **Guevara, M.**, Martínez, F., Arévalo, G., Gassó, S., Baldasano, J.M., 2013. An improved system for modelling Spanish emissions: HERMESv2.0, Atmospheric Environment 81, 209-221.

F-9 BIOGRAPHICAL SKETCH

Name Jaume Marrugat	**Title** Doctor	**BIRTH DATE** *(Month, Day, Year)* 12/08/1954

Education (*Begin with baccalaureate training and include postdoctoral training*)

INSTITUTION AND LOCATION	**DEGREE**	**YEAR CONFERRED**	**FIELD OF STUDY**
Universitat Autònoma de Barcelona	Medicine & Surgery	1980	Medicine & Surgery
Universitat Autònoma de Barcelona	Medicine & Surgery	1990	Medicine & Surgery
Ministerio de Educación y Ciencia	Specialist Public Health & Preventive Medicine	2003	Medicine & Public Health

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: *Concluding with present position, list in chronological order previous employment, experience, and honors. List, in chronological order, the titles and complete references to recent representative publications, especially those most pertinent to this application.*

2012 – act.	Senior Consultant 3	IMIM-PSMAR
2008 –2014	RICAD Research Program Director	IMIM-PSMAR
2007 – act.	REGICOR Group Coordinator	IMIM-PSMAR
2003-2007	Preventive Medicine and Public Health Tutor	UPF, Hospital del Mar, IMIM
1996-2007	Associated Professor	UAB
1992 – 2007	Head of Lipids&CV Epidemiology Research Unit	IMIM-PSMAR
1989 – 1992	Senior Medicine Technician	IMIM-PSMAR
1982 – 1988	Medical Director	Hospital de Lloret de Mar

PUBLICATIONS (selected from a total of 355):

1.- Molina L, Sarmiento M, Peñafiel J, Donaire-González D, Garcia-Aymerich J, Gómez-Pérez MA, Ble M, Ruiz-Bustillo S, Francés A, Schröder H, **Marrugat J,** Elosua R[*], Validation of the Regicor Short Physical Activity Questionnaire for the Adult Population, PLoS ONE 2017; 12(1): e0168148. (FI: 3.057).

2.- NCD Risk Factor Collaboration (NCD-RisC) (...,Elosua R, **Marrugat J**, Porta M,...). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants. Lancet 2017; 389(10064): 37-55. (FI: 44.002).

3.- Baena-Diez JM, Peñafiel J, Subirana I, Ramos R, Elosua R, Marin-Ibañez A, Guembe MJ, Rigo F, Tormo-Díaz MJ, Moreno-Iribas C, Cabré JJ, Segura A, García-Lareo M, Gómez de la Cámara A, Lapetra J, Quesada M, **Marrugat J**, Medrano MJ, Berjón J, Frontera G, Gavrila D, Barricarte A, Basora J, García J, Pavone NC, Lora-Pablos D, Mayoral E, Franch J, Mata M, Frances A, Grau M*, on behalf of the FRESCO Investigators. Risk of Cause-Specific Death in Individuals With Diabetes: A Competing Risks Analysis. Diabetes Care 2016; 39(11): 1987-1995. (FI: 8.934).

4.- Elosua R*, Lluís-Ganella C, Subirana I, Havulinna A, Läll K, Lucas G, Sayols-Baixeras S, Pietilä A, Alver M, Cabrera de León A, Sentí M, Siscovick D, Melander O, Fischer K, Salomaa V, **Marrugat J** Cardiovascular Risk Factors and Ischemic Heart Disease: Is the Confluence of Risk Factors Greater than the Parts? A Genetic Approach. Circ Cardiovasc Genet 2016; 9(3): 279-286. (FI: 3.719).

5.- Di Cesare M, Bentham J, Stevens GA, Zhou B, Danaei G, Lu Y, Bixby H, Cowan MJ, Riley LM, Hajifathalian K, Fortunato L, Taddei C, Bennett JE, Ikeda N, Khang YH, Kyobutungi C, Laxmaiah A, Li Y, Lin HH, Miranda JJ, Mostafa A, Turley ML, Paciorek CJ, Gunter M, Ezzati M*, NCD Risk Factor Collaboration (NCD-RisC) (...,**Marrugat J**, Porta M,...). Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. Lancet 2016; 387(10026): 1377-1396. (FI: 44.002).

6.- Marcelino-Rodríguez I, Elosua R, Rodríguez-Pérez MC, Fernández-Berges DJ, Guembe MJ, Vega-Alonso T, Felix FJ, Almeida-González D, Ortiz-Marrón H, Rigo F, Lapetra J, Gavrila D, Segura A, Fitó M, Peñafiel J, **Marrugat J,** Cabrera de León A*. On the problem of type 2 diabetes-related mortality in the Canary Islands, Spain. The DARIOS Study. Diabetes Res Clin Pract 2016; 111: 74-82. (FI: 3.045).
7.- Dégano IR, Salomaa V, Veronesi G, Ferrieres J, Kirchberger I, Laks T, Havulinna AS, Ruidavets JB, Ferrario MM, Meisinger C, Elosua R, **Marrugat J***, The Acute Myocardial Infarction Trends in Europe (AMITIE) Study Investigators. Twenty-five-year trends in myocardial infarction attack and mortality rates, and case-fatality, in six European populations. Heart 2015; 101(17): 1413-1421. (FI: 5.693).

