Socioeconomic inequalities in the prevalence and management of hypertension: analyses of the Chilean National Health Surveys 2003, 2010 and 2017

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I, Álvaro Passi-Solar, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

Background: Up-to-date information on hypertension prevalence and management indicators (awareness, treatment, control); measures of its socioeconomic inequalities; and their impacts are required in Chile. This PhD aims to quantify the prevalence of these indicators, the magnitude of their socioeconomic inequalities, and their association with mortality risk among adults in Chile 2003, 2010, and 2017.

Methods: First, using 2003, 2010, and 2017 Chilean national health surveys (ENS) I analysed secular changes in levels of hypertension outcomes by demographic variables. Secondly, I analysed socioeconomic position (SEP) inequalities in hypertension outcomes using individual-level measures (educational level, income, and health insurance). Thirdly, using a multilevel approach, I evaluated the association between individual educational level and hypertension prevalence, before and after adjustment for socioeconomic environment measures (county-level income inequality, poverty, and unemployment). Finally, I analysed all-cause and cardiovascular mortality rates by educational level and hypertension status using ENS data linked with mortality registries.

Results: Between 2003 and 2017, hypertension prevalence decreased (34%-31%), awareness increased slightly (58%-66%), whereas treatment (38%-65%) and control (13%-34%) levels increased substantially. Hypertension management levels were lower among males than females. Secondly, hypertension prevalence was higher among adults with lower levels of education. Inequalities by education in hypertension prevalence, untreated, and uncontrolled hypertension were more pronounced among females. Thirdly, multilevel analyses showed that the magnitude of inequalities by education level were minimally affected by socioeconomic environment measures. Finally, I found a higher risk of all-cause and cardiovascular mortality in participants with hypertension and at the lowest educational level.

Conclusions: Despite favourable changes in hypertension outcomes over time, Chile currently needs innovative and collaborative strategies to improve hypertension management (especially among males), and simultaneously decrease SEP inequalities in hypertension outcomes (mainly among females). Interventions decreasing hypertension prevalence, improving hypertension management, and increasing educational levels could help to decrease the burden of premature mortality.

Impact Statement

This project provides evidence about changes in levels of hypertension prevalence and management in Chile between 2003 and 2017. I believe this evidence (published in BMC Public Health, 2020) can help to update the local burden of disease estimates used by the Chilean Ministry of Health (MINSAL). My PhD is the first study providing evidence about recent favourable changes in hypertension outcomes: decreasing hypertension prevalence while increasing treated and controlled hypertension, which I believe can be attributed to the healthcare reforms and other major public health interventions implemented in the last decade. My findings can help to boost these advances, by highlighting groups with worse levels of hypertension management (e.g. males), helping to target further public health interventions.

Crucially, this research also shows that these favourable changes in hypertension levels in Chile coexist with emerging SEP inequalities in hypertension-related outcomes. I believe these findings highlight the need to evaluate whether current public health interventions are generating SEP inequalities, but also, to implement new (and strengthen current) interventions aiming to decrease these inequalities. Evidence from my PhD also provides evidence about the relevance of the county in explaining hypertension prevalence, which could help to design public health interventions, highlighting the need to consider the neighbourhood where people live.

Finally, my PhD shows the relevance and usefulness of linking health examination surveys with mortality registries, allowing a unique opportunity to assess mortality risk by individual-level characteristics that are usually not available in administrative data sources. Results from this research provide evidence that hypertension increases the risk of not only cardiovascular mortality but from all causes in Chile, fostering the need to continue national efforts to decrease hypertension.

My PhD showed that having a low education level in Chile is not only related to higher hypertension prevalence and higher levels of untreated and uncontrolled hypertension but also to higher mortality rates. These findings provide further support for national interventions to increase educational opportunities and to improve, in general, the socioeconomic profile of the Chilean population.

In February 2022, I presented to the MINSAL's Department of Non-Communicable Diseases (MINSAL-NCDs) some key results of my PhD on SEP inequalities in the prevalence and management of hypertension. In addition to their interest in my research, they suggest I include a definition of controlled hypertension considering a lower BP threshold (130/80 mmHg instead of 140/90 mmHg) for those with very high cardiovascular risk, diabetes, or chronic kidney disease. Following this request, I included some specific goals and analyses using this definition.

In March 2022, MINSAL-NCDs invited me to participate in a project to update the cardiovascular risk stratification used by the Chilean health system (the Framingham score adapted to Chile). They were interested in my PhD survival results and asked me to give a brief presentation. After this presentation, they formally asked me to apply the survival analysis methods I developed in my PhD to the specific goals of the Chilean Framingham score (see the letter of invitation in the Appendix).

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List of Abbreviations

ABPM	Ambulatory BP Monitoring
ACC	American College of Cardiology
ACI	Absolute concentration index
AHA	American Heart Association
ANID	Chilean National Research and Development Agency
AOBP	Attended Automated Office BP Measurement
ATC	Anatomic Therapeutic Chemical classification (WHO)
AUDIT	Alcohol Use Disorders Identification Test
AUGE	Universal Access with Explicit Guarantees (Chile)
BMI	Body mass index
BP	Blood pressure
CARMELA	Assessment of cardiovascular risk in seven Latin American cities
CASEN	Chilean National Socioeconomic Characterization Survey
CESCAS	Centre of Excellence in Cardiovascular Health
CI	Confidence intervals
CKD	Chronic kidney disease
CLP	Chilean peso
CONICYT	National Commission for Scientific and Technological Research (Chile)
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DEIS	Statistics and Health Information Department (Chile)
DM	Diabetes mellitus
eGFR	Estimated glomerular filtration rate
ENDES	Demographic and Family Health Survey, Peru
ENS	Chilean National Health Survey
ESH	European Society of Hypertension
EU	European Union
FOFAR	Pharmacy funds (Chile)
FONASA	Chilean National Health Fund
GBP	Great Britain pounds
GDP	Gross domestic product
GES	Explicit Health Guarantees (Chile)
GFR	Glomerular filtration rate
GP	General practitioners

HDL	High-density lipoprotein
HES	Health examination survey
HIC	High income country
HM	Hypertension management
HR	Hazard ratio
HSE	Health Survey for England
HTN	Hypertension
ICC	Intraclass correlation
ICD	International Classification of Diseases
IHD	Ischaemic heart disease
INE	Chilean National Statistics Institute
ISAPRE	Private Health Insurers (Chile)
JNC 7	The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
LACC	Latin American and Caribbean country
LDL	Low-density lipoproteins
LIC	Low-income country
LMIC	Low-and middle-income country
LPM	Linear probability model
MAR	Missing at random
MAUCO	Maule Cohort (Chile)
MDRD	Modification of diet in renal disease equation
MIC	Middle-income countries
MICE	Multiple imputation by chained equations
MINSAL	Ministry of Health, Chile
NCD	Non-communicable diseases
NCD-RisC	NCD Risk Factor Collaboration
NHANES	National Health and Nutrition Examination Survey, US
OECD	Organisation for Economic Cooperation and Development
OR	Odds ratio
PAHO	Pan American Health Organization
PH	Proportional hazards
PMM	Predictive mean matching
pp	Percentage point
PR	Prevalence ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PUC	Pontificia Universidad Católica de Chile
PURE	Prospective Urban and Rural Epidemiological
RII	Relative index of inequality

RR	Risk ratio
SABE	Health, Well-Being and Ageing cohort (Brazil)
SAGE	Study on Global Ageing and Adult Health
SBP	Systolic blood pressure
SDH	Social determinants of health
SE	Standard error
SEP	Socioeconomic position
SII	Slope index of inequality
SNS	National Health Service (Chile)
SWiM	Synthesis Without Meta-analysis
UK	United Kingdom
US	United States of America
USD	US dollar
WHO	World Health Organization

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I would like to thank my first supervisor, Dr. Shaun Scholes, who provided me with his constant support and guidance during these last four and a half years of my PhD. I would also like to thank my second and third supervisors, Prof. Jennifer Mindell and Dr. Milagros A Ruiz, who guided me with their feedback and support.

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And finally, I would like to thank my mom, dad, sisters, and Mar, and my friends for their trust, company, and emotional support.

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Chapter 1: Background

This chapter introduces my research area and outlines the background and rationale for my PhD. First, I briefly describe the framework of the social determinants of health that informs the study. Secondly, using this framework I describe the main characteristics of Chile. Thirdly, I describe the global relevance of hypertension and present Chilean evidence before my study on its prevalence, attainment of hypertension management indicators (i.e. levels of awareness, treatment, and control), key risk factors (and their recent changes over time), policies and guidelines.

1.1. Social determinants of health

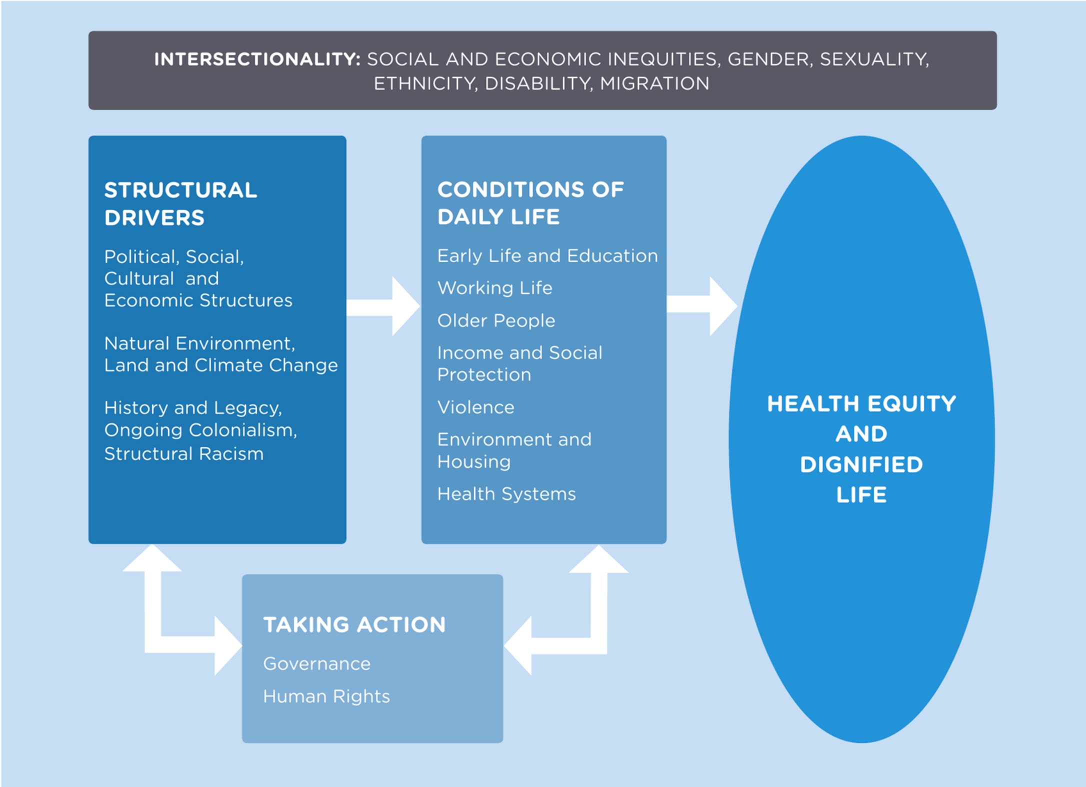
1.1.1. Definition and framework

Social determinants of health (SDH), including living conditions, environmental factors, and health behaviours, are not equally distributed between socioeconomic groups. Several frameworks for the SDH have been developed in recent decades in order to organise these factors and to understand how they affect health and healthcare use.[1] Overall, the frameworks concur on the importance of the social structure and social factors which produce health and disease through a range of complex pathways. Most frameworks include (i) **distal factors** (e.g. social structure), (ii) **intermediate factors** (e.g. social position, educational attainment) and (iii) **proximal factors** (e.g. health behaviours, age).[1] Whilst distal factors are *upstream* (indirectly affecting health), proximal factors are *downstream* (directly affecting health).

Somehow, these social determinants are translated into the health of individuals in a process called by some authors as *embodiment*.[2] A number of pathways have been used to explain the embodiment process, including (i) psychosocial, (ii) social production and (iii) ecosocial.[2] Briefly, the psychosocial pathway highlights the psychological stress related to social inequality. This stress can alter the neuroendocrine function, changing the susceptibility of the host or favouring behaviour that is harmful to health. The social production pathway explains social inequalities in health as a result of the economic and political institutions and decisions that generate social inequality but does not systematically try to integrate biological perspectives to understand health inequalities. Lastly, the ecosocial pathway combines the psychosocial and social production pathways but also expands its theory to integrate other concepts of ecology and multilevel approaches.[2]

Recently, the Pan-American Health Organization (PAHO) Commission on Equity and Health Inequalities in the Americas revised the conceptual framework on the SDH that was developed by the World Health Organization’s (WHO) Commission on Social Determinants of Health. This adaptation (Figure 1.1) was carried out to better represent the conditions of the Americas (as a continent), giving more emphasis to colonialism; racism; climate change; human rights; and inequities according to age, gender, sexual orientation, ethnicity and disability.[3] According to the PAHO, the SDH can be classified as (i) *structural drivers*, those related to the socioeconomic and political context, and (ii) *daily life conditions*, such as early life and education, working life, income and health systems. *Intersectionality* encompasses structural drivers and conditions of daily life, which emphasises inequities occurring across several factors (e.g. poverty, gender, ethnicity) that compound the adverse effects of individual social determinants of health. Addressing health inequalities requires intersectoral action on the *causes of the causes*. *Taking action* in governance arrangements and human rights are the key factors that shape the patterns and magnitude of health inequities.

Figure 1.1: Conceptual framework of the PAHO Equity Commission.



Source: PAHO (2018).

Health *inequalities* and *inequities* are related but different concepts: inequalities denote differences (e.g. between socioeconomic groups), while *inequities* emphasise unfair and avoidable differences arising from poor governance, corruption or cultural exclusion. *Health inequities* are systematic differences in health that could be avoided and addressing them is an issue of social justice.[4] Many types of *health inequities* are observed by groups of age, gender, ethnicity, religion, region, or by markers of socioeconomic position (SEP) such as income and educational status.

There are several ways to define and classify SEP in epidemiological research. In general, SEP describes the social resources and economic factors that determine the position that an individual holds within the structure of a society.[5] SEP is widely related to several exposures that can affect health and healthcare use. Each SEP indicator has its own advantages and disadvantages when used to empirically investigate associations with health. Some SEP indicators are better at representing childhood SEP (e.g. parent's educational status), while others are better at representing adulthood SEP (e.g. years spent in formal education), SEP during active professional life (e.g. income, employment and occupation), and SEP during retirement (e.g. household income and wealth). However, SEP indicators in epidemiological research are generally chosen because of their availability in datasets (national health examination surveys such as the Health Survey for England, for example, do not measure childhood SEP) and to be comparable with previous studies. The most common SEP indicators used are education, income and occupation.[5]

In most countries, SEP groups tend to be geographically segregated. This segregation brings special characteristics within each area (i.e. contextual factors), including physical characteristics (e.g. availability of health services, housing quality, food resources) and social characteristics (e.g. levels of poverty, unemployment, income inequality and crime). A large body of research in health inequalities recognises the need to distinguish between *individual* and *contextual* SEP factors, as the observed social disparities in health outcomes are often not fully explained by individual-level SEP factors. Contextual factors have been associated with inequalities in several health outcomes, including hypertension, even after adjustment for individual-level SEP.[6–8] Similarly, associations between individual-level SEP and hypertension may persist even after adjustment for contextual SEP factors. In addition, there may be effect modification, whereby the associations between individual-level SEP and health outcomes may vary across levels of contextual SEP.[7]

Epidemiological research on health inequalities has been carried out mainly in high-income countries (HICs). Whilst the traditional individual-level SEP measures have a similar definition and interpretation in HICs and in low- and middle-income countries (LMICs), there are some differences that should be considered when generalising evidence from HICs into LMICs (e.g. informal labour is more frequent in LMICs than in HICs).[9] Some differences in SEP characteristics between HICs and LMICs also apply to the Chilean context. Whilst being one of South America's most prosperous nations, Chile is one of the most income-unequal countries worldwide and shares several characteristics with middle-income countries (MICs).[10]

1.2. Social determinants of health in Chile: an overview

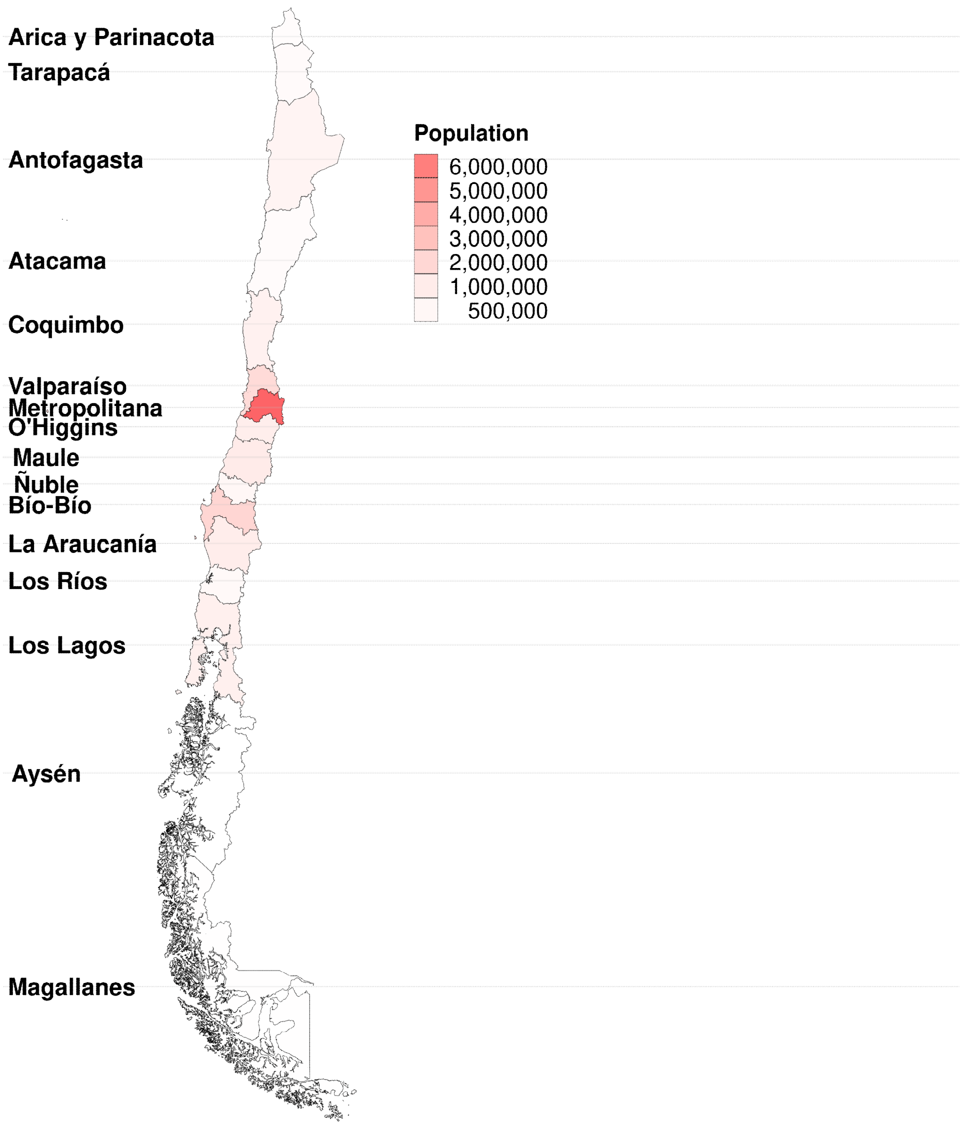
Using the PAHO conceptual framework set out above, the following section summarises aspects of the structural and daily-life conditions in Chile.

1.2.1. Structural drivers

Political, social, cultural and economic structures

Chile has 17.6 million inhabitants (2017), with 11% aged ≥64y, and 37% living in the Metropolitan region (Santiago, Figure 1.2). It is currently one of the most prosperous economies in Latin America, classified by the World Bank as a HIC since 2013.

Figure 1.2: Population size by region.



Source: Instituto Nacional de Estadísticas, Chile 2017.

The 1980 Political Constitution established that Chile is a unitary State with a democratic republic. The Constitution established that the State administration is functionally and territorially decentralised (into 16 regions). The President of the

Republic is the Head of State. Sebastián Piñera (liberal-conservative politician) was president of Chile between 2017 and 2022; Gabriel Boric (social-democrat) was recently elected in 2022. A national plebiscite was held in 2020 to decide whether a new constitution should be written and, if so, how it should be written. Almost 80% of the Chilean adult population agreed that members elected directly for this convention should draft a new constitution.

The Chilean economy is characterised by being open to free trade and is a country with the most signed treaties worldwide. It is a member of the Organisation for Economic Co-operation and Development (OECD). Chile ranks as the 35th largest export economy worldwide, characterised by the exploitation and export of raw materials (e.g. copper, fruit, seafood, cellulose, wine). The gross domestic product (GDP) in 2019 was 282 billion US dollars (USD) and 25,000 USD per capita (well below the OECD average, ranking 35/38).[11]

Natural environment, land and climate change

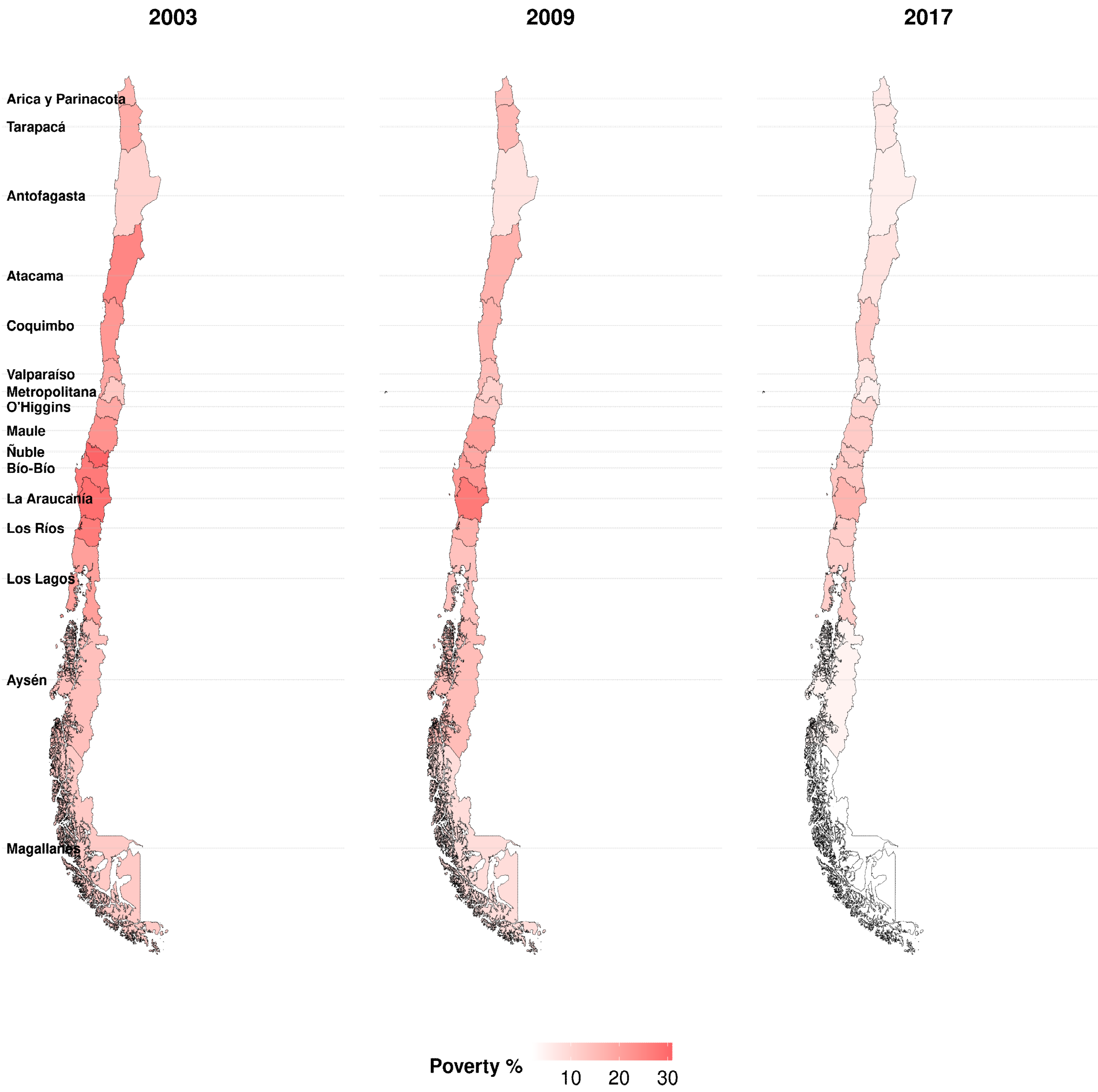
At the southwest end of South America, bordering Peru, Bolivia, and Argentina, Chile is the longest and narrowest country in the world, with a north-south distance of 2,653 miles. The Andes mountain range and the Pacific Ocean act as natural borders. A great variety of landscapes can be found: the northern zone has very dry climates (mostly desert), the central zone has temperate climates (and agricultural lands), and the southern zone has the coldest and most humid climate. Chile is highly vulnerable to climate change, especially in the central zone, where most of the population lives. This is expected to increase levels of both infectious diseases (e.g. malaria, dengue) and non-communicable diseases (e.g. hypertension, diabetes) because of the effects on water and food availability, and levels of air pollution.

The long and diverse Chilean territory is also reflected in regional differences in the levels of risk factors for cardiovascular disease (CVD). For example, as shown by analyses of the Chilean National Health Survey (ENS) 2017, the prevalence of obesity (defined as a body mass index (BMI) ≥30 kg/m²) among adults showed wide regional variation, ranging from 24% in Antofagasta (North) to 43% in Aysén (South).

Likewise, the prevalence of survey-defined diabetes (i.e. fasting blood sugar >7 mmol/L or self-reported diagnosed diabetes) varied from 8% in O'Higgins (Centre) to 18% in Atacama (North).[12]

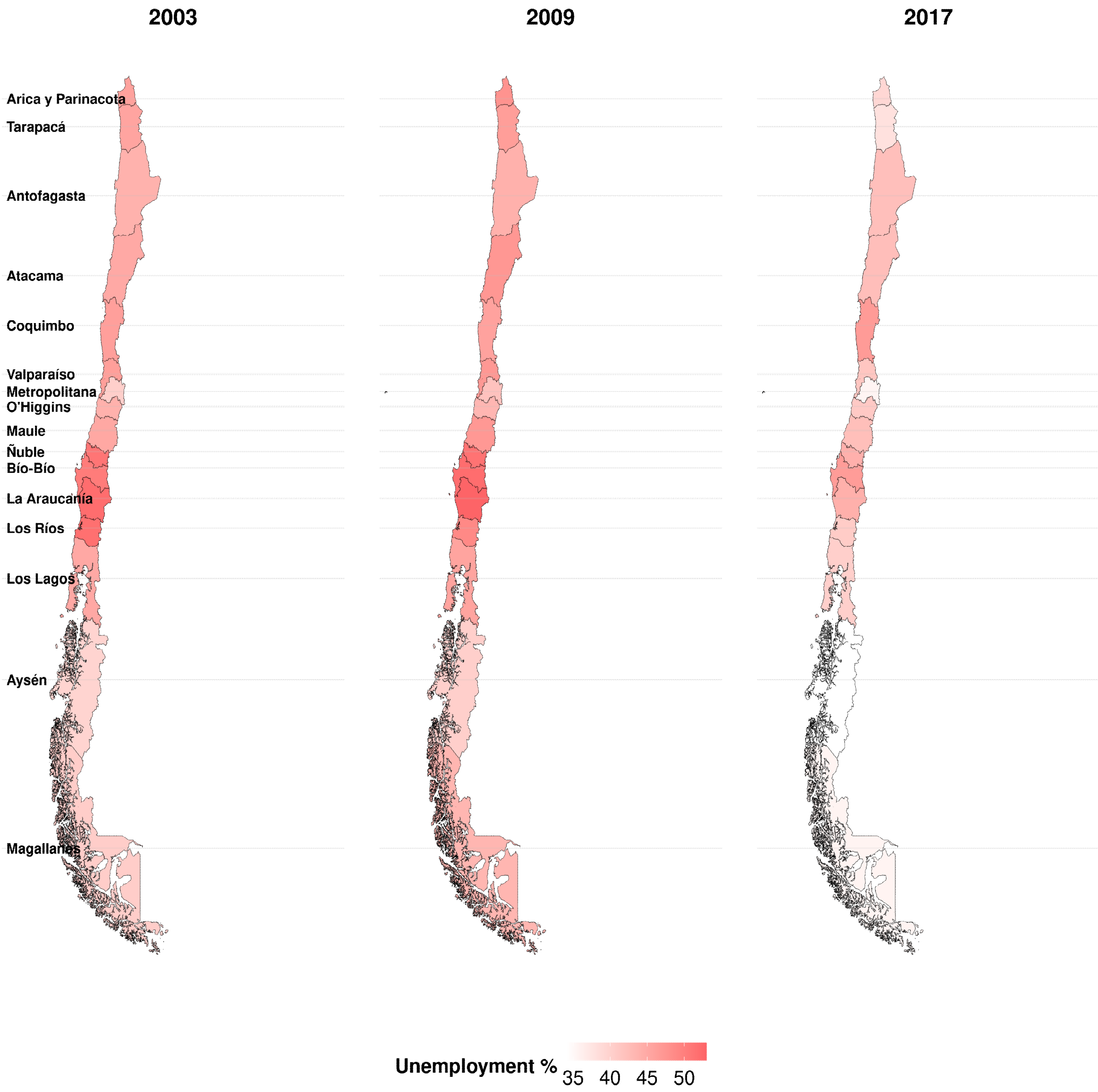
Although Chile became a HIC in 2013, half of its regions (where a third of the population lives) still have an upper-middle-income profile.[11] In order to illustrate regional socioeconomic differences and changes over time, I estimated regional levels of poverty (Figure 1.3) and unemployment (Figure 1.4) for Chile in 2003, 2009 and 2017. Since 2003, poverty levels have decreased in all regions, but they remain highly heterogeneous, with higher levels concentrated in the extreme North and Central-South. Unemployment levels also decreased and remained heterogeneous, with higher levels in the North and Central regions.

Figure 1.3: Poverty rate by region and year.



Source: Chilean National Socioeconomic Characterization Survey (CASEN) 2003, CASEN 2009, and CASEN 2017. Poverty: population (%) living in households with insufficient income to meet the basic needs of their members according to the individual minimum basket for the satisfaction of food and non-food needs.

Figure 1.4: Unemployment rate by region and year.



Source: Chilean National Socioeconomic Characterization Survey (CASEN) 2003, CASEN 2009, and CASEN 2017. Unemployment: population (%) aged 15-64y who reported that they did not work in gainful employment for at least one hour in the previous week and who did not have a job that they were absent from during the reference week.

