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ASSOCIATION OF EARLY SOCIOECONOMIC CIRCUMSTANCES WITH LUNG FUNCTION IN CHILDREN: A STUDY IN THE GENERATION XXI COHORT

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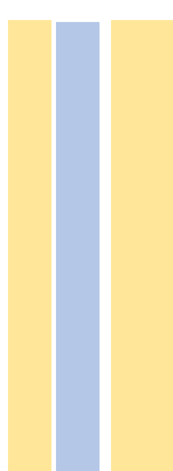

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Dissertação de candidatura ao grau de Mestre em Saúde Pública apresentada à Faculdade de Medicina da Universidade do Porto e ao Instituto de Ciências Biomédicas Abel Salazar.

Porto, 2022

O presente trabalho foi realizado no Instituto de Saúde Pública da Universidade do Porto no âmbito da coorte Geração XXI. Os objetivos desta dissertação inserem-se no projeto de investigação "HIneC: When do health inequalities start? Understanding the impact of childhood social adversity on health trajectories from birth to early adolescence" (POCI-01-0145-FEDER-029567; Reference: PTDC/SAU-PUB/29567/2017), financiado pelo Fundo Europeu de Desenvolvimento Regional (FEDER) através do Programa Operacional Fatores de Competitividade e por Fundos Nacionais através da Fundação para a Ciência e a Tecnologia (FCT). O trabalho foi apoiado pela Unidade de Investigação em Epidemiologia - Instituto de Saúde Pública da Universidade do Porto (EPIUnit) (UIDB/04750/2020), e o Laboratório para a Investigação Integrativa e Translacional (ITR) (LA/P/0064/2020).

ACKNOWLEGEMENTS

I am so excited to be completing this phase of my academic journey, it is indeed a dream come true for me.

My sincere gratitude goes to my supervisors Prof. Sílvia Fraga and Dr. Sara Soares for their advice, trust, and guidance which gave me the much-needed support throughout the master's program. Thank you for this opportunity to learn and develop my skills, it was indeed a pleasant experience. A big thank you to all members of Instituto de Saúde Pública da Universidade do porto (ISPUP), and Generation XXI birth cohort for providing all the necessary resources and materials needed to make the research a success.

A special gratitude to my darling husband and Mentor, who has been so supportive through the ups and down of this master's program, making sure everything goes smoothly. Thank you for your endless support, motivation and for believing in me it sure paid off. Perhaps, we can say we did this together. To my dearest sonshine, Erin André who was with me through it all keeping mummy occupied and motivated, we did it baby! My appreciation further goes to my parents Mr. and Mrs. J.S Toluhi for their constant prayers, support, words of encouragement, immense love, and for always believing in me. And to my siblings Abiola, Yemisi, Bunmi, Dola, Kayode, Rachel, U. Konkey thank you for always being there for your baby sister I love you all!

I also would like to extend my gratitude to my Nigeria friends in Porto, I call them my Porto family. Thank you for making my stay in Porto a pleasant one filled with lots of memories. I like to particularly thank Dr. and Mrs. Aboderin and their kids for everything they do for us, you are indeed family to us. And to my friends and extended family, the list is long I best not name each one, I say thank you all for your love and support always.
To myself, I say well done for putting in the work and nursing Erin at the same time, you did amazingly well. And finally, but not the least acknowledging I am nothing without God, I am externally grateful to God for everything. Greater things to come….

Muito Obrigada a todos!

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LIST OF ABBREVIATIONS

BMI - Body Mass Index

COPD - Chronic Obstructive pulmonary disease

FEV1 - Forced Expiratory Volume in 1 second

FVC - Forced Vital Capacity

SES - Socioeconomic Status

SDH - Social Determinants of Health

WHO - World Health Organization

ABSTRACT

Background

Child development reaches its peak during childhood. During this period the foundations for every individual's physical and mental health capacities and attainment are laid, influencing growth, development and well-being in adolescence and adulthood. Thus, the study of the effects of exposure to socioeconomic deprivation is essential to understand the origin of health inequalities. Literature documents that socioeconomic deprivation experienced in childhood is associated with a greater risk of developing health problems in adulthood, and of premature death. However, the biological incorporation of these experiences during childhood and their impact on health has not yet been explored. Particularly, exposure to socioeconomic deprivation during early life has been shown to negatively affect lung function in adulthood. However, only a few studies have investigated the association of childhood socioeconomic circumstances with lung function in children. Thus, the aim of this work is to investigate the association of early childhood socioeconomic circumstances with lung function in the first decade of life using data from Generation XXI.

Methods

Information from the Portuguese birth cohort Generation XXI was used. Socio-economic indicators, including the mother's and father's education and occupation, and household income, were collected in the first cohort assessment. At 10 years of age, spirometry data from 5060 children were analyzed and measurements of forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) were obtained. The FEV1/FVC ratio was then calculated. Linear regression models were fitted to estimate the association between socioeconomic indicators and lung function (FEV1/FVC). The models were adjusted as follows: Model 1, adjusted for small for gestational age; Model 2, adjusted for smoking during pregnancy; Model 3, adjusted for 2nd hand smoking; Model 4, adjusted for acute infections (C-reactive protein); and the final model, adjusted for all covariates.

Results

Participants from more disadvantaged socioeconomic status present higher ratio of FEV1/FVC at 10 years of age, compared with more advantaged counterparts. Our results show that there is a dose-response association between early socioeconomic status and lung function i.e., increasing FEV1/FVC ratios are observed with decreasing categories of socioeconomic indicators. The same trend is observed when analyses are conducted stratified by gender. Children from more disadvantaged socioeconomic status presented lower lung function compared with more advantaged counterparts. In general, the trend was very similar in girls and boys and for all indicators, with children whose parents had the lowest SES having the highest FEV1/FVC ratio.

For instance, children whose parents had a low educational level, presented higher FEV1/FVC ratio than those whose fathers had higher educational levels.

Conclusions

Children born in a socioeconomically disadvantaged context will present worse lung function compared to children born in more affluent environments.

These results show that health inequalities resulting from social inequalities can be observed already in the first ten years of life. Thus, the observed inequalities in lung function seem to be socially patterned, showing that lung function in children can be negatively affected at a very early stage of life.

This emphasizes the importance of investing in social policies and family support to provide children with a better start in life for better long-term health. Factors identified during childhood by their modifiable nature provide the perfect opportunity for local and global public health interventions aimed at alleviating or reducing socioeconomic inequalities and their health effects, starting at earlier ages.

RESUMO

Introdução

O desenvolvimento da criança atinge o seu pico durante a infância e é nos primeiros anos de vida que se estabelecem as bases para um crescimento saudável e consequente saúde física e mental ao longo da vida. Assim, o estudo dos efeitos da exposição a situações adversidade socioeconómica, é fundamental para compreender a origem das desigualdades em saúde. Na literatura está já documentado que a privação socioeconómica experienciada no período da infância está associada maior risco de desenvolvimento de problemas de saúde na vida adulta, e com maior risco de morte prematura. No entanto, a incorporação biológica destas experiências já durante a infância e o seu impacto na saúde não foi ainda muito explorado. Em particular, foi demonstrado que a exposição a privação socioeconómica durante o início da vida afeta negativamente a função pulmonar na idade adulta. No entanto, apenas alguns estudos investigaram a associação das circunstâncias socioeconómicas na infância com a função pulmonar em crianças. Assim, o objetivo deste trabalho é investigar a associação das circunstâncias socioeconómicas da primeira infância com a função pulmonar na primeira década de vida usando dados da Geração XXI.

Métodos

Foi usada informação proveniente da coorte de nascimentos portuguesa Geração XXI. A informação sobre os indicadores socioeconómicos, incluindo a educação e a profissão da mãe e do pai, e o rendimento do agregado familiar, foi recolhida na primeira avaliação da coorte. Aos 10 anos de idade, dados de espirometria de 5060 crianças foram analisados e obtiveram-se medidas do volume expiratório forçado no primeiro segundo (FEV1) e a capacidade vital forçada (FVC). Foi depois calculado o rácio FEV1/FVC. Modelos de regressão linear foram ajustados para estimar a associação entre os indicadores socioeconómicos e a função pulmonar (FEV1/FVC). Os modelos foram ajustados da seguinte forma: Modelo 1, ajustado para pequeno para idade gestacional; Modelo 2, ajustado para consumo de tabaco durante a gravidez; Modelo 3, ajustado para exposição a fumo de tabaco; Modelo 4, ajustado para infecções agudas (Proteína C reativa); e o modelo final, ajustado para todas as covariáveis.

Resultados

Em geral, a tendência foi muito semelhante nos dois géneros e nos diferentes indicadores socioeconómicos, e crianças de famílias, famílias socioeconomicamente menos favorecidas apresentam um rácio FEV1/FVC maior aos 10 anos de idade. Em particular, crianças cujos pais apresentam níveis de escolaridade mais altos, apresentam um rácio FEV1/FVC menores do que filhos de pais com menores níveis de escolaridade.

Conclusões

Observou-se que as crianças nascidas em contextos socioeconomicamente menos favorecidos apresentam pior função pulmonar em comparação com crianças nascidas em ambientes mais afluentes.

Estes resultados parecem mostrar que as desigualdades em saúde resultantes das desigualdades sociais podem ser observadas já nos primeiros dez anos de vida. Desta forma, as desigualdades da observadas na função pulmonar parecem ser socialmente padronizadas já na primeira década de vida, mostrando que a função pulmonar em crianças pode ser afetada negativamente numa fase muito precoce da vida.

