UNIVERSITÀ DEGLI STUDI DI VERONA

INSTITUTO DE HIGIENE E MEDICINA TROPICAL DE LISBOA

DEPARTMENT OF

Diagnostics and Public Health

GRADUATE SCHOOL OF

Life and Health Sciences

DOCTORAL PROGRAM

Applied Sciences of Life and Health

(Epidemiology and Biostatistics)

Cycle / year (1° year of attendance): 36° Cycle (2020)

Vulnerability in healthcare: from concept to methods insights from three case studies

S.S.D. MED/01

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Vulnerability in healthcare: from concept to methods

insights from three case studies

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Tesi di Dottorato
Verona, Novembre 2023
ISBN

“Questo ricordatelo Saskia, non cercare mai di ripeterti. Vivi ora.”

Tiziano Terzani, La fine è il mio inizio.

Sommario

In questo manoscritto esploreremo il concetto di vulnerabilità in salute.
Rispondendo alle questioni: 'Quali popolazioni sono considerate vulnerabili? Quali i determinanti di vulnerabilità? Con quali metodi e quali approcci studiare le vulnerabilità in salute?', tenteremo di fornire una visione strutturata del problema e approfondirne i risvolti nell'ambito della Salute Pubblica. Dopo aver delineato il concetto in un contesto generale, procederemo a presentare tre studi che esemplificano i fattori di vulnerabilità legati all'accesso ai servizi sanitari o agli esiti di salute.
Il primo studio presenta l'elaborazione di dati secondari, provenienti da tre indagini nazionali trasversali condotte in Mozambico, negli anni 2011, 2015, 2018. Nello specifico, in questo studio si sono analizzate tendenze temporali e differenze geografiche riguardanti la copertura di visite prenatali materne all'interno del paese. È stata calcolata la copertura di visite materne prenatali (percentuale di madri che avessero effettuato un minimo di quattro visite durante la gravidanza) nei tre anni di riferimento e il relativo tasso di crescita/decremento annuale, su ciascun sotto-strato del disegno di studio.
Questa indagine aveva come obiettivo primario quello di investigare, il possibile impatto del conflitto armato, che dal 2017 affligge il Nord del paese, sull'accesso alle cure prenatali. Per una completezza dello studio sono stati, infine, analizzati i possibili fattori determinanti la probabilità di attendere il desiderato numero di visite prenatali, facendo riferimento ai dati estratti dalla più recente indagine nazionale disponibile online (2018).
Il secondo studio presenta i risultati di un'indagine trasversale condotta sull'Isola di Santiago (Capo Verde), al fine di misurare i tassi di prevalenza di asma, rinite e eczema, tra bambini di età compresa tra i 6 e 7 anni e investigarne i possibili fattori di rischio. In questa analisi si sono confrontate, inoltre, le risultanti associazioni stimate tra esposizioni e outcomes a livello individuale, usando modelli generalizzati di regressione logistica, con le risultanti associazioni aggregate a livello scuola, usando modelli multilivello.
Il terzo e ultimo studio, infine, presenta l'analisi dei tassi di test per COVID-19 tra bambini residenti in cinque distretti dell'area metropolitana di Lisbona (Portogallo).

Obiettivo principale di questa indagine era quello di investigare differenze di accesso al sistema sanitario, in tale contesto, tra bambini immigranti e no, tenendo in considerazione altri fattori potenzialmente associati alla probabilità di accesso ai test e al numero di test condotti, durante il periodo pandemico.

Con questi tre studi ci prefiggiamo di descrivere, in contesti tra di loro differenti, come fattori di vulnerabilità individuali e/o a livello di comunità, si intersechino strettamente con risultati sanitari, ripercuotendosi sia sui tassi di accesso alle cure che sui tassi di prevalenza di determinate malattie.

Nonostante un'ampia letteratura esista su questo tema, nuovi approcci di studio basati su una progettazione multidisciplinare e nuove metodologie di analisi, potrebbero portare la ricerca a nuovi conoscimenti, con favorevoli ripercussioni in termini di attività programmatica del sistema sanitario.

Abstract

This manuscript explores the concept of vulnerability in health.

Answering the questions: ‘Which populations or individuals are vulnerable? What are the determinants of vulnerability? What methods and approaches are used to study vulnerability in health?', we attempt to provide a comprehensive description of the problem and explore its Public Health implications. After outlining health vulnerability conceptualization in general terms, we present three case-studies that illustrate vulnerability factors in relation to access to health services or health outcomes. The first study that we present, analysed trends in time and geographical variations in antenatal care uptake, in Mozambique. Secondary data from three national surveys, conducted in 2011, 2015, 2018, were used. Annual trend growth rates of antenatal care coverage were calculated between 2015 and 2018, in each of the surveys design substrata. Primary focus of this study was to investigate the possible impact of the armed conflict, which has plagued the North of the country since 2017, on antenatal care utilization among mothers. Also, factors possibly associated with the outcome ‘attending at least four antenatal visits before pregnancy’ were analysed, using published data from last available survey (2018).

The second study presents results of a cross-sectional survey conducted in the Island of Santiago (Cape Verde), to measure the prevalence of asthma, rhinitis and eczema, among resident children aged 6-7 years old, and their possible associated risk factors. Individual-level exposure-outcomes associations estimated from standard logistic models were compared to school-level associations estimated from multilevel logistic models. The third and last study analysed COVID-19 testing rates among children living in five districts of the Lisbon metropolitan area (Portugal). Primary focus of this study was to investigate differences in access to the health system, between immigrant and non-immigrant children, while also taking into account other factors potentially associated with the likelihood of accessing or not at least one test and number of tests performed in mean, during the pandemic period.

With these three studies, we aim to report, in different contexts, how individual and/or community-level vulnerability factors are closely linked to health outcomes, affecting both access to care and prevalence rates of specific diseases.

Although there is a large body of literature on this topic, new approaches to research, based on multidisciplinary design and new methods of analysis, could lead to new knowledge, with beneficial implications for health system planning.

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Acknowledgments

When I set out to write this thesis, I wanted to give it a personal touch, something lasting that would go beyond data and figures, something beyond the merely writing of an academic work. The concept of 'Vulnerability' resonated in me immediately. It's part of my life, as it is for the lives of other human beings. I am firmly convinced that the context in which we live plays a crucial role in shaping who we are, both physically and psychologically and in determining self and external perception of ourselves.

I wish to dedicate this thesis to my mother, the person who I wanted to keep alive with my life, but also to my beloved grandmother, to her sweet humility, simplicity, resilience and fragility, that she passed to me growing up; but I want also to dedicate it to the future me, the person I am trying to be at the best of my possibilities.

I would like to thank the University of Verona, specifically the Department of Diagnostics and Public Health to have given me the opportunity to do this PhD journey, for the empowering psychological challenges this has taken me to, and for having had in this way the chance to know this country where I found a second house and a family, made of friends, colleagues, unknown people that I recognize and they recognize me on the street. I would like to express my gratitude to my supervisor Professor Maria Do Rosario Oliveira Martins, that gave me this opportunity too, introduced me to the friendly research team in Lisbon, and with whom I could participate in a field data collection experience that was my research prototype dream.

I would like to acknowledge all those friends who companied me in my life in Italy, with whom I grew up, all those I met around the world and brought me here now, all those who are companying me now, the new families we choose on the walk of life. Without good relations, good connections we are nothing. Friendship, human relations give us a sense of life, a sense of being 'more', a sense of enjoying the journey in the present, make us more self-confident, make us less vulnerable.

Statement of candidate contribution

This thesis contains work prepared for publication, some of which has been co-authored.

In the specificity, the second case-study (reported in chapter three), is a project conducted by the leading doctor Maria Do Ceu Teixeira in Cape Verde, from which an abstract has been already submitted to the 17th World Congress of Public Health in Rome, and an article will be produced in the future, and where I will be assigned the role of second author:

"Prevalence of asthma, rhinitis and eczema symptoms and its determinants in children aged 6-7 years, Santiago Island, Cape Verde"

Authors: Teixeira, MCRT; Panunzi, S; Ramos, J; Fernandes, E[2]; Semedo, C[6]; Pereira, W[6]; Alves, J[2]; Semedo, J[2]; Moreira, P[2]; Sanches, O[1]; Ferreira, M.[3] Araújo, IIMP[2,3]; Martins, MRO[3]

The third case-study (Chapter 4) was a projected leaded by Iolanda Alves, for which an article was already submitted and is in phase of journal approval:

"Have immigrant children been left behind in COVID-19 testing rates? - A quantitative study in the Lisbon Metropolitan Area between March 2020 and May 2023"

Authors: Iolanda B. Alves, Silvia Panunzi, António C. Silva, Regina B.R. Loesch, Sofia C. R. Pereira, M. Rosário O. Martins

Chapter 1 General Introduction

1.1 Health vulnerability concept

The word "vulnerability" is derived from the Latin word "*vulnerabilis*", the adjectival form of *"vulnus"*. It means capable of being wounded or susceptible to injury.
The concept of specific groups or people having a greater likelihood of experiencing health problems due to different factors has long been recognised in medicine and public health. The expression gained popularity in the late 20th and early 21st centuries as a means of describing the higher possibility of specific populations or individuals developing health issues. Several factors, such as poverty, poor education, age, and gender, or exposure to pollution and natural disasters, impediments to access healthcare for prevention or treatment, can increase the risk of health issues. The right of everyone to timely access to affordable, preventive and curative care of good quality is one of the key principles of the recently proclaimed European Pillar of Social Rights (1) however, disparities and inequities persistently exist and increase, among individuals and communities. Researchers and policymakers aim to comprehend and reduce health weaknesses, to guarantee that each person and social group can attain good health and well-being, this has become especially crucial in the context of worldwide health emergencies, including pandemics and conflicts.
The postulation of the concept of vulnerability in the medical field has evolved over time as our understanding of health and healthcare has become more complex. Vulnerability in medicine refers to a person's or a population's susceptibility to adverse health outcomes or difficulties in accessing healthcare. This concept is closely tied to the concept of social determinants of health (SDOH), namely the societal and environmental conditions that influence individual health and well-being. These factors include socioeconomic status, education, housing, employment, access to healthcare, and the physical and social environment. Scientific research on SDOHs has led to recognize certain groups people or populations as more vulnerable to poor health outcomes, due to systemic disadvantages.
Historically, medicine focused predominantly on individual risk factors and clinical

treatments. Later, it became evident that addressing vulnerability required a broader perspective. Vulnerability can be attributed to systemic and structural factors such as poverty, discrimination, lack of education, or inadequate housing. For example, individuals from disadvantaged socioeconomic backgrounds may have limited access to healthy food, quality healthcare, and safe living conditions, which can lead to increased vulnerability to various health problems. Vulnerable populations, such as low-income communities, racial and ethnic minorities, the elderly, and those with chronic illnesses, are often disproportionately affected by health disparities, such as higher rates of chronic diseases, reduced life expectancy.

The definition and characterization of health vulnerability can differ greatly across countries due to cultural, social, economic and political nuances. These disparities can lead to different approaches to healthcare, understandings of health and experiences of vulnerability.

Consider the following key points:

- Different cultures typically align with different attitudes towards the nature of health issues, the reasons behind afflictions, and suitable techniques for treatment. Cultural traditions and societal beliefs significantly influence the comprehension of health vulnerability.
- Access to healthcare is a fundamental factor that change from one region to another. In wealthier nations, individuals typically benefit from good access to healthcare, education, and economic opportunities, which ultimately reduces the level of vulnerability. Conversely, financially deprived regions may face deficiency of resources and limited access to healthcare, contributing to increased health vulnerability.
- Geographic location plays a significant role in determining access to healthcare. Individuals residing in remote or rural areas may have restricted access to healthcare facilities and services, thereby increasing their vulnerability. Moreover, those living in regions prone to natural disasters or environmental hazards may face specific health risks.
- Government policies and healthcare systems vary widely across different nations.

The models for delivering healthcare also differ, ranging from universal healthcare to private insurance-based systems. These systems can have a significant impact on how health vulnerability is addressed and managed.

- Epidemiological factors, including the prevalence of specific diseases and health conditions, also vary between regions. Some areas may carry a higher burden of infectious diseases, whilst others may suffer from more chronic health issues, impacting health vulnerability.

Understanding these differences is crucial for creating effective public health systems policies and interventions that meet the specific requirements of diverse communities and regions.

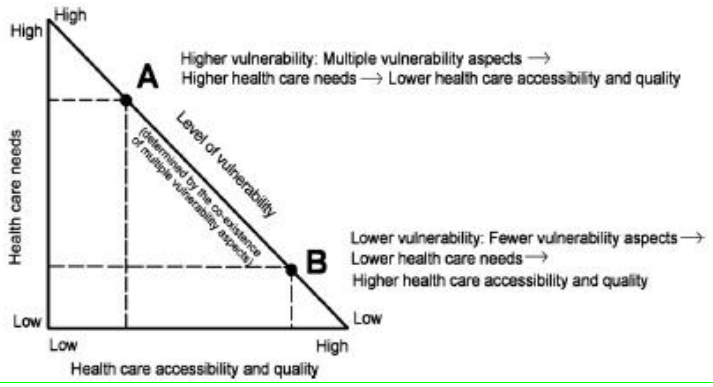
1.2 Literature review

The Belmont Report (2) published in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research in the United States, is recognized as the first human research ethics guideline to identify vulnerable groups, specified that those identified as vulnerable need extra protections during research participation. The application of the concept of vulnerability has expanded from research ethics to the broader field of health care and health technologies, and beyond the individual context; families, groups, communities, populations and countries can be described as vulnerable (3).

Up to date, a significant body of literature is dedicated to the study of vulnerable populations. Some of these studies introduce and discuss conceptual models for understanding the origins and consequences of vulnerability on poor health outcomes.

However, Grabovschi et al (2013) (3) extensively criticized how research often do not focus on examining health care disparities or explicitly explore the links between these and multiple aspects of vulnerability. The author scoping review interesting confirmed the dynamic vulnerability model of health care disparities based on the Inverse Care Law (ICL) (4), that states how high levels of vulnerability, work on increasing health care needs but in the same time, are paradoxically companied by reduced health care accessibility and quality (Figure 1.1).

Figure 1.1. Inverse Care Law. Grabovschi et al. (3)

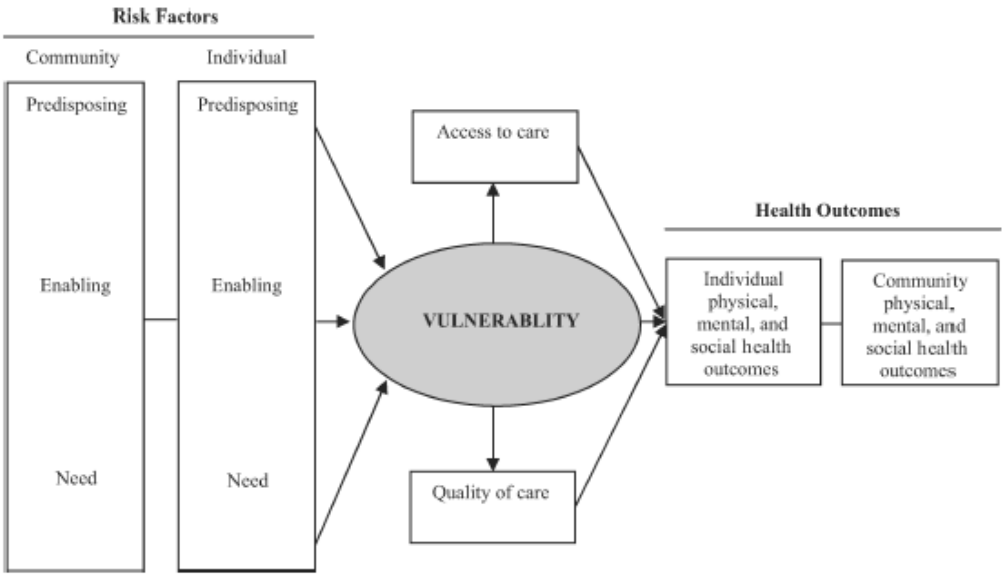


Grabovschi et al operationalized vulnerability as increased susceptibility to health and health care disparities, coming from a combination of individual (inborn or acquired) and environmental (physical or socioeconomic environment) factors.

Andersen and Aday (5), discussed the concept of vulnerability within the context of access to medical care, proposing a framework for understanding access to healthcare made by the following key components:

- Predisposing Factors: factors that make individuals vulnerable to accessing healthcare; include demographics (age, gender), social structure (education, occupation), and health beliefs.
- Enabling Factors: resources and means that facilitate or hinder individuals' access to healthcare; include income, health insurance coverage, and the availability of healthcare services in a given area.
- Need Factors: individual's perception of their health status, which can be influenced by physical symptoms, psychological distress, or diagnosed health conditions.

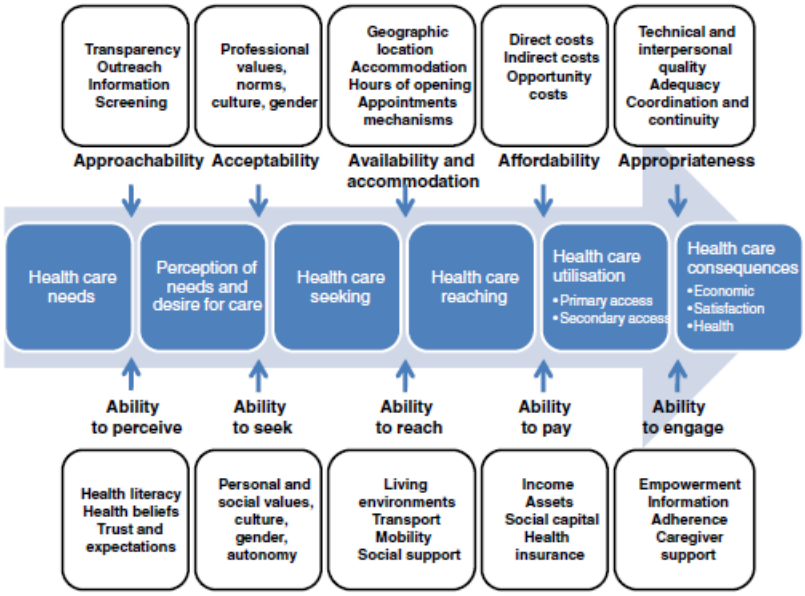
Figure 1.2. Enhancing the Measurement of Health Disparities for Vulnerable Populations (6).



Over time, the Behavioural Model, first conceptualized by Andersen in the late 1960s has undergone revisions and updates to include new measures of health services use, recognizing improvement of health status as explicit outcomes and goals of health services delivery (7) (Figure 1.2). Penchansky and Thomas, in 1981, defined access as resulting from the interface between the characteristics of persons, households, social and physical environments and the characteristics of health systems, organisations and providers (8). Levesque, in 2013 (9) presented access to health care services as resulting from the interaction of determinants pertaining to characteristics of individuals (e.g. the place where they live, their economic resources and their social status) and of services (e.g. quantity, location of facilities, costs) (Figure 1.3). Characteristics of resources, individuals and communities can determine various dimensions simultaneously.

Several models have been formulated according to the circumstances and beliefs of the time. Some of these have considered only part of the characteristics that make up vulnerability.

Figure 1.3. A conceptual framework of access to health care (9).

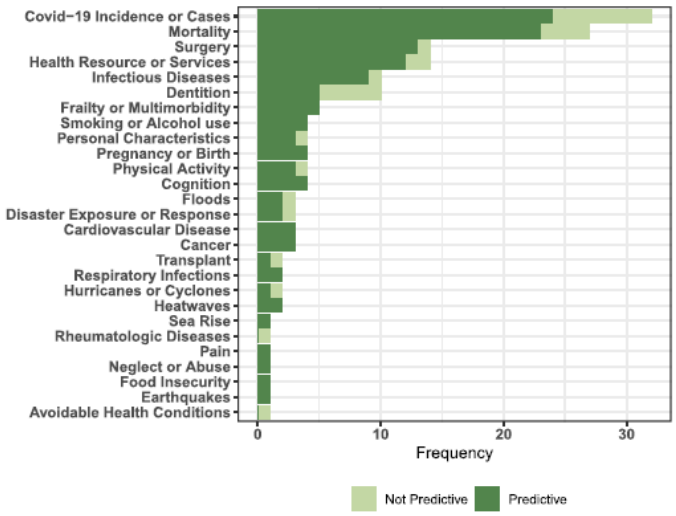


1.3 Measure of vulnerability

To estimate social vulnerability multi-dimensional indexes, aggregating social factors, has been developed, for different scopes as to assess disaster risk, environmental hazards, healthcare access in underserved regions, communities' resilience (10).

The SVI developed by the Centre for Disease Control and Prevention (CDC) (11), is an example. In the recent years, Mah et al' scoping review (12), examined literature on SVIs to map their composition and contests of utilization such as predictive power with respect to health outcomes (Figure 1.4).

Figure 1.4. Social Vulnerability Index predictive power on health outcomes (12).



Betancur et al. in 2015 (13) formulated a Relative Index of Inequality (RII), that resemble the Social Vulnerability Index (SVI) in its idea, constituting a measurement of socioeconomic inequalities in health outcomes. Using a structured regression, they provided a framework to enable comparisons of associations across different populations, ultimately improving understanding of health vulnerability in different contexts, regions and countries.

1.4 The many dimensions of vulnerability

In the following section, we report on specific examples from the literature, that explore factors leading to health vulnerability, both for individuals and for populations:

- Geographical vulnerability: is rooted in the disparities in healthcare infrastructure and resources across different regions. Rural areas, often characterized by limited healthcare facilities and specialized services, face accessibility challenges. Populations residing in remote or isolated areas, such as islands or mountainous regions, encounter difficulties accessing healthcare due to constrained transportation options and healthcare facilities. Limited geographical access to health facilities can result in insufficient resources for disease control. A comprehensive review from 2021 (14) demonstrated, indeed, how poor spatial accessibility to health care was

found to be associated with higher disease incidence, more severe health outcomes, and higher mortality in the majority of the studies analysed.

- Social Vulnerability: revolves around the influence of socio-demographic factors on healthcare access. Older adults, for example, may face barriers due to limited mobility, transportation challenges, and complex health needs; homeless individuals, lacking stable housing, encounter difficulties accessing consistent healthcare services. Studies, such as the one by Baggett et al. (15) highlight the increased likelihood of homeless populations developing infectious diseases like tuberculosis and respiratory infections. People within prisons often face challenges in accessing healthcare due to restricted mobility and limited availability of medical services.
- Ethnic/Cultural Vulnerability: refers to the increased risk of experiencing healthcare disparities and limited access to quality care due to an individual's ethnic or cultural background. It encompasses various factors such as language barriers, lack of culturally sensitive healthcare services, cultural differences on health beliefs, behaviours and expectations, stigma and discrimination experiences within healthcare settings. Furthermore, immigrants may encounter problems on obtaining a legal status and refugee and migrant population on even have services provided (16).
- Systemic Vulnerability: focuses on structural and systemic factors contributing to healthcare disparities and limited access to healthcare services. These include inadequate healthcare policies, that fail to address disparities and access issues; fragmented healthcare systems, lacking coordination and integration; systemic discrimination within healthcare systems; insufficient resources for addressing healthcare disparities. These factors can lead to higher disease prevalence across various conditions, including mental health disorders, chronic diseases, or infectious diseases.
- Economic Vulnerability: is characterized by financial constraints that limit access to healthcare services, including preventative care, medications, and specialized treatments. It encompasses various aspects, such as: lack of health insurance or inadequate coverage hinders access to healthcare services. Economically vulnera-

ble populations may experience higher disease prevalence related to chronic conditions, as demonstrated in research by Jayathilaka et al (2020) (17).

- Technology-Related Vulnerability: refers to disparities in access to healthcare services and information due to limited technological resources or literacy. It encompasses challenges in accessing telemedicine, for example, or difficulties in accessing and understanding online health information; limited access to digital health tools, which have become increasingly important in healthcare delivery (18).
- Environmental Vulnerability: encompasses exposure to environmental hazards, climate change effects, and natural disasters that can disproportionately affect certain populations. These environmental factors can impact healthcare access and lead to the development of various diseases, including respiratory, cardiovascular, and infectious diseases (19).

1.5 Studies designs and methodological approaches

A large variety of study designs has been used to research on the topic of health vulnerability, each of these offering distinct advantages:

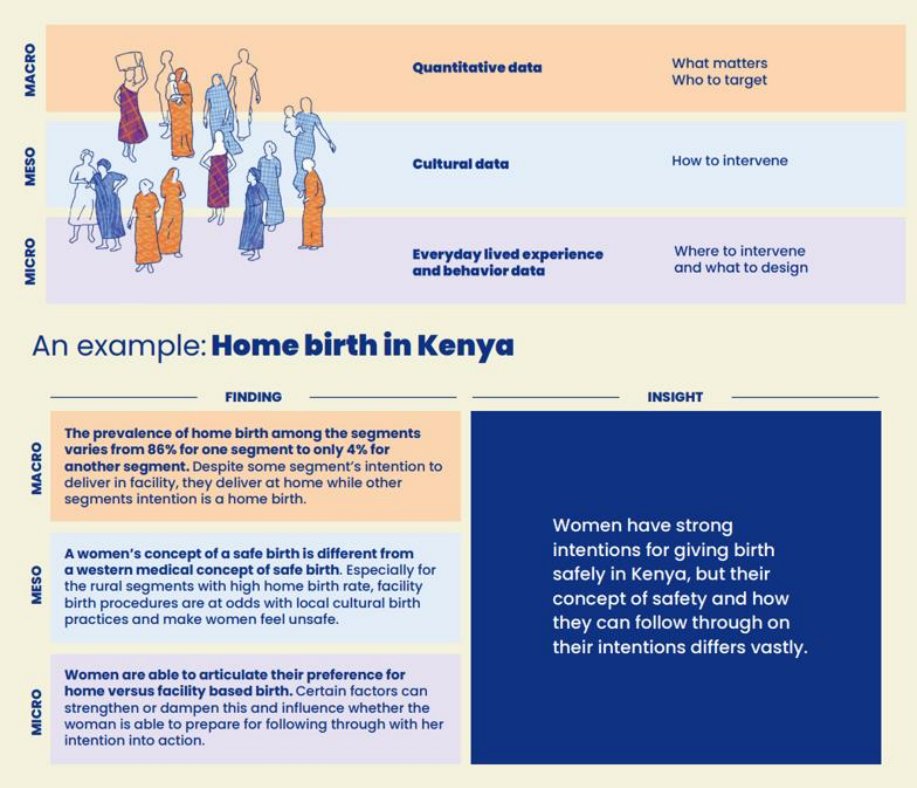
- Cross-Sectional Studies: provide a snapshot of a population's health status at a particular point in time. They are valuable for identifying prevalent health disparities, as they allow researchers to assess the association between various factors and vulnerabilities simultaneously.
- Cohort Studies: offer the advantage of tracking a group of individuals over time, making them well-suited for understanding the development of health vulnerabilities and their long-term consequences.
- Case-Control Studies: are highly effective in investigating the causes of specific health outcomes within vulnerable populations, by comparing individuals with a particular health condition to those without and analysing their past exposures.
- Longitudinal Studies: excel at capturing changes in health vulnerabilities and their effects over an extended period. These studies are valuable for understanding the dynamic nature of vulnerabilities and how they evolve.

- Ecological Studies: are advantageous when exploring population-level vulnerabilities and their effects on health outcomes. They are well-suited for identifying broad associations between exposures and outcomes at the community or regional level, while they cannot establish individual-level relationships.
- Interventional Studies (Randomized Controlled Trials): particularly randomized controlled trials, are essential for assessing the effectiveness of interventions designed to mitigate health vulnerabilities and improve access.

1.6 Potential gaps

While reviewing literature on health vulnerability, it became clear that multidisciplinary approaches are rarely used in research. Investigations usually approach the topic from a unique, while direct, perspective. However, given the multidimensional nature of the problem, there is an urgent need for comprehensive research planning and collaboration across disciplines; integrating insights and expertise from different fields, including public health, sociology, economics and environmental science, is essential to design studies and conduct analyses to truly understand the complex web of factors influencing health vulnerabilities.

