Universitat de Girona
Facultat de Medicina

Bachelor Thesis

Does Air Quality Matter? 24-hour Exposure to PM2.5 Particles and Blood Pressure Registers

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1. ABBREVIATIONS

ABPM	Ambulatory Blood Pressure Measurement
ANS	Autonomous Nervous System
ºC	Celsius degrees
CV	Cardiovascular
DALY	Disability-adjusted life year
DBP	Diastolic Blood Pressure
dL	decilitre
g	gram
h	hour
HBPM	Home Blood Pressure Measurement
HPA Axis	Hypothalamic Pituitary Adrenal Axis
ID	Identity Document
IL-6	Interleukin-6
LDL	Low-density Lipoprotein
mg	milligram
µg/m^3	microgram/cubic metre
min	minute
µm	micrometre
mmHg	millimetres of Mercury
OBPM	Office Blood Pressure Measurement
SBP	Systolic Blood Pressure
PC	Personal Computer
PHC	Primary Healthcare Centre/s
PM	Particulate Matter
UPAS	Ultrasonic Personal Aerosol Sampler
UFP	Ultrafine Particle
WHO	World Health Organization

2. ABSTRACT

Background: Hypertension is a global and national public health issue, with large human and economic costs, both in developed and developing countries. Ambient pollution is one of the leading risk factors on mortality and loss of quality-of-life burden. Recent evidence has shown how these two factors could be related, and how a great part of the cardiovascular disruptions could be explained by the interaction of pollutants with our organism. Particulate matter is especially dangerous and, moreover, the smaller these particles are, the more hazardous they become. Previous studies have linked the exposure to PM2.5 with cardiovascular and blood pressure alterations.

Objective: The goal of this study is to measure the association between the exposure to PM2.5 and an increased blood pressure at an individual level, before and after adjusting for comorbidities. Additionally, the strength of this association by socioeconomical status will be evaluated.

Study design: We present a prospective cohort study considering a continuous measure of exposure to PM2.5 particles.

Participants: This study will require the participation of the Primary Healthcare Centres users in the city of Barcelona (Spain) who meet the inclusion criteria and none of the exclusion ones. The final n will be 462.

Methodology: For 8 months, 24-hour data of blood pressure registers and the same period pollution exposure will be collected by an ABPM and a relatively new machine, the UPAS monitor. 24-hour, the diurnal and the nocturnal average blood pressures (systolic and diastolic) and other blood pressure variations will be considered the outcomes. Total PM2.5 exposure during the 24 hours will be used as the exposure variable. Other confounding factors such as age, sex, ethnicities comorbidities and socioeconomical status will be included in the analyses.

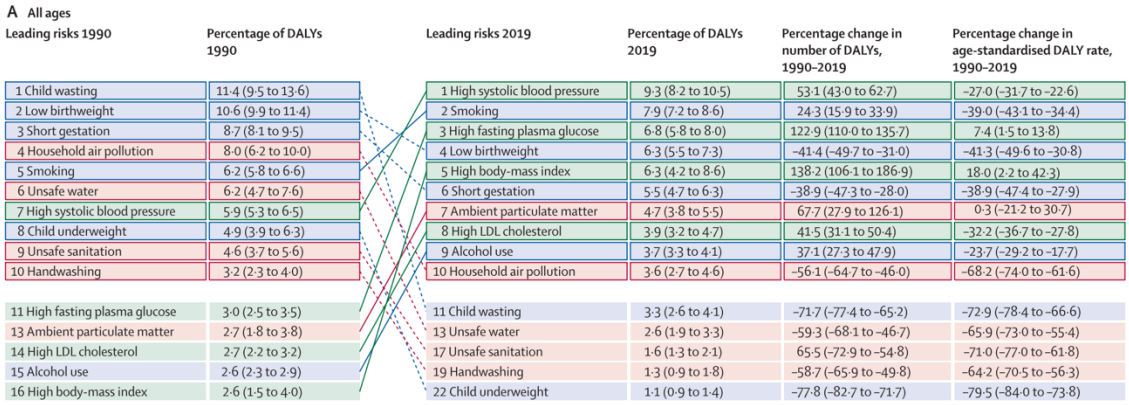
Key Words: Hypertension, blood pressure, PM2.5, ABPM, UPAS monitor.

3. INTRODUCTION

3.1 HYPERTENSION OR HIGH BLOOD PRESSURE

Epidemiology and Global Burden

Hypertension or high blood pressure has become the most relevant risk factor of morbimortality the last decades (1,2). 1.13 billion adult patients suffered from hypertension in 2015, and every year, 9.4 million people die from its complications (3). High SBP was considered the first (in women) and second (in men) Level 2 risk factors for mortality in 2019 (4), as shown on Figure 1 (next page). In addition, the DALYs rate caused by high blood pressure goes up to 200 million (5) and high SBP was the leading risk factor in terms of percentage of attributable DALYs for all ages in 2019 (4), as shown in Figure 2.



A All ages

Leading risks 1990	Percentage of DALYs 1990	Leading risks 2019	Percentage of DALYs 2019	Percentage change in number of DALYs, 1990–2019	Percentage change in age-standardised DALY rate, 1990–2019
1 Child wasting	11·4 (9·5 to 13·6)	1 High systolic blood pressure	9·3 (8·2 to 10·5)	53·1 (43·0 to 62·7)	−27·0 (−31·7 to −22·6)
2 Low birthweight	10·6 (9·9 to 11·4)	2 Smoking	7·9 (7·2 to 8·6)	24·3 (15·9 to 33·9)	−39·0 (−43·1 to −34·4)
3 Short gestation	8·7 (8·1 to 9·5)	3 High fasting plasma glucose	6·8 (5·8 to 8·0)	122·9 (110·0 to 135·7)	7·4 (1·5 to 13·8)
4 Household air pollution	8·0 (6·2 to 10·0)	4 Low birthweight	6·3 (5·5 to 7·3)	−41·4 (−49·7 to −31·0)	−41·3 (−49·6 to −30·8)
5 Smoking	6·2 (5·8 to 6·6)	5 High body-mass index	6·3 (4·2 to 8·6)	138·2 (106·1 to 186·9)	18·0 (2·2 to 42·3)
6 Unsafe water	6·2 (4·7 to 7·6)	6 Short gestation	5·5 (4·7 to 6·3)	−38·9 (−47·3 to −28·0)	−38·9 (−47·4 to −27·9)
7 High systolic blood pressure	5·9 (5·3 to 6·5)	7 Ambient particulate matter	4·7 (3·8 to 5·5)	67·7 (27·9 to 126·1)	0·3 (−21·2 to 30·7)
8 Child underweight	4·9 (3·9 to 6·3)	8 High LDL cholesterol	3·9 (3·2 to 4·7)	41·5 (31·1 to 50·4)	−32·2 (−36·7 to −27·8)
9 Unsafe sanitation	4·6 (3·7 to 5·6)	9 Alcohol use	3·7 (3·3 to 4·1)	37·1 (27·3 to 47·9)	−23·7 (−29·2 to −17·7)
10 Handwashing	3·2 (2·3 to 4·0)	10 Household air pollution	3·6 (2·7 to 4·6)	−56·1 (−64·7 to −46·0)	−68·2 (−74·0 to −61·6)
11 High fasting plasma glucose	3·0 (2·5 to 3·5)	11 Child wasting	3·3 (2·6 to 4·1)	−71·7 (−77·4 to −65·2)	−72·9 (−78·4 to −66·6)
13 Ambient particulate matter	2·7 (1·8 to 3·8)	13 Unsafe water	2·6 (1·9 to 3·3)	−59·3 (−68·1 to −46·7)	−65·9 (−73·0 to −55·4)
14 High LDL cholesterol	2·7 (2·2 to 3·2)	17 Unsafe sanitation	1·6 (1·3 to 2·1)	65·5 (−72·9 to −54·8)	−71·0 (−77·0 to −61·8)
15 Alcohol use	2·6 (2·3 to 2·9)	19 Handwashing	1·3 (0·9 to 1·8)	−58·7 (−65·9 to −49·8)	−64·2 (−70·5 to −56·3)
16 High body-mass index	2·6 (1·5 to 4·0)	22 Child underweight	1·1 (0·9 to 1·4)	−77·8 (−82·7 to −71·7)	−79·5 (−84·0 to −73·8)

Figure 2: Leading 10 Level 4 risks by attributable DALYs, from 1990 to 2019 for all ages (4)

All these data suggest the big relevance and the burden of this disease and establish it as a global and public health issue. We find it important to emphasise how this disease is unevenly distributed among countries and social groups (3,5).

In Spain, hypertensive patients have been estimated to cost to the health system the double that a normotensive patient would (6). An investigation group who studied Catalan population estimated that an hypertensive patient costs 1,312.10€ to the Primary Healthcare, depending on the level of morbidity and without taking into account the costs of these patients' complications and hospital care when needed (7).