8.- Pérez-Grau L*, Wolf K, Hennig F, Pennell J, Basagaña X, Aguilera I, Agis D, Beelen R, Brunekreef B, Cyrys J, Fuks K, Adam M, Baldassare D, Cirach M, Elosua R, Dratva J, Hampel R, Koenig W, **Marrugat J**, de Faire U, Pershagen G, Probst-Mensch NM, de Nazelle A, Nieuwenhuijsen M, Rathmann W, Rivera M, Seissler J, Schindler C, Thiery J, Hoffmann R, Peters A, Künzli N. Air Pollution and Atherosclerosis: A Cross-Sectional Analysis of Four European Cohort Studies in the ESCAPE Study. Environ Health Perspect 2015; 123(6): 597-605. (FI: 8.443).

9.- Pérez-Grau L*, Wolf K, Hennig F, Pennell J, Basagaña X, Aguilera I, Agis D, Beelen R, Brunekreef B, Cyrys J, Fuks K, Adam M, Baldassare D, Cirach M, Elosua R, Dratva J, Hampel R, Koenig W, **Marrugat J,** de Faire U, Pershagen G, Probst-Mensch NM, de Nazelle A, Nieuwenhuijsen M, Rathmann W, Rivera M, Seissler J, Schindler C, Thiery J, Hoffmann R, Peters A, Künzli N. Air Pollution and Atherosclerosis: A Cross-Sectional Analysis of Four European Cohort Studies in the ESCAPE Study. Environ Health Perspect 2015; 123(6): 597-605. (FI: 8.443).

10.- Stitziel NO, (...), **Marrugat J**, (...), Kathiresan S*, The Myocardial Infarction Genetics Consortium Investigators. Inactivating Mutations in NPC1L1 and Protection from Coronary Heart Disease. New Engl J Med 2014; 371(22): 2072-2082. (FI: 55.873).

11.- Foraster M*, Künzli N, Aguilera I, Rivera M, Agis D, Vila JS, Bouso L, Deltell A, **Marrugat J**, Ramos R, Sunyer J, Elosua R, Basagaña X. High Blood Pressure and Long-Term Exposure to Indoor Noise and Air Pollution from Road Traffic. Environ Health Perspect 2014; 122(11): 1193-1200. (FI: 7.977).

12.- Fuks K*, (...), **Marrugat J**, (...), Tsai MY, Turunen AW, Peters A, Hoffmann R. Arterial Blood Pressure and Long-Term Exposure to Traffic-Related Air Pollution: An Analysis in the European Study of Cohorts for Air Pollution Effects (ESCAPE). Environ Health Perspect 2014; 122(9): 896-905. (FI: 7.977).

F-9 BIOGRAPHICAL SKETCH

Name Susanne Moebus	**Title** Prof. Dr. rer. nat., MPH	**BIRTH DATE** *(Month, Day, Year)* 06/09/1958

Education

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Department of Plant and Cell Biology, University of Bremen,	Master of Biology	1988	Biology
Department of Plant and Cell Biology, University of Bremen,	PhD (Dr. rer. nat.)	1994	Biology
Faculty for Public Health, University of Bielefeld, Germany	Master of Public Health (MPH)	1997	Public Health

RESEARCH AND/OR PROFESSIONAL EXPERIENCE:

Susanne Moebus is Professor of Urban Epidemiology at the University of Duisburg-Essen, where she represents the medical faculty in the Urban Systems master's program. She is Director of the Centre for Urban Epidemiology (CUE) in the Institute of Medical Informatics, Biometry and Epidemiology (IMIBE) at the University Clinics of Essen, where she is also Deputy Director. She teaches clinical environmental medicine and epidemiology to medical students at the University Clinics of Essen and several graduate seminars to masters students at the University of Duisburg-Essen. Besides urban epidemiology her research interests include cardiovascular epidemiology, prevention and health promotion. Professor Moebus is Co-PI of the German National Cohort Study at the Study Centre Essen, PI of the 1000Brain Study, the Heinz Nixdorf Recall Study and the Heinz Nixdorf Recall MultiGenerationStudy. She has been involved in several research and development projects funded by European Union, the German Research Foundation and numerous other public and private funding bodies. She is a member of several large national and international research consortia, and has published widely in international peer-reviewed journals.

1992-1993 Research associate, Institute for Cell Biology, Biochemistry and Biotechnology, University of Bremen

1996 Research associate, Chartered Institute of Environmental Health (CIEH), London

1996-1999 Research associate, Institute for Medical Informatics, Biometry and Epidemiology (IMIBE), University Clinics Essen, Germany

1999-2012 Head, Unit of Cardiovascular Epidemiology & Prevention and Head, Project Group Complementary Medicine, IMIBE, University Clinics Essen, Germany

2008 Habilitation and venia legendi for Epidemiology and Medical Biometry at the Medical Faculty of the University of Duisburg-Essen, Germany

Since 2012 Full professor for Urban Epidemiology, University Hospital Essen, University of Duisburg-Essen. Director of the Center of Urban Epidemiology, and Deputy Director of IMIBE

Activities in the Scientific Community

2002-2006 Member of the Steering Committee of Complementary and Alternative Medicine

Since 2002 Editorial Advisory Board of Research of the Journal of Complementary and Classical Natural Medicine

2002-2010 Speaker Working Group Cardiovascular Epidemiology of the German Society of Epidemiology (DGEpi), German Society of Medical Informatics, Biometry and Epidemiolgy (GMDS) and German Society of Social Medicine and Prevention (DGSMP)

Since 2009 Member of the *Main Research Area Urban System,* University of Duisburg-Essen; spokesperson for "Medical Sciences". Responsible for "Urban Health" of the Mastersprogram "Urban Systems"

Since 2009 Member of the Steering and Use & Access Committee of the *German National Cohort*
Since 2016 President of the German Society for Social Medicine and Prevention (DGSMP)
2016 Host of Annual Conference of the German Society for Social Medicine and Prevention (DGSMP)

Selected Publications

Tzivian L, Dlugaj M, Winkler A, Weinmayr G, Hennig F, Fuks KB, Vossoughi M, Schikowski T, Weimar C, Erbel R, Jöckel KH, **Moebus S**, Hoffmann B. Long-Term Air Pollution and Traffic Noise Exposures and Mild Cognitive Impairment in Older Adults: A Cross-Sectional Analysis of the HNR Study. Environ Health Perspect. 2016,124:1361.