Figure 1.5. Pathways approach to design studies: three lenses for organizing and thinking with different data streams (top). Home birth insights derived from macro-meso-micro lens analysis example in practise (bottom). © 2022 Sonder



A landmark paper was published just a year ago by Johnson and Wendland (2022); introducing a novel, design-driven, interdisciplinary research approach to study vulnerability (20). This approach, known as the 'Pathways' approach, has three core components: a vulnerability framework, population-representative household segmentation solutions and a set of qualitative stories and insights that bring the framework and segmentation to life. Its main objective is to enable health systems stakeholders to categorize their users based on the social, environmental and cultural vulnerabilities associated with poor health outcomes, in a range of areas, including reproductive, maternal, newborn and child health, nutrition, and women's health and well-being. As an illustration of this approach, Figure 1.5 shows the formulation of this approach in the contextualised exploration of the lived experiences of Kenyan women and their families

within the cultural contexts that shape their lives (Figure 1.5).

There is, also, untapped potential in borrowing research methods from other disciplines, such as economics, for health research.

Conjoint analysis (CA), for example, is an analytical tool commonly used in marketing research and customer analysis, that could be easily re-adapted to explore policies and interventions preferences among vulnerable populations in low- and middle-income countries (LMICs) (21).

In resource-constrained settings where data-driven decision making is critical, CA has the potential to shed light on how vulnerable individuals make choices about health care options and to identify the key features of health services. The involvement of the local community in the collection of data can promote community engagement, empower community members to participate in decision-making processes, and instil a sense of ownership of health care programmes and initiatives.

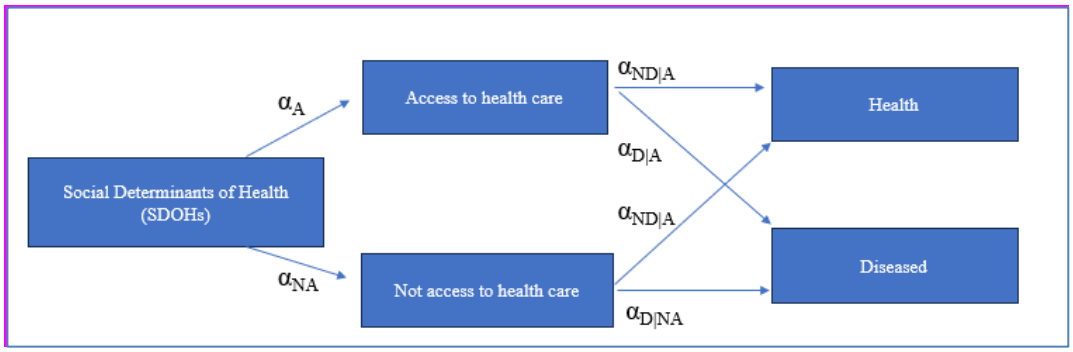
Other valuable methods of data analysis remain underused in the study of the link between vulnerability and health. To estimate in which extent social determinants of health (SDOHs) may impact health outcomes, while controlling for confounding variables, standard multivariate regression models are generally fitted.

To assess the impact of the implementation of policies or health interventions aimed at reducing health vulnerabilities and improving overall well-being, the method of difference-in-difference (DiD) estimation can be a valuable tool. DiD compares changes in an outcome of interest between two or more groups over two different time periods. It controls for pre-existing differences (22).

Causal analysis is often overlooked when studying vulnerabilities. While many studies have identified associations between determinants and health inequalities, only a few have delved into the causal pathways involved. Cross-population comparisons can provide valuable insights into how variation in the distribution of risk factors influences differences in disease occurrence, as exemplified by Betancur et al. (2018) (21). This causal approach, rooted in counterfactual analysis, is underrepresented in health vulnerability research but has the potential to inform policy decisions and interventions more effectively.

Finally, developing a structured regression approach that considers the influence of vulnerabilities on underutilization of health access, modelling causal associations between SDOHs and health outcomes' development, could improve the analysis to tangle under discovered pathways (Figure 1.6).

Figure 1.6. Formulation of model' structure that combines in two steps analysis of determinants to health access and their conditional impact on health outcomes, in a causal pathway. Note: α are conditional probabilities.



1.7 Summary

This manuscript started presenting the concept of vulnerability in its generality. This topic is of paramount importance in the current context of global public health, where health inequalities continue to growth because of social and economic inequalities. Investigating the "who, how, where, what, when, why and what" in health vulnerability research might be crucial to understand determinant factors and inform targeted interventions, guiding the global policy's development and strengthen public health systems response. By identifying specific vulnerable groups, public health can implement a tailored approach for resource allocation, maximizing the effective improvement or avoidance of adverse health outcomes. It is only in this way that it will be possible to work towards a more equitable health system that ensures access to quality health care for all (Universal Health Coverage UHC).

While significant progress has been made in health vulnerability research, certain regions of the world and dimensions remain still understudied.

Vulnerabilities in low-resource countries (LMICs), marginalised populations and neglected health areas require increasing attention. Also, it's important to consider that factors that lead to vulnerability, of any type, vary and evolve over time and space. Countries might be vulnerable to shocks such as natural disasters, pandemics and cross-border population movements/displacement or economic and political crises, which can exacerbate pre-existing vulnerabilities. In addition, new vulnerabilities arise from urbanisation, globalisation and technological advances and require further study to promote inclusive health strategies.

Vulnerability is, therefore, a dynamic phenomenon, also affecting disproportionately groups that were already disadvantaged.

Building adaptable health systems, it’s imperative to adequately address and reduce vulnerabilities. Presence of organisations dedicated to preventing, mitigating and recovering from unexpected conditions, like shocks or emergencies, is crucial to ensure universal access to health care for vulnerable populations (23).

Identifying vulnerabilities at individual or community level requires a nuanced analysis of context, spatial dynamics, temporal trends, and biological specificities. These elements interact to shape health experiences and vulnerabilities of different groups. The influence of geography, cultural practices, historical context, and genetic predispositions underscores the need for tailored interventions that address specific population vulnerabilities. It is therefore only through a multidisciplinary approach that it is possible to carry out appropriate research in this area.

Chapter 2 Antenatal care coverage in conflict

2.1 Introduction

In the realm of health disparities and population vulnerabilities, this thesis chapter examines the interplay between armed conflicts and health care trends. Previous literature has broadly argued how severe adverse outcomes can arise from armed conflicts, on the health of women and children, always considered vulnerable individuals (24–30). However, this issue remains often insufficiently explored, enabling appropriate Global Health's response actions. Creating and implementing measures for healthcare systems reinforcement and facilitating access to medical care for vulnerable groups, are and should always be, primary objectives of Public and Global Health.

A significant obstacle in quantifying direct or indirect impact of conflicts and wars on health outcomes, lays on the difficulty to disentangle their specific effects from the multitude of concomitant factors, also related.

Conflicts not only result in increased mortality rates. Vulnerable populations, bear a disproportionate burden during armed conflicts due to heightened risks to their health and well-being (31). Disruptions in healthcare services, compromised sanitation and hygiene, food insecurity, displacement, and exposure to violence significantly impact these vulnerable groups, leading to increased maternal morbidity and mortality, malnutrition, and infectious diseases (32). The precarious conditions exacerbate pre-existing health inequalities and heighten the vulnerability of these populations, demanding urgent attention and targeted interventions.

In 2015, the United Nations supported the Sustainable Development Goals (SDGs) with a major aim: to reach a global maternal death rate of less than 70 for every 100,000 live births by 2030 (33). Nevertheless, the current trend indicates that this vital objective is not being achieved. To tackle this urgent issue, a group of various partners dedicated to maternal health created the Ending Preventable Maternal Mortality (EPMM) scheme. It aims to prepare for, react to, and endure emergencies while emphasizing humanitarian settings, where the problem is particularly severe.

2.2 Literature Review

A recent and comprehensive systematic review from Alibhai et al (2022) (25) extensively reported barriers, facilitators, and overall factors that very likely impact antenatal care (ANC) uptake in countries or regions classified as fragile and conflict-affected situations (FCAS), as for World Bank's definition (34). It was evidenced that women living in FCAS are, compared to women worldwide, significantly less likely to seek ANC early in pregnancy or attend a total of four ANC visits.

This review, referencing to the Andersen's Model of Healthcare Utilization (7), conceptualized healthcare utilization as function of the interaction between predisposing, enabling, and need factors that influence whether women are able to seek antenatal care. Four factors were frequently cited as influencing the uptake, frequency, and timing of antenatal care, in general: mothers' education, gender dynamics (gendered power relations which inhibit women's lack of decision-making power about when and where to seek care, driving inequality) (35), socioeconomic status, geographical distance from the health facility and quality of health service.

Although conflict is not always reported as a barrier, it is axiomatic that they indirectly cause a poor uptake of antenatal care services, for mothers living in areas where facilities are affected by attacks, practitioners flee from rural to urban areas to escape from kidnapping dangers, clinics run out of resources, and all the other not mentioned outturns. Disrupted events also result in women experiencing displacement and consequently poor quality of healthcare, lack of infrastructures or difficulties in accessing them, because of walking distances, lack of transportation or fear of experiencing violence travelling alone to the closest hospital (36).

Understanding the intricate interplay between conflicts and the other determinants is of paramount importance for addressing health disparities experienced by vulnerable mothers, in these contests and for devising efficacious interventions geared toward enhancing their overall well-being.

2.3 Antenatal care framework

Antenatal care (ANC) is an essential aspect of maternal healthcare, comprising a range of medical and supportive services administered to expectant mothers to guarantee a safe pregnancy and childbirth. According to the World Health Organization (WHO), ANC, encompasses the "care administered by competent healthcare professionals to pregnant women and adolescent girls to uphold optimal health for both mother and baby throughout pregnancy, childbirth, and the postnatal phase" (37).

Its purpose is to monitor the pregnancy's progress, identify and manage complications, deliver vital health information, and supply relevant interventions to enhance the well-being of both mother and child.

ANC effectiveness depends on a key indicator denoted as ANC4+ coverage, that represent the percentage of women aged 15-49 with a live birth, in a given time period, that received antenatal care four or more times (38). It is reported that receiving antenatal care at least four times increases the likelihood of receiving effective maternal health interventions during the antenatal period. This indicator is listed in the Global Strategy for Women's, Children's and Adolescents' Health (2016-2030) Monitoring Framework, and is one of the tracer indicators of health services for the universal health coverage (SDG indicator 3.8.1) (39).

Several studies have shown that meeting this threshold has a positive impact on maternal and neonatal health, leading to improved outcomes; these benefits include detecting and managing complications early, reducing maternal and neonatal mortality, improving birth preparedness, increasing the likelihood of providing care in medical settings, and enhancing the use of essential interventions such as iron and folic acid supplementation and tetanus toxoid vaccination (40).

Considering developing evidence and heightened objectives towards the enhancement of maternal and child health outcomes, the World Health Organization has revised its guidance and increased the minimum number of suggested ANC visits from four to a minimum of eight during pregnancy (23). This alteration intends to expand and improve ANC objective, allowing for greater access to health assessments, education, and interventions. However, achieving the desirable number of visits often poses challenges, especially in LMICs countries. In these settings obstacles persist in term of

deficient healthcare infrastructures, financial constraints, cultural beliefs, and geographical accessibility that impede women from reaching the recommended number of ANC visits (41). A comprehensive enhancement of the healthcare system, addressing socio-economic inequalities, and improving public awareness and engagement is required, especially in those cases.

2.4 Study objective

In this chapter we present a case study from Mozambique, in which data from national surveys were used to analyse antenatal coverage trends in time and differences between geographical areas (provinces), while also investigating into potential factors associated to undergo the desirable number of ANC visits.

Our primary research question was: 'May living in regional areas more affected by the civilian conflict started in 2017 potentially influenced women's accesses to antenatal visits in the country?'.

2.5 Study Setting

Mozambique is a southern East African country with an estimated population of 32.5 million inhabitants, primarily residing in rural areas (65%). About half (51.6%) of the population are women, with 36.7 births estimated over 1000 habitants, a fertility rate of 4.8 (number of children for each woman) and a 63,9% of infant mortality rate (42). Presently, the country is classified as a low-income country (LIC) by the World Bank, with a gross domestic product per capita (average annual income) of USD 467 in 2020 (43). According to the United Nations 2020 Human Development Index, Mozambique was ranked 181 out of 189 countries, decreasing by one point from its ranking in 2019 and 2018 (44).

Antenatal care service provision in Mozambique has undergone a remarkable transformation since the early 1990s. Back in 1990, only around 30% of women received antenatal care. Over the subsequent years, concerted efforts have been made to enhance maternal healthcare, with the implementation of national and international healthcare

programs. The Health Sector Reform Programme, introduced in 1997, was a significant milestone that paved the way for the development of healthcare infrastructure and the provision of essential services. Collaborative endeavours amongst international agencies gathered impetus through initiatives like the "Millennium Development Goals (MDGs)" (2000-2015) and subsequent "Sustainable Development Goals (SDGs)" (2016-present), which encompassed objectives directed primarily towards diminishing maternal mortality rates and improving antenatal care coverage. During this period multiple national initiatives were enforced, such as the "Mozambique Health Sector Strategic Plan (PESS)" in 2014, highlighting maternal health as a top priority, as well other programs like the "Integrated Community Case Management (iCCM)" aimed at remote regions, greatly increasing the accessibility of maternal healthcare services.

However, since October 2017, Mozambique has been grappling with a militant uprising originated in Cabo Delgado province, resulting in significant loss of life and livelihoods. The armed conflict has caused widespread violence, displacement, and instability in the northern provinces of the country. According to data from the Armed Conflict Location & Event Data Project (ACLED) (45), the conflict has resulted in thousands of deaths and the displacement of hundreds of thousands of people, leading to severe humanitarian crises.

It's been only since 2021 that Mozambique appears in the list of fragile and conflict-affected situations annually released by the World Bank Group (WBG) with the aim to inform strategic and operational decision-making within the WBG (34).

The escalation has resulted in healthcare facilities and infrastructures disruption, hindering access to health services, and exacerbating existing health inequalities. Maternal and child health have been severely affected, with ANC services facing significant strain. Efficiency and effectiveness of humanitarian aid, resources' allocation and targeted support become, especially in this context, crucial to ensure sufficient and quality antenatal care coverage and mitigate adverse outcomes. Research and data collection are fundamental to monitor indicators in time and promptly inform decision maker to plan evidence-based policies and strategies, to safeguard the well-being of Mozambique's population and strengthen the health system.

2.6 Methods

2.6.1 Data sources

The Demographic and Health Surveys (DHS) program (46) is a globally recognized initiative that conducts comprehensive, nationally representative surveys, in low- and middle-income countries. These surveys are designed to collect characteristics at household level that include mothers and children health status. To collect data comparable across countries, surveys are organized in model questionnaires, administered to women aged between 15 and 49 years, including inquiries about household's socio-demographic, economic and health status, living environment, health behaviour, and pre- and post-natal care utilization.

Data for this analysis were retried from Mozambique DHS 2011 (47), AIS (AIDS Indicator Survey) 2015 survey (48) and MIS (Malaria Indicator Survey) 2018 (49).

2.6.2 Study design

DHS, AIS and MIS surveys use a complex multi-stage stratified cluster sampling design to ensure representativeness of the population and allow for efficient data collection (50).

In the first stage, the survey area (namely the country) is divided into smaller geographical units called clusters or primary sampling units (PSUs). These clusters are usually based on administrative boundaries, such as villages or neighbourhoods. From this defined list of PSUs, a systematic random sample of clusters is selected. The selection is made with a probability proportional to the size of the cluster, ensuring that larger clusters have a higher chance of being selected and considering the allocation of the PSU sample over the sample strata, that are typically regions and urban/rural residence. Once the clusters are selected, field teams conduct an exhaustive household listing or census in each one, to help creating a comprehensive and up-to-date list of households within them and collecting geographical coordinates of the cluster itself.

The second stage involves, therefore, a random selection of a predetermined number of households within the list, within each selected cluster.. All women aged 15-49 years

from the selected household, within each cluster, finally constitute the eligible sample to be interviewed.

This two-stage process helps control the cost and time involved in interviewing every household, making the data collection process manageable and logistically feasible, especially in large or geographically dispersed regions. It also improves the representativeness of the survey by providing a systematic and unbiased selection of households at each stage. The use of probability sampling at both stages ensures that each selected household has a known probability of being selected, reducing the potential for bias and allowing the estimation of sampling error. In addition, the use of stratification at the first stage (dividing the population into homogeneous subgroups or strata) helps to ensure that different geographical or demographic segments of the population are represented. This is essential to obtain a comprehensive and accurate picture of the entire population within the survey area.

Sample sizes for DHS surveys are calculated by inflating the standard formula for the sample size of a proportion, by a design effect (Deft), a measure of efficiency of cluster sampling compared to simple random sampling of individuals, defined as the ratio between the standard error using the given sample design and the standard error that would result if a simple random sample had been used:

$$n = \text{Deft}^2 \times \frac{(1/P - 1)}{\alpha^2}$$

α^2 is the precision and p the selected proportion; a default value of 1.5 is used for Deft if not specified.

After determining the total sample size and allocating it to different survey domains/strata, it should be decided the number of individuals (sample take) to be interviewed per sample cluster and convert the domain/stratum sample size to number of clusters. Normally a sample take of 20 to 25 households in urban clusters and between 25 to 30 households in rural clusters, has been proved to be appropriate (50).

To account for the complex sampling design sampling weights are assigned to each household sampled. Sampling weights are calculated based on the inverse of the probability of selection at each stage and any adjustments for non-response.

The household design weight (all households in the same cluster share same weight), therefore, correspond to:

$$W_H = \frac{1}{P_{1hi}P_{2hij}}$$

P_{1hi} are first-stage or cluster sampling probability, of cluster *i* in stratum *j*

P_{2hij} are second-stage or household sampling probability of household *j*, of cluster *i* in stratum *j*

To adjust for non-response, the weight above is then divided by the product of the cluster response rate and the household response rate, for each of the sampling stratum. Individuals' sampling weights of cluster *i* in stratum *h* are, in the same way, calculated by dividing the household design weight by the product of the cluster response rate, the household response rate and the individual response rate, for each of the sampling strata.

In the analysis phase, these weights are applied to calculate health indicators, to correct for the under- or over-sampling of different strata during sample selection.

The responses of each sampled household are multiplied by the assigned weight, so that each interviewed unit becomes representative of similar units in the target population.

2.6.3 Study Sample

In this study, we analysed a pooled dataset of three Mozambique's sub-nationally representative household surveys: Demographic Health Surveys 2011(DHS), HIV Indicator Survey 2015 (AIS) and Malaria Indicator Survey 2018 (MIS). Data collection was implemented between April and November 2011, June and September 2015, March to June 2018 respectively. Surveys response rates were 99% in 2011, 95% in 2015 and 98% in 2018, the higher response rate was always registered among women living in rural areas, compared to urban areas.

We analysed only data from women with at least one child aged at the most twelve months, at the time of the survey, were considered.

2.6.4 Ethics and permissions

Permission to use these datasets was granted by the Monitoring and Evaluation to Assess and Use Results Demographic and Health Survey (MEASURE-DHS).

2.6.5 Variables

The study outcome variable is defined as having or not a received a minimum of four antenatal care visits (ANC4+) for mothers under study. It was derived from the question "How many times did you receive antenatal care during this pregnancy?", the responses were recoded into a binary variable.

Independent variables for which the association with the outcome was investigated, were included based on literature review and data availability. Mother's age at the date of the survey, educational level defined in three categories (no education, primary, secondary or higher, working status, household size (more or less than 6), wealth index in five categories, area of residence (rural or urban), province of residence.

2.6.6 Statistical Analysis

Descriptive statistics as means and standard deviations for continuous variables and frequencies with percentages for categorical variables were used to summarise sample characteristics.

The percentage of mothers attending at least four visits before pregnancy (ANC4 coverage) was computed for each survey at province level, applying sampling probability weights, retrieved from DHS datasets. Also, annual exponential growth rates (AGR) of ANC4 were estimated between subsequent surveys, using this formula:

$$\text{AGR from year s to s} * = e\,\frac{\log(\text{ANC4s} *) - \log(\text{ANC4s})}{\text{year s} * - \text{year s}}$$

Where s* and s represent years of the two subsequent surveys. To compute ANC4 coverage indicator sampling weights were applied.

QGIS software (QGIS Desktop 3.22.7) was used to map cluster-level ANC4 coverage percentages from AIS 2015 clusters (of mothers with a live child aged at the most 12 months at the time of the survey) (number of clusters=294) and MIS 2018 (number of

clusters=219), linking clusters' GPS coordinates (latitude and longitude) to women's questionnaires data by cluster id code.

Also, for the most recent survey (MIS 2018), we modelled associations between mothers' socio-demographic characteristics and ANC4 outcome, to analyse factors associated with antenatal care utilization. We used complex sample logistic regression, applying sample probability weights, as before. Results were reported as odds ratios (ORs) and confidence intervals (95% CIs for a significance level of $\alpha = 0.05$) and model goodness of fit was evaluated.

Statistical analyses were performed in R software (version 4.0.3).

2.7 Results

In total, a subsample of 4779 women (aged 15-49) who participated in the three surveys (DHS 2011, AIS 2015 and MIS 2018) was included in the study (n_{2011}=2558, n_{2015}=1152, n_{2018}=1069). We specifically selected only women who had given birth in the year before the questionnaire was administered.

In all three surveys, most mothers were 25-34 years old and lived in rural areas. In terms of educational attainment, the majority had no or primary education. The percentage of uneducated mothers decreased from 2011 (33%) to 2018 (23%), and the percentage of women with secondary education increased from 15% in 2011 to 24% in 2018. Mothers were almost equally distributed among household wealth index classes, in all three years under study. Sample demographic characteristics are described in Table 2.1 (Table 2.1). Supplementary table S2.1 (Table S2.1) testify the harmonized distribution of mothers among the 21 design strata, in the three surveys under study and table S2.2 (Table S2.2) evidence great mothers' participation in answering antenatal care questions, with very few missing answers, over all provinces and surveys. In Supplementary table S2.3 (Table S2.3) reports mothers' education levels and household wealth index levels, among the three surveys.

Overall, percentage of mothers with no education was higher in rural areas, for all the provinces and years, there was a very low percentage of higher educated mothers in all

the areas (equal to zero in rural areas) and for all the years, percentage of mothers with a poorest level of wealth index was higher in 2015 compared to 2011 and lower in 2018 compared to 2015, apart from mothers living in the provinces of Sofala, Cabo Delgado and Nampula. Also, percentage of mothers with the richest level of wealth index were lower overall in 2018 compared to 2015, apart from the provinces of Manica, Gaza and Maputo.

Table 2.1. Mothers' sociodemographic characteristics, for the three surveys under study. Data are presented for the sample overall and stratified for ANC4+ binary outcome. Note: percentages reported in parenthesis, are computed with respect to column total. P-values are computed from Wilcoxon tests for continuous variables and Chi-squared tests for categorical variables.

	DHS 2011				**AIS 2015**				**MIS 2018**			
Variables	**Overall (n=2558)**	**no ANC4+ (n=1252, 49%)**	**ANC4+ (n=1288, 51%)**	**p**	**Overall (n=1152)**	**no ANC4+ (n=420,39%)**	**ANC4+ (n=668, 61%)**	**p**	**Overall (n=1069)**	**no ANC4+ (n=460, 44%)**	**ANC4+ (n=583, 56%)**	**p**
% of total women sample	19%				15%				17%			
% of mothers sample	34%				30%				32%			
Age in 5-year groups (%)				0.487				0.068				0.078
15-19	465 (18.2)	220 (17.6)	242 (18.8)		272 (23.6)	104 (24.8)	151 (22.6)		253 (23.7)	126 (27.4)	122 (20.9)	
20-24	666 (26.0)	315 (25.2)	347 (26.9)		308 (26.7)	111 (26.4)	186 (27.8)		306 (28.6)	118 (25.7)	181 (31.0)	
25-29	578 (22.6)	290 (23.2)	284 (22.0)		232 (20.1)	80 (19.0)	138 (20.7)		197 (18.4)	79 (17.2)	112 (19.2)	
30-34	423 (16.5)	214 (17.1)	204 (15.8)		166 (14.4)	55 (13.1)	99 (14.8)		154 (14.4)	60 (13.0)	90 (15.4)	
35-39	302 (11.8)	149 (11.9)	152 (11.8)		117 (10.2)	38 (9.0)	71 (10.6)		99 (9.3)	50 (10.9)	46 (7.9)	
40-44	89 (3.5)	50 (4.0)	38 (3.0)		41 (3.6)	24 (5.7)	15 (2.2)		52 (4.9)	23 (5.0)	28 (4.8)	

Variables	DHS 2011				AIS 2015				MIS 2018			
	Overall (n=2558)	**no ANC4+ (n=1252, 49%)**	**ANC4+ (n=1288, 51%)**	**p**	**Overall (n=1152)**	**no ANC4+ (n=420,39%)**	**ANC4+ (n=668, 61%)**	**p**	**Overall (n=1069)**	**no ANC4+ (n=460, 44%)**	**ANC4+ (n=583, 56%)**	**p**
45-49	35 (1.4)	14 (1.1)	21 (1.6)		16 (1.4)	8 (1.9)	8 (1.2)		8 (0.7)	4 (0.9)	4 (0.7)	
Residencial area = Rural (%)	1720 (67.2)	923 (73.7)	790 (61.3)	<0.001	720 (62.5)	307 (73.1)	369 (55.2)	<0.001	692 (64.7)	340 (73.9)	335 (57.5)	<0.001
Education level (%)				<0.001				<0.001				<0.001
no education	845 (33.0)	486 (38.8)	354 (27.5)		283 (24.6)	132 (31.4)	126 (18.9)		244 (22.8)	136 (29.6)	102 (17.5)	
primary	1311 (51.3)	650 (51.9)	651 (50.5)		595 (51.6)	223 (53.1)	341 (51.0)		544 (50.9)	253 (55.0)	280 (48.0)	
secondary	381 (14.9)	114 (9.1)	264 (20.5)		267 (23.2)	65 (15.5)	194 (29.0)		261 (24.4)	69 (15.0)	183 (31.4)	
higher	21 (0.8)	2 (0.2)	19 (1.5)		7 (0.6)	0 (0)	7 (1.0)		20 (1.9)	2 (0.4)	18 (3.1)	
Wealth index (%)				<0.001				<0.001				<0.001
poorest	463 (18.1)	281 (22.4)	181 (14.1)		214 (18.6)	96 (22.9)	99 (14.8)		201 (18.8)	120 (26.1)	74 (12.7)	
poorer	456 (17.8)	267 (21.3)	189 (14.7)		219 (19.0)	105 (25.0)	100 (15.0)		219 (20.5)	122 (26.5)	95 (16.3)	
middle	539 (21.1)	277 (22.1)	259 (20.1)		211 (18.3)	96 (22.9)	105 (15.7)		196 (18.3)	89 (19.3)	100 (17.2)	
richer	553	241 (19.2)	306 (23.8)		262	78 (18.6)	179 (26.8)		253	83 (18.0)	168 (28.8)	

Variables	DHS 2011				AIS 2015				MIS 2018			
	Overall (n=2558)	**no ANC4+ (n=1252, 49%)**	**ANC4+ (n=1288, 51%)**	**p**	**Overall (n=1152)**	**no ANC4+ (n=420,39%)**	**ANC4+ (n=668, 61%)**	**p**	**Overall (n=1069)**	**no ANC4+ (n=460, 44%)**	**ANC4+ (n=583, 56%)**	**p**
richest	(21.6) 547 (21.4)	186 (14.9)	353 (27.4)		(22.7) 246 (21.4)	45 (10.7)	185 (27.7)		(23.7) 200 (18.7)	46 (10.0)	146 (25.0)	
Nr of children 5 and under in household (mean (SD))	2.00 [1.00, 2.00]	2.00 [1.00, 3.00]	2.00 [1.00, 2.00]	<0.001	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	0.003	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	2.00 [1.00, 2.00]	0.598

2.7.1 ANC4+ coverage and trends from 2011 to 2018

Among the selected subsample, 18 mothers (0.7%) for 2011 survey, 26 (5.6%) for 2015 and 64 (2.4%) for 2018, didn't answer the question about antenatal care visits, focus of this analysis. No pattern emerged while investigating distribution of missingness among provinces (Table S2.2).

From DHS 2011, it resulted that 52% of the selected subsample of mothers had fewer than 4 antenatal care visits (undesired antenatal care). This percentage lowered down in 2015 (41%) and then back increased in 2018 (51%). The proportion of mothers who had no visits at all was 8% in 2011, 6% in 2015 and 5% in 2018, while the proportion of mothers who had only one visit was 4%, 5% and 5% respectively. Among mothers having at least one ANC visit, the median (IQR) of visits was 4 (3-5), in all the three years and among the same mothers, only 30 (1%) in 2011, 37 (3%) in 2015 and 34 (3%) in 2018, had at least 8 visits. Socio-economic and demographic disparities were consistently observed between mothers with a desirable number of visits (ANC4+) and those without (no ANC4+) (Table 2.1). In the group of mothers with ANC4+ the proportion living in rural areas was 61% in 2011, 55% in 2015 and 58% in 2018, whether in the complementary group, was around 74% in all three years.