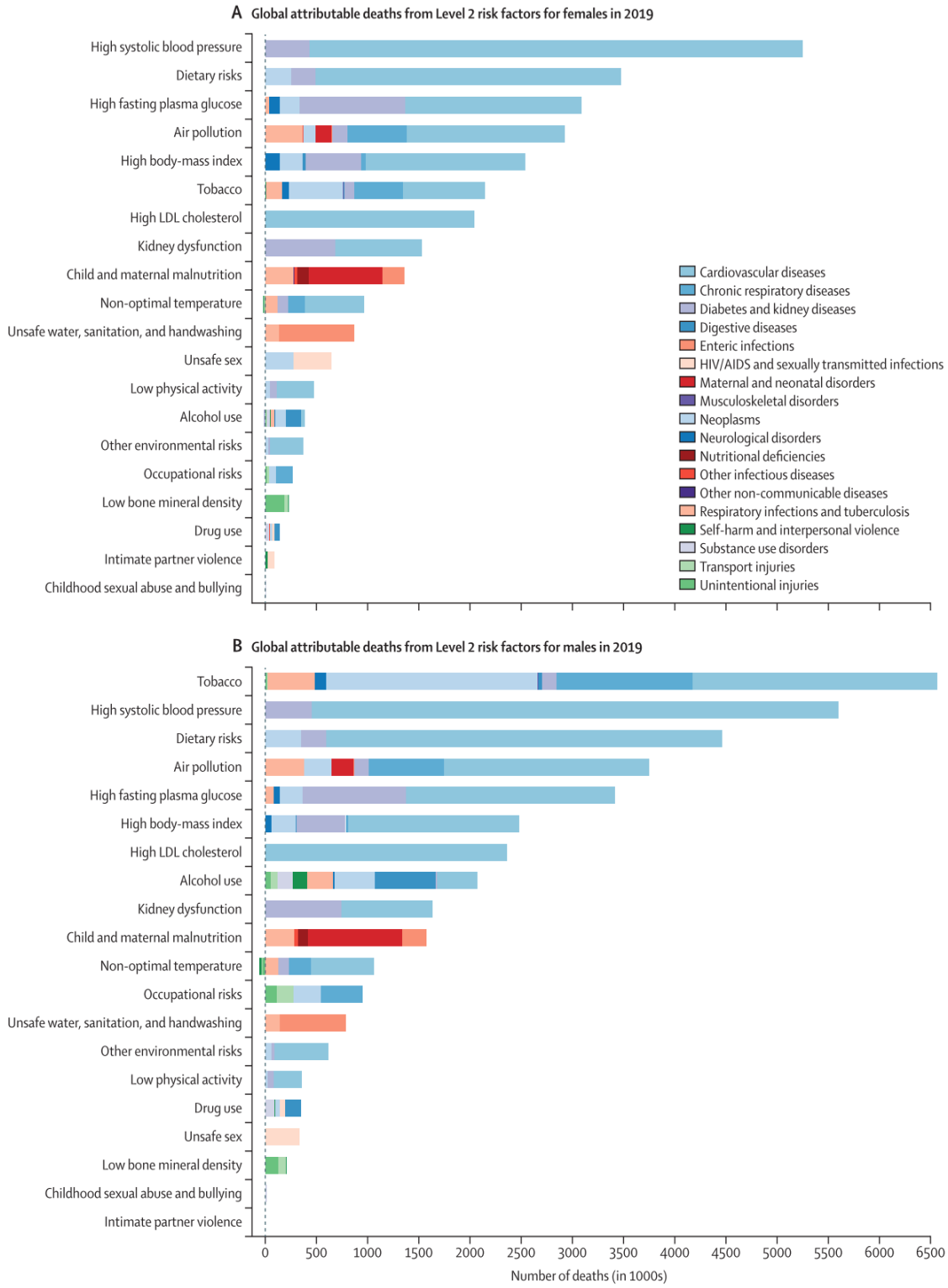


Figure 1: Leading Level 2 risk factors for mortalities for women and men in 2019(4)

Definition and Clinical Relevance

Blood pressure is the force by which the blood is pushed through the arterial system, causing a pressure against its walls. 2 values are considered: the systolic pressure that corresponds the blood pressure in the vessels when the heart contracts, and the diastolic pressure that represents the pressure when the heart relaxes. Optimal values are set on <120mmHg for the systolic pressure and <80mmHg for the diastolic pressure on adult patients. When the blood pressure is too high, reaching levels > 140mmHg for the SBP and/or levels > 90mmHg for the DBP, we talk about hypertension or high blood pressure (3,5).

There are some controversies on setting a threshold to define high blood pressure among different medical societies (8,9). The European and the American thresholds to define blood pressure are explained on Table 1 (12). The relevance of this differentiation lays on the fact that when choosing one criteria or the other to define hypertension, the prevalence of this disease changes substantially; currently, the prevalence of hypertension in Spain goes up to 32% using the European standards (8), but if the American criteria were used, the number could almost reach the 50% of the population. However, all medical societies agree on the relationship between high blood pressure and the risk of developing CV and renal affections. Table 2 exposes the main diseases and syndromes related to high blood pressure (5,(10). We can nowadays predict the benefit on treating patients, and know how much the risk of other CV diseases, chronic renal disease or even all-cause mortality decrease every 10mmHg of the SBP, as shown it Figure 3 (11).

Table 1: Definition of Hypertension according to the ESH/ESC and American guidelines (12)

	ESC/ESC 2018	ACC/AHA 2017
SBP < 120 mmHg and DBP <80 mmHg	Optimus	Normal
SBP 120-129 mmHg and/or DBP 80-84 mmHg	Normal	-
SBP 120-129 mmHg and DBP < 80 mmHg	-	Elevated
SBP 130-139 mmHg and/or DBP 85-89 mmHg	Normal-elevated	-
SBP 130-139 mmHg or DBP 80 - 89 mmHg	-	Hypertension stage 1
SBP 140-159 mmHg and/or DBP 90-99 mmHg	Hypertension stage 1	Hypertension stage 2
SBP 169-179 mmHg and/or DBP 100-109 mmHg	Hypertension stage 2	
SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg	Hypertension stage 3	

Table 2: Consequences of high blood pressure. Adapted from (5,10)		
Short and long-term consequences	Long-term consequences	
Stroke	Hypertensive cardiomyopathy	Peripheral arterial disease
Coronary heart disease	Heart failure with preserved	Chronic kidney disease
Heart failure	ejection fraction	Dementias
Cardiovascular death	Atrial fibrillation	Diabetes mellitus
	Valvular heart disease	Erectile dysfunction
	Aortic syndrome	Hypertensive retinopathy

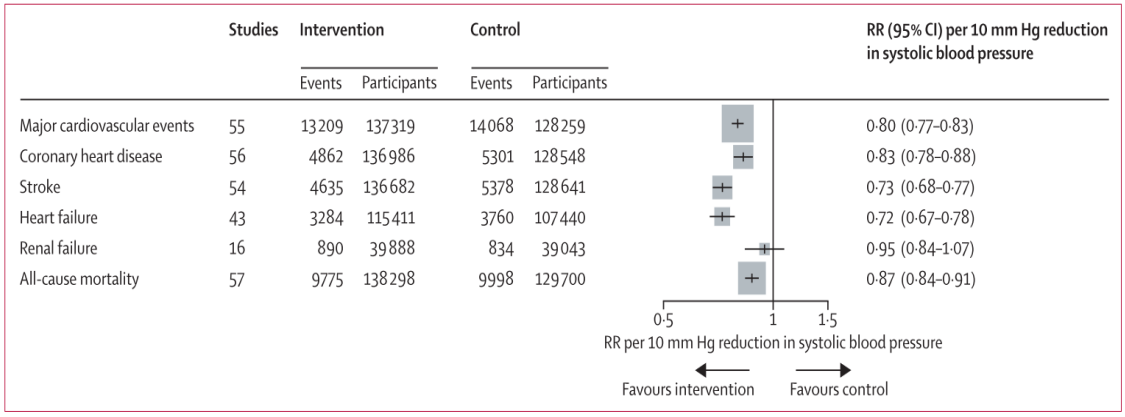


Figure 3: Standardised effect of a 10 mmHg reduction in SBP (11)

Pathophysiology and Risk Factors

The first cause of high blood pressure is Primary or Essential Hypertension, causing the 90% of the cases. 10% of the patients suffer from an underlying disease that produces a Secondary Hypertension (8).

We will suspect of Secondary Hypertension in a young patient without the main cardiovascular risk factors, that are much more associated with Essential Hypertension, and who shows the corresponding signs during the physical exploration. Some of the main diseases that may cause a Secondary Hypertension are renal parenchymal disease, hyperaldosteronism, obstructive sleep apnoea syndrome or drug-induced hypertension (5,8).

The Essential Hypertension, which will be the main target in this project, has an unclear pathophysiology. Some forms of secondary hypertension can be explained by a single-gene mutation. However, other forms of hypertension are related with multiple mutations, each one of them related with a small effect on the blood pressure.

Therefore, we understand that essential hypertension has a genetic base, which predispose a person to develop high blood pressure when exposed to different factors. The exposition to environmental risk factors on certain people would lead to the characteristic vascular alterations of hypertension, with endothelial disruption and hemodynamic alterations. These environmental risk factors are well-known and the main medical societies consider them to be overweight and obesity, sodium and potassium intake, physical fitness and alcohol (8,13).

Hypertension prevalence depends on age, sex and ethnicity; it is more prevalent on older groups, with men and black population having an earlier and higher incidence as shown on Figure 4 (13); therefore, these 3 variables are factors to take into account when studying this disease (14). In addition, since cardiovascular risk factors tend to cluster, we will find a higher incidence of insulin-resistance and type 2 diabetes, dyslipidaemia and obesity on the patients who suffer from high blood pressure (14).

	SBP/DBP ≥130/80 mm Hg or Self-Reported Antihypertensive Medication†		SBP/DBP ≥140/90 mm Hg or Self-Reported Antihypertensive Medication‡	
Overall, crude	46%		32%	
	Men (n=4717)	Women (n=4906)	Men (n=4717)	Women (n=4906)
Overall, age-sex adjusted	48%	43%	31%	32%
Age group, y				
20–44	30%	19%	11%	10%
45–54	50%	44%	33%	27%
55–64	70%	63%	53%	52%
65–74	77%	75%	64%	63%
75+	79%	85%	71%	78%
Race-ethnicity§				
Non-Hispanic white	47%	41%	31%	30%
Non-Hispanic black	59%	56%	42%	46%
Non-Hispanic Asian	45%	36%	29%	27%
Hispanic	44%	42%	27%	32%

Figure 4: Prevalence of Hypertension depending on 2 different thresholds in USA in 2014 segregating by age, sex and ethnicity (13)

Diagnosis

Hypertension diagnosis requires a good measure of the blood pressure, obtained with the proper conditions. Blood pressure can be measured during a medical visit or out-of-office. The second enables the medical team to obtain more reliable measurements. The 3 main methodologies used are 1) office blood pressure measurement, 2) home blood pressure measurement and 3) ambulatory blood pressure measurement (5,13). Table 3 compares these different methods and the information obtained.