Myocardial Infarction Genetics and CARDIoGRAM Exome Consortia Investigators. Stitziel NO, …, **Moebus S**, …, Willer CJ, Kathiresan S, Deloukas P, Samani NJ, Schunkert H. Coding Variation in ANGPTL4, LPL, and SVEP1 and the Risk of Coronary Disease. N Engl J Med. 2016;374:1134-44

McClelland RL, Jorgensen NW, Budoff M, Blaha MJ, Post WS, Kronmal RA, Bild DE, Shea S, Liu K, Watson KE, Folsom AR, Khera A, Ayers C, Mahabadi AA, Lehmann N, Jöckel KH, **Moebus S**, Carr JJ, Erbel R, Burke GL. 10-Year Coronary Heart Disease Risk Prediction Using Coronary Artery Calcium and Traditional Risk Factors: Derivation in the MESA (Multi-Ethnic Study of Atherosclerosis) With Validation in the HNR Study and the DHS (Dallas Heart Study). J Am Coll Cardiol. 2015;66:1643-53.

Weinmayr G, Hennig F, Fuks K, Nonnemacher M, Jakobs H, Möhlenkamp S, Erbel R, Jöckel KH, Hoffmann B, **Moebus S**. Long-term exposure to fine particulate matter and incidence of type 2 diabetes mellitus in a cohort study: effects of total and traffic-specific air pollution. Environ Health. 2015;14:53

Winkler A, Dlugaj M, Weimar C, Jöckel KH, Erbel R, Dragano N, Moebus S. Association of diabetes mellitus and mild cognitive impairment in middle-aged men and women. J Alzheimers Dis. 2014; 42:1269-77.

Hennig F, Fuks K, **Moebus S**, Weinmayr G, Memmesheimer M, Jakobs H, Bröcker-Preuss M, Führer-Sakel D, Möhlenkamp S, Erbel R, Jöckel KH, Hoffmann B. Association between Source-Specific Particulate Matter Air Pollution and hs-CRP: Local Traffic and Industrial Emissions. Environ Health Perspect. 2014 Apr 22.

Kälsch H, Hennig F, **Moebus S**, Möhlenkamp S, Dragano N, Jakobs H, Memmesheimer M, Erbel R, Jöckel KH, Hoffmann B. Are air pollution and traffic noise independently associated with atherosclerosis: the HNR Study. Eur Heart J. 2014;35:853-60

Icks A, Albers B, Haastert B, Pechlivanis S, Pundt N, Slomiany U, Erbel R, Jöckel KH, Kruse J, Kulzer B, Nowotny B, Herder C, Giani G, **Moebus S**. Risk for high depressive symptoms in diagnosed and previously undetected diabetes: 5-year follow-up results of the Heinz Nixdorf Recall study. PLoS One. 2013; 8(2):e56300

Fuks K, **Moebus S**, Hertel S, Viehmann A, Nonnemacher M, Dragano N, Möhlenkamp S, Jakobs H, Kessler C, Erbel R, Hoffmann B; Heinz Nixdorf Recall Study Investigative Group. Long-Term Urban Particulate Air Pollution, Traffic Noise and Arterial Blood Pressure. Environ Health Perspect. 2011 Dec;119(12):1706-11.

Moebus S, Göres L, Lösch C, Jöckel KH. Impact of time since last caloric intake on blood glucose levels. Eur J Epidemiol. 2011; 26:719-28

Bauer M, **Moebus S**, Möhlenkamp S, Dragano N, Nonnemacher M, Fuchsluger M, Kessler C, Jakobs H, Memmesheimer M, Erbel R, Jöckel KH, Hoffmann B. Urban particulate matter air pollution is associated with subclinical atherosclerosis – results from the HNR Study. JACC 2010 23;56:1803-8.

Moebus S, Stang A, Möhlenkamp S, Dragano N, Schmermund A, Slomiany U, Hoffmann B, Bauer M, Bröcker M, Mann K, Siegrist J, Erbel R, Jöckel KH. Association of impaired fasting glucose and coronary artery calcification as a marker of subclinical atherosclerosis in a population-based cohort. Results of the HNR Study. Diabetologia 2009; 52:81-9.

Dragano N, Hoffmann B, Stang A, **Moebus S**, Verde PE, Weyers S, Möhlenkamp S, Schmermund A, Mann K, Jöckel KH, Erbel R, Siegrist J. Subclinical coronary atherosclerosis and neighbourhood deprivation in an urban region. Eur J Epidemiol. 2009; 24:25- 35

F-9 BIOGRAPHICAL SKETCH

NAME	TITLE	BIRTH DATE
Mark Nieuwenhuijsen	Professor	24-01-1965

Education

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Agricultural University of Wageningen, Wageningen, Holland	BSc/MSc	1989	Environmental Science with specialization in health
Department of Occupational and Environmental Medicine National Heart and Lung Institute, University of London	PhD	1993	Occupational Hygiene/Epidemiology
Department of Epidemiology and Preventive Medicine, University of California Davis, Davis, CA. USA.	Post doc	1996	Epidemiology

RESEARCH AND/OR PROFESSIONAL EXPERIENCE:

2007- Research Professor at ISGlobal, formerly the Centre for Environmental Epidemiology (CREAL), Barcelona

2003- 2006 Reader at the Department of Epidemiology and Public Health, and Health risk assessment, management and policy option convenor, Imperial College of Science, Technology and Medicine, London.