History and legacy, ongoing colonialism and structural racism

Chile became independent from Spain in 1810, and its history with democracy is longer than in many Latin American and Caribbean countries (LACCs). Some ongoing effects of colonialism include the current economy, which is based on natural resources and international trade. However, colonialism built the basis for racial and ethnic discrimination and income inequality. The most recent Census (2017) in Chile showed that 13% of the population belonged to minority ethnic groups (80% Mapuche). Moreover, poverty levels are higher in minority ethnic groups and access to healthcare is unequal, leading to very large differences by ethnicity in levels of life expectancy, infant mortality, and poor mental health.[13, 14]

1.2.2. Conditions of daily life

Quality of life has improved in Chile over the last decades, approaching the OECD average for many dimensions, ranging from jobs, income, social connections and work-life balance to health and well-being (Table 1.1).[11]

Table 1.1: Indicators of daily living conditions: Chile and OECD.

Indicators of daily life	Chile	OECD[a] Median (min-max)	Ranking[b]
Health			
Infant mortality (deaths/1,000 live births)	7	3 (1-17)	5
Children overweight or obese (%, 5-9y)	38	31 (8-43)	5
Health expenditure (% of GDP)	9	9 (4-17)	20
Housing			
Overcrowding rate (% households)	9	9 (1-33)	13
Dwellings without basic facilities (%)	9	1 (0-26)	5
Income and wealth			
Total income poverty (%)	16	11 (5-20)	8
Child income poverty (%)	22	12 (3-27)	4
Income inequality (Gini index)	0.46	0.3 (0.24-0.5)	2
Knowledge and skills			
Tertiary education (%, 25-64y)	25	40 (18-59)	32
Children not enrolled in school (%, 5-14y)	2	1 (0-2)	12
Lack of adult skills in numeracy (%)	14	8 (3-14)	2
Other dimensions			
Gender wage gap (%, median male/female)	12	12 (4-32)	18
Voter turnout (%)	47	68 (45-92)	37
Air pollution (µg/m3)	16	14 (3-28)	12
Satisfied with water quality (%)	71	84 (65-99)	33
Homicides (rate per 100,000 deaths)	3	1 (0-27)	6
Not feeling safe at night (%)	55	21 (7-56)	2
Lack of social support (%)	11	6 (2-22)	9
Life satisfaction (0-worst to 10-best)	6	7 (5-8)	22

[a] OECD values exclude Chile. [b] OECD ranking in decreasing order (1=highest; 38=lowest). Source: OECD data, 2020 or nearest year. OECD definitions: http://stats.oecd.org

Early life

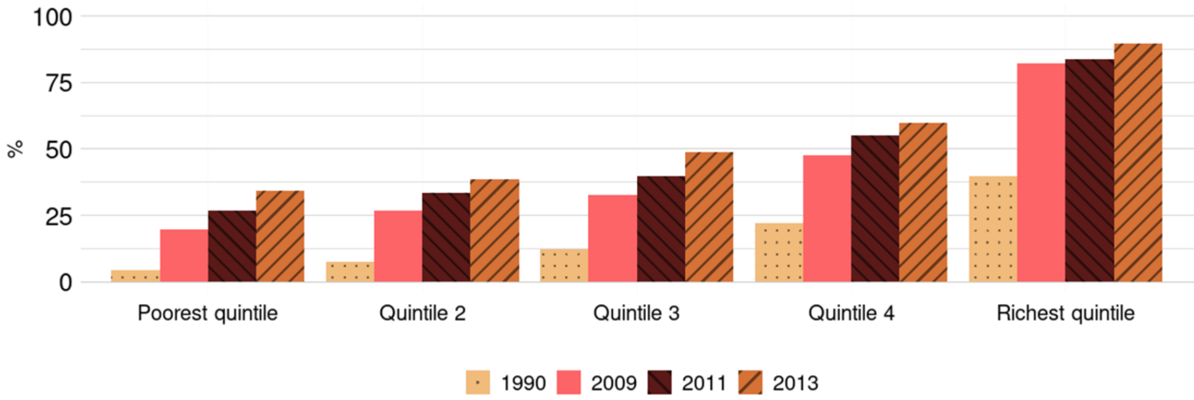
The under-5 mortality rate per 1,000 live births decreased from 157 in 1960 to 7 in 2017.[10] This impressive decline is mostly linked to the creation of the National Healthcare System in 1952, known as the Servicio Nacional de Salud (SNS). Since then, SNS has sought to reduce malnutrition levels through the free distribution of powdered milk and breastfeeding promotion. Other important SNS interventions were the implementation of oral rehydration for diarrhoea cases, increasing the proportion of deliveries with professional care, and early vaccination strategies.[15] However, evidence suggests that the decline in infant mortality has stagnated in recent years: some authors hypothesise that this could be related to increasing SEP inequalities in the distribution burden of mortality.[16] Currently, Chile has high levels of child poverty (OECD ranking 4/38) and one of the highest rates of infant mortality (ranking 5/38).[11] Obesity levels among children aged 6-7y have recently doubled in absolute terms, from 12% in 1993 to 24% in 2017.[17, 18] Moreover, 38% of children aged 5-9y were classified as overweight in 2017, representing one of the highest levels in the OECD (ranking 5/38).[11]

Education

Levels of educational attainment improved considerably in the last decade. The proportion of the population with tertiary education increased from 17% to 25% between 2009 and 2017. However, this proportion remains below the OECD average (ranking 32/38).[11]

The proportion of children aged 5-14y not enrolled in school in 2016 was low (2%), similar to most OECD countries (ranking 12/38).[11] However, schooling is socially segregated, in favour of privately managed schools, with levels of private schooling being higher than the OECD average. Access to tertiary education has been growing since 1990 across all income groups. However, the gap between the poorest and richest income quintiles in access to tertiary education remains large (Figure 1.5).[11]

Figure 1.5: Access to tertiary education by income quintiles, 1990-2013.



Source: OECD Economic Surveys: Chile 2015.

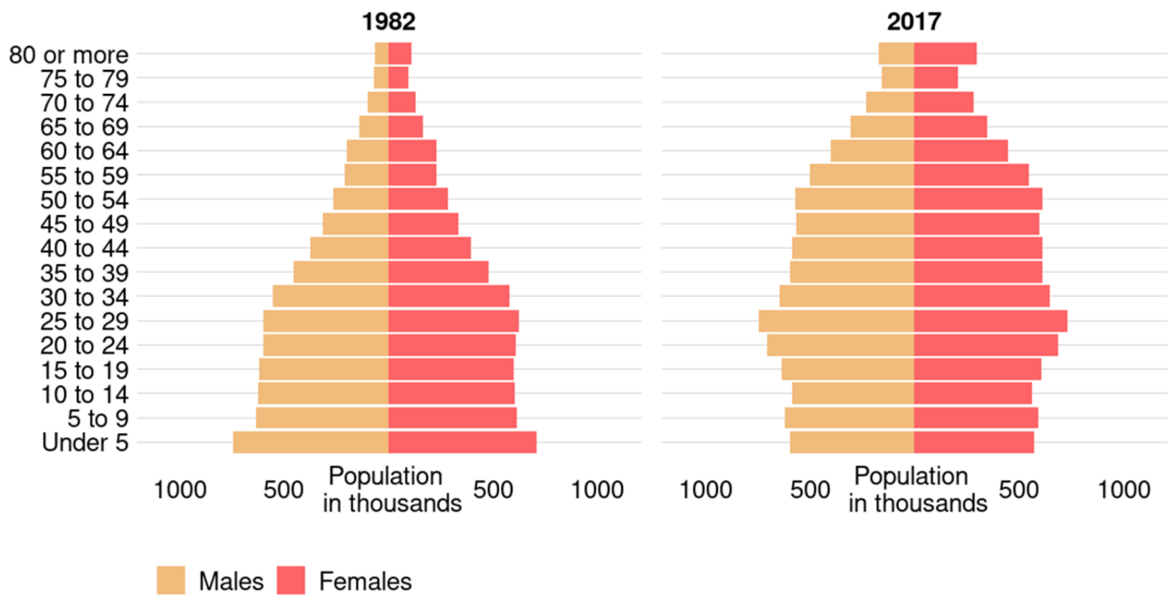
Working life

The unemployment rate among people aged 15y or more was higher among females (28% males; 41% females).[13] This gender difference decreased in absolute terms between 2005 and 2017 (from 32 to 13 percentage points). Unemployment levels vary by region (Figure 1.4) and by income, with the poorest group having the highest unemployment rate (66% versus 23% among the richest).[13]

Older people

Chile has reached an advanced stage of the demographic transition (i.e. transformation of a society from a traditional to a highly modernised state), due to achieving low levels of both fertility and premature mortality, resulting in ageing of the population, as observed in the population pyramids for 1982 and 2017 (Figure 1.6).[11]

Figure 1.6: Chilean population pyramids, 1982 and 2017.



Source: Chilean population projections Census 2017.

Overall, levels of self-reported quality of life among people aged ≥60y increased between 2007 and 2016, especially in the subindex of affective relationships.[19] However, older persons also showed low levels of material conditions.[19] The legal retirement ages are 60y and 65y for men and women, respectively. However, 40% of men and 25% of women aged ≥60y are still working (especially as self-employed), with higher levels of employment among the highly educated.[19] One-fifth of persons aged ≥60y have never contributed to the Chilean pension system, with this proportion being higher among women and among those with a basic educational level.[19] On average, pensions are low in monetary value, and 23% of persons aged ≥60y describe them as not being sufficient to meet their needs.[19] Evidence shows that improving the Chilean pension system is essential to addressing levels of income inequality.[11]

Income and social protection

The percentage of Chileans living in poverty (those with income per capita below the poverty threshold, based on the cost of a basket of essential food and non-food items) was 29% in 2006, but this decreased to 9% in 2017.[13] Extreme poverty levels (those below the minimum per capita income to meet basic food needs) decreased in a more pronounced way over the same time period, from 13% to 4%.[13]

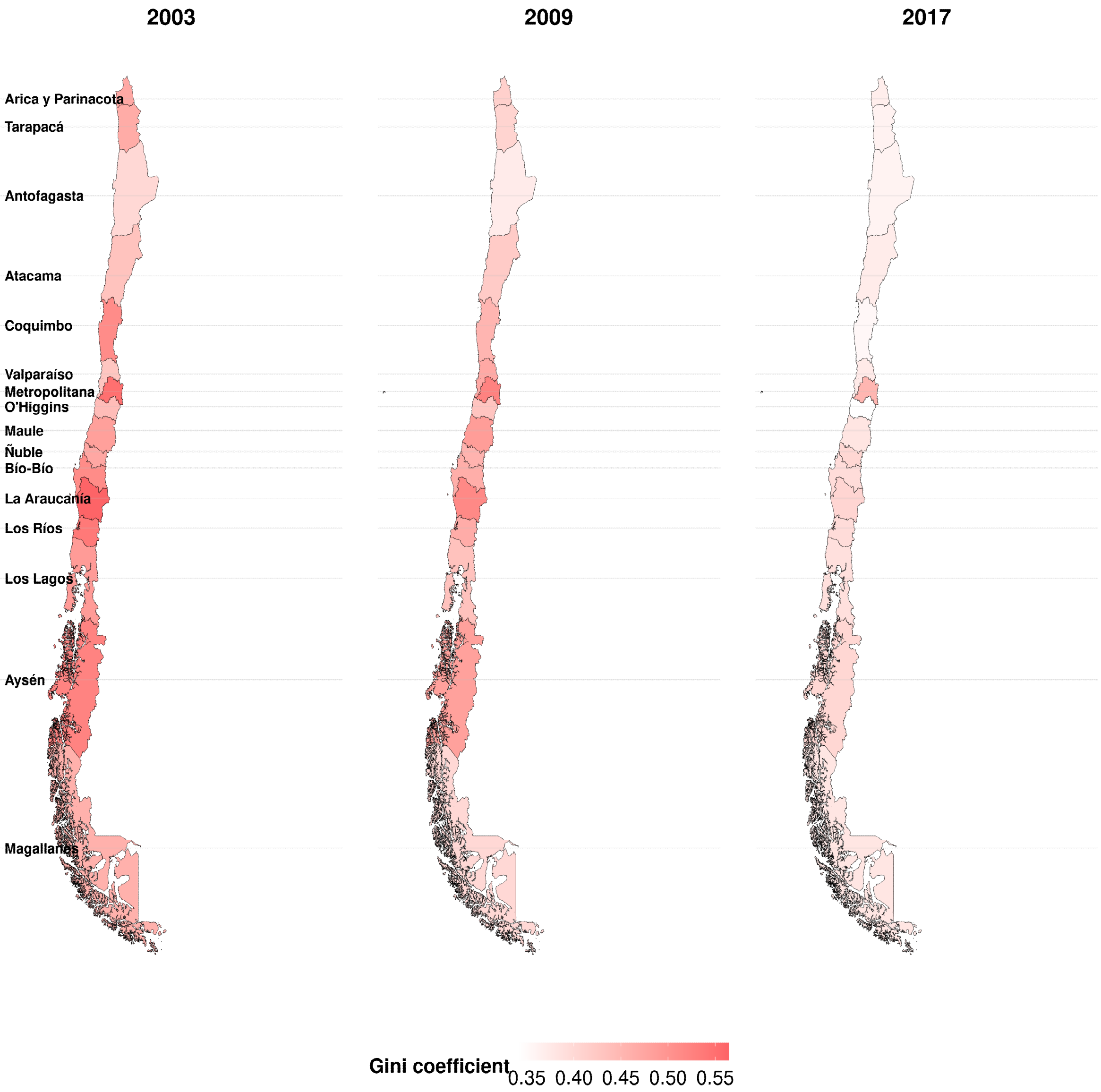
Government benefits (i.e. contributions in money received from the State through social programmes) as a percentage of total household income almost doubled from 1.5% in 2006 to 3.3% in 2017.[13] Benefits contribute a much higher percentage to total income in the lowest income group, being 45% in the poorest decile and 15% in the second poorest decile, decreasing to 0.2% in the richest decile.[13]

Income levels and wealth inequality

The Gini coefficient is a summary measure of inequality in income and wealth distributions; varying from 0 (perfect equidistribution/equality) to 1 (perfect inequality, i.e. all income being held by one person). In 2020, among OECD countries, Chile had the second-highest Gini coefficient (just below Costa Rica). Inequality levels in Chile between 1987 and 2017 were similar to the average for all LACCs. Although inequality levels have decreased (the Gini coefficient decreased from 0.56 in 1987 to 0.46 in 2017), it remains well above the OECD average (ranking 2/38).[10]

Figure 1.7 shows the decrease in income inequality levels since 2003 in Chile. It also shows the heterogeneity between regions, with the highest level of income inequality in 2017 being observed in the Metropolitan region.

Figure 1.7: Income inequality levels (Gini coefficient) by region, 2003-2017.



Source: Chilean National Socioeconomic Characterization Survey (CASEN) 2003, CASEN 2009, and CASEN 2017. Gini values based on the monthly equivalised household income (including government benefits).

Violence and personal safety

Compared with other OECD countries, Chile performs poorly regarding levels of violence and personal safety.[20] The homicide rate is one of the highest in the OECD (ranking 6/38) and 55% of the population report feeling unsafe walking alone at night (ranking 2/38).[20] Nevertheless, compared with the other LACCs, Chile has one of the lowest homicide levels and has the lowest proportion of the population who reported limiting recreation related to insecurity or who reported being a victim of crime in the previous 12 months.[20]

Environment and housing

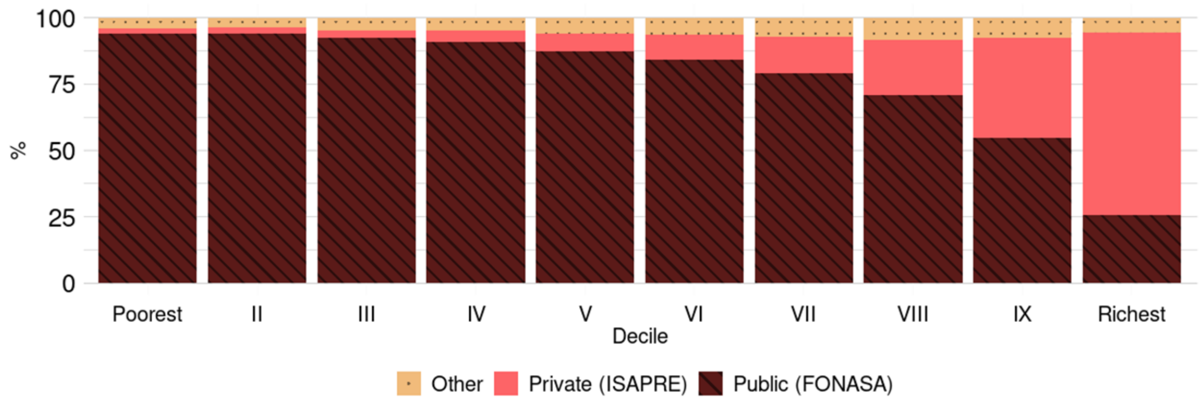
Indicators of housing affordability, overcrowding, and access to sanitation facilities have improved in the last 20 years, reaching levels similar to the OECD average in 2015.[11] However, in 2017, only 71% of the population was satisfied with the quality of water in their area (ranking 33/38) and the level of air quality in Chile was below the OECD average (ranking 12/38).[11]

Healthcare system and explicit guarantees for health conditions

Levels of health expenditure, as a percentage of GDP, increased during the last decades (from 6% in 2006 to 9% in 2020), reaching levels similar to the median of other OECD countries (ranking 20/38).[11]

The Chilean healthcare system is composed of two main subsystems, public and private, both for insurance and the provision of health services. The public subsystem, **FONASA**, and the private subsystem, **ISAPRE**, covered around 78% and 14% of the population in 2017, respectively.[13] Specific groups, such as the armed forces and the police, and specific groups of workers have separate healthcare schemes (covering 3% of the population). A small minority are not formally registered in any health insurance scheme (e.g. unemployed, homeless, or in an irregular migratory situation). By default, these individuals are covered by FONASA which gives access to basic medical treatment in public hospitals, but they face more barriers in accessing care for non-basic health needs. Registration in private health insurance is distributed unevenly by income, being considerably higher in the richest income decile (Figure 1.8).[13]

Figure 1.8: Health insurance status by income decile, 2017.



Source: Chilean National Socioeconomic Characterization Survey (CASEN) 2017. Decile in monthly equivalised household income (including government benefits).

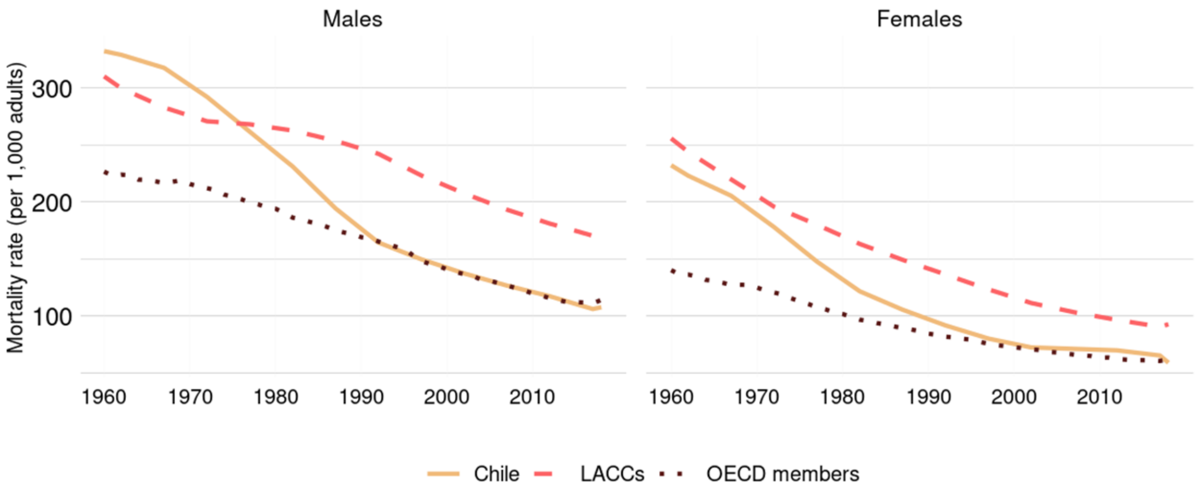
There are 85 health conditions of high burden, severity or mortality cost (including hypertension, myocardial infarction, and diabetes) for which the State provides explicit guarantees to ISAPRE's or FONASA's registrants.[21] These guarantees began in 2005 with the AUGE plan (*Acceso Universal con Garantías Explícitas*, translated as *Universal Access with Explicit Guarantees*), later named as GES (*Garantías Explícitas en Salud*, translated as *Explicit Health Guarantees*). The GES plan guarantees:

i) Access to health services
ii) Maximum waiting times (both for diagnosis confirmation and treatment initiation)
iii) Financial protection (the State pays 80-100% of treatment costs)
iv) Quality of care (accredited health care services).

Epidemiological trends

Between 1960 and 2018, mortality rates for people aged 15-60y decreased from 332 to 108 per 1,000 among males, and from 232 to 59 per 1,000 among females.[10] Since the 1990s, mortality rates in Chile have been similar to those observed among OECD members and have remained below those observed in LACC (Figure 1.9).[10] Life expectancy at birth increased by 23y during the same period (from 57y to 80y), an increase greater than the average increase across LACCs.[10] Although the reduction in infant and childhood mortality explains most of the increase in life expectancy, it is also due to the increase in longevity.

Figure 1.9: Mortality rates by gender: Chile, OECD members, and LACCs, 1960-2018.



Source: World Bank. Mortality rate (per 1,000) among adults aged 15-60y.

Although people are increasingly living longer, life at middle- and older-ages is affected by chronic diseases. As shown in analyses of Chilean survey data in 2003 (ENS2003), 2009-2010 (ENS2010) and 2016-2017 (ENS2017), for those aged ≥17y, there is both a high and increasing prevalence of CVD and CVD-related risk factors such as obesity, high levels of low-density lipoproteins (LDL) cholesterol, and sedentarism.[22–24] The previous and current epidemiological profile in Chile indicates that the peak of the chronic disease burden is yet to come.

As in many other countries, the leading causes of death have changed in Chile during the last 50 years, with a considerable increase in mortality from diseases of the circulatory system and tumours, and a decrease in mortality from infection and perinatal diseases.[25] As described in Section 1.3, a high proportion of deaths from diseases of the circulatory system is related to hypertension, one of the most frequent health conditions in Chile and worldwide.

1.2.3. Taking action

Human rights

The State of Chile ratified the international convention on the elimination of all forms of racial discrimination in 1971. Since then, Chile has ratified several international conventions, including the Geneva Conventions, the Declaration of the Rights of the Child, and the Universal Declaration of Human Rights.

However, many Chileans were victims of human rights violations during the 1973-1990 coup of Augusto Pinochet. The armed and law enforcement institutions committed violations against indigenous populations, student unions, and trade unions, as well as against the larger civilian population during the process of transition to democracy. Despite the improvement in human rights since 1990, large student mobilisations took place in 2006 and 2011, while large-scale mobilisations of women on International Women's Day, and protests about the pension system have occurred in recent years. The mobilisations were strengthened during 2018 when a social and political crisis erupted in gestation after decades of lack of response to social demands from the political system. During this crisis, serious human rights violations occurred.[26]

The *right to the highest attainable standard of health* is one of the major concerns of the Chilean State since the transition to democracy in 1990. Despite a steady improvement in several health indicators, the Chilean health system, designed and implemented during the military regime, is often criticised as failing to confront the persistent SEP inequalities in health and in healthcare. Long waiting lists in the public system and discrimination by gender, age and pre-existing health conditions, among other factors, in the private system are examples of the problems experienced by the Chilean population. The health reform in 2005 (see next section) was one of the key steps taken by the Chilean State to address the epidemiological needs of the population, improve the quality of care and reduce the gap in health outcomes between registrants in the private and public systems.

1.3. Hypertension in Chile

This section first describes the relevance of hypertension, and aspects of its management (mainly awareness, treatment, and control) in Chile and worldwide. Secondly, I describe policies affecting hypertension prevalence and indicators of its management in Chile. Thirdly, I briefly describe SEP inequalities in hypertension outcomes. Finally, I outline the current trends in risk factors for hypertension.

1.3.1. Hypertension prevalence, and aspects of its management: an overview

Hypertension (sustained high blood pressure, BP) continues to be one of the most important health challenges, being a major risk factor for cardiovascular morbidity and mortality worldwide.[27, 28] Notably, high systolic BP (SBP) is the most important cause of attributable deaths worldwide (19.2% of all deaths in 2019) and in Chile (19.3% of all deaths in 2019).[28] Hypertension is associated with coronary heart disease and cardiovascular events,[29] and is the major risk factor for heart failure,[30] stroke,[31] and kidney disease.[32] LMICs have experienced the sharpest increase in hypertension worldwide during the last four decades,[33] explained only partially by population ageing.

Hypertension prevalence

Estimating the global prevalence of hypertension is difficult. One common operational definition, based on *health examination survey* (HES) data, is *high BP or use of antihypertensive medication*.[34] Being on treatment is often included in the definition as these participants are presumed to have been prescribed antihypertensive medication as a result of satisfying the clinical definition of hypertension.[35] Antihypertensive medication can effectively reduce high BP levels, therefore some participants with hypertension would be missed if the survey-defined hypertension is based only on the current BP level.

Even using this operational definition, considerable heterogeneity exists across different studies related to different data collection methods (e.g. the number of BP measurements and measurement device used) or different SBP and diastolic BP (DBP) thresholds for high BP (including lower BP thresholds for those classified as having very high cardiovascular risk, such as people with diabetes).

Evidence on hypertension prevalence in LACCs is scant. However, most studies have estimated the prevalence to be around 30%, in line with the estimated global prevalence.[34] In Chile, hypertension prevalence (BP ≥140/90 mmHg or use of antihypertensive medication) for adults aged ≥15y in 2017 was 30%.[24]

Hypertension prevalence, and levels of uncontrolled hypertension, would be even higher if a stricter definition based on lower thresholds for defining elevated BP is adopted. According to the 2017 American College of Cardiology/American Heart Association guidelines (2017 ACC/AHA), the commonly used Seventh Joint National Committee (JNC 7) clinic-based threshold for high BP (BP ≥140/90 mmHg) should be lowered to BP ≥130/80 mmHg.[36, 37] The 2017 ACC/AHA recommendation to lower BP thresholds was based on evidence from large observational studies and clinical trials, which showed a dose-response association between BP levels and cardiovascular morbidity and mortality.[36] The recommended 2017 ACC/AHA's lower BP thresholds aim to identify patients with earlier stages of cardiovascular disease and thereby reduce cardiovascular morbidity and mortality by improving treatment levels and control.[36] Lowering the BP threshold increases hypertension prevalence and increases the number of persons eligible for treatment. In the United States, it is estimated that 31 million additional people are now eligible for BP-lowering medication after reducing the threshold.[38, 39] As most of the hypertension research that has been conducted in LACCs predates this recommendation, most studies defined high BP using the 140/90 mmHg threshold.

Even when the same BP thresholds are used, it is challenging to monitor, interpret and compare secular changes in prevalence, since hypertension is often defined not only using BP data but also using information about treatment. The *true* prevalence and its change over time may be attributed not to changes in *underlying* BP levels but to changes in the prescription patterns and use of antihypertensive medication (possibly due to changes in hypertension guidelines). Survey participants who report currently using BP-lowering treatment are likely to have measured BP values that are lower than their underlying BP values.[40] This problem is common for any operational definition that includes the use of treatment to establish the prevalence of chronic diseases.[41]

Data from 1975 to 2015 show that BP levels have been steadily falling worldwide, except in some areas of Asia and Africa.[33] This decrease in BP could be partially explained through the increased detection of raised BP levels by healthcare professionals (awareness/diagnosis), and subsequent wider uptake of treatments, and also partially by potential decreases in several major risk factors for hypertension (e.g. lower salt intake has been reported in some countries,[42, 43] although not worldwide).[44] However, the decrease in BP levels also occurred among the youngest age groups, where treatment coverage is often low.[45] Evidence also suggests that the falls in mean BP levels began before the recent increase in awareness and treatment levels,[33, 46] and despite the increase in several risk factors for high BP, such as high BMI and diabetes.[47]

Following this trend, between 2000 and 2010, hypertension prevalence (BP ≥140/90 mmHg or use of antihypertensive medication) decreased from 28% to 26% among HICs (including Chile) but increased from 32% to 39% among LMICs.[33] Evidence from LACCs suggests divergent trends in hypertension prevalence for males and females between 2000 and 2010. Hypertension increased from 27% to 33% among females (including Brazil, Argentina, Colombia, Cuba, Ecuador, Haiti, Mexico, Peru and Venezuela), but remained unchanged among males (around 30%).[33]

Indicators of hypertension management

Different analytical approaches can be used to assess health system performance in hypertension. One of these, the cascade care approach, has been widely used to monitor the performance of HIV programmes within health systems over the past two decades and is now being applied to a range of other chronic conditions, including hypertension.[48, 49] In the study of hypertension using a *cascade of care approach*, the probability of reaching any given stage is conditional on having reached all previous stages, that is, being treated for hypertension is conditional on being aware, and having BP controlled is conditional on being aware and being treated.[49]

Another analytical approach is the use of a broader focus on attainment of *hypertension management indicators*. The hypertension management approach does condition on adults being hypertensive (e.g. having survey-defined hypertension). However, being treated for hypertension is not conditional on being aware, and having BP controlled is not conditional on being treated. Following most previous studies, using standard definitions, my thesis focuses on levels of hypertension management. These key hypertension management indicators are defined as follows:

• **Awareness**: people with hypertension reporting a prior diagnosis of high BP or hypertension by a healthcare professional.

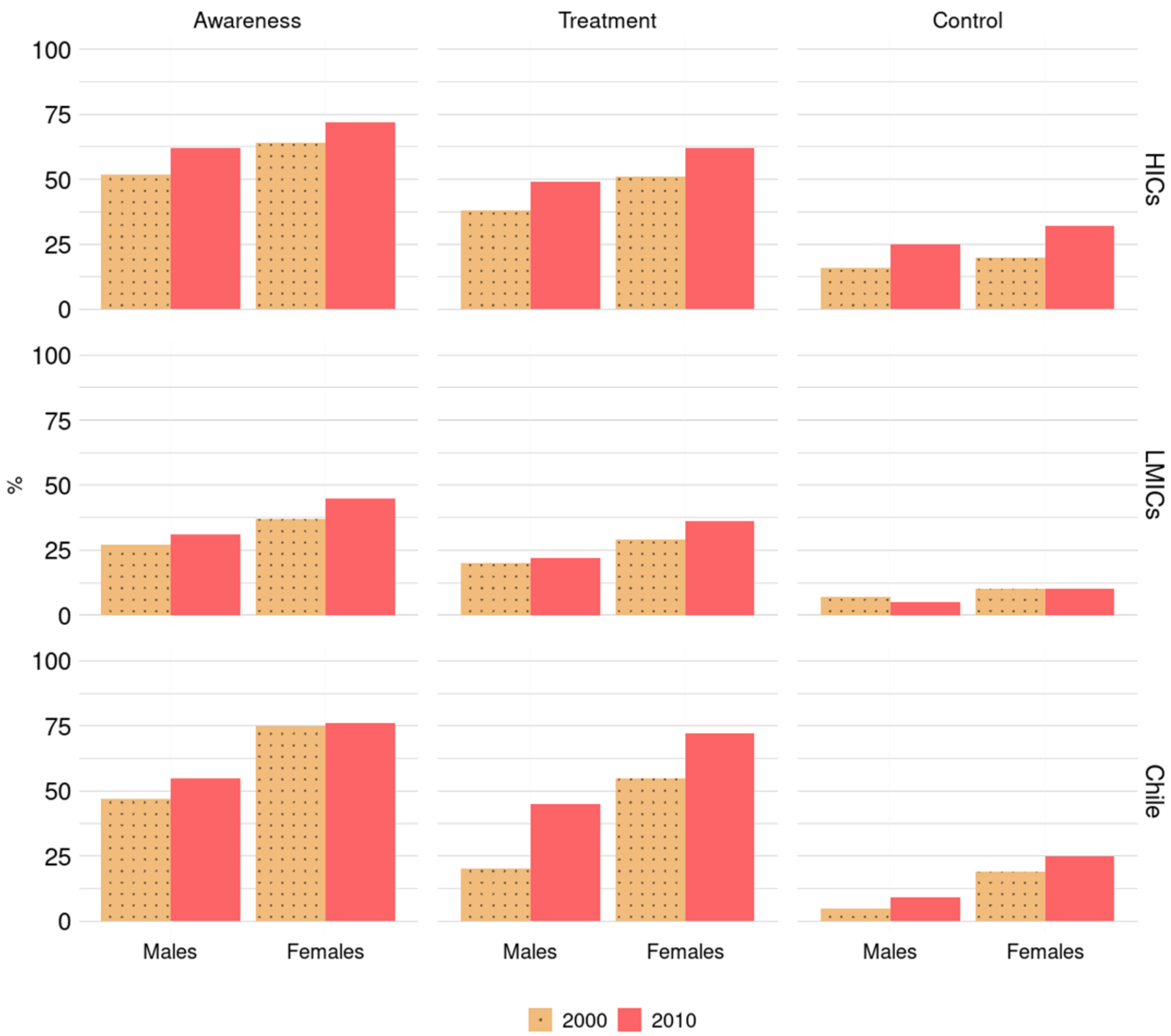
• **Treatment**: people with hypertension using antihypertensive medication.