Table 3: Comparison of the different forms of BP measurements. Adapted from (Torguet, P)

	OBPM	HBPM	ABPM
Real BP values	Questionable	Yes	Yes
Dipper status	No	No	Yes
Morning increase	No	Questionable	Yes
BP variability	No	Questionable	Yes
Duration of pharmaceutical effect	No	Yes	Yes

ABPM consists of a 24-hour register of the SBP and DBP. With this, we can obtain a great number of blood pressure lectures, which describes its variations during the patient's usual activities and daily life. The Figure 5 shows the device used on this monitoring (15). The ABPM device requires a digital blood pressure monitor attached to a belt and connected to a cuff around the patient's upper arm. Once the patient completes the 24-hour monitoring, the evaluated information is the average blood pressure the patient had during the whole day, during the diurnal and the nocturnal period; the hypertensive burden (%) during the whole day, the diurnal and the nocturnal periods; and the pattern of variation between the sleeping and the awaken periods (15). All these data have a clinical relevance and relates to a cardiovascular risk (5). In addition, ABPM is the only method to evaluate nocturnal hypertension, which has a very significant value and is a very good estimator of cardiovascular risk (16).

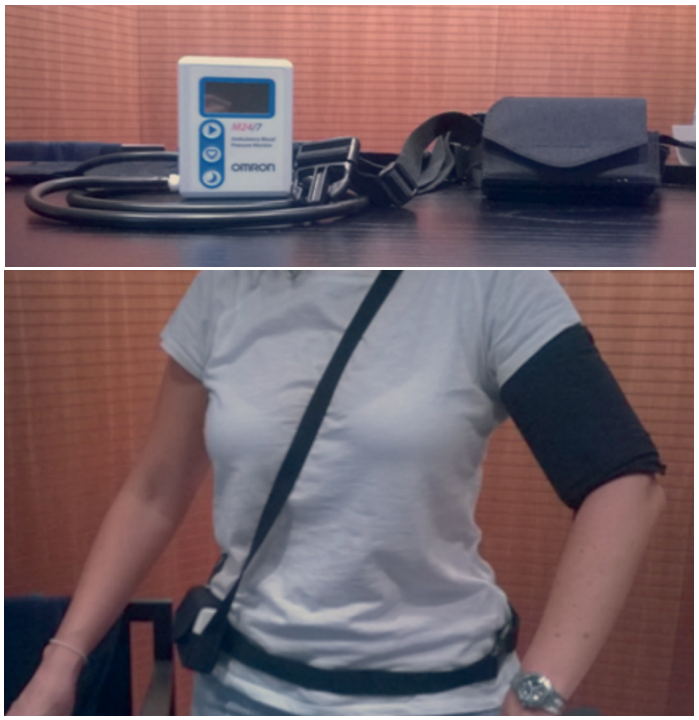


Figure 5: ABPM device before (A) and after (B) being equiped (15)

Compared to OBPM, ABPM can provide us with more precise control of blood pressure and can even offer other measurements that have proven to be clinically relevant to assess the patient's CV risk. We have seen in Table 3 that ABPM offers us more reliable information. In relation with the "Dipper Status" exposed, we usually find nocturnal descends of the blood pressure in healthy patients (Dipper patients or Extreme dipper patients). Those patients who do not have these decreases or even have higher blood pressures at night (Non-dipper or Riser) have a higher CV risk and must be managed accordingly (17,18). These statuses are summarized in Table 4.

Table 4: Dipper status according to % of nocturnal systolic and diastolic descend relative to the diurnal SBP. Adapted from (Torguet, P)

>20 % descend	Extreme Dipper status	
10 – 20 % descend	Dipper status	
0 – 10 % descend	Non-dipper	Higher CV risk
<0% descend or >0% increase	Riser	

Also, some patients' who suffer white-coat hypertension and masked hypertension, defined in Table 5, will only be detected and properly diagnosed with the ABPM, thus these patients benefit the most from this measure (5,13).

Table 5: Diagnosis in different situations. Adapted from (Torguet, P)		
	ABPM <135/85	ABPM > 135/85
OBPM > 140/90	White-coat hypertension	Real hypertension
OBPM < 140/90	Real normotension	Masked hypertension

ABPM can also register the blood pressure variability, which can also be relevant to evaluate the patient CV risk.

Treatment

High blood pressure treatment is nowadays based mostly on 2 mainstays: lifestyle changes and pharmacological therapy, which include antihypertensive treatment and medical treatment for other CV risk factors when necessary (5). Other techniques and medical devices are regarded in case of resistant hypertension, but generally, most of them still lack evidence or knowledge (5).

Lifestyle changes are the base of high blood pressure prevention and are almost always previous to pharmacological interventions. With them, the physician aims for a weight reduction, mostly on overweighted and obese patients; dietary changes, with sodium restriction and more potassium intake, together with an overall healthier diet; moderation of alcohol; and to increase the physical activity (8).

3.2 POLLUTION AND PARTICLE MATTER

When talking about air pollution, it is almost impossible to avoid seeing the big picture of today's ecological and global challenges. Every now and then, we hear about climate change, migratory crisis due to climatic catastrophes, massive Amazon rainforests fires, unpredictable storms in an unseen way… And all of these have a relationship to the way the humankind relates with the ecosystem and the rest of the planet. Even the current Coronavirus Disease 19 pandemic is believed to be linked to the way humans interact with nature. We believe changing this is on our hands and may be beneficial for the planet but also for the human species (19).

Global Burden

Air pollution has become a major public health issue. Ambient air pollution killed 4.2 million people worldwide in 2016. There is a greater impact on low and middle-income areas, suffering the 91% of the pollution burden. However, pollution affects all the areas in the planet, and everyone at a greater or lower level. More than half the deaths attributed to pollution are related to ischaemic heart disease and strokes. The numbers are much lower for chronic obstructive pulmonary disease and even lower for lung cancer (20). Moreover, ambient particulate matter became the 4th Level 2 risk factor (for both women and men) on mortality. See Figure 1 above. At the same time, ambient particulate matter was the 7th risk factor and household air pollution was the 10th risk factor on DALYs percentage in 2019 for all ages (4). See Figure 2 above.

Concepts

When talking about air pollution, we refer to a great mixture of gases and particles emitted to the atmosphere that have an adverse effect on humans or the rest of the ecosystem. Some of these pollutants can be divided according to their chemist composition (nitrogen oxides, ozone, sulphur dioxide and many more) and others will bond and condense, creating what is known as PM or simply, particles. At the same time, this PMs can be divided according to their aerodynamic diameter.

We find PM10 (with and aerodynamic diameter <10μm), PM2.5 (with and aerodynamic diameter <2.5μm) and ultrafine particles or UFP (with and aerodynamic diameter <0.1μm). The fact that particles have different sizes enable them to reach different parts of our system and make them more or less dangerous; we consider that PM10 reach the pharynx, whereas PM2.5 and UFP can reach the pulmonary alveoli. The main sources of PM pollution come from traffic and mobile sources, industries such as power plants or factories and local sources like house heaters (21,22). Figure 6 compares the particles' size (22).

It is important to differentiate between outdoor or ambient air pollution and indoor or household air pollution. Indoor air pollution is relevant in those houses and spaces where activities that require combustion take place. It is clearly related to bad ventilation systems, typical from low-income and marginalised countries and areas.

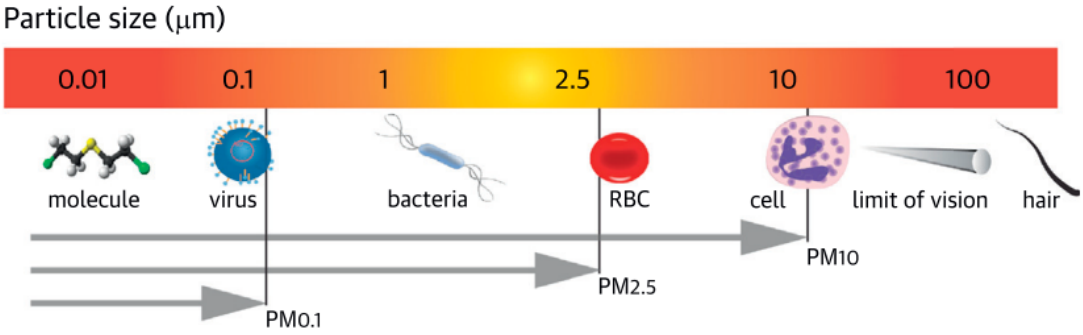


Figure 6: PM sizes comparisson (22)

Biomechanisms of CVD associated with pollution

The mechanisms that explain the effects of PM2.5 on our organism are still being studied. However, some authors have tried to understand the pathways that could be activated and would promote cardiovascular pathology because of these particles. Each previous study explains these mechanisms differently, but they are all superposable (21–24). Figure 7 summarizes the following explanation.