Enfatiza-se assim a importância de investir em políticas sociais e de apoio às famílias para que se proporcione às crianças um melhor começo de vida para uma melhor saúde a longo prazo. Fatores identificados durante a infância pela sua natureza modificável, proporcionam a oportunidade para intervenções locais e globais em saúde pública direcionadas para atenuar ou reduzir as desigualdades socioeconómicas e os seus efeitos na saúde, começando em idades mais precoces.

1 INTRODUCTION

The health of individuals can be impacted by their behavior and lifestyle choices such as diet, exercise, vaccinations, access to healthcare, smoking, and drinking among others. Their health can also be influenced by the health infrastructure and policies of their nations such as the timeliness and access to healthcare, affordable health insurance, and health prevention and promotion strategies[1]. However, there has been evidence showing a strong relationship between the living and working conditions of individuals and their health outcomes thereby drawing attention to the influence of the social environment on the health of individuals[1]. These social factors such as income, education, occupation/employment, and housing can impact the health of individuals or the population positively or negatively[2] and, as such, cannot be ignored.

These social factors are referred to as Social Determinants of Health (SDH)[3] which are aspects of people's lives that are not directly related to their health because they are non-medical but play a major role in determining health outcomes. The social determinants related to the political, economic, and cultural environment in which people live can vary widely between individuals and are capable of determining whether one gets a particular sickness or not and even the extent of such sickness. Since these determinants are non-medical, they cannot be addressed with typical clinical approaches to health issues [4] implying that medical care alone is not sufficient to greatly improve the overall health of the population. Therefore, social factors such as the environment people find themselves in, their socioeconomic position, as well as their social identity (gender, tribe, race, associations) needs to be addressed concerning how they impact their health.

1.1 Social Determinants of Health

According to the World Health Organization (WHO), Social Determinants of Health are the conditions in which people are born, grow, work, live, and age, and a range of other factors and systems that directly influences the day to day living.[3] These conditions are embedded in social, economic, and political systems that result in an individual´s division into various socioeconomic indicators such as education, income, occupation, gender and race amongst others.[3] An individual can be more susceptible or exposed to certain health conditions as a result of their socioeconomic status. For example, a rural farmer will be more susceptible to diseases caused by exposure to harmful chemicals and pesticides than people who work in built environments, while people exposed to household second-hand smoke will be more susceptible to respiratory illnesses than those who are not subjected to such exposures.

There have been lots of studies showing associations, pathways, and biological mechanisms pointing to the fact that social factors play a major role in determining health outcomes across a population[5]. Although, this does not rule out the role of medical factors but indeed shows that it is not limited to medical care alone[4,5]. Whether in low-income or high-income countries, health outcomes are correlated with social factors, with people of lower socioeconomic circumstances ending up with the worst health outcomes and shorter life expectancy as compared with those who are well-off.

1.1.1 The Conceptual Framework

The conceptual framework to study the Social Determinants of Health was developed by WHO to understand how social factors affect population health and how to tackle them to improve public health. The framework emphasizes that the goal of studying these social factors is to achieve health equity which is the absence of unfair and avoidable differences in health among groups of people or population[3]. The framework addresses socioeconomic and political contexts comprising of a wide range of factors that are immeasurable at individual levels in the society but consist of structural, cultural, and functional aspects that greatly determine one´s ranking in society and, by extension, one´s health.

The WHO framework maintains that social, economic and political mechanisms result in socioeconomic positions as they generate social hierarchy in the population. As shown in Figure 1.1, these mechanisms include labor, educational, political systems, and societal cultural values. Socioeconomic position is influenced by education, income, occupation, gender, race as well as other factors. Accordingly, these socioeconomic factors shape the health status of an individual through material circumstances (e.g., financial means to buy healthy food or live in healthy environments), behavioral circumstances (e.g., consumption of alcohol or tobacco) and psychosocial circumstances (e.g., stressful living situations).

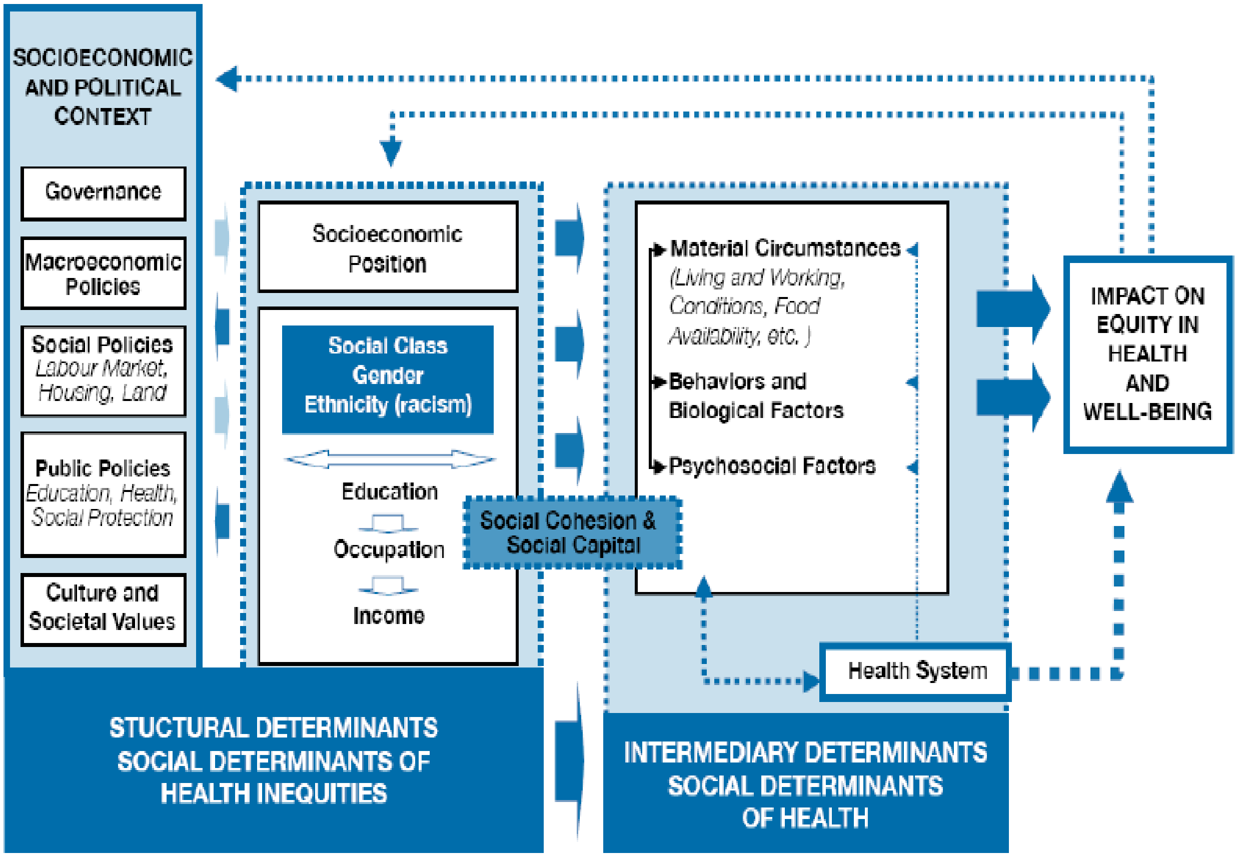

Figure 1.1 The WHO Conceptual Framework[3]

The WHO framework also considers healthcare as a social determinant of health, as not everyone has equal access to healthcare leading to differential consequences of illnesses (Figure 1.1). It further highlights that illness can give ‘feedback’ on an individual’s social status, this can be seen in cases of losing employment opportunities or resigning due to ill health which translates to reduced income that further impacts health negatively.

The epidemic disease could also give feedback as it could greatly affect social, economic, and political organizations.

Three key policy approaches suggested to address health inequity are 1. Programs targeted at improving the health of individuals with lower socioeconomic status 2. Closing health gaps between different social groups 3. Addressing the association between socioeconomic position and health in the entire population.

1.1.2 Socioeconomic Indicator

There are several socio-economic indicators used in population studies, each measuring different aspects of social stratification and having its significance in relation to health outcomes. Some of these indicators are relevant to different health outcomes and at different phases in the life course. Every indicator is important in population studies but the choice of indicator to be used will depend on the research in question as different socioeconomic indicators answer questions about different aspects.[6,7] Some commonly adopted socioeconomic indicators are summarized below:

Education: Education as a socioeconomic indicator has been used a lot in population studies[6] and has been shown to play a major role in determining some health outcomes (e.g., studies have shown that children from homes where parents have some level of education tend to enroll/take the needed vaccinations in comparison with children whose parents are not educated[8], some other studies have also shown how children with parents who are not educated having higher cases of malnutrition or obesity, as some do not have the necessary health information on nutrition[5,9]. It improves health via knowledge acquisition and promotes healthy behaviors. Since education is strongly determined by parental status, it reflects the material resources of the parents[6,10] and thus provides some level of information about an individual´s early socioeconomic status.[3] Attainment of education can help to improve literacy and increase health knowledge and behavior. This can be reflected in the way individuals are receptive to health information, how they obtain or search for this information, how they can seek or access healthcare, communicate their health needs, and make decisions about their health. People with higher levels of education have been associated with better health behaviors such as diet, exercise, smoking and drinking habits, disease, or health management among other things.[11]

Educational attainment can also determine employment opportunities and income, as highly educated people are more likely to get better jobs with better working conditions and environment including health insurance, retirement plans and compensations in case of work-related hazards[5,7,12]. Studies have shown that unemployed individuals tend to have worse health conditions than their employed counterparts.[13] Greater educational attainment can reflect social class, social standing, income resources and material assets of an individual[6].