• **Control**: people with hypertension with BP levels below thresholds (such as <140/90 mmHg).

While hypertension prevalence (BP ≥140/90 mmHg or use of antihypertensive medication) across 90 countries remained stable between 2000 and 2010 at around 30%, its management indicators increased slightly from 41% to 47% (awareness); 32% to 37% (treatment); and 34% to 37% (control).[34] Despite the existence of highly effective antihypertensive medications, most treated people with hypertension do not achieve BP control.[34]

Awareness levels in 2000 and 2010 for people aged ≥20y were higher among HICs than LMICs: levels in Chile were similar to the former (Figure 1.10). Levels of awareness increased from 2000 to 2010, but this varied by gender. In 2010, Chilean females had similar levels of awareness to females from other HICs. For Chilean males, however, levels were well below the 2010 average and more closely resembled the average across HICs in 2000.[22, 23, 34] Treatment levels in 2000 and 2010 were higher among HICs than LMICs; levels in Chile were similar to the former. Treatment levels increased from 2000 to 2010 and were higher among females.[22, 23, 34] Levels of controlled hypertension in 2000 and 2010 were higher among HICs than among LMICs and in Chile. These levels increased between 2000 and 2010, but only in HICs (including Chile).[22, 23, 34]

Figure 1.10: Hypertension management indicators in HICs, LMICs and Chile, 2000 and 2010.



Source: Mills et al. (2016): High-income countries (HICs) and low- and middle-income countries (LMICs).[34] Chile: National Health Survey (ENS), ENS2003 and ENS2010. Awareness: prior diagnosis of high BP; Treatment: use of antihypertensive medication; and Control: BP <140/90 mmHg. Levels of awareness, treatment, and control estimated amongst people with hypertension (BP ≥140/90 mmHg or use of antihypertensive medication).

Different explanations for these HICs vs LMICS differences observed in 2000 and 2010 have been offered: Mills et al. (2016) showed that scientific knowledge relating to the efficacy (i.e. the power to produce a direct result or effect) and effectiveness of lifestyle modifications and BP-lowering treatments to prevent hypertension and other

CVDs has not been fully applied to populations living in LMICs.[34] Numerous barriers at the levels of (i) the healthcare system; (ii) healthcare providers; and (iii) patients are described by Mills et al. (2016) as factors that are likely impeding the prevention and control of hypertension.[34] Such barriers include lack of access to care, costly medications, and low patient health literacy.

In Chile, levels of awareness, treatment, and control were higher among females than males at both time points (i.e. 2000 and 2010), at least partially reflecting gender differences in healthcare service utilisation.[50] Differences between population subgroups in hypertension management indicators are worrisome, as successful control of BP helps to reduce the long-term risk of CVD events and premature death.[51] I will provide more evidence from the three Chilean national health surveys on these differences and their change over time in the following chapters.

1.3.2. Policies affecting hypertension prevalence and its management indicators in Chile

Policies affecting hypertension prevalence

Sustained efforts have been made to provide care to people with hypertension since the 1980s through its Mixed Healthcare system (public and private), with 75% of the population using public-health insurance and services in 2017.[52, 53] Since the 1980s, two major health system interventions have been introduced to improve levels of diagnosed, treated, and controlled hypertension. First, in 2002, the former hypertension disease-specific programme in primary public care was transformed into an integrated risk-stratified based model: the *Cardiovascular Health Programme* and secondly, in 2005, a law was passed (GES) which warranted timely access and financial coverage (e.g. medicines free-of-charge) to all insured Chileans (public and private) for the most prevalent chronic diseases, including hypertension.[54] These efforts were aligned with the health goals for 2010 to 2020 of increasing levels of controlled hypertension (BP <140/90 mmHg) in relative terms by 50%.[55] Addressing inequalities in health was also one of the key priorities of the healthcare reforms implemented in 2005.

BP levels are affected by several individual and contextual factors. These include current and past healthy lifestyle behaviours, and the social and environmental context, such as early-life conditions,[56] diet,[57] alcohol consumption,[58] tobacco consumption,[59] physical activity,[60] use of medication,[61] air pollution,[62] exposure to noise,[63] psychosocial stress,[64] socioeconomic background,[65] temperature and geographical latitude.[66] In this context, the WHO outlines four main recommendations aimed at preventing and successfully controlling high BP: these cover health and lifestyle behaviours, namely (i) increasing physical activity, (ii) reducing harmful alcohol consumption, (iii) stopping tobacco use, and (iv) eating a healthy diet.[67]

The Chilean National Health Strategy (2011-2020) is aligned with these recommendations, as it aimed to increase prevalence levels of protective cardiovascular factors (i.e. not smoking; being in the normal range of BMI; being physically active for ≥150 minutes/week; consuming ≥5 portions/day of fruit and vegetables; and achieving low levels of BP (<120/80 mmHg); total cholesterol (<5.2 mmol/L); and fasting glycaemia (<5.6 mmol/L).[55] The Chilean government planned individual and population-based interventions targeting each WHO recommendation.[68–71] One of the main interventions over the last 20 years was the modification of the Tobacco Law (2005), which enforced more restrictions on tobacco companies and smokers. Tobacco advertising was banned; the size of the warning message on packages was increased; more tobacco-free public spaces were declared, and taxes were increased.[71]

A further key intervention was the Food Labelling and Advertising Law (enacted in 2012, applied since 2016), which added stop signs onto packaged foods; increased the taxation of sugar-sweetened beverages; and reduced children’s exposure to unhealthy foods by banning marketing; advertising and sales that targeted children.[72]

Policies affecting hypertension management in Chile

The WHO recommends integrated health programmes for hypertension and other associated non-communicable diseases (NCDs), especially at the primary care level, with trained health workers and standardised guidelines covering essential equipment (e.g. BP measurement devices); unbranded medicines; and counselling to improve treatment adherence.[73] Following the WHO recommendations, the Chilean State has made sustained efforts to improve hypertension management since 1980. First, with the sub-programme of hypertension in primary care (1980-1999); secondly, through the Cardiovascular Health Programme in primary care (2000-2004);[74] and thirdly, through the AUGE-GES plan (GES-hypertension, 2005-to the present).[75]

Between 2005 and 2022, three Chilean hypertension guidelines have been implemented, developed by the Ministry of Health (2005, 2010, and 2018 guidelines).[75] The GES-hypertension guidelines address the diagnosis, treatment and follow-up of adults with hypertension. They form a reference for patient care in the GES-hypertension plan. These guidelines used the classification of the European Society of Hypertension (ESH) which defines hypertension as BP ≥140/90 mmHg.[76] The treatment to be started follows the pharmacological approach proposed by the English Hypertension Guidelines 2004.[77] BP goals and the initial treatment (Table 1.2) are based on the Chilean cardiovascular risk stratification, based on results from the US Framingham Heart study and adapted to the Chilean population.[78] The Chilean hypertension guidelines suggest using a lower threshold of BP control (BP <130/80 mmHg) for adults with very high cardiovascular risk (defined as those with previous CVD), diabetes or proteinuric nephropathy.[75]

Table 1.2: Blood pressure goals and treatment by cardiovascular risk: Chilean hypertension guidelines.

Cardiovascular risk stratification	Blood pressure control goal (mmHg)	Initial hypertensive treatment
Low cardiovascular risk	<140/90	Lifestyle changes
Moderate cardiovascular risk	<140/90	Lifestyle changes + monotherapy antihypertensive medication
High cardiovascular risk or BP ≥160/100 mmHg	<140/90	Lifestyle changes + combined antihypertensive medication
Very high cardiovascular risk, diabetes or proteinuric nephropathy	<130/80	Lifestyle changes + combined antihypertensive medication

Source: Ministerio de Salud, Chile 2010.[54]. Cardiovascular risk stratification according to Framingham risk scores adapted to Chile. Lifestyle changes encompass eating a healthy diet, taking regular exercise, reducing salt intake, reducing alcohol consumption and tobacco cessation.

Hypertension is one of the costliest health conditions in Chile and worldwide: Chilean evidence of this high expenditure has been available since 2003 (before the introduction of the GES-hypertension plan) and mainly reflects the costs of antihypertensive medication.[79] Treatment costs for patients are low (£5/year/person in 2018), but high prevalence translates to high costs for the State.[80] For example, the GES-hypertension plan in 2018 cost £88M (5% of total GES costs).[80] The State pays most of the costs of patients related to hypertension: this amounts to between 80% and 100% of treatment costs, depending on SEP and health insurance type.[21]

1.3.3. SEP inequalities in hypertension

A growing body of evidence shows that risk factors for CVD (e.g. hypertension, diabetes, physical inactivity, sedentary behaviour, obesity and salt intake) and CVD-related mortality are more frequent among lower versus higher SEP groups.[65, 81–

86] Particularly, evidence supports the association between SEP and hypertension prevalence and in indicators of its management. Nevertheless, scarce research on SEP inequalities has been done using contextual socioeconomic factors or individual-level SEP factors among LACCs.

The association between socioeconomic position and hypertension using individual-level data has been well examined over various decades. A 2015 systematic review and meta-analysis of international studies by Leng et al. showed inequalities in hypertension by several SEP indicators: those with lower levels of education or occupational status had significantly higher odds of hypertension.[87] Leng et al. also showed that the magnitude of SEP inequalities in hypertension were higher among LACCs than the global estimates. Although hypertension inequalities have been documented in countries with recent epidemiological transitions such as Chile, there is scarce evidence of SEP inequalities in hypertension management indicators, and their trends over time.[87] To better inform my empirical investigation of these SEP inequalities in subsequent chapters of my PhD, I first undertook a systematic review of the literature on SEP inequalities in hypertension management in LACCs. This is presented in the next chapter.

Policies related to social determinants of health in Chile

One of the first efforts to reduce SEP inequalities in health in Chile was the creation of the *Chilean Equity Gauge* in 2001. This group, supported by the Rockefeller Foundation, aimed “to improve the monitoring of health equity in Chile and to build capacity for research, advocacy and community participation to improve health equity”. Following the SDH Commission’s recommendations, Chile, in 2015, adopted an intersectoral approach in its national health policy that emphasised the need to embrace all key sectors of society, not just the health sector. In 2005, the health reform and the launch of GES initiated major changes that aimed to improve equality in health. Specific efforts targeting social determinants and health equity in the redesign of health programmes in Chile included (i) the first measurement of health inequalities by county in 2005, and (ii) implementation of *13 steps to equality in* *health* in 2008, marking the first attempt to align the SDH commission with an inter-sectoral perspective.[88]

Within the *13 steps to equality in health* initiative, an evaluation of barriers in the cardiovascular programme identified that males aged 45-64y with a low educational level, unstable employment and low income, or workers living in districts with high levels of poverty, had major difficulties in accessing cardiovascular health care.[88] These evaluation efforts also found barriers within the Cardiovascular Health Programme itself, including inflexible working hours at health-care centres, high levels of staff turnover, distant locations and unaffordable transportation costs.[88]

Between 2009 and 2014 (during Piñera's administration), no major interventions targeting SDH were implemented. In 2014 (during Bachelet's administration), the SDH were prioritised again. In 2016, the Chilean Ministry of Health created the *Equity Commission, Social Determinants of Health and Health in All Policies*. By doing so, the Ministry of Health assumed the collective responsibility of guaranteeing the well-being, equity and protection of the population, considering health as a fundamental human right. In particular, this commission aims to (i) promote the *healthy municipalities, communes and communities strategy*; (ii) provide training on equality in *All policies*; (iii) develop *guidelines and recommendations* for health in *All policies*, social determinants and equity; and (iv) create *regional groups* across the country to promote work on equity, social determinants of health, and health in *All Policies*.

1.3.4. Trends in risk factors for hypertension

Changes since 2003 in the major risk factors for hypertension have been mixed among Chilean adults (Table 1.3). Although high total cholesterol levels, high LDL cholesterol, obesity, and diabetes have increased, levels of current smoking and passive exposure to smoke have decreased. Levels of fruit and vegetable consumption, the proportion of participants with excessive dietary intake of sodium,[89] and levels of alcohol consumption have remained stable.[24]

Table 1.3: Risk factors and related health conditions, 2003-2017.

	Prevalence (%) by year		
Risk factor	**2003**	**2010**	**2017**
Health condition			
Obesity	23	25	34
Diabetes	4	9	13
Measurement			
Excessive dietary intake of sodium	‡	96	96
Decreased HDL	40	46	47
High triglycerides	27	31	33
Behaviour			
Sedentary leisure time	91	89	87
Insufficient fruit-vegetable consumption	‡	85	85
Alcohol consumption in last month	‡	58	54
Smoking	42	40	33
Risk of alcohol abuse/dependence	‡	11	13

Source: ENS2003, ENS2010, ENS2017. Obesity: body mass index ≥30 kg/m²; Diabetes: fasting blood sugar >7 mmol/L or self-reported diabetes diagnosis; Excessive dietary intake of sodium: excessive dietary intake of sodium along with insufficient potassium (urinary sodium-to-potassium ratio >1); Decreased HDL: males <1 mmol/L or females <1.3 mmol/L; High triglycerides: ≥1.8 mmol/L; Sedentary leisure time: <30 min of exercise 3 times/week during leisure time; Insufficient fruit-vegetables: <5 portions/day; Smoking: current or occasional; Risk of alcohol abuse/dependence: Alcohol Use Disorders Identification Test (AUDIT) score >8.[90]
‡: Measured in 2010 and 2017 only.

1.4. Overview of the following chapters

In my PhD, I used data from the Chilean National Health Surveys (ENS2003, ENS2010, and ENS2017) to investigate SEP inequalities in the prevalence and management of hypertension. To better understand SEP inequalities, I first conducted a systematic review of the literature covering SEP inequalities in hypertension management in LACCs (presented in Chapter 2). I used the results of this review to develop my conceptual model; and identify the research questions, aims and hypotheses (presented in Chapter 3) that informed my empirical analyses (presented in Chapters 4 to 7).

Among all adults (i.e. irrespective of SEP), I first explored the “big picture” of levels of hypertension prevalence and management indicators, and how these have changed over time (Chapter 4). These results helped frame the analysis of SEP inequalities in hypertension and its management indicators (using individual-level measures of SEP), and their respective secular changes (Chapter 5). Individual-level SEP inequalities were further explored in a multilevel modelling approach by simultaneously considering several contextual SEP factors (Chapter 6). I also evaluated how hypertension status and educational status were associated with all-cause and cardiovascular mortality using ENS-mortality-linked data (Chapter 7). Finally, Chapter 8 presents a summary of the results of the four empirical chapters, and places the findings in a Chilean, LACC and global context. The policy implications of my study are presented and I highlight potential areas for future empirical research.

Chapter 2: Systematic review of socioeconomic inequalities in hypertension management in Latin American and Caribbean countries

2.1. Introduction

Hypertension continues to be a leading contributor to mortality worldwide,[27, 28] and is well known to be socially graded in HICs: those with fewer resources are more likely than those with more resources to have higher levels of CVD-related risk factors (e.g. hypertension, obesity, and diabetes), morbidity, and mortality.[65, 81–83, 91, 92] In contrast, evidence of social gradients in hypertension remains limited in LMICs,[83, 93, 94] and show mixed results, showing higher prevalence among the most advantaged,[81, 95] or null SEP-hypertension associations.[96] A systematic review of global disparities by Mills et al. (2016) showed a higher prevalence of hypertension among LMICs versus HICs.[34] Social gradients in hypertension are magnified by disparities in levels of awareness, treatment, and control.[34] Rates of under-diagnosis, non-treatment and poor BP control were found to be twice as high in LMICs compared with HICs;[34, 97] suggesting the relevance of examining SEP inequalities in hypertension management in the LMIC context.

Although knowledge about the association between markers of SEP and hypertension prevalence in LACCs has accumulated in recent years, including a global systematic review and meta-analysis by Leng et al. (2015),[87] evidence of SEP inequalities in hypertension management (SEP-HM) is scarce worldwide and is exceptionally rare in LACCs. Recent systematic reviews on SEP-CVD associations have highlighted the lack of information in LACCs.[82, 83, 98] Factors that are associated with SEP inequalities in hypertension management may differ from those related to SEP inequalities in hypertension prevalence, and moreover, the factors associated with each could change over time within the same population.[99–102]

Leng et al. (2015) reported the magnitude of SEP inequalities in hypertension globally and by region, including LACCs.[87] Using the pooled global data, they found significant inequalities in hypertension by educational status (OR lowest vs highest: 2.02, 95% CI: 1.55–2.63) and occupation (OR lowest vs highest: 1.31, 95% CI: 1.04–1.64). Inequalities by income almost reached statistical significance (OR lowest vs highest: OR 1.19, 95% CI: 0.96–1.48). Leng et al. (2015) showed that the magnitude of SEP inequalities in hypertension were higher among LACCs (OR lowest vs highest education: 2.56, 95% CI: 1.11-5.89; OR lowest vs highest occupation: 1.66, 95% CI: 1.34-2.06; OR lowest vs highest income: 1.48, 95% CI: 1.18-1.84).[87]

Since a relatively recent systematic review of SEP inequalities in hypertension prevalence that included LACCs has been published, my systematic review presented here focuses on SEP inequalities in the management of hypertension among LACCs. Detailed exploration is required to inform policy-making efforts designed to better address the burden in the region and for monitoring the progress of efforts to improve hypertension care across all SEP groups and to reduce inequalities.

The following section presents the aims and methods of the review. Then I describe the results, including the flow diagram of the articles retrieved by the search; discuss the range of analytical techniques used to assess SEP-HM associations; and summarise the direction of the associations. The chapter ends with a discussion of the main findings and the implications for my subsequent research aims (set out in Chapter 3) and empirical work (Chapters 4 to 7) based on analyses of Chilean health examination survey data.

2.2. Aim and objectives

This systematic review aims to describe the current evidence of SEP-HM associations in LACCs. Five specific objectives for this review are as follows:

i. Describe the most common SEP associations with hypertension awareness.

ii. Describe the most common SEP associations with treatment of hypertension.

iii. Describe the most common SEP associations with controlled hypertension.

iv. Describe the most common analytical techniques used to estimate these associations, including the definition of hypertension and its management outcomes, and the chosen statistical measure(s) of inequality.

v. Where relevant, objectives i to iii will also consider gender- and country-specific SEP-HM associations.

2.3. Literature search methods

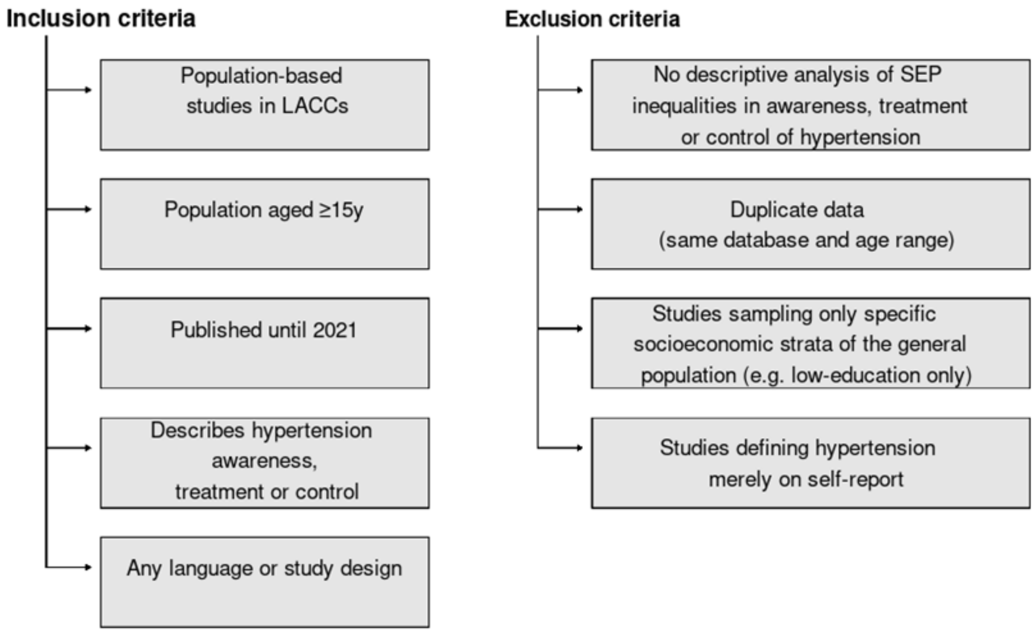
2.3.1. Search strategy and eligibility criteria

I prepared this systematic review according to the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA-2020) guidelines.[103] In this review, I did not perform a meta-analysis because of the heterogeneity of the study designs and reporting of outcomes; I conducted a narrative synthesis of the key findings according to the *Synthesis Without Meta-analysis* (SWiM) guidelines.[104]

I conducted a systematic literature search using two search engines: OvidSP and BVSalud, without language limitations. For this chapter, the search was first conducted in April 2018 and then updated in April 2021. Although I last updated the systematic review more than a year ago, more recent articles were included in later chapters of my PhD where relevant.

Eligibility criteria were designed to be more sensitive than specific (Figure 2.1). In this way, an article evaluating an adult population-based setting describing at least one indicator of hypertension management was included for full-text reading.

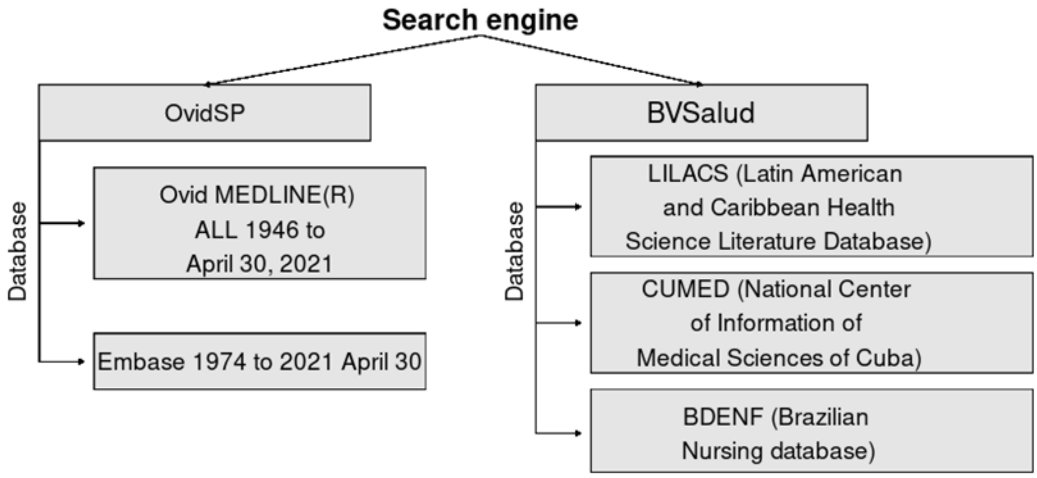
Figure 2.1: Inclusion and exclusion criteria for the systematic review.



2.3.2. Information sources

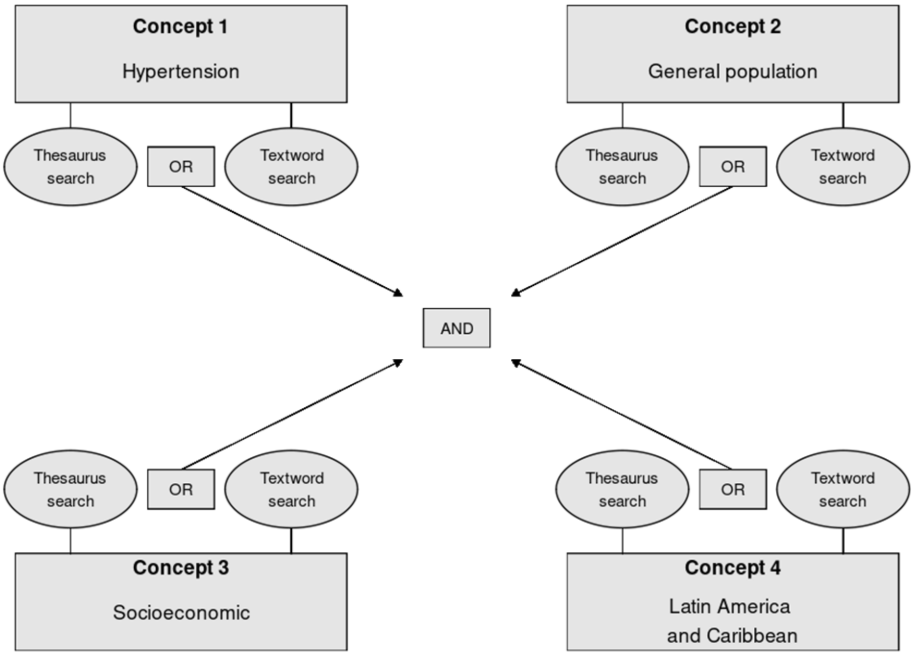
Two search engines and several electronic databases were used, as described in Figure 2.2.

Figure 2.2: Search engines and databases used in the systematic review.



Four concepts: (i) hypertension, (ii) general population, (iii) socioeconomic, and (iv) Latin America and the Caribbean were built. I used a combination of controlled vocabulary (thesaurus terms/subject headings, including MeSH terms) and textwords (free text, using truncations and *wild-cards*) strategy. Thesaurus terms and textwords were combined into a single syntax using Boolean operators (Figure 2.3). I repeated this process once for both OvidSP databases and once for the three BVSalud databases. Hypertension management was not included as a fifth concept/term, as the search failed to retrieve several important articles that I had identified beforehand.

Figure 2.3: Creation process for search syntax.



I searched for additional literature within the references section of selected sources for full-text reading and within reports on LACCs' National Health Surveys. I downloaded a full-text version of all potentially relevant articles, theses, and dissertations from electronic databases. If not found, I requested the article by e-mail from the authors.

2.3.3. Definition of terms included in the search strategy

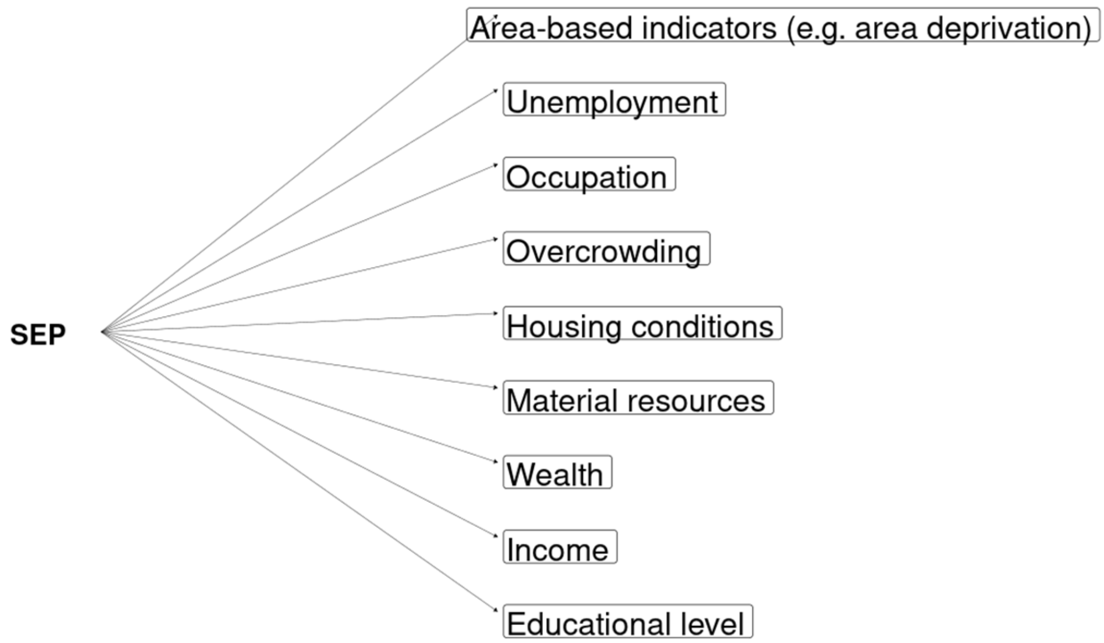
The four concepts covered by this review are briefly defined below.

Concept 1: **Hypertension** was defined as high BP or use of antihypertensive medication. Studies were restricted to those using BP measurement and so studies relying exclusively on self-report data were excluded.

Concept 2: **General population** was defined as the population excluding those who reside in an institution (e.g. hospital, prison). No other restrictions were applied, except for the place of residence (being outside LACCs) and age (<15y).

Concept 3: **SEP** refers to the social and economic factors that influence what positions individuals or groups hold within the structure of a society.[9] As discussed in Chapter 1, there is no single best indicator of SEP, as it depends on the outcome to be evaluated and on the population being researched. Area-level markers of socioeconomic circumstances were also included to capture factors that potentially influence levels of hypertension awareness, treatment, and control over and above those accounted for by individual-level markers of SEP.[105, 106] The full list of SEP indicators included in the search syntax is presented in Figure 2.4.

Figure 2.4: SEP indicators included in the search syntax.



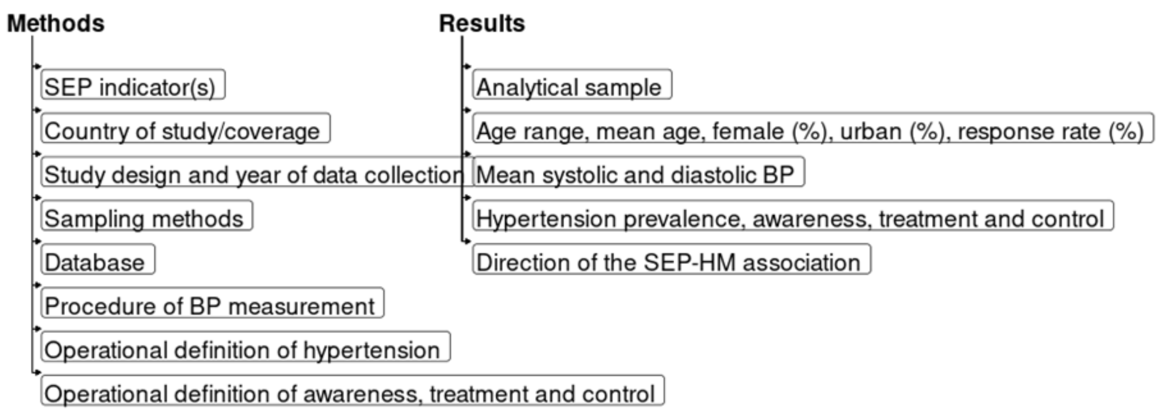
Concept 4: **LACCs** comprise 19 sovereign states and several territories covering an area from the northern Mexican border to the southern tip of South America, including the Caribbean.