When particles are inhaled and reach the alveolar parenchyma, they result in different consequences. Generally, we can speak about 1) the direct blood translocation and release of other substances into the bloodstream; 2) a local and posterior systemic inflammation; and 3) all the systemic effects on the organism. According to some authors, the first step to occur would be the production of reactive oxygen species, that would catalyse the rest of the mechanisms. Proinflammatory mediators such as cytokines, interleukins (specially IL-6) or tumour necrosis factor would have an important role, enhancing the rest of the inflammatory system. At the same time, the particles inhaled, now on the bloodstream, would be able to activate thrombotic pathways by interacting with platelets and coagulation factors and inhibit the liberation of endogenous nitric oxide, an endogenous vasodilator. All these effects would promote an endothelial dysfunction on the short-term.

Simultaneously, the endothelial disruption and the proinflammatory state would have systemic and long-term consequences. Regarding the CV system, this would be translated into a higher risk of atherosclerosis and high blood pressure. The nervous system would also interact with all these responses, leading to an alteration of the ANS, promoting a sympathetic action with an alteration of the blood vessels, and affecting the neuroendocrinological nucleus, with an enhanced activation of the HPA Axis.

Other systems could also be affected by this global response, with alterations on the adipose tissue, the liver, the heart and the skeleton. In the long run, PM inhalation has been related to metabolic alterations such as insulin resistance, hyperglycaemia, obesity and also atherosclerosis and plaque instability (24) and also with other CV events such as cardiac arrythmias and ischemic heart disease (22).

Some authors have also stated that pollution and PM inhalation could produce epigenetic changes and alterations on the gut microbiome (22,24), with new evidence still required.

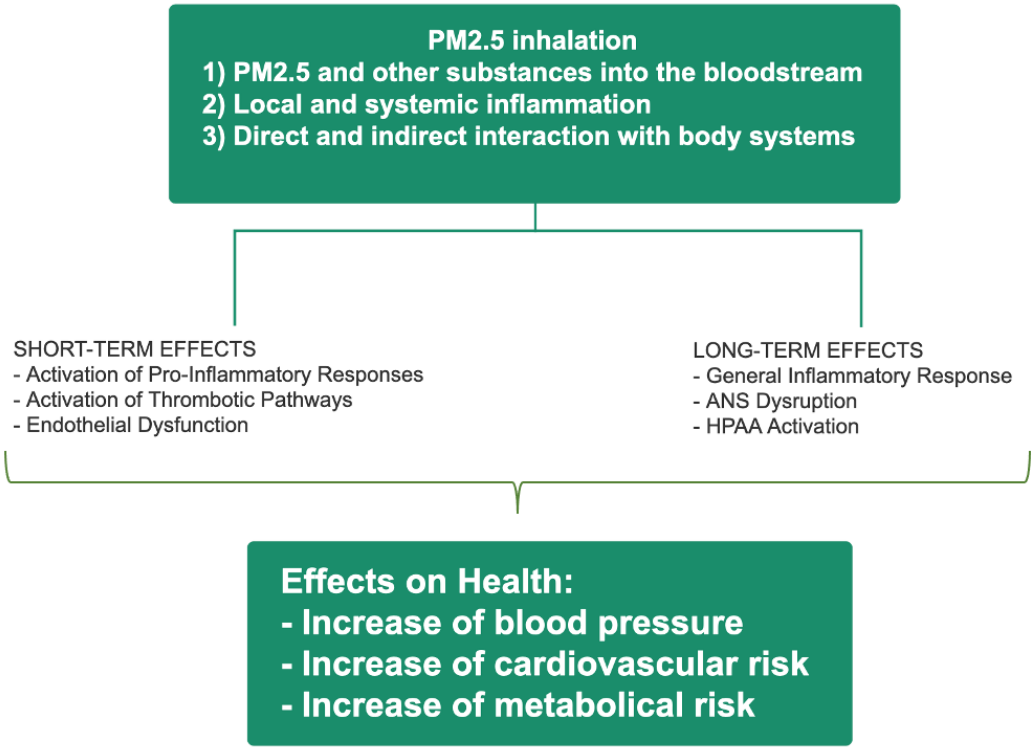


Figure 7: Main pathogenic mechanisms of the inhalation of PM2.5 particles

Some authors have reported a link between the active form of vitamin D3 and an attenuation of the inflammatory reaction induced by the PM2.5 particles on in-vitro human bronchial epithelium (25). Vitamin D has also proved to be clinically relevant on protecting against the respiratory symptoms triggered by PM2.5 particles of obese asthmatic children (26).

3.3 CLINICAL RELATION BETWEEN POLLUTION AND BLOOD PRESSURE

We can already find some studies that support a relationship between PM and blood pressure alterations. This relationship has been established in different populations and different kinds of patients. In 2019, a Brazilian investigation team found an association between PM2.5 levels and a raise on blood pressure and heart rate on urban workers, with a bigger effect on diabetic and hypertensive patients (27). That same year, PM10 and PM2.5 were seen to increase blood pressure and high blood pressure diagnostics on children and teenagers in China (28). Also, in Canada, numerous pollutants were related to higher blood pressures and an increase on emergency department visits related to high blood pressure in 2015 (29). A German study in 2011 was already stating that the smaller the particles we inhale, the more dangerous it can be, proving how UFP had a bigger effect on CV diseases and high blood pressure crisis than PM2.5 and PM10 (30). Finally, a Spanish study set in Barcelona related UFP with an increase of blood pressure, especially diastolic blood pressure (31).

As we have previously stated, most of the deaths attributed to pollution were related to ischaemic heart disease and strokes (20,22,24,32). It is relevant to remind how high blood pressure is a main risk factors of both these diseases (5,13), and how its relationship could be caused secondarily by the effect pollution has on blood pressure.

4. JUSTIFICATION

Hypertension is a major public health issue that affects more than 1 billion people all over the world, and millions die from its complications every year. The link between hypertension and CV risk has been well-established and it affects the patients' quality of life and implies a great expenditure to our public health system (1-5, 7).

At the same time, pollution has also become an increasing risk factor during last decades. Even though new investigation is still required, the current evidence proves its many effects on human health (4, 18). However, many people believe that public health policies against the rise of pollution and its detrimental consequences are not assessed the way it is needed.

Given this scenario, new studies have been addressing the relationship between pollution and an increase on blood pressure and have even been able to explain a biological plausibility to it (19-27). Still, medical societies and health policies do not regard pollution as a modifiable ambient risk factor for hypertension.

We would like to see if this relationship can be seen in our environment. Barcelona is a Spanish city in the North-Eastern coast and is the most extend urban area in Catalonia. Its annual average levels for PM2.5 exceed the thresholds set by the WHO, and in some parts, these levels even exceed the European Union ones (33).
Previously, Soldevila's investigations in 2019 proved how UFP can be related to an increase of diastolic blood pressure in Barcelona (27). The problem for us was that this study assumed a homogenous distribution of pollution for the people all over the city.

This protocol presents a new study that will try to individualise the PM2.5 levels for each participant and could therefore be more precise on studying the relationship between these particles and blood pressure. For that, we will be using ABPM devices, which has been proven to be the best method of evaluating the patients' BP (13, 15-17). Also, we have not found any reference on how this association can differ between different socioeconomical groups. We will try to establish the effect of this variable on the

mentioned association. Learning this, will be helpful to adjust public health policies and medical guidelines for a better and more equitable control of high blood pressure and CV health.

5. HYPOTHESIS

Main hypothesis

A major exposition to PM2.5 particles increases the 24-hour, diurnal and nocturnal on SBP and DBP numbers on demandant population from Barcelona.

Secondary hypothesis

- A major exposition to PM2.5 particles has a greater effect on the 24-hour blood pressure numbers on demandant low-income population from Barcelona, than on higher income people.
- A major exposition to PM2.5 particles increases the rates of pathological circadian blood pressure variability on demandant population from Barcelona.

6. OBJECTIVES

Main objective

To find how higher rates of exposure to PM2.5 translates into more elevated blood pressure numbers detected by ABPM register on Barcelona's demandant population.

Secondary objectives:

- To seek different relationships between PM2.5 exposition and blood pressure on populations of different socioeconomical statuses.
- To find if other CV risk data obtained by ABPM such as daily variation and dipper-behaviour also increase with PM2.5 ratios.
- To evaluate in which patients the relationship we want to study is bigger according to age, sex, ethnicity and comorbidities.

7. METHODOLOGY

7.1 STUDY DESIGN AND SETTINGS

Our study will be an observational prospective cohort study. Instead of an exposed group a non-exposed one, we will evaluate different levels of exposition, monitoring the 24 hours exposition of our patients to PM2.5 particles and seeking progressive differences.

Blood pressure will be registered by ABPM devices and exposition to PM2.5 particles will be controlled with the UPAS monitor (explained on Section 7.4).

7.2 STUDY POPULATION

The study population will be selected from people attending PHC in the city of Barcelona, from the sanitarian region of Barcelona (Annex 1). We have chosen Barcelona city because it is an extent urban area where similar studies have taken place, and with annual average differences of PM2.5 particles depending on neighbourhoods and streets. The following figure exposes these differences in the city (Figure 8) (33). As we can observe, no part of the city respects the levels recommended by the WHO and some even exceed the ones set by the European Union.