Income: Income is a socioeconomic indicator that is oftentimes considered a direct indicator to measure material resources. As with other indicators, income can influence a lot of material circumstance that directly impacts health in various ways by the conversion of money and assets into health-enhancing commodities.[14] Some studies have also found an association between income and life expectancy finding that individuals with higher income have a longer life expectancy as they can afford the resources needed to prevent or treat illness as well as access healthcare in comparison to low-income earners[15,16]. Income in some cases could determine who has access to health care or other enabling resources that promote health e.g., housing and even education. It could also influence the kind of lifestyle people live, as people with less income might not be able to afford certain resources needed for a healthy lifestyle such as eating nutritious meals, leisure activities etc.[17] It can also reflect socioeconomic status over an aggregate period and can change over a short period.[18] Ill health could also lead to lower income as an individual is either unable to work or spend most of their income treating illnesses. [19,20] Oftentimes, household income is measured rather than individual income as this reflects the income of the home particularly since all members of the household share the elements of consumption of the income. [6]

Occupation: Occupation is another socioeconomic indicator used in a lot of population studies. It shows an individual's position in society, intellect as well as income. [6]Occupation could reflect income as it translates to resources and other privileges associated with work which can determine health outcomes. These benefits can shape individuals' access to healthcare, better level of education and neighborhood environment. Occupation could also have a psychosocial effect on individuals as it determines their social support, work stress, social standing, and control. Individuals can also end up with certain health conditions because of their occupational exposure. For example, a worker that does a job that requires repeating certain movements over and over could be exposed to musculoskeletal disorders, a painter is more exposed to chemicals contained in paints as he works daily [21] or a worker whose job is sedentary has an increased risk of obesity. [22]In studies related to childhood or early socioeconomic status (SES), occupations of parents are usually used either alone or with an individual's occupation at several stages across their life. In some cases, the occupational socioeconomic status of an individual, for example, the head of the house or a combination of individuals, could be used to measure the SES of a dependent or partner in the household. One major setback of occupation as an indicator is that it cannot be assigned to people who are currently unemployed or retired. As such, it should be used alongside other indicators to adequately capture socioeconomic differentials.

Housing/Neighborhood: Housing characteristics and neighborhood conditions can influence health outcomes in several ways. They are used in population studies to measure SES and can provide information about specific pathways or mechanisms that can be directly linked to health outcomes e.g., water or air quality. Conditions such as water quality, air quality, overcrowding, green spaces for exercise, proximity to healthcare facilities, transport, nearness to facilities that emit or store harmful chemicals, exposure to secondhand smoking, dust, etc. can either lead to illness or worsen certain health conditions. [23,24] Also studies have shown that neighborhoods with better social interaction and community togetherness have been linked with better physical and mental health, and with lower cases of homicides. [25]Conversely, illnesses such as mental health disorders are prevalent in neighborhoods with fewer social interactions. [26] This indicator could be used both for developed and under-developed countries though characteristics measured/assessed may differ between countries. Housing amenities and conditions are usually used as a measure of material resources. Housing contracts are usually one of the common characteristics used to assess housing, whether the house is rented, owned or bought on a mortgage and in rural populations owing farmlands.[6]

1.1.3 Health inequalities and health inequities

Social determinants of health have a strong impact on health inequities. Health inequities refer to unfair or unjust disparities in health or social determinants that favor social groups that were already more advantaged.[27] The disparity, in this case, is not merely differences between groups of people but specific differences that arise because of the social position people occupy in the population. For example, the kind of job, resident geographic area or educational qualification can place people at different levels of social advantages or privileges in the population.[28] It is worth noting that, not all health disparities are unfair as some are natural such as men having prostate problems while women do not, or women having mensural issues while men do not. In these cases, the disparities are termed health inequality. However, when such inequalities arise due to systematic unfairness in rules or policy that adversely affects a particular group, it is referred to as health inequity. Therefore, health inequity is an inequality in health that is unfair or unjust.[28]

Health inequities arise due to the circumstances in which people are born into, grow up, live, work, age, and the available systems to tackle illnesses. All these conditions in which people are born and die are influenced by social, economic, and political factors. And they go a long way in determining whether an individual will live a flourishing life or have a shorter life expectancy. For example, in some countries access to education depends on gender, in other parts of the world it could be access to clean water or healthcare that is dependent on the Income or Race of individuals. In these examples, certain privileges or access are denied or limited because of the social group people identify with within the population.

On the other hand, health inequities refer to systematic, unjust, and avoidable differences in health care across the population or between groups of people. Health inequalities can be due to several factors including social circumstances into which people are born, grow and live.[29] These inequalities have been shown to begin very early in life, even from conception as traits and circumstances can be transferred between generations.[30]Socio-economic factors such as parental education, income, employment status, ethnicity, and environmental exposure can influence a child´s development and can continue to determine health status even into adulthood.[31]

Inequity in health or healthcare cannot be directly measured, however, inequalities between more advantaged and less advantaged social groups can reflect inequities as those less advantaged are further disadvantaged in their health and healthcare.[32] To achieve health equity, every member of the population must be valued/treated equally while also paying attention to avoidable inequalities, systematic and historical bias as well as disparities in health and healthcare[33] The main aim of addressing health inequities is to ensure everyone can attain their full health potentials equally with no one been disadvantaged because of their social group or position or because of other socioeconomic circumstances they find themselves.[34]

This thesis focuses on understanding how socioeconomic circumstances impact lung function, so the next sections will summarize the meaning of lung function, the factors that determine lung function and some studies linking social inequities to lung function.

1.2 Lung function and its determinants

To determine the level of functionality of the lungs, lung function tests also referred to as pulmonary function tests are usually performed. Spirometry is often used to screen for diseases affecting the lungs as well as the airways. Lung volume testing and diffusing capacity tests can also be performed to measure the volume of air in the lungs and how oxygen enters the bloodstream. These lung function test helps to identify the possible existence of lung diseases and their severity as well as assess response to respiratory-related interventions in terms of treatment. Anthropometric factors such as weight, height, age, and gender[35] have long been used for the interpretation of lung function. However, over time several studies have found other factors/associations very relevant in assessing lung function, these include physical factors (menstrual cycle[36], chest diameter, trachea size etc.), social and healthcare factors (socioeconomic status [37]e.g., Income, education, occupation), environmental factors (Air pollution[38], climatic conditions[39]), Race/ethnic group[40], Lifestyle (diet/nutrition[41], exercise[42], smoking), genetic factors[43], childhood circumstances[44], pregnancy[45], and other diseases.

Age is one of the factors used in assessing lung function. Studies have shown that the maturity of the lung is usually attained at around the age of 20-25 years[46], after which lung function begins to decrease.[47] The forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) are the variables that decline the most with age. [48] Some other studies have also found an association between respiratory diseases and low birth weight[49], women that have attained menopause[50], as well as certain exposures in childhood that impacts lung function negatively in adulthood.[51] The height of individuals can also determine lung capacity and volume, as taller individuals are said to have higher lung capacity with shorter individuals having decreased lung volume at older age.[52] Weight /BMI (body mass index) has also been seen to cause a decrease in total lung capacity although the reduction might be insignificant.[53] Some studies have also shown that airways can be limited because of obesity[54], and abdominal obesity has been linked with reduced FEV1 and FVC, especially in women and specific age groups.[55] As regards gender, in men and women with the same weight and height, women tend to have smaller lungs in comparison to men and an association was found between gender and the occurrence, susceptibility and severity of some lung diseases.[56]

1.2.1 Social inequalities in lung function

Social inequalities exist in the growth and development of the lungs which results in how it functions whether optimally or not. Understanding the social patterning of lung function would help in proffering interventions to address social issues associated with lower lung function, especially from early childhood.[57]

Socioeconomic status is associated with lung function both in childhood and adult life. Socioeconomic status such as income/resources, housing environment, the occupation people do and what they are exposed to while working, as well as their educational levels, can cause social inequalities that impact their lung function positively or negatively. Several studies have found positive associations between higher SES and lung function and vice versa.[43,58–61] Some studies in adults show that the origin of lung problems can be traced back to socio-economic circumstances occurring during early childhood.[51,62] The lifestyle of individuals such as the kind of food they eat, their physical activities and habits such as smoking can also affect their lung function. Studies have also found that differences in lung function exist based on the race/ethnic groups people belong to.[63]

Occupation/occupational pollutants have been associated with respiratory diseases such as Chronic obstructive pulmonary disease (COPD), mesothelioma, and lung cancer. Studies have also shown that individuals with less or no skills and educational qualifications end up with menial jobs with a lot of occupational hazards[1] Individuals that are unemployed have been linked with ill health and other disabilities in comparison to their employed counterparts. Poor housing conditions such as the presence of dampness, dust, and molds, including overcrowding have also been linked with respiratory diseases such as asthma as well as respiratory irritation. These conditions are usually seen in poorly constructed houses or damp areas and these houses are usually occupied by individuals of low socioeconomic status who can't afford better housing.[6,64] Likewise, homeless individuals are likely to have respiratory issues like chest infection, asthma, COPD, among others.[65]

Environmental air pollution with substances such as nitrogen dioxide (NO2) and particulate matter (PM) can cause can also worsen or cause lung diseases. Individuals who work or live near factories that produce these substances are at greater risk of respiratory diseases.[38,66] Similarly, air pollution in the environment where people live can be an important factor that negatively impacts lung function. This can be particularly detrimental in childhood when lungs are still developing and are more susceptible to diseases that can linger to adulthood. It is therefore imperative to study how socioeconomic circumstances affect lung function in early childhood.