2.3.4. Articles meeting the inclusion criteria

I screened relevant articles by selecting first by title and then by the abstract. Some articles were excluded during this stage as they did not comply with the inclusion criteria. The rest were assessed for full-text reading, and those meeting the inclusion criteria were included for data extraction.

Data were entered into a spreadsheet form organised by methods and results (Figure 2.5). The direction of SEP-HM associations and statistical methods used to summarise inequalities in hypertension management (e.g. age adjustment, and whether inequalities were estimated on absolute or relative scales) were the key summary measures used in this review.

Figure 2.5: Data extracted from the selected articles.



SEP: socioeconomic position, HM: hypertension management

2.3.5. Classification of the outcome measures

The key indicators of hypertension management covered in the review apply to persons with hypertension. However, studies defined hypertension differently. Table 2.1 briefly describes the five main definitions of hypertension used in studies included in this review.

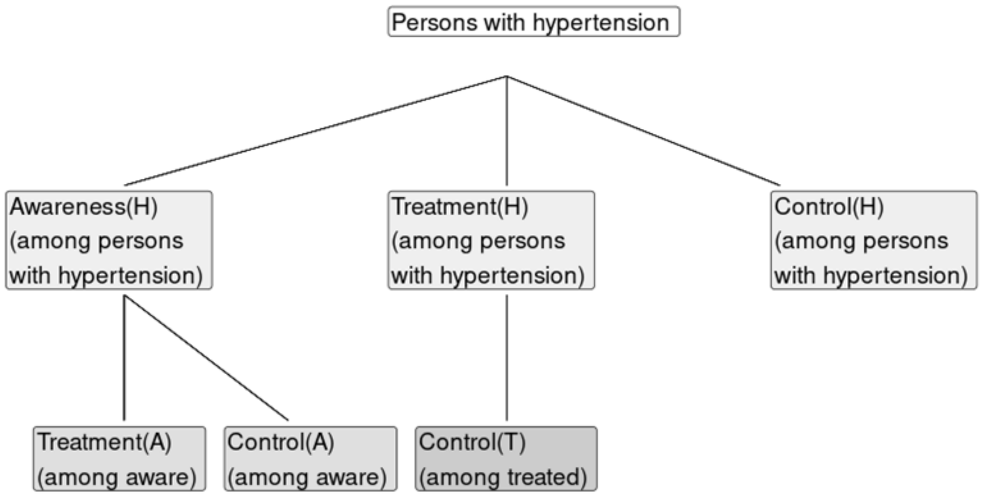
Table 2.1: Hypertension definitions.

Definition	Description
1	BP ≥140/90 mmHg or use of antihypertensive medication
2	BP ≥140/90 mmHg or self-reported prior diagnosis of hypertension made by a healthcare professional
3	BP ≥140/90 mmHg or use of antihypertensive medication or self-reported prior diagnosis of hypertension made by a healthcare professional
4	BP ≥140/90 mmHg
5	BP ≥160/95 mmHg‡ or use of antihypertensive medication

‡ *Defined as an "old threshold" for high BP.[107]*

There is no standard definition of awareness, treatment, or control, as different denominators could be used for calculating prevalence (Figure 2.6).[35] For example, levels of controlled hypertension could be calculated using as the denominator: (i) all persons with hypertension; (ii) only those with self-reported diagnosed hypertension (i.e. levels of control among those aware); or (iii) only those classified as currently using antihypertensive medication (i.e. levels of control among those treated). SEP-HM associations in a particular study may therefore vary according to the choice of denominator.

Figure 2.6: Hypertension management denominators.



2.3.6. Classification of SEP

Four out of the nine SEP indicators listed in Figure 2.4 were found in the review using different definitions:

• **Educational level**: the articles included in the review used educational attainment as a SEP indicator. Educational level was classified using ordinal categories of the highest attained level (e.g. completed education at the primary school level, university graduates) or total years of completed education.

• **Financial resources**: classified using ordinal categories of (individual or household) income or wealth.

• **Occupation**: classified using non-hierarchical groups (e.g. government employee, non-government employee, self-employed, student, homemaker, retired or unemployed).

• **Employment status**: classified using non-hierarchical groups (e.g. unemployed or employed).

2.3.7. Classification of measures of health inequality

Measures of health inequality have been classified by the WHO as simple or complex.[108] Simple measures involve pairwise comparisons between SEP groups (e.g. using the odds ratio (OR) to compare the odds of an outcome for persons in the least versus most educated groups). Complex measures (e.g. relative index of inequality (RII), slope index of inequality (SII), and concentration index) use data from all SEP groups to assess inequality using a single number that summarises the estimated difference in a health outcome between the highest and lowest SEP. For both simple or complex measures, inequalities can be quantified on an absolute or relative scale (Table 2.2). Absolute inequalities quantify the difference in levels (e.g. percentage point (pp) differences in outcome); relative inequalities quantify proportional differences (e.g. prevalence ratios).

Table 2.2: WHO classification of measures of health inequality and examples.

Type of measure	Simple measure of inequality	Complex measure of inequality
Absolute	Proportion difference	Slope Index of inequality (SII), Absolute concentration index
Relative	Odds Ratio (OR), Risk Ratio (RR), Prevalence Ratio (PR)	Relative Index of inequality (RII), Relative concentration index

Source: WHO (2013).[108]

2.3.8. Data synthesis

Classification of the SEP-HM associations

In this review, I use the terms **pro-poor**, **null**, and **pro-rich** to summarise the direction of SEP-HM associations, as briefly described in Table 2.3. I use the terms *pro-poor* and *pro-rich* as shorthand for *better outcomes for the more advantaged* and *better outcomes for the more disadvantaged*, respectively. These terms should not be taken to imply it is solely material circumstances driving any differences. In this chapter, the hypertension management indicators are defined in terms of awareness, treatment, and control (i.e. *favourable or positive* outcomes). Higher levels of management in the highest versus the lowest SEP groups are therefore classified as a pro-rich finding. Associations using employment or occupational status with non-hierarchical groups (i.e. based on nominal rather than ordinal categories) are described separately.

Table 2.3: Direction of SEP-HM associations.

Direction of association	Definition
Pro-poor	Inverse, statistically significant SEP-HM association (e.g. lower financial resources associated with higher levels of awareness).
Null	Non-significant SEP-HM association.
Pro-rich	Positive, statistically significant SEP-HM association (e.g. higher financial resources associated with higher levels of awareness).

I classified the statistical significance of SEP-HM associations using the reported two-tailed p-values (threshold set at <0.05). If the SEP indicator had more than two categories, I used the overall (joint) test of significance or the test for trend (when available). When no test was reported, I evaluated the association by examining the p-value of the difference between the highest and lowest SEP groups. I classified SEP-HM associations as null if the results suggested a curvilinear trend (e.g. when only the middle SEP differed significantly from the reference category). If an article presented both unadjusted and age-adjusted results, I classified the association based on the latter as age potentially confounds SEP-HM associations. I evaluated the distribution of pro-poor, null, and pro-rich associations by SEP indicator, gender, and country. Associations reported by gender or presented by more than one complex measure (i.e. RII, SII, concentration index) were included separately.

Gender-specific analyses of SEP-HM associations

The WHO guidelines for inequality analysis suggest evaluation of whether dimensions of inequality (e.g. SEP, gender, race, rurality) intersect and recommend analysis by performing double disaggregation (e.g. by SEP and gender).[108] As MacIntyre and Hunt (1997) mention, the intersection of gender and SEP in influencing health needs to be systematically considered using comparable SEP indicators.[109]

Notably, my analyses were stratified by gender because SEP indicators and hypertension outcomes are distributed differently by gender. For example, according to Chilean data, females have higher rates of poverty and spend fewer years in formal education than males.[13] In addition, global and Chilean evidence shows that levels of awareness, treatment, and control are higher among females.[34, 110, 111] Previous evidence shows that SEP inequalities in hypertension differ by gender.[40, 87, 99] For example, according to the meta-analysis conducted by Leng et al. (2015), women in the lower versus higher socioeconomic groups had significantly higher levels of hypertension.[87] In contrast, inequalities were less consistent among men. Leng et al. (2015) attributed the wider inequalities in hypertension among women to the fact that women in the highest SEP may be more exposed to health information and be more likely to change unhealthy lifestyle behaviours than men.[87]

2.3.9. Quality sensitivity analysis

I performed a sensitivity analysis in order to examine the strength of the SEP-HM associations amongst those associations grouped by (i) inequality measure (simple versus complex), (ii) age adjustment (yes versus no), (iii) documentation of response rate to the survey (yes versus no) and (iv) sample size for estimating levels of hypertension management indicators (i.e. n of participants with hypertension in three categories: 0-500, 501-2,000, >2,000). To test for differences in the distribution of pro-poor, null, and pro-rich associations, I performed a Chi-square test (χ^2). Analyses were performed in R (version 4.0.4).

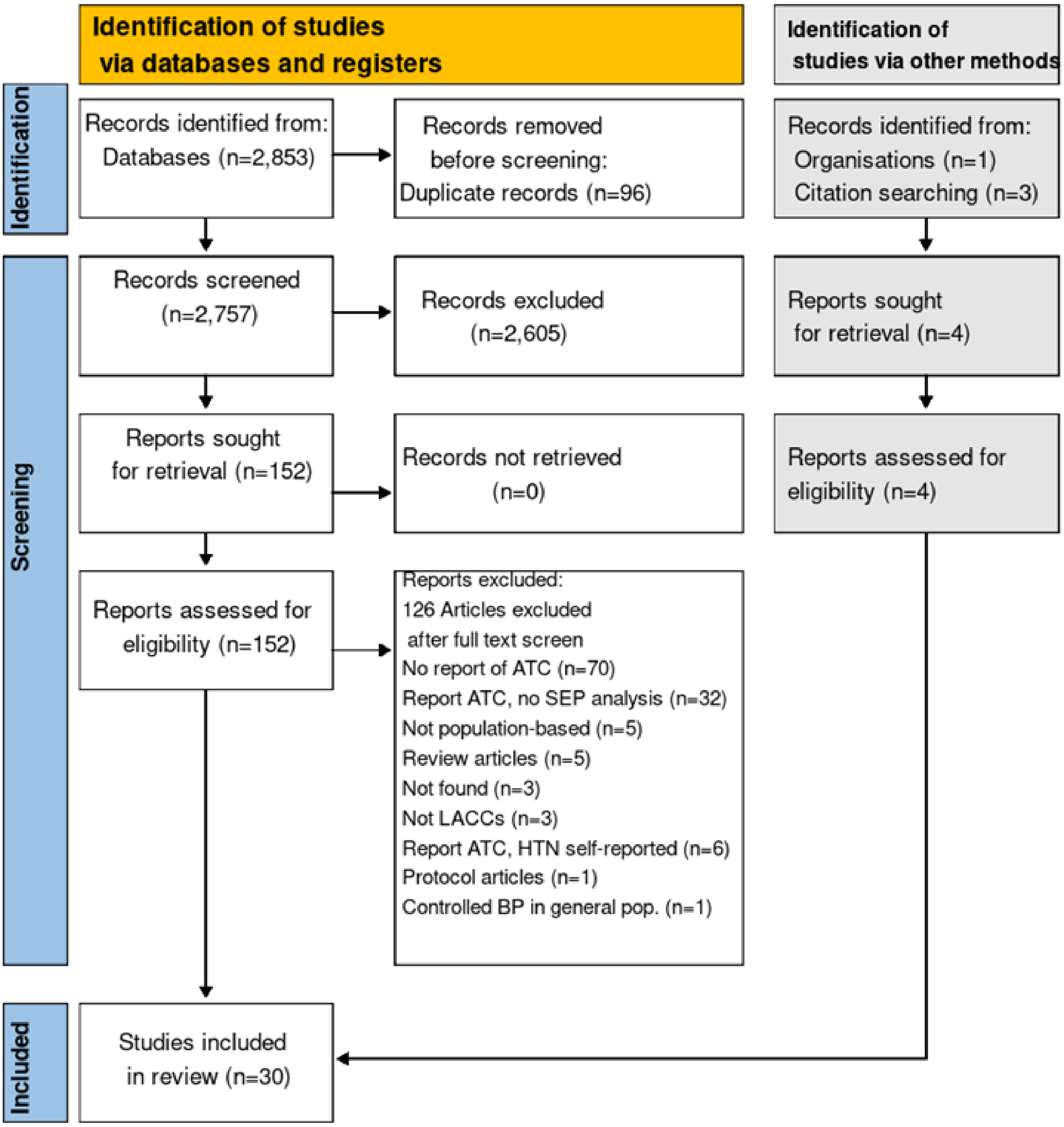
2.4. Results

2.4.1. Study selection

The search strategy retrieved 2,757 unique and potentially relevant titles. After scanning titles and abstracts, I identified 152 articles (5%) for inclusion, of which I then excluded 126. Figure 2.7 shows the criteria used to select the articles included.

After scanning the references of the articles retrieved, a further four articles were included. I selected 30 articles for data extraction.

Figure 2.7: PRISMA flowchart.



Date of search: 30 April 2021.
ATC: Awareness, Treatment or Control; HTN: hypertension.

2.4.2. Choice of the denominator

In the following sections, I use three different denominators to summarise the results. 30 articles were included (Denominator 1). Four articles outlined SEP-HM associations in more than one population (e.g. from different LACCs or from the same LACC but across different years of data collection). Because of this, the denominator increased from 30 articles to 41 populations (Denominator 2). Specifically, Irazola et al. (2016) described results in four LACCs (Argentina, Chile, Peru, and Uruguay) and Palafox et al. (2016) from four LACCs (Argentina, Brazil, Chile, and Colombia).[112, 113] Gutierrez et al. (2016) described results in Mexico across three survey years (2000, 2006 and 2012).[114] Three articles reported pooled results from several LACCs without describing the results by country: these were considered as results from individual populations. Particularly, Geldsetzer et al. (2019) used pooled data from 10 LACCs (Belize, Brazil, Chile, Costa Rica, Ecuador, Grenada, Guyana, Mexico, Peru, Saint Vincent and the Grenadines);[110] Rubinstein et al. (2016) from three LACCs (Argentina, Chile, and Uruguay);[115] and Lamelas et al. (2019) from six LACCs (Argentina, Brazil, Chile, Colombia, Peru, and Uruguay).[116] Finally, these 41 populations contained 193 unique SEP-HM associations (Denominator 3).

2.4.3. Study characteristics

Table 2.4 (sorted alphabetically by LACC) presents the study (first) author, study location, geographical coverage, study design, year of data collection, age range, response rate, sample size, and definition of hypertension for each of the 41 populations covered by the 30 articles.

Table 2.4: Articles included in the systematic review.

First author	Country	Year (data collection)	Coverage	Design	Age range	Response (%)	HTN	Total sample size•
Palafox[113]	Argentina	2006	SN	L‡	35-70	N/A	1	7,497
Irazola[112]	Argentina	2010	SN	C	35-74	73	1	3,990
Gus[117]	Brazil	1999	SN	C	≥20	N/A	1	918
Moreira[118]	Brazil	2004	SN	C	≥40	N/A	1	1,492
Palafox[113]	Brazil	2005	SN	L‡	35-70	N/A	1	5,581
Chrestani[119]	Brazil	2007	SN	L‡	≥20	N/A	1	2,949
Santimaria[120]	Brazil	2008	SN	C	≥65	N/A	2	3,478
Zattar[121]	Brazil	2009	SN	C	≥60	89	3	1,705
Sousa[122]	Brazil	2010	SN	C	≥60	98	1	912
Margozzini[123]	Chile	2003	N	C	≥17	64	1	3,619
Palafox[113]	Chile	2006	SN	L‡	35-70	N/A	1	3,270
Irazola[112]	Chile	2010	SN	C	35-74	73	1	1,925
Passi (A)[124]	Chile	2010	N	C	≥15	85	1	1,149
Passi (B)[125]	Chile	2017	N	C	≥17	N/A	1	13,605
Camacho[126]	Colombia	2002	SN	L‡	35-70	N/A	1	7,444
Palafox[113]	Colombia	2006	SN	L‡	35-70	N/A	1	7,506
Mendez[127]	Costa Rica	2004	N	L‡	≥60	76	3	2,827
Ordunez[128]	Cuba	2001	SN	C	25-74	80	1	1,475
Felix[129]	Ecuador	2018	SN	L‡	35-70	N/A	1	2,020
Geldsetzer[110]	LACCs	2009	N	C	≥15	66-94	1	155,572

First author	Country	Year (data collection)	Coverage	Design	Age range	Response (%)	HTN	Total sample size•
Rubinstein[115]	LACCs	2010	SN	C	35-74	73	1	7,524
Lamelas[116]	LACCs	2010	SN	L‡	35-70	N/A	1	33,276
Gutierrez[114]	Mexico	2000	N	C	≥20	N/A	2	45,300
Gutierrez[114]	Mexico	2006	N	C	≥20	87	2	33,366
Barquera[130]	Mexico	2006	N	C	≥20	80	4	33,366
Lloyd[131]	Mexico	2007	N	C	≥50	52.4	1	2,281
Basu[132]	Mexico	2007	N	C	≥18	N/A	4	2,733
Gutierrez[114]	Mexico	2012	N	C	≥20	N/A	2	10,898
Campos (A)[133]	Mexico	2012	N	C	≥20	N/A	4	10,898
Campos (B)[134]	Mexico	2016	N	C	≥20	92	4	8,054
Laux[135]	Nicaragua	2009	SN	C	20-60	77-86	4	1,355
Valladares[136]	Nicaragua	2016	SN	C	≥18	90.7	1	577
Lerner[137]	Peru	2007	SN	C	≥30	N/A	4	987
Irazola[112]	Peru	2010	SN	C	35-74	75	1	3,601
Zavala[138]	Peru	2012	SN	L	≥35	82	3	717
Villarreal[139]	Peru	2015	N	C	≥15	N/A	4	27,412
Villarreal[139]	Peru	2016	N	C	≥15	N/A	4	26,680
Villarreal[139]	Peru	2017	N	C	≥15	N/A	4	27,142
Villarreal[139]	Peru	2018	N	C	≥15	N/A	4	28,167
Gulliford[107]	Trinidad and Tobago	2001	SN	C	24-89	87	5	461
Irazola[112]	Uruguay	2010	SN	C	35-74	73	1	1,584

Survey-defined hypertension (HTN): (1) BP ≥140/90 mmHg or use of antihypertensive medication, (2) BP ≥140/90 mmHg or diagnosis, (3) BP ≥140/90 mmHg, (4) BP ≥140/90 mmHg or treatment or diagnosis, (5) BP ≥160/95 mmHg or treatment. BP: Blood pressure.
•*Sample size for calculating hypertension prevalence.*
N/A: Not available; Coverage (N: National, SN: Subnational).
Study design (C: Cross-sectional, L: Longitudinal). ‡: Cross-sectional analysis of cohort baseline data.

Research on SEP inequalities in hypertension management was available for 12 out of 19 LACCs (Figure 2.8). Most of the research was conducted in Mexican (8/41 populations), Brazilian (7/41), Peruvian (7/41), and Chilean (5/41) populations.

Figure 2.8: LACCs included in the systematic review.

The earliest year of data collection was 1999,[117] and the most recent was 2018.[129] Only one article used data collected before 2000. Roughly half of the data (54%, 22/41 populations with a reported year of collection) were collected before 2010.

A cross-sectional study design was reported in 23/30 articles; 7/30 were prospective cohort studies: *Pelotas* (Brazilian cohort),[119] *PURE* (Chilean, Argentine, Brazilian, Ecuadorian, and Colombian cohort),[113, 116, 126, 129] *CRONICAS* (Peruvian cohort),[116, 138] and *CESCAS* (Argentine, Chilean, and Uruguayan cohort).[116] Twelve articles were based on data from nationally-representative samples, the remaining samples were representative at a subnational level.

The lowest minimum age included in the articles was 15y, however, most focused on populations aged ≥20y. Twenty-six of the 41 populations did not include an upper age limit; the rest used an upper age limit between 60y and 89y. The response rate was reported in 18/41 populations: of these, most exceeded 70% (range: 52%-98%).

In Table 2.1, I outlined five different definitions of hypertension. The most common definition used by the included studies (17/30) was Definition 1 (BP ≥140/90 mmHg or use of antihypertensive medication). Seven of the 30 articles used Definition 2 (BP ≥140/90 mmHg or self-reported diagnosed hypertension).

Most articles reported hypertension levels before presenting levels of awareness, treatment, or control. Sample sizes for estimating hypertension prevalence had a large variation, ranging from 461[107] to 155,572[110] participants (Table 2.4). Sample sizes for estimating levels of awareness, treatment or control were smaller, by definition (Table 2.5), as the denominator was persons with hypertension or a subset of those (e.g. those on treatment). In Table 2.5, I show the relevant denominator for the hypertension management indicators via a letter in parentheses.

Table 2.5: Number of associations and sample size by outcome.

Outcome	Associations	Sample size		
		Min	Median	Max
Awareness(H)	71	95	1,810	38,963
Treatment(H)	40	95	1,974	38,963
Treatment(A)	11	162	600	3,669
Control(H)	41	95	1,974	38,963
Control(A)	14	290	850	3,669
Control(T)	16	162	550	2,163

Denominator in parentheses: H: persons with hypertension; A: those aware; T: those on treatment.

As described above, four SEP indicators (educational status, financial resources, occupation and employment status) were found in this review. The number of associations for each SEP was as follows: (i) education: 78/193; (ii) financial resources: 104/193; (iii) occupation: 5/193; and (iv) employment: 6/193 (data not shown).

According to the WHO classification (set out earlier in Table 2.2), 144/193 and 49/193 SEP-HM associations were evaluated through simple and complex measures of health inequality, respectively (Table 2.6).

Table 2.6: Associations by inequality measure.

Inequality measure		Associations
Simple measure of inequality (pairwise comparisons)	Difference (proportion descriptions or χ^2 test)	104
	Odds ratio (OR)	40
Complex measure of inequality	Absolute concentration index (ACI)	12
	Relative index of inequality (RII)	13
	Slope index of inequality (SII)	24

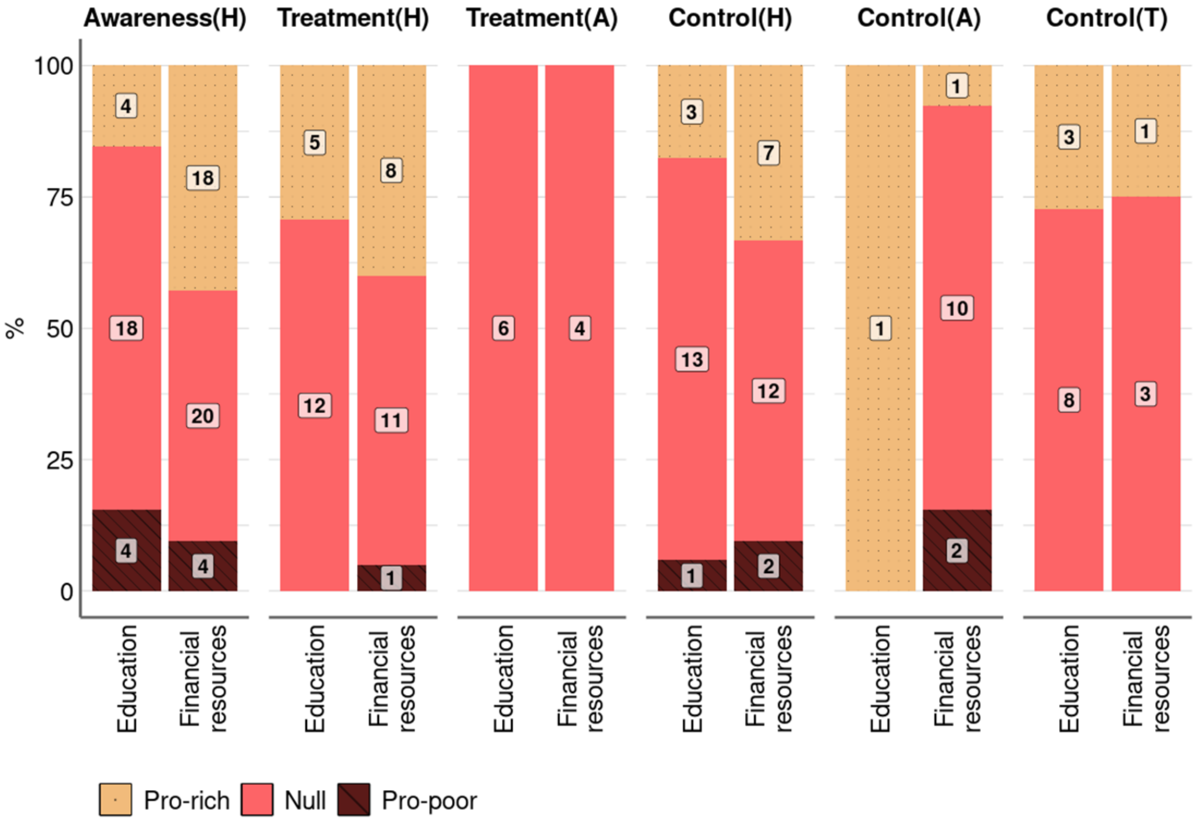
Age and gender stratification or adjustment were performed in (i) all estimations using the SII, RII, and concentration index; (ii) 25/40 estimations using the OR; and (iii) 12/104 estimations using proportions or χ^2 test.

2.4.4. Associations by awareness, treatment, and control

Half of the selected articles (15/30) examined inequalities over the entire pathway of care (awareness, treatment, and control). As presented earlier in Table 2.5, the most reported SEP-HM association was for awareness(H) (n=71), followed by control(H) (n=41) and treatment(H) (n=40).

From the total of 193 associations, I classified 182 associations as either pro-rich, null, or pro-poor (Figure 2.9). The remaining 11 associations were based on nominal indicators of SEP (employment and occupation) and are described separately.

Figure 2.9: Outcome-specific associations by ordinal measures of SEP.



SEP: socioeconomic position. Denominator in parentheses: H: persons with hypertension; A: those aware; T: those under treatment. Number of associations inside bars.

Levels of hypertension awareness by ordinal SEP

Twenty-five of 30 articles reported levels of awareness, all using persons with hypertension as the denominator (awareness(H)), with levels of awareness that varied between 31% (Mexico, 2006[114]) and 84% (Brazil, 2007[119]).

A total of 68 SEP-awareness(H) associations were found, with a higher proportion of pro-rich than pro-poor associations (32% and 12% of associations, respectively), especially when financial resources was used as the SEP measure (Figure 2.9).

Country-specific associations

The studies conducted in Chile, Nicaragua, Ecuador, Trinidad and Tobago, and Uruguay showed only null SEP-awareness associations. In Brazil, 2/11 associations were pro-poor, and 1/11 was pro-rich. The equivalent figures in Mexico were 5/22 and 12/22. In Colombia, two pro-rich, and in Argentina, one pro-poor association, were reported when financial resources was used as the SEP measure.

Gender-specific associations

Few SEP-awareness associations were stratified by gender. Of these, 7/14 associations were evaluated in females: one used education as the SEP measure (null) and six used financial resources (two pro-poor and four pro-rich). Seven of 14 associations were reported in males: six used financial resources as the SEP measure (all pro-rich) and one used education as the SEP measure (null).

Levels of treated hypertension by ordinal SEP

Nineteen articles reported levels of treated hypertension by SEP. Most articles defined treatment based on self-reported use of antihypertensive medication. Two different denominators were used for calculating levels of treatment: 16/30 articles used treatment(H), and 5/30 used treatment(A). Overall, treatment(H) levels varied between 19% (Peru, 2017[139]) and 95% (Brazil, 2008[120]). Half of the reported treatment(H) levels were below 50%. Treatment(A) levels were generally higher, varying between 78% (Uruguay, 2010[112]) and 95% (Nicaragua, 2016[136]).

The studies included in this review contained 37 SEP-treatment(H) and 10 SEP-treatment(A) associations: of these, 62% and 100% were null, respectively (Figure 2.9). Pro-poor and pro-rich SEP-treatment(H) associations were found using both SEP indicators (financial resources and educational status).

Country-specific associations

Studies from Argentina, Brazil, Nicaragua, and Uruguay reported only null SEP-treatment(H) and SEP-treatment(A) associations. Mexican studies reported two SEP-treatment(H) associations (one null and one pro-rich using education and financial resources as the SEP measure, respectively). Studies conducted in

Colombia reported only pro-rich SEP-treatment(H) associations (three with income and one with education as the SEP measure).

Gender-specific associations

Few SEP-treatment associations were gender specific. One and two pro-rich associations between treatment(H) and educational status were reported among males and females, respectively. Two null associations between educational status and treatment(H) were reported by gender (divided equally between genders).

Levels of controlled hypertension by ordinal SEP

Twenty-two articles reported SEP-Control associations. Almost all defined controlled hypertension as BP <140/90 mmHg. Three different denominators for estimating levels of controlled hypertension were found: 18/30 articles reported control(H), 3/30 articles reported control(A), and 11/30 reported control(T). Levels of control(H) varied between 5% (Peru, 2018[139]) and 51% (Brazil, 2010[122]); levels of control(A) varied from 36% (Mexico, 2000[114]) to 56% (Mexico, 2006[130]); and levels of control(T) varied from 30% (Peru, 2007[137]) to 71% (Peru, 2010[112]).

Thirty-eight SEP-control(H), 14 SEP-control(A) and 15 SEP-control(T) associations were found in the included studies. Most SEP-Control associations were classified as null. Control(A) showed a lower percentage of pro-rich associations compared with control(H) and control(T), with respective figures of 14%, 26%, and 73%.

Country-specific associations

Looking at the associations over SEP as a whole, studies conducted in Chile, Mexico, Nicaragua, Trinidad and Tobago, and Uruguay reported only null SEP-control(H) associations. Studies from Argentina reported three associations with control(H), two pro-poor and one null. Brazilian studies reported six associations with control(H), one pro-poor and five null. Pro-rich SEP-control(H) associations were reported in Colombia, Peru, and among pooled data from LACCs. Mexican and Cuban studies reported SEP-control(A) associations. In Mexico, associations were 2/13 being pro-poor, 10/13 null, and 1/13 being pro-rich using financial resources as the SEP measure; in Cuba, one pro-rich association was found using education as the SEP measure. Studies conducted in Argentina, Chile, Mexico, Nicaragua, Peru, and Uruguay presented only null SEP-control(T) associations. Brazilian studies reported 2/2 pro-rich SEP-control(T) associations (split between education and financial resources as measures of SEP).