2000- 2003 Senior Lecturer at the Department of Environmental Science and Technology, and Health risk assessment, management and policy option convenor, Imperial College of Science, Technology and Medicine, London.

1996- 2000 Lecturer at the TH Huxley School of Environment, Earth Sciences and Engineering, and Health risk assessment, management and policy option convenor, Imperial College of Science, Technology and Medicine, London.

References

Nieuwenhuijsen M, Khreis H. Green space is important for health. The Lancet. 2017 Feb 18;389(10070):700

Nieuwenhuijsen MJ, Khreis H, Triguero-Mas M, Gascon M, Dadvand P. Fifty Shades of Green: Pathway to Healthy Urban Living. Epidemiology. 2017;28: 63–71

de Keijzer C, Agis D, Ambrós A, Arévalo G, Baldasano JM, Bande S, Barrera-Gómez J, Benach J, Cirach M, Dadvand P, Ghigo S, Martinez-Solanas È, **Nieuwenhuijsen M**, Cadum E, Basagaña X; MED-HISS Study group. The association of air pollution and greenness with mortality and life expectancy in Spain: A small-area study. Environ Int. 2017 ;99:170-176

Gascon M, Triguero-Mas M, Martínez D, Dadvand P, Rojas-Rueda D, Plasència A, **Nieuwenhuijsen MJ**. Residential green spaces and mortality: A systematic review. Environ Int. 2015; 2: 86:60-67

Tamosiunas A, Grazuleviciene R, Luksiene D, Dedele A, Reklaitiene R, Baceviciene M, Vencloviene J, Bernotiene G, Radisauskas R, Malinauskiene V, Milinaviciene E, Bobak M, Peasey A, **Nieuwenhuijsen MJ**. Accessibility and use of urban green spaces, and cardiovascular health: findings from a Kaunas cohort study. Environ Health. 2014; 13 :20

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F-9 BIOGRAPHICAL SKETCH

Name Ester Orban	**Title** M.Sc.	**BIRTH DATE** *(Month, Day, Year)* 10/28/1987

Education (*Begin with baccalaureate training and include postdoctoral training*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
University of Bremen	B. A.	2010	Public Health
Ludwig-Maximilians-University Munich	M. Sc.	2012	Epidemiology

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: *Concluding with present position, list in chronological order previous employment, experience, and honors. List, in chronological order, the titles and complete references to recent representative publications, especially those most pertinent to this application.*

Ester Orban holds a Master's degree in Epidemiology. She joined the Centre for Urban Epidemiology (CUE) in 2012. Her main research interest is in effects of the urban environment, particularly traffic noise and surrounding greenness, on mental and general health outcomes. Further interests lie in topics of environmental justice and the role of socioeconomic status in the context of urban health. Next to her PhD project, she is involved in teaching Epidemiology for medical students at the University Clinics and project seminars within the Master program *Urban Systems* at the University of Duisburg Essen. She further studies the associations of air pollution with the adaptive immune system within the scope of the DFG-funded Airflamm III project.

Employment until present

10/2008 – 07/2010
University of Bremen
Student associate, tutor for Epidemiology
Teaching

08/2011 – 12/2011 **Helmholtz Centre Munich, Institute for Epidemiology II**
Internship
- Preparation of a study protocol for a meta-analysis
- Systematic literature review
  Analysis and report

11/2011 – 9/2012 **IMS Health GmbH, Munich**
Student associate
- Helping with reports and presentations of pharmaceutical trial results
- Helping with AMNOG dossiers

Since 10/2012 **Centre for Urban Epidemiology (CUE), Institute for Medical Informatics, Biometry and Epidemiology, University Hospital Essen, University of Duisburg-Essen, Germany**

Research associate and doctoral candidate

- Research and analysis in the field of environmental and urban epidemiology, mental and general health
- Preparing of publications, reports and abstracts
- Presenting results at scientific conferences
- Teaching
- Schooling and supervision of study personnel

List of publications

E. Orban, R. Sutcliffe, N. Dragano, K.-H. Jöckel, S. Moebus. Residential Surrounding Greenness, Self-Rated Health and Interrelations with Aspects of Neighborhood Environment and Social Relations. J Urban Health (2017). doi:10.1007/s11524-016-0112-3.

E. Orban und R. Sutcliffe, Salman Ahmed, S. Moebus. Potentials of spatial epidemiology in the Ruhr Metropolis. [German] Public Health Forum 2016; 24(4): 281–284, DOI: 10.1515/pubhef-2016-2134.

E. Orban, K. McDonald, R. Sutcliffe, B. Hoffmann, K.B. Fuks, N. Dragano, A. Viehmann, R. Erbel, K.-H. Jöckel, N. Pundt, S. Moebus. Residential Road Traffic Noise and High Depressive Symptoms after Five Years of Follow-up: Results from the Heinz Nixdorf Recall Study. Environ Health Perspect 2016; 124:578–585; http://dx.doi.org/10.1289/ehp.1409400.

R. Sutcliffe, **E. Orban**, K. McDonald, S. Moebus. The German Energiewende – a matter for health? Eur J Public Health. 2015 Dec 29, DOI: 10.1093/eurpub/ckv212.