Several studies have shown associations between socioeconomic status and lung function, with lower SES leading to health inequalities in lung function. A study that assessed the association between socioeconomic status and severity of Asthma found that asthma was more prevalent in children from lower socioeconomic groups than those from higher socioeconomic groups.[67] Similarly, an association was found that showed that adolescents from families with low income have lower lung function than those with higher income.[68] Social patterning of lung function was also studied at different ages showing that SES disparity in lung function increases with age, especially in men and that early life factors can predict inequity during younger years of life.[57,69] This association has also shown time evolution from childhood to adolescence with children with lower SES having a lower respiratory function in adolescence than higher SES and that boys had higher respiratory inequalities compared to girls.[61]

1.3 Early socioeconomic circumstances and respiratory health in childhood

In the early stages of life, the environment where a child is raised is very vital for the overall health of the child.[51] Socioeconomic status influences the health and well-being of children at several levels (family and environment). In most studies involving child development, socioeconomic status is always looked at as it is believed to be one of the ways through which health outcomes of a child can be tracked using parental socioeconomic status to ascertain the resources and opportunities the child is exposed to. [70]

Individuals with less advantaged socioeconomic circumstances (SEC) at early ages have been shown to end up with the worst health outcomes through life course.[51,62] This might be explained by the fact that the period from birth to adolescence is where the most crucial growth or development of body organs occurs and system functions are formed, and thus determined by social and economic circumstances. Previous studies have shown pathways that link adverse childhood circumstances with increased risk of mortality to several diseases as well as chronic diseases in adulthood such as coronary heart diseases, different kinds of cancer, and respiratory problems involving low lung function among others.[71,72],[57] Some early life factors such as childhood infection, low birth weight, prematurity, and maternal smoking, among others which can be linked to low socioeconomic circumstances have been associated with reduced lung function in early life as well as adolescence.[73–76]

Studies in adults show that the origin of lung problems can be traced back to socio-economic circumstances occurring during early childhood when lungs are still developing and thus vulnerable to various unfavorable conditions such as poor housing, poor diet, and exposure to second-hand smoking amongst others. These conditions can inhibit proper lung growth and lead to lower lung function in adults.[51,62] Some respiratory diseases have also been traced back to epigenetic programming resulting from exposures to certain conditions or environments influencing how genes work.[51,77,78]

However, a previous review showed that only a few studies have explored the association of childhood SEC with lung function in children using prospective data.[79] Therefore, studying such association can be used to understand at what point during early life the effect of SEC on lung function starts manifesting in children and can additionally be useful in detecting early life differences in lung growth. Although, it is quite complex to explore this relationship as children do not have their socioeconomic status but are indirectly impacted by those of their parents/guardians[71], usually maternal education is used and, in a few cases, parental occupation and income. The choice of indicators to use as a measure of SEC should always be evidence-based to avoid bias in reported results.[6]

Most of the studies on the association of SEC with lung function in children have been based on physician diagnoses reported by the parents and thus can be subject to memory bias.[80–82] More objective metrics of lung function such as forced expiratory volume in 1 second (FEV1) or forced vital capacity (FVC) are required to properly assess the association.[68] Other results using these metrics found an association between low SEC and children´s reduced lung function[83] although the result appears to be inconsistent with others carried out on children between the ages of 5 and 17 where social differences were only found in boys but not girls.[68,84] Studies have implied that differences in gender impact lung structure and growth and can determine the vulnerability and severity of several lung problems.[85] This might explain the difference in the SEC-lung function association with gender but requires further study.

During the early period of life, the bases are laid for the individual physical and mental ability, affecting growth, development, and health. Therefore, improving health and developmental outcomes in childhood is a top priority, since every child should have the best start in life. Studying inequalities in children is important as it can help inform social policies that are targeted at children and families with low SEC to prevent and reduce its adverse impact on children's health.
Ascertaining the effect of childhood socioeconomic circumstances on respiratory function is essential to avoid uneven lung function growth between different socioeconomic groups, which could lead to the disproportionate prevalence of respiratory illnesses over the life course. Therefore, the goal of this thesis is to estimate the association between SEC and lung function in children using data from the Portuguese population-based birth cohort- Generation XXI.

1.4 Public Health approach to social health inequalities

Health inequalities are disparities in health outcomes, these disparities can be observed in individuals, social groups, within a population, or between countries. These health inequalities can be observed among individuals from early childhood until old age (i.e., throughout life course). Most of these inequalities in health are unjust and avoidable as they result from policies and government actions that are unfavorable to specific groups of individuals. To address health Inequality, first, the sources of these inequalities need to be identified and the root causes such as living conditions, access to healthcare, employment opportunities, and exposures among others that lead to inequalities addressed. Also, Conditions such as income, employment, occupation, housing, nutrition, healthcare etc. are some of the social determinants of health. These social determinants of health can enhance the health outcomes of individuals who have access to them while adversely affecting the health of individuals who can't access them in the population. How these social determinants of health are distributed among the population is what leads to inequality in health.

During the early period of life, the bases are laid for the individual physical and mental ability affecting growth, development, and health. Therefore, improving the health and developmental outcome in childhood is a top priority, since every child should have the best start in life. Tackling health inequalities at the early stages of life greatly reduces inequalities, especially among the most vulnerable children in the population.

Factors that can help reduce health inequalities include ensuring there is a strong database of evidence in which policymakers can refer to make life-changing decisions, an intersectoral approach (engaging other sections outside the health sector to jointly improve the social determinants of health and health equity, develop effective programs and interventions targeted at children at the early years of development, among others.

2 THESIS OBJECTIVES

This thesis aims to investigate the association of early childhood socioeconomic circumstances with lung function in the first decade of life using data from the Generation XXI population-based birth cohort. More precisely, the study aims:

- to estimate the association between childhood socioeconomic circumstances and respiratory function (FEV1/measures) among 10-year-old children.

In line with this, the secondary objectives of the thesis are:

- to investigate if there are social differences in lung function according to gender.
- to investigate if social differences are independent from the role of perinatal characteristics, health behaviors, exposure to second-hand smoking, and the presence of infections at these early ages on lung function.

3 METHODOLOGY

3.1 Study Design

The prospective study sample consists of children who took part in the Generation XXI Portuguese population-based birth cohort that enrolled 8647 newborns delivered in 2005/2006 in the Porto Metropolitan Area, Northern Portugal. Children were invited to attend the subsequent study waves in 2009-2011, 2012-2014 and 2016-2017 at the ages of four, seven, and ten years old, respectively. Birthweight and length were extracted from the clinical records at birth. Anthropometric measures were recorded in all study waves, following the same standardized procedures. Data on demographic and socioeconomic characteristics, personal history of disease and health-related behaviors were collected by trained interviewers through structured questionnaires administered at all study waves.

3.2 Participants

Participant recruitment was carried out between April 2005 and August 2006 at five public maternity units of Porto Metropolitan Area that provide obstetrical and neonatal care, as at the time: Centro Hospitalar de Vila Nova de Gaia, Centro Hospitalar do Porto - Maternidade de Júlio Dinis, Hospital de São João, Centro Hospitalar do Porto - Hospital de Santo António and Unidade Local de Saúde de Matosinhos - Hospital Pedro Hispano. All the maternities had perinatal support and were level III units. In 2004, 91.6% of the deliveries in the whole population occurred in these maternities, with the remaining percentage occurring in private hospitals and clinics.

Eligible participants were women living in the recruitment area- one of the six municipalities of the metropolitan area of Porto (Figure 3.1) and who delivered a live-born child with more than 23 weeks of gestation in one of the five maternities unit, during the recruitment period. Seventy per cent of the eligible mothers were invited and out of these 91.4% accepted to participate. As shown in figure 3.2, a total of 8647 infants and their mothers (n=8495) were enrolled on the cohort study.