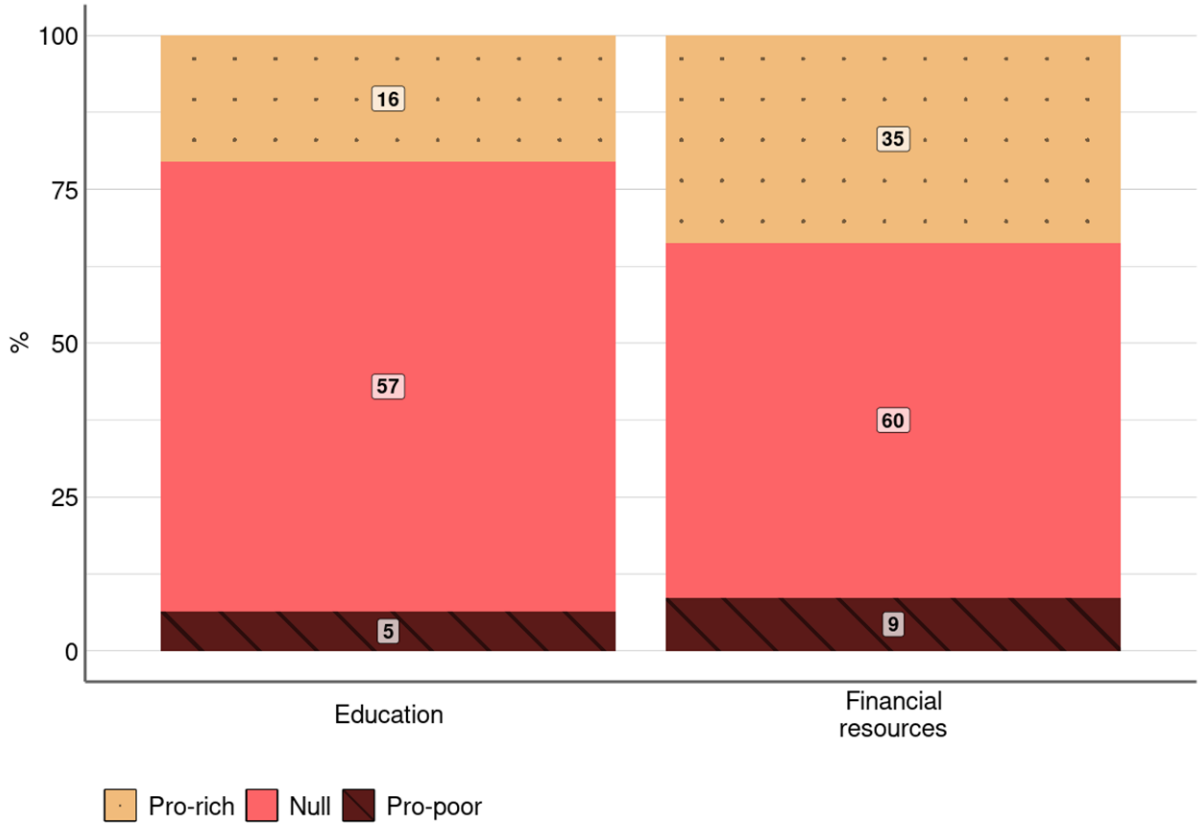
Gender-specific associations

Eighteen SEP-Control associations were reported separately for males and females. Two SEP-control(H) associations were reported for females (both null) and two were reported for males (both null). Six SEP-control(A) associations were reported for females (two pro-poor, three nulls, one pro-rich) and six were reported for males (all null). Two SEP-control(T) associations by gender were found, one pro-rich for males and one null for females.

2.4.5. Associations by ordinal SEP, country, and gender

Overall (across the three management indicators), the results of the 182 separate ordinal SEP-HM associations showed 8% pro-poor, 64% null, and 28% pro-rich associations. Higher proportions of pro-rich associations were reported when financial resources was used as the SEP measure (Figure 2.10).

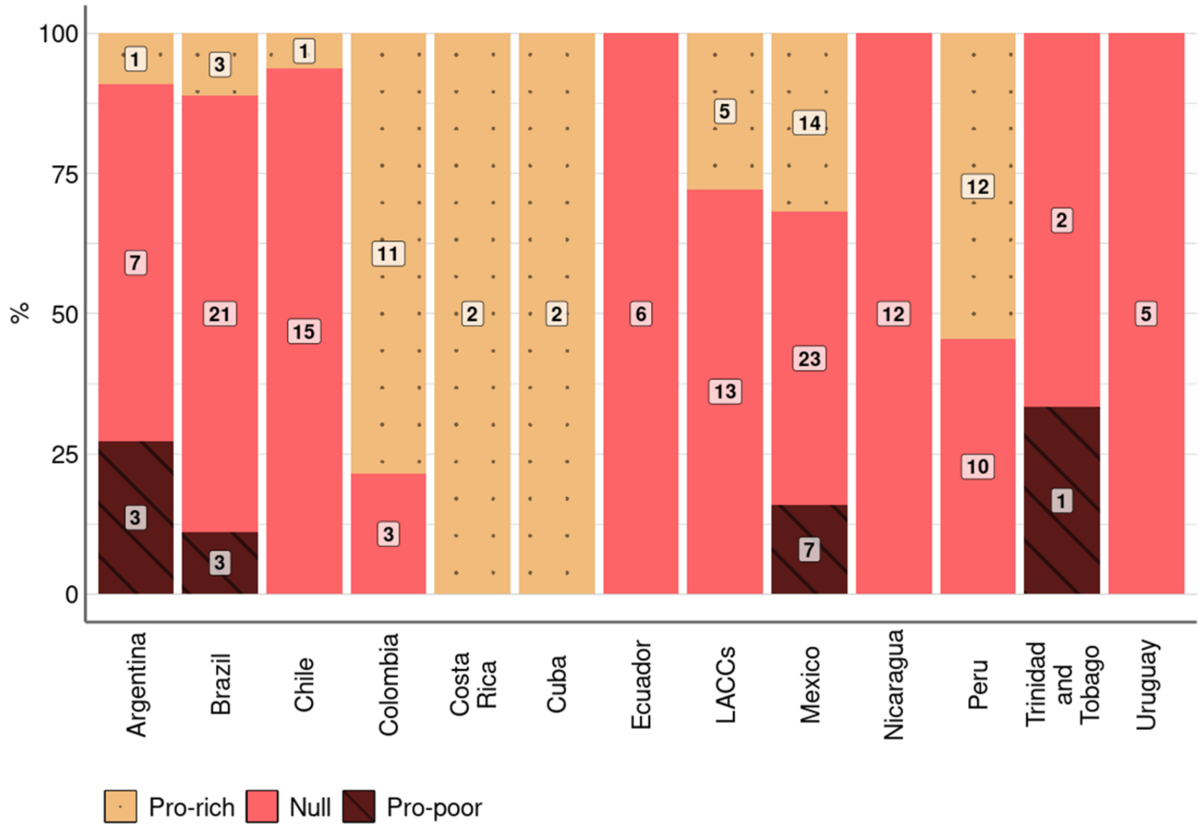
Figure 2.10: Associations by ordinal SEP (across all hypertension indicators).



SEP-HM: inequalities by socioeconomic position in hypertension management. Number of associations inside bars.

SEP-HM associations were reported most commonly in Mexico, followed by Brazil, Peru, and Chile. Studies conducted in Chile, Colombia, Costa Rica, Cuba, Peru, and Mexico showed a higher proportion of pro-rich than pro-poor associations. Argentina, Brazil, Mexico, and Trinidad and Tobago were the only LACCs reporting pro-poor associations. All SEP-HM associations in Ecuador, Nicaragua and Uruguay were found to be null (Figure 2.11).

Figure 2.11: SEP-HM associations by LACC (across all hypertension indicators).

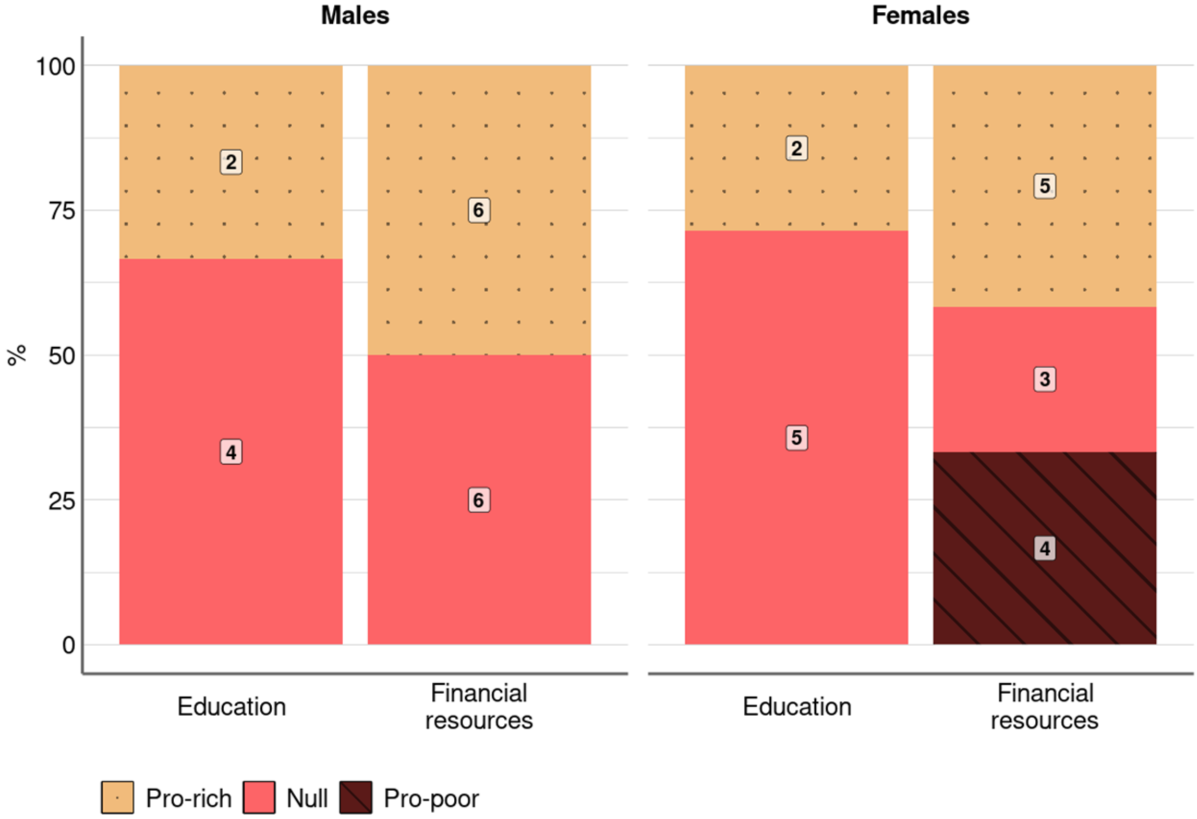


SEP-HM: inequalities by socioeconomic position in hypertension management. LACCs include data from Argentina, Brazil, Chile, Colombia, Peru, and Uruguay. Number of associations inside bars.

The distribution of pro-poor, null, and pro-rich associations showed some evidence of change over time within countries. For instance, evidence suggested that Chile (2003-2017), Colombia (2002-2006), and Peru (2007-2018) shifted from having null associations only to having pro-rich associations only. In Mexico (2000-2016), on the other hand, the proportion of pro-rich associations decreased over time, while the proportion of pro-poor associations remained stable.

5/30 articles[114, 115, 124, 127, 135] reported 37 gender-specific SEP-HM associations. Pro-poor associations were found only among females and only when financial resources was used as the SEP measure (Figure 2.12).

Figure 2.12: SEP-HM associations by gender (across all hypertension indicators).



SEP-HM: inequalities by socioeconomic position in hypertension management. Number of associations inside bars.

2.4.6. Associations by occupation and employment

Only 2/30 articles reported SEP-HM associations using employment [120] or occupation [136] as the SEP measure. Non-hierarchical groups were used to analyse these SEP measures. Regarding employment status, a Brazilian study by Santimaria et al. (2019) that presented results by region showed that levels of awareness(H) were higher among the unemployed in the South; while differences by employment status in the North were null.[120] Levels of treatment(H) were higher among the unemployed in both the North and South; whilst levels of control(H) did not vary by employment status in either region.[120] Finally, regarding occupational status, the study by Valladares et al. (2019) using data from Nicaragua reported higher levels of awareness, treatment, and control among those retired, homemakers and unemployed compared with government employees, non-government employees, self-employed or students.[136] However, these occupational inequalities were not discussed by the authors and were likely affected by several confounding factors, including age, health behaviours, and comorbidities. The latter may have led to an increased likelihood of being out of the labour market, increased chances of BP measurement and therefore, increased chances of having diagnosed, treated, and controlled hypertension.

2.4.7. Quality sensitivity analyses

I performed a sensitivity analysis to examine the SEP-HM associations, grouped by four study features:

(i) Inequality measure (simple versus complex).

(ii) Age adjustment (yes versus no).

(iii) Documentation of response levels to the survey (yes versus no).

(iv) Study sample size for hypertension management indicators (n of participants with hypertension, grouped into categories).

The results are shown in Table 2.7. SEP-HM associations (evaluated by Pearson's chi-squared test) were statistically significant in each quality test. The proportions of statistically significant SEP-HM associations were higher when complex (versus simple) measures of inequality (p=0.003) and age adjustment (versus no adjustment) (p=0.001) were used. The proportion of statistically significant associations was higher in studies that reported the levels of response to the survey (p=0.003). Of the associations in studies with 500 or fewer participants, 94% of the SEP-HM associations were null compared with 36% of the SEP-HM associations among studies with over 2,000 participants (p<0.001).

Table 2.7: Sensitivity analysis for the SEP-HM associations.

Study feature		n	Pro-poor (%)	Null (%)	Pro-rich (%)	p-value
Statistical method	Simple	133	5	71	25	0.003
	Complex	49	16	47	37	
Response rate	Not reported	95	7	54	39	0.003
	Reported	87	8	76	16	
Adjusted by age	No	96	6	77	17	0.001
	Yes	86	9	50	41	
Sample size	0-500	31	3	94	3	<0.001
	501-2,000	81	5	78	17	
	>2,000	70	13	36	51	

SEP-HM: inequalities by socioeconomic position in hypertension management. Row percentages are shown. P-values from Chi-square tests. Study sample size for hypertension management indicators.

2.5. Discussion

2.5.1. Main findings of the systematic review

The 'rule of halves' as the rule for levels of hypertension management in LACCs?

The *rule of halves* establishes that approximately half of patients with high BP are undiagnosed, half of those diagnosed are untreated, and half of those treated have uncontrolled BP levels.[140, 141] This rule is not the current reality for HICs nor LMICs. Evidence suggests that HICs have improved their levels of hypertension management in recent decades, presenting levels of undiagnosed, untreated, and uncontrolled hypertension of around 30%.[142] However, hypertension management levels in LMICs have remained well below optimal.[34, 99, 132, 137, 143] Most of the articles included in this review reported levels of hypertension management (i.e. awareness, treatment, and control) below 50%. The lower levels of hypertension management in LACCs affect all SEP groups (though not necessarily equally) and suggest pervasive problems, such as under-diagnosis, barriers to accessing appropriate treatment, and the provision of inadequate treatment (e.g. ineffective drugs, inadequate dosing, improper combinations of drugs) or non-adherence to antihypertensive treatment. More research is needed to understand the determinants of the low levels of hypertension management in LACCs.

Socioeconomic inequalities in hypertension management in LACCs

Inequalities in hypertension that favour the most advantaged are magnified by pro-rich inequalities in levels of awareness, treatment, and control. The lack of information on SEP inequalities in hypertension management is a barrier to reducing both the burden of hypertension and its unequal distribution. To the best of my knowledge, this is the first systematic review of the literature on socioeconomic inequalities in hypertension management in LACCs. However, SEP-HM associations could only be evaluated to date in 12 of 19 LACCs. I found a mixture of pro-rich and pro-poor associations. Based on ordinal measures (financial resources and educational status), a large proportion of the SEP-HM associations (64%) were null. Some of the null associations among LACCS may be genuine, i.e. suggesting equality by SEP groups for some of the hypertension management indicators. However, it is important to note that null associations do not necessarily imply *true* equality. Null associations could arise if SEP inequalities in hypertension management were not linear or due to analyses being underpowered due to small numbers in comparison groups or small analytic samples. Specifically, achieving sufficient statistical power to detect *true* differences in levels of hypertension management across SEP groups can be difficult for subgroup analyses of nationally-representative HES data.[144] Medium to large differences in levels of awareness, treatment, and control between SEP groups may fail to achieve statistical significance if the sample sizes among those with hypertension are small to moderate.[145]

Most research to date has analysed BP control among persons with hypertension as the key indicator of hypertension management, followed by awareness, and treatment among persons with hypertension. Educational level, financial resources (i.e. income), employment, and occupation were used to evaluate SEP inequalities in levels of hypertension management.

My review has found that most evidence on SEP-HM among LACCs is based on data collected in the last two decades. Patterns in socioeconomic inequalities in hypertension management are perhaps more complex and challenging to interpret than those for hypertension prevalence. The direction of inequalities (pro-poor, null, or pro-rich) in LACCs differs considerably by outcome, country, year of data collection, gender, and marker of SEP. Nevertheless, there are some underlying patterns in the body of evidence to date.

SEP inequalities in diagnosed hypertension

Regarding self-reported diagnosed hypertension, the proportion of pro-rich associations was higher than pro-poor. The lower levels of diagnosis in low SEP groups demonstrates the importance of measuring BP within nationally-representative HES and of not relying exclusively on self-reported diagnosed hypertension or surveys conducted solely among users of healthcare services.[146]

SEP inequalities in treated hypertension

Regarding treatment, inequalities were found using persons with hypertension as the denominator, but not when the denominator was restricted to those who were aware. The latter finding could reflect lower statistical power (i.e. smaller samples when restricted to those with diagnosed hypertension: especially if levels of diagnosis were low). Alternatively, it could be that after limiting the denominator to those with a previous diagnosis (and so have had some access to healthcare), there is more of an equal distribution between SEP groups in levels of treatment (especially if there are no costs for treatment). Mixed results of financial resources-treatment(H) associations were reported, with pro-rich associations reported in Mexican and Colombian populations, possibly reflecting the unaffordability or the unavailability of cardiovascular drugs for those in lower SEP groups.[147–149]

SEP inequalities in controlled hypertension

Regarding BP control, there was a tendency to find more pro-rich than pro-poor associations when the denominator comprised those on treatment. Having higher financial resources could improve access to better treatment (e.g. more optimal combinations and dosage of drugs) or improve adherence to treatment compared with having fewer resources.[150] Each SEP-control(A) association found in this review was from Mexican populations: one pro-rich (2003), and one pro-poor (2006).[114] Potentially, this shift in the direction of associations could have resulted from the increase in health insurance coverage that occurred in Mexico with the health reform of 2003, when the 'System for Social Protection in Health' began.[151]

2.5.2. Country-specific SEP-HM associations

As reported by Murphy et al. (2016), differences between countries in levels of health-care expenditure (e.g. as a % of GDP) are a reliable predictor of inequalities in the treatment coverage of secondary prevention for CVD.[147] According to my review, Mexico was the LACC with the most research to date on SEP-HM inequalities, and one with the highest proportion of pro-rich associations. This could be related to its lower health care expenditure compared with other LACCs: according to World Bank data, Mexico in 2016 spent 6% of its GDP on health, while the other countries included in my review spent an average of 7%.[10] Furthermore, as mentioned earlier, some evidence suggests that SEP-HM inequalities have changed over time within countries, including Mexico, where the proportion of pro-rich associations decreased between 2000 and 2016. Health expenditure increased in Mexico from 5% of GDP in 2000 to 6% in 2016;[10] this agrees with the report by Sousa et al (2019) of lower SEP inequalities in hypertension and in diabetes management using more up-to-date HES data.[114] Other factors must be considered to better understand the change in inequalities in hypertension management indicators over time within countries, including policies to reduce SEP inequalities, and the implementation of a universal health system, as discussed below.

Differences in the pro-poor or pro-rich associations between countries could be related to the degree of implementation of a universal healthcare system. Atun et al. (2015) developed an index (ranging between 0 and 100) to summarise the level of universal coverage per country based on 23 specific health conditions, including diabetes and ischaemic heart disease (IHD).[152] The authors of that study could not develop an index for hypertension because of the inferior quality or quantity of the data. As a proxy for hypertension, the IHD indices for the LACCs included in my systematic review were as follows: Chile (98), Peru (93), Uruguay (87), Costa Rica (80), Ecuador (80), Argentina (79), Colombia (73), Brazil (66), Mexico (64), Nicaragua (56), Cuba (52) and Trinidad and Tobago (47).[153] Overall, studies from LACCs with a higher IHD index (i.e. greater evidence of a more universal health care system) reported more frequent pro-rich associations (Chile, Colombia, Costa Rica, Cuba, Peru and Mexico), on the contrary, studies from countries with higher pro-poor associations (Argentina, Brazil, Mexico, and Trinidad and Tobago) showed a lower IHD index. This counterintuitive finding could be related to the *inverse equity hypothesis*, which shows that newly introduced health interventions (e.g. health services provided in the universal healthcare system among LACCs) are likely to first bring more benefit to the socially privileged population.[154]

2.5.3. Financial resources and educational status as SEP measures

My review found a higher proportion of pro-rich and pro-poor associations with financial resources (income, wealth) as the SEP measure when compared with using educational status. However, the distribution of associations changed between countries and mixed results within a country were found when comparing these SEP measures.[155] For example, studies of the Brazilian population showed mixed results in SEP-HM associations: null associations were found using financial resources as the SEP measure, whilst pro-rich associations were found using educational status.[121] The universal public health system in Brazil and its Family Health Strategy deliver targeted health care to individuals with low incomes,[156] with a demonstrated reduction of inequality in levels of access to healthcare.[157] Conventional treatments are often free, and the programme provides community-based services, improving healthcare access and treatment adherence for those with fewer resources.[156] In this way, in Brazil and in other countries with universal coverage and strategies to reduce socioeconomic inequalities in health and in health care, financial resources (as measured for example through current income) might not be the primary driver of inequalities in hypertension management.[101]

However, differences in educational status might impact levels of access to the healthcare system and levels of treatment adherence, with more educated groups having not only higher levels of economic and financial resources but also higher levels of knowledge about health conditions, health-related behaviours, and more social and psychosocial resources than the least educated.[158] This may be particularly important as hypertension is frequently asymptomatic in its early stages and, as a result, educational status is an important factor in influencing the likelihood of diagnosis among persons with high BP.[159]

A few articles that evaluated both income and educational-based inequalities in hypertension outcomes (prevalence and management indicators), reported differences by educational status but not by income.[121, 126, 133] The null SEP-control(T) associations with income but significant associations using educational status reported by Camacho et al. (2016) could be explained at least in part by the limitations of income as a SEP measure: levels of income can be unstable over time (especially among younger and older age groups), while the highest level of educational attainment is normally completed in early adulthood. Furthermore, income is usually more difficult to register accurately (one survey participant is typically asked to report on the income of each household member) and typically contains more missing data than educational status.[5]

More research is needed to understand the pro-rich inequalities in levels of controlled hypertension reported in Cuba, a country well-known for its low levels of inequality and high levels of education and healthcare.[160] Those findings were not discussed by the authors.[128]

2.5.4. Occupation and employment as SEP measures

Little research has been conducted in LACCs on SEP-HM associations using occupation and employment as SEP measures. The articles I found did not report age-adjusted results, making it difficult to interpret the findings.

2.5.5. Gender-specific SEP-HM associations

Recent studies from outside LACCs have further highlighted the need for gender-specific analyses of SEP inequalities in hypertension and its management indicators.[161, 162] For instance, Scholes et al. (2020) using data from the Health Survey of England (HSE) 2011-2016 (pooled data to maximise sample sizes), reported statistically significant income-related inequalities in hypertension among women only, while men in low-income households had a marginally lower probability of being undiagnosed than men in high-income households (no income difference in undiagnosed hypertension was found among women).[162]

Consequently, there is no reason to expect SEP-HM associations to be similar for males and females in LACCs. Reports of gender-specific variations in SEP-HM associations within LACCs were scarce. I identified five studies reporting SEP inequalities by gender.[114, 115, 124, 127, 135] Since only a few studies reported gender-specific associations (and with mixed results), no definitive conclusions on gender differences in the direction of SEP-HM associations can be made. Rubinstein et al. (2016) reported (pro-rich) income-based inequalities in controlled hypertension among males but not among females.[115] On the other hand, Gutierrez et al. (2016) and Laux et al. (2012) reported SEP inequalities in controlled hypertension only among females.[114, 135] None of the five articles discussed potential explanations for the observed gender differences in SEP inequalities in these hypertension management indicators. Nevertheless, the evidence related to differences in SEP inequalities by gender in this review and elsewhere highlights the need to report SEP-HM associations separately by gender and investigate the reasons for observed gender differences.[159, 163, 164]

2.5.6. Main statistical methods used to evaluate SEP-HM associations

It is recommended to use complex measures (e.g. SII, RII) to quantify the magnitude of inequalities in health since they consider information on all SEP groups (not just the extremes) and reflect the direction of the gradient (assuming a linear association).[108, 165] However, simple measures that do not consider the entire SEP spectrum (e.g. pairwise comparisons such as odds- or prevalence-ratios) should also be reported as such evidence is more suitable to a broader, non-technical audience, including policy makers.[166] The SII, the RII, and the concentration index were the only complex measures of inequality reported in the studies included in this review.

Furthermore, it is recommended to report both absolute and relative measures of inequality when feasible as they represent different aspects of inequality.[167–169] Presenting both provides a complete picture as inequalities can be higher on the relative rather than absolute scale if the overall levels of an outcome are low.[170, 171] This is also important in the assessment of changes in inequalities over time: an unbiased assessment requires using both absolute and relative measures of inequality.

2.5.7. Strengths and limitations of the systematic review

A strength of my review is the systematic exploration of different indicators of hypertension management and of SEP in LACCs. However, some limitations should be considered when interpreting the results. Due to the small number of articles quantifying the magnitude of associations and the heterogeneity in statistical approaches, a meta-analysis (i.e. a quantitative statistical procedure that estimate an overall effect, by integrating data of relevant independent studies considered to be combinable) could not be performed. Therefore, only the statistical significance of the SEP-HM associations was evaluated in this review.

Although several null findings were reported in the reviewed studies, publication bias remains a potential limitation. Hypertension management outcomes were evaluated among persons with hypertension or a subset of them (e.g. among those treated). Because of the low sample sizes typically available in national HES, most associations were likely to be statistically underpowered to some extent. In contrast to HICs such as England and the United States which collect data continuously (and so data can be pooled across years to maximise sample sizes), surveys in LACCs are typically conducted about once every five years.

This could explain at least in part the high proportion of null associations. According to this review, there was a tendency for a higher percentage of null associations when sample sizes to estimate hypertension management indicators were relatively small (<500). This is especially important when the SEP indicator is used in the analysis as a categorical rather than a continuous variable (statistical power is higher for the latter)[172] or by analysing subgroups (e.g. gender-specific analyses). Moreover, sample sizes may be reduced by lower response rates in the study population, which are often differential across SEP groups (usually lower in disadvantaged SEP groups).[173, 174] However, most population-based surveys try to compensate for any observed SEP bias in non-response through weighting adjustments.[175–177]

By analysing data at the SEP-HM association level (rather than study level), more weight was given to those studies that reported more associations. Also, I summarised SEP-HM associations in a single analysis that, in some cases, covered a reasonably long time period (e.g. 2000-2016 in Mexico). This could have masked changes over time within a country in levels of hypertension management, SEP distributions, and SEP-HM associations.

Other methodological differences between the included studies could also have influenced the results. The sensitivity analysis within this review helped to some extent to understand how some of these differences affected the main conclusions about SEP-HM associations in LACCs. For example, a larger proportion of pro-poor and pro-rich associations (over null results) were described when analyses were age-adjusted and were summarised using complex rather than simple measures of inequality.

2.5.8. Gaps and implications for my PhD research

This systematic review has highlighted the need for country-specific analyses within the LACC region, as differences in economic circumstances and in levels of healthcare provision and access prevent extrapolation of data from other countries. The differences in the direction of the SEP-HM associations related to the choice of SEP measure highlight the importance of evaluating inequalities in hypertension management using several SEP measures. The articles included in this review only used education level, financial resources (mainly current income), occupation, and employment as the SEP measure. However, a more comprehensive understanding of SEP inequalities in hypertension management by more contemporary markers of economic status is important. In Chapter 5 of this thesis, I present results using educational status and financial resources (income) as measures of individual-level SEP, but I also present results using health insurance status.

Furthermore, as the SEP-HM associations could change in magnitude and/or direction over time within the same population,[164] it is relevant to analyse whether any inequalities in hypertension management outcomes have changed over time in Chile using data from the three available ENS (2003, 2010, and 2017).

The most advanced statistical methods were the SII, RII, and concentration index; however, no studies presented inequalities on both the absolute and relative scales (and using both simple and complex measures) as recommended in the health inequalities literature.[167] In Chapters 5 and 6, I report both simple and complex measures of inequalities on the absolute and relative scales.

Only a few articles reported SEP-HM associations stratified by gender. As shown in my review and based on evidence outside of LACCs, SEP-HM associations can be gender specific and should be systematically evaluated. In Chapters 5 and 6, I estimate gender differences in socioeconomic inequalities in HM, although such analyses have lower statistical power than those which combine data across genders (and so might mask gender differences in SEP-HM associations).

2.6. Conclusion

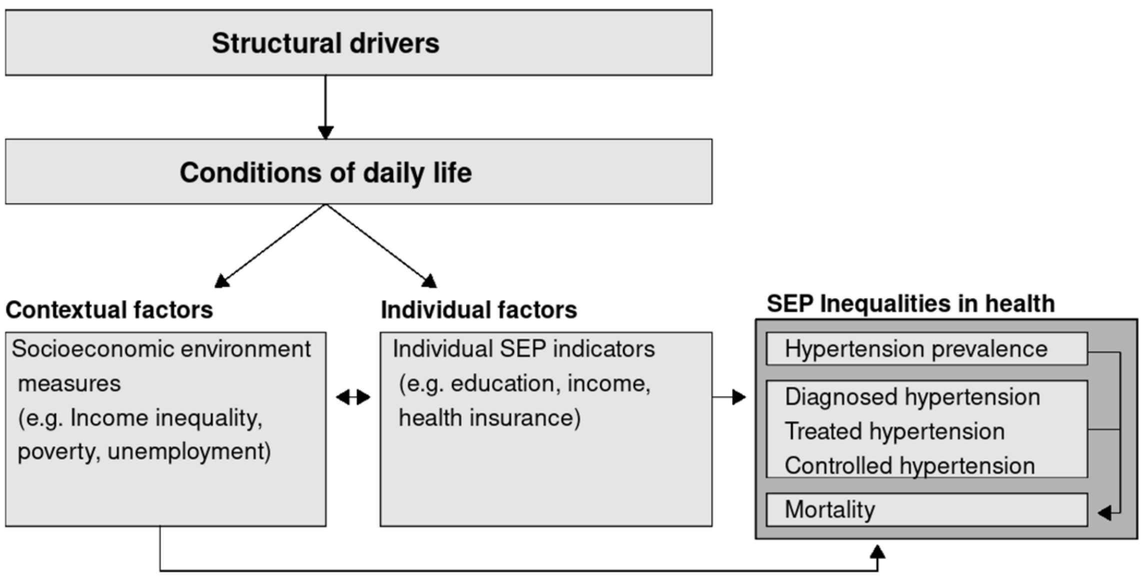
In summary, levels of awareness, treatment, and control differ widely within LACCs. Empirical data on SEP inequalities in levels of hypertension management are scarce in LACCs. The directions (pro-poor, null, and pro-rich) of inequalities in diagnosed, treated, and controlled hypertension are mixed and vary according to factors including choice of SEP measure; outcome definition (choice of denominator); year of data collection; and summary measure of inequalities. There is a clear need for an in-depth understanding of the magnitude and the direction of socioeconomic inequalities in hypertension management in Chile, and whether such inequalities have persisted over time. This is the principal topic of my PhD.