Among mothers in the ANC4+ group, the proportion having secondary or higher education (22% in 2011, 30% in 2015 and 34.5% in 2018) and with household wealth index falling in the 'richer' or 'richest' categories (51.2% in 2011, 54.5% in 2015, 53.8% in 2018), were consistently higher than in the group with undesirable ANC (9.3%, 15.5%, 15.4% for secondary/higher education and 34.1%, 29.3%, 28% for richer/richest wealth index). Table 2.2 reports distribution of mother undergoing or not the four visits during pregnancy, among the ten provinces and the three surveys.

To measure antenatal coverage trend over time of antenatal in each of the 21 studies design substrata (provinces divided in urban and rural areas), we calculated weighted ANC4+ percentages along with standard errors and 95% confidence intervals, for each of the 21 study substrata (Table 2.3). Sampling weights were applied during the calculation and from these, we computed substrata-level growth rates from 2015 to 2018 (Table 2.4).

Table 2.2. Distribution of the sample of mothers, among the ten provinces in Mozambique, for the three surveys and stratifying by the outcome ANC4+ uptake. Chi-squared tests were applied to calculate p-values.

Province	DHS 2011			AIS 2015			MIS 2018		
	no ANC4+	**ANC4+**	**p**	**no ANC4+**	**ANC4+**	**p**	**no ANC4+**	**ANC4+**	**p**
niassa	0.61	0.39	<0.001	0.46	0.54	<0.001	0.48	0.52	<0.001
cabo delgado	0.45	0.55		0.31	0.69		0.77	0.23	
nampula	0.68	0.32		0.52	0.48		0.68	0.32	
zambézia	0.58	0.42		0.55	0.45		0.4	0.6	
tete	0.6	0.4		0.36	0.64		0.65	0.35	
manica	0.33	0.67		0.64	0.36		0.33	0.67	
sofala	0.45	0.55		0.27	0.73		0.33	0.67	
inhambane	0.53	0.47		0.33	0.67		0.27	0.73	
gaza	0.42	0.58		0.21	0.79		0.37	0.63	
maputo province	0.38	0.62		0.17	0.83		0.21	0.79	
maputo city	0.33	0.67		0.25	0.75		0.16	0.84	

Table 2.3. Estimated ANC4+ coverage percentages, by the 21 strata design, for the three surveys. Standard errors (SE) and 95% CIs are also reported. Sampling weights were applied during computation.

	DHS 2011				AIS 2015				MIS 2018			
Province	**ANC4+**	**SE**	**Low CI**	**Upper CI**	**ANC4+**	**SE**	**Low CI**	**Upper CI**	**ANC4+**	**SE**	**Low CI**	**Upper CI**
niassa urban	0.56	0.09	0.37	0.74	0.65	0.05	0.54	0.75	0.48	0.13	0.23	0.73
niassa rural	0.35	0.04	0.27	0.43	0.52	0.07	0.38	0.65	0.5	0.06	0.39	0.61
cabo delgado urban	0.7	0.07	0.56	0.84	0.71	0.1	0.51	0.91	0.39	0.12	0.15	0.62
cabo delgado rural	0.47	0.05	0.36	0.58	0.68	0.06	0.56	0.8	0.12	0.06	0	0.24
nampula urban	0.35	0.06	0.23	0.48	0.66	0.09	0.49	0.82	0.46	0.13	0.2	0.72
nampula rural	0.32	0.04	0.25	0.4	0.41	0.1	0.21	0.6	0.24	0.07	0.1	0.39
zambezia urban	0.48	0.07	0.35	0.62	0.7	0.1	0.51	0.9	0.95	0.05	0.87	1.04
zambezia rural	0.41	0.05	0.31	0.5	0.41	0.08	0.25	0.57	0.5	0.07	0.36	0.64
tete urban	0.68	0.06	0.56	0.8	0.73	0.08	0.58	0.88	0.56	0.08	0.41	0.71
tete rural	0.42	0.07	0.29	0.55	0.6	0.07	0.46	0.74	0.27	0.08	0.1	0.43
manica urban	0.69	0.04	0.6	0.77	0.55	0.09	0.37	0.72	0.66	0.06	0.55	0.78
manica rural	0.66	0.05	0.56	0.77	0.31	0.04	0.23	0.39	0.67	0.08	0.52	0.82
sofala urban	0.66	0.04	0.59	0.74	0.88	0.05	0.78	0.98	0.69	0.1	0.49	0.89
sofala rural	0.45	0.04	0.36	0.53	0.62	0.06	0.5	0.73	0.63	0.06	0.52	0.74
inhambane urban	0.55	0.1	0.36	0.74	0.68	0.11	0.46	0.91	0.83	0.03	0.77	0.88
inhambane rural	0.42	0.04	0.34	0.51	0.69	0.05	0.59	0.79	0.63	0.05	0.54	0.72
gaza urban	0.56	0.1	0.37	0.75	0.66	0.11	0.45	0.86	0.59	0.07	0.45	0.72
gaza rural	0.59	0.05	0.5	0.69	0.84	0.04	0.77	0.92	0.66	0.07	0.53	0.79

Province	DHS 2011				AIS 2015				MIS 2018			
	ANC4+	SE	Low CI	Upper CI	ANC4+	SE	Low CI	Upper CI	ANC4+	SE	Low CI	Upper CI
maputo provincia urban	0.62	0.05	0.52	0.73	0.85	0.07	0.71	0.98	0.85	0.07	0.72	0.98
maputo provincia rural	0.64	0.07	0.5	0.78	0.73	0.12	0.5	0.96	0.77	0.06	0.64	0.9
maputo city urban	0.67	0.04	0.59	0.75	0.73	0.05	0.63	0.83	0.85	0.05	0.76	0.94

Some of the provinces showed a strong decrease trend pattern from 2015 to 2018, compared to the general trend, namely Cabo Delgado (rural and urban), Tete and Nampula rural areas showed an AGRp lower than -10%, Cabo Delgado rural area had a -35% AGRp from 2015 to 2018 and Cabo Delgado urban area -20.5%, Tete rural area -19% and Nampula rural area a -10% AGRp.

On contrast, Inhambane, Manica, Sofala, Zambezia and Maputo city, Maputo province urban area, Niassa urban area, showed an improvement trend from 2015 to 2018 (Figure 2.1).

Figure 2.1. Trends of ANC4+ coverage among the 21 strata design, during the three years (2011, 2015, 2018).

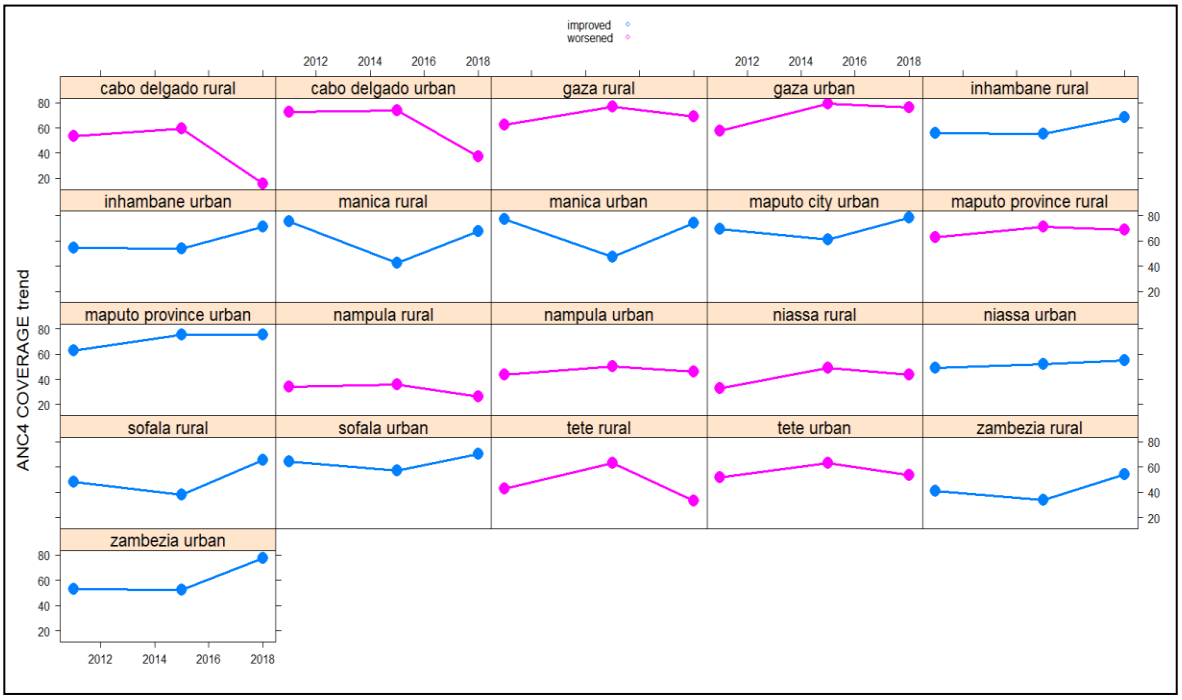


Table 2.4. Annual Exponential growth rates (%) for ANC4+ coverage, computed for all the 21 design strata. Trends are computed from 2011 to 2015 and from 2015 to 2018.

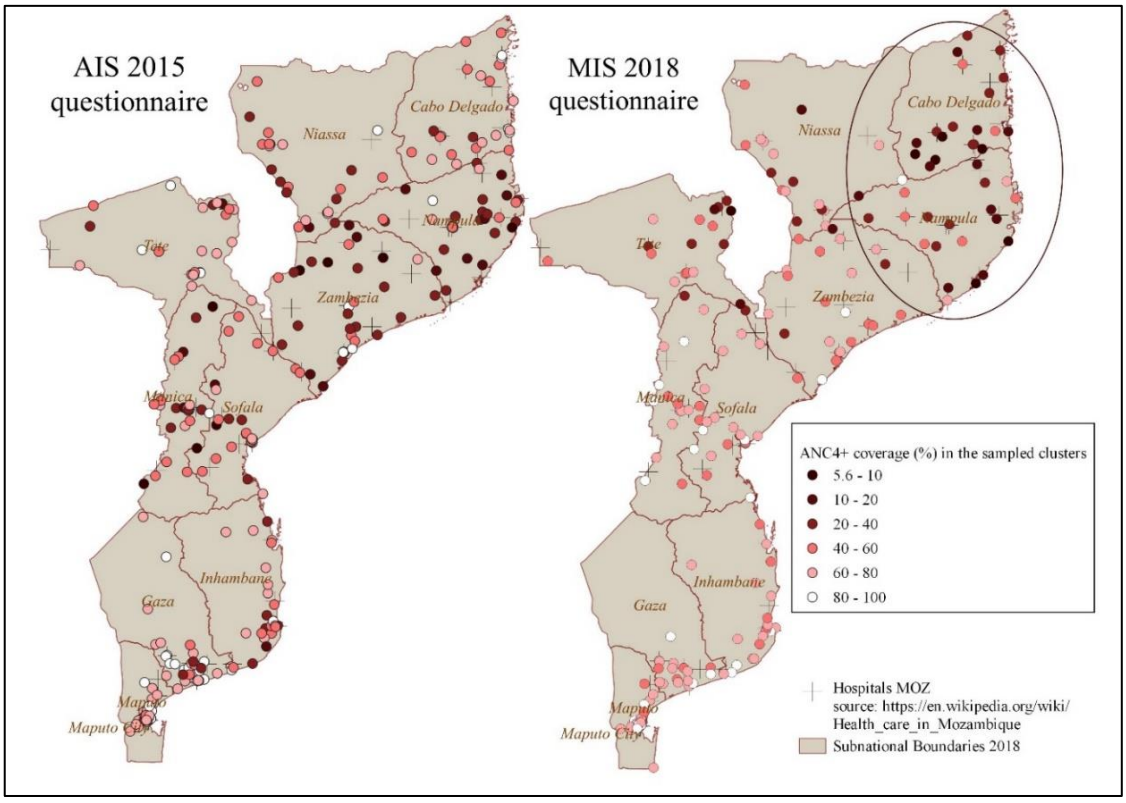
Province	% Annual Exponential Growth Rate for ANC4+	
	2011-2015	2015-2018
cabo delgado rural	9.85	-44.77
tete rural	9.39	-23.73
cabo delgado urban	0.29	-18.18
nampula rural	5.81	-15.70
nampula urban	16.78	-11.11
niassa urban	3.90	-9.71
tete urban	1.83	-8.43
sofala urban	7.28	-7.85
gaza rural	9.10	-7.83
gaza urban	4.01	-3.83
inhambane rural	12.88	-2.85
niassa rural	10.53	-1.28
maputo provincia urban	8.06	0.18
sofala rural	8.47	0.86
maputo provincia rural	3.35	1.79
maputo city urban	2.27	4.92
inhambane urban	5.64	6.51
manica urban	-5.63	6.67
zambezia rural	0.30	6.70
zambezia urban	9.81	10.71
manica rural	-17.36	29.55

2.7.2 Mapping ANC4+ at cluster-level

In a second stage of this analysis, we calculated cluster-level percentages of mothers undertaking at least four antenatal care visits (ANC4+) for 291 clusters in 2015 and 217 in 2018. Sampling weights were applied. We then proceeded to compare scenarios between the two years mapping, side-by-side, clusters-level ANC4+ coverage using

graduated colours symbology (six-levels categories) to highlight geographical areas at lower antenatal care access (Figure 2.2). While general improvement was still clear for the country overall, with this descriptive analysis the worsening in specific area of the North was even more evident.

Figure 2.2. Maps of ANC4+ coverage at cluster-level, comparing year 2015 (before conflict) and 2018 (during conflict). Surveys' clusters from AIS 2015 and MIS 2018 are represented by points, with graduated colours, to follow levels of ANC4+ (in dark brown the clusters with the lowest percentage).



2.7.3 Factors related to ANC4+ in the most recent survey (MIS 2018)

For the subsample of 1069 mothers responding to last available survey (MIS 2018), we investigated factors possibly associated with undertaking or not the minimum number of four antenatal.

Results of complex sample logistic regression are shown in Table 2.5. Adjusted odds

ratios and 95% CI have been reported. Compared to mothers who didn't have formal education, those with a higher education level were 7.51 times (aOR = 7.51, 95% CI [1.72; 32.88]) more likely to undergo at least four antenatal visits. Mothers with household wealth index following in the middle, richer and richest quintiles had 1.51 times (aOR = 1.51, 95% CI [0.88; 2.58]), 3.43 times (aOR = 3.43 , 95% CI [1.67; 7.04]) and 3.23 times, (aOR = 3.23, 95% CI [1.18; 8.85]) higher odds of undergoing the desirable number of visits, compared to mothers living in households classified among the poorest quintile.

No statistical association was found between living in a rural area (compared to living in an urban area), mother's age class, number of children 5 or under 5 living in the same household, and the outcome under study.

Table 2.5. Complex sample logistic regression's results for the outcome ANC4+ uptake, analysing data from the MIS 2018 survey. Clustering, stratification, and weights are considered when fitting the model. Adjusted odds ratios (aOR) and 95% CIs are reported.

	aOR	**95% CI**	**p-value**
Age in 5-year groups (%) (Ref. 15-19)			
20-24	1.52	[0.85; 2.73]	0.158
25-29	0.99	[0.57; 1.73]	0.977
30-34	1.29	[0.67; 2.49]	0.45
35-39	0.97	[0.53; 1.77]	0.916
40-44	2.12	[0.97; 4.62]	0.058
45-49	0.55	[0.09; 3.29]	0.509
Residencial area = Rural (%)	0.73	[0.38; 1.39]	0.339
Province of residence (Ref. maputo city)			
niassa	0.79	[0.25; 2.42]	0.672
cabo delgado	0.14	[0.04; 0.47]	0.002

	aOR	95% CI	p-value
nampula	0.25	[0.08; 0.8]	0.02
zambézia	1	[0.32; 3.11]	0.996
tete	0.25	[0.08; 0.84]	0.025
manica	1.11	[0.38; 3.3]	0.843
sofala	1.11	[0.37; 3.36]	0.852
inhambane	0.85	[0.3; 2.45]	0.764
gaza	0.71	[0.24; 2.12]	0.538
maputo province	1.16	[0.4; 3.36]	0.782
Education level (%) (Ref. no education)			
primary	1.34	[0.86; 2.08]	0.198
secondary	1.51	[0.75; 3.01]	0.244
higher	7.51	[1.72; 32.88]	0.008
Wealth index (%) (Ref. poorest)			
poorer	1.26	[0.81; 1.97]	0.308
middle	1.51	[0.88; 2.58]	0.13
richer	3.43	[1.67; 7.04]	0.001
richest	3.23	[1.18; 8.85]	0.023
Nr of children 5 and under in household (mean (SD))	0.97	[0.82; 1.14]	0.684

2.8 Discussion

It is challenging to discern the extent to which research on maternal care delivery and utilisation in conflict settings accurately reflects actual field situations, given the various hardships involved. Furthermore, effectiveness of health interventions is rarely reported in these settings (26).

Antenatal care (ANC) is a very important component on maternal and child healthcare, providing women with supervision, information and support during pregnancy. ANC is essential for the well-being of both mother and child, helping to timely identify and

manage complications and monitor fetal development and health, leading to better outcomes and reduced delays in accessing emergency care when needed (51). ANC also supports timely administration of vaccinations and prevention of mother-to-child transmission of ailments, including HIV, which significantly decreases the risk of vertical transmission. During antenatal visits, expectant mothers receive education and advice on proper nutrition and healthy lifestyles, as well as information on breastfeeding and postnatal care. In addition, antenatal care serves as a gateway to the health system and increases the use of health services (52). Women who receive antenatal care are more likely to continue accessing healthcare services for themselves and their children, leading to improved health-seeking behaviour and health outcomes within the family. Higher rates of ANC attendance have been associated with lower rates of maternal and neonatal mortality and morbidity. ANC also enables timely intervention and care, ultimately helping to save lives (52).

This study investigates trends in ANC coverage in Mozambique from 2011-2018. Specifically, we examined ANC4+ coverage indicator trends; this has been defined, as from the World Health Organization definition, as the proportion of women who have completed four or more antenatal visits, across various provinces and years. For this analysis secondary data were used. We retrieved data from three national cross-sectional surveys: Demographic and Health Survey (2011), designed to gather data on reproductive health, maternal and child health, nutrition, and endemic diseases at both national and provincial levels, AIDS survey (2015) designed to calculate indicators on immunization, malaria and HIV and Malaria Indicators Survey (2018).

Primary focus of this study was investigating whether, how, and to what extent the armed conflict originated in 2017 in the North of the country, and still ongoing at present time, negatively impacted antenatal services uptake for women living in Mozambique. We used publicly available data to examine trends in ANC coverage indicator at provinces' level, both prior to (2015) and after (2018) the conflict. We determined ANC4+ coverage among the 21 provinces substrata composing the three surveys' design under study. We subsequently calculated relative annual growth rates, between 2015 and 2018, for the same substrata. A pattern emerged while exploring subnational

trends. Some of the provinces showed evident worsening in antenatal care coverage, from 2015 to 2018. Cabo Delgado rural area, among the others, registered the most plummeting annual decrease rate of -44%.

Other geographical areas, such as Tete rural (-24%), Cabo Delgado urban (-18%), Nampula rural and urban (-16%, -11%) also registered very high negative growth rates. Of notice, these areas are located in the North of the country, where the conflict originated.

Humanitarian crises, displacement of the local population, and difficulties accessing essential services such as healthcare and education are typically negative outcomes in conflict settings. Not only pregnant women in conflict-affected regions face obstacles due to geographic isolation, limited transportation options, and security concerns, but also shortages of healthcare workers and resources exacerbate the situation, making it increasingly difficult to provide adequate and high-quality antenatal care services.

Disentangling the distinct effects of the conflict on antenatal care coverage from simultaneous shifts occurring both at the broader population level and within the healthcare system itself is a challenge. In general, conflicts may intertwine with a complex web of dynamics that influence numerous aspects of life, including healthcare utilization. Factors such as population movements, political economic dynamics, social disparities and public policies all concurrent with the conflict, blur the direct correlation between conflict and ANC coverage. Without a comprehensive understanding and separation of these multifaceted influences, accurately attributing changes in ANC coverage solely to the conflict becomes exceedingly complex.

Furthermore, these contests themself inhibit quality of data collection and representativeness. Indirect effects, such as disrupted supply chains and the destruction of healthcare facilities, further complicate data collection and surveys' participation.

Comprehensive research, interdisciplinary approaches, and meticulous data analysis are imperative to attain a precise comprehension of the influence of conflicts on the utilization of antenatal care.

On the other hand, a positive trend was recorded at national level overall (from 2011 to 2018). However, the overall annual percentual global growth rate was relatively low

(0.25), conditioned by a strong worsening in the period between 2015 and 2018 (+5.5 from 2011 to 2015 and -6.1 from 2015 to 2018).

Several factors may have contributed to the positive trend at national level, including the implementation of national policies and initiatives to improve access to health services, investments in health infrastructure such as the construction of new health facilities and the expansion of health centres and clinics, which may have improved access to antenatal care for both urban and rural populations. Community-based approaches to health care delivery began to be promoted during the years, with community health workers (CHWs) educating and engaging communities, reinforcing the importance of antenatal care, and raising awareness among pregnant women to encourage them to seek care. Efforts to reduce financial barriers also might have represented a key driver of improved antenatal care utilisation.

To analyse individual factors that may be associated with attending the desired number (four) of antenatal visits, a complex sample logistic model was fitted to the 2018 MIS data (53). In line with other studies evidence (54,55), it was found that mothers with higher levels of education and living in families with wealth indices in the middle, wealthy and wealthiest quintiles were more likely undertake four or more visits during pregnancy. However, on contrast to previous results, no association was found in this case between living in an urban (vs rural) and ANC4+ outcome.

2.9 Limitations

Monitoring long-term trends in global health indicators using national cross-sectional surveys is instrumental in assessing progress toward achieving universal sustainable goals. Nonetheless, these data sources come with certain limitations that temper their practicality. These surveys rely on paper-based questionnaires, which are inherently susceptible to errors and time-consuming. Responders may be influenced by recall bias since they often report on events that transpired years ago. Moreover, these surveys are not designed for short-term trend analyses, which is particularly crucial in humanitarian

emergencies where health systems need to swiftly respond to shocks, and their representativeness is typically limited to regional levels.

Furthermore, at the time of this assessment, more up-to-date data were unavailable to investigate the long-term trends of the ANC indicator and investigate more deeply consequences of the conflict over time.

Routine facilities data, conversely, offer superior precision, more detailed information, and a deeper understanding of the health system's status, especially in hard-to-reach areas such as conflict zones. In such contexts, data collected from individuals can be less accurate due to various factors like post-traumatic stress and underreporting of high-risk pregnancies, leading to potentially higher sampling errors.

Data representativeness could also be compromised in our analysis. With respect to this, we identified three main challenges.

First, DHS, AIS, and MIS surveys were not specifically designed to estimate antenatal care coverage; second, we didn't include all women in the coverage computation, but instead we selected a specific subsample of women who gave birth during the year before the interview, leaving out all the others. This choice was taken to limit the antenatal care visits registered in 2018 survey, to correspond to the time window going from the beginning of the conflict onwards.

However, women dataset is representative of the Mozambique population (of women) in all the surveys, therefore data were themselves harmonized even if not specifically representing the population of mothers. One way to correct this possible bias would be using calibration methods, based on updated census data, not available in this case.

Third all three surveys were designed based on population data dated back to 2007 census. Several years elapsed between the census and data collection in the 2018 MIS, several changes in population distribution likely occurred in between as a result also of displacement due to conflict. Therefore, the sample size allocation procedure may be subject to bias, and the data representativeness may be affected.

Overall, ANC uptake might be underestimated as a result of the war and conflict effect on ANC uptake might be underestimated, too.

When considering factors associated with mothers' adherence to the recommended four

ANC visits, we couldn't take into consideration residential distance of the mothers from the closest facility or point of care, since this variable wasn't collected in 2018 MIS survey. This variable can critically influence access and utilization of healthcare services, especially in LMICs.

It is also important to remember that even when health facilities are geographically accessible and ready to serve the population, there are settings where various dynamics can create strong barriers that make it practically unattainable. Indeed, in conflict areas, insecurity, lack of transport infrastructure and other contextual elements can significantly impede actual access to points of care. The estimated model resulted, indeed, in wide confidence intervals that reflect less precise population estimates.

Because of study design, it is not possible to establish causality for associations found between mothers' socio-demographic characteristics and their likelihood to undergo the minimum desirable number of antenatal visits. Furthermore, simply counting the number of ANC visits, as we have done here, may not be sufficiently detailed, as it doesn't capture the adherence to quality standards of care or the inclusion of skilled care attendance.

Data on post-natal care, emergency obstetric attendance and routine data from health facilities should be collected to give a comprehensive picture of the situation in this reality.

2.10 Conclusions

Previous literature revealed that women in fragile and conflict-affected regions fall significantly short of meeting WHO ANC recommendations, particularly in terms of early ANC seeking and visit frequency. Attacks on healthcare facilities, practitioner threats, and resource scarcity in these conflict-affected areas indirectly affect ANC, causing barriers. Education, gender dynamics, socioeconomic status, distance, and ANC quality have been shown to be interrelated factors influencing ANC utilization. In line with these findings, our study also evidenced education and household wealth index to play a significant role, with women more educated and living in household with higher

wealth index being more likely to undergo the minimum desirable number of four visits during pregnancy.

Although in 2016 the World Health Organization introduced new guidelines advocating for a desirable number of eight antenatal care visits model (ANC8) to replace the traditional four times antenatal care contacts (ANC4), the percentage of mothers who adhered to the new standard didn't increase at all from 2015.

We explored trends of antenatal care (ANC) coverage across different provinces in Mozambique from 2011 to 2018, specifically we investigated growth/decrease rates occurring from 2015, just prior to the conflict outbreak in Cabo Delgado, to 2018, the year just after the start of the conflict. It was shown a consistent decrease on the indicator in the northern provinces of the country (Cabo Delgado, Nampula, Tete provinces) that coincide with the areas most affected by the conflict.

The province of Cabo Delgado experienced a staggering worsening in ANC4+ utilization, with antenatal care decreasing from a coverage of 68% in 2015 to a troubling 12% in 2018, in the rural area and from 71% to 39% in the urban area.

On contrast, from 2011 to 2018 the provinces of Inhambane, Manica, Maputo City, and Zambezia demonstrated an upward trend. Nampula and Tete experience a completely opposite trend, especially during the three years from 2015 to 2018. These results call for targeted region-specific interventions policy changes to ensure the continued provision of essential maternal healthcare services in areas affected by conflict.

To our knowledge, this was the first study assessing trend ANC coverage in Mozambique, between 2011 and 2018.

Availability of more up-to-date data would have helped to conduct a long-term monitoring of the health consequences of the conflict in the country. Measuring ANC trend in the longer term, would help to state more precise suggestions for policy makers in terms, for a target strengthen of the health systems all over the country, and more specifically in the area affected by the conflict. Implementing robust monitoring and evaluation systems to track the progress of antenatal care coverage is essential to drive interventions.

Collaboration among local policymakers, women, and global organizations, promotion

of community-based care and support from local healthcare providers, can be critical to effectively address these complex barriers and enhance ANC access in fragile settings and therefore should be stimulated.

To encourage the recommended frequency of antenatal care (ANC) visits, it is essential to foster a collaborative effort spanning across different sectors. For instance, ministries such as Labor/Employment, Education, Development, Women's Affairs, and Finance could partner with the Ministry of Health to attain universal ANC coverage.

Further studies are advisable to investigate the impact of conflict on healthcare access and uptake in Mozambique. Collecting more disaggregated data may be crucial to conduct comprehensive geographical analyses, also in relation to other maternal health related indicators but availability of accurate public data is essential to make research open and reproducible for as many investigators as possible, especially in these contexts where conducting multifaceted assessments becomes even more critical.

2.11 Supplementary material

Supplementary Table 2.1. Distribution (percentages) of the analysed sample of mothers, among design strata (provinces divided in rural/urban areas), for the three surveys under study.