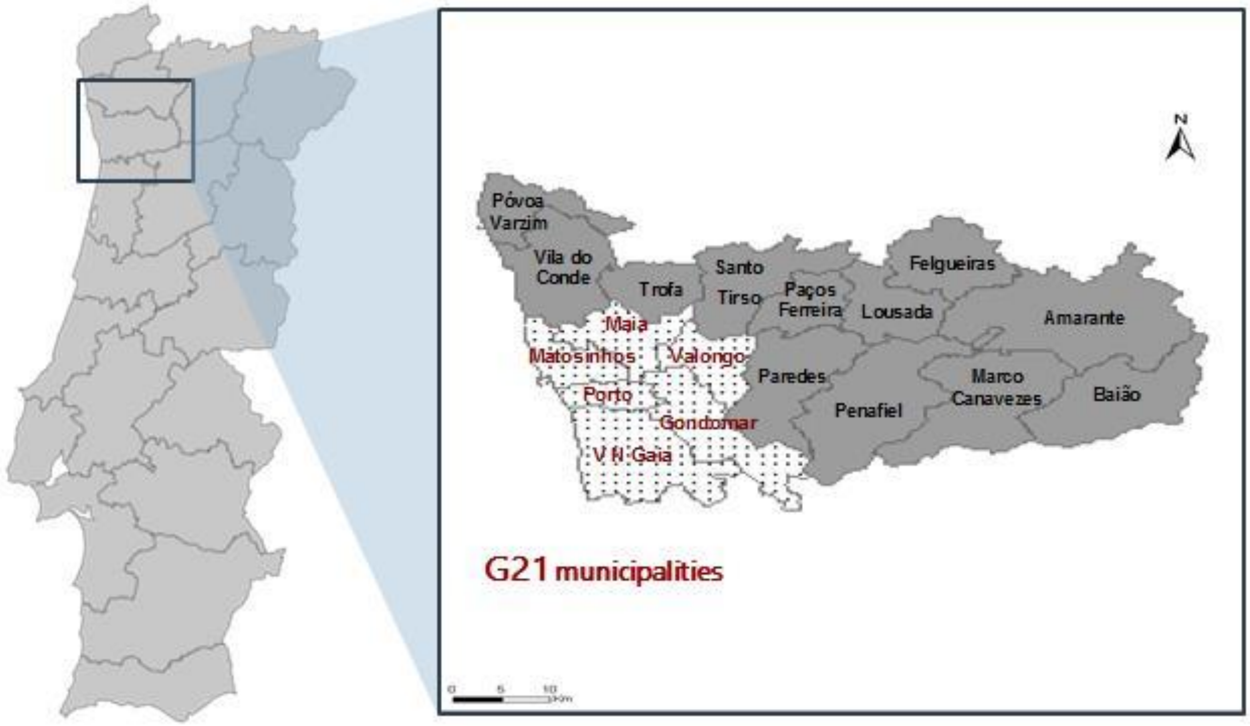

Figure 3.1 Representation of the six municipalities of the metropolitan area of Porto.

3.3 Data Collection

At baseline, trained interviewers assigned to the five hospitals were in charge of presenting the Generation XXI study and inviting mothers who had just delivered in the first 24 to 72 hours during their hospital stay to participate. Data were obtained in a face-to-face interview and clinical records at birth were reviewed by the trained interviewers.

The cohort's subsamples were evaluated at the ages of 6 months (n=1555), 15 months (n=1043) and 2 years (n=855). A follow-up evaluation of the entire cohort was done four years after birth, between April 2009 and July 2011, and 7459 children (86.3% of the cohort), were re-evaluated. Of these, 5987 children (69.2% of the cohort) were evaluated in a face-to-face interview while 1472 children (17.0% of the cohort), that were unable to attend an in-person evaluation, had their legal guardian complete a shorter version of the questionnaire in a telephone interview. A 7- year follow-up evaluation of the cohort was conducted from April 2012 to April 2014, where all families were invited to attend. Overall, 6889 children were reassessed (79.7% of the entire cohort), of which 5849 children (67.6% of the cohort) were evaluated in person and 1040 (12.0% of the cohort) provided information by telephone interview.

Between July 2015 and July 2017, a subsequent evaluation of the cohort took place, when children were 10 years old, and 6397 children (76.0% of the cohort) were re-evaluated.

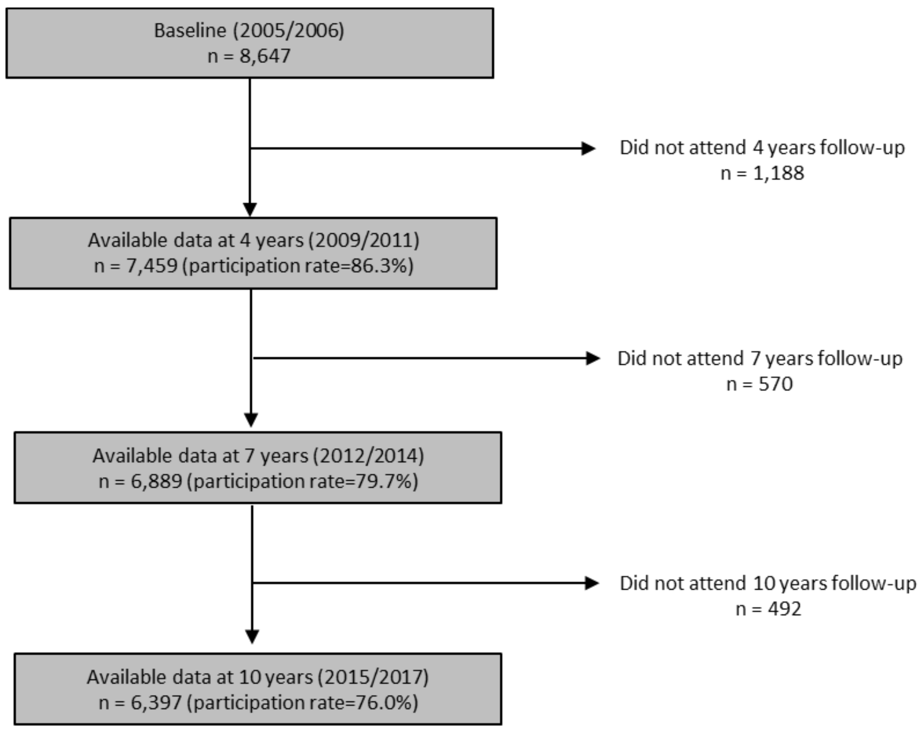

Figure 3.2 Flow-chart of participants

Follow-up evaluations of the cohort took place at Departamento de Ciências da Saúde Pública e Forenses, e Educação Médica in the University of Porto Medical School. Standard procedures have been established and adopted in all cohort evaluations. A multidisciplinary team of interviewers and health professionals, that are periodically trained and supervised by the Generation XXI administration team, are responsible for the application of structured questionnaires, performing the physical examination of children and biological parents and extracting information from clinical records and National Health Service official health books.

Below is the description of procedures specific to data collection sections from the baseline, and age four, seven and ten-years-old follow-up evaluations. These were cohort evaluation waves from which data to answer the objectives of this thesis were obtained.

a) ***Questionnaires***

Structured questionnaires were designed for face-to-face interviews and administrated by a multidisciplinary team to obtain information on the following areas:

· Family demographic information such as age, gender, and the number of individuals in the household; socioeconomic status included parental occupation, parental education, and household income as well as lifestyle information such as smoking habits, exposure to secondhand smoking, nutrition etc. were obtained. Also, information on child and family medical history such as the existence of chronic or respiratory diseases was collected.

Self-administered questionnaires were used for parents or legal guardians and children to provide data on sensitive topics such as household financial support needs etc.

b) ***Physical examination***

Physical examination of the child was conducted, including anthropometric and respiratory evaluation. The devices used for measurement were properly standardized and regularly calibrated.

c) ***Anthropometric assessment*** was also carried out with the child standing barefooted in underwear, using stadiometers and scales. The length, height and weight of the children were measured.

3.4 Main variables description

3.4.1 Early life Socioeconomic Indicators

Early childhood socioeconomic circumstances were assessed using the information on parental education, occupation and disposable household income per month obtained at baseline.

Parental Education

Education was measured by years of schooling completed and categorized according to the International Standard Classification of Education 2011 classes (ISCED)[86], which corresponds to lower educational level (9 years or less); intermediate education (12 years) and higher education (more than 12 years) of formal education.

Parental Occupation

Parental occupational attainment was categorized according to the National Classification of Occupations[86] and grouped into three categories: low (blue collar: farmers, skilled and unskilled workers, craftsmen, machine operators, and assembly workers); intermediate (lower white collar: administrative and related workers, service and sales workers); and high (upper white collar: executive civil servants, industrial directors, scientists, middle management, and technicians).

Disposable Income

Household disposable income per month data was collected and grouped as low disposable income (1000€ per month or less and where both parents receive the national minimum wage of (374.70€ in 2005 and 385.90€ in 2006).[87,88] The intermediate category was between 1001€ and 2000€ each month, and the highest disposable income was more than 2000€ per month.

3.4.2 Lung function

Spirometry refers to the basic lung function test which measures the amount of airflow in and out of the lung. It is the most common pulmonary function test widely used to assess lung function to obtain tangible information used in the diagnosis of lung diseases as well as for monitoring lung health.[89,90] It is very useful in the early detection of changes to the lung and its progression, quantifying lung impairment, monitoring the effects of exposure in cases of environmental and occupational hazards, as well as monitoring the effects of medications during treatment. Spirometry test helps to diagnose conditions such as lower lung function, COPD, Asthma, and Interstitial pulmonary fibrosis, among others. The three basic measurements are time, volume, and flow. Spirometry measures some factors:

- Expiratory forced vital capacity (FVC)- It measures the highest amount of air exhaled as fast as possible when blowing out.

- Forced expiratory volume in 1 s (FEV1)- It measures the maximum amount of air exhaled in one sec.
- FEV1/FVC ratio- It is the percentage of the lung capacity to exhale in one sec.

The FEV1/FVC ratio reflects the amount of air that can forcefully bed exhaled from the lungs, and this can help in the diagnoses and monitoring of lung diseases. For this thesis, we will be using the ratio FEV1/FVC for our analysis.

3.4.3 Covariates

The following are the variables used in the analysis:

- Small for gestational age is a term used to describe babies who are smaller than usual for the number of weeks of pregnancy. These babies have birth weight below the 10th percentile. This means they are smaller than many other babies of the same gestational age. This was measured using a measuring tape to determine if the babies were small or "normal" sized for their gestational age.
- Smoking during pregnancy was accounted for by asking mothers if they smoked during pregnancy.
- Second-hand smoke was also accounted for by asking parents for how long the child was exposed to second-hand smoke. Parents were asked for how long they smoked: on the balcony, inside the house in the same room as the child, in the house but in a different room as the child and the car. If the answer was more than one hour, the child was considered exposed to second-hand smoke.
- C-reactive protein levels was assessed following an overnight fast, a venous blood sample was collected before 11 a.m. by trained nurses in our research center after applying a topical analgesic cream (EMLA cream). The samples were centrifuged at 3500 rpm for 10 min and plasma was aliquoted. Biomarkers were assayed in fresh blood samples. Hs-CRP was assayed using CardioPhase hsCRP Flex and the Dimension Vista System from Siemens. All blood evaluations were performed at the Clinical Pathology Service, São João Hospital Center, Porto, Portugal.