Chapter 3: Research justification, aims, and ethical considerations

3.1. Conceptual framework

In Chapter 1, I described the concept of the social determinants of health (SDH), along with the relevance of hypertension worldwide and in Chile. In Chapter 2, I evaluated the evidence on SEP inequalities in hypertension management in LACCs. In this brief chapter, I include three main hypertension-related outcomes (Figure 3.1 below) to the PAHO's adaptation of the WHO's conceptual framework on the SDH that was set out earlier (Figure 1.1, Chapter 1). This conceptual model helped to formulate the research problems, aims, objectives and hypotheses that informed the following four empirical chapters.

Figure 3.1: Conceptual model of the study.



The framework distinguishes between three main outcomes: (i) hypertension prevalence, (ii) the three key hypertension management indicators (diagnosed, treated, and controlled hypertension), and (iii) mortality. Mortality was included in the conceptual framework since indicators of SEP, hypertension as a condition (chronic disease), and having diagnosed, treated, and controlled hypertension have separately been associated with mortality.[178–181] I placed these three main hypertension-related outcomes in separate boxes because those factors potentially associated with SEP inequalities in hypertension management may differ from those related to SEP inequalities in hypertension and from those associated with the risk of all-cause and cardiovascular mortality.

The framework distinguishes between *individual* and *contextual* factors. Individual factors include the individual-level SEP indicators covered in the systematic review of inequalities in hypertension management in LACCs (e.g. education and income) but also include those particularly relevant to the Chilean context (i.e. health insurance). Contextual factors, including *socioeconomic environment measures* (e.g. those summarising the socioeconomic level of a region or county), are also included to capture factors that potentially influence inequalities in each hypertension related outcome over and above those accounted for by individual-level SEP factors. The framework sets the scene for the four empirical chapters of my PhD by illustrating the importance of statistically controlling and quantifying the impact of potential confounders or moderators (e.g. survey year, age, gender) on the magnitude and direction of SEP-inequalities in these outcomes.

3.2. Research problems

More specifically, the four research problems outlined below will be the focus of the empirical chapters:

- Available evidence on hypertension prevalence and management in Chile is limited to health survey data from 2003 and 2010.[22, 23] Therefore, more up-to-date research using data from the most recent ENS2017 is needed to update evidence on the hypertension outcomes and to evaluate whether (and if so, how) the most recent secular changes modify the national picture of the prevalence and management of hypertension in Chile.

- Chilean evidence has shown SEP inequalities in hypertension prevalence.[65] However, information on SEP inequalities in hypertension management indicators (diagnosis, treatment, and control) in Chilean adults is only partially known.
- Chilean evidence about educational-based inequalities in hypertension outcomes using a multilevel approach is available for hypertension prevalence in 2003 and 2010 only.[65] Therefore, up-to-date research based on multilevel modelling using ENS2017 data and extending the focus to other hypertension outcomes (i.e. undiagnosed, untreated, and uncontrolled hypertension) is needed.
- There is no information available on the differences in all-cause and cardiovascular mortality rates in the Chilean adult population by hypertension nor by individual educational level.

3.3. Aims

Related to these research problems, the overarching aim of my thesis is to:

Examine socioeconomic inequalities in hypertension prevalence and in aspects of its management (undiagnosed, untreated, and uncontrolled hypertension) in Chile.

The aims of the following four empirical chapters are:

- To quantify gender-specific secular changes in hypertension prevalence and in diagnosed, treated, and controlled hypertension; to quantify the impact of lowering BP thresholds on these hypertension outcomes; and to estimate levels of controlled hypertension using a disease-specific BP goal (**Chapter 4**).

- To examine the gender-specific magnitude of SEP inequalities in hypertension prevalence and in undiagnosed, untreated, and uncontrolled hypertension, and their change over time in Chilean adults since 2003, using individual-level measures of SEP. (**Chapter 5**).
- To contextualise gender-specific individual-level educational inequalities in hypertension and in hypertension management indicators in Chilean adults in 2003, 2010, and 2017 by considering the role of socioeconomic environment measures using a multilevel analytical approach (**Chapter 6**).
- To evaluate gender-specific associations between (i) hypertension status and (ii) individual-level educational status on all-cause and cardiovascular mortality. (**Chapter 7**).

The specific objectives and hypotheses for each aim are stated within the relevant chapter.

3.4. Ethics approval and consent to participate

The Ethics Committee of the Pontificia Universidad Católica de Chile (PUC) approved the study protocol for this PhD (IDs: 200205003 and 211116004, certificates provided in Appendices 4 and 7). The PUC ethics committee and the Chilean Ministry of Health approved the Chilean National Health Survey (ENS) study protocol and ethical consent forms (ENS2003: number not retrieved; ENS2010 ID: 09-113; ENS2017 ID: 16-019). Persons selected for inclusion in the Chilean health surveys provided informed and signed consent before participation.

Chapter 4: Secular changes in the prevalence and management of hypertension among adults in Chile

4.1. Introduction

This chapter presents nationally-representative cross-sectional estimates of hypertension prevalence and in indicators of its management (awareness, treatment, and control) in Chile, and examines changes in these over time, through an analysis of data from the three most recent National Health Surveys (ENS 2003, 2010, and 2017). An article based on the main findings from this chapter (*"Hypertension care cascade in Chile: a serial cross-sectional study of national health surveys 2003-2010-2017"*) was published in *BMC Public Health* in 2020.[111]

As described in Chapters 1 and 2, hypertension (sustained high BP) continues to be one of the most important health challenges, being a major risk factor for cardiovascular morbidity and mortality worldwide.[27, 28] Recent trends show decreasing levels of BP on average in most world regions.[33] The decrease in average BP levels has occurred at the same time as increasing levels of major risk factors for high BP, including high BMI, and persistently high levels of other risk factors, such as high salt consumption and insufficient physical activity. Furthermore, according to the NCD Risk Factor Collaboration (NCD-RisC), the decrease in average BP levels at the population level between 1975 and 2015 was only partially explained by the increase in hypertension treatment levels.[33] Although evidence of trends in BP levels by antihypertensive treatment status is scarce, some studies have reported a decrease in average BP levels at the population level in both treated and non-treated participants.[142, 182] Differences in hypertension outcomes by levels of macroeconomic development were also reported in Chapters 1 and 2, with the prevalence of raised BP falling in HICs and in some MICs, whereas it has remained unchanged elsewhere.[34]

To date, there is scarce evidence of recent secular changes in the three key hypertension management indicators from countries such as Chile, which have experienced fast epidemiologic transitions. To the best of my knowledge, no studies to date in LACCs have quantified changes over time using nationally-representative data, measured BP data, and only one study (in Peru) has assessed the implications of lowering BP thresholds in line with the 2017 ACC/AHA guidelines (as described in Section 1.3), albeit using an indicator of high BP alone.[183] In addition, Chilean GES-hypertension guidelines suggest using a more aggressive BP goal among patients with hypertension and accompanying *high-risk* comorbidities (prior stroke or infarction, diabetes mellitus (DM), or chronic kidney disease (CKD));[54] levels of BP control based on this guideline have not been reported in Chile to date. Therefore, up-to-date evidence on (i) changes over time in hypertension prevalence and indicators of its management, and (ii) levels of hypertension and BP control based on different BP thresholds is required.

4.2. Research problem, aim, objectives and hypotheses

Problem

Available evidence on hypertension prevalence and management in Chile is limited to health survey data from 2003 and 2010.[22, 23] Therefore, more up-to-date research using data from the most recent ENS2017 is needed to update evidence on the hypertension outcomes and to evaluate whether (and if so, how) the most recent secular changes modify the national picture of the prevalence and management of hypertension in Chile.

Aim

Using data from three nationally-representative Chilean HES covering a 15-year period (2003, 2010, 2017), this chapter aims to quantify gender-specific secular changes in hypertension prevalence and in diagnosed, treated, and controlled hypertension; to quantify the impact of lowering BP thresholds on

these hypertension outcomes; and to estimate levels of controlled hypertension using a disease-specific BP goal.

Specific objectives

The specific objectives for this empirical work are as follows:

- Estimate levels of hypertension prevalence and of each hypertension management indicator (awareness, treatment, and control) in 2003, 2010, and 2017.
- Describe differences in levels of hypertension prevalence and of each hypertension management indicator by gender, age group, and urban/rural residence.
- Estimate changes over time in levels of hypertension prevalence and of each hypertension management indicator by gender.
- Estimate changes over time in mean levels of SBP and DBP by gender and treatment status.
- Estimate hypertension prevalence and levels of each hypertension management indicator, applying lower BP thresholds.
- Estimate levels of controlled hypertension based on a disease-specific BP goal.

Hypotheses

The three main hypotheses for this empirical work are:

- **H4.1**: Hypertension prevalence decreased over time for both genders.
- **H4.2**: Hypertension awareness, treatment, and control levels increased over time for both genders.
- **H4.3**: Mean BP levels decreased over time among treated and non-treated adults.

4.3. Methods

4.3.1. Study design and setting

This chapter is based on analyses of cross-sectional data from the three most recent Chilean National Health Surveys (ENS 2003, 2010, 2017). The study designs were similar for the three surveys. First, ENS2003 participants were selected using a stratified random subsample from participants of the Quality of Life and Health Survey 2000.[184] The Quality of Life and Health Survey's sampling frame was household information from the National Census of 1992, and sampling was carried out by a stratified and cluster design. The subsample of participants for the ENS2003 was selected using the same age-gender-regional structure of the original sample frame, except for the oversampling of the Bio-Bío Region, where additional funds from PAHO were available to increase the sample size. Fresh samples were selected for the 2010 and 2017 surveys based on stratified cluster sampling. Sampling for these two surveys was based on the master sample frame of the Chilean National Institute of Statistics and the Population and Housing Census of Chile (2002).

Each ENS was a nationally-representative cross-sectional survey of the free-living general population aged ≥17y (2003) or aged ≥15y (2010 and 2017). In this chapter, my analytical sample was restricted to those aged ≥17y. Institutionalised and non-Spanish speaking individuals were excluded. Respondents who were pregnant at the time of the survey were also excluded. Persons aged ≥65y were oversampled in each ENS. Within selected households, one eligible person was randomly selected for interview using a Kish grid.[185] ENS survey instruments and protocols are described in more detail elsewhere.[175]

4.3.2. Data collection

Similar methods of data collection were used across the three surveys. In the first home visit, a trained interviewer applied health questionnaires face-to-face via Computer-Assisted Personal Interview. Participants provided demographic information, including their date of birth (age was calculated on the day of the first interview), gender (assigned by the interviewer as male or female) and residential address. The address was classified into urban-rural residence, as defined by the Chilean National Statistics Institute (INE). The INE defines urban as an area with >2,000 inhabitants, or between 1,001 and 2,000 inhabitants when less than half of the population is economically active in primary activities; rural otherwise.

The interviewer also applied the following questions regarding **hypertension awareness**: *“Have you ever been told by a doctor, nurse or healthcare provider that you have high blood pressure?”* and **hypertension treatment** (regardless of awareness): *“Are you currently under a treatment programme prescribed by a health professional to keep your blood pressure under control?”*. Participants who reported that they were on treatment were asked about the type of treatment (response options: medications, treatment without medication, or both). Self-reported history of doctor-diagnosed infarction, stroke, and diabetes mellitus (DM) was obtained through the questions: (i) *“Have you ever been told by a doctor that you had or have suffered a heart attack?”*; (ii) *“Have you ever been told by a doctor that you had or have suffered a vascular accident or cerebral thrombosis (or stroke)?”*; and (iii) *“Have you ever been told by a doctor, nurse or healthcare provider that you have diabetes (high blood sugar)? (other than during pregnancy)”*, respectively.

During the second visit, a trained nurse measured BP, recorded the medications that participants were currently using (prescribed or not) and performed biological sampling (including a fasting blood sample). Sitting BP was measured after a five-minute rest using an upper arm monitor (Omron, Healthcare Co Ltd, Kyoto, Japan: models HEM713C, HEM742 and HEM7200 in 2003, 2010, and 2017, respectively) with appropriately sized arm cuffs, with a two-minute pause between readings. In 2003, two BP readings were taken, while three readings were taken in 2010 and 2017. To ensure like-for-like comparisons, I used the mean of the first- and second-readings in each year in my main analysis. I decided at the outset of the present study that this approach would provide the most accurate estimate of the change in levels of hypertension across the three surveys, giving more value to the reproducibility of the results to estimate changes over time.[186]

Medications were collected via a detailed inventory and classified using the ATC classification system.[187]

Kidney function was evaluated by measuring blood creatinine, used to calculate the estimated glomerular filtration rate (eGFR) according to the updated *modification of diet in renal disease* (MDRD) equation.[188, 189]. Further details about ENS laboratory procedures and blood creatinine are available elsewhere.[190]

4.3.3. Definitions of hypertension outcomes

Hypertension

Hypertension was defined as BP ≥140/90 mmHg or use of antihypertensive medication (the most common definition found in my systematic review in Chapter 2). Estimates of hypertension prevalence vary by choice of high BP cut-points.[36] As described in Chapter 1, the ACC/AHA in 2017 recommended lowering the (clinic-based) BP threshold from 140/90 mmHg to 130/80 mmHg.[36] In this chapter, I evaluate the potential impact of implementing this lower BP threshold by comparing two different definitions of hypertension. First, I identified participants with hypertension based on the JNC 7 guideline: BP ≥140/90 mmHg or use of antihypertensive medication.[37] Secondly, I identified participants with hypertension based on the 2017 ACC/AHA guidelines: BP ≥130/80 mmHg or use of antihypertensive medication.[36] Comparing these two definitions provides evidence on the potential changes in hypertension prevalence that the adoption of the 2017 ACC/AHA guidelines could bring to Chile.

Hypertension management indicators: standard definitions

I focused on three management indicators: awareness, treatment, and control. I used standard definitions,[35, 191] in use by the Chilean GES-hypertension guidelines,[54] and by the studies included in my systematic review of SEP inequalities in levels of hypertension management in LACCs (Chapter 2). Among those participants with survey-defined hypertension, I defined: (i) **awareness** as the report of prior diagnosis of high BP by a healthcare professional; (ii) **treatment** as the use of antihypertensive medication as identified in the medicine inventory (ATC codes: C02, C03, C07, C08, C09); and (iii) **control**: BP <140/90 mmHg.

4.3.4. Statistical analyses

Only participants aged ≥17y were included in the analyses, to ensure comparability across the three surveys. The final analytical sample excluded a total of n=1,350 (n=198; 447; and 705 in 2003, 2010, and 2017, respectively) participants with missing values for BP or treatment (most of these were interviewed but did not receive the follow-up nurse visit). Analyses were weighted using the weights available on the datasets which account for differences in selection probability (i.e. selection of one person per household and oversampling of those aged ≥65y) and differences in non-response rates. P-values <0.05 were classified as statistically significant (two-tailed), but I also interpret p-values as continuous values in order to avoid using an arbitrary cut-point.[192] All analyses were conducted in R (version 4.0.4) accounting for the complex survey design of the ENS. I conducted seven main statistical analyses described in turn below.

I. Sample characteristics

I summarised the sociodemographic profile of the analytical sample by demographic characteristics (age in three categories: 17-44y; 45-64y and ≥65y years, gender, and urban-rural residence) and estimated mean levels of SBP and DBP in each survey amongst all participants with valid BP and medicine data.

II. Hypertension and indicators of its management

I estimated levels of hypertension prevalence and, amongst those classified as hypertensive (JNC 7 guideline), I estimated levels of hypertension awareness, treatment, and control. Levels of each hypertension outcome with accompanying 95% confidence intervals (95% CIs) were described by survey year, gender, age group, and urban-rural residence. In this chapter, descriptive values were not age-standardised in order to present the current burden of hypertension.[35]

III. Age-adjusted differences in hypertension and its management indicators by gender, and urban-rural residence

To estimate differences in outcomes by gender, and urban-rural residence, I used logistic regression models on pooled 2003-2010-2017 data (to obtain a general estimate and increase statistical power) with adjustments for age (continuous variable) and survey year (as a three-level factor: 2003, 2010, and 2017). Analysis of differences by urban-rural residence were further adjusted for gender. Results were summarised using Odds Ratios (ORs) with accompanying 95% CIs.

IV. Age-adjusted secular changes in hypertension and its management indicators by gender

Pooling data across years, I used age-adjusted logistic regression to estimate the gender-specific changes over time in hypertension (JNC 7 guideline). Among those with hypertension, I used age-adjusted logistic regression to calculate gender-specific changes over time in awareness, treatment, and control. In each analysis, survey year was entered into the models as a three-category independent variable and age as a single continuous variable. Most of the models were gender-specific, however, to provide an overall picture for all adults, I also ran models that pooled data across genders (further adjusted for gender). Pairwise comparisons were used to evaluate change in outcomes over time (i.e. 2010 vs 2003; 2017 vs 2010; and 2017 vs 2003). Results were summarised using ORs with accompanying 95% CIs.

V. Age-adjusted secular changes in mean BP levels by gender and treatment status

Age-adjusted linear regression models were used to test for significant changes over time in mean levels of SBP and DBP by gender (regardless of treatment and separately by treatment status). Pairwise comparisons were used to evaluate changes in the outcomes over time. I reported absolute differences in mean SBP and DBP with accompanying 95% CIs.

VI. Hypertension prevalence based on lower BP thresholds

I quantified the difference in hypertension prevalence and in levels of awareness, treatment, and control between the current (JNC 7) and proposed (2017 ACC/AHA) guidelines.[36, 37] Participants in ENS2017 were classified into one of four mutually exclusive groups. According to the JNC 7 guidelines, these groups were defined as follows: (i) **normotensive** (<140/90 mmHg, not on treatment); (ii) **treated and controlled** (<140/90 mmHg); (iii) **treated, but uncontrolled** (≥140/90 mmHg); and (iv) **untreated** (≥140/90 mmHg). The corresponding classification using the 2017 ACC/AHA guidelines used the 130/80 mmHg threshold. Applying the 2017 Chilean census data to the ENS2017 data,[193] I estimated the number of additional adults who would be eligible for treatment based on the 2017 ACC/AHA guidelines.

VII. Controlled hypertension based on a disease-specific BP goal

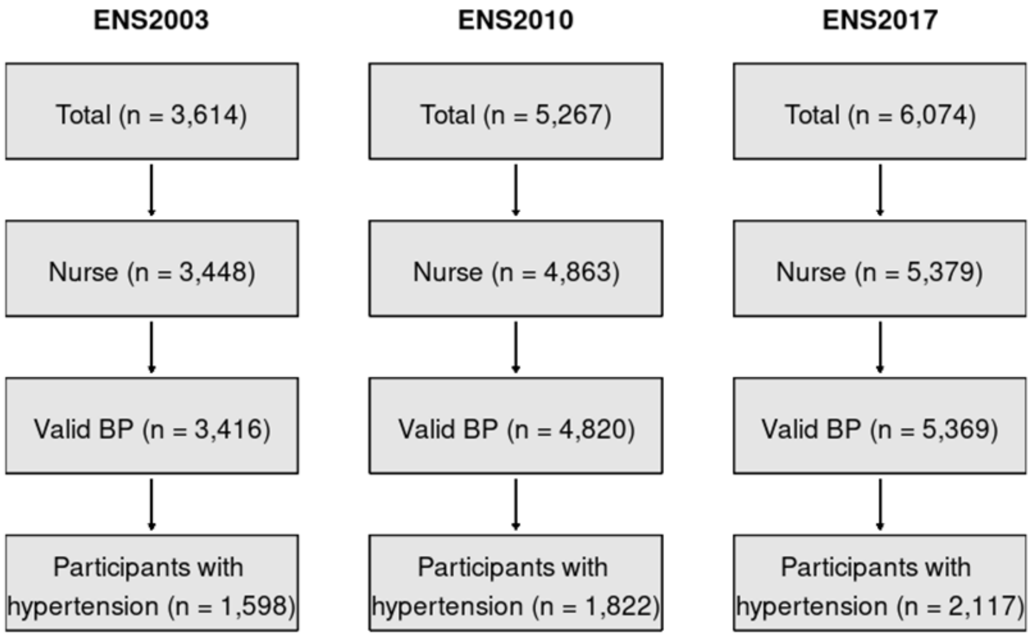
The Chilean GES-hypertension, JNC 7, and 2017 ACC/AHA guidelines consider a different BP goal for people with hypertension and very high CVD risk (prior stroke or infarction), DM, or CKD.[36, 37, 54] I estimated levels of controlled hypertension among ENS2017 participants with hypertension and with at least one comorbidity (*high risk*) and with no comorbidities (*not high risk*). The high-risk group had at least one of the following three comorbidities: (i) very high CVD risk: those with self-reported previous stroke or infarction, (ii) self-reported doctor-diagnosed DM; and (iii) CKD: identified as an estimated eGFR >15 and <60 mL/min/1.73m². Two definitions of controlled hypertension were compared: (i) **control (general definition)**: BP <140/90 mmHg for all adults (i.e. those with and without high risk); and (ii) **control (disease-specific definition)**: BP <130/80 mmHg for those with high risk and BP <140/90 mmHg for those with no high risk. In this way, any decrease in levels of controlled hypertension is the result of the subset of adults with very high risk who achieve BP control under the standard definition (<140/90 mmHg) but not under the more aggressive disease-specific BP goal (<130/80 mmHg). For this set of analyses, ENS participants with missing data on any of the three comorbidities used to classify adults as high risk were excluded.

4.4. Results

4.4.1. Sample characteristics

The number of selected households (and response rate) for ENS 2003, 2010, and 2017 were 5,469 (63%); 7,212 (75%); and 9,901 (67%), respectively. Overall, 3,614; 5,267; and 6,074 adults aged ≥17y participated in the ENS 2003, 2010, and 2017, respectively (Figure 4.1). The analytical sample (valid BP and medicine data) comprised 13,605 adults: 3,416; 4,820; and 5,369 for the three surveys, respectively.

Figure 4.1: Flowchart of participants in the study.



Valid BP: valid blood pressure (BP) and medicine data.

Summary statistics of the sociodemographic profile, as well as mean levels of SBP/DBP in each survey year, are reported in Table 4.1. Characteristics were similar across the three surveys. However, there was a slight increase over time in the proportion of participants in the older age groups, those residing in urban settings, and a small decrease in mean SBP and DBP levels.

Table 4.1: Analytical sample by survey year.

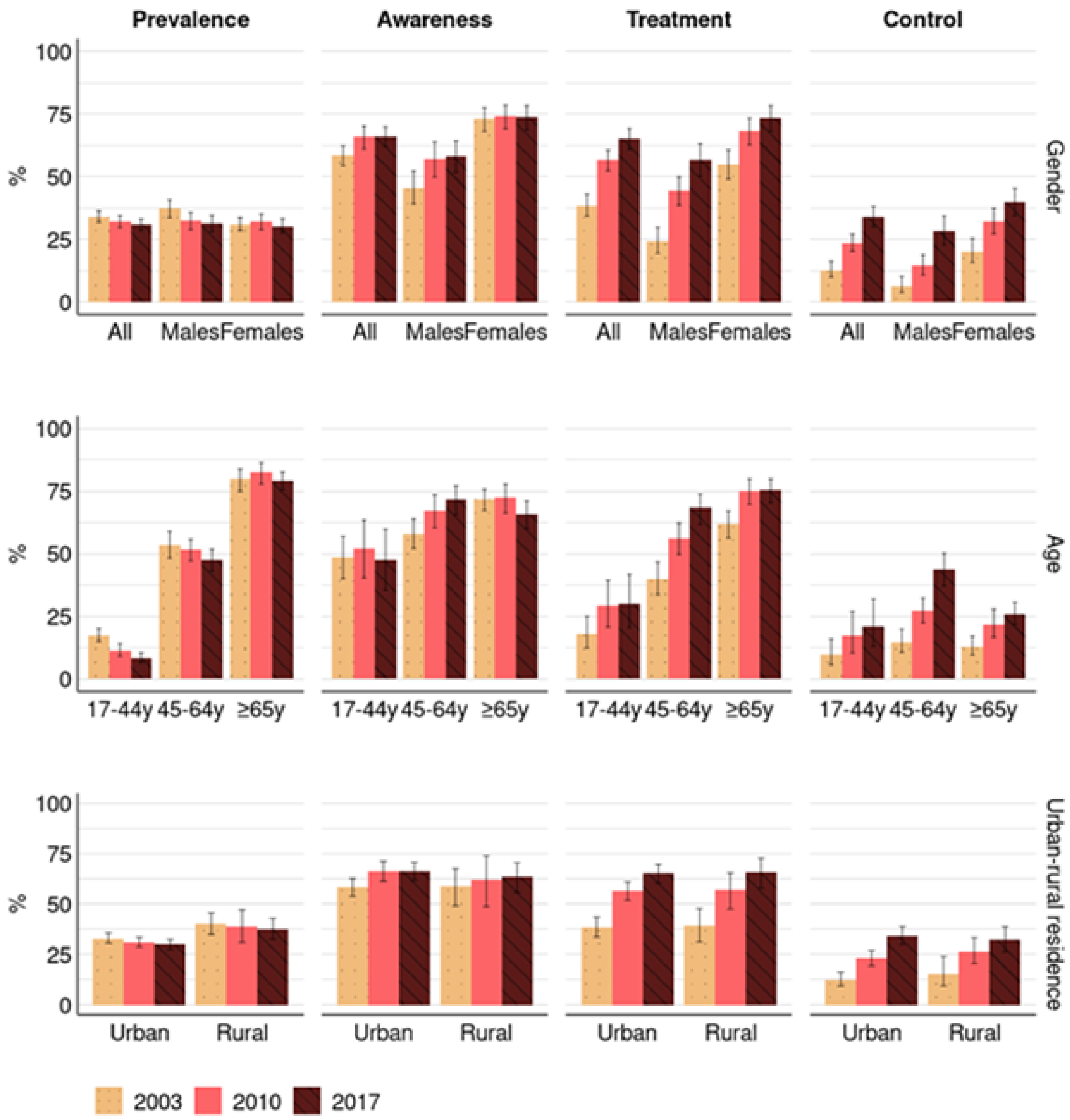
Variable		2003		2010		2017	
		n	% or mean (SE)	n	% or mean (SE)	n	% or mean (SE)
Total	All	3,416		4,820		5,369	
Gender	Males	1,558	49	1,919	48	1,945	49
	Females	1,858	51	2,901	52	3,424	51
Age	17-44y	1,446	62	2,235	58	2,155	54
	45-64y	1,094	27	1,641	30	1,857	32
	≥65y	876	11	944	12	1,357	14
Area	Urban	2,798	86	4,099	87	4,513	89
	Rural	618	14	721	13	856	11
SBP (mmHg)	Mean	3,416	127.8 (0.62)	4,820	126.9 (0.51)	5,369	124.9 (0.49)
DBP (mmHg)	Mean	3,416	79.9 (0.34)	4,820	76.6 (0.27)	5,369	74.7 (0.26)

Participants with valid BP and medicine data. n: unweighted sample size. Estimates are weighted for the complex survey design. BP: blood pressure; SBP: systolic BP; DBP: diastolic BP; SE: standard error.

4.4.2. Hypertension and indicators of its management

According to JNC 7 guidelines (BP ≥140/90 mmHg or use of antihypertensive medication), Figure 4.2 shows the levels of hypertension and indicators of its management across the three surveys (not age-standardised: hereafter referred to as observed). Estimates by gender are presented in the summary table of this section. Results by age and urban-rural residence are provided in Appendix 4.

Figure 4.2: Hypertension prevalence, awareness, treatment, and control by gender, age, and urban-rural residence.



Observed estimates (% and 95% CI).

Change in hypertension outcomes between 2003 and 2017 by gender

For brevity, I report here on the change in hypertension outcomes between the first (2003) and last (2017) surveys. Tests for changes over time in outcomes by gender are presented in a later section. As shown in Figure 4.2, among all adults, the prevalence of hypertension decreased from 34% (95% CI: 32-36) to 31% (95% CI: 28-33). Prevalence decreased among males from 37% (95% CI: 34-41) to 31% (95% CI: 28-35) and decreased slightly among females from 31% (95% CI: 28-34) in 2003 to 30% (95% CI: 28-33) in 2017.

Levels of hypertension management indicators mainly showed improvement (Figure 4.2). Among all adults, levels of treated and controlled hypertension increased between 2003 and 2017 (38% to 65% for treatment; 13% to 34% for control). Levels of awareness among males increased from 46% (95% CI: 39-52) to 58% (95% CI: 52-64); these levels were higher among females in each year but remained stable at around 73%. Treatment levels among males increased from 24% (95% CI: 20-30) to 57% (95% CI: 50-63) and increased among females from 55% (95% CI: 49-61) to 74% (95% CI: 68-78). Levels of control among males increased from 6% (95% CI: 4-10) to 28% (95% CI: 23-34) and increased among females from 20% (95% CI: 16-25) to 40% (95% CI: 34-45). Figure 4.2 shows that levels of awareness and treatment among females in 2003 were higher or similar to the increased levels observed among males in 2017.

Change in hypertension outcomes between 2003 and 2017 by age group

Hypertension between 2003 and 2017 in the youngest age group (17-44y) decreased from 18% (95% CI: 15-20) to 8% (95% CI: 7-11), but remained at around 80% in the oldest age group (≥65y). Levels of awareness, treatment, and control increased across all age groups, but with a larger increase (in absolute terms) among those aged 45-64y. Between 2003 and 2017, levels of treatment increased from 18% (95% CI: 12-25) to 30% (95% CI: 21-42) among those aged 17-44y; from 40% (95% CI: 34-47) to 68% (95% CI: 62-74) among those aged 45-64y; and from 62% (95% CI: 56-67) to 75% (95% CI: 70-80) among those aged ≥65y.

Change in hypertension outcomes between 2003 and 2017 by urban-rural residence

Similar decreasing levels in hypertension prevalence and increasing levels of hypertension management were observed in both rural and urban settings. Hypertension prevalence in urban settings in 2003 and 2017 was 33% (95% CI: 31-36) and 30% (95% CI: 28-32), respectively. The corresponding values in rural settings were 40% (95% CI: 35-46) and 38% (95% CI: 33-43). Levels of awareness, treatment, and control were higher in 2017 than in 2003 in urban and rural settings. For instance, levels of treatment in urban settings increased from 38% (95% CI: 34-43) in 2003 to 65% (95% CI: 60-70) in 2017. Respective figures in rural settings were 39% (95% CI: 31-48) and 66% (95% CI: 58-73).

4.4.3. Differences in hypertension and its management indicators by gender, and urban-rural residence (data pooled across years)

In this section, using data pooled over the three survey years, I present age-adjusted differences in the four hypertension outcomes by gender, and urban-rural residence.

Differences in hypertension outcomes by gender: pooled data

The age-adjusted odds of hypertension were significantly lower for females than for males (OR: 0.73 (95% CI: 0.63-0.84)). The odds of diagnosed (OR: 2.26 (95% CI: 1.82-2.81)), treated (OR: 2.53 (95% CI: 2.07-3.09)), and controlled (OR: 2.35 (95% CI: 1.83-3.02)) hypertension were significantly higher for females than for males.