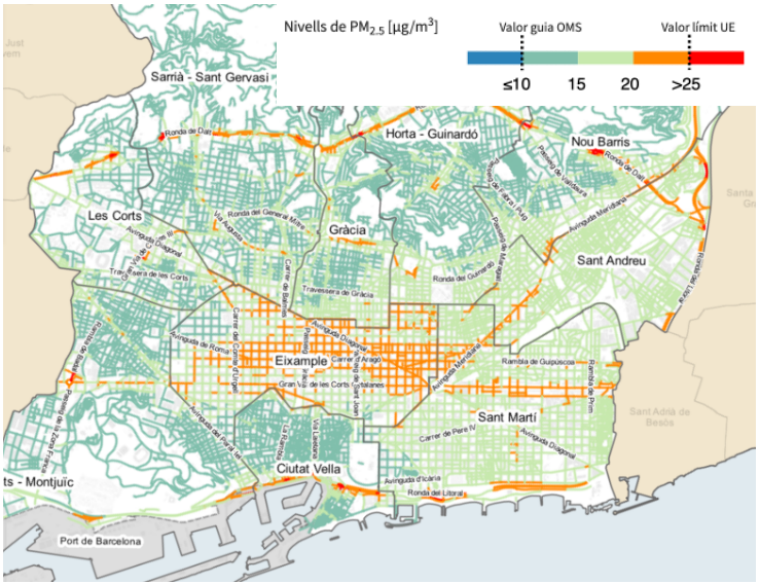


Figure 8: Anual average levels of PM2.5 pollution in different street sections in Barcelona, 2019 (32)

Inclusion criteria:

- Patients aged 18-65 years old
- Patients who attend PHC in Barcelona
- Patients who are able to carry out daily activities without external help
- Patients who can wear the ABPM and the UPAS devices and who can understand its basic functioning

Exclusion criteria:

- Patients who do not meet the inclusion criteria
- Patients who do not want/cannot answer or compromise on anything included in the protocol.
- Patients with a language barrier, with whom the healthcare providers cannot communicate and cannot make sure he or she understands everything needed.
- Patients diagnosed with refractory or resistant hypertension
- Patients with any medical condition that may difficult the obtaining or the evaluation of the results according to the investigators.
- Patients who do not want to participate in the study or do not want to sign the Informed Consent Sheet (Annex 2).

7.3 SAMPLE

Sampling Method

We will contact the Territorial Management of Barcelona and ask for the participation of the PHC in Barcelona city. The participants will be selected by their general doctors according to the inclusion and exclusion criteria and will be informed with the corresponding sheets (Annex 3).

Once we complete the needed sample selection and all the participants' information is collected properly (Annex 4), the patients will be informed to attend their PHC an exact day, where they will be given the devices that will register their blood pressure and pollution exposure for 24 hours.

Sample size

Previous similar studies, such as the one carried out by Soldevila et al in 2019, used a sample of 521 subjects (31).

We have also calculated the ideal sample size. We assumed a two-sided test, with an alpha risk equal to 5% and a beta risk of 0.2%. The prevalence of hypertension in Spain is estimated at 32% of the adult population according to the European criteria. We do not think we will lose a big number of patients, but maybe the registers will not always be valid. Therefore, we assumed a 10% drop-out rate. All these data make us need 462 patients for our study.

7.4 VARIABLES AND MEASUREMENT INSTRUMENTS

Considering the objectives of this study, we will define the following variables:

Independent variables:

The independent variable in this study is the 24-hour PM2.5 exposition. It is a continuous quantitative variable measured in $\mu g/m^3$. This will be evaluated with the UPAS monitor, shown on Figure 9 (34).

The UPAS is a personal dust monitor that can detect different kinds of particles, in which PM2.5 are included, and has the capacity to be operative during more than 24-hour periods. A specific inlet lets in air with particles of a particular size which reach de detection part of the monitor. There, the particles are read and quantified. The system is also integrated by a pump that keeps the air flowing. Its registers are easy to access and can be uploaded immediately.

Figure 9: Ultrasonic Personal Aerosol Sampler (UPAS) (31)

The UPAS has been previously evaluated and compared to other forms of particles detection (35) and it has also been used on previous studies to test patients' exposition and compared to other devices (36,37). The following Figure 10 shows some tests that justify its application on previous studies (35,36).

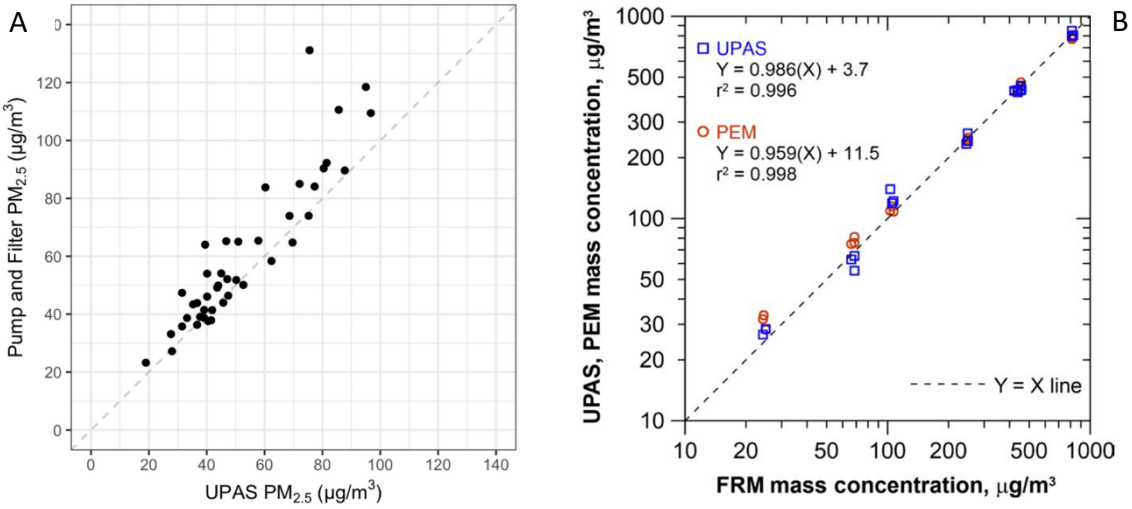


Figure 10: Validation of UPAS on previous studies. Image A compares the UPAS with another tested device (35). Image B compares the UPAS to the Federal Reference Method (36)

Regarding the UPAS characteristics, it is important to know most of the devices used to monitor particles can be expensive and cost several hundreds of euros. The UPAS is a more affordable option, that costs 1,369.58 euros and presents very interesting features summarized on Table 6, which make this device easily wearable and useful to assess our objectives (34). Images of patients wearing the UPAS are available on Figure 11 (35,36).

Table 6: Summary of UPAS device characteristics (33)	
Exterior Size (millimetres)	128x70x23
Weight (grams)	230
Noise	<40dB (less than the noise of a silent library)
Operation Temperature (ºC)	0-50
Battery Endurance	>35h at a 1 Litre per minute (some studies have proved 25h of function at a rate of 2 Litres per minute detected)
Data Obtention	Via Bluetooth, connectable to mobile phone or PC

Figure 11: Participants of other studies wearing the UPAS device together with other monitors. A) The UPAS is the white monitor on the patient's chest (36). B) The patient has cut a whole on her clothes to expose the UPAS inlet (35)

More information of the UPAS device can be found on Annex 5

Dependent variables:

The dependent variables will be those obtained by the ABPM register. As we have exposed in section 3.1, the ABPM does not only offer us blood pressure numbers; it also enables us to check the patients' circadian variation over the day. We have defined the average blood pressure numbers as the main dependent variable and the other data as secondary dependent variables.

Average blood pressures: these will be measured as a continuous quantitative variable, with a systolic and a diastolic value measured in mmHg. We will consider the 24-hour blood pressure average, the diurnal and the nocturnal one. Diurnal and nocturnal periods can whether be prefixed or established by the patients' usual life.

Hypertension: these will be measured as a dichotomous qualitative variable (**Yes** / **No**), considering 24-hour blood pressured averages higher than 135mmHg for the systolic blood pressure and/or 85mmHg for the diastolic blood pressure.

Dipper status: it will be measured as a nominal qualitative variable. (**Extreme dipper** / **Dipper** / **Non-dipper** / **Riser**).

Covariates:

We will need to consider the following variables in order to interpret the results. These covariates have been selected for their proven cardiovascular effect and because of the objectives of this protocol. This information will be collected on the Data Collection Sheet (Annex 4)

- Age: It will be presented as a continuous quantitative variable and will be measured in **years**. Hypertension prevalence increases with age and it is one of its main non-modifiable risk factors. It will be measured by anamnesis and/or with the ID card.
- Sex: It will be presented and a dichotomous qualitative variable (**Male** / **Female**). Sex is a significant risk factor for hypertension, with higher male prevalence, especially before the age of 65. It will be measured by anamnesis and/or with the ID card.
- Ethnicity: It will be presented as a nominal qualitative variable (**Asian** / **Hispanic** / **Non-hispanic white** / **Non-hispanic black**). Ethnicity is a complex concept. Most of the current guidelines agree on the fact that black people have a higher risk of hypertension. We have wanted to illustrate that considering these 4 categories, although we acknowledge our simplification of the subject. It will be measured by physical exam and anamnesis.
- Smoking: It will be measured as a nominal qualitative variable (**Non-smoker** / **Smoker** / **Ex-smoker**). Tobacco increases the incidence of Hypertension. It will be measured by anamnesis.
- Current medical treatment: It will be measured as a dichotomous qualitative variable (**Yes** / **No**). For the people who answer with YES, we will collect which drugs are being taken considering **antihypertensive drugs** / **SGLT2 inhibitors** / **asthma treatment** / **others**.
- Central obesity: It will be measured as a dichotomous quantitative variable (**Yes** / **No**). At the same time, it will be defined by the abdominal perimeter. Those patients with a **≥ 102 centimetres of abdominal perimeter for men** and **≥ 88 centimetres of abdominal perimeter for women** will be considered obese. It will be measured during the physical exam.