3.5 Data Analysis

Sample characteristics were summarized descriptively using counts and percentages and means and standard deviation, stratified by sex. Chi-square test was used to test for associations between sociodemographic characteristics and lung function. Analyses were performed together for all participants and separately for girls and boys. Linear regression models (Beta coefficients and corresponding 95% Confidence Intervals) were fitted to estimate the association between socioeconomic indicators and lung function (FEV1/FVC). Models were adjusted as follows: Model 1, adjusted for small gestational age; Model 2, adjusted for smoking during pregnancy; Model 3, adjusted for second-hand smoking; Model 4, adjusted for acute infections (C-reactive Protein); and the final model, adjusted for small for gestational age, smoking during pregnancy, second-hand smoking, and acute infections.

Analyses were conducted using SPSS statistical software (IBM Corp. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.).

3.6 Ethics

Generation XXI was approved by the Portuguese Data Protection Authority and all study wave protocols were submitted and approved by the ethics committee of São João Hospital. Data confidentiality and protection were guaranteed in all procedures according to the Declaration of Helsinki Medical Research Involving Human Subjects. Oral informed consent was obtained for all participants and signed informed consent was obtained for their legal guardian at every study wave. Alternatively, verbal consent was explicitly solicited for telephone interviews.

4 RESULTS

Sociodemographic characteristics and health-related outcomes of study participants are presented in Table 1. The sample consists of a total of 5060 children, of which 2476 are girls and 2584 are boys, from the Generation XXI cohort. About 9.1% of both girls and boys had a birth weight lower than 2500g while the mean length at birth was 48.3cm in girls and 49.0 cm for boys. Similar proportion of girls and boys were born as small for gestational age (14.0% girls and 14.1% boys). At the age of 10 years, both genders had similar heights (141cm). Some differences were observed for the FEV1/FVC ratio, slightly higher in boys (0.468) when compared with girls (0.444).

Majority of fathers were in high and intermediate occupational levels while majority of mothers were in the intermediate category. Regarding education, both fathers and mothers were more frequently (~40%) in the lowest category of education. Only 18% of the parents were classified as high-income earners (>2000€) whereas the income of most of the parents was in intermediate and low levels income.

Only 20% of the mothers reported smoking during pregnancy. However, a larger proportion (65.9%) reported children's exposure to secondhand smoking with boys (65%) being more exposed than girls (34%). For C-reactive protein, more girls were in the highest tertile than boys (36.6% vs 30.3%).

Table 4.1 Characteristics of the participants included by sex (n=5060)

	Girls (n= 2476)	Boys (n= 2584)	Total
ANTHROPOMETRICS			
Birth weight, mean (SD), g	3288.7 (737.96)	3240.3 (3250.00)	3151.4 (535.37)
Birth weight			
<2500g (%)	187 (9.1)	192 (9.1)	379 (9.1)
≥2500g	1862 (90.9)	1919 (90.9)	3781 (90.9)
Length at birth, mean (SD), cm	48.3 (2.34)	49.0 (2.57)	48.6 (2.48)
Small for gestational age			
No	2047 (86.0)	2137 (85.9)	4184 (86.0)
Yes	332 (14.0)	350 (14.1)	682 (14.0)
Age, mean (SD), y	10.18 (0.351)	10.15 (0.328)	10.16 (0.340)
Height, mean (SD), cm	141.35 (6.843)	140.97 (6.369)	141.16 (6.61)
LUNG FUNCTION, mean (SD)			
FEV1	-0.053 (0.9691)	-0.107 (1.0268)	-0.081 (0.9993)
FVC	-0.268 (0.9889)	-0.342 (1.0032)	-0.306 (0.9968)
FEV1/FVC	0.444 (1.0726)	0.468 (1.1075)	0.456 (1.0905)
SOCIOECONOMIC STATUS, n (%)			
Paternal occupational position			
High	638 (33.9)	632 (32.4)	1270 (33.2)
Intermediate	467 (24.8)	483 (24.8)	950 (24.8)
Low	775 (41.2)	835 (42.8)	1610 (42.0)
Maternal occupational position			
High	699 (30.1)	745 (30.4)	1444 (30.3)
Intermediate	1133 (48.8)	1194 (48.8)	2327 (48.8)
Low	488 (21.0)	510 (20.8)	998 (20.9)
Paternal educational level			
High (>12th grade)	483 (24.3)	504 (23.7)	987 (24.0)
Intermediate (10th-12th grade)	570 (28.7)	625 (29.3)	1195 (29.0)
Low (<9th grade)	934 (47.0)	1001 (47.0)	1935 (47.0)
Maternal educational level			
High (>12th grade)	718 (32.0)	776 (32.4)	1494 (32.2)
Intermediate (10th-12th grade)	683 (30.4)	740 (30.9)	1423 (30.7)
Low (<9th grade)	845 (37.6)	877 (36.6)	1722 (37.11)
Income			
High (>2000€)	396 (18.1)	404 (17.6)	800 (17.9)
Intermediate (1001-2000€)	1006 (46.1)	1112 (48.5)	2118 (47.3)
Low (<1000€)	782 (35.8)	779 (33.9)	1561 (34.9)
EXPOSURE TO SMOKING, n (%)			
During pregnancy			
No	1951 (79.8)	2038 (80.0)	3989 (78.6)
Yes	494 (20.2)	509 (20.0)	1003 (20.1)
Second-hand smoking			
No	1456 (65.9)	816 (34.8)	1568 (34.4)
Yes	752 (34.1)	1529 (65.2)	2985 (65.6)
INFLAMMATION			
C-reactive protein, mean (SD)	1.167 (0.0431)	0.990 (0.0380)	1.073 (0.0286)
C-reactive protein			
Upper tertile	494 (36.6)	466 (30.3)	960 (33.3)
Lowest tertiles	856 (63.4)	1070 (69.7)	1926 (66.7)

Legend: FEV1: z-scores of forced expiratory volume in the first-second age and height-adjusted; FVC: z-scores of forced vital capacity age and height-adjusted; FEV1/FVC: z-scores of ratio is the ratio of the forced expiratory volume in the first one second to the forced vital capacity of the lungs.

The lung function, measured by the mean of the ratio FEV1/FVC, is calculated for the different socioeconomic indicators. As seen in Figure 4.1., there is a dose-response association between early socioeconomic status and lung function i.e., increasing FEV1/FVC ratios is observed with decreasing categories of socioeconomic indicators. The same trend is observed when analyses are conducted stratified by gender (Figure 4.2).

In general, the trend was very similar in girls and boys with children whose parents had the lowest SES having the highest FEV1/FVC ratios. Children whose parents had high occupational levels, presented lower FEV1/FVC ratio than those whose fathers had low occupational levels. The same trend is observed in the other socioeconomic indicators as well. Lower FEV1/FVC ratios are observed in girls whose fathers had high educational levels, while the highest FEV1/FVC ratios are observed in children whose parents had low occupational levels (Figure 4.2).

Parents in the lowest socioeconomic levels (education, occupation and income) generally had children with higher FEV1/FVC ratios, as seen in the Figure 4.1. This trend is observed for parental education with lower parental educational levels being associated with higher FEV1/FVC ratio, and similar when the SES indicator used is household income.

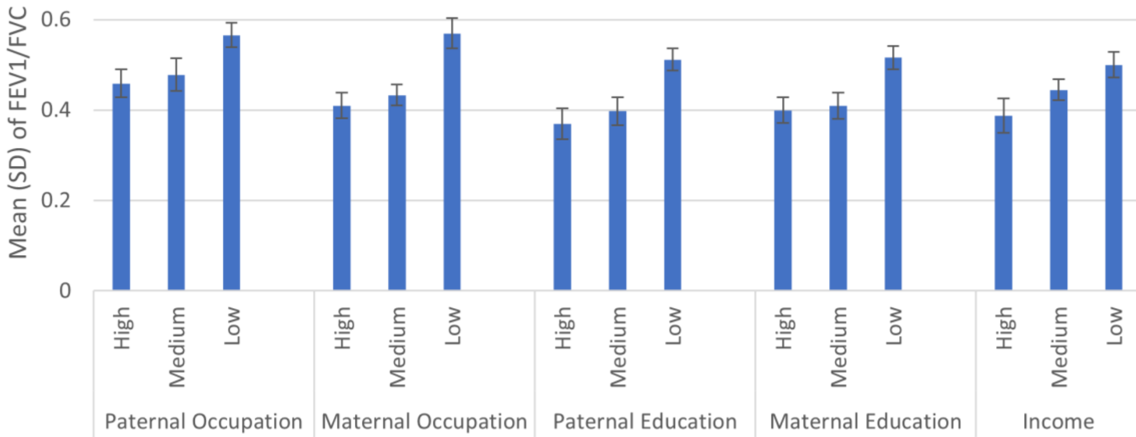

Figure 4.1 Graphical depiction of the lung function measure (FEV1/FVC) (mean, SD) by socioeconomic status indicator.