Province	DHS 2011	AIS 2015	MIS 2018
niassa urban	0.02	0.04	0.03
niassa rural	0.07	0.06	0.08
cabo delgado urban	0.02	0.03	0.03
cabo delgado rural	0.07	0.05	0.06
nampula urban	0.03	0.04	0.04
nampula rural	0.05	0.07	0.08
zambezia urban	0.02	0.03	0.02
zambezia rural	0.09	0.09	0.08
tete urban	0.01	0.03	0.02
tete rural	0.09	0.07	0.06
manica urban	0.02	0.03	0.04
manica rural	0.08	0.07	0.09
sofala urban	0.04	0.05	0.04
sofala rural	0.07	0.07	0.07
inhambane urban	0.02	0.02	0.03
inhambane rural	0.06	0.04	0.05
gaza urban	0.02	0.03	0.02
gaza rural	0.07	0.08	0.05
maputo province urban	0.06	0.04	0.03
maputo province rural	0.02	0.02	0.03
maputo city urban	0.07	0.06	0.06

Supplementary Table 2.2. Number and percentage of missing answers on the question related to antenatal care visits, in the three surveys under study, stratified by provinces.

Province	**DHS 2011**	**AIS 2015**	**MIS 2018**
niassa	2 (11.11%)	2 (3.13%)	0 (0%)
cabo delgado	1 (5.56%)	10 (15.63%)	2 (7.69%)
nampula	2 (11.11%)	7 (10.94%)	0 (0%)
zambezia	0 (0%)	8 (12.5%)	8 (30.77%)
tete	2 (11.11%)	8 (12.5%)	1 (3.85%)
manica	0 (0%)	5 (7.81%)	2 (7.69%)
sofala	0 (0%)	10 (15.63%)	5 (19.23%)
inhambane	1 (5.56%)	0 (0%)	2 (7.69%)
gaza	5 (27.78%)	4 (6.25%)	1 (3.85%)
maputo province	3 (16.67%)	5 (7.81%)	3 (11.54%)
maputo city	2 (11.11%)	5 (7.81%)	2 (7.69%)
Total	18	26	64

Supplementary Table 2.3. Distribution (percentages) of mothers for educational level, for the three years, among the 21 design strata.

	DHS 2011				AIS 2015				MIS 2018			
Province	**no education**	**primary**	**secondary**	**higher**	**no education**	**primary**	**secondary**	**higher**	**no education**	**primary**	**secondary**	**higher**
niassa urban	0.14	0.34	0.5	0.02	0.17	0.39	0.44	0	0.15	0.55	0.3	0
niassa rural	0.59	0.35	0.06	0	0.37	0.56	0.07	0	0.42	0.54	0.04	0
cabo delgado urban	0.3	0.44	0.24	0.02	0.26	0.42	0.32	0	0.33	0.39	0.21	0.06
cabo delgado rural	0.47	0.51	0.02	0	0.23	0.65	0.12	0	0.27	0.69	0.03	0
nampula urban	0.28	0.62	0.09	0	0.14	0.5	0.32	0.05	0.26	0.38	0.33	0.03
nampula rural	0.44	0.55	0.02	0	0.34	0.59	0.07	0	0.31	0.63	0.06	0
zambezia urban	0.28	0.58	0.14	0	0.13	0.42	0.42	0.03	0.1	0.52	0.38	0
zambezia rural	0.34	0.62	0.03	0	0.41	0.55	0.04	0	0.28	0.62	0.1	0
tete urban	0.15	0.29	0.5	0.06	0.15	0.41	0.44	0	0	0.52	0.48	0
tete rural	0.53	0.42	0.04	0	0.42	0.54	0.05	0	0.35	0.55	0.11	0
manica urban	0.09	0.56	0.35	0	0.1	0.28	0.62	0	0.05	0.28	0.62	0.05
manica rural	0.29	0.57	0.14	0	0.36	0.56	0.09	0	0.35	0.45	0.2	0
sofala urban	0.19	0.49	0.29	0.04	0.02	0.4	0.58	0	0.2	0.32	0.4	0.07
sofala rural	0.59	0.4	0.02	0	0.52	0.39	0.09	0	0.38	0.54	0.08	0
inhambane urban	0.02	0.59	0.37	0.02	0.04	0.48	0.39	0.09	0.06	0.39	0.53	0.03
inhambane rural	0.36	0.52	0.12	0	0.16	0.45	0.39	0	0.04	0.69	0.28	0
gaza urban	0.22	0.57	0.2	0.02	0.07	0.79	0.14	0	0.04	0.46	0.46	0.04
gaza rural	0.3	0.6	0.11	0	0.21	0.6	0.2	0	0.06	0.83	0.11	0
maputo province urban	0.05	0.57	0.37	0.01	0.05	0.43	0.52	0	0.11	0.21	0.64	0.04
maputo province rural	0.11	0.77	0.12	0	0	0.86	0.14	0	0.19	0.49	0.32	0
maputo city urban	0.04	0.49	0.43	0.05	0.03	0.51	0.43	0.03	0.03	0.17	0.65	0.14

Supplementary Table 2.4. Distribution (percentages) of mothers for household wealth index, for the three years, among the 21 design strata

Province	DHS 2011					AIS 2015					MIS 2018				
	poor-est	poore r	mid-dle	riche r	rich-est	poor-est	poore r	mid-dle	riche r	rich-est	poor-est	poore r	mid-dle	riche r	rich-est
niassa urban	0.05	0.07	0.17	0.38	0.33	0.05	0.02	0.24	0.49	0.2	0.06	0.15	0.3	0.33	0.15
niassa rural	0.11	0.34	0.46	0.07	0.01	0.52	0.32	0.11	0.05	0	0.37	0.46	0.12	0.05	0
cabo delgado urban	0.22	0.14	0.24	0.14	0.26	0	0.1	0.13	0.52	0.26	0.15	0.18	0.18	0.3	0.18
cabo delgado rural	0.3	0.46	0.18	0.06	0.01	0.28	0.44	0.19	0.09	0	0.31	0.42	0.16	0.1	0.02
nampula urban	0.23	0.12	0.15	0.31	0.19	0	0	0.14	0.48	0.39	0.31	0.05	0.08	0.23	0.33
nampula rural	0.45	0.25	0.27	0.03	0	0.4	0.4	0.16	0.04	0	0.4	0.31	0.2	0.09	0.01
zambezia urban	0.3	0.16	0.16	0.28	0.09	0.35	0.06	0.06	0.26	0.26	0.14	0.05	0.19	0.48	0.14
zambezia rural	0.5	0.29	0.15	0.05	0	0.47	0.37	0.12	0.03	0	0.44	0.23	0.24	0.09	0
tete urban	0.03	0	0.12	0.18	0.68	0.1	0	0	0.33	0.56	0	0	0	0.52	0.48
tete rural	0.33	0.22	0.29	0.12	0.03	0.36	0.35	0.27	0.02	0	0.32	0.38	0.18	0.12	0
manica urban	0.02	0.09	0.13	0.42	0.35	0.07	0.03	0.1	0.38	0.41	0.03	0	0.03	0.41	0.54
manica rural	0.11	0.19	0.32	0.32	0.06	0.19	0.35	0.33	0.14	0	0.17	0.34	0.3	0.18	0.01
sofala urban	0.03	0.05	0.14	0.38	0.41	0.02	0.04	0.04	0.21	0.7	0.03	0.05	0.17	0.42	0.32
sofala rural	0.23	0.29	0.32	0.16	0	0.1	0.32	0.48	0.08	0.01	0.26	0.44	0.22	0.08	0.01
inhambane urban	0	0	0.12	0.37	0.51	0.04	0.04	0.17	0.43	0.3	0.03	0	0.14	0.67	0.17
inhambane rural	0.07	0.11	0.27	0.49	0.05	0.02	0.04	0.33	0.53	0.08	0	0.04	0.43	0.5	0.04
gaza urban	0.02	0.02	0.12	0.37	0.48	0	0.03	0.07	0.45	0.45	0	0	0	0.38	0.62
gaza rural	0.03	0.05	0.23	0.54	0.15	0.05	0.06	0.25	0.58	0.06	0.02	0.04	0.34	0.51	0.09
maputo province urban	0	0	0.01	0.1	0.89	0	0	0	0.19	0.81	0	0	0	0.18	0.82
maputo province rural	0.04	0.05	0.07	0.63	0.21	0	0	0.33	0.48	0.19	0	0	0.14	0.54	0.32
maputo city urban	0	0	0	0.02	0.98	0	0	0	0.07	0.93	0	0	0	0.02	0.98

Chapter 3

Respiratory diseases in children in Santiago Island: a multilevel logistic approach

3.1 Introduction

Respiratory diseases in children cover a wide range of conditions that affect the lungs, airways, and breathing mechanisms. Bacharier et al, 2008 (56), identified asthma to be the most common chronic disease in children, with increasing trends on its prevalence and severity.

What makes children particularly vulnerable to respiratory illness is a combination of factors. First, their developing immune systems may struggle to fight off infections effectively (57); second, the proximity they often share in school and daycare settings facilitates the rapid transmission of respiratory pathogens. In addition, children are often exposed to new environments and potential allergens. Lack of prior exposure to other pathogens and their smaller airways apparat can exacerbate symptoms as well.

Symptoms of asthma, allergic rhinitis, and atopic eczema in children cluster at both the individual and population levels, indicating a complex interplay of genetic predisposition, environmental factors, and immune responses. Understanding these clusters is essential for developing effective prevention and treatment strategies.

3.2 Literature review

A vast amount of literature exists in the field of respiratory. Many of them not only investigates prevalence and incidence rates but also factors associated with the health outcomes, such as:

- Environmental exposures, such as poor indoor air quality, tobacco smoke, indoor allergens, and living in areas with high levels of pollution are proved to exacerbate respiratory conditions (58).
- Respiratory infections, particularly viral infections like common cold, influenza,

and respiratory syncytial virus (RSV) can trigger or worsen respiratory diseases in children, especially in those with asthma (59)

- Family history and genetics can play a role in a child's susceptibility to respiratory diseases. If there is a family history of asthma or allergies, a child may be at a higher risk (60).
- Premature birth and low birthweight are risk factors for respiratory conditions, including bronchopulmonary dysplasia (BPD) and asthma. Premature infants often have underdeveloped lungs (61).
- Children exposed to second-hand smoke are more likely to develop respiratory illnesses, including bronchitis, ear infections and asthma (62).
- Childhood obesity has been linked to an increased risk of asthma, affecting lung function and increase inflammation (63).
- Dust mites, cockroach droppings, and mold in the home (indoor allergens) can exacerbate respiratory conditions (64).
- Pollen, grass, and other outdoor allergens can trigger allergic reactions, leading to respiratory symptoms (65)
- A diet lacking in fruits and vegetables and high in processed foods may contribute to inflammation and weaken the immune system, making individuals more susceptible to respiratory diseases (66).
- Psychological stress, including family stress and trauma, has been associated with an increased risk of respiratory conditions in children (67).
- Children in daycare or school settings are more likely to be exposed to infectious agents and may have an increased risk of respiratory infections (68).

3.3 Study objective

This chapter presents prevalence data on current asthma, current rhinitis and current eczema diseases, among children in Santiago Island, Cape Verde. It also aims to analyse how socio-demographic, environmental factors, health behaviours might be associated to this population susceptibility.

3.4 Study setting

Santiago Island, located in the archipelago of Cape Verde in the Atlantic Ocean, is a diverse and ecologically significant island known for its unique geography, rich history, and vibrant communities. The island extends for approximately 991 square kilometres, making it the largest and most populous island in Cape Verde. Spanning between valleys, mountains and arid plains, the distinct island geography poses challenges to healthcare service distribution. Limited healthcare infrastructure, particularly in remote areas, hamper access to quality medical services.

Whether living in a specific environment such as an island, with all the specific characteristics this involve, could be potentially itself associated with higher chances to develop respiratory symptoms in the general population has been originally debated. An article from Jeffs, Grainger, and Powell (69), exposed the question in the specific contest of a UK island, where parents and clinicians, living in an offshore environment, were claiming their children developing symptoms of wheezing and other allergies more likely compared to other children in the mainland. Factors that were supposed to influence this higher likelihood included influence of a moist maritime climate, periods of high rainfall, variations in ozone levels, and differences in housing construction that foster the growth of mould and other respiratory allergens; also, a potential higher presence of private cars and its use on a limited land area was supposed to be a component of the potential phenomenon.

However, a comparison of health data from these islands with a larger UK study did not confirm a significantly higher prevalence of these conditions. This study also referred to prior research about differences in the prevalence of asthma amongst island (70,71).

Challenges of investigating causes through geographical variation in epidemiological studies are acknowledged, as these studies require a varying distribution of exposure to ascertain disease aetiology. Furthermore, factors varying geographically such as climate, diet, and outdoor environment, may not be the primary determinants of respiratory diseases' prevalence.

A very recent paper from Varela et al.(2023) (72) examined the spatiotemporal evolution of mortality in Cape Verde from 1995 to 2018. Among others respiratory diseases were considered as possible cause of death accounting for 8.9% of cases, they occupy the 5th position in the group of causes of death. Respiratory diseases exhibited a growing trend for both genders since 2005, with consistently higher mortality rates in males compared to females. Although the burden of asthma is higher in developing countries and underserved populations, LMICs (low and middle-income countries) still face many barriers to appropriate allergy and asthma care, resulting in significant morbidity (73).

Previous studies on respiratory diseases were conducted in the country. In 1993 the PAC Study, conducted in the island of Sal, measured a prevalence of 10.6% of current asthma in a sample of children aged 6-16 years old; in 1994, in the island of São Vicente a 7.0% prevalence of current asthma was measured in another sample of children aged 6-10 years old (74). A study from 2006 analysed a different sample of adolescents or adults, over 20 years old, who sought care at health centres and emergency services at the two central hospitals on the islands of São Vicente and Santiago, 10.9% had a clinical diagnosis of asthma (75).

Of relevance, in Cape Verde, such as in other African countries (e.g. Angola and Mozambique), there is no national program for asthma control, no national recommendations and standardized procedures for diagnosis, treatment, access to healthcare and essential medications for its management, are therefore available.

3.5 Methods

3.5.1 Study sample and study design

This is a cross-sectional study, for which data were collect, between April and September 2022 in children aged 6-7 years old, attending primary schools in the Island of Santiago.

The sample size was determined based on the number of children aged 6 and 7 of both sexes on the island of Santiago, i.e. 12,150 children (12,014 plus 1.1%), using the usual

formula for a prevalence study with a margin of error of 2% and a 95% confidence interval. A prevalence of 10.5% was used for the calculation, since studies carried out in Cape Verde have estimated prevalences of 10.6% (students aged between 6 and 16 on the Island of Sal), 7% (in children aged between 6 and 10 on the Island of São Vicente) and 6.7% (in individuals aged over 20 who went to the Health Centres and Emergency Services of the 2 Central Hospitals on the Islands of S. Vicente and Santiago) (76). Schools were selected with simple random sampling (n=42). To ensure that the sample was representative, the number of participants was then stratified by municipality and school according to the population of each municipality and school.

3.5.2 Data collection

Data were collected in the field, using ISAAC (International Study of Asthma and Allergies in Childhood) questionnaire (77). This is a self-reported questionnaire, filled by parents, to evaluate asthma, allergic rhinitis, and eczema in childhood, while retrieving information about responders' lifestyle and environmental behaviour. ISAAC questionnaire was designed, in 1995 by Asher et al. (78) and since its inception has been largely used worldwide and translated in 42 different languages, Portuguese (official language in Cape Verde) among these. Pretesting questionnaires were administered and a pilot study was conducted to assess adaptability to the contest.

3.5.3 Ethics and permissions

The study protocol was approved complying with the codes of ethics for research in the humanities, the Code of Ethics of the Cape Verdean Medical Association and the guidelines of the Ethics Committee for health research (Decree-Law 26/2007). Authorisation from the National Data Protection Commission of Cape Verde to collect personal data through a questionnaire with sensitive data, approval from the National Ethics Committee for Health Research and authorisation from the Ministry of Education and the Directorates of Primary Schools on the Island of Santiago, were obtained.
All parents signed a written consent form.

3.5.4 Outcomes definition

The three main outcomes of interest, current asthma, rhinitis and eczema, are defined using previous ISAAC protocol.

Specifically, current asthma was defined by a positive response to the following question: “Has your child had wheezing or whistling in the chest in the past 12 months?
Current rhinitis was defined by positive responses to the following questions: “In the past 12 months has your child had a problem with sneezing, or a runny, or blocked nose when he/she did not have a cold or the flu?” - “In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?”. Eczema was defined by positive responses to the following questions: “Has your child had an itchy rash at any time in the past 12 months?” - “Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?”
The three outcomes were considered separately (with no to their intercorrelation), each of the symptoms was then considered in absence of the others (uni-morbidity) and finally coexistence of asthma with rhinitis and rhinitis with eczema were evaluated (in multi-morbidity).

3.5.5 Independent variables

The questionnaire contained questions about children and their families’ characteristics, early life and present exposures, as well as nutritional and daily life habits. Only some of the collect variables entered in the analyses; these were chosen, from literature review, among those already shown to potentially influence the symptoms under study. Some of the categorical variables were reduced to binary categories (frequency of trucks on the road close to the house, source of energy used for cooking, time spent in front of television/monitor/other electronic devices). Also, some of the original ISAAC questions have been readapted to the setting and validated. Variables included in the models were selected as those confirmed to be potentially influencing for the outcomes, by previous literature (79).

3.5.6 Statistical analysis

To model associations between exposures and the three outcomes we used fixed effects Logistic regressions and Multilevel Logistic models, where school were settled as random effects (intercepts) and compared estimated individual-level effects with averaged school-level effects. In multilevel models we rescaled child’s birthweight and years of

mother's education variables, to prevent fitting problems; resulting coefficients represent, therefore, the change in the dependent variable for a one-standard-deviation change in the independent variable.

For each of the analysis above mentioned and for each of the outcomes, we formulated three version of models: the first one provided a simpler set of independent variables as reference (sex of the child, birthweight, living area (urban vs rural) and years of mother's education as independent variables), the second further adjusted for past exposures, whether in the third we further adjusted for present exposures.

AIC and BIC criteria were reported for the fitted regressions.

3.6 Results

3.6.1 Sample characteristics

Our final sample included 1045 children, of these 50.1% were residing in the Municipality of Praia and 49.5% were boys. Almost all parents responded to questions regarding their children's symptoms, with only one missing response for asthma outcomes and four missing responses for rhinitis and eczema.

The prevalence of asthma symptoms ever in life was 24% (95%CI: [21.5, 26.8]) and of current asthma was 10.5% [8.7, 12.5], 20% [17.7, 22.7] for current rhinitis and 12% [10.2, 14.3] for eczema. The 4% (n=42) of children had symptoms of current asthma not accompanied by other respiratory symptoms, the 9% (n=102) of current rhinitis alone and the 6% (n=63) of current eczema alone. Among children with current asthma (n=110), 54% (n=65) had also current rhinitis, 18% (n=20) current eczema and among the whole sample 30.5% (n=319) presented symptoms for all the three outcomes together. able 3.1 reports sample's characteristics, environmental exposures and variables referred to family past and present lifestyle behaviours, in the sample overall and stratifying by occurrence of the three diseases (Table 3.1).

Higher prevalence was observed for current asthma and current rhinitis among males (compared to females) and among children living in Praia district when compared with inland Santiago (the other eight districts) for current rhinitis and eczema.

Table 3.1 Distribution of children characteristics, health behaviours and present/ past exposure factors, among the sample overall, and stratified for each of the outcomes under study.

		CURRENT ASTHMA			CURRENT RHINITIS			CURRENT ECZEMA		
Variables	**Overall (N=1045)**	**no (n=934)**	**yes (n=110)**	**p**	**no (n=831)**	**yes (n=210)**	**p**	**no (n=914)**	**yes (n=127)**	**p**
child's sex=Male	517 (49.5)	452 (48.4)	65 (59.1)	0.043	387 (46.6)	128 (61.0)	<0.001	448 (49.0)	67 (52.8)	0.487
child's birthweight (kg)	3.06	3.06	3.04	0.585	3.05	3.10	0.705	3.06	3.08	0.521
(%) (median [IQR])	[2.80, 3.48]	[2.80, 3.49]	[2.75, 3.35]		[2.80, 3.45]	[2.80, 3.51]		[2.79, 3.45]	[2.89, 3.50]	
living in Praia (vs other districts) (%)	524 (50.1)	462 (49.5)	61 (55.5)	0.277	386 (46.5)	135 (64.3)	<0.001	445 (48.7)	78 (61.4)	0.009
years mother's education	9.00	9.00	9.00	0.53	9.00	11.00	0.004	9.00	9.00	0.793
(median [IQR])	[6.00, 12.00]	[6.00, 12.00]	[6.00, 12.00]		[6.00, 12.00]	[7.00, 12.00]		[6.00, 12.00]	[6.00, 12.00]	
child nationality= Cape Verde (%)				0.158	tor (%)		0.764	(%)		0.851
no	36 (3.4)	29 (3.1)	7 (6.4)		27 (3.2)	9 (4.3)		32 (3.5)	4 (3.1)	
yes	1003 (96.0)	900 (96.4)	103 (93.6)		800 (96.3)	200 (95.2)		878 (96.1)	122 (96.1)	
NA	6 (0.6)	5 (0.5)	0 (0.0)		4 (0.5)	1 (0.5)		4 (0.4)	1 (0.8)	
trucks on the road (%)				0.519			0.765			0.297
low	754 (72.2)	679 (72.7)	75 (68.2)		599 (72.1)	153 (72.9)		667 (73.0)	85 (66.9)	
high	288 (27.6)	253 (27.1)	35 (31.8)		230 (27.7)	57 (27.1)		245 (26.8)	42 (33.1)	
NA	3 (0.3)	2 (0.2)	0 (0.0)		2 (0.2)	0 (0.0)		2 (0.2)	0 (0.0)	
source of cooking energy (%)				0.707			0.002			0.203

		CURRENT ASTHMA			CURRENT RHINITIS			CURRENT ECZEMA		
Variables	**Overall (N=1045)**	**no (n=934)**	**yes (n=110)**	**p**	**no (n=831)**	**yes (n=210)**	**p**	**no (n=914)**	**yes (n=127)**	**p**
eletric or gas	771 (73.8)	687 (73.6)	84 (76.4)		595 (71.6)	175 (83.3)		671 (73.4)	100 (78.7)	
others	270 (25.8)	244 (26.1)	26 (23.6)		233 (28.0)	35 (16.7)		241 (26.4)	26 (20.5)	
NA	4 (0.4)	3 (0.3)	0 (0.0)		3 (0.4)	0 (0.0)		2 (0.2)	1 (0.8)	
refreezing device (%)				0.169			0.604			0.731
no	608 (58.2)	542 (58.0)	66 (60.0)		479 (57.6)	127 (60.5)		535 (58.5)	71 (55.9)	
yes	434 (41.5)	391 (41.9)	43 (39.1)		350 (42.1)	83 (39.5)		377 (41.2)	56 (44.1)	
NA	3 (0.3)	1 (0.1)	1 (0.9)		2 (0.2)	0 (0.0)		2 (0.2)	0 (0.0)	
parent smoking (%)				0.595			0.613			0.463
no	925 (88.5)	825 (88.3)	100 (90.9)		740 (89.0)	182 (86.7)		812 (88.8)	110 (86.6)	
yes	114 (10.9)	104 (11.1)	10 (9.1)		87 (10.5)	27 (12.9)		97 (10.6)	17 (13.4)	
NA	6 (0.6)	5 (0.5)	0 (0.0)		4 (0.5)	1 (0.5)		5 (0.5)	0 (0.0)	
breastfeeding (%)				0.005			0.915			0.199
no	28 (2.7)	20 (2.1)	8 (7.3)		22 (2.6)	6 (2.9)		22 (2.4)	6 (4.7)	
yes	1009 (96.6)	907 (97.1)	102 (92.7)		803 (96.6)	203 (96.7)		885 (96.8)	121 (95.3)	
NA	8 (0.8)	7 (0.7)	0 (0.0)		6 (0.7)	1 (0.5)		7 (0.8)	0 (0.0)	
contact with farm animals during mother pregnancy (%)				0.569			0.077			0.241
no	612 (58.6)	552 (59.1)	60 (54.5)		473 (56.9)	137 (65.2)		528 (57.8)	83 (65.4)	
yes	430 (41.1)	380 (40.7)	50 (45.5)		356 (42.8)	73 (34.8)		384 (42.0)	44 (34.6)	
NA	3 (0.3)	2 (0.2)	0 (0.0)		2 (0.2)	0 (0.0)		2 (0.2)	0 (0.0)	

		CURRENT ASTHMA			CURRENT RHINITIS			CURRENT ECZEMA		
Variables	**Overall (N=1045)**	**no (n=934)**	**yes (n=110)**	**p**	**no (n=831)**	**yes (n=210)**	**p**	**no (n=914)**	**yes (n=127)**	**p**
contact with farm animals when child aged 1 year old (%)				0.781			0.071			0.178
no	616 (58.9)	552 (59.1)	64 (58.2)		476 (57.3)	137 (65.2)		531 (58.1)	84 (66.1)	
yes	423 (40.5)	378 (40.5)	45 (40.9)		350 (42.1)	73 (34.8)		379 (41.5)	42 (33.1)	
NA	6 (0.6)	4 (0.4)	1 (0.9)		5 (0.6)	0 (0.0)		4 (0.4)	1 (0.8)	
cat in the house when child aged 1 year old (%)				0.059			0.06			0.688
no	724 (69.3)	637 (68.2)	87 (79.1)		562 (67.6)	159 (75.7)		630 (68.9)	91 (71.7)	
yes	317 (30.3)	294 (31.5)	23 (20.9)		266 (32.0)	51 (24.3)		281 (30.7)	36 (28.3)	
NA	4 (0.4)	3 (0.3)	0 (0.0)		3 (0.4)	0 (0.0)		3 (0.3)	0 (0.0)	
dog in the house when child aged 1 year old (%)				0.891			0.875			0.838
no	594 (56.8)	533 (57.1)	61 (55.5)		474 (57.0)	119 (56.7)		523 (57.2)	70 (55.1)	
yes	449 (43.0)	400 (42.8)	49 (44.5)		356 (42.8)	91 (43.3)		390 (42.7)	57 (44.9)	
NA	2 (0.2)	1 (0.1)	0 (0.0)		1 (0.1)	0 (0.0)		1 (0.1)	0 (0.0)	
drugs for fever when child aged 1 year old (%)				0.158			0.949			0.257
no	330 (31.6)	303 (32.4)	27 (24.5)		262 (31.5)	67 (31.9)		280 (30.6)	48 (37.8)	
yes	673 (64.4)	593 (63.5)	80 (72.7)		537 (64.6)	134 (63.8)		597 (65.3)	75 (59.1)	
NA	42 (4.0)	38 (4.1)	3 (2.7)		32 (3.9)	9 (4.3)		37 (4.0)	4 (3.1)	
antibiotics when child				0.001			0.115			0.084

		CURRENT ASTHMA			CURRENT RHINITIS			CURRENT ECZEMA		
Variables	**Overall (N=1045)**	**no (n=934)**	**yes (n=110)**	**p**	**no (n=831)**	**yes (n=210)**	**p**	**no (n=914)**	**yes (n=127)**	**p**
aged 1 year old (%)										
no	472 (45.2)	438 (46.9)	34 (30.9)		385 (46.3)	84 (40.0)		405 (44.3)	66 (52.0)	
yes	474 (45.4)	405 (43.4)	69 (62.7)		365 (43.9)	109 (51.9)		417 (45.6)	55 (43.3)	
NA	99 (9.5)	91 (9.7)	7 (6.4)		81 (9.7)	17 (8.1)		92 (10.1)	6 (4.7)	
cat in the house during last year (%)				0.871			0.721			0.613
no	672 (64.3)	602 (64.5)	70 (63.6)		533 (64.1)	138 (65.7)		583 (63.8)	86 (67.7)	
yes	370 (35.4)	330 (35.3)	40 (36.4)		296 (35.6)	72 (34.3)		329 (36.0)	41 (32.3)	
NA	3 (0.3)	2 (0.2)	0 (0.0)		2 (0.2)	0 (0.0)		2 (0.2)	0 (0.0)	
dog in the house during last year (%)				0.833			0.666			0.268
no	582 (55.7)	521 (55.8)	61 (55.5)		462 (55.6)	119 (56.7)		503 (55.0)	79 (62.2)	
yes	459 (43.9)	410 (43.9)	49 (44.5)		366 (44.0)	91 (43.3)		408 (44.6)	48 (37.8)	
NA	4 (0.4)	3 (0.3)	0 (0.0)		3 (0.4)	0 (0.0)		3 (0.3)	0 (0.0)	
use of paracetamol (or others) for fever during last year (%)				<0.001			<0.001			0.596
no	436 (41.7)	408 (43.7)	28 (25.5)		374 (45.0)	61 (29.0)		387 (42.3)	48 (37.8)	
yes	598 (57.2)	516 (55.2)	82 (74.5)		447 (53.8)	149 (71.0)		518 (56.7)	78 (61.4)	
NA	11 (1.1)	10 (1.1)	0 (0.0)		10 (1.2)	0 (0.0)		9 (1.0)	1 (0.8)	
consuming fastfood (%)				0.075			0.118			0.835
no	870 (83.3)	784 (83.9)	86 (78.2)		696 (83.8)	172 (81.9)		762 (83.4)	105 (82.7)	