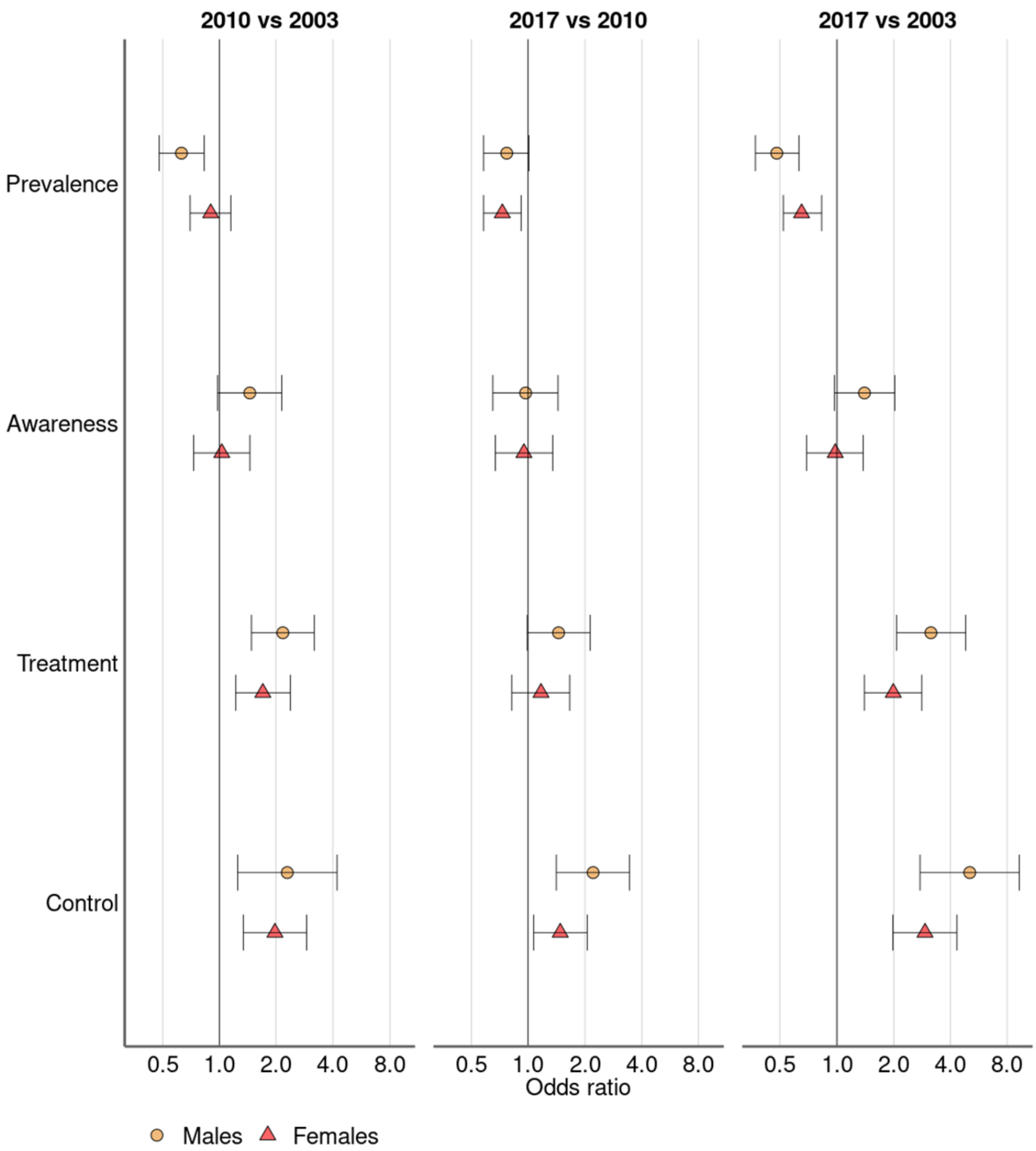
Differences in hypertension outcomes by urban-rural residence: pooled data

The odds of hypertension were higher for those residing in urban vs rural settings (OR: 1.25 (95% CI: 1.03-1.52)). Odds ratios for awareness, treatment, and control by urban-rural residence were not statistically significant (see Appendix 4).

4.4.4. Secular changes in hypertension and its management indicators by gender

Figure 4.3 shows the age-adjusted changes over time in hypertension outcomes stratified by gender, based on logistic regression models.

Figure 4.3: Age-adjusted change over time in hypertension prevalence, awareness, treatment, and control by gender.



Odds ratios and 95% CIs estimated from age-adjusted logistic regressions.

Among males, compared with 2003, the odds of hypertension were significantly lower in 2010 and in 2017 (e.g. 2017 vs 2003 OR: 0.48 (95% CI: 0.37-0.63)); the corresponding decrease between 2010 and 2017 almost reached statistical significance (2017 vs 2010 OR: 0.77 (95% CI: 0.58-1.01)). The odds of hypertension decreased significantly among females between 2003 and 2017 and between 2010 and 2017 (e.g. 2017 vs 2003 OR: 0.65 (95% CI: 0.52-0.83)).

Overall, Figure 4.3 shows that apart from controlled hypertension, the improvements in hypertension management indicators occurred to a much greater extent between the first two surveys with minor (if any) changes since then. The odds of awareness among males, and the odds of treated and controlled hypertension among both genders, increased over time. Among males, the increase in the odds of awareness from 2003 to 2010 almost attained statistical significance (2010 vs 2003 OR: 1.45 (95% CI: 0.98-2.14)). Compared with 2003, the odds of treated and controlled hypertension were significantly higher in 2010 and in 2017 for both genders. For instance, the 2017 vs 2003 OR for diagnosed hypertension was 3.15 (95% CI: 2.07-4.81) for males and 1.99 (95% CI: 1.40-2.82) for females. Respective ORs for controlled hypertension were 5.06 (95% CI: 2.76-9.27) and 2.93 (95% CI: 1.98-4.32).

For presentation purposes, the main estimates discussed previously are summarised in Table 4.2. I provide the full set of estimates for changes over time in hypertension and its management indicators in Appendix 4.

Table 4.2: Summary of secular changes in hypertension prevalence, awareness, treatment, and control.

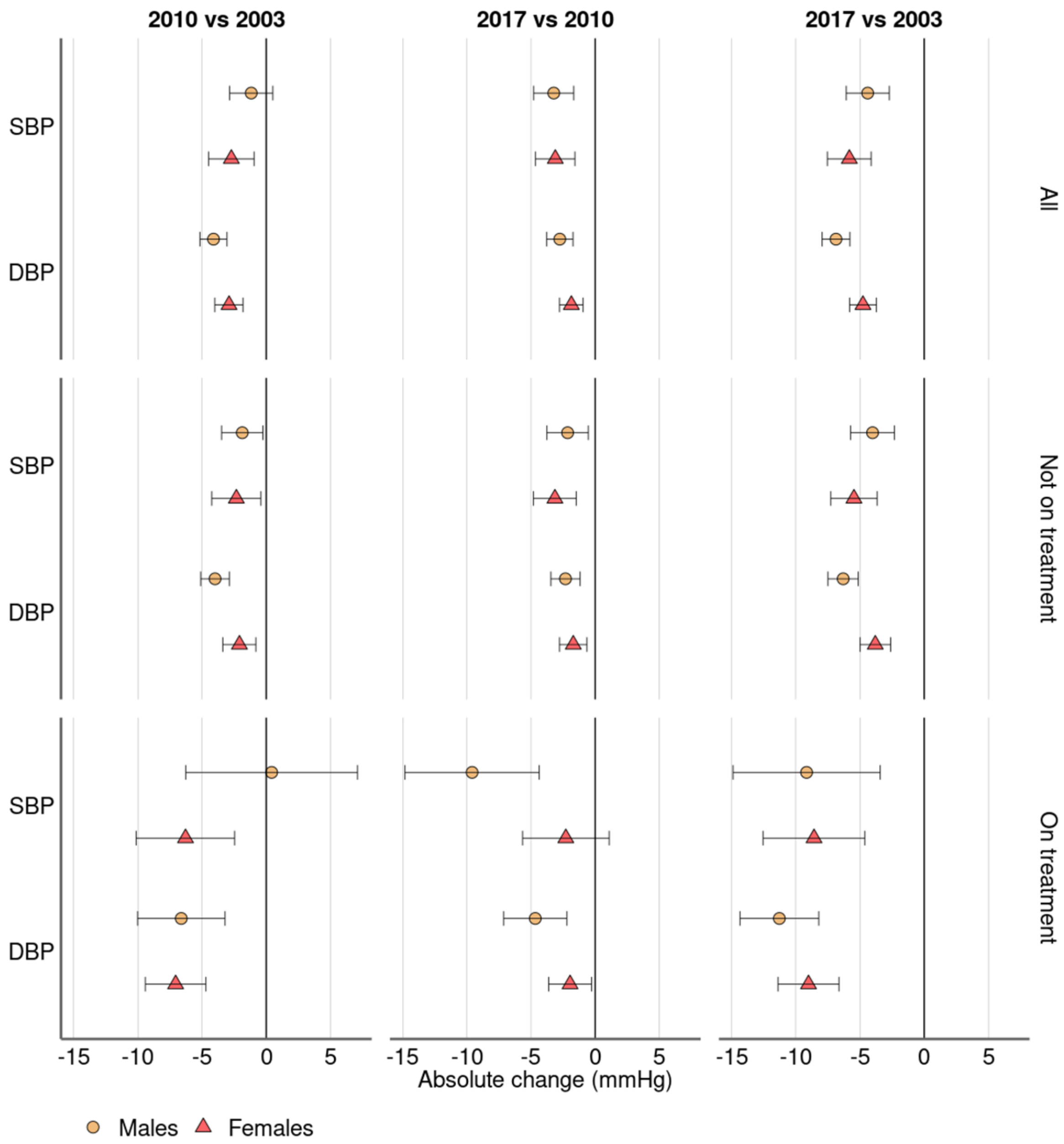
	Prevalence by survey year			
Outcome	**2003**	**2010**	**2017**	**OR 2017 vs 2003**
Adults				
Hypertension	34% (32-36)	32% (30-34)	31% (28-33)	**0.56 (0.46-0.67)**
*Awareness	58% (54-62)	66% (61-70)	66% (62-70)	1.21 (0.94-1.55)
*Treatment	38% (34-43)	56% (52-61)	65% (61-69)	**2.51 (1.88-3.34)**
*Control	13% (10-16)	23% (20-27)	34% (30-38)	**3.61 (2.56-5.09)**
Males				
Hypertension	37% (34-41)	32% (29-36)	31% (28-35)	**0.48 (0.37-0.63)**
*Awareness	46% (39-52)	57% (50-64)	58% (52-64)	1.40 (0.97-2.03)
*Treatment	24% (20-30)	44% (39-50)	57% (50-63)	**3.15 (2.07-4.81)**
*Control	6% (4-10)	14% (11-19)	28% (23-34)	**5.06 (2.76-9.27)**
Females				
Hypertension	31% (28-34)	32% (29-35)	30% (28-33)	**0.65 (0.52-0.83)**
*Awareness	73% (68-77)	74% (69-78)	74% (69-78)	0.98 (0.69-1.38)
*Treatment	55% (49-61)	68% (63-73)	74% (68-78)	**1.99 (1.40-2.82)**
*Control	20% (16-25)	32% (27-37)	40% (34-45)	**2.93 (1.98-4.32)**

Observed estimates (% and 95% CI). Odds ratios (ORs) calculated from age-and survey year-adjusted logistic regressions. Values in bold indicate a statistically significant change ($p<0.05$). Models that pooled data across genders were further adjusted for gender.
** Measured among participants with hypertension.*

4.4.5. Secular changes in mean BP levels by gender and treatment status

After adjustment for age, mean SBP and DBP levels among all adults (i.e. regardless of treatment status) decreased significantly over the 15-year period for both genders. For example, mean SBP decreased by 4.4 mmHg (95% CI: 2.7-6.1) and by 5.8 mmHg (95% CI: 4.1-7.5) between 2003 and 2017 among males and females, respectively (Figure 4.4). Additional analyses stratified by treatment status showed that mean BP levels decreased significantly among all groups, except for mean SBP among females on treatment between 2010 and 2017. The largest decrease in average BP levels was observed among males on treatment, with an absolute decrease between 2003 and 2017 of 9.2 mmHg (95% CI: 3.4-14.9) in SBP and 11.3 mmHg (95% CI: 8.2-14.3) in DBP.

Figure 4.4: Secular changes in mean SBP/DBP by gender and treatment status.

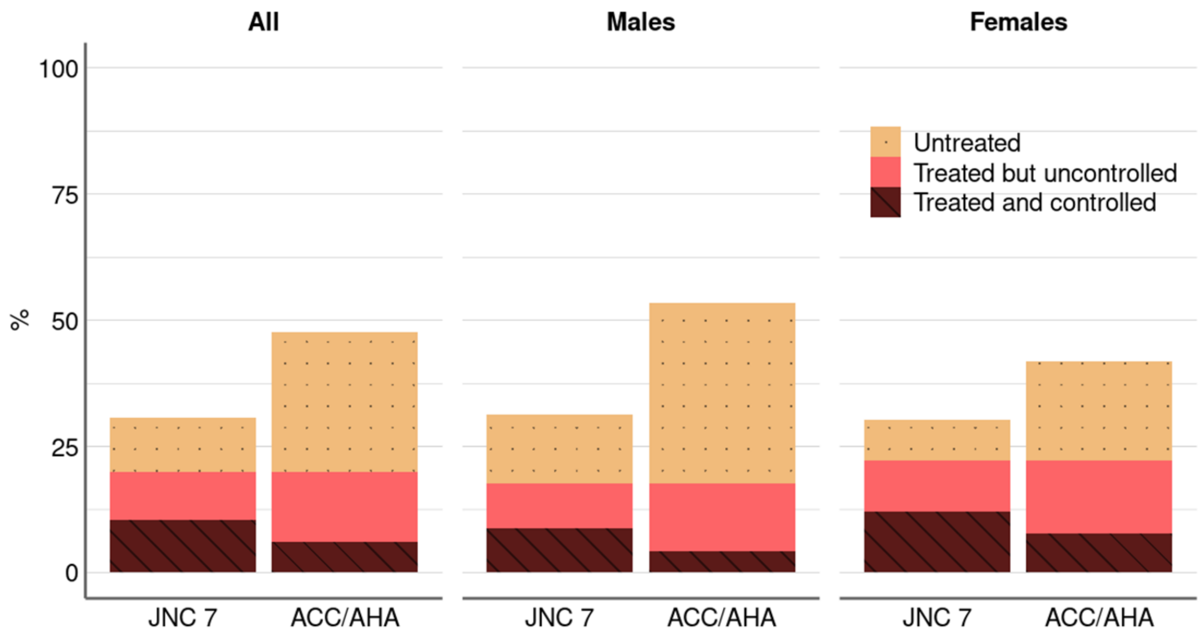


Coefficients and 95% CIs from age-adjusted linear regressions. BP: Blood pressure; SBP: Systolic BP; DBP: Diastolic BP; Treated or not treated based on the use of antihypertensive medication.

4.4.6. Hypertension prevalence based on lower BP thresholds

Based on the ENS2017 data, Figure 4.5 shows the difference in hypertension prevalence and in the proportion of adults with hypertension attaining each hypertension management indicator based on the 2017 ACC/AHA and JNC 7 guidelines. Overall, hypertension prevalence in 2017 would be about 17 percentage points (pp) higher in absolute terms if the BP threshold were lowered to <130/80 mmHg (2017 ACC/AHA: 48% (95% CI: 45-50); JNC 7: 31% (95% CI: 29-33)), a relative increase of around 55%. Based on the 2017 census, an additional 2.3 million adults aged ≥17y would therefore be classified as having hypertension and so be eligible for treatment. The proportion of adults observed to be on treatment (with either controlled or uncontrolled hypertension) is unchanged across the definitions: the higher hypertension prevalence based on ACC/AHA is due to the subset of persons not on treatment with SBP (130-139 mmHg) / DBP (80-89 mmHg) being classified as hypertensive by ACC/AHA and as normotensive by JNC 7.

Figure 4.5: Hypertension prevalence and management: JNC 7 and 2017 ACC/AHA guidelines by gender in 2017.



Seventh Joint National Committee (JNC 7) (i) normotensive (BP <140/90 mmHg, not on antihypertensive medication); (ii) treated and controlled (BP <140/90 mmHg); (iii) treated, but uncontrolled (BP ≥140/90 mmHg); and (iv) untreated (≥140/90 mmHg). 2017 American College of Cardiology/American Heart Association guidelines (ACC/AHA) used 130/80 mmHg instead of 140/90 mmHg.

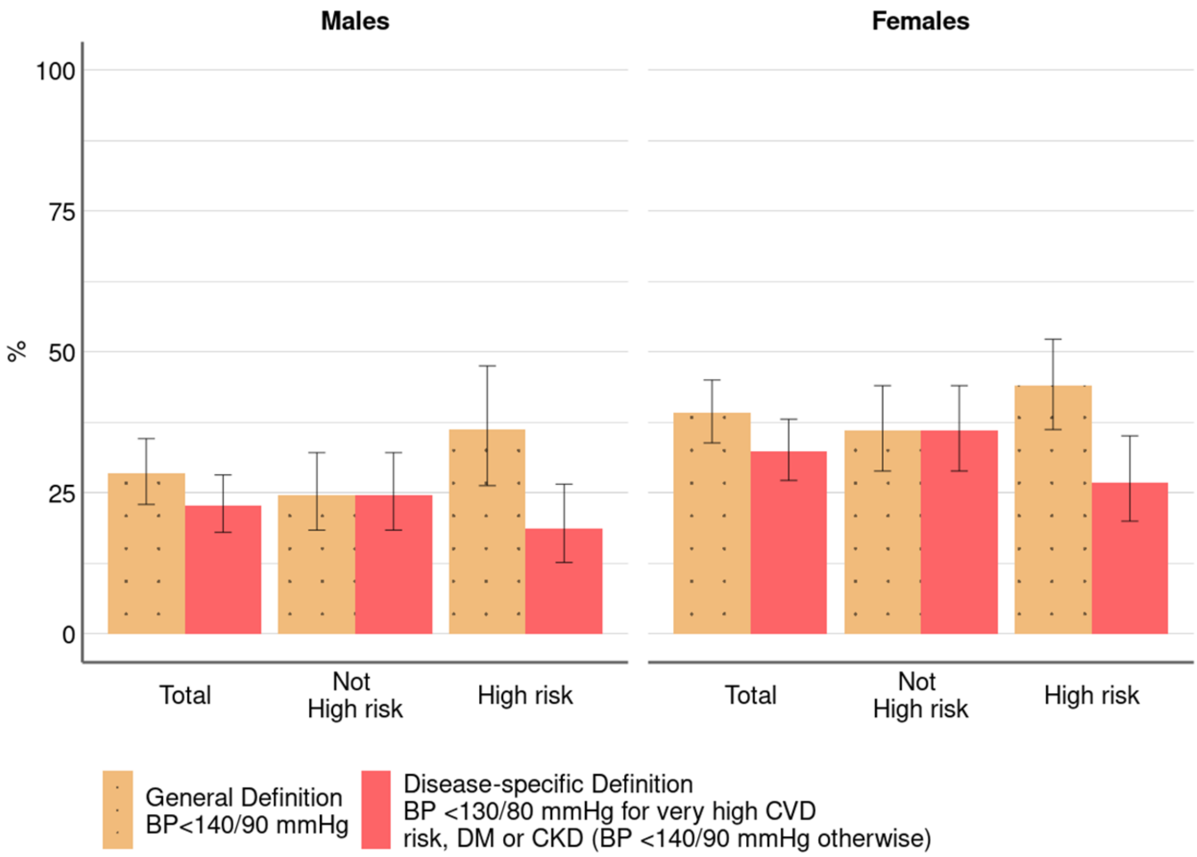
I estimated that the proportion of adults in the population with untreated hypertension in 2017 using the 2017 ACC/AHA guideline would be about 4 pp lower (2017 ACC/AHA: 6% (95% CI: 5- 7); JNC 7: 10% (95% CI: 9-12)); whilst the proportion of adults with treated but uncontrolled hypertension would be about 4 pp higher (2017 ACC/AHA: 14% (95% CI: 12-16); JNC 7: 10% (95% CI: 8-11)). A full set of estimates and accompanying 95% CIs are provided in Appendix 4.

4.4.7. Controlled hypertension based on two BP goals

Among participants with hypertension in 2017, 3% of males and 4% of females had missing values on kidney function (eGFR), self-reported history of stroke, infarction, or DM diagnosis, and so were excluded from the following analysis. Among those with valid data, *high risk* prevalence was 33% (95% CI: 27-39) among females and 40% (95% CI: 35-45) among males.

Figure 4.6 shows the difference in the estimated levels of controlled hypertension using two BP goals: (i) *control (general definition)* and (ii) *control (disease-specific definition)*. Overall, levels of controlled hypertension were 5 pp and 7 pp lower in absolute terms when using the disease-specific versus general definition among males (23% disease-specific vs 28% general) and females (32% disease-specific vs 39% general), respectively. Among participants with *high risk*, the absolute difference in controlled hypertension was 17 pp among both males (19% disease-specific vs 36% general) and females (27% disease-specific vs 44% general). Among participants with *not high risk*, the estimated levels of controlled hypertension (<140/90 mmHg) were 25% and 36% among males and females, respectively.

Figure 4.6: Controlled hypertension by disease-specific BP goal.



Very high CVD risk: history of stroke or infarction. DM: self-reported diagnosis. CKD: estimated glomerular filtration rate (eGFR) > 15 and <60 mL/min/1.73m². High risk: Very high CVD risk, DM, or CKD.

4.5. Discussion

A detailed discussion of the results presented in this chapter and their policy implications are included in Chapter 8 of this thesis. Here, I briefly summarise the main results, followed by a brief discussion of the strengths and limitations of this empirical work.

4.5.1. Main findings

Analysing the three most recent Chilean HES data (2003, 2010, and 2017), the aim of this first empirical chapter was to quantify gender-specific secular changes in hypertension prevalence and in diagnosed, treated, and controlled hypertension; to quantify the impact of lowering BP thresholds on these hypertension outcomes; and to estimate levels of controlled hypertension using a disease-specific BP goal.

This work was informed by three hypotheses:

- **H4.1**: Hypertension prevalence decreased over time for both genders.
- **H4.2**: Hypertension awareness, treatment, and control levels increased over time for both genders.
- **H4.3**: Mean BP levels decreased over time among treated and non-treated adults.

I estimated that around 30% of the Chilean population aged ≥17y had hypertension (BP ≥140/90 mmHg or use of antihypertensive medication). My analyses support hypothesis **H4.1**: the prevalence of hypertension showed a small but statistically significant decline between 2003 and 2017 (from 37% to 31% for males; from 31% to 30% for females). My analyses also support hypothesis **H4.2**: between 2003 and 2017, two indicators of its successful management (treatment and control) significantly increased among both genders. Levels of diagnosed hypertension almost showed a statistically significant increase among males but were higher and stable among females. Finally, mean SBP and DBP levels significantly declined over the same period regardless of treatment status, supporting hypothesis **H4.3**.

After age adjustment, my analyses showed significant differences by gender, with lower odds of hypertension among females. Levels of attainment for each hypertension management indicator were higher among females. Furthermore, levels of diagnosed hypertension among females in 2003, 2010, and 2017 were higher than the increased levels reached by males in 2017; levels of treated hypertension for females in 2003 were at the level achieved by males in 2017.

Hypertension prevalence in 2017 would be about 17 pp higher in absolute terms if the BP threshold were lowered from <140/90 mmHg to <130/80 mmHg (2017 ACC/AHA: 48%; JNC 7: 31%): this higher prevalence is due to the inclusion of adults not on treatment but with SBP of 130 mmHg to 139 mmHg or with DBP of 80 mmHg to 89 mmHg.

Finally, among all persons with hypertension, levels of controlled hypertension using a disease-specific versus general BP goal were 5 pp (23% vs 28%) and 7 pp (32% vs 39%) lower in absolute terms among males and females, respectively. The lower level of controlled hypertension is due to the more aggressive 130/80 mmHg BP target for those with very high CVD risk, DM, or CKD. Among this subset, levels of controlled hypertension using the disease-specific versus general BP goal were 17 pp lower among both genders (males: 19% vs 36%; females: 27% vs 44%).

4.5.2. Strengths and limitations

A strength of my study is the use of nationally-representative HES data (covering all 16 regions in Chile), in contrast to the PURE study that covers the adult population aged 35–74y from only one city in the South (Temuco).[116] The second strength is the use of BP measurements, which overcomes the limitations of self-reported data (e.g. underestimation of prevalence due to persons being unaware of having high blood pressure). Using BP levels in the survey-definition of hypertension also decreases the risk of reporting bias linked to differences in levels of undiagnosed hypertension potentially related to systematic differences in levels of contact with the healthcare system. Moreover, BP measurements and self-reported hypertension-related data (awareness and treatment) were collected following similar protocols on each survey and with similar standards to other HES conducted worldwide.[35, 191] In this way, ENS data and the use of standard definitions of hypertension prevalence and management indicators allows for comparisons over time in Chile and also with other HES with reasonable confidence.[146]

Nevertheless, my study has a number of limitations. First, to ensure comparability across the three surveys, I used the mean of the first and second BP readings. Typically, analyses of national HES such as HSE and the US National Health and

Nutrition Examination Surveys (NHANES) collect three BP measurements and use the mean of the second and third BP readings. This is to adjust for a *white coat effect* that causes a transitory increase in BP levels related to the presence of a healthcare professional.[35] Previous research has shown that the fall in BP between the first and second measurements is much greater than that between the second and third.[194, 195] The difference between the third and fourth measurements is even smaller, and including the fourth reading does not give a substantial change in the overall prevalence of high BP.[196] Compared with using the mean of the second and third readings, my approach could have overestimated hypertension prevalence and underestimated levels of controlled hypertension.[195] I assessed the magnitude of this overestimation using ENS2017: the prevalence of hypertension (BP ≥140/90 mmHg or use of antihypertensive medication) was slightly (<1 percentage point) overestimated based on the mean of the first and second BP measurements (31%, 95% CI: 28-33; results not reported) compared with the second and third BP measurements (30%, 95% CI: 28-32). Reassuringly, my findings regarding changes in hypertension over time were similar when I repeated the main analyses by taking the mean of the second and third readings in the 2010 and 2017 survey datasets (details of this analysis are provided elsewhere).[111]

Secondly, although my analyses were adjusted for age and stratified by gender, I cannot rule out the possibility of residual confounding and assume that comparisons over time were completely like-for-like. Particularly, the interpretation of a decrease in average BP levels among participants with treated hypertension should consider changes in hypertension guidelines (i.e. diagnosis thresholds, eligibility for treatment) and changes in access to healthcare. Over the time period of my study, due to changes in hypertension guidelines and also improvements in the levels of access to healthcare, some adults (e.g. those at high risk of CVD) would have been more likely to be treated at lower levels of BP.

Thirdly, according to the JNC 7, 2017 ACC/AHA, and Chilean GES-hypertension guidelines, the diagnosis of hypertension should be made at follow-up visits.[36, 37] BP measurement during a single visit (as done in ENS surveys) can overestimate the *true* prevalence, as raised BP is not necessarily persistent. The *white coat effect* could partially explains this effect. According to analyses of Chilean data (follow-up of the total subsample of ENS2010 participants residing in the metropolitan region), a small but statistically significant reduction in hypertension prevalence (1%) was found when BP measurement was repeated in a follow-up visit.[197] This overestimation related to the white coat effect could partially attenuate masked hypertension (i.e. non-elevated BP in clinical but elevated in ambulatory monitoring). Nevertheless, estimations based on follow-up visits are also prone to measurement bias. A recent study, based on a sample of 309 patients from a primary healthcare setting in Chile, evaluated the concordance in hypertension prevalence by comparing two methods (i) Attended Automated Office BP Measurement (AOBP; in follow-up visits) versus (ii) 24-hour Ambulatory BP Monitoring (ABPM). According to the results of this study, both the *white coat effect* (defined as AOBP: BP ≥140/90 mmHg and ABPM: BP <130/80 mmHg) and *masked hypertension* (AOBP: BP <140/90 mmHg and ABPM: BP ≥130/80 mmHg) were very frequent (26% and 8% of patients, respectively).[198] Unfortunately, the potential of any white coat effect or masked hypertension could not be estimated using ENS data.

Fourthly, recall bias could also have affected the estimated levels of hypertension awareness and treatment. Ascertaining use of antihypertensive medication based on ATC codes from the medicine inventory could have produced a slight overestimation of prevalence, since some medicines can be used for other conditions without the co-existence of hypertension. However, the results from my sensitivity analysis (comparing use of ATC codes with self-reported data to ascertain treatment status) showed that the magnitude of the bias was very small in 2003 and 2017, and was only slightly higher in 2010 (data not shown, details of this analysis are provided elsewhere).[111] This finding suggested (i) very little recall bias in participants' self-reports or (ii) the low use of cardiovascular medications for conditions other than hypertension.

Finally, levels of response to the ENS decreased from 75% in 2010 to 67% in 2017. However, the current levels of response are comparable to those achieved by other national HES.[174] My analysis showed that the proportion of female and younger participants in the analytical samples for the work presented here increased over time, suggesting increasing rates of non-response among males and older adults (data not shown). However, the impact of any differential non-response over time would be reduced by my decision to adjust for age, stratify analyses by gender, and use non-response weights.

4.6 Conclusion

In conclusion, mean levels of blood pressure have declined in Chile during the last 15 years irrespective of treatment status, while levels of treated and controlled hypertension have increased. The introduction of the GES-hypertension plan in 2005 may have accounted at least partly for these increases since 2003. Regardless of the hypertension definition, innovative and collaborative strategies are needed to improve levels of attainment of each hypertension management indicator, including the promotion of screening and access to care, together with interventions to increase treatment coverage and its adherence, especially among males.

Chapter 5: Individual-level socioeconomic inequalities in the prevalence and management of hypertension

5.1. Introduction

Evidence accumulated in the last three decades shows persisting, worldwide SEP inequalities in several health outcomes, including obesity, hypertension and CVD.[65, 81–83] Both country-specific observational studies and systematic reviews of the literature have documented that hypertension is more frequent in lower SEP groups.[65, 87, 99–102] Leng et al.'s systematic review and meta-analysis (2015) found that those in lower versus higher SEP (measured at the individual-level) had increased risk of hypertension, whether using income (OR: 1.19, 95% CI: 0.96–1.48), or education (OR: 2.02, 95% CI: 1.55–2.63) as the measure of SEP.[87] Leng et al. (2015) found that SEP inequalities were significant in HICs and were more prominent among females, but less consistent among males.[87] However, evidence about SEP inequalities in hypertension management indicators (awareness, treatment, and control) is scarce worldwide and among LACCs.[82, 83, 98] Results from my systematic review (presented in Chapter 2) showed that SEP inequalities in levels of hypertension management among LACCs vary by country, gender, and choice of SEP indicator. Within countries, SEP inequalities also varied over time, but the limited available evidence makes it difficult to assess any trends of these inequalities. Accordingly, the association between individual SEP indicators and hypertension outcomes was framed as a key component of the conceptual model of my PhD (Chapter 3).