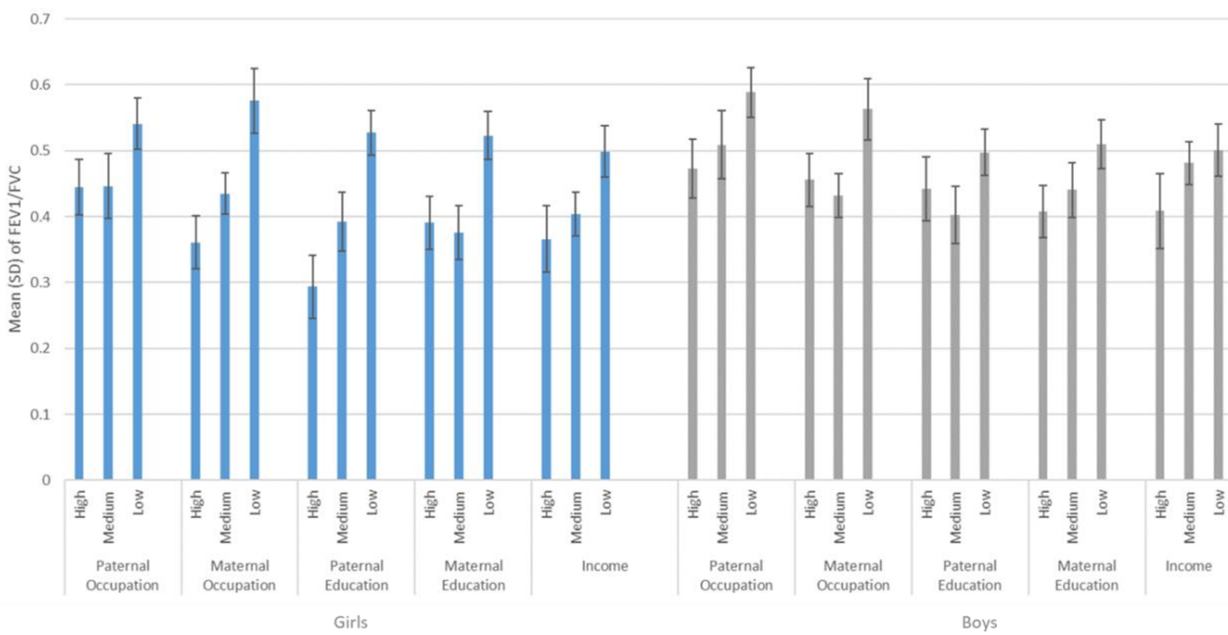

Figure 4.2 Graphical depiction of the lung function measure (FEV1/FVC) (mean, SD) by socioeconomic status, according to gender

Table 4.2 shows the association between socioeconomic indicators and FEV1/FVC for all participants (girls and boys). Children born into families whose father's occupation is in the lower category presented a FEV1/FVC ratio **0.188** (95% CI: 0.120; 0.256) higher than those in the highest category. After adjustment for small for gestational age, smoking during pregnancy, second-hand smoking, and C-reactive Protein, the difference increased to **0.258** (95% CI: 0.165; 0.350). The same trend is observed for maternal occupation, and those born from mothers in the lowest occupational category, present a FEV1/FVC ratio **0.148** (95% CI: 0.063; 0.233) higher than children born from mothers in the highest occupation category. After adjustment for all covariates, the difference increased to **0.152** (95% CI: 0.036; 0.268).

Also, children born in families whose father´s education is in the lower category presented a FEV1/FVC ratio **0.075** (95% CI: 0.006; 0.143) higher than those born from fathers in the highest category of education. After adjustment for small for gestational age, smoking during pregnancy, second-hand smoke, and C-reactive Protein, the difference increased to **0.152** (95% CI: 0.048; 0.244). A similar trend is observed for maternal education, were those born from mothers in the lowest category of education, present a FEV1/FVC ratio **0.079** (95% CI: 0.008; 0.150) higher than those born from mothers in the highest category of education. The difference increased to **0.136** (95% CI: 0.095; 0.236) after adjustment for covariates.

Regarding household income, children born in families whose parental income is in the lower category presented a FEV1/FVC ratio **0.076** (95% CI -0.003: 0.155) higher than those born from fathers in the highest category of income. After adjustment for small for gestational age, smoking during pregnancy, second-hand smoke and C-reactive Protein, the association was slightly strengthened and remained statistically significant. The difference increased to **0.089** (95% CI: 0.009; 0.170) in model 1, decreased by **0.084** (95% CI: 0.004; 0.164) in model 2, slightly increased to **0.097** (95% CI: 0.015; 0.178) in model 3. However, this statistical power was lost after model 3 and after fully adjusting for covariates it increased to **0.108** (95% CI-0.002; 0.218).

Table 4.2 Association of socioeconomic disadvantage with lung function (FEV1/FVC) for all participants.

	FEV1/FVC							
	OR (95%CI)							
	Crude model	**Model 1**	**Model 2**	**(Model 1+2)**	**Model 3**	**Model 4**	**(Model 3+4)**	**Fully adjusted model[1]**
Paternal occupational position								
High	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Intermediate	**0.101 (0.019; 0.182)**	**0.103 (0.020; 0.185)**	**0.108 (0.027; 0.190)**	**0.110 (0.027; 0.194)**	**0.109 (0.024; 0.194)**	0.086 (-0.022; 0.193)	0.107 (-0.003; 0.217)	**0.125 (0.013; 0.237)**
Low	**0.188 (0.120; 0.256)**	**0.195 (0.125; 0.264)**	**0.191 (0.123; 0.260)**	**0.198 (0.128; 0.268)**	**0.199 (0.128; 0.271)**	**0.230 (0.141; 0.319)**	**0.238 (0.147; 0.329)**	**0.258 (0.165; 0.350)**
Maternal occupational position								
High	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Intermediate	0.011 (-0.056; 0.079)	0.012 (-0.057; 0.081)	**0.021 (-0.048; 0.090)**	**0.021 (-0.049; 0.091)**	0.017 (-0.055; 0.088)	-0.005 (-0.095; 0.085)	0.008 (-0.085; 0.100)	0.013 (-0.081; 0.107)
Low	**0.148 (0.063; 0.233)**	**0.149 (0.063; 0.236)**	**0.150 (0.065; 0.236)**	**0.153 (0.066; 0.240)**	**0.157 (0.069; 0.245)**	**0.140 (0.029; 0.252)**	**0.140 (0.027; 0.254)**	**0.152 (0.036; 0.268)**
Paternal educational level								
>12th grade	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
10th-12th grade	-0.039 (-0.118; 0.039)	-0.023 (-0.103; 0.057)	-0.050 (-0.129; 0.029)	-0.033 (-0.114; 0.048)	-0.004 (-0.087; 0.079)	-0.028 (-0.133, 0.077)	-0.001 (-0.109; 0.107)	0.001 (-0.109; 0.112)
<9th grade	**0.075 (0.006; 0.143)**	**0.083 (0.013; 0.153)**	**0.071 (0.002; 0.140)**	**0.079 (0.008; 0.150)**	**0.118 (0.044; 0.193)**	**0.116 (0.024; 0.208)**	**0.148 (0.053; 0.244)**	**0.146 (0.048; 0.244)**
Maternal educational level								
>12th grade	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
10th-12th grade	-0.028 (-0.103; 0.047)	-0.029 (-0.105; 0.047)	-0.025 (-0.101; 0.050)	-0.027 (-0.103; 0.050)	0.015 (-0.064; 0.094)	-0.052 (-0.152; 0.049)	-0.026 (-0.129; 0.077)	-0.019 (-0.124; 0.086)
<9th grade	**0.079 (0.008; 0.150)**	**0.080 (0.008; 0.153)**	**0.085 (0.014; 0.157)**	**0.086 (0.013; 0.159)**	**0.127 (0.051; 0.202)**	**0.103 (0.008; 0.199)**	**0.130 (0.032; 0.228)**	**0.136 (0.035; 0.236)**
Income								
>2000€	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
1001-2000€	0.021 (-0.053; 0.095)	0.024 (-0.051; 0.100)	0.016 (-0.059; 0.091)	0.019 (-0.181; -0.003)	0.031 (-0.046; 0.108)	0.013 (-0.085; 0.111)	0.021 (-0.079; 0.120)	0.029 (-0.073; 0.131)
<1000€	0.076 (-0.003; 0.155)	**0.089 (0.009; 0.170)**	**0.084 (0.004; 0.164)**	**0.097 (0.015; 0.178)**	**0.084 (0.001; 0.167)**	0.075 (-0.030; 0.180)	0.092 (-0.016; 0.199)	0.108 (-0.002; 0.218)

Legend: FEV1: z-scores of forced expiratory volume in the first-second age and height-adjusted; FVC: z-scores of forced vital capacity age and height-adjusted; FEV1/FVC: z-scores of ratios is the ratio of the forced expiratory volume in the first one second to the forced vital capacity of the lungs; B: beta-coefficient of linear regression models; CI: confidence interval; In bold statistically significant values.
Model 1: Adjusted for small for gestational age; Model 2: Adjusted for smoking during pregnancy; Model 3: Adjusted for second-hand smoking; Model 4: Adjusted for infections (C-reactive Protein).
1Fully Adjusted model: Adjusted for small for gestational age, smoking during pregnancy, second-hand smoking and infections (C-reactive Protein).