- Previous Hypertension diagnosis: It will be measured as a dichotomous qualitative variable (**Yes** / **No**). It will be checked on the patients' medical history.
- Previous CV event or disease: It will be presented as a dichotomous variable (**Yes** / **No**). It will be measured by anamnesis and by checking the patient's clinical history. Ischaemic or congestive heart disease, atrial fibrillation, vasculopathy, amputations, strokes, transient ischaemic attack and other records will account positive for previous CV event.
- Diabetes mellitus (DM): It will be measured as a dichotomous qualitative variable (**Yes** / **No**). We will diagnose Diabetes Mellitus according to the *American Diabetes Association criteria* (38) if it does not appear in the patient's clinical history.
- Dyslipidaemia: It will be measured as a dichotomous qualitative variable (**Yes** / **No**). For those patients with no previous diagnosis of dyslipidaemia and no recent exams, we will run new blood exams, and will consider those with **≥ 130 mg/dL of LDL** as dyslipidaemic.
- Chronic Kidney Disease: It will be measured as a dichotomous qualitative variable (**Yes** / **No**). For those patients with no previous diagnosis of chronic kidney disease and no recent exams, we will run new blood exams, and will consider those with a **glomerular filtrate rate < 60mL/min/1.73m2** and/or **albumin/creatinine ratio > 30 mg/g** for **more than 3 months**.
- Socioeconomical status: It will be measured by 3 ordinal qualitative variables, based on the *Enquesta de Salut de Catalunya (ESCA)* as a dichotomous qualitative variable (39):
    - Studies level: **no studies** or **primary studies** / **secondary studies** / **university degree**
    - Social class: **class I** (managers, university professionals, directors) / **class II** (intermediate occupations, sel-employed workers) / **class III** (manual workers)
    - Employment situation: **housework** / **unemployed** / **active worker**

7.5 DATA COLLECTION

For data collection, the manager of the Barcelona city PHC will be contacted. We will inform and ask for their collaboration, to coordinate the sample selection and the posterior obtention of the results.

Once the PHC are enrolled in the project, the sample selection will start. We will ask all the general physicians in these centres to ask their patients if they want to participate in the study. Every tenth (the tenth, the twentieth…) patient who meets the inclusion criteria will be asked to be part of the study and will be given the information sheet and the informed consignment (Annex 2 and Annex 3). The patient's data will be collected in the Data Collection Sheet (Annex 4) by the physicians.

Since most of the patients will be usual primary healthcare patients, we expect to have most of their information. However, a second visit to their usual centre may be needed to complete blood tests and evaluate the patients' comorbidities if they are not specified or studied on their medical records.

In the first or this second visit, we will decide with the patients what date is better for them to use the ABPM and the UPAS monitor, knowing that they will need to attend their centre the first day at 9:00 in the morning and will need to come back the next day. These dates will be organized in a shared document to which all the physicians will have access.

We have decided to pay for 10 ABPM devices and 10 UPAS monitors. A technician will work with us every day in order to deliver 5 ABPM and 5 UPAS devices during the morning before 9.00 am, and after that, collecting the devices that were used the previous day. This same person, once he or she collects the devices used during the day before, will have to download the information and charge all the devices for them to be ready to use the following day. He or she will have to clean the machines and prepare them for the next day.

We will be collecting information from Monday to Friday with 24 hours periods of time. This gives us 4 periods of data collection every week, and in each period of 24 hours, we expect to collect the information of 5 people. This gives us a total of 20 records per week. If we want to collect 462 patients' records, we will need a total of 23.5 weeks of work, which is a little bit less than 6 months or half year. In order to make sure all the patients can collaborate and find a date that suit them, we have thought of extending the collecting period to 8 months. Table 7 summarizes the week organization.

At the end of this period, we expect to have all the data put together in the same computer, which will be given to the investigating team and who will apply all the statistics analysis needed.

Table 7: Weekly organization of the data collection.
The 20 devices will be separated in 2 groups of 5 ABPM devices and 5 UPAS monitors
(Group A – Orange; Group B – Blue)

	Monday (1)	Tuesday (2)	Wednesday (3)	Thursday (4)	Friday (5)
9:00 AM					
Technician's job	Each day, the technician must: - On day 1, the technician must deliver Group A devices before 9.00AM - On day 2, the technician must deliver Group B devices before 9.00AM and then collect Group A devices. After that, Group A devices' information is downloaded and the batteries, charged. - On day 3, the technician must deliver Group A devices before 9.00AM and then collect Group B devices. After that, Group B devices' information is downloaded and the batteries, charged. - On day 4, the technician must deliver Group B devices before 9.00AM and then collect Group A devices. After that, Group A devices' information is downloaded and the batteries, charged. - On day 5, the technician must collect Group B devices. After that, Group B devices' information is downloaded and the batteries, charged.				

8. STATISTICAL ANALYSIS

8.1 DESCRIPTIVE ANALYSIS

The characteristics of the sample of the study will be summarized in this section.

The quantitative outcome variables such as the 24-hour, the diurnal and nocturnal blood pressures, differentiating systolic and diastolic, the means will be calculated with the corresponding standard deviation. The same analysis will be carried out with the 24-hour PM2.5 exposure, calculating its mean and standard deviation. It will be segregated by quintiles in order to analyse if there are differences between groups.

We will also have to summarize the variables related to the diagnosis of Hypertension on our patients and the circadian blood pressure variation with the dipper status. The hypertensive and dipper statuses will be summarized with percentages distribution of each category of our sample.

For the covariates, we will use the average and standard deviation to evaluate the age. The rest of the covariates, which are qualitative variables, will be expressed in percentage for each category

8.2 BIVARIATE AND MULTIVARIATE ANALYSES

In the main analyses, we will estimate the association between PM2.5 and the outcomes: 1) blood pressure (measured in a continuous scale); 2) hypertension diagnosis; and 3) dipper status. For each of these models, adjusted and unadjusted models will be calculated. Adjusted models will allow us to account for the presence of confounding factors.

For all models, a generalised linear regression model will be used. For blood pressure (continuous), an identity link will be specified. For hypertension diagnosis (binary outcome), a logistic regression will be used. For dipper status, a multinominal model will be specified.

All the analyses will be performed using R software version 3.3.3.

9. WORKING PLAN. CRONOGRAM

9.1 STUDY PERSONNEL

The study will require the following staff:

- Study's Investigators: Joan Vidiella Martin, Pere Torguet Escuder
- Coordinator of Research Groups
- Nursery Team
- Technician
- Data and Statistics Consultant
- External collaborators: External investigators, General Physicians

9.2 STUDY STAGES

The complete study has been separated in the following stages.

- **Stage 0: Study Design**. September 2020 – January 2021

  This stage has required a bibliographical research and the elaboration of this protocol.

- **Stage 1: Ethical Evaluation**. January 2021 – February 2021

  The protocol will be submitted to the Clinical Research Ethical Comitee (CEIC) at Hospital Universitari Doctor Josep Trueta de Girona for its approval.

- **Stage 2: Presentation and initial Coordiantion**. March 2021 – May 2021

  The main investigators will contact a Research Coordinator and will hold a meeting with the Barcelona Primary Healthcare Managers in order to involve as many centres as possible in the project.

- **Stage 3: Sample Selection**. June 2021 – September 2021

  During these 4 months, the patients who attend the mentioned centres, will be asked to take part in this study by their general physician. We expect most of the patient's information to be already uploaded to their medical register. However, some of them may need to complete some exams and tests in order to know all their clinical required information.

- **Stage 4: Data Collection**. October 2021 – May 2022

  During the following 8 months, the data will be collected as explained in section 7.5. In this stage, the nursery and technician's collaboration are essential.

- **Stage 5: Statistics Analysis**. June 2022 – July 2022

  Once all the required data is collected, the statistical analysis will be performed.

- **Stage 6: Final Article Elaboration and Publication**. August 2022 – September 2022.

  The final article will be elaborated, and the results will be published.

9.3 CHRONOGRAM

The following Table 8 summarizes the whole project working plan.

Table 8: Chronogram of the Total Project

		Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Stage 6
2020	S							
	O							
	N							
	D							
2021	J							
	F							
	M							
	A							
	M							
	J							
	J							
	A							
	S							
	O							
	N							
	D							
2022	J							
	F							
	M							
	A							
	M							
	J							
	J							
	A							
	S							

10. BUDGET

We have considered the total expenditure, explained on the Table 9.

Table 9: Summary of the Study Budget		
Personnel Expenses		
Nursery Team	1 nurse per patient for 1 hour 5 patients per day 5 days of work per week 23.5 - 32 weeks in total 25€ per hour	14,687.5 – 2,000
Technician	5 hours per day 5 days of work per week 23.5 – 32 weeks in total 25€ per hour	14,687.5 – 20,000
Research Coordinator	19 months of work 1,500€ per month	28,500€
Data and Statistics Consultant	80 hours of total work 35 € per hour	2,800€
Material Expenses		
ABPM devices	10 devices 1,500€ per device 150€ for external batteries 3 extra tension cuffs with different sizes, 300€ each	16,500€
UPAS monitor	10 devices 1,369.58€ per device (machine) 130.42€ per device (uncounted expenses) 1,500€ per device (total)	15,000€
Blood Tests	<50% of the sample will require a total blood test 470 participants 80€ per blood test	15,000€
Coordination and Dissemination Expenses		
Coordination meetings with PHC Services		1,500€
Article Publication		1,500€
Investigation Meetings		1,500€
TOTAL		111,675 – 122,300€

We have tried to expose all the expenses that have to be taken into consideration.

We believe that the Research Coordinator will not have a great workload, which will be mostly concentrated on the Stage 2, and then will just require a basic follow-up.

For the required machines, and mostly for the ABPM devices, we believe primary healthcare centres and/or hospitals, will be interested on them once we no longer require them. This way, even though we have counted the whole price of the devices, we believe part of their cost will be covered by other projects or institutions.

As we have mentioned on Section 7.5, we believe we will have most of the patient's information. However, we have counted to require extra blood tests for less than half of the patients. We have considered these as part of our study budget, but we believe that most of the required tests are part of the expected medical attention in our country, so this cost may not be finally counted.