B. Bisdorff, K. Kenn, D. Nowak, J. Schlichtiger, J. Bäuml, **E. Orban**, K. Radon. Asthma and vocal cord dysfunction related symptoms in the general population-a pilot study. Ann Allergy Asthma Immunol. 2014 Sep 17. pii: S1081-1206(14)00590-0, DOI: 10.1016/j.anai.2014.08.009

E. Orban, S. Schwab, B. Thorand, C. Huth. Association of iron indices and type 2 diabetes: a meta-analysis of observational studies. Diabetes Metab Res Rev 2014 Jul; 30(5):372-94. DOI: 10.1002/dmrr.2506

F-9 BIOGRAPHICAL SKETCH

NAME	**TITLE**	**BIRTH DATE** *(Month, Day, Year)*
María Teresa Pay	Researcher	04/20/1982

Education (*Begin with baccalaureate training and include postdoctoral training*)

INSTITUTION AND LOCATION	**DEGREE**	**YEAR CONFERRED**	**FIELD OF STUDY**
University of Murcia, Spain	Bsc	2006	Chemical Engineering
Technical University of Catalonia, Spain	Msc	2008	Environmental Engineering
Technical University of Catalonia, Spain	PhD	2011	Environmental Engineering
L'École Polytechnique, Palaiseau, France	PostDoc	2013	Environmental Engineering

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: *Concluding with present position, list in chronological order previous employment, experience, and honors. List, in chronological order, the titles and complete references to recent representative publications, especially those most pertinent to this application.*

Dr Pay's research activities are focused on the use of chemical transport model (CTM) to understand better and predict the chemical composition of the atmosphere, and its effects on air quality (AQ), health and ecosystems. During her PhD, she developed profound skills on atmospheric chemistry and AQ modelling at regional and urban scale using cutting-edge High-Performance Computing. In 2011, she got the Special Doctoral Award by the Technical University of Catalonia for her PhD. Her PhD contributed to implement an AQ forecast system at high spatial and temporal resolution for Spain (CALIOPE system, www.bsc.es/caliope) founded by the Spanish Environmental Ministry. These works have allowed her to be involved in CTM inter-comparison exercises at EU scale (e.g. EURODELTA). After her PhD, she moved to the Laboratoire of Météorologie Dynamique (L'École Polytechnique, Palaiseau) where she studied in-depth the relationship between AQ and synoptic circulation patterns to explain in what extends meteorological situations can explain air pollution dynamic. During last years, she have focused my research on determining the contribution of emission from activity sources to air pollutant concentrations, so she studied the potential of the source apportionment (SA) algorithms implemented in CTM, and she moved to the U.S. Environmental Protection Agency to learn how to run and interpreted them. Now at the Barcelona Supercomputing Center, as part of the Earth Sciences Department, she is using SA techniques at high spatial and temporal resolution to understand air pollution dynamic of secondary pollutants (PM and O_3) in Europe. Through these experiences, she has participated as a scientific expert in the Forum for Air Quality Modelling (FAIRMODE) to harmonise the use of SA techniques in EU. Also, she takes part of the modelling group working at the UNECE Convention on Long-range Transboundary Air Pollution Task Force on Measurements and Modelling (TFMM) analyzing the trends of AQ in Europe to assess the efficiency of air pollution mitigation strategies over the past 20 years. Furthermore, she has been involved in a range of different AQ research projects (10 national and 4 international projects), which illustrate the impressive breadth of her experience and research training to date on AQ, as well as her ability to acquire new search knowledge. Her capacity to manage research has already been demonstrated by the successful supervision of a 1 PhD student and the coordination of four projects as Principal Investigator. Currently, she is the PI of the PAISA project, funded by the Spanish Ministry of Economy and Competitiveness (MINECO, CGL2016-75725-R).

Dr Pay is a young, experienced and knowledgeable researcher (OrcID: 0000-0001-7985-9253) who has shown great commitment to her research so far and is clearly determined to succeed in science. This is evidenced by the 20 publications in international peer-reviewed journals (5 publications as the first author), more than 261 citations and an h-index of 8 (source SCOPUS), with long lists of co-authors, and as well as the various highly prestigious fellowships she got in competitive calls (1 pre-doc and 1 Marie Curie post-doc).

Selected publications:

1. **Pay, M.T.**, Piot M, Jorba O, Basart S, Gassó S, Jiménez-Guerrero P, Gonçalves M, Dabdub D, Baldasano JM, 2010. A full year evaluation of the CALIOPE-EU air quality system in Europe for 2004: a model study. Atmos Environ, 44, 3322-3342.
2. **Pay, M.T.**, Jiménez-Guerrero P, Baldasano JM, 2011. Implementation of resuspension from paved roads for the improvement of CALIOPE air quality system in Spain. Atmos Environ, 45, 802-807.
3. Baldasano JM, **Pay, M.T.**, Jorba O, Gassó S, Jiménez-Guerrero P, 2011. An annual assessment of air quality with the CALIOPE modeling system over Spain. Sci Total Environ, 409, 2163-2178.
4. Jiménez-Guerrero P., Jorba O, **Pay, M.T.**, Montávez JP, Jerez S, Gomez-Navarro JJ, Baldasano JM, 2011. Comparison of two different sea-salt aerosol schemes as implemented in air quality models applied to the Mediterranean basin. Atmos Chem Phys, 11, 4833-4850.
5. **Pay, M.T.**, Jiménez-Guerrero P, Jorba O, Basart S, Pandolfi M, Querol X, Baldasano JM, 2012. Spatio-temporal variability of levels and speciation of particulate matter across Spain in the CALIOPE modeling system. Atmos Environ, 46, 376-396.
6. Basart S, **Pay, M.T.**, Jorba O, Pérez C, Jiménez-Guerrero P, Schulz M, Baldasano JM, 2012. Aerosol in the CALIOPE air quality modelling system: validation and analysis of PM levels, optical depths and chemical composition over Europe. Atmos Chem Phys, 12, 3363-3392.
7. **Pay, M.T.**, Jiménez-Guerrero P, Baldasano JM, 2012. Assessing sensitivity regimes of secondary inorganic aerosol formation in Europe with the CALIOPE-EU modeling system. Atmos Environ, 51, 146-164.
8. Aguilera, I., Basagaña, X., **Pay, M.T**., Agis, D., Bouso, L., Foraster, M., Rivera, M., Baldasano, J.M., Künzli, N., 2013. Evaluation of the CALIOPE air quality forecasting system for epidemiological research: the example of NO2 in the province of Girona (Spain). Atmos Environ., 72, 134-141.
9. Guevara, M., **Pay, M.T**., Martínez, F., Soret, A., Denier van der Gon, H.A.C., Baldasano, J.M., 2014. Inter-comparison between HERMESv2.0 and TNO-MACC-II emission data using the CALIOPE air quality system (Spain). Atmos. Environ., 98, 134-145.
10. **Pay, M.T**., Martínez, F., Guevara, M., Baldasano, J.M., 2014. Air quality forecasts at kilometer scale grid over Spanish complex terrains. Geosci. Model Dev., 7, 1979–1999.
11. Valverde, V., **Pay, M.T**., Baldasano, J.M., 2014. Circulation-type classification derived on a climatic basis to study air quality dynamics over the Iberian Peninsula. International Journal of Climatology, doi: 10.1002/joc.4179.
12. Valverde, V., **Pay, M.T.** and Baldasano, J.M., 2015. A model-based analysis of SO2 and NO2 dynamics from coal-fired power plants under representative synoptic circulation types over the Iberian Peninsula. *Scienc. Tot. Environ*., 541, 701-713.
13. Valverde, V., **Pay, M.T.** and J.M. Baldasano, 2015. Ozone attributed to Madrid and Barcelona on-road transport emissions: characterization of plume dynamics over the Iberian Peninsula. *Scienc. Tot. Environ*, 543, 670-682, doi:10.1016/j.scitotenv.2015.11.070.

F-9 BIOGRAPHICAL SKETCH

NAME	TITLE	BIRTH DATE *(Month, Day, Year)*
Carlos Pérez García-Pando	PhD	25/06/1977

Education (*Begin with baccalaureate training and include postdoctoral training*)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Polytechnic University of Catalonia	Msc	2001	Industrial Engineering
École Centrale Paris	Msc	2001	Ingénieur des Arts et Manufactures
Polytechnic University of Catalonia	PhD	2006	Environmental Engineering

RESEARCH AND/OR PROFESSIONAL EXPERIENCE: *Concluding with present position, list in chronological order previous employment, experience, and honors. List, in chronological order, the titles and complete references to recent representative publications, especially those most pertinent to this application.*

CURRENT POSITIONS

10/2016– **Head of the Atmospheric Composition Group**
AXA Professor on Sand and Dust Storms
Ramon y Cajal Researcher
Earth Sciences Department, Barcelona Supercomputing Center (BSC), Spain

PREVIOUS POSITIONS

2011-2016 **Associate Research Scientist**
NASA Goddard Institute for Space Studies, New York
Department of Applied Physics and Applied Math, Columbia University, New York

2009-2011 **Earth Institute Fellow**
The Earth Institute at Columbia University, New York
NASA Goddard Institute for Space Studies, New York
International Research Institute for Climate and Society, New Jersey

2009 **Visiting Scientist**
NOAA National Centers for Environmental Prediction, Camp Springs, Maryland.

2006-2009 **Research Scientist**
Mineral Dust Group Leader
Earth Sciences Department, Barcelona Supercomputing Center, Spain

COMPETITIVE FELLOWSHIPS, AWARDS, PRIZES AND DISTINCTIONS

2016 – 2030 **AXA Chair on Sand and Dust Storms**. Endowment of EUR 1.7 million awarded by the AXA Research Fund to support my research program at BSC, Spain.

2016 – 2020 **Ramon y Cajal Fellowship** awarded by the Ministry of Economy, Industry and Competitiveness, Spain (ranked #1 in Earth Sciences)

2014 Co-author of the Best Publication of 2014 at NASA Goddard Institute for Space Studies

2014 Best Science Brief of 2014 at NASA Goddard Institute for Space Studies

2009 – 2011 **Earth Institute Fellowship** (~5% success rate) awarded by the Earth Institute at

	Columbia University, New York.
2009	Mobility grant José Castillejo awarded by the Ministry of Science and Innovation, Spain,
2001 – 2005	PhD Thesis fellowship awarded by the Polytechnic University of Catalonia, Spain.
2007	Poster presentation prize at the 11th International Conference on Harmonisation within atmospheric dispersion modelling for atmospheric purposes.
1998 – 2000	EU Fellowship to obtain the double Spanish-French Engineering degree at the École Centrale Paris, France

AEROSOL-CHEMISTRY MODEL DEVELOPER

BSC-DREAM8b model, MONARCH (NMM/BSC-CTM), NASA Earth System ModelE, Dust forecasts (http://sds-was.aemet.es, http://dust.aemet.es), Air quality forecasts (http://www.bsc.es/caliope/es)