4.1 DISCUSSION

This study shows that inequalities can be observed since early ages with children from more disadvantaged socioeconomic circumstances presenting lower lung function, measured by higher FEV1/FVC ratios, at 10 years of age compared to their more advantaged counterparts. The effects of socioeconomic disadvantage were observed on the FEV1/FVC ratio since it largely reflects the ratio of forced expiratory volume in 1 second (FEV1) to forced vital capacity and it is used in children as it is an objective method to measure lung function and less prone to bias.[91] This significant association observed between low SES and lower lung function in the first decade of life was maintained even after adjusting for gestational age, smoking during pregnancy, second-hand smoke, and infection (C-reactive protein).

There is a well-known relationship between childhood disadvantage circumstances and adult health, and this relationship is known to begin very early in the life course. Low SES results in poorer health outcomes e.g., lower lung function both in children and in adults.[92] Epidemiological studies have described this inverse relationship between SES and lung function for several decades, whether measured by education, occupation, income and housing/neighborhood, this social gradient has been evident in most studies relating to pulmonary/lung function.

These different socioeconomic indicators which are parental education, occupation and income may play different roles in a child's life, reflecting childcare, behaviors, exposures as well as overall child's health. [6] Parental education can reflect literacy and knowledge about health-related issues and choices. Education is also associated with how parents are receptive to health information, access to healthcare and health-related behaviors e.g., vaccination.[6,93] Another indicator used to measure early socioeconomic status is parental occupation, which might be more related to material resources. It also reflects an individual's position in society, intellect, as well as income. Some studies have shown that parental occupation, especially paternal has a direct association with an individual's health.[94]

We observed from our study that FEV1/FVC ratios were quite high in both girls and boys from less educated parents. However, the lowest FEV1/FVC ratios were observed in girls whose fathers were in the highest educational categories. This could be explained by the role high parental educational levels play in a child's wellbeing and overall care.[94] In general, high parental education is associated with better childcare since their education facilitates healthy and informed choices such as avoiding smoking during pregnancy, favorable behaviors/lifestyle e.g., physical activities, vaccination, and even nutrition such as eating balance diets and healthy meals which all influence lung growth and function.[95]

Also, the highest FEV1/FVC ratios were observed in children with parents in low occupational categories for both girls and boys. This association may be explained by the fact that occupation can be translated to material assets and can directly influence child's health. [6] These benefits can determine a child's better access to healthcare, better level of education and healthy neighborhood environment which can influence lung function. In our study, a significant association was observed between low parental income and lower lung function in both girls and boys of the same age group. Literature has shown contradictory results with studies showing similar significant association between low education and income levels with lower lung function in children of the same age group,[72,96,97] and others showing a significant association between low income and lower lung function in boys aged 8-17 years but not in girls of the same age group.[98,99] This association can be explained by the fact that children in low-income households might be more exposed to toxins and smoke due to the environment they live in and household conditions which could lead to airway inflammation and other lung-related issues, as well as the lesser access to healthcare [100]. Another study also found an association between low parental occupation and lower lung function in boys and not in girls [101], which contradicts our study's results that showed a significant association between lower parental occupation and lower lung function in both girls and boys.

Similarly, to other studies,[61,79,96,97,102] we observed the strongest association between children with low socioeconomic circumstances and lower lung function in all three socioeconomic indicators: educational level, occupation and income. Prior studies[58,61,68,82,102,103] sought to explain this association by the fact that the effects of educational level, occupation, income in lung function seem to be an important and consistent upstream risk factor for low lung function since early ages. However, further research is needed to disentangle the precise mechanism(s) underlying this association. Thus, enhancing populations' educational level might help improve respiratory health, but this hypothesis warrants further investigation. On the other hand, the educational level, occupation and income were the indicators associated with lower lung function, in girls and boys, demonstrated to be the indicators especially determining the health and wellbeing of a child in the early years. For instance, attainment of education has been associated with literacy, increased health knowledge and healthier behavior of parents, particularly maternal education. Previous studies have shown how this indicator can be indirectly reflected on a child's health either via childcare, nurturing, adherence to healthy lifestyles or avoiding health risk factors, all of these can promote a good child’s health in particular lung growth and development.[104–106]

Overall, the association was quite similar in both sexes with no striking difference in the FEV1/FVC ratios between boys and girls. Boys seem to have slightly higher FEV1/FVC ratios than girls. This could be because lung function has been shown to be associated with height, in which taller individuals tend to have higher lung function than their counterparts.[102,107–110] There is a brief period in adolescence during the onset of puberty growth when girls are taller than boys of the same age group, which might explain why girls would have slightly lower FEV1/FVC ratios. However, studies have found higher lung function in boys than in girls of the same height. This is attributed to the fact that boys tend to have larger lungs which are associated with wider airway diameter and respiratory bronchioles.[111] This difference in lung function between boys and girls increased over time with growth process, as boys tend to be eventually taller than girls.[91,102,108,112] Nevertheless, further investigations are needed to establish this hypothesis.

This study contributes to an understanding and estimation of the association between early childhood socioeconomic circumstances and lung function in the first decade of life. The results of this study show that social inequalities begin very early in life which is a crucial period in the life of a child for subsequent respiratory health. A previous review showed that only a few studies have explored the association of childhood SES with lung function in children using prospective data[79], therefore this study increases the understanding that the effect of SES on lung function starts manifesting in children at a very early stage and this can also be useful in detecting early life differences in lung growth. The results help us to understand that social inequalities exist already at early ages in children and are independent from other factors. Early socioeconomic circumstances have a significant role to establish trajectories of lung function during childhood which is a critical time for future respiratory health. This study can aid social policies aimed at children and families with low SEC to prevent and reduce its adverse impact on children’s respiratory health.

4.2 STRENGTHS AND LIMITATIONS

One of the key strengths of this thesis is the use of data from the Portuguese population-based birth cohort Generation XXI. With these data, we could observe and analyze lung function, and establish a potential causal relationship between the exposure, early socioeconomic circumstances, and the outcome, FEV1/FVC ratio. However, as is common in a prospective birth cohort, there has been attrition over time, leading to a reduction in the sample size and a more socioeconomically advantaged group of participants at older ages. Nevertheless, we believe that the inclusion of the more disadvantaged group would have widened the differences observed.

Also, information on the family's early socioeconomic circumstances for both parents as well as socioeconomic indicators obtained at childbirth, helped to reduce recall bias and provide detailed information about the family socioeconomic status. Education and occupation are quite reliable sources of information about the socioeconomic status of a family even though they are self-reported as they are easy to measure.[6] On the other hand, there is a possibility that income can be underestimated.[113] The result of our findings shows an association between early socioeconomic status and lower lung function in children in the first decade of life. Generally, it is anticipated that all socioeconomic indicators play a role in influencing a child’s health and distinguishing social differences in children at these ages. Although little is known about the moment when socioeconomic circumstances matter the most or how long they need to last, the results show the effects of early socioeconomic status on lung function in the first decade of life. Thus, implying that early SES does have a strong impact on children’s lung function from very early in life.

In most studies, the FEV1/FVC ratio is the mostly used index to assess respiratory function[91]

FEV1 index largely provides information on airflow based on airway caliber and elasticity. The FEV1/FVC ratio is used to ascertain or detect the presence of airway obstruction and to diagnose how well the lungs are functioning. It helps to distinguish if the lung has an obstructive or restrictive condition, as well as to monitor lung function to see how well it is responding to treatment. It is generally a simple, safe and non-invasive procedure that helps to prevent, identify and quantify respiratory diseseses.[90,114] The procedure can also be performed anywhere and by anyone with good training. Although in some cases, when carrying out the procedure some people

might feel out of breath or lightheaded when blowing forcefully. There is also a small risk of an asthma attack for individuals who are asthmatic or have temporary severe breathing problems[115]
In this study, asthma was not considered as none of the children included had an asthma diagnosis. Including children with asthma in the study would introduce some bias in the results as this could act as a confounder. We would expect that those with asthma would have a lower lung function, and if they are on medication for asthma this might improve their lung function.

4.3 IMPLICATIONS FOR PUBLIC HEALTH

An understanding of the association between early childhood socioeconomic circumstances and lower lung function in the first decade of life will significantly help to understand the social patterning of lung function, inequalities in lung function, as well as the differences in lung function between boys and girls. This knowledge will help to inform the development of public health policies aimed at children and families with low SES to prevent and reduce its adverse impact on children's health. Also, a clear understanding of factors affecting the development, growth and loss of lung function is very vital in planning strategies and interventions to tackle respiratory/lung diseases both in children and adults, especially among the more vulnerable ones.
Studies have shown that childhood socioeconomic disadvantage leading to poorer adult health and health inequity can be partially or fully overcomed by upward socioeconomic mobility.[92] As we know that childhood SES can adversely impact one's health even in adulthood, interventions and social policies to improve the socioeconomic status of individuals may improve health outcomes for those who have experienced childhood socioeconomic disadvantage.[57,72]

The association found in this study is vital to inform the design, development and implementation of effective tailored strategies to be included in the programs/interventions targeting to mediate or reduce risk factors that play key roles in adversely impacting lung function both in childhood and adulthood. These interventions will go a long way to significantly improve the prevention and treatment of lung diseases.

5 CONCLUSIONS

Results from this thesis show that exposure to disadvantaged socioeconomic circumstances is incorporated and its effects are already expressed in the first 10 years of life. Therefore, and by using data from a prospective ongoing birth cohort, in future studies, we can assess if the social and health inequalities observed at these ages will be maintained, widen or shrink throughout life. Since early childhood is a critical period in the overall growth and development of a child, it is crucial to ensure that children receive optimal care to minimize the effects of SES. Interventions and strategies targeted at early childhood to reduce health inequalities in lung function should be encouraged.

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