11. HEALTH AND CLINICAL IMPACT

As we have already explained on Sections 3 and 4, hypertension and pollution are two related major global health issues. Both of them are of great transcendence on human health, both on years and quality of life, and on national healthcare expenditure. Also, we have seen how the hypertension clinical guidelines do not consider pollution as a relevant factor on its physiopathology or as a factor to change on lifestyle modifications, and cities around the world have an unsolved problem with pollution.

This study may increase our knowledge on the effect that PM2.5 particles have on blood pressure, with valid information that could be used in a personal and global assessment.

If we can finally see personal exposure to pollution as a CV risk factor, we will be able to justify certain recommendations to the patients to reduce its impact on their health. The secondary objectives of this study may also help identify those patients who suffer pollution burden on cardiovascular health the most and who need a specific attention.

However, we clearly believe that an individual action would not be sufficient, and that institutions must be the main agent to dynamize a change in our cities and on our emissions. Therefore, we believe that the documentation of this relationship is essential to pressure the national governments, the city halls and any other form of administration to act on global emissions, reducing pollution, climate change advance and all the ecological and human problems related to them.

12. ETHICAL CONSIDERATIONS

The protocol will be submitted to the Clinical Research Ethical Comitee (CEIC) at Hospital Universitari Doctor Josep Trueta de Girona for its approval.

All patients who take part in the study will be properly informed by their physician with the information sheet (Annex 3) and will be asked to sign voluntarily for the informed consent (Annex 2), making clear how the lack of collaboration will not have any effect on their medical attention from that point. All patients will be identified with a number that will be used instead of their names, and the information will be confidential.

This protocol presents a study conducted in agreement with the ethical principles and guidelines established by the *Declaration of Helsinki of Ethical Principles for Medical Research Involving Human Subjects* signed in October 2013 by the World Health Association, and by the *Orden Ministerial SAS/3470/2009* defined currently in the Spanish legislation in relation with the development of observational studies.

Also, the study will be done according to the *Regulation 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to their processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation)*, and the *Ley Orgánica 3/2018, de 5 de diciembre, de Proteccción de Datos Personales y Garantía de los derechos digitales and the Real Decreto 1720/2007, de 21 de diciembre por el que se aprueba el Reglamento de desarrollo de la Ley Orgánica 15/1999*, by which the personal data cession, information collection, data processing and confidentiality of the patients is to be guaranteed and respected.

All the collected information will only be used for the development of the study.

The four Principles of Beauchamp and Childress will be respected during the development of this study.

The authors of this protocol declare to have no conflict of interests with any organ related to the study.

13. FEASIBILITY

We consider our sample to have a significant size. However, we have found previous studies with similar samples of the same population that successful collected all the required patients for their study. We have considered 68 PHC (Annex 1) to collaborate with us in the city of Barcelona city. This mean that if we consider a sample of 462 patients, each centre will have to collect no more than 7 patients, which we believe to be a reasonable number.

Regarding the budget, we believe it relevant to consider how we have tried to regard all the costs and have estimated them taking into account several expenses that we believe will finally be lower as explained in section 10. On the other hand, more than 50% of our total budget corresponds to personnel expenses, which will be hard to cut back.

14. LIMITATIONS

We considered the following limitations that may interfere with our research process:

In this study we investigate the association between PM2.5 and blood pressure, and the results should not be interpreted as casual. Given our non-experimental methodology, variation in exposure to PM2.5 may be driven by unobserved individual characteristics, thus leading to endogeneity in our estimation.

To partially address this, neighbourhoods fixed effects may be included in the multivariate analysis, therefore exploiting within-neighbourhood variation in PM2.5 exposures. Nonetheless, the use of within-neighbourhoods fixed effects could be counterproductive if within-neighbourhood variation in exposure is limited. Because of this, we do not include them in our model.

An alternative (which would fall outside the scope of this protocol) validated in previous literature that studied other topics (40), would be the exploiting quasi-experimental variations from sudden changes in laws or natural disasters.

Many studies have observed similar tendencies on different pollutants rates, basically because of the many common sources. This synergy of the pollutants' behaviour makes the individual evaluation of each of them difficult to assess.

Since we select our sample from a demandant group of patients, we have to consider the real application of the study's result on general population. We believe our study can offer new information on how the different comorbidities alter the relationship between PM2.5 and blood pressure, but by doing so, the applicability on other populations may differ.

Also, we exclude patients who cannot cooperate or understand the required information. We cannot find a reason to think the results could not be applied to these patients, but new evidence is required to confirm so.

The UPAS device is a low-cost personal pollution measuring device which has been tested and used previously, thus we believe it to be a really good tool to use. However,

the current data may seem insufficient and may require other forms of validation by an engineering team.

Nowadays, other public health studies that evaluate personal pollution, also use GPS systems to relate moments of minimum or maximum pollution exposure with the corresponding locations. This was not part of our objectives, but could be interesting on future studies, given the fact that we will be monitoring the PM2.5 exposure during the whole day.

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16. ANNEXES

16.1 Annex 1 – List of Barcelona Primary Healthcare Centres

CAP Adrià - Equip Marc Aureli
CAP Adrià - Equip Sant Elies
CAP Barceloneta
CAP Besòs
CAP Bon Pastor
CAP Bordeta-Magòria
CAP Carles I
CAP Casanova
CAP Casc Antic
CAP Centre Integral de Salut Cotxeres
CAP Chafarinas
CAP Ciutat Meridiana
CAP Comte Borrell
CAP Doctor Carles Ribas
CAP Doctor Lluís Sayé
CAP Drassanes
CAP El Carmel
CAP El Clot
CAP Guinardó
CAP Guineueta
CAP Gòtic
CAP Horta - Equip Barcelona 7D
CAP Horta - Equip Barcelona 7F
CAP La Marina
CAP La Pau
CAP La Sagrera
CAP Larrard - Equip La Salut
CAP Larrard - Equip Lesseps
CAP Les Corts
CAP Les Hortes
CAP Les Planes
CAP Manso - Equip Poble Sec Montjuïc
CAP Manso - Equip Sant Antoni
CAP Manso - Equip Universitat
CAP Manso - Equip Via Roma
CAP Montnegre - Equip Les Corts
Pedralbes
CAP Montnegre - Equip Montnegre
CAP Numància
CAP Pare Claret
CAP Passeig Maragall - Equip Congrès
CAP Passeig de Maragall - Equip Camp
de l'Arpa
CAP Passeig de Maragall - Equip
Encants
CAP Passeig de Sant Joan
CAP Poblenou
CAP Ramon Turró
CAP Roger
CAP Roger de Flor - Equip Dreta
Eixample
CAP Roger de Flor - Equip Monumental
CAP Roquetes - Canteres
CAP Río de Janeiro - Equip Porta
CAP Río de Janeiro - Equip Prosperitat -
Verdum

CAP Sagrada Família - Equip Barcelona 2 I

CAP Sagrada Família - Equip Barcelona 2 K

CAP Sanllehy

CAP Sant Andreu

CAP Sant Martí - Equip Sant Martí

CAP Sant Martí - Equip Verneda Sud

CAP Sant Rafael

CAP Sants

CAP Sardenya

CAP Sarrià

CAP Trinitat Vella

CAP Turó

CAP Vallcarca-Sant Gervasi - Equip Sant Gervasi

CAP Vallcarca-Sant Gervasi - Equip Vallcarca

CAP Vallvidrera

CAP Vila Olímpica

CAP Vila de Gràcia-Cibeles

16.2 Annex 2 – Informed Consent Sheet

CONSENTIMENT INFORMAT

Jo (Nom i Cognoms).....

declaro que:

- Se m'ha ofert i he llegit el full d'informació per pacients sobre l'estudi.
- He rebut la informació adequada de manera clara.
- He pogut fer totes les preguntes necessàries respecte l'estudi.
- He estat informa/da pel meu metge/metgessa de capçalera, amb nom i cognoms ....., amb número de col·legiat ..... de les implicacions i finalitats de l'estudi.
- Entenc que la meva participació és voluntària
- Entenc que es respectarà la confidencialitat de les meves dades i puc demanar conèixer-les.
- Entenc que puc revocar el meu consentiment en qualsevol moment del procés d'investigació i que la meva negativa a iniciar o continuar en el projecte no afectarà en la meva atenció mèdica.

Accepto participar en l'estudi de manera voluntària.

Accepto que l'equip mèdic i d'investigació contactin amb mi si ho requereixen en un futur mitjançant el meu número de telèfon i/o correu electrònic:

.....

Signatura del/la pacient Signatura de l'investigador

Data: ....., ... de/d'..... de l'any .....

REVOCACIÓ DEL CONSENTIMENT

Jo (Nom i Cognoms), ...,
revoco el consentiment de participació a l'estudi on prèviament faig acceptar participar.

Signatura del/la pacient

Data: ....., ... de/d'..... de l'any .....

16.3 Annex 3 – Study Information Sheet

FULL D'INFORMACIÓ PER EL/LA PACIENT

Benvolgut/Benvolguda,

Ens adrecem a vostè per convidar-lo/la a participar en el següent estudi. La seva col·laboració i participació és d'inestimable ajuda i ens permetrà desenvolupar una millor atenció i cura de la població. A continuació li fem saber els motius del projecte i com pot vostè col·laborar.

TÍTOL DE L'ESTUDI

Does Air Quality Matter? 24-Hour Exposure to PM2.5 Particles and Blood Pressure Registers

GENERALITATS DE L'ESTUDI

Aquest estudi es realitzarà a Barcelona i es seleccionaran persones que vinguin a Centres d'Atenció Primària de tota la ciutat. El projecte ha estat avaluat i validat pel Comitè d'Ètica d'Investigació Clínica de l'Hospital Universitari Doctor Josep Trueta de Girona.