10 RECENT PUBLICATIONS (H-Index 28, ~3096 citations google scholar)

1. Di Tomaso, E., N.A.J. Schutgens, O. Jorba, and **C. Pérez García-Pando,** 2017: Assimilation of MODIS Dark Target and Deep Blue observations in the dust aerosol component of NMMB-MONARCH version 1.0. Geosci. Model Dev., in press. 2017
2. Badia, A., O. Jorba, A. Voulgarakis, D. Dabdub, **C. Pérez García-Pando,** A. Hilboll, M. Gonçalves, and Z. Janjic, 2017: Description and evaluation of the Multiscale Online Nonhydrostatic AtmospheRe CHemistry model (NMMB-MONARCH) version 1.0: Gas-phase chemistry at global scale. Geosci. Model Dev., 10, 609-638, doi:10.5194/gmd-10-609-2017. 2016
3. Bell, J.E., S.C. Herring, L. Jantarasami, C. Adrianopoli, K. Benedict, K. Conlon, V. Escobar, J. Hess, J. Luvall, **C. Pérez García-Pando**, D. Quattrochi, J. Runkle, and C.J. Schreck, III, 2016: Ch. 4: Impacts of extreme events on human health. In The Impacts of Climate Change on Human Health in the United States: A Scientific Assessment. A. Crimmins, J. Balbus, J.L. Gamble, C.B. Beard, J.E. Bell, D. Dodgen, R.J. Eisen, N. Fann, M.D. Hawkins, S.C. Herring, L. Jantarasami, D.M. Mills, S. Saha, M.C. Sarofim, J. Trtanj, and L. Ziska, Eds. U.S. Global Change Research Program, 99-128, doi:10.7930/J0BZ63ZV.
4. **Pérez García-Pando, C.,** R.L. Miller, J.P. Perlwitz, S. Rodríguez, and J.M. Prospero, 2016: Predicting the mineral composition of dust aerosols: Insights from elemental composition measured at the Izaña Observatory. Geophys. Res. Lett., 43, no. 19, 10520-10529, doi:10.1002/2016GL069873.2015
5. Perlwitz, J.P., **C. Pérez García-Pando,** and R.L. Miller, 2015: Predicting the mineral composition of dust aerosols — Part 1: Representing key processes. Atmos. Chem. Phys., 15, 11593-11627, doi:10.5194/acp-15-11593-2015.
6. Perlwitz, J.P., **C. Pérez García-Pando,** and R.L. Miller, 2015: Predicting the mineral composition of dust aerosols — Part 2: Model evaluation and identification of key processes with observations. Atmos. Chem. Phys., 15, 11629-11652, doi:10.5194/acp-15-11629-2015.
7. Ceccato, P., S. Trzaska, **C. Pérez García-Pando,** O. Kalashnikova, J. del Corral, R. Cousin, M.B. Blumenthal, M. Bell, S.J. Connor, and M.C. Thomson, 2014: Improving decision-making activities for meningitis and malaria. Geocarto Int., 29, no. 1, 19-38, doi:10.1080/10106049.2013.827749.
8. Hickman, J.E., R.J. Scholes, T.S. Rosenstock, **C. Pérez García-Pando**, and J. Nyamangara, 2014: Assessing non-CO2 climate-forcing emissions and mitigation in sub-Saharan Africa. Curr. Opin. Environ. Sustain., 9-10, 65-72, doi:10.1016/j.cosust.2014.07.010.
9. **Pérez García-Pando, C.,** M. Stanton, P. Diggle, S. Trzaska, R.L. Miller, J.P. Perlwitz, J.M. Baldasano, E. Cuevas, P. Ceccato, P. Yaka, and M. Thomson, 2014: Soil dust aerosols and wind as predictors of seasonal meningitis incidence in Niger. Environ. Health Perspect., 122, no. 7, 679-686, doi:10.1289/ehp.1306640.
10. **Pérez García-Pando, C.,** M.C. Thomson, M. Stanton, P. Diggle, T. Hopson, R. Pandya, and R.L. Miller, 2014: Meningitis and climate: From science to practice. Earth Perspect., 1, 14, doi:10.1186/2194-6434-1-14.

F-10 ADDITIONAL SUBMISSIONS

Please refer to the instructions for details. Headers that do not apply to your application can be deleted.

Human Participants *(see also form F-11)*

All ISGlobal and IMIM researchers are self-regulated by the Code of Good Scientific Practice (http://www.prbb.org/system/uploads/attachment/file/3/en/eng_a4.pdf). Research studies in Spain are regulated by the International, European and National legislations and ethical rules that will be fulfilled during the course of the THeCUE:

- The Nuremberg Code (1947) addressing volunteer consent and proper acting;
- The Revised Declaration of Helsinki in its last version of 2013
- The convention for the protection of human rights and dignity of human being with regard to the application of biology and medicine called the "Convention on Human Rights and Biomedicine" (Council of Europe, 1997) and its additional protocol on biomedical research (2005)
- The Recommendation Rec (2006)4 of the Committee of Ministers to member states on research on biological materials of human origin (Council of Europe) are the main international guidelines for medical research.
- Convention of the Council of Europe on Human Rights and Biomedicine signed in Oviedo on 4 April 1997, and the Additional Protocol on the Prohibition of Cloning Human Beings signed in Paris 12 January 1998;
- The Spanish Law on Biomedical Research (14/2007, of 3rd July) which regulates biomedical research in Spain
- The charter of Fundamental rights of the EU Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to processing of personal data and on the free movement of such data;

ISGlobal (Campus Mar) and IMIM are bond to the PS-Mar Ethics Committee (Clinical Research Ethics Committee of the Municipal Health Care Service, created and accredited for the first time on November 11th, 1993 by the General Direction of Health Resources of the Department of Health of the Government of Catalonia, in accordance with the Order of 26 October 1992). The PS-Mar CEIC evaluates all research protocols in humans conducted by ISGlobal (Campus Mar) researchers. According to Spanish regulations, our local Ethic Committee will follow the implementation of the study by giving its approval to every protocol (including Participant Information Sheet and Consent Form) that will be developed through the study. Adequate measures to ensure personal data protection and confidentiality will be taken, according to European directive on the protection of individuals with regard to the processing of personal data and free movement of such data (95/46/EC, 24th October). National The Spanish Personal Data Protection Law (15/1999, 13th December) and the Royal Degree that exapnds the Personal Data Protection Law (1720/2007, 21st December) will be implemented to guarantee the highest standards in personal data management. Besides, ISGlobal, CUE and IMIM have their own internal policies on personal data protection which follows the national regulations.