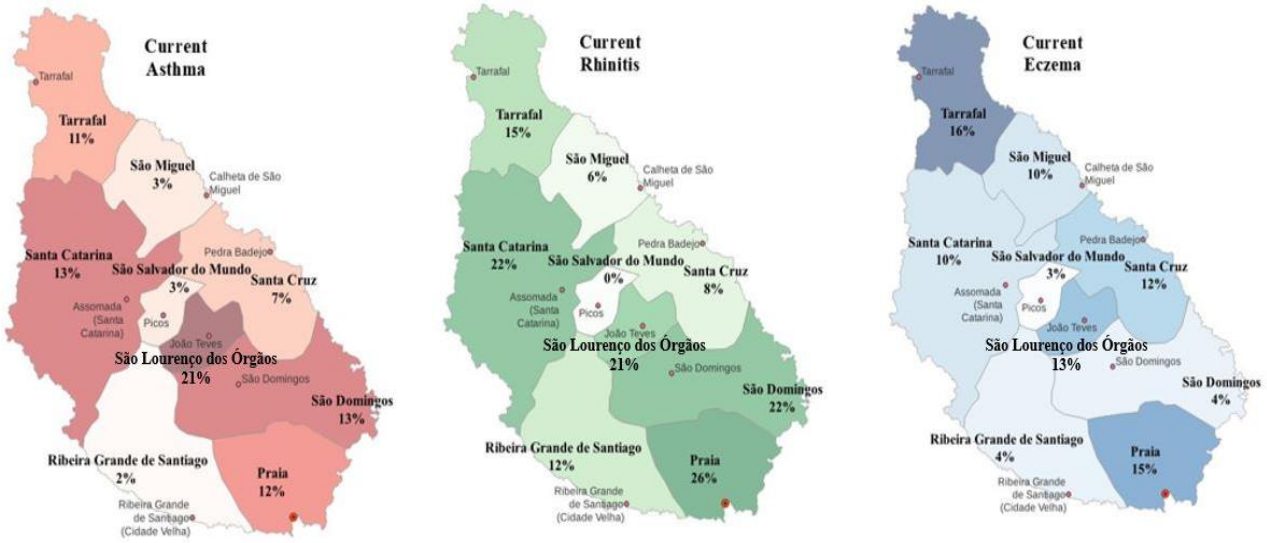
		CURRENT ASTHMA			CURRENT RHINITIS			CURRENT ECZEMA		
Variables	**Overall (N=1045)**	**no (n=934)**	**yes (n=110)**	**p**	**no (n=831)**	**yes (n=210)**	**p**	**no (n=914)**	**yes (n=127)**	**p**
yes	161 (15.4)	137 (14.7)	24 (21.8)		123 (14.8)	38 (18.1)		140 (15.3)	21 (16.5)	
NA	14 (1.3)	13 (1.4)	0 (0.0)		12 (1.4)	0 (0.0)		12 (1.3)	1 (0.8)	
time in front of eletric devices (%)				0.284			0.092			0.004
high	322 (30.8)	289 (30.9)	33 (30.0)		244 (29.4)	78 (37.1)		271 (29.6)	51 (40.2)	
low	175 (16.7)	161 (17.2)	14 (12.7)		139 (16.7)	36 (17.1)		146 (16.0)	28 (22.0)	
medium	533 (51.0)	470 (50.3)	63 (57.3)		435 (52.3)	95 (45.2)		483 (52.8)	48 (37.8)	
NA	15 (1.4)	14 (1.5)	0 (0.0)		13 (1.6)	1 (0.5)		14 (1.5)	0 (0.0)	

Note: p-values were derived from Chi-squared test and Wilcoxon-test.

In Figure 3.1, we plotted prevalences of asthma, rhinitis, and eczema, calculated at district-level, to explore for potential geographical patterns (Figure 3.1).

Chi-square tests for associations between district of residence and the three outcomes, evidenced only for current rhinitis a differential distribution among districts ($p<0.001$).

Figure 3.1. Santiago Island districts coloured by prevalences of respiratory symptoms (graduated scales colours). Note: the sample is not representative at district level.



A more in-depth descriptive analysis that considers mean prevalences at school locations wasn't possible because GPS coordinates weren't available for most of the schools located outside Praia district.

3.6.2 Comparison of risk factors for current asthma, current rhinitis, and current eczema

Table 3.2 reports Generalized Logistic adjusted models results, for the three outcomes under study (considered separately, without taking account coexistence of symptoms) and for presence of at least one of the three symptoms in the child.

Individual-level associations were modelled between socio-demographic and environmental characteristics and past or present exposures variables and the outcomes.

Male children were shown to be more likely to have symptoms of current asthma (OR=1.58, 95%CI [1.03, 2.46]) and rhinitis (OR=1.86 [1.33, 2.61]) as compared to females. Living in Praia Municipality (considered urban residence area) was shown to be a potential risk factor for current rhinitis (OR=1.73 [1.24, 2.44]) as compared to live in the other districts (considered as rural areas). Children with mothers having more years of education were more likely to have current rhinitis symptoms (OR=1.05 [1.01, 1.09]). Administration of antibiotics in children's first year of life was shown to be potential risk factors for current asthma (OR=2.46 [149, 4.18]) and rhinitis (OR=1.62 [1.11, 2.37]), whether exposure to cats, in the same period, seemed to be a protective factor for current asthma (OR=0.39 [0.21, 0.71]). Frequent exposure, in the 12 months before the interview, to trucks in the closeness to children house, was recognized as potential risk factor for eczema (OR=1.59 [1.02, 2.45]) and cooking with wood or carbon was shown as potentially protective for rhinitis (OR=0.61 [0.37, 0.98]).

All the models above were reformulated as Multilevel logistic models, setting schools as random intercepts. Estimated school-level averaged associations are shown in Table 3.3. Hausman tests (80) consistently reported random intercept models to be more efficient, even with low intraclass correlation coefficients (81) (ICCs <0.4).

In this case no significant associations were found, at school-level, for children sex and years of mothers' education and current asthma, and between source of energy used for cooking and eczema. The other associations were found, instead, consistent to those estimated at individual-level.

Uni-morbidity multilevel models were also fitted, considering each of the disease in absence of the others (Table 3.4). Also, in this analysis use of antibiotics was shown to be a potential risk factor for presence of asthma alone (OR=2.55 [1.11, 5.87]); no significant association, instead, resulted between exposure to cats in the first year of childhood and symptoms of asthma alone. Being a male (OR= 1.61 [1.04, 2.48]) and living in Praia district (OR= 1.96 [1.25, 3.07]) were shown to be potential risk factors for current rhinitis alone, whether mothers' years of education were no more associated with the uni-morbidity outcome. Use of paracetamol, or other drugs to combat fever in the first year of childhood, was shown to be potentially protective from having current

rhinitis alone or eczema alone. Use of antibiotics in the first year was no more associated with symptoms of rhinitis alone, whether cooking with carbon or wood (as compared to cooking with electricity or gas) was now showed to be potentially protective from having current rhinitis alone (OR=0.41 [0.20, 0.82]). No association was found between current exposure to trucks in the living area and symptoms for eczema alone. Finally, coexistence of the rhinitis and asthma and rhinitis with eczema were considered in multi-morbidity models (Table 3.5).

Children's sex, mothers' years of education and use of antibiotics during the first year of childhood were still recognized as potential risk factors, for coexistence of current asthma and rhinitis. Consistently, to previous findings exposure to cats during their first year of childhood was found to be a potential protective factor from having asthma and rhinitis together. Furthermore, exposure to dogs in the first year of childhood was found to be a potential risk factor for asthma and rhinitis together (OR= 2.06 [1.01, 4.24]).

No association was found between socio-demographic variables and lifestyle habits, with likelihood of having rhinitis and eczema simultaneously.

Table 3.1. Logistic regression models results, for the three outcomes considered separately and presence of at least one of the symptoms.

Variables	CURRENT ASTHMA			CURRENT RHINITIS			CURRENT ECZEMA			ASTHMA OR RHINITIS OR ECZEMA		
	Ref. Model	Past Exposures	Present Exposures	Ref. Model	Past Exposures	Present Exposures	Ref. Model	Past Exposures	Present Exposures	Ref. Model	Past Exposures	Present Exposures
child's sex=Male	1.58 * [1.03; 2.46]	1.52 [0.96; 2.44]	1.60 * [1.04; 2.50]	1.86 * [1.33; 2.61]	1.65 * [1.15; 2.36]	1.93 * [1.37; 2.72]	1.13 [0.75; 1.70]	0.97 [0.63; 1.49]	1.07 [0.71; 1.62]	1.62 * [1.33; 1.90]	1.48 * [1.17; 1.79]	1.61 * [1.32; 1.91]
birthweight (kg) rescaled	0.91 [0.63; 1.30]	0.98 [0.66; 1.43]	0.96 [0.66; 1.38]	0.98 [0.74; 1.29]	1.02 [0.76; 1.37]	1.01 [0.76; 1.34]	1.11 [0.79; 1.55]	1.08 [0.75; 1.53]	1.04 [0.73; 1.48]	0.95 [0.71; 1.19]	0.98 [0.73; 1.24]	0.95 [0.70; 1.19]
living in Praia (vs other districts)	1.13 [0.73; 1.75]	1.26 [0.75; 2.14]	1.13 [0.70; 1.82]	1.73 * [1.24; 2.44]	1.79 * [1.20; 2.70]	1.50 * [1.04; 2.17]	1.48 [0.98; 2.26]	1.45 [0.89; 2.39]	1.37 [0.87; 2.17]	1.58 * [1.29; 1.87]	1.58 * [1.24; 1.93]	1.33 * [1.02; 1.65]
years mother's education rescaled	1.04 [0.99; 1.10]	1.06 * [1.00; 1.13]	1.05 [0.99; 1.10]	1.05 * [1.01; 1.09]	1.06 * [1.01; 1.11]	1.05 * [1.00; 1.09]	0.99 [0.94; 1.04]	0.99 [0.94; 1.04]	0.98 [0.93; 1.03]	1.03 [0.99; 1.06]	1.04 * [1.00; 1.08]	1.02 [0.98; 1.06]
factory's animals in pregnancy =yes		1.67 [0.78; 3.55]			0.96 [0.52; 1.76]			1.04 [0.51; 2.08]			0.95 [0.44; 1.46]	
factory's animals first year =yes		0.86 [0.40; 1.83]			1.02 [0.55; 1.86]			0.93 [0.46; 1.88]			1.06 [0.55; 1.57]	
cat first year =yes		0.39 * [0.21; 0.71]			0.67 [0.43; 1.03]			0.93 [0.55; 1.54]			0.69 [0.32; 1.07]	
dog first year =yes		1.58 [0.94; 2.64]			1.28 [0.85; 1.92]			1.07 [0.65; 1.73]			1.25 [0.90; 1.60]	
fever first months =yes		1 [0.57; 1.78]			0.75 [0.50; 1.13]			0.85 [0.53; 1.38]			0.72 [0.37; 1.07]	
antibiotics first months =yes		2.46 * [1.49; 4.18]			1.62 * [1.11; 2.37]			0.89 [0.57; 1.40]			1.59 * [1.26; 1.91]	
cat last year =yes			1.11 [0.69; 1.77]			1.13 [0.78; 1.63]			1.01 [0.63; 1.59]			1.04 [0.72; 1.36]
dog last year =yes			1.26 [0.79; 1.99]			1.14 [0.80; 1.63]			0.82 [0.52; 1.27]			1.07 [0.76; 1.38]
trucks =high			1.16 [0.71; 1.84]			0.96 [0.65; 1.39]			1.59 * [1.02; 2.45]			1.12 [0.80; 1.45]
fastfood =yes			1.6 [0.90; 2.72]			1.15 [0.72; 1.79]			0.92 [0.51; 1.59]			1.18 [0.78; 1.57]
source of cooking energy =wood,carbon			0.92 [0.51; 1.62]			0.61 * [0.37; 0.98]			0.88 [0.49; 1.51]			0.67 [0.27; 1.06]
time at television,pc,.. =high			0.93 [0.58; 1.47]			1.25 [0.88; 1.77]			1.18 [0.76; 1.81]			1.23 [0.92; 1.53]
parent smoking =yes			0.59 [0.24; 1.25]			0.86 [0.48; 1.47]			0.99 [0.49; 1.85]			0.99 [0.51; 1.46]

Note: Table reports estimated individual-level odds ratios and 95% CIs. Models were firstly adjusted for sex, maternal education and living district (Ref. Model) and further adjusted for exposures referred to past events (Model for past exposures) or to present events (Models for present exposures). *denotes significant associations.

Table 3.2. Multilevel logistic regression results, for the three outcomes separately and for presence of at least one of the symptoms

Variables	CURRENT ASTHMA			CURRENT RHINITIS			CURRENT ECZEMA			ASTHMA OR RHINITIS OR ECZEMA		
	Ref. Model	Past Exposures	Present Exposures	Ref. Model	Past Exposures	Present Exposures	Ref. Model	Past Exposures	Present Exposures	Ref. Model	Past Exposures	Present Exposures
child's sex=Male	1.51 [0.96; 2.38]	1.48 [0.91; 2.42]	1.53 [0.97; 2.42]	1.84 * [1.31; 2.58]	1.62 * [1.13; 2.33]	1.92 * [1.36; 2.71]	1.13 [0.75; 1.69]	0.97 [0.63; 1.49]	1.07 [0.71; 1.62]	1.59 * [1.19; 2.13]	1.45 * [1.06; 1.98]	1.59 * [1.18; 2.14]
birthweight (kg) rescaled	0.98 [0.78; 1.22]	1 [0.78; 1.28]	1.01 [0.80; 1.26]	0.99 [0.84; 1.16]	1.02 [0.85; 1.21]	1.01 [0.85; 1.19]	1.06 [0.87; 1.30]	1.04 [0.85; 1.29]	1.02 [0.83; 1.26]	0.96 [0.75; 1.23]	0.99 [0.76; 1.29]	0.95 [0.74; 1.23]
living in Praia (vs other districts)	1.14 [0.58; 2.25]	1.34 [0.63; 2.84]	1.09 [0.55; 2.16]	1.72 * [1.18; 2.51]	1.81 * [1.12; 2.92]	1.49 * [1.01; 2.20]	1.48 [0.98; 2.25]	1.45 [0.89; 2.38]	1.37 [0.87; 2.16]	1.58 * [1.11; 2.26]	1.62 * [1.08; 2.44]	1.33 [0.92; 1.92]
years mother's education rescaled	1.16 [0.91; 1.48]	1.29 [0.98; 1.68]	1.17 [0.91; 1.50]	1.23 * [1.03; 1.47]	1.28 * [1.05; 1.56]	1.21 * [1.01; 1.46]	0.95 [0.77; 1.18]	0.95 [0.76; 1.19]	0.92 [0.73; 1.14]	1.03 [0.99; 1.07]	1.04 [1.00; 1.08]	1.02 [0.98; 1.06]
factory's animals in pregnancy =yes		1.83 [0.81; 4.09]			0.96 [0.52; 1.78]			1.04 [0.51; 2.10]			0.95 [0.56; 1.60]	
factory's animals first year =yes		0.87 [0.39; 1.93]			1.04 [0.56; 1.92]			0.93 [0.46; 1.88]			1.08 [0.64; 1.81]	
cat first year =yes		0.37 * [0.20; 0.71]			0.66 [0.42; 1.03]			0.93 [0.55; 1.56]			0.69 [0.47; 1.00]	
dog first year =yes		1.44 [0.83; 2.48]			1.29 [0.85; 1.94]			1.07 [0.66; 1.74]			1.25 [0.87; 1.78]	
fever first months =yes		0.98 [0.54; 1.77]			0.75 [0.49; 1.13]			0.85 [0.53; 1.37]			0.72 [0.50; 1.03]	
antibiotics first months =yes		2.69 * [1.56; 4.62]			1.65 * [1.12; 2.41]			0.89 [0.57; 1.40]			1.61 * [1.16; 2.24]	
cat last year =yes			1.03 [0.63; 1.69]			1.13 [0.78; 1.64]			1.01 [0.64; 1.60]			1.04 [0.75; 1.44]
dog last year =yes			1.26 [0.78; 2.02]			1.15 [0.80; 1.64]			0.82 [0.53; 1.28]			1.06 [0.78; 1.45]
trucks =high			1.18 [0.72; 1.95]			0.96 [0.66; 1.40]			1.59 * [1.03; 2.46]			1.11 [0.80; 1.55]
fastfood =yes			1.5 [0.84; 2.68]			1.13 [0.72; 1.79]			0.92 [0.52; 1.62]			1.14 [0.76; 1.71]
source of cooking energy =wood,carbon			0.87 [0.47; 1.62]			0.62 [0.38; 1.01]			0.88 [0.50; 1.53]			0.67 * [0.44; 1.00]
time at television,pc,.. =high			0.97 [0.60; 1.59]			1.25 [0.88; 1.78]			1.18 [0.77; 1.81]			1.25 [0.91; 1.70]
parent smoking =yes			0.67 [0.29; 1.55]			0.86 [0.49; 1.50]			0.99 [0.51; 1.92]			0.98 [0.61; 1.59]
AIC	605.76	531.26	609.03	900.79	806.1	888.04	670.19	623.34	662.67	1118.45	1001.43	1097.86
BIC	634.75	587.8	671.39	929.77	862.61	950.37	699.16	679.84	724.98	1147.42	1057.91	1160.16
Log Likelihood	-296.88	-253.63	-291.52	-444.4	-391.05	-431.02	-329.1	-299.67	-318.33	-553.23	-488.71	-535.93
Num. obs.	927	822	895	925	820	893	924	819	892	923	818	891
Num. groups: school	44	44	44	44	44	44	44	44	44	44	44	44
Var: school (Intercept)	0.59	0.56	0.52	0.06	0.13	0.03	0	0	0	0.09	0.09	0.07

Note: Table reports estimated school-level averaged odds ratios and 95% CIs. Models were adjusted for sex, maternal education and living district (Ref. Model) and further adjusted for exposures referred to past events (Models for past exposures) or to present events (Models for present exposures). *denotes significant associations.

Table 3.3. Uni-morbidity multilevel logistic models results.

Variables	ASTHMA ONLY			RHINITIS ONLY			ECZEMA ONLY		
	Ref. Model	Past Exposures	Present Exposures	Ref. Model	Past Exposures	Present Exposures	Ref. Model	Past Exposures	Present Exposures
child's sex=Male	0.99 [0.50; 1.95]	1.06 [0.51; 2.19]	0.98 [0.49; 1.95]	1.61 * [1.04; 2.48]	1.58 [0.99; 2.51]	1.67 * [1.07; 2.60]	1.15 [0.66; 1.99]	1.06 [0.59; 1.88]	1.04 [0.59; 1.83]
birthweight (kg) rescaled	0.74 [0.41; 1.34]	0.84 [0.45; 1.58]	0.74 [0.40; 1.36]	0.83 [0.58; 1.19]	0.87 [0.60; 1.28]	0.86 [0.59; 1.24]	1.17 [0.74; 1.87]	1.06 [0.65; 1.72]	1.06 [0.65; 1.73]
living in Praia (vs other districts)	0.85 [0.36; 2.00]	0.85 [0.33; 2.21]	0.66 [0.27; 1.63]	1.96 * [1.25; 3.07]	1.99 * [1.16; 3.43]	1.51 [0.93; 2.46]	1.43 [0.71; 2.88]	1.42 [0.67; 2.99]	1.25 [0.57; 2.75]
years mother's education rescaled	1.03 [0.95; 1.12]	1.04 [0.95; 1.15]	1.03 [0.94; 1.12]	1.04 [0.98; 1.09]	1.04 [0.98; 1.10]	1.02 [0.97; 1.08]	0.97 [0.90; 1.04]	0.97 [0.90; 1.04]	0.95 [0.88; 1.02]
factory's animals in pregnancy =yes		0.8 [0.24; 2.64]			0.83 [0.37; 1.87]			0.63 [0.24; 1.68]	
factory's animals first year =yes		1.41 [0.44; 4.56]			1.19 [0.53; 2.67]			1.64 [0.63; 4.29]	
cat first year =yes		0.48 [0.18; 1.30]			0.96 [0.54; 1.68]			1.41 [0.73; 2.74]	
dog first year =yes		0.94 [0.40; 2.17]			0.92 [0.54; 1.57]			1.1 [0.57; 2.14]	
fever first months =yes		1.5 [0.57; 3.98]			0.58 * [0.35; 0.97]			0.53 * [0.28; 0.99]	
antibiotics first months =yes		2.55 * [1.11; 5.87]			1.6 [0.98; 2.61]			0.89 [0.48; 1.65]	
cat last year =yes			0.79 [0.36; 1.75]			1.01 [0.62; 1.65]			0.91 [0.48; 1.72]
dog last year =yes			0.88 [0.42; 1.85]			1.25 [0.79; 1.98]			0.88 [0.48; 1.62]
trucks =high			1.2 [0.57; 2.55]			0.67 [0.39; 1.14]			1.23 [0.66; 2.29]
fastfood =yes			2.19 [0.98; 4.89]			0.72 [0.37; 1.38]			0.65 [0.27; 1.55]
source of cooking energy =wood,carbon			0.67 [0.25; 1.77]			0.41 * [0.20; 0.82]			0.82 [0.38; 1.76]
time at television,pc,.. =high			0.89 [0.42; 1.88]			1.29 [0.82; 2.03]			1.37 [0.76; 2.47]
parent smoking =yes			1.27 [0.41; 3.88]			1.16 [0.59; 2.27]			1.39 [0.61; 3.18]
AIC	317.66	286.11	323.53	607.4	547.89	594.91	430	401.2	424.87
BIC	346.65	342.65	385.89	636.39	604.42	657.25	458.96	457.68	487.17
Log Likelihood	-152.83	-131.05	-148.77	-297.7	-261.95	-284.45	-209	-188.6	-199.44
Num. obs.	927	822	895	926	821	894	923	818	891
Num. groups: school	44	44	44	44	44	44	44	44	44
Var: school (Intercept)	0.52	0.44	0.52	0	0	0	0.29	0.16	0.39

Note: School-level estimated odds Ratios and 95%CIs are reported. Models were adjusted for sex, maternal education and living district (Ref. Model) and further adjusted for exposures referred to past events (Models for past exposures) or to present events (Models for

Table 3.4. Multi-morbidity multilevel logistic models results.

	ASTHMA AND RHINITIS			RHINITIS AND ECZEMA		
Variables	**Ref. Model**	**Past Exposures**	**Present Exposures**	**Ref. Model**	**Past Exposures**	**Present Exposures**
child's sex=Male	2.21 * [1.20; 4.04]	2.13 * [1.09; 4.14]	2.26 * [1.23; 4.18]	1.2 [0.67; 2.18]	0.97 [0.52; 1.82]	1.22 [0.67; 2.23]
birthweight (kg) rescaled	1.2 [0.74; 1.93]	1.22 [0.71; 2.09]	1.32 [0.81; 2.15]	1.09 [0.67; 1.79]	1.14 [0.69; 1.91]	1.09 [0.66; 1.82]
living in Praia (vs other districts)	1.24 [0.51; 3.01]	1.81 [0.57; 5.73]	1.4 [0.55; 3.52]	1.6 [0.84; 3.06]	1.59 [0.77; 3.28]	1.49 [0.75; 2.94]
years mother's education rescaled	1.06 [0.98; 1.14]	1.10 * [1.01; 1.20]	1.07 [0.99; 1.16]	1.04 [0.96; 1.12]	1.04 [0.96; 1.12]	1.04 [0.96; 1.12]
factory's animals in pregnancy =yes		2.35 [0.79; 7.00]			0.91 [0.32; 2.61]	
factory's animals first year =yes		0.82 [0.28; 2.42]			0.95 [0.33; 2.73]	
cat first year =yes		0.36 * [0.16; 0.82]			0.61 [0.26; 1.42]	
dog first year =yes		2.06 * [1.01; 4.24]			0.96 [0.47; 1.97]	
fever first months =yes		0.62 [0.29; 1.33]			1.38 [0.65; 2.90]	
antibiotics first months =yes		3.14 * [1.51; 6.54]			1.06 [0.55; 2.04]	
cat last year =yes			1.08 [0.58; 2.03]			1.09 [0.55; 2.13]
dog last year =yes			1.77 [0.96; 3.29]			0.72 [0.37; 1.39]
trucks =high			1.14 [0.60; 2.18]			1.67 [0.89; 3.13]
fastfood =yes			1.15 [0.52; 2.53]			1.3 [0.62; 2.76]
source of cooking energy =wood,carbon			1.07 [0.49; 2.36]			0.73 [0.30; 1.81]
time at television,pc,.. =high			1.01 [0.54; 1.89]			1.06 [0.57; 1.97]
parent smoking =yes			0.44 [0.13; 1.52]			0.7 [0.24; 2.05]
AIC	405.83	354.46	409.52	378.43	353.27	382.92
BIC	434.82	411	471.88	407.42	409.79	445.26
Log Likelihood	-196.91	-165.23	-191.76	-183.22	-164.63	-178.46
Num. obs.	927	822	895	926	821	894
Num. groups: nome_escola	44	44	44	44	44	44
Var: nome_escola (Intercept)	0.92	1.57	0.9	0.06	0	0.04

Note: School-level estimated odds Ratios and 95%CIs are reported. Models were adjusted for sex, maternal education and living district (Ref. Model) and further adjusted for exposures referred to past events (Models for past exposures) or to present events (Models for present exposures). *denotes significant associations.

3.7 Discussion

This is, so far, the first population-based study to assess asthma, rhinitis and eczema prevalence, in children aged 6-7 years old, in Santiago Island, and one of the first studies to examine the same diseases, among this age group, in Africa.

A 10.5% prevalence for current asthma, 20% for rhinitis and 12% for eczema were observed in the same under study.

Among children reporting symptoms of asthma, the 54% also presented concomitant symptoms of rhinitis, whether only the 4% had asthma alone. Asthma and allergic rhinitis often coexist in the same individuals (82).

Previous investigation of asthma prevalence in other Portuguese-speaking countries, for the same age group of children, reported higher rates compared to this study (83–86). Overall, mean prevalence of asthma in Africa, for 6-7 years old children, has been also measured around 10%. Global mean prevalence of asthma is 9.3%; whether global mean prevalence of rhinitis 8.5% (85).

This study also aimed to investigate risk factors potentially related to each of the three symptoms. The outcomes were firstly considered separately; secondly, we considered each of the diseases, in the absence of the others (uni-morbidity). Lastly, we modelled coexistence of asthma with rhinitis and rhinitis with eczema (multi-morbidity). Results were compared. Furthermore, we compared associations estimated at individual-level using generalized logistic regression and school-level averaged associations, estimated from multilevel logistic models, between the exposures and the outcomes. Individual-level and school-level odds ratios were found to be very similar in direction and magnitude, with only few associations disappearing when averaging at school-level.

This evidence helps to exclude effect of reverse causation, phenomenon in which the outcome precedes and cause the exposure (e.g. use of antibiotics or the avoidance of pets in the home in allergic families) (87,88).

As asthma, rhinitis and eczema cluster together at the individual-level; it is, therefore, possible that associations exposures-outcome for each one of the conditions can be confounded by factors associated with the others. Nonetheless, coefficients resulted

from uni-morbidity models were very similar in magnitude and direction to those estimated without considering outcomes correlation.

Multi-morbidity models resulted in stronger associations, between child's sex and use of antibiotics in the first year of child's life and symptoms of current asthma and rhinitis together. However, no significant association was identified between the considered exposures and coexistent symptoms of current rhinitis and eczema.

Therefore, we can state that multi-morbidity alone doesn't seem to explain the common epidemiological patterns encountered between the exposures and the three diseases.