OBJECTIUS I FINALITAT DE L'ESTUDI

En aquest estudi proposem valorar la relació que pot existir entre l'exposició diària a la contaminació urbana (concretament a una partícula anomenada PM2.5) i alteracions en la pressió arterial, monitoritzades ambdues informacions durant 24 hores seguides.

També utilitzarem els resultats obtinguts per veure en quins grups de la població, aquesta relació és més severa, i per tant necessitem replantejar l'atenció que se'ls hi ofereix

BENEFICIS QUE DERIVARAN D'AQUEST ESTUDI

Els resultats d'aquest estudi ens poden permetre conèixer millor la hipertensió arterial i les causes d'augment de la pressió sanguínia en els/les pacients.

A més a més, en la situació actual de mala qualitat de l'aire a la ciutat, creiem que aquest tipus d'estudi és una eina amb les quals la ciutadania pot reclamar millores ambientals I urbanístiques als dirigents polítics que han de vetllar pel seu benestar.

QUÈ SE LI DEMANA COM A PARTICIPANT EN L'ESTUDI

Si ha estat informat/da d'aquest projecte, significa que el seu metge de família considera que compleix els criteris necessaris per participar. La seva participació també requerirà que signi el "Consentiment Informat" i que puguem obtenir totes les dades necessàries mostrades en el "Full d'Informació del Pacient", pel que pot ser necessari una visita extra i exàmens de sang al seu CAP habitual si falta informació en la seva història clínica.

Un cop completada tota la informació, se li assignarà un dia a acordar amb vostè on haurà de ser al seu CAP habitual a les 9:00 del matí i se li posarà una màquina que li valorarà els nivells de pressió arterial durant les properes 24h i una monitor que valorarà l'exposició a la contaminació durant el mateix període de temps. Només li demanem que faci la seva vida habitual, anant als espais habituals (feina, transport, casa seva, exterior…) i que al dia següent torni a les 9:00 del matí on se li retirarà ambdós dispositius.

Respecte la màquina de tensió arterial, ha de saber que anirà lligada al seu braç durant tot el dia i notarà com es va apretant periòdicament. Només li demanem que quan això passi vostè estigui tranquil/tranquil·la i segueixi fent les seves activitats habituals.

Pel que fa a la màquina que mesura la contaminació, necessitem que la porti descoberta com en les imatges mostrades. Quan estigui a casa seva la pot deixar a una cadira o taula a la mateixa habitació on s'estigui però amb el detector de partícules encarat cap a munt. Aquesta màquina pesa menys de mig kilogram i pot fer un soroll similar al de una biblioteca (<40dB). Durant el dia es pot escalfar, però pensi que la ha de tenir per fora la roba, no entre la pell i la roba.

Ha de saber que la seva participació és totalment voluntària i el fet de no participar en aquest estudi no afectarà l'atenció que rep en aquest centre. Té dret a abandonar la aquest projecte en qualsevol moment del procés. No rebrà cap compensació econòmica per participar en aquest estudi.

ACCÉS A LES DADES OBTINGUDES

De la mateixa manera, les seves dades individuals que obtinguem seran compartides amb vostè si així ho desitja. Les dades es tractaran amb les mesures corresponents i es garantiran la seva confidencialitat en compliment de la *Llei Orgànica 3/2018 del 5 de desembre* i la *Regulació 2016/679 del Parlament Europeu*, que fan referència a la protecció de dades dels pacients en investigacions.

CONTACTE

Si té qualsevol pregunta no dubti en contactar amb les persones encarregades de dur a terme l'estudi:

Principals investigadors: Joan Vidiella Martin, Pere Torguet Escuder

Adreça de correu electrònic:

.....//.....

Número de contacte:

.....//.....

16.4 Annex 4 – Data Collection Sheet

RECOLLIDA DE DADES DEL/LA PARTICIPANT

DATA: ..... REFERÈNCIA DEL/LA PARTICIPANT: .....

CONTACTE (adreça mail i/o telèfon): .....//.....

Com està especificat en l'apartat 7.4, els diagnòstics es valoraran segons la història clínica dels/les pacients. Si alguna malaltia no està registrada i no hi ha exàmens recents, caldrà fer estudis amb els corresponents criteris:

Diagnòstic Diabetis Mellitus → valorar criteris de l'American Diabetis Association

Diagnòstic Dislipèmia → valorar LDL segons protocol

Diagnòstic Malaltia Renal Crònica → valorar Filtrat Glomerular i Quocient Alb/Cr segons protocol

1. EDAT (anys): .....
2. SEXE:
   - ☐ Dona
   - ☐ Home
3. GRUP ÈTNIC:
   - ☐ Asiàtic/a
   - ☐ Blanc/a No-Hispànic/a
   - ☐ Hispànic/a
   - ☐ Negre No-Hispànic/a
4. TABAQUISME:
   - ☐ Ex Fumador/a
   - ☐ Fumador
   - ☐ No fumador
5. MEDICACIÓ ACTUAL:
   - ☐ Medicació per la Hipertensió Arterial
   - ☐ Inhibidors de SGLT-1 (glucosúrics)
   - ☐ Medicació per l'Asma

☐ Altres

6. PERÍMETRE ABDOMINAL (cm): ..... → OBESITAT CENTRAL:

☐ Si ☐ No

7. MALALTIA O ALTRES ANTECEDENTS CARDIOVASCULARS:

☐ Si ☐ No

8. DIAGNÒSTIC DE DIABETIS MELLITUS:

☐ Si ☐ No

9. DIAGNÒSTIC DE DISLIPÈMIA:

☐ Si ☐ No

10. DIAGNÒSTIC DE MALALTIA RENAL CRÒNICA:

☐ Si ☐ No

11. ESTATUS SOCIOECONÒMIC:

    a. Estudis Cursats:

    ☐ No estudis o Estudis 1aris

    ☐ Estudis 2aris

    ☐ Estudis universitaris

    b. Classe Social (segons ocupació):

    ☐ 1: Gestor/a, Professional Universitari, Directiu

    ☐ 2: Autònom/a, Ocupació Intermèdia

    ☐ 3: Treballador/a manual

    c. Situació Laboral:

    ☐ Aturat/da

    ☐ Treballador/a actiu/va

    ☐ Treballador/a de la llar

16.5 Annex 5 – UPAS Data Sheet

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PORTABLE DUST MONITOR

UPAS
Ultrasonic Personal Air Sampler

"Imagine if personal air sampling was simple.

One, lightweight, quiet, pre-programmed, and tamper proof unit.

No calibration. No tubes. No tape. Simple."

The Ultrasonic Personal Air Sampler (UPAS) provides a new paradigm of exposure assessment for particulate matter air pollution.

Variable Particle Sizes

Depending on the user there are typically 3 particle sizes of interest, the smallest being PM 2.5 and largest being PM 10. In between there's Respirable, usually referenced to Silica. The UPAS has different inlets to size-select the particles you want to collect. Those inlets are also sized differently for different flow rates.

Benefits of Tubeless Design

The UPAS is a self-contained, filter-integrated sampler. It's ultrasonic pumping technology provides substantial reductions in size, weight, noise, and cost along with increased durability over traditional sampling equipment.

Additionally the hassle-free tubeless design allows the UPAS to fit directly onto a person with no tubes or tape required. It is silent and light enough to be worn directly in the subject's breathing zone. Therefore it is easy for the subject to wear while performing daily activities.

Reliable Steady Flow Rate

In addition to being quiet and energy efficient, the mass flow sensor enables the device to maintain a constant sampling flow rate and measures changes in pressure drop across the filter media, giving the UPAS the advantage of having reliably steady flow rate over time.

APPLICATIONS
- Construction
- Outdoor Studies
- Indoor Studies

- Industrial Hygienists
- Environmental Consultants
- Researchers
- Epidemiologists

FEATURES
- Integrated Size Selective inlets
- 35+ hours of battery life
- GPS tracking
- Wireless connectivity
- UPAS App control

a1-cbiss | DATA SHEET PORTABLE DUST MONITOR

SPECIFICATION

• Exterior Size	128mm x 70mm x 23mm
• Weight	230g
• Noise	<40 dB
• Filter Cartridge	37 mm (quick inter-changeable cartridge)
• Battery Type	Li-ion
• Operation Temperature	0-50°C
• Flow Rates	0.5LPM to 3.0 LPM (±5%) accuracy
• Particle Size	PM2.5 - PM10
• Battery Endurance	>35 hours at 1 L min-1 (std) External Battery (optional)
• On-board Sensors	Mass Flow Control Atmospheric Pressure Temperature Relative Humidity GPS Filter Differential Pressure
• Mounting	Body - Armband, clothing clip, lanyard, safety vest etc Fixed - Standard tripod mount

Easy Setup

In all gravimetric samples, filter media must be pre and post-weighed before and after sample collection. Most users work with their local laboratory to weigh the filter and return the mass data. The UPAS collects all of the data during a sample session and logs that to a file the can be exported over Bluetooth or extracted directly from the micro SD card that is part of the UPAS hardware.

The logfiles hold additional information that provide details of the sample, time stamps, GPS, temperature, humidity and pump flow control throughout the sample. Other pumps must have their flow checked before/after each sample run to ensure that the flow was maintained at the correct flow. Note that some test standards/ methods require this anyway even though the UPAS maintains the flow rate on its own.

Easy Access to Data

The UPAS app is primarily a method to program the UPAS and set up the sample parameters along with various options for initiating the sample (now, at a future time, or next press of the start button). It can be quickly programmed from any tablet or phone to fit the users' needs across various applications. Collected data can be uploaded wirelessly to a phone or computer with the UPAS app. Data is easily accessible while keeping the UPAS deployed.

Less Maintenance

Because it is designed with no moving parts, it requires less time for overall maintenance and service.

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