Written consent has been obtained from all the participants in the two cohorts to use their personal data. All material obtained in the framework of the project is identified trough a code, the name and/or other personal data that could allow the identification of the participant will never be indicated. This unique identifier links all basic data required for the study. The master key file linking the centre's study numbers with personal identifiers will be maintained in a password protected file with limited access.

- All files containing personal data will be stored in encrypted and password-locked files. Access to these files will be limited to authorized project personnel;
- Only researchers linked to the project will have access to personal data.
- Personal data will not be transferred, except in the cases considered by law.

- Reported study results will pertain to analyses of aggregate data. No individual's name will be associated with any published or unpublished report of this study.

All project personnel will be trained in the importance of confidentiality of individual records and required to sign a confidentiality agreement.

Laboratory Animals
N/A

Sponsor Participation *(if checked "Yes" on form F-6)*
N/A

Consultant(s)
N/A

Statistician(s)

The PI of the project, Xavier Basagaña, has a PhD in Biostatistics from Harvard Universtity, has been leading or participating in the statistical group of several international projects, and has extensive experience in data analysis and in the development of new statistical methods. Dr. Basagaña has written the statistical part of the present proposal, will be in charge of writing the statistical analysis plan and will supervise all analyses conducted within the project.

OMB No. 0990-0263
Approved for use through 3/31/2015

F-11 Protection of Human Subjects
Assurance Identification/IRB Certification/Declaration of Exemption
(Common Rule)

Policy: Research activities involving human subjects may not be conducted or supported by the Departments and Agencies adopting the Common Rule (56FR28003, June 18, 1991) unless the activities are exempt from or approved in accordance with the Common Rule. See section 101(b) of the Common Rule for exemptions. Institutions submitting applications or proposals for support must submit certification of appropriate Institutional Review Board (IRB) review and approval to the Department or Agency in accordance with the Common Rule.

Institutions must have an assurance of compliance that applies to the research to be conducted and should submit certification of IRB review and approval with each application or proposal unless otherwise advised by the Department or Agency.

1. Request Type	2. Type of Mechanism	3. Name of Federal Department or Agency and, if known, Application or Proposal Identification No.
_X_ ORIGINAL __ CONTINUATION __ EXEMPTION	_X_ GRANT __ CONTRACT __ FELLOWSHIP __ COOPERATIVE AGREEMENT __ OTHER: _____	U. S. Environmental Protection Agency
4. Title of Application of Activity Unraveling the effects of traffic on cardiometabolic and mental health from the complex network of urban exposures (THeCUE)		5. Name of Principal Investigator, Program Director, Fellow, or Other Dr. Xavier Basagaña

6. Assurance Status of this Project *(Respond to one of the following)*

[X] This Assurance, on file with Department of Health and Human Services, covers this activity:
Assurance Identification No _FWA00017711__, the expiration date _22 May 2022____ IRB Registration No. _IRB00003847____
[ ] This Assurance, on file with *(agency/dept)*_____, covers this activity.
Assurance No. _____, the expiration date_____ IRB Registration/Identification No._____ *(if applicable)*
[ ] No assurance has been filed for this institution. This institution declares that it will provide an Assurance and Certification of IRB review and approval upon request.
[ ] Exemption Status: Human subjects are involved, but this activity qualifies for exemption under Section 101(b), paragraph _____

7. Certification of IRB Review (Respond to one of the following IF you have an Assurance on file)
[ ] This Activity has been reviewed and approved by the IRB in accordance with the Common Rule and any other governing regulations. By:
[ ] Full IRB Review on (date of IRB meeting) _____ or [ ] Expedited Review on (date) _____
[ ] If less than one year approval, provide expiration date _____
[X] This activity contains multiple projects, some of which have not been reviewed. The IRB has granted approval on condition that all projects covered by the Common Rule will be reviewed and approved before they are initiated and that appropriate further certification will be submitted.

8. Comments

9. The official signing below certifies that the information provided above is correct and that, as required, future reviews will be performed until study closure and certification will be provided.	10. Name and Address of Institution BARCELONA INSTITUTE FOR GLOBAL HEALTH (ISGLOBAL) C/ Rosselló, 132, 5-2 08036 Barcelona Spain	
11. Phone No. +34 93 227 98 92		
12. Fax No. +34 93 227 18 50		
13. Email: projects@isglobal.org		
14. Name of Official Gonzalo Vicente	15. Title Managing Director	
16. Signature		17. Date 14/07/17

ISGlobal Barcelona Institute for Global Health

According to the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number. The valid OMB control number for this information collection is 0990-0263. The time required to complete this information collection is estimated to average 30 minutes per response. If you have comments concerning the accuracy of the time estimate(s) or suggestions for improving this form, please write to: U.S. Department of Health & Human Services, OS/OCIO/PRA, 200 Independence Ave., S.W., Suite 336-E, Washington D.C. 20201, Attention: PRA Reports Clearance Officer.