Our results were consistent with previous evidence. For example, living in urban areas, (defined as living in Praia Municipality in our setting) has been previously recognized to be a potential risk factor for asthma. Other studies have also shown that male children might be more likely to have asthma as compared to females (89–91,91–98).

Coexistence of allergic rhinitis and asthma was previously shown to be predominant in males during childhood, pattern that switch direction in adolescents (99).

The higher prevalence of asthma in males in paediatric age can be also explained by the smaller diameter and higher tone of the airways compared to females.

Children's diagnosis of asthma has previously been recognized to be associated to healthcare access and caregivers' health literacy (100). In this study, children with mothers having higher number of education years were shown to be more likely to have symptoms of current asthma and rhinitis. This evidence, contextualized with the study setting, might indicate that parents with higher literacy levels may recognize better their children's symptoms, or have higher health awareness levels.

ISAAC phase III data already revealed an association between antibiotic use in the first year of life and current asthma symptoms in children aged 6-7 (92); outdoor and indoor air pollution were previously associated with respiratory symptoms in children (101,102).

Furthermore, previous studies confirmed a potential protective effect of early exposure to domestic animals for asthma, particularly in developed countries (103,104); even though, in other cases it was pointed for evidence in the exact opposite direction, as

affirming an increasing risk, among children exposed, for future sensitisation and allergic pathology (94,105).

Coexistence of the diseases may also may be associated with children's greater impairment of daily activities and lower quality of life, leading to higher risk of worse outcomes (106).

This study contributed to measure prevalences of respiratory symptoms and identify factors to these associated, on the paediatric population of Santiago Island (Cape Verde). It provides valuable information that is essential for the design of public policies and the creation of effective plans and strategies for the prevention, management and treatment of asthma. In addition, it sheds light on the prevalence of asthma in this specific region and serves as a fundamental step in understanding how asthma and related allergic diseases evolve over time in this area of the world.

3.8 Limitations

ISAAC questionnaire has substantial advantages, being applied in numerous studies with large sample sizes worldwide, it provides a valid standardised methodology for the analysis of respiratory symptoms and related risk factors. However, as a self-reported symptoms-based questionnaire both the definition of disease outcomes and the ascertainment of risk factors might be biased. Misclassification of disease or risk factor information could be non-systematic, leading to weaker associations, or systematic, potentially exaggerating, or masking associations. Of particular concern are individual threshold's differences in symptoms reporting. This could exaggerate clustering of the three diseases within individual children. However, this do not affect risk factor associations in unmorbid analyses. Clinical information on allergic sensitisation, measured by skin prick testing and serum allergen specific IgE are notably useful for a precise diagnostic and should accompany self-reported evidence. Furthermore, in our specific setting prevalence of asthma might be underestimated because some of the parents did not know the concept of 'wheezing', possibly causing difficulties in symptoms' recognition or not acceptance of the same.

Focusing on 6-7 years may limit the ability to capture the full spectrum of factors related to asthma, rhinitis, and eczema, which can develop at different ages and participants in school-based studies may not be representative of all children on Santiago Island, particularly if there are barriers to school attendance or participation, with possible under-representation of prevalences.

The cross-sectional design of the study doesn't allow sufficient understanding of the interrelationships between different diseases in terms of complex patterns of multimorbidity.

Controlling for all potential confounding variables in observational studies, which can make it difficult to establish clear cause-and-effect relationships; for example, this analysis did not consider exposure to pollutants or greenspace indexes, recognized to be strong risk factors for respiratory diseases in other studies (107).

This investigation only reports intermediate results on the measure of prevalence of asthma, rhinitis, and eczema in Cape Verde, being circumscribed to the Island of Santiago; may not be generalizable to other regions or populations, as factors related to these conditions can vary significantly based on geographic, environmental, and cultural factors.

3.9 Conclusions

To our knowledge, this was the first study to analyse respiratory diseases prevalence and their associated risk factors, using different modelling approaches, among children in Santiago Island. It was shown that asthma, rhinitis, and eczema should be considered public health problems in Santiago Island. A higher prevalence of respiratory symptoms was observed among boys and in the main city of Praia.

The estimated prevalences of asthma, rhinitis and eczema were consistent with other African countries data.

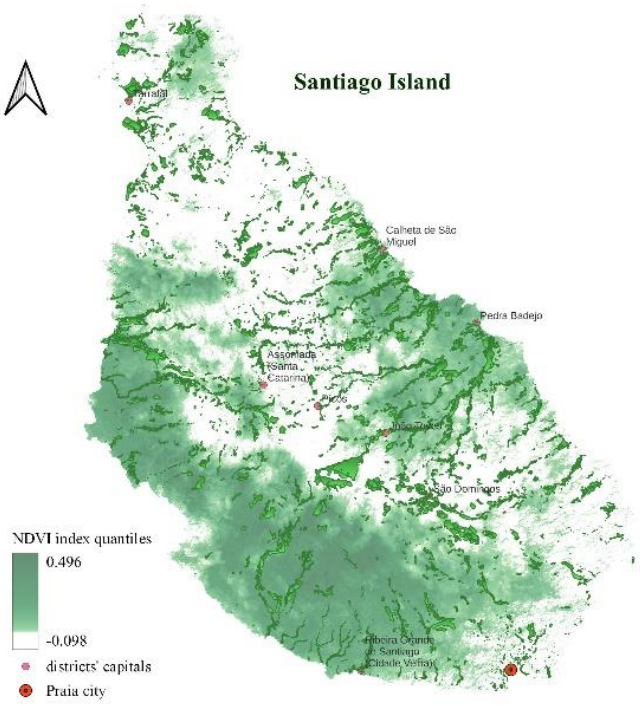
When developing strategies and health policies to improve children's respiratory health, particular attention should be paid to the factors identified here as potential influences on the three respiratory outcomes. Our study plays a pivotal role in filling critical gaps

in under-reported diagnoses, revealing previously unrecognised health problems prevalent in the study region. In doing so, they provide essential insight and guidance not only to policy makers but also to healthcare providers and, more importantly, raise awareness of the problem in the community. In general, scientific research helps to increase the health literacy of the population, facilitating early recognition of health symptoms and potentially guiding individuals towards preventive behaviours that could avert adverse health outcomes.

In essence, these findings may help identified vulnerabilities related to respiratory symptoms in children, call for improvement in access to healthcare among this population and for a comprehensive educational campaign aimed at empowering individuals. This study could act as a catalyst for a healthier future for the children of Santiago Island.

3.10 Supplement material

Supplementary Figure 3.1. Santiago Island. Vegetation index (NDVI) is reported (calculated in QGIS using QuickOSM tool)



Chapter 4

Analysis of COVID-19 testing among immigrant and non-immigrant children in Lisbon

4.1 Introduction

Ethnic minorities, immigrants and refugees are frequently classifiable as vulnerable populations (108).

Many studies in literature have investigated factors influencing migrants and refugee health care delivery in high income countries. Brandenberger et al in a comprehensive review, from 2019, structured the so called '3C Model' identifying the major challenges in migrant health delivery namely communication, continuity of care and confidence. Furthermore, contextual variables in the host country were recognized as largely determining the conditions, in which the three categories above mentioned can be provided (109).

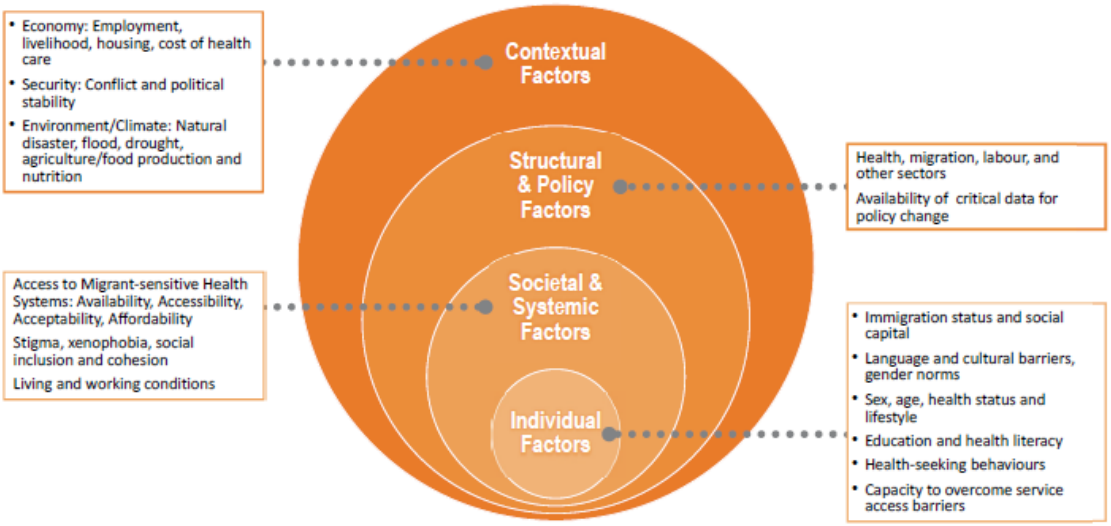
Nevertheless, inequalities vary with healthcare sector and subpopulation of migrants and socio-economic status cannot explain them alone. Ethnicity is an important determinant of health care utilization included in the Behavioural Model of Health Services Use, also called Andersen Model (110).

Facing multiple barriers to accessing health care in the host country, may turn immigrants consecutively more vulnerable to diseases development.

Overcoming these barriers requires a comprehensive and proactive strategy within health systems. Strategic interventions on multiple fronts are needed to address legal, cultural, linguistic and systemic barriers. A cornerstone of this approach is advocacy for inclusive government policies and tailored health programmes and insurance coverage. Equally important is promoting cultural competence among health care providers through comprehensive and diverse training, language services and culturally sensitive care. Engaging communities directly through targeted programmes that provide information, education and access to health services, in collaboration with government

agencies, NGOs, community groups and health providers, pools resources to better meet the health needs of immigrants. Access to health services can vary depending on individual circumstances and on health system organization. This complexity creates a challenging landscape in which equitable access to healthcare remains an ongoing concern. We report some of the factors discouraging or impeding immigrants to seek care: speaking a different language from that of healthcare providers can hinder effective communication, cultural differences create different health practices beliefs and expectations, limited knowledge of the host country's healthcare organization may be a challenge for them, affecting immigrants' ability to navigate the system effectively, access primary care providers or engage in preventive care. Experiences of discrimination or stigma in healthcare settings and institutions can also act as strong barriers. Economic and financial aspects such as lack of health insurance, unemployment, low wages or household instability and transportation issues are notably crucial determinants influencing health behaviours and discriminating inequalities in health access. Furthermore, immigrant people often lack social support networks in the host country, which can compound the difficulties they face. These networks are very important to provide valuable information and assistance in accessing health services. All the factors presented and others more (111) can also vary over time, as contests change, and individuals adapt to new environments .

Figure 4.1. Health vulnerability and resilience factors for migrants: Resetting the Agenda. Report of the 2nd Global (111)



In the contest of COVID-19 pandemic a disproportional negative impact has been evidenced in vulnerable groups, unrevealing the complex links existing between economic and financial stressors, health inequalities and healthcare outcomes. During the pandemic, immigrant people often encountered barriers, of multiple sources, in accessing health care, compared to non-immigrants. COVID-19 testing emerged playing a crucial role in controlling the spread of the virus; timeliness and accuracy of testing have been critical to case identification, effective contact tracing and breaking transmission chains. However, vulnerable populations often faced challenges or delays in accessing testing, due to socioeconomic barriers, lack of awareness and language barriers, or at times, mistrust of health systems.

By analysing COVID-19 testing rates among children, usually recognized as vulnerable group, it is possible to glean insights into systemic healthcare inequalities and identify areas for intervention to ensure equitable healthcare access for all children, irrespective of their immigration status. This focus not only aligns with the ongoing efforts to mitigate health inequalities exacerbated by the pandemic but also highlights the need for targeted public health strategies to support vulnerable groups effectively.

Differences between immigrants and non-immigrants people on COVID-19 were testified in several countries. In Italy, for example, immigrants were shown to have an average delay of two weeks in taking the test was (112). In North America and in Denmark immigrant populations, including children, showed lower reduced testing rates, compared to the general population (113–116).

4.2 Study objective

The study we present in this chapter, aimed to analyse immigrant status as a possible discriminant factor for COVID-19 testing rates, in children residing in the Lisbon Metropolitan area (Portugal).

4.3 Study setting

Although in Portugal, legally resident foreigners can access health services through the National Health Service (NHS), navigating the system can be struggling and while most medical services are covered, some may have small fees. A recent study in the country, found that immigrant children, compared to non-immigrants, undertake fewer check-up visits at the age of four (117) and made large use of hospital emergency services (before and during the pandemic) (118).

Lack of comprehensive data on COVID-19 testing among immigrants in Portugal impedes the efficient development of targeted policies and strategies to reduce access inequalities among immigrants. This analysis might, therefore, reveal crucial evidence, to rethink public health interventions to reduce health inequalities.

The study was conducted in five municipalities in the Lisbon metropolitan area of Portugal (Figure S4.1). These municipalities comprise 22 primary health centres and three referral hospitals (119,120) and the 17% of the resident population is foreign-born (121).

4.5 Methods

4.5.1 Study design

A cross-sequential design was used to examine health outcomes and access to healthcare for children of different ages.

4.5.2 Study sample

The sample included children aged 2 to 8, born in 2015, 2018, and 2020, living in the five municipalities of Lisbon Metropolitan Area (Portugal) and attending primary health centres. All children classified as immigrants who attended a consultation and vaccination during recruitment were included in the study and in each centre each non-immigrant child was matched with one immigrant child, to maximize comparison over time. Were defined 'immigrant' children as those Portuguese residents who were born outside of the EU or had at least one parent born outside of the EU.

Recruitment took place sequentially, with children born in 2015 starting to be recruited before the pandemic. Enrolment of children born in 2018 and 2020 began in May 2022 and is still ongoing, at the time of this manuscript writing.

The original birth cohort, called "CRIAS", from which this sample was generated is described in a published reference paper (118).

4.5.3 Data collection

We analysed data for the sample testing, from 31 March 2020 to 18 May 2023.

For each age-cohort, a comprehensive set of socioeconomic and demographic data was collected through face-to-face Strengths and Difficulties Questionnaires (SDQ) (118), administered to children's parents or caregivers in dedicated areas of the sampled primary health centres. Portuguese was the primary language used during interviews, however other languages were accommodated based on individual preferences and needs. Notifications of children laboratory COVID-19 test results (RT-PCR and antigen tests) were also obtained from the Portuguese General Directorate of Health's laboratory surveillance system for COVID-19 and linked through unique identifier to data from questionnaires.

4.5.4 Outcome

We modelled two different outcomes to analyse children access to COVID-19 tests: a dichotomous outcome indicating whether children had performed at least one COVID-

19 test during the study period (yes/no), and the counts of COVID-19 tests undertaken during the study period.

4.5.5 Independent variables

The Andersen and Newman's model, in its revisited version, was taken as primary reference source to identify independent variables to include in our analysis, as previously done in similar studies (122). While the original Andersen model primarily focused on individual-level factors, the Andersen and Newman model expanded to include environmental and systemic factors, health behaviours and outcomes providing a more holistic view. Greater emphasis is placed on how health policy and system-level factors affect individual health service utilization and more attention is attributed to issues of equity and access, examining how social determinants and systemic barriers contribute to disparities in health service utilization (123) (Figure S4.2) .

Caregiver's age and sex (male/female), family structure (single parent family/traditional family), child immigration status (non-immigrant; immigrant), household density (HD) (high/low), caregiver's education (less than secondary/upper secondary/university degree), caregiver's employment status (unemployed/employed), were considered in quality of predisposing, enabling and perceived need factors conditioning health access.

House density was defined as the ratio of people to the number of bedrooms in the household, and we considered a high HD as a ratio greater than 1, monthly net household income was dichotomized using the minimum country salary as cut-off (≤750€/ >750€), child health insurance was defined as having or not health insurance, the child's birthweight as high/normal/low/very low, and the caregiver's perception of the child's health status as very good/good/reasonable/poor and very poor. Children birthweight was included as a variable for perceived health care needs because it significantly influences the likelihood of mortality, morbidity, and disability during the critical early stages of life, particularly for newborns, infants, and children (124).

4.5.6 Statistical Analysis

Sample socio-demographic characteristics were reported as percentages for categorical variables and means with standard deviations for continuous variables (Table 4.1).

Characteristics were categorized as predisposing, enabling and need factors for healthcare access (7,122).

We computed univariate a Robust Poisson regression to model associations occurring between independent variables and the binary outcome (being tested) and a Standard Poisson regression to model associations with number of tests undertaken. We reported prevalence ratios (PR) and risk ratios (RR) and 95% confidence intervals (Figure 4.2, Table S4.2, Table S4.3). We also reported, for the adjusted models, variance inflation factors (GVIF), to test for models' multicollinearity (Table S4.1).

For the outcome being tested or not for COVID-19, we compared results of Robust Poisson model with Log-binomial and Probit regression alternatives, for binary outcomes. Log-binomial regression (logistic) is considered a less accurate option when models may suffer of misspecification, Robust Poisson model is the preferred choice for estimating unbiased coefficients, especially when the prevalence of the outcome is unbalanced and covariates are continuous (125).

Statistical analyses were performed in R software (version 4.0.3).

4.5.7 Ethical approval

The Ethics Committee for Health of the Regional Health Administration of Lisbon and Tagus Valley, Portugal (001/CES/INV/2019 and 071/CES/INV/2021, respectively) approved both cohort studies and COVID-19 interim study (9-2020/CES/2020). Moreover, one of the child's primary caregivers signed an information and consent form before participating in the study.

4.6 Results

Overall, 722 children were analysed; 420 children were born in 2015, 133 in 2018 and 169 in 2020. In the time window spanning from March 2020 to May 2023, participants underwent in total 637 tests, with a median of 2 tests (range 0-12). The 78.8% (95% CI: 75.8 - 81.7) of children received at least one COVID-19 test; among these, the majority (52.4%) were non-immigrants children. Median of number of tests was 3 (range 1.75 - 5) among non-immigrants and 2 (range 0-3) among immigrants ($p <$

0.001). Overall African countries and Brazil were the most represented nationalities among immigrants; among these, Cape Verde accounted for 25.9%, Angola for 15.7%, Brazil for 14.7%, Guinea Bissau for 12.6%, São Tomé and Principe for 7.3%, and Mozambique for 2.9%.

Table 4.1. Children's and households' characteristics, overall and stratified by the outcome 'being or not tested for COVID-19' and categorized following the Andersen Model (7)

Factors **n**	**Overall** **722**	**Not tested** **153**	**Tested** **569**
PREDISPOSING FACTORS			
Caregiver's age (years); mean ± SD	34.85 ± 7.42	34.82 ± 7.75	34.86 ± 7.34
Caregiver's sex = Female (%)	629 (87.1)	134 (87.6)	495 (87.0)
Caregiver's educational level (%)			
Less than secondary education	233 (32.3)	52 (34.0)	181 (31.8)
Upper secondary education	287 (39.8)	65 (42.5)	222 (39.0)
University degree / professional education	201 (27.8)	36 (23.5)	165 (29.0)
Family structure (%)			
Single parent family	437 (60.5)	89 (58.2)	348 (61.2)
Caregiver's employment status (%)			
employed	522 (72.3)	105 (68.6)	417 (73.3)
House density^2 (%)			
high	615 (85.2)	129 (84.3)	486 (85.4)
Child's immigrant status (%)			
Immigrant children	382 (52.9)	111 (72.5)	271 (47.6)
ENABLING FACTORS			
Household net income/month			
>750eur	503 (69.7)	107 (69.9)	396 (69.6)
Child's health insurance (%)			
having	308 (42.7)	53 (34.6)	255 (44.8)

NEED FACTORS			
Child's perceived health status (%)			
Very good	228 (31.6)	49 (32.0)	179 (31.5)
Good	344 (47.6)	75 (49.0)	269 (47.3)
Reasonable	128 (17.7)	26 (17.0)	102 (17.9)
Bad / Very bad	17 (2.4)	1 (0.7)	16 (2.8)
Child's birthweight			
High (≥ 4 kg)	76 (10.5)	23 (15.0)	53 (9.3)
Normal (≥ 2.5 - < 4kg)	568 (78.7)	114 (74.5)	454 (79.8)
Low (≥ 1.5 - < 2.5kg) / Very low (< 1.5kg)	46 (6.4)	10 (6.5)	36 (6.3)

Immigrant status resulted to be significantly associated to both the considered outcomes, with immigrant children being 18% (PR=0.82 [0.76, 0.89]) less likely to be tested for COVID-19 and undertaking in mean a 26% (RR=0.74 [0.67, 0.82]) less of number of tests, after adjusting the models for the other covariates (Figure 4.2, Table S4.3).

Children's perceived health status was also shown to significantly associated with both the likelihood to be tested and the number of tests undertaken in mean. Children who were perceived by their caregivers being bad/very healthy, as compared to those perceived in very good health status, were 15% (PR=1.15 [1.00, 1.33]) more likely to undergo at least one COVID-19 test and were undertaking, in mean, the 38% (RR=1.38 [1.03, 1.81]) more of number of tests. Also, those children perceived in good and reasonably good health status were undertaking a significantly higher number of tests in mean, as compared to those perceived very good by their caregivers (RR=1.14 [1.02, 1.28] and RR=1.24 [1.07, 1.43]).

Children with normal birthweight significantly underwent a higher number of tests, in mean, as compared to those with low birthweight (RR=1.18 [1.01, 1.40]).

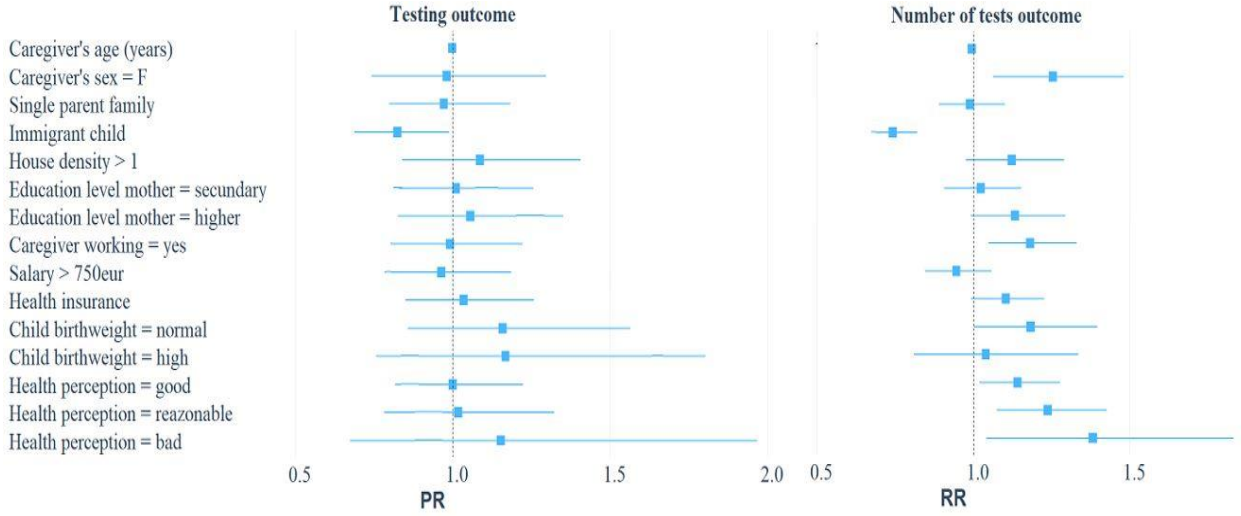
Caregiver's age and employment status were significantly associated with number of tests undertaken by their children (RR=1.25 [1.07, 1.49] and RR=1.18 [1.05,1.33]).

Figure 4.2 show comparison of results from Robust Poisson, Log-binomial and Probit

models, for the binary outcome being tested (Figure 4.2). Interpretation of coefficients

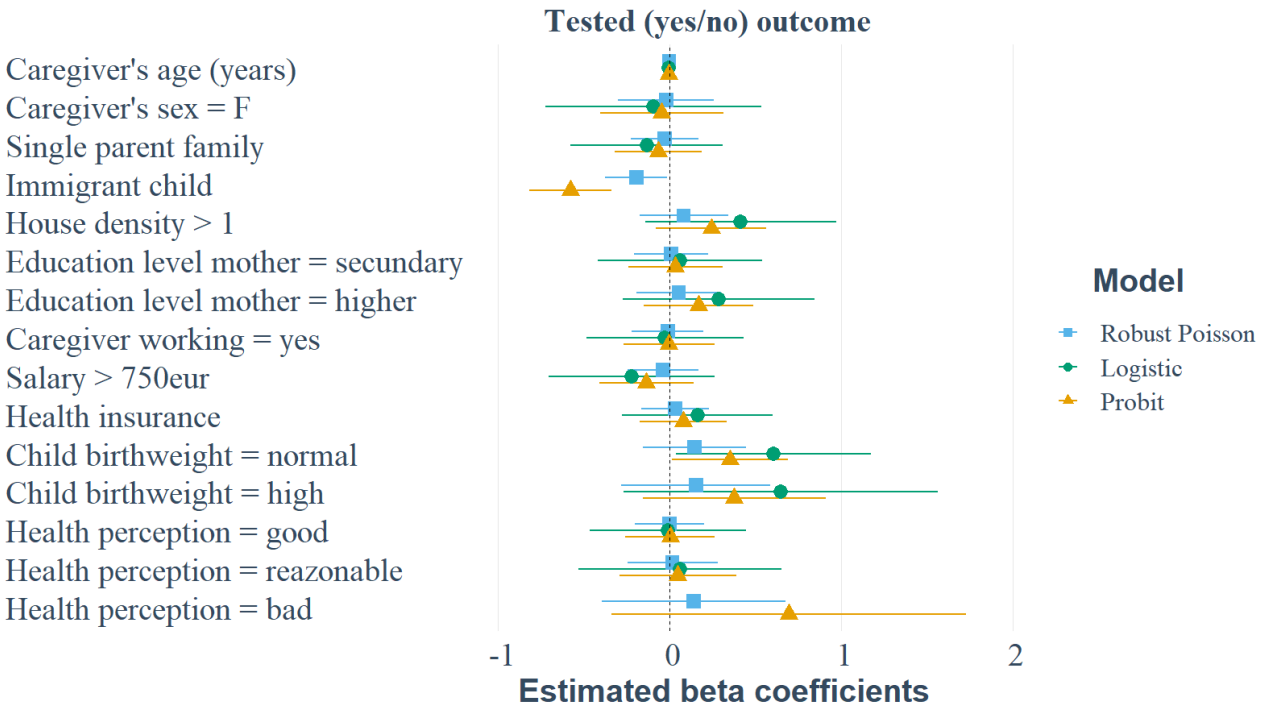
Figure 4.2. Estimated coefficients and CIs, for the associations among sample characteristics and the two outcomes (ever tested for COVID-19 and number of tests performed). Results Robust Poisson (left) and Standard Poisson (right) regressions.

of probit models is slightly different from those of the other models; since they repre-



sent a change in the z-score of the outcome, exponents are not reducible to prevalence or odds ratios. Although the three models identified the same significant associations between the considered variables and the outcome, log-binomial model resulted in wider confidence intervals (Figure 4.3).

Figure 4.3. Estimated coefficients and CIs, for the associations among sample characteristics and the binary outcome ever tested for COVID-19. Results from Logistic (orange), Probit (green) and Robust Poisson (light blue) regressions.



4.7 Discussion

The WHO Refugee and Migration Health Program (126) emphasizes that refugees and migrants are some of society's most vulnerable members, facing daunting challenges including xenophobia, discrimination, substandard living conditions, and inadequate access to healthcare. Amid the COVID-19 pandemic, these groups, encountered heightened risks of infection and mortality, disproportional adverse outcomes might also be influenced by reduced attendance to the healthcare practise.

Rethinking the system is imperative to ensure healthcare services sensitive to the specific needs of migrant communities.

Our study investigated immigration as possible discriminant factor for healthcare underutilization, reframing the question to a more specific setting: access to COVID-19

tests during the pandemic, among immigrant children in Lisbon metropolitan area. Testing rates and median number of performed tests were calculated, during the time window spanning from March 2020 till October 2023, and compared between immigrants and non-immigrants children. Factors associated to testing patterns were also analysed. Several variables can influence immigrants' choice to access health systems in the host countries, either for health prevention or treatment purposes. Barriers may have different origins and vary from country to country, region to region and case to case. The structure, organisation, accessibility and cost of the health care system, as well as individual-level characteristics and the degree of integration in the host country, play a fundamental role in determining differences in uptake.

Only few studies in literature investigated COVID-19 testing coverage among immigrant population. A study in North Carolina revealed that ethnic minorities completed 18% to 31% fewer tests than the general population (114); another one, in Italy, observed a significant higher proportion of nasal swabs among Italians, compared to migrants across all Regions, difference that disappeared in the following periods, probably due to a major availability of diagnostic tests (127).

In our sample, 78.8% of children underwent COVID-19 testing during the analysed period. However, a disproportion was observed between non-immigrants and immigrants, with the first one having testing rates.

Immigrant status was identified as a discriminant factor statistically associated to probability of being testing at least once for COVID-19, even after adjusting for the other covariates. Non-immigrant children were also shown to undertake a higher number of tests, in mean. Caregivers' higher educational level, age, employment status, perception of children health status and children birthweight were also significantly associated with the binary outcome.

Many factors may hinder health care access for immigrant population, for example lack of transportation services (private or public) in their residential areas (usually underserved), lack of health insurance because of legal bureaucracy or economic reasons, full employment schedule hindering their time off work, and lastly lack of confidence with the healthcare system organizational structure (128).

Our analysis was confined to five municipalities in Lisbon metropolitan area. In 2022, 16.7% of children in Portugal were registered as born inside the country but having mothers with different nationality. Immigration plays a significant role in the country and can have, therefore, strong implications for public health practise and management. During health crises such as the COVID-19 pandemic, comprehensive testing is a critical measure to contain the spread of disease and mitigate its adverse impact on health systems. However, under-testing of migrants and migrant communities often leads to inaccurate estimation of positivity rates, making it difficult to accurately assess spread of the disease among these groups. Lack of accurate information hampers health interventions in resource allocation and system planning, which are critical to effectively managing and containing outbreaks. In addition, it can lead to delayed or inadequate support and medical care, exacerbating vulnerabilities and health risks faced by these communities and individuals.

4.8 Limitations

This study may have some limitations. It is important to acknowledge that not all potential factors that can confound differences in accesses to tests, between immigrants and non-immigrants, might be here considered. To address these limitations and gain a more comprehensive understanding, future research could integrate qualitative methodologies. Qualitative studies could delve into the obstacles and experiences faced by immigrant families when accessing COVID-19 testing and healthcare services in general, providing valuable insights beyond quantitative data. Also, geographical location of children's residence, might be considered in the models.

Time of access to COVID-19 tests was not investigated, with no chance to reveal is a delayed perception of the emergency existed among immigrants and investigate eventual time-period related factors influencing accesses.

Because of the observational design of the study, it is not possible to infer causality from the disclosed associations. Moreover, further refinement could involve distin-

guishing non-immigrant children by their country of origin to discern potential variations in access rates within this group. This could undiscover nuanced disparities that were overlooked in this study's analysis.

Our findings are not generalizable to other regions or countries with different healthcare systems, policies, or demographics. Each locale has its unique set of factors influencing healthcare access, and what holds true for Lisbon's metropolitan area may not apply universally. In this analysis we also didn't distinguish immigrants for their nationality. Cultural differences may influence their health behaviour and perception.

Furthermore, examining the testing strategies employed during the study period, particularly those targeting children, and understanding any changes over time could provide valuable context for interpreting the results. Variations in testing availability, prioritization criteria, and public health messaging could significantly influence testing rates and accessibility. For instance, shifts in policy regarding who should be tested, the introduction of mass testing campaigns, or changes in school testing protocols may have impacted the data. By accounting for these factors, the analysis could better differentiate between structural barriers to healthcare access and the effects of evolving public health strategies.

Lastly, immigrants seeking healthcare services might not represent the entire immigrant population; to the contrast, more deprived families may be less likely to attend primary healthcare centres and therefore findings on testing rates might be already underestimated at start.

4.9 Conclusion

Our findings indicate that immigrant children compared to non-immigrants were less likely to undergo COVID-19 tests in the region under study. This holds substantial implications for health policy formulation and intervention strategies aimed at achieving equitable healthcare access for immigrant populations. Policy initiatives which focus on tailored outreach efforts, ensuring culturally sensitive education campaigns and

addressing specific concerns and perceptions related to testing prevention for infections, within immigrant communities are advisable.

Health system policies should actively tackle barriers such as language diversity, cultural nuances, legal complexities, and socio-economic disparities that hinder healthcare access. Strategies might involve providing interpreter services, cultural competency training for healthcare providers, and financial support programs to bridge these gaps.

Collaborative partnerships between healthcare providers, community organizations, and migrant support networks are crucial for fostering trust and facilitating streamlined access to healthcare services.

Interventions to promote access should involve active community engagement, initiatives to improve health literacy within immigrant populations, and training healthcare professionals to deliver culturally competent care.

Further studies might investigate influence of children residence's closeness to testing locations on the outcome; or even more generally investigate residence area characteristics such as transport availability and deprivation index might, to possibly unravel important determinants that should be considered.

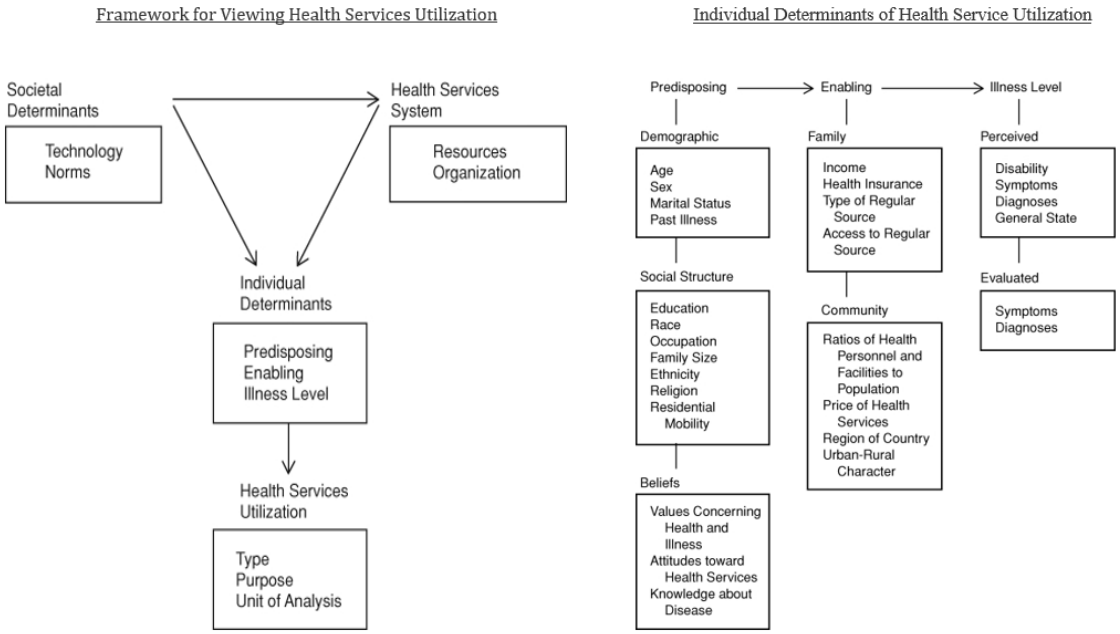
Also, other research directions should explore aspects regarding immigrant experiences in and perception of the healthcare system, related to access during public health crises, combining quantitative with qualitative data collection. Longitudinal studies tracking healthcare access patterns among immigrants and comparative analyses between different immigrant groups and non-immigrant populations would provide deeper insights and guide targeted interventions.

Finally, evaluating the impact of policy interventions is crucial to assess their effectiveness in improving healthcare access for immigrants. This evidence-based approach is essential in guiding future system development and address the complex dynamics influencing healthcare access and as consequence, health outcomes among immigrant populations.

4.10 Supplementary Material

Supplementary Figure 4.1. Map of Lisbon Metropolitan district. Created using QGIS software).

Supplementary Figure 4.2. Andersen and Newman concept framework of Health Service Utilization. Below are presented figures 1 and 4 from the original article "Societal and Individual determinants of medical care utilization in the United States" (123).



Supplementary Table 4.1. Variance inflation coefficients (GVIFs) resulting from the two fully adjusted regressions (left: Robust Poisson, right: Standard Poisson). modelling the outcomes 'being tested' and 'number of tests undertaken'.

OUTCOME:	**Tested (yes/no)**	**Nr of tests undertaken**
	GVIF	**GVIF**
Caregiver's age	1.10	1.11
Caregiver's sex	1.07	1.06
Caregiver's education level	1.24	1.25
Caregiver's employment status	1.13	1.12
Single parent family	1.19	1.19
Household density	1.09	1.09
Child Immigrant status	1.19	1.07
Household net income/month >750€	1.13	1.11
Child's health insurance	1.25	1.25
Child's birthweight	1.04	1.04
Child's perceived health status	1.08	1.08

Supplementary Table 4.2. Comparison of estimated univariate (uPR and uRR) and adjusted prevalence and risk ratios, computed for the two outcomes under study (being tested and number of tests undertaken).

OUTCOME:	**Tested (yes/no)**				**Nr of tests undertaken**			
	uPR	**95%CI**	**aPR**	**95%CI**	**uRR**	**95%CI**	**aRR**	**95%CI**
Caregiver's age	1.00	[0.99; 1.01]	0.98	[0.87, 1.11]	1.00	[0.99; 1.01]	1.25	[1.07, 1.49]
Caregiver's sex = Female (Ref. Male)	0.99	[0.88; 1.11]	1.00	[0.99, 1.01]	1.22	[0.78; 1.27]	0.99	[0.99, 1.00]
House family structure = single parent	1.02	[0.95; 1.11]	0.97	[0.89, 1.06]	1.03	[0.87; 1.21]	0.99	[0.89, 1.10]
Immigrant child (Ref. Non-immigrant)	0.81	[0.75; 0.87]	0.82	[0.76, 0.89]	0.69	[0.69; 0.95]	0.74	[0.67, 0.82]
House density^2 = high	1.02	[0.91; 1.14]	1.09	[0.96, 1.22]	1.01	[0.81; 1.3]	1.12	[0.98, 1.29]
Caregiver's educational level (Ref. Less than secondary)								
Upper secondary education	1.00	[0.91; 1.09]	1.01	[0.91, 1.12]	1.01	[0.82; 1.21]	1.02	[0.91, 1.15]
University degree/professional	1.06	[0.96; 1.16]	1.06	[0.95, 1.18]	1.13	[0.86; 1.3]	1.13	[0.99, 1.29]
Caregiver working status = employed (Ref. Unemployed)	1.05	[0.96; 1.15]	0.99	[0.9, 1.09]	1.21	[0.87; 1.27]	1.18	[1.05, 1.33]
Household income salary >750eur (Ref. < 750eur)	0.97	[0.89; 1.06]	0.96	[0.89, 1.05]	1.00	[0.81; 1.18]	0.95	[0.85, 1.06]
Child's health insurance = having	1.09	[1.01; 1.17]	1.03	[0.95, 1.13]	1.21	[0.92; 1.29]	1.10	[0.99, 1.23]
Child's birthweight (Ref. = low (<2.5 kg))								

OUTCOME:	Tested (yes/no)				Nr of tests undertaken			
	uPR	**95%CI**	**aPR**	**95%CI**	**uRR**	**95%CI**	**aRR**	**95%CI**
Normal (> 2.5 - < 4 kg)	1.15	[0.98; 1.34]	1.16	[0.99, 1.36]	1.24	[0.87; 1.54]	1.18	[1.01, 1.40]
High (< 4 kg)	1.12	[0.9; 1.39]	1.17	[0.95, 1.44]	0.99	[0.73; 1.71]	1.04	[0.81, 1.33]
Child's perceived health status								
(Ref. Very good)								
Good	1.00	[0.91; 1.09]	1.00	[0.91, 1.1]	1.16	[0.83; 1.2]	1.14	[1.02, 1.28]
Reasonable	1.02	[0.91; 1.13]	1.02	[0.91, 1.14]	1.24	[0.79; 1.29]	1.24	[1.07, 1.43]
Bad / Very bad	1.20	[1.04; 1.38]	1.15	[1, 1.33]	1.44	[0.69; 1.93]	1.38	[1.03, 1.81]

Supplementary Table 4.3. Estimated coefficients (coeff) and standard errors (SE) from the three alternative regressions used to model the binary outcome 'being tested at least once for COVID-19'.

Model:	**Robust Poisson**		**Log-binomial**		**Probit**	
	coeff	**SE**	**coeff**	**SE**	**coeff**	**SE**
Caregiver's age	-0.001	(-0.003)	-0.006	(-0.014)	-0.003	(-0.008)
Caregiver's sex = Female (Ref. Male)	-0.019	(-0.064)	-0.092	(-0.32)	-0.044	(-0.184)
House family structure = Single parent	-0.028	(-0.045)	-0.132	(-0.226)	-0.065	(-0.13)
Immigrant child (Ref. Non-immigrant)	-0.193 ***	(-0.041)	-1.005 ***	(-0.22)	-0.575 ***	(-0.122)
House density^2 = high	0.083	(-0.061)	0.416	(-0.284)	0.243	(-0.164)

Model:	**Robust Poisson**		**Log-binomial**		**Probit**	
	coeff	**SE**	**coeff**	**SE**	**coeff**	**SE**
Caregiver's educational level (Ref. Less than secondary)		(0.011)		(0.062)		(0.036)
Upper secondary education	0.011	(-0.051)	0.062	(-0.243)	0.036	(-0.141)
University degree/professional	0.055	(-0.057)	0.288	(-0.285)	0.171	(-0.163)
Caregiver working status = employed (Ref. Unemployed)	-0.009	(-0.049)	-0.026	(-0.234)	-0.002	(-0.135)
Household income salary >750eur (Ref. < 750€)	-0.036	(-0.043)	-0.22	(-0.247)	-0.134	(-0.141)
Child's health insurance = having	0.034	(-0.043)	0.164	(-0.224)	0.08	(-0.129)
Child's birthweight (Ref. = low (<2.5 kg))		(0.147)		(0.606 *)		(0.352 *)
Normal (> 2.5 - < 4 kg)	0.147	(-0.081)	0.606 *	(-0.29)	0.352 *	(-0.173)
High (< 4 kg)	0.155	(-0.108)	0.648	(-0.467)	0.377	(-0.272)
Child's perceived health status (Ref. Very good)		(0.001)		(-0.009)		(0.004)
Good	0.001	(-0.046)	-0.009	(-0.231)	0.004	(-0.133)
Reasonable	0.017	(-0.06)	0.062	(-0.302)	0.05	(-0.173)
Bad / Very bad	0.142 *	(-0.072)	1.251	(-1.06)	0.696	(-0.527)
AIC	1269.883		643.734		643.533	
BIC	1341.192		715.042		714.841	
Log Likelihood	-618.942		-305.867		-305.766	

Model:	**Robust Poisson**		**Log-binomial**		**Probit**	
	coeff	**SE**	**coeff**	**SE**	**coeff**	**SE**
Deviance	225.883		611.734		611.533	
Num. obs.	637		637		637	
*** p < 0.001; ** p < 0.01; * p < 0.05						

Chapter 5 General Discussion

Vulnerabilities intricately intertwine with health, manifesting through both direct and indirect impact on healthcare access and outcomes.

Global health research on health inequalities and disparities is continuously evolving, with the important effort to recognize and intervene to counteract determinant factors. This area of research may benefit from a multifaceted investigation that spans the life course and highlights the complex links between childhood experiences and adult vulnerability. Year after year, Public Health moves closer to achieve universal health coverage. However, still much work must be done in addressing the root causes of health inequalities, looking into social determinants such as income inequality, education levels, access to nutritious food, housing stability, and exposure to environmental hazards. When adverse factors converge, they create a breeding ground for health vulnerability. Policies and initiatives implementation often faces hurdles due to systemic barriers and different priorities among nations. Additionally, access to healthcare itself remains a critical challenge, especially in marginalized communities where resources are scarce. Despite progress made, we have to consider that vulnerability is not a static concept. Vulnerabilities might change and accumulate over time and are shaped by a variety of social factors that span generations.

The collection and analysis of quantitative data has been instrumental in unravelling the interdependencies between vulnerability factors and understanding how they cluster together, revealing their association with deteriorating health outcomes and the complex dynamics at play. However, to catalyse a more effective shift in global health initiatives, a shift in focus towards holistic approaches that combine qualitative and quantitative data and multiple disciplines should be prioritised. Only by recognising the interconnectedness of different dimensions of health, social, systemic and individual it would be possible to develop strategies that address broader systemic and societal factors, leading to more effective and inclusive interventions.

In this manuscript, we have presented two case studies focusing on vulnerability factors that may determine uptake of health care, for antenatal care visits and disease

testing. Furthermore, we reported a study discussing vulnerability factors that may influence the development of adverse respiratory outcomes in children.

In chapter two we analysed differences in trends, in time and among provinces in antenatal care coverage in Mozambique. We commented on the fragility of the health infrastructure in conflict areas, on healthcare underutilization, healthcare worker shortages, and how it is important to shift priorities from merely emergency interventions to prevention plans, in these contexts. The inability to adapt to conflict zones showcases the importance of resilient health systems capable of navigating challenging contexts. Vulnerabilities stemming from conflict and displacement, reconfigure the perception and conception of health itself.

In chapter four, we analysed testing differences among immigrant and non-immigrant children, during COVID-19 pandemic in Lisbon Metropolitan area district (Portugal). The study elucidates general subtleties of vulnerabilities in shaping healthcare-seeking behaviours. Family education, economic status, culture and nationality create a web of complexities that indirectly impact healthcare access, as well as distinct health perceptions could mould different responses to health crises.

In chapter three, we analysed individual and community-level factors possibly associated with asthma, rhinitis and eczema diseases among 6-7 years old children, in Santiago Island (Cape Verde). In this context, vulnerabilities were shown to be embedded within the community system—family education levels, environmental characteristics, and even dietary habits are interwoven, synergistically elevating probabilities of disease development.

The complex interplay of health vulnerability factors shows how outcomes are not determined by individual characteristics alone but are strongly influenced by contextual factors.

5.1 Data sources and methodological challenges

While vulnerabilities hold a critical role in shaping health outcomes, data collection

methods employed in their assessments introduce its own complexity. Recall and reporting biases inherent in self-reported characteristics may bias measures of vulnerabilities. These and other methodological limitations call for careful interpretation and cautious reliance on self-reported data. Collecting data for research on health vulnerabilities can involve various methodologies and sources, to capture their intricate and interconnected nature. Useful data, for example, can be gathered through population-wide surveys that assess health indicators, administrative health records documenting disease prevalence and access to care, socioeconomic and census databases offering insights into living conditions. Qualitative research can be very useful to deep into individual experiences and narratives of vulnerability.

Data representativeness problems can often emerge. For example, secondary data from national public surveys are readily available, but they are generally collected for different purposes. This was the case with DHS, MIS and AIS data for data on antenatal care coverage in Mozambique.

Data collection can also pose significant challenges when it comes to reaching vulnerable populations. For example, in settings such as areas affected by conflict, displacement or migration, there are significant logistical and geographical barriers to overcome. On the other hand, even when contact is established, vulnerable individuals might be reluctant to participate in studies, for reasons closely related to their own vulnerability, such as mistrust, fear of repercussions or past traumatic experiences, among others.

The Inverse Care Law, we have mentioned in Chapter 1 (4), also, highlights a stark reality: vulnerable populations, those most in need of health care, tend to seek it less, use it with lower access rates and receive inadequate services. Even in countries that are close to accomplish universal health coverage, vulnerable individuals are recognised less likely to access care services for health maintenance, chronic disease management and disease prevention. This cycle perpetuates their vulnerability and creates a scenario where those most in need of care have limited access to it.

Disparity in the distribution of health resources complicates research efforts aimed at understanding and addressing the health vulnerabilities of these communities.

Collecting meaningful data and designing interventions that are truly inclusive and effective requires nuanced and comprehensive multidisciplinary approaches.

In general, research on health vulnerability could benefit from pursuing two lines of research: one focusing on aggregated data to identify trends, patterns and overarching determinants of vulnerability across populations or regions. This approach can help researchers identify systemic issues and societal determinants that influence vulnerability. Conversely, a second strand focusing on individual experiences, narratives and contexts of vulnerability can provide nuanced insights into specific challenges faced by individuals or communities.

Policymakers can use macro-level insights to design broad strategies, while leveraging micro-level understandings to tailor interventions that address the specific needs and experiences of vulnerable populations.

As final remark, variability of definitions and measurements of vulnerability across contexts, can also arise complications for a worldwide and time-static interpretation of analyses' findings.

5.2 Policies and interventions

Addressing vulnerabilities in public health mandates a paradigm shift in policies and approaches. The case studies reported in this manuscript contributed to highlight the need for tailor-made interventions that consider the context-specific vulnerabilities that contribute to health inequalities. Conflict settings, for example, call for adaptive health systems that prioritise flexible and mobile health facilities. Such systems respond to the unique challenges posed by vulnerabilities resulting from displacement and conflict. According to Flaskerud and Wislow "vulnerability stems from a lack of socioeconomic and environmental resources (129). Health systems need to intervene by adopting solutions to achieve health equity and universal coverage; improve accessibility, affordability and cultural competence of health services; promote prevention and early intervention; forge partnerships with community organisations; and advocate for policies that address the root causes of health inequalities. Recognising that different

populations may have different needs and face different challenges, even when the same vulnerability factors are at play, is crucial to effectively tailoring interventions and resources. Health systems should continually reassess their strategies, adapt to changing circumstances and update practices.

Public awareness and advocacy, play a significant role in addressing health vulnerabilities and the Inverse Care Law (4).

Engaging the community and fostering a sense of collective responsibility for improving healthcare access is an important component of this comprehensive approach.

Continuity of data collection and analysis is essential to measure interventions' effectiveness and consequently plan improvements. Focus on outcomes and transparency also helps to build trust and accountability within the healthcare system.

Effective coverage measurement (130) becomes the compass in navigating and quantifying vulnerabilities in access and utilization, probing not just the reach of healthcare services but also their adequacy and equity among vulnerable groups. It's the synergy between these concepts that unveils critical insights, aiding policymakers and healthcare providers in pinpointing gaps, tailoring interventions, and ensuring that healthcare services effectively bridge the disparities faced by vulnerable communities. This link not only illuminates the hurdles but also offers a pathway towards equitable healthcare provisioning for those most in need.

The ultimate objective is to create healthcare systems that not only treat illnesses but also actively work to prevent them.

Understanding and recognizing coping and resilient strategies that individuals imply to face health vulnerabilities, can lead to plan more empowering strategies in health promotion, diagnosis, treatment, fostering new developments and approaches to care.

Individuals and communities develop innovative ways to manage chronic conditions, and these strategies can be incorporated into healthcare models to empower patients to take an active role in their care. Patient-centred care is a cornerstone of this approach. Vulnerable individuals frequently become experts in their own health conditions. By involving them in the decision-making process, healthcare providers not only improve

treatment outcomes but also empower patients to advocate for their well-being. Vulnerable populations often rely on strong community support networks. Healthcare systems can harness these networks to promote health education, outreach, and community-based care. Collaborating with community organizations can facilitate access to care and ensure that resources are effectively utilized. Cultural competence is essential when working with vulnerable populations; incorporating cultural values into treatment or interventions' plans can foster trust and improve healthcare outcomes.

Innovations in healthcare models can stem from vulnerability; use of telemedicine and mobile clinics and community health workers can, for example, help to reach underserved populations improving their access to healthcare.

Advocacy and policy changes often arise from the experiences of vulnerable populations. Their insights can drive reforms that address the root causes of health disparities, leading to more equitable access to care and better outcomes for all.

Promotion of health equity is a natural outcome of recognizing the strengths within vulnerable populations. It encourages healthcare systems to actively work to reduce disparities in access and outcomes, fostering a more inclusive and equitable healthcare environment.

5.3 Conclusive remarks

The aim of this manuscript was to reframe the endless topic of health vulnerability research, presenting practical examples of how vulnerability factors act in practise and discussing about their inherent impact on public health management.

We first introduced the concept of vulnerability from a general point of view and then delved into its conceptualization in the health care framework.

We presented a review of the existing literature and included a discussion of the methodological designs and analyses commonly used to study the topic. We tried to highlight possible gaps and future suggestions for research development.

In the first chapter, we set the stage for a holistic understanding of vulnerability in different contexts. In the following chapters, we reported on three different case studies

as examples of vulnerability in health outcomes and access to health care, demonstrating the multifaceted nature of the question under investigation. We have explored the interplay of socio-economic, cultural and political factors that shape health inequalities, causing populations, communities, individuals' vulnerabilities. We have sought to provide a comprehensive understanding of vulnerability, looking at multiple dimensions and highlighting the urgency of tailoring interventions to address context-specific challenges. It is important to note that this analysis can lead to important considerations that go beyond the findings and observations of individual case studies. We have discussed, how interplaying scenarios in low- and middle-income countries (LMICs), can combine to increase population's health vulnerability. In these settings health data underreporting, absence or inadequacy of policies, lack or lower level of health literacy, shortage of skilled health workers and limited diagnostic resources, significantly, combined with lower socio-economic levels, can lead to lower rates of healthcare access, hampering timely disease detection and increasing diseases burden and susceptibility to health crises. We argued for interdisciplinary studies, refined methodologies, cross-sectoral collaboration and contextually relevant interventions to effectively address health vulnerabilities globally. It paves the way for future research efforts and policy interventions that respond skilfully and dynamically. Promoting universal coverage is a fundamental pillar in reducing health vulnerability. Ensuring access to health services for all, regardless of their socio-economic status or background, is central to safeguarding against vulnerability. This inclusive approach not only improves health outcomes, but also promotes societal resilience by reducing inequalities. In scenarios where barriers to access persist, the use of cost-effectiveness analysis facilitates the optimisation of the allocation and reallocation of limited health resources.

Reframing global health challenges through the lens of the vulnerable could represent a transformative shift in research design, moving away from traditional top-down approaches and adopting a bottom-up perspective that values the lived experiences, needs and voices of vulnerable populations in planning analyses. This shift would require researchers to actively engage and collaborate with communities to ensure their involvement in the research process and could be a revolutionary opportunity to promote

inclusive, empathetic, and impactful studies that truly addresses the health inequities experienced by the world's most vulnerable populations.

Chapter 6 References

1. European Commission. Directorate General for Employment, Social Affairs and Inclusion., Luxembourg Institute of Socio Economic Research (LISER)., Applica., European Social Observatory (OSE). Inequalities in access to healthcare: a study of national policies 2018. [Internet]. LU: Publications Office; 2018 [citato 1 dicembre 2023]. Disponibile su: https://data.europa.eu/doi/10.2767/371408

2. Nambisan P. Relevance of Ethics in Biotechnology. In: An Introduction to Ethical, Safety and Intellectual Property Rights Issues in Biotechnology [Internet]. Elsevier; 2017 [citato 6 dicembre 2023]. p. 127–48. Disponibile su: https://linkinghub.elsevier.com/retrieve/pii/B9780128092316000053

3. Grabovschi C, Loignon C, Fortin M. Mapping the concept of vulnerability related to health care disparities: a scoping review. BMC Health Serv Res. dicembre 2013;13(1):94.

4. The Lancet. 50 years of the inverse care law. The Lancet. febbraio 2021;397(10276):767.

5. Andersen R, Aday LA. Access to Medical Care in the U.S.: Realized and Potential. Medical Care. 1978;16(7):533–46.

6. Shi L, Stevens GD, Lebrun LA, Faed P, Tsai J. Enhancing the Measurement of Health Disparities for Vulnerable Populations. Journal of Public Health Management and Practice. novembre 2008;14(6):S45–52.

7. Andersen RM. Revisiting the Behavioral Model and Access to Medical Care: Does it Matter? Journal of Health and Social Behavior. marzo 1995;36(1):1.

8. Penchansky R, Thomas JW. The Concept of Access: Definition and Relationship to Consumer Satisfaction. Medical Care. 1981;19(2):127–40.

9. Levesque JF, Harris MF, Russell G. Patient-centred access to health care: conceptualising access at the interface of health systems and populations. Int J Equity Health. 2013;12(1):18.

10. Armaș I, Gavriș A. Social vulnerability assessment using spatial multi-criteria analysis (SEVI model) and the Social Vulnerability Index (SoVI model) – a case study for Bucharest, Romania. Nat Hazards Earth Syst Sci. 18 giugno 2013;13(6):1481–99.

11. Flanagan BE, Gregory EW, Hallisey EJ, Heitgerd JL, Lewis B. A Social Vulnerability Index for Disaster Management. Journal of Homeland Security and Emergency Management [Internet]. 5 gennaio 2011 [citato 1 dicembre 2023];8(1). Disponibile su: https://www.degruyter.com/document/doi/10.2202/1547-7355.1792/html

12. Mah JC, Penwarden JL, Pott H, Theou O, Andrew MK. Social vulnerability indices: a scoping review. BMC Public Health. 28 giugno 2023;23(1):1253.

13. Moreno-Betancur M, Latouche A, Menvielle G, Kunst AE, Rey G. Relative Index of Inequality and Slope Index of Inequality: A Structured Regression Framework for Estimation. Epidemiology. luglio 2015;26(4):518–27.

14. Hierink F, Okiro EA, Flahault A, Ray N. The winding road to health: A systematic scoping review on the effect of geographical accessibility to health care on infectious diseases in low- and middle-income countries. Marotta C, curatore. PLoS ONE. 4 gennaio 2021;16(1):e0244921.

15. Baggett TP, O'Connell JJ, Singer DE, Rigotti NA. The Unmet Health Care Needs of Homeless Adults: A National Study. Am J Public Health. luglio 2010;100(7):1326–33.

16. Egede LE. Race, ethnicity, culture, and disparities in health care. J Gen Intern Med. giugno 2006;21(6):667–9.

17. Sommet N, Spini D. Financial scarcity undermines health across the globe and the life course. Social Science & Medicine. gennaio 2022;292:114607.

18. Saeed SA, Masters RM. Disparities in Health Care and the Digital Divide. Curr Psychiatry Rep. settembre 2021;23(9):61.

19. European Environment Agency. Flood risks and environmental vulnerability: exploring the synergies between floodplain restoration, water policies and thematic policies. [Internet]. LU: Publications Office; 2016 [citato 2 dicembre 2023]. Disponibile su:

https://data.europa.eu/doi/10.2800/039463

20. Johnson TP, Wendland M. A Role for Design in Global Health: Making the Concept of Vulnerability Actionable. She Ji: The Journal of Design, Economics, and Innovation. 2022;8(4):486–503.

21. Lim AH, Ng SW, Teh XR, Ong SM, Sivasampu S, Lim KK. Conjoint analyses of patients' preferences for primary care: a systematic review. BMC Prim Care. 9 settembre 2022;23(1):234.

22. Impact Evaluation in Practice, First Edition [Internet]. [citato 7 dicembre 2023]. Disponibile su: https://openknowledge.worldbank.org/entities/publication/f090e5a0-16f6-5795-a3b2-7f711c8b7eb7

23. New guidelines on antenatal care for a positive pregnancy experience [Internet]. [citato 7 dicembre 2023]. Disponibile su: https://www.who.int/news/item/07-11-2016-new-guidelines-on-antenatal-care-for-a-positive-pregnancy-experience

24. Amberg F, Chansa C, Niangaly H, Sankoh O, De Allegri M. Examining the relationship between armed conflict and coverage of maternal and child health services in 35 countries in sub-Saharan Africa: a geospatial analysis. The Lancet Global Health. giugno 2023;11(6):e843–53.

25. Alibhai KM, Ziegler BR, Meddings L, Batung E, Luginaah I. Factors impacting antenatal care utilization: a systematic review of 37 fragile and conflict-affected situations. Confl Health. dicembre 2022;16(1):33.

26. Munyuzangabo M, Gaffey MF, Khalifa DS, Als D, Ataullahjan A, Kamali M, et al. Delivering maternal and neonatal health interventions in conflict settings: a systematic review. BMJ Glob Health. febbraio 2021;5(Suppl 1):e003750.

27. Singh NS, Ataullahjan A, Ndiaye K, Das JK, Wise PH, Altare C, et al. Delivering health interventions to women, children, and adolescents in conflict settings: what have we learned from ten country case studies? The Lancet. febbraio 2021;397(10273):533–42.

28. Amsalu R, Firoz T, Lange IL, Tappis H. Editorial: Maternal Health in Conflict Settings. Front Glob Womens Health. 10 marzo 2022;3:807257.

29. Keasley J, Blickwedel J, Quenby S. Adverse effects of exposure to armed conflict on pregnancy: a systematic review. BMJ Glob Health. ottobre 2017;2(4):e000377.

30. Ferreira JBB, Santos LLD, Ribeiro LC, Rodrigues Fracon BR, Wong S. Vulnerability and Primary Health Care: An Integrative Literature Review. J Prim Care Community Health. gennaio 2021;12:215013272110497.

31. Bornemisza O, Ranson MK, Poletti TM, Sondorp E. Promoting health equity in conflict-affected fragile states. Social Science & Medicine. gennaio 2010;70(1):80–8.

32. Bendavid E, Boerma T, Akseer N, Langer A, Malembaka EB, Okiro EA, et al. The effects of armed conflict on the health of women and children. The Lancet. febbraio 2021;397(10273):522–32.

33. Indicators [Internet]. [citato 2 dicembre 2023]. Disponibile su: https://www.who.int/data/gho/data/indicators

34. Classification of Fragile and Conflict-Affected Situations [Internet]. [citato 6 dicembre 2023]. Disponibile su: https://www.worldbank.org/en/topic/fragilityconflictviolence/brief/harmonized-list-of-fragile-situations

35. Morgan R, Tetui M, Muhumuza Kananura R, Ekirapa-Kiracho E, George AS. Gender dynamics affecting maternal health and health care access and use in Uganda. Health Policy and Planning. 1 ottobre 2017;32(suppl_5):v13–21.

36. Glass N, Jalalzai R, Spiegel P, Rubenstein L. The crisis of maternal and child health in Afghanistan. Confl Health. 12 giugno 2023;17(1):28.

37. World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience [Internet]. Geneva: World Health Organization; 2016 [citato 22 novembre 2023]. 152 p. Disponibile su: https://iris.who.int/handle/10665/250796

38. Antenatal care coverage - at least four visits (%) [Internet]. [citato 3 dicembre 2023]. Disponibile su: https://www.who.int/data/gho/indicator-metadata-registry/imr-details/80

39. Antenatal care coverage - at least four visits (%) [Internet]. [citato 2 dicembre 2023]. Disponibile su: https://www.who.int/data/gho/indicator-metadata-registry/imr-details/80

40. Abir T, Ogbo FA, Stevens GJ, Page AN, Milton AH, Agho KE. The impact of antenatal care, iron–folic acid supplementation and tetanus toxoid vaccination during pregnancy on child mortality in Bangladesh. Van Wouwe JP, curatore. PLoS ONE. 1 novembre 2017;12(11):e0187090.

41. Dahab R, Sakellariou D. Barriers to Accessing Maternal Care in Low Income Countries in Africa: A Systematic Review. IJERPH. 16 giugno 2020;17(12):4292.

42. Instituto Nacional de Estatistica - INE - INE [Internet]. [citato 3 dicembre 2023]. Disponibile su: https://www.ine.gov.mz/web/guest

43. GNI per capita, Atlas method (current US$) - Mozambique | Data [Internet]. [citato 3 dicembre 2023]. Disponibile su: https://data.worldbank.org/indicator/NY.GNP.PCAP.CD?locations=MZ

44. Human Development Index | Human Development Reports [Internet]. [citato 3 dicembre 2023]. Disponibile su: https://hdr.undp.org/data-center/human-development-index#/indicies/HDI

45. ACLED | Bringing Clarity to Crisis [Internet]. [citato 3 dicembre 2023]. Disponibile su: https://acleddata.com/

46. The DHS Program - Country Main [Internet]. [citato 3 dicembre 2023]. Disponibile su: https://dhsprogram.com/Countries/Country-Main.cfm?ctry_id=61

47. The DHS Program - Mozambique: Standard DHS, 2011 [Internet]. [citato 7 dicembre 2023]. Disponibile su: https://dhsprogram.com/methodology/survey/survey-display-362.cfm

48. The DHS Program - Mozambique AIS, 2015 - Final Report (English, Portuguese)

[Internet]. [citato 7 dicembre 2023]. Disponibile su: https://dhsprogram.com/publications/publication-ais12-ais-final-reports.cfm

49. The DHS Program - Mozambique: MIS, 2018 - MIS Final Report (Portuguese) [Internet]. [citato 7 dicembre 2023]. Disponibile su: https://dhsprogram.com/publications/publication-mis33-mis-final-reports.cfm

50. The DHS Program - An Analysis of Sample Designs and Sampling Errors of the Demographic and Health Surveys (English) [Internet]. [citato 7 dicembre 2023]. Disponibile su: https://dhsprogram.com/publications/publication-ar3-analytical-studies.cfm

51. Monitoring birth preparedness and complication readiness: Tools and indicators for maternal and newborn health – Healthy Newborn Network [Internet]. [citato 7 dicembre 2023]. Disponibile su: https://www.healthynewbornnetwork.org/resource/monitoring-birth-preparedness-and-complication-readiness-tools-and-indicators-for-maternal-and-newborn-health/

52. McClure EM, Nalubamba-Phiri M, Goldenberg RL. Stillbirth in developing countries. Intl J Gynecology & Obste. agosto 2006;94(2):82–90.

53. DHS-Analysis-Code/Intro_DHSdata_Analysis/6_ExampleAnalysis/ExampleAnalysis.R at main · DHSProgram/DHS-Analysis-Code · GitHub [Internet]. [citato 26 giugno 2024]. Disponibile su: https://github.com/DHSProgram/DHS-Analysis-Code/blob/main/Intro_DHSdata_Analysis/6_ExampleAnalysis/ExampleAnalysis.R

54. Raru TB, Ayana GM, Zakaria HF, Merga BT. Association of Higher Educational Attainment on Antenatal Care Utilization Among Pregnant Women in East Africa Using Demographic and Health Surveys (DHS) from 2010 to 2018: A Multilevel Analysis. IJWH. febbraio 2022;Volume 14:67–77.

55. Duodu PA, Bayuo J, Mensah JA, Aduse-Poku L, Arthur-Holmes F, Dzomeku VM, et al. Trends in antenatal care visits and associated factors in Ghana from 2006 to 2018. BMC Pregnancy Childbirth. dicembre 2022;22(1):59.

56. Bacharier LB, Boner A, Carlsen K -H., Eigenmann PA, Frischer T, Götz M, et al. Diagnosis and treatment of asthma in childhood: a PRACTALL consensus report. Allergy.

gennaio 2008;63(1):5–34.

57. Fitzpatrick AM, Teague WG. Severe Asthma in Children: Insights from the National Heart, Lung, and Blood Institute's Severe Asthma Research Program. Pediatric Allergy, Immunology, and Pulmonology. giugno 2010;23(2):131–8.

58. Gehring U, Wijga AH, Hoek G, Bellander T, Berdel D, Brüske I, et al. Exposure to air pollution and development of asthma and rhinoconjunctivitis throughout childhood and adolescence: a population-based birth cohort study. The Lancet Respiratory Medicine. dicembre 2015;3(12):933–42.

59. Jartti T, Bønnelykke K, Elenius V, Feleszko W. Role of viruses in asthma. Semin Immunopathol. febbraio 2020;42(1):61–74.

60. Paaso EM, Jaakkola MS, Rantala AK, Hugg TT, Jaakkola JJ. Allergic diseases and asthma in the family predict the persistence and onset-age of asthma: a prospective cohort study. Respir Res. dicembre 2014;15(1):152.

61. Seidman DS, Laor A, Gale R, Stevenson DK, Danon YL. Is low birth weight a risk factor for asthma during adolescence? Archives of Disease in Childhood. 1 maggio 1991;66(5):584–7.

62. Strachan DP, Cook DG. Parental smoking and childhood asthma: longitudinal and case-control studies. Thorax. 1 marzo 1998;53(3):204–12.

63. Sutherland ER. Obesity and Asthma. Immunology and Allergy Clinics of North America. agosto 2008;28(3):589–602.

64. Huss K, Adkinson NF, Eggleston PA, Dawson C, Van Natta ML, Hamilton RG. House dust mite and cockroach exposure are strong risk factors for positive allergy skin test responses in the Childhood Asthma Management Program. Journal of Allergy and Clinical Immunology. gennaio 2001;107(1):48–54.

65. Erbas B, Jazayeri M, Lambert KA, Katelaris CH, Prendergast LA, Tham R, et al. Outdoor pollen is a trigger of child and adolescent asthma emergency department presentations: A systematic review and meta-analysis. Allergy. agosto 2018;73(8):1632–41.

66. Chatzi L, Apostolaki G, Bibakis I, Skypala I, Bibaki-Liakou V, Tzanakis N, et al. Protective effect of fruits, vegetables and the Mediterranean diet on asthma and allergies among children in Crete. Thorax. 1 agosto 2007;62(8):677–83.

67. Oren E, Martinez FD. Stress and asthma. Annals of Allergy, Asthma & Immunology. ottobre 2020;125(4):372-373.e1.

68. Schuez-Havupalo L, Toivonen L, Karppinen S, Kaljonen A, Peltola V. Daycare attendance and respiratory tract infections: a prospective birth cohort study. BMJ Open. settembre 2017;7(9):e014635.

69. Jeffs D, Grainger R, Powell P. Is childhood allergy more common amongst an island population? Journal of the Royal Society for the Promotion of Health. dicembre 2000;120(4):236–41.

70. Carey MJ, Cordon I. Asthma and climatic conditions: experience from Bermuda, an isolated island community. BMJ. 4 ottobre 1986;293(6551):843–4.

71. Sánchez Palacios A, Schamann F, García JA, Sánchez MA. Epidemiological aspects of asthma in the Canary Islands. J Investig Allergol Clin Immunol. 1997;7(5):298–9.

72. Varela DV, Martins MDRO, Furtado A, Mendonça MDLL, Fernandes NM, Santos I, et al. Spatio-temporal evolution of mortality in Cape Verde: 1995–2018. Asweto CO, curatore. PLOS Glob Public Health. 10 marzo 2023;3(3):e0000753.

73. Trikamjee T, Comberiati P, Peter J. Pediatric asthma in developing countries: challenges and future directions. Current Opinion in Allergy & Clinical Immunology. aprile 2022;22(2):80–5.

74. de Almeida MM, Pinto JR. Bronchial asthma in children: clinical and epidemiologic approach in different Portuguese speaking countries. Pediatr Pulmonol Suppl. 1999;18:49–53.

75. Rosado-Pinto J, Gaspar A, Morais-Almeida M. Epidemiology of asthma and allergic diseases in Portuguese speaking regions. Revue Française d'Allergologie et d'Immunologie Clinique. aprile 2006;46(3):305–8.

76. Martins P, Rosado-Pinto J, Do Céu Teixeira M, Neuparth N, Silva O, Tavares H, et al. Under-report and underdiagnosis of chronic respiratory diseases in an African country. Allergy. luglio 2009;64(7):1061–7.

77. ISAAC Tools [Internet]. [citato 26 giugno 2024]. Disponibile su: https://isaac.auckland.ac.nz/resources/tools.php

78. Asher M, Keil U, Anderson H, Beasley R, Crane J, Martinez F, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. Eur Respir J. 1 marzo 1995;8(3):483–91.

79. Rutter CE, Silverwood RJ, Asher MI, Ellwood P, Pearce N, Garcia-Marcos L, et al. Comparison of individual-level and population-level risk factors for rhinoconjunctivitis, asthma, and eczema in the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three. World Allergy Organization Journal. giugno 2020;13(6):100123.

80. Hausman JA. Specification Tests in Econometrics. Econometrica. novembre 1978;46(6):1251.

81. The coefficient of determination R2 and intra-class correlation coefficient from generalized linear mixed-effects models revisited and expanded - PubMed [Internet]. [citato 25 giugno 2024]. Disponibile su: https://pubmed.ncbi.nlm.nih.gov/28904005/

82. Bousquet J, Schünemann HJ, Samolinski B, Demoly P, Baena-Cagnani CE, Bachert C, et al. Allergic Rhinitis and its Impact on Asthma (ARIA): Achievements in 10 years and future needs. Journal of Allergy and Clinical Immunology. novembre 2012;130(5):1049–62.

83. Arrais M, Lulua O, Quifica F, Rosado-Pinto J, Gama JMR, Taborda-Barata L. Prevalence of asthma and allergies in 13–14-year-old adolescents from Luanda, Angola. int j tuberc lung dis. 1 giugno 2017;21(6):705–12.

84. Mavale-Manuel S, Joaquim O, Nunes E, Pedro A, Bandeira S, Eduardo E, et al. Prevalence of asthma-like symptoms by ISAAC video questionnaire in Mozambican schoolchildren. Monaldi Arch Chest Dis [Internet]. 10 febbraio 2016 [citato 5 dicembre 2023];65(4). Disponibile su: https://www.monaldi-

archives.org/index.php/macd/article/view/548

85. Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. The Lancet. agosto 2006;368(9537):733–43.

86. Sole D, Camelo-Nunes IC, Wandalsen GF, Mallozi MC. Asthma in children and adolescents in Brazil: contribution of the International Study of Asthma and Allergies in Childhood (ISAAC). Rev paul pediatr. marzo 2014;32(1):114–25.

87. Silverwood RJ, Rutter CE, Mitchell EA, Asher MI, Garcia-Marcos L, Strachan DP, et al. Are environmental risk factors for current wheeze in the International Study of Asthma and Allergies in Childhood (ISAAC) phase three due to reverse causation? Clin Experimental Allergy. aprile 2019;49(4):430–41.

88. Rutter CE, Silverwood RJ, Williams HC, Ellwood P, Asher I, Garcia-Marcos L, et al. Are Environmental Factors for Atopic Eczema in ISAAC Phase Three due to Reverse Causation? Journal of Investigative Dermatology. maggio 2019;139(5):1023–36.

89. Mitchell EA, Clayton T, García-Marcos L, Pearce N, Foliaki S, Wong G, et al. Birthweight and the risk of atopic diseases: the ISAAC Phase III study. Pediatric Allergy Immunology. maggio 2014;25(3):264–70.

90. Strachan DP, Aït-Khaled N, Foliaki S, Mallol J, Odhiambo J, Pearce N, et al. Siblings, asthma, rhinoconjunctivitis and eczema: a worldwide perspective from the International Study of Asthma and Allergies in Childhood. Clin Experimental Allergy. gennaio 2015;45(1):126–36.

91. Wong GW, Brunekreef B, Ellwood P, Anderson HR, Asher MI, Crane J, et al. Cooking fuels and prevalence of asthma: a global analysis of phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). The Lancet Respiratory Medicine. luglio 2013;1(5):386–94.

92. Foliaki S, Pearce N, Björkstén B, Mallol J, Montefort S, Von Mutius E. Antibiotic use in infancy and symptoms of asthma, rhinoconjunctivitis, and eczema in children 6 and

7 years old: International Study of Asthma and Allergies in Childhood Phase III. Journal of Allergy and Clinical Immunology. novembre 2009;124(5):982–9.

93. Ellwood P, Asher MI, García-Marcos L, Williams H, Keil U, Robertson C, et al. Do fast foods cause asthma, rhinoconjunctivitis and eczema? Global findings from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three. Thorax. aprile 2013;68(4):351–60.

94. Brunekreef B, Von Mutius E, Wong G, Odhiambo J, García-Marcos L, Foliaki S. Exposure to Cats and Dogs, and Symptoms of Asthma, Rhinoconjunctivitis, and Eczema. Epidemiology. settembre 2012;23(5):742–50.

95. Björkstén B, Aït-Khaled N, Innes Asher M, Clayton TO, Robertson C. Global analysis of breast feeding and risk of symptoms of asthma, rhinoconjunctivitis and eczema in 6–7 year old children: ISAAC Phase Three. Allergologia et Immunopathologia. novembre 2011;39(6):318–25.

96. Beasley R, Clayton T, Crane J, Von Mutius E, Lai CK, Montefort S, et al. Association between paracetamol use in infancy and childhood, and risk of asthma, rhinoconjunctivitis, and eczema in children aged 6–7 years: analysis from Phase Three of the ISAAC programme. The Lancet. settembre 2008;372(9643):1039–48.

97. Brunekreef B, Stewart AW, Anderson HR, Lai CKW, Strachan DP, Pearce N, et al. Self-Reported Truck Traffic on the Street of Residence and Symptoms of Asthma and Allergic Disease: A Global Relationship in ISAAC Phase 3. Environ Health Perspect. novembre 2009;117(11):1791–8.

98. Mitchell EA, Beasley R, Keil U, Montefort S, Odhiambo J, and the ISAAC Phase Three Study Group. The association between tobacco and the risk of asthma, rhinoconjunctivitis and eczema in children and adolescents: analyses from Phase Three of the ISAAC programme. Thorax. novembre 2012;67(11):941–9.

99. Fröhlich M, Pinart M, Keller T, Reich A, Cabieses B, Hohmann C, et al. Is there a sex-shift in prevalence of allergic rhinitis and comorbid asthma from childhood to adulthood? A meta-analysis. Clin Transl Allergy. dicembre 2017;7(1):44.

100. Annesi-Maesano I, Sterlin C, Caillaud D, De Blay F, Lavaud F, Charpin D, et al. Factors related to under-diagnosis and under-treatment of childhood asthma in metropolitan France. Multidiscip Respir Med. dicembre 2012;7(1):24.

101. Khreis H, Cirach M, Mueller N, De Hoogh K, Hoek G, Nieuwenhuijsen MJ, et al. Outdoor air pollution and the burden of childhood asthma across Europe. Eur Respir J. ottobre 2019;54(4):1802194.

102. Breysse PN, Diette GB, Matsui EC, Butz AM, Hansel NN, McCormack MC. Indoor Air Pollution and Asthma in Children. Proceedings of the American Thoracic Society. 1 maggio 2010;7(2):102–6.

103. Frei R, Roduit C, Ferstl R, O'Mahony L, Lauener RP. Exposure of Children to Rural Lifestyle Factors Associated With Protection Against Allergies Induces an Anti-Neu5Gc Antibody Response. Front Immunol. 16 luglio 2019;10:1628.

104. Fall T, Lundholm C, Örtqvist AK, Fall K, Fang F, Hedhammar Å, et al. Early Exposure to Dogs and Farm Animals and the Risk of Childhood Asthma. JAMA Pediatr. 2 novembre 2015;169(11):e153219.

105. Ji X, Yao Y, Zheng P, Hao C. The relationship of domestic pet ownership with the risk of childhood asthma: A systematic review and meta-analysis. Front Pediatr. 22 luglio 2022;10:953330.

106. Mallol J, Crane J, Von Mutius E, Odhiambo J, Keil U, Stewart A. The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three: A global synthesis. Allergologia et Immunopathologia. marzo 2013;41(2):73–85.

107. Ferrante G, Asta F, Cilluffo G, De Sario M, Michelozzi P, La Grutta S. The effect of residential urban greenness on allergic respiratory diseases in youth: A narrative review. World Allergy Organization Journal. gennaio 2020;13(1):100096.

108. Refugees and Migrants [Internet]. [citato 6 dicembre 2023]. Disponibile su: https://refugeesmigrants.un.org/

109. Brandenberger J, Tylleskär T, Sontag K, Peterhans B, Ritz N. A systematic literature

review of reported challenges in health care delivery to migrants and refugees in high-income countries - the 3C model. BMC Public Health. dicembre 2019;19(1):755.

110. Klein J, Von Dem Knesebeck O. Inequalities in health care utilization among migrants and non-migrants in Germany: a systematic review. Int J Equity Health. dicembre 2018;17(1):160.

111. Health of Migrants: Resetting the Agenda - Report of the 2nd Global Consultation on Migrant Health - World | ReliefWeb [Internet]. [citato 7 dicembre 2023]. Disponibile su: https://reliefweb.int/report/world/health-migrants-resetting-agenda-report-2nd-global-consultation-migrant-health

112. Fabiani M, Mateo-Urdiales A, Andrianou X, Bella A, Del Manso M, Bellino S, et al. Epidemiological characteristics of COVID-19 cases in non-Italian nationals notified to the Italian surveillance system. European Journal of Public Health. 1 febbraio 2021;31(1):37–44.

113. OECD [Internet]. [citato 6 dicembre 2023]. Disponibile su: https://read.oecd-ilibrary.org/view/?ref=1155_1155529-kmivt4sbol&title=What-has-been-the-impact-of-the-COVID-19-pandemic-on-immigrants-An-update-on-recent-evidence

114. Brandt K, Goel V, Keeler C, Bell GJ, Aiello AE, Corbie-Smith G, et al. SARS-CoV-2 testing in North Carolina: Racial, ethnic, and geographic disparities. Health & Place. maggio 2021;69:102576.

115. Mannheim J, Konda S, Logan LK. Racial, ethnic and socioeconomic disparities in SARS-CoV-2 infection amongst children. Paediatric Perinatal Epid. maggio 2022;36(3):337–46.

116. ICES | COVID-19 in Immigrants, Refugees and Other Newcomers in Ontario: Characteristics of Those Tested and Those Confirmed Positive, as of June 13, 2020 [Internet]. [citato 6 dicembre 2023]. Disponibile su: https://www.ices.on.ca/publications/research-reports/covid-19-in-immigrants-refugees-and-other-newcomers-in-ontario-characteristics-of-those-tested-and-those-confirmed-positive-as-of-june-13-2020/

117. Migrantes - viver e trabalhar em Portugal - ePortugal.gov.pt [Internet]. [citato 6

dicembre 2023]. Disponibile su: https://eportugal.gov.pt/migrantes-viver-e-trabalhar-em-portugal

118. Muggli Z, Mertens T, Amado R, Teixeira AL, Vaz D, Pires M, et al. Cohort profile: Health trajectories of Immigrant Children (CRIAS)–a prospective cohort study in the metropolitan area of Lisbon, Portugal. BMJ Open. ottobre 2022;12(10):e061919.

119. ACES Amadora [Internet]. [citato 6 dicembre 2023]. Disponibile su: https://bicsp.min-saude.pt/pt/biufs/3/30014/Pages/default.aspx

120. ACES Arco Ribeirinho [Internet]. [citato 6 dicembre 2023]. Disponibile su: https://bicsp.min-saude.pt/pt/biufs/3/30019/Pages/default.aspx

121. Portugal: População residente segundo os Censos: total e por naturalidade | Pordata [Internet]. [citato 6 dicembre 2023]. Disponibile su: https://www.pordata.pt/portugal/populacao+residente+segundo+os+censos+total+e+por+naturalidade-3799

122. Pengid S, Peltzer K, De Moura Villela EF, Fodjo JNS, Siau CS, Chen WS, et al. Using Andersen's model of health care utilization to assess factors associated with COVID-19 testing among adults in nine low-and middle-income countries: an online survey. BMC Health Serv Res. dicembre 2022;22(1):265.

123. Andersen R, Newman JF. Societal and Individual Determinants of Medical Care Utilization in the United States. Milbank Quarterly [Internet]. dicembre 2005 [citato 25 giugno 2024];83(4). Disponibile su: https://onlinelibrary.wiley.com/doi/10.1111/j.1468-0009.2005.00428.x

124. K. C. A, Basel PL, Singh S. Low birth weight and its associated risk factors: Health facility-based case-control study. Pradhan PMS, curatore. PLoS ONE. 22 giugno 2020;15(6):e0234907.

125. Chen W, Qian L, Shi J, Franklin M. Comparing performance between log-binomial and robust Poisson regression models for estimating risk ratios under model misspecification. BMC Med Res Methodol. dicembre 2018;18(1):63.

126. Refugee and migrant health - Global [Internet]. [citato 3 dicembre 2023]. Disponibile su: https://www.who.int/health-topics/refugee-and-migrant-health#tab=tab_1

127. Díaz González JL, Rusciani R, Spadea T, Leoni O, Bortolan F, Cacciani L, et al. Access to SARS-CoV-2 diagnostic tests: are there barriers for the immigrants in Italy? E&P. Luglio 2022;46(4 Suppl. 1):33–40.

128. Pandey M, Kamrul R, Michaels CR, McCarron M. Identifying Barriers to Healthcare Access for New Immigrants: A Qualitative Study in Regina, Saskatchewan, Canada. J Immigrant Minority Health. febbraio 2022;24(1):188–98.

129. Flaskerud JH, Winslow BJ. Conceptualizing Vulnerable Populations Health-Related Research: Nursing Research. marzo 1998;47(2):69–78.

130. Ng M, Fullman N, Dieleman JL, Flaxman AD, Murray CJL, Lim SS. Effective coverage: a metric for monitoring Universal Health Coverage. PLoS Med. settembre 2014;11(9):e1001730.