As described in Chapters 1 and 4, the Chilean state implemented health reforms in 2005 to improve the quality of care and reduce the gap in health outcomes between registrants in the private and public systems. The Chilean state has made considerable efforts in recent decades to improve the management of hypertension, including the launch of the GES-hypertension plan in 2005. Despite the availability of effective and low-cost BP-lowering medicines, the high prevalence means that hypertension is one of the costliest health conditions worldwide. Indeed, the GES-hypertension plan is the second most expensive Chilean health plan (CKD being the costliest).[80] The GES-hypertension plan aimed to improve the levels of diagnosed, treated, and controlled hypertension while decreasing SEP inequalities. In this way, up-to-date information on SEP inequalities in hypertension and its management indicators, using comparable estimates, is needed to better understand the impact of this considerable investment.[54, 55, 199]

5.2. Research problem, aim, objectives and hypotheses

Problem

Chilean evidence has shown SEP inequalities in hypertension prevalence.[65] However, information on SEP inequalities in hypertension management indicators (diagnosis, treatment, and control) in Chilean adults is only partially known.

Aim

This chapter aims to examine the gender-specific magnitude of SEP inequalities in hypertension prevalence and in undiagnosed, untreated, and uncontrolled hypertension, and their change over time in Chilean adults since 2003, using individual-level measures of SEP.

Specific objectives

The specific objectives for this empirical work are as follows:

- Estimate SEP inequalities in hypertension by gender in 2003, 2010, and 2017.
- Estimate changes over time in SEP inequalities in hypertension by gender comparing 2010 vs 2003, 2017 vs 2010, and 2017 vs 2003.
- Estimate SEP inequalities in undiagnosed, untreated, and uncontrolled hypertension by gender in 2003, 2010, and 2017.

- Estimate changes over time in SEP inequalities in undiagnosed, untreated, and uncontrolled hypertension by gender, comparing 2010 vs 2003, 2017 vs 2010, and 2017 vs 2003.
- Estimate the difference in levels of uncontrolled hypertension in 2017 using a disease-specific (<130/80 mmHg) vs general BP goal (<140/90 mmHg) by educational level and gender.

Hypotheses

The five main hypotheses are:

- **H5.1**: Levels of hypertension prevalence are higher in lower SEP groups among both males and females.
- **H5.2**: SEP inequalities in hypertension have persisted over time among both males and females.
- **H5.3**: Levels of undiagnosed, untreated, and uncontrolled hypertension are higher in the lower SEP groups among both males and females.
- **H5.4**: SEP inequalities in undiagnosed, untreated, and uncontrolled hypertension have decreased over time among both males and females.
- **H5.5**: The absolute difference in controlled hypertension using a disease-specific than a general BP goal is larger among those in the lowest than highest educational level among both males and females.

5.3. Methods

The Chilean HES datasets analysed in this chapter are the same as those used in Chapter 4 (Section 4.3). I describe here the particular methods relevant to the empirical work presented in this chapter.

5.3.1. Definitions of hypertension and hypertension management

Hypertension is defined as BP ≥140/90 mmHg or use of antihypertensive medication (as ascertained by ATC codes). In Chapters 2 and 4, the three key hypertension management indicators were defined in terms of awareness, treatment, and control (*favourable or positive* outcomes). In order to simplify the interpretation of inequalities, in this chapter, I define these in terms of undiagnosed, untreated, and uncontrolled hypertension. By doing so, hypertension and the three management indicators are defined as *unfavourable or negative* outcomes.

Similar to Chapter 4, I used two definitions of controlled hypertension, according to both BP goals stated in the Chilean hypertension guidelines: (i) **control (general definition)**: BP <140/90 mmHg for all adults (i.e. those with and without high risk); and (ii) **control (disease-specific definition)**: BP <130/80 mmHg for those with high risk (history of stroke/infarction, DM or CKD) and BP <140/90 mmHg for those with *not high risk*.

5.3.2. Definition of individual-level SEP indicators

Education, income, and health insurance were used as individual-level indicators of SEP. These were defined as follows:

- **Educational status**: this indicator was based on self-reported years of formal education. Two questions were used to collect these data: (i) *"What is the highest level reached or the current educational level?"* (in categories: *never attended school*, *nursery*, *primary school*, *secondary school*, *technical training*, *professional institute*, *university education*, *postgraduate university*), and (ii) *"At that educational level, what was the last year you passed (for those who are not studying) or are you currently taking (for those who are studying)?"* (discrete variable). Educational status was grouped into three categories as follows: (i) **low** (<8y, equivalent to *primary or no education*); (ii) **medium** (8-12y, equivalent to *secondary school*), and (iii) **high** (>12y, equivalent to studying one year or more after *secondary school*). These educational categories have been previously associated with other health outcomes using Chilean data from ENS and CASEN.[200, 201]

- **Equivalised income quartile**: this variable was calculated from data collected in ENS2010 and ENS2017, reported by the participant (not necessarily the head of the household). The question used for this purpose was *"How much is approximately the monthly net income of the whole household, that is, adding all the income of the household members? (net income is the amount of money you receive by taking out the discounts)"*. In 2010, answers were collected using 11 income ranges (in Chilean pesos (CLP) < $65,000; $65,000 to $136,999; $137,000 to $180,999; $181,000 to $250,999; $251,000 to $350,999; $351,000 to $450,999; $451,000 to $650,999; $651,000 to $850,999; $851,000 to $1,050,999; $1,051,000 to $1,250,999; >$1,251,000. Year 2010 exchange: £1 GBP = $800 CLP). The midpoint of the range was used to obtain a numeric value (except for the last category, which was set equal to the cut-off point). In 2017, monthly income was collected as a numeric variable.

  Income values in both surveys were equivalised to the household's size (divided by the number of individuals living in the household; children were considered identical to adults for this equivalisation). Separately for each survey year, the numeric income variable was grouped into quartiles (poorest; Q2; Q3; richest).

- **Health insurance**: whilst health insurance status is not usually defined as an individual-level measure of SEP, it is strongly related to both levels of income and the time spent in formal education in Chile.[13] As described in Chapter 1, the two main components of the Chilean health insurance system are (i) FONASA (the single public insurance entity, the National Health Insurance Fund), which covers about 75% of the population, and (ii) ISAPRE (several private health insurance firms) which cover around 18% of the population.

  The question used to collect information on health insurance in ENS2010 and ENS2017 was as follows: *"What health insurance system do you belong to,* *either as a contributor or a dependent?”*. The response categories were: (i) *FONASA* (public system), (ii) *ISAPRE* (private system), (iii) *army*, (iv) *none*, (v) *other*, and (vi) *don’t know*. A binary variable for health insurance status (public or private) was used in the following analyses. *Don’t know* and other responses were assigned to missing in the descriptive analyses. Accordingly, inequalities by health insurance were restricted to public (FONASA) and privately (ISAPRE) insured participants.

5.3.3. Statistical analyses

Analyses were restricted to adults aged ≥17y to ensure comparability across the three surveys. My main analyses were based on complete cases (those participants with no missing data on the variables of interest, including SEP) and were weighted to account for the differences in selection probability (i.e. selection of one person per household and oversampling of persons aged ≥65y) and non-response rates. Two-tailed p-values <0.05 were classified as statistically significant. As in previous chapters, I will interpret this as an arbitrary cut point since p-values are continuous (range: 0-1), and as such their interpretation should be thought of as a continuum of probabilities.[192] Analyses were conducted in R (version 4.0.4) adjusting for the complex survey design of the ENS.

Gender-specific analyses

For several reasons I decided to stratify the analysis of inequalities by gender. As mentioned in previous chapters, the WHO guidelines for inequality analysis suggest evaluating whether dimensions of inequality intersect and whether to perform double disaggregation (e.g. by SEP and gender).[108] Some authors have mentioned that the intersection of gender and SEP affecting health outcomes should be evaluated systematically.[109] Several agencies, including the Canadian Institutes of Health Research, the European Commission, and the US National Institutes of Health, are requesting gender-specific analysis in health inequalities research.[202] Evidence from my previous chapters and from other authors has shown differences by gender in levels of hypertension outcomes, which further emphasise the importance of gender-specific research in this area.[110, 111] For instance, in my analyses of

Chilean data (Chapter 4), I showed that females had lower odds of age-adjusted hypertension and higher odds of awareness, treatment, and control than males. Also, there is evidence for gender differences in SEP indicators: females have higher rates of poverty and spend fewer years in formal education.[13] In addition, previous evidence shows that the magnitude of inequalities in hypertension differs by gender,[203–207] at least partly due to women in lower SEP groups being less exposed than women in higher SEP groups to health information and facing greater barriers to health services, and as a result, being less likely to change unhealthy lifestyle behaviours that are associated with increased risk of raised blood pressure.[87]

I conducted five sets of analyses, which are described in turn below.

I. Descriptive analyses

First, in each survey year, I estimated levels of survey-defined hypertension and the three management indicators according to the three individual-level SEP measures. I estimated *observed* (i.e. non age-standardised) levels to present the current burden of hypertension within groups[35] and *age-standardised* levels. I used the direct method of standardisation by age and gender to adjust for differences in the age distribution between SEP groups, using as the reference population (i) the gender-specific age composition of the Chilean adult population from the Census 2017 for hypertension prevalence (age groups: 17-44y; 45-64y; and ≥65y); and (ii) the weighted age composition of participants with hypertension in ENS2017 (age groups: 17-44y; 45-64y; 65-74y, and ≥75y) for the three management indicators.[35] The statistical significance of the differences between SEP groups in hypertension outcomes was evaluated using Pearson’s chi-squared test.

II. Simple measures of inequalities

I built regression models to estimate simple measures of inequalities (pairwise comparisons) in hypertension outcomes. To analyse SEP inequalities on a relative scale, I built logistic regressions using generalised linear models (Equation 5.1) with a binomial distribution and a logit link.

Equation 5.1:

$$g(Y) = intercept + \beta_1 SEP + \beta_2 age$$

Where $g(Y)$ is the mean of the transformed binary outcome (the logarithm of the odds, logit) and the coefficient of main interest (β1) represents the coefficient for the simple measure of inequality (pairwise comparisons between SEP groups). Age-adjusted ORs (age entered as a continuous variable, years) were estimated for the SEP indicators stratified by survey year. Reference categories for the SEP variables were as follows: (i) high education level (>12 y), (ii) richest income quartile, and (iii) private health insurance. The coefficient for SEP represents the main OR of interest (e.g. comparing the public vs privately insured). The null hypothesis of no association between SEP and the outcomes is OR=1.

In order to increase the sample size (and the statistical power), I additionally reported a pooled analysis for adults (combining the data for males and females) if the gender-specific ORs showed the same direction of associations but did not attain statistical significance (models for adults were adjusted for gender). Similarly, most analyses were survey year-specific but in particular situations (similar patterns of year-specific inequalities, but with associations that did not reach statistical significance) I evaluated inequalities among adults using pooled ENS2003-2010-2017 data (with survey year adjustment as a three-level factor: 2003, 2010, and 2017).

III. Complex measures of inequalities

To better monitor the population health burden of inequalities over time, health inequality measures should be sensitive to two sources of change: (i) change in the size of the population subgroups involved, and (ii) change in the level of health within each subgroup. When the assessment of inequalities involves only comparisons of specific groups (e.g. public vs private health insurance), then pairwise comparisons may be sufficient. When the objective is to provide a summary across all SEP groups (e.g. educational levels), then the use of summary measures of inequality is warranted. Also, over time, the distribution of the population across SEP groups may change (e.g. a rise in the proportion of adults classified as highly educated due to expansion of university education), and it is advantageous for a measure of inequality in health to be sensitive to such changes.[208]

In order to provide single quantifications of inequalities in a metric recommended for national health inequality statistics,[108] the distribution of ordinal markers of SEP (education and income) were used to generate ridit scores (range: 0 (most advantaged) to 1 (least advantaged)). Each SEP group was assigned a score (fractional rank) based on the midpoint of its range in the cumulative distribution in the dataset (also known as a cumulative mean proportion).[209] Ridit scores were year-specific and calculated separately for the analyses of hypertension (using the general population sample) and its management indicators (using the subsample with hypertension). In this way, the use of ridit scores enables comparisons across survey years while accounting for the differences in the proportion of participants in each SEP group.

By entering the ridit scores into the model as a single continuous variable, the SEP coefficient in a linear regression model (Slope Index of Inequality (SII)) can be interpreted as the estimated absolute difference in outcomes between the lowest (rank 1) and highest SEP (rank 0). For example, for hypertension, this forms a linear probability model (LPM)—the absolute difference in the probability of hypertension between the lowest and highest SEP. As suggested by the WHO, the absolute measure of inequality (SII) should be complemented by a relative measure: the Relative Index of Inequality (RII). It is important to present both absolute and relative measures as the choice of measure has been shown to influence conclusions about whether inequalities in health are increasing or decreasing over time.[108] Using the ridit scores, I used (i) *Gaussian* models with an identity link function to calculate the **SII**, and *Poisson* models with a log link function to compute the **RII**. Both indices were estimated with 95% CI with the following generalised linear model:

Equation 5.2:

$$g(Y) = intercept + \beta_1 SEPridit + \beta_2 age$$

The coefficient of main interest (β1) represents the complex measure of inequality. The null hypothesis of no association between SEP and the outcome was an SII of 0 and an RII of 1. The term *SEP.ridit* in Equation 5.2 corresponds to the ridit scores used instead of the original (ordinal) SEP variable. Estimates were adjusted for age (continuous variable) and stratified by survey year.

Again, with the intention of increasing the sample size (and thus increasing the statistical power) of the analysis, I pooled the data across genders or survey years with similar patterns of gender/year-specific inequalities and with associations that did not reach statistical significance.

The predicted values for the two extremes (rank 1, lowest SEP; rank 0, highest SEP) can be used to calculate the SII and RII, which can be interpreted as the rate difference (Equation 5.3) and rate ratio (Equation 5.4) comparing the extremes of the SEP hierarchy, respectively. For each outcome, a SII > 0 and a RII > 1 indicates higher levels of the unfavourable outcome in the lowest SEP group.

Equation 5.3:

$$SII = Predicted\ value\ for\ rank\ 1 - Predicted\ value\ for\ rank\ 0$$

Equation 5.4:

$$RII = \frac{Predicted\ value\ for\ rank\ 1}{Predicted\ value\ for\ rank\ 0}$$

These complex measures of inequalities should be used only when the dose-response gradient is approximately linear.[210] I assessed the linearity assumption by visual inspection of descriptive plots. Consequently, I used the SII and RII only if descriptive results and simple measures of inequality (OR) were compatible with a linear association between the ordinal SEP variable and the outcome. In the case of non-linearity, using the ordinal SEP variable instead of ridit scores, I used a simple measure of inequality to compare the lowest vs highest SEP groups: ORs (exponentiated β) from logistic regression models, and absolute differences (β) from LPM models.

IV. Secular changes in the magnitude of inequalities

Using pooled ENS2003-2010-2017 data, changes over time in inequalities were analysed by including two-way interaction terms (SEP indicator by survey year) to age-adjusted models stratified by gender. Survey year was included as a categorical variable in order to estimate change over time comparing 2010 vs 2003; 2017 vs 2010; and 2017 vs 2003. Results were summarised using the interaction term coefficients with accompanying 95% CIs.

V. Inequalities in controlled hypertension based on a disease-specific BP goal

In a similar manner to the previous chapter (Section 4.4.7), I analysed educational-based inequalities in levels of controlled hypertension among ENS2017 participants with and without comorbidities using the two different BP goals: (i) **control (general definition)**: BP <140/90 mmHg for all adults (i.e. those with and without high risk); and (ii) **control (disease-specific definition)**: BP <130/80 mmHg for those with high risk (at least one of three comorbidities: CKD or self-reported prior diagnosis of stroke, infarction, or DM) and BP <140/90 mmHg for those with *not high risk*.

5.3.4. Sensitivity analyses

Multiple imputation to replace missing values in household income

The only SEP variable with a high proportion of missing values was income: n=1,459 (14%) participants in the pooled 2010-2017 ENS dataset had missing data on income, and these were excluded from my main analyses. As mentioned in Chapter 2, because of the low sample sizes typically available in national HES (especially those conducted in LACCs), most associations in previous studies examining inequalities in hypertension management were likely to be statistically underpowered to some extent. In the presence of a large amount of missing data, relying on complete cases in this study might weaken the power to detect SEP inequalities in both hypertension and hypertension management indicators. In a sensitivity analysis, I therefore used the multiple imputation using chained equations (MICE) method to avoid excluding participants with valid BP and medicine data, but with missing income data. Compared with complete-case analyses, multiple imputation has several advantages, including greater statistical precision and power.[211] My analyses were consistent with the assumption that income was missing at random (MAR), meaning that the probability of income data being missing can be explained by differences in observed data.[211] This assumption was supported by an exploratory analysis in which I found that the pattern of missing income values was at least partially explained by differences in hypertension status and educational level: I found a lower percentage of missing income values among those with hypertension and among those with lower educational levels.

To impute income values, I implemented the MICE technique using the *predictive mean matching* (PMM) method implemented in the *mice* package in R. Missing values were replaced by randomly selecting one of the observed values from a pool of 10 nearest-neighbour donors (those with the closest predictive mean from the imputation model).[212] The imputation model included i) the variables involved in the analyses (i.e. dependent variables: survey-defined hypertension and indicators of undiagnosed, untreated and uncontrolled hypertension; and the SEP exposure to be imputed: income), ii) and auxiliary variables, such as potential predictors of income values or their missing values (i.e. educational level, health insurance, and gender), and variables to increase the plausibility of the MAR assumption (i.e. survey design variables, survey year, SBP and DBP).100 imputations were made with 20 iterations for each. With each imputed dataset, I used the complex survey design features of the ENS to estimate the relative inequalities for each outcome. Estimates were combined across the imputed datasets using Rubin's rules.[213] Results were summarised using age-adjusted ORs (comparing the poorest vs richest income quartile) stratified by survey year.

Mutual adjustment for multiple indicators of SEP

I decided a priori to run separate models for the three individual-level SEP indicators (educational level, income, and health insurance) rather than estimate inequalities using a single model that mutually adjusted for multiple indicators of SEP. My analytical approach is mainly to monitor SEP inequalities (i.e. descriptive) and so does not seek to establish causal associations. Furthermore, I wished to avoid the ‘potential interpretative pitfalls’ that mutual adjustment for different SEP measures might bring.[214] As explained by Green and Popham (2019), since different SEP measures overlap to capture the overall socioeconomic position (*core SEP*), mutual adjustment (and so estimating just the independent effects of the *unique* aspects of a SEP measure) ignores aspects of SEP that are common to all SEP measures.[214] However, as a robustness check, using 2010 and 2017 data, I evaluated the change in educational-based inequalities (using age-adjusted ORs stratified by survey year) before and after adjustment for health insurance. The percentage relative change in the ORs was computed as $(adjusted - unadjusted)/unadjusted \times 100$.

5.4. Results

In this section, I describe SEP inequalities in hypertension and in hypertension management indicators. For both sets of analyses, I describe (i) the socioeconomic characteristics of the analytical sample, (ii) age and gender-standardised prevalence, (iii) simple and complex measures of inequality and (iv) changes in inequalities over time.

5.4.1. Inequalities in hypertension prevalence

Socioeconomic characteristics of the analytical sample

5,422 males and 8,183 females from ENS 2003, 2010, and 2017, aged ≥17y with valid BP and medicine data, were included in the analysis (Table 5.1 males; Table 5.2 females). Between 2003 and 2017, there was a 50% increase in the proportion of participants with the highest educational attainment (>12 years of formal education) in relative terms. Between 2010 and 2017, the median monthly equivalised income of participants also increased by 50% in relative terms, from 83,000 CLP (£71, according to the 2021 exchange rate) to 125,000 CLP (£116). The distribution of income quartiles showed that females were poorer than males in 2010 and 2017 (e.g. the percentage in the poorest quartile in 2017 was 14% and 22% for males and females, respectively). The percentage of males with public health insurance was

74% and 71% in 2010 and 2017 (females: 80% and 86%), respectively. Fewer than 3% of participants had missing values for educational level and health insurance. In contrast, 12% and 20% of participants had missing values for income in 2010 and 2017, respectively.

Table 5.1: Analytical sample by survey year among males.

		2003		2010		2017	
Variable		**n**	**%**	**n**	**%**	**n**	**%**
Total	All	1,558	100	1,919	100	1,945	100
Age	17-44y	703	64	897	60	803	56
	45-64y	481	27	657	30	658	32
	≥65y	374	9	365	11	484	12
Educational level	Low	558	21	469	17	409	14
	Medium	766	57	1,037	57	1,037	53
	High	230	22	377	25	483	33
	Missing	4	0	36	1	16	1
Income	Poorest	‡		309	19	233	14
	Q2			512	24	351	19
	Q3			370	21	359	21
	Richest			566	24	613	26
	Missing			162	12	389	20
Health insurance	Public	‡		1,435	74	1,521	71
	Private			213	13	245	19
	Army			65	2	51	2
	None			143	9	101	7
	Missing			63	2	27	1

Participants with valid BP and medicine data. n: unweighted sample size. Estimates are weighted for the complex survey design. Totals may not sum to 100% due to rounding. Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. ‡: Measured in 2010 and 2017 only.

Table 5.2: Analytical sample by survey year among females.

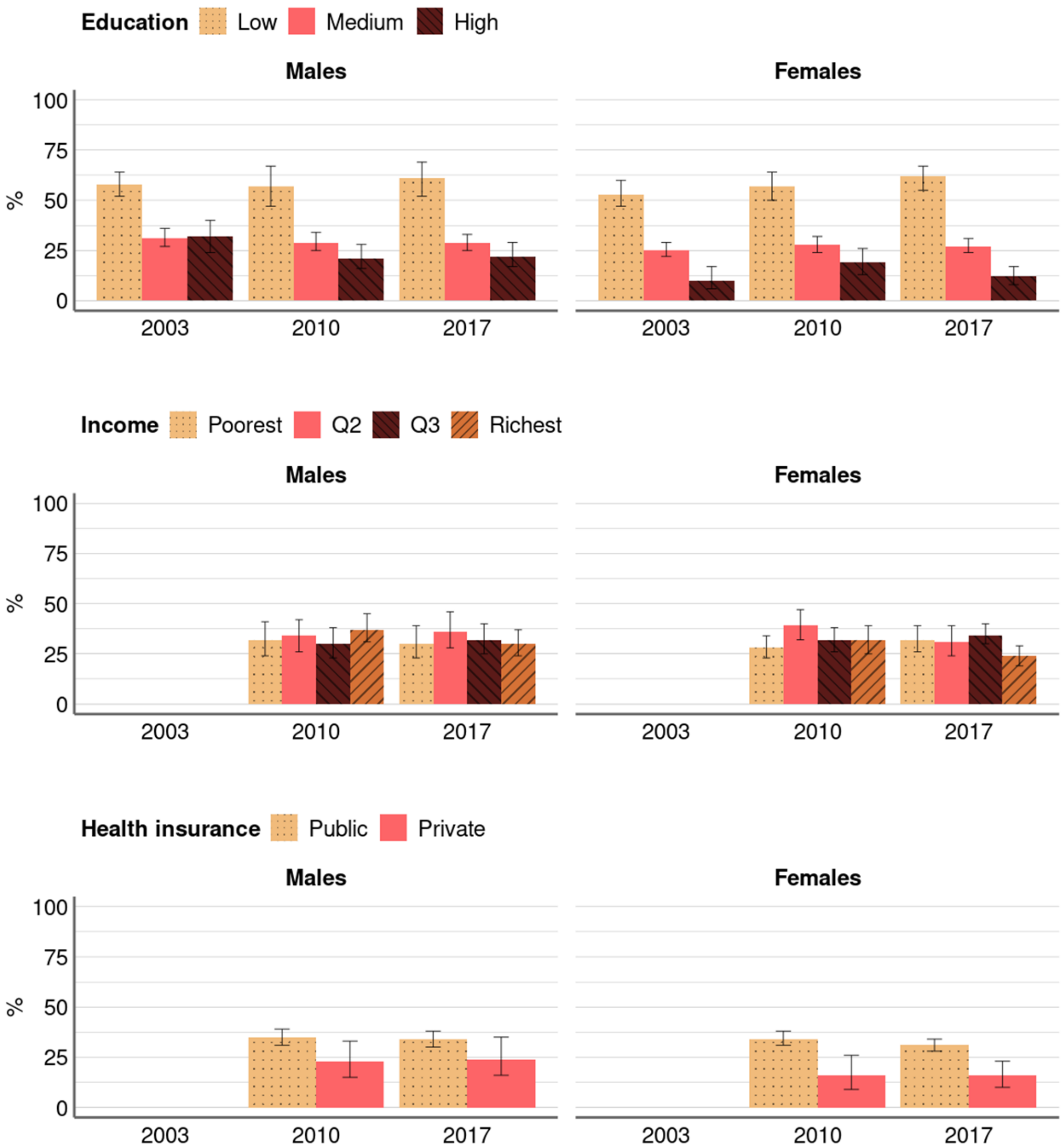
Variable		2003 n	2003 %	2010 n	2010 %	2017 n	2017 %
Total	All	1,858	100	2,901	100	3,424	100
Age	17-44y	743	61	1,338	57	1,352	53
	45-64y	613	27	984	30	1,199	32
	≥65y	502	13	579	14	873	15
Educational level	Low	804	29	808	21	910	20
	Medium	859	54	1,494	53	1,771	55
	High	191	17	535	25	712	25
	Missing	4	0	64	1	31	1
Income	Poorest	‡		612	24	561	22
	Q2			761	21	618	18
	Q3			683	24	783	23
	Richest			624	19	775	16
	Missing			221	11	687	20
Health insurance	Public	‡		2,378	80	2,978	86
	Private			236	11	240	8
	Army			78	2	65	1
	None			113	4	103	4
	Missing			96	2	38	1

Participants with valid BP and medicine data. n: unweighted sample size. Estimates are weighted for the complex survey design. Totals may not sum to 100% due to rounding. Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. ‡: Measured in 2010 and 2017 only.

Descriptive analysis

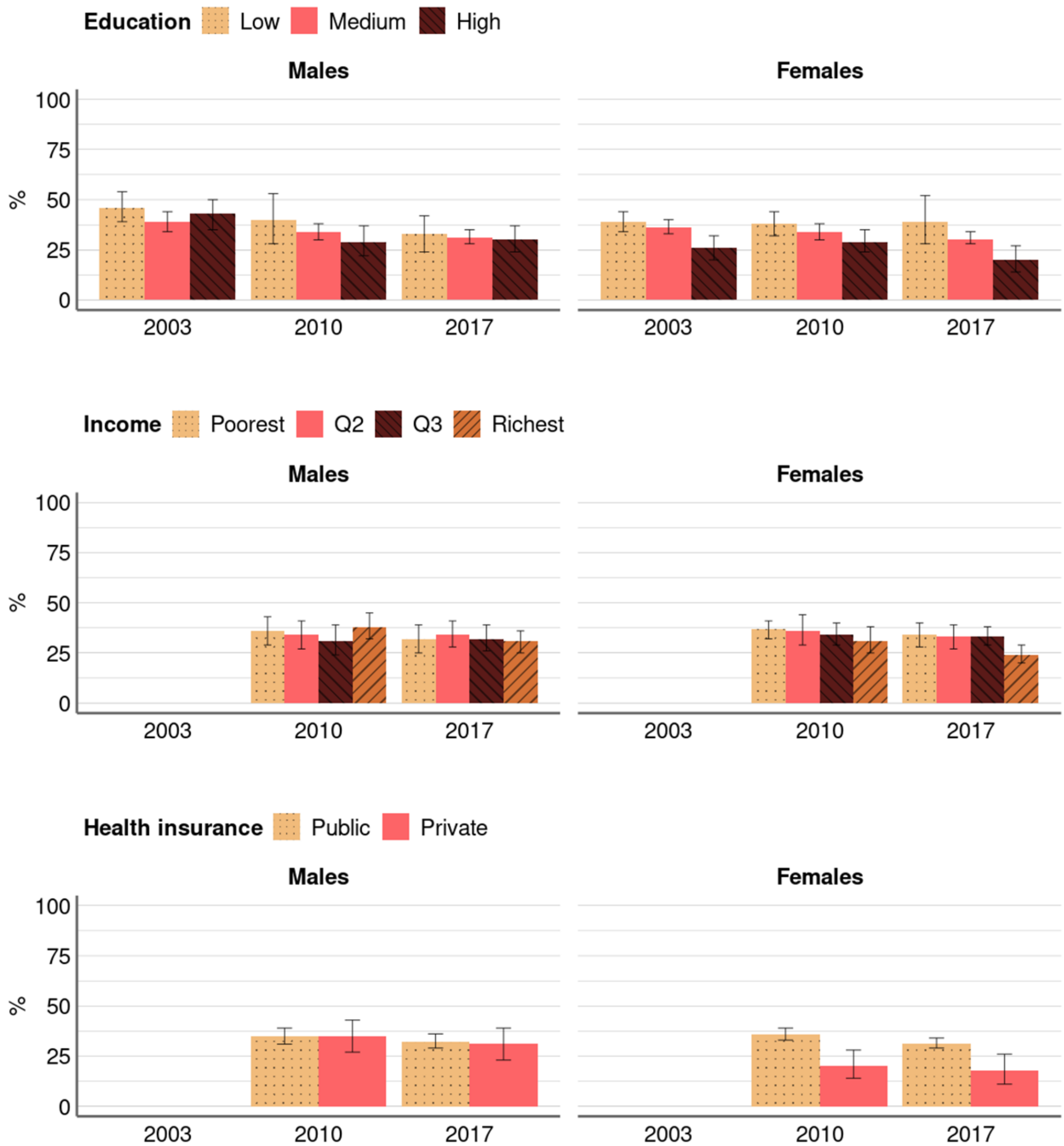
The *observed* (non-age standardised) estimates for survey-defined hypertension by year are presented in Figure 5.1; while *age-standardised* (directly age- and gender-standardised) estimates are presented in Figure 5.2.

Figure 5.1: Hypertension prevalence by SEP indicator and gender (observed).



Observed estimates (% and 95% CI). Educational level: low (<8y); medium (8-12y); high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. Income and health insurance measured in 2010 and 2017 only.

Figure 5.2: Hypertension prevalence by SEP indicator and gender (age-standardised).



Values and 95% CIs were directly age-gender-standardised using data from Census 2017 (age groups: 17-44y; 45-64y; ≥65y). Educational level: low (<8y); medium (8-12y); high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. Income and health insurance measured in 2010 and 2017 only.

I describe briefly the age-standardised estimates by educational level, income, and health insurance in turn below. I also report p-values of the chi-squared test for the age-standardised differences between SEP groups in hypertension outcomes. A full set of observed and age-standardised estimates is provided in Appendix 5.

Educational level: The gap in hypertension between the low and high educational groups was wider among females than males. Hypertension among males was similar in the low and high educational levels in 2003 (low: 43% (95% CI: 35-50); high: 46% (95% CI: 39-54); p=0.475). A transient non-significant increase in this gap was observed in 2010 (low: 40% (95% CI: 28-53); high: 29% (95% CI: 22-37); p=0.128), whereas similar values were observed in 2017 (low: 33% (95% CI: 24-42); high: 30% (95% CI: 24-37); p=0.654). Persisting differences in hypertension by educational level that favoured those most advantaged were evident in females. Among females with low educational level, 39% (95% CI: 34-44), 38% (95% CI: 32-44) and 39% (95% CI: 28-52) had survey-defined hypertension in 2003, 2010, and 2017, respectively. The corresponding figures (and p-values comparing low vs high education level in each year) among females with high educational level were 26% (95% CI: 20-32; p=0.001), 29% (95% CI: 24-35; p=0.035) and 20% (95% CI: 14-27; p=0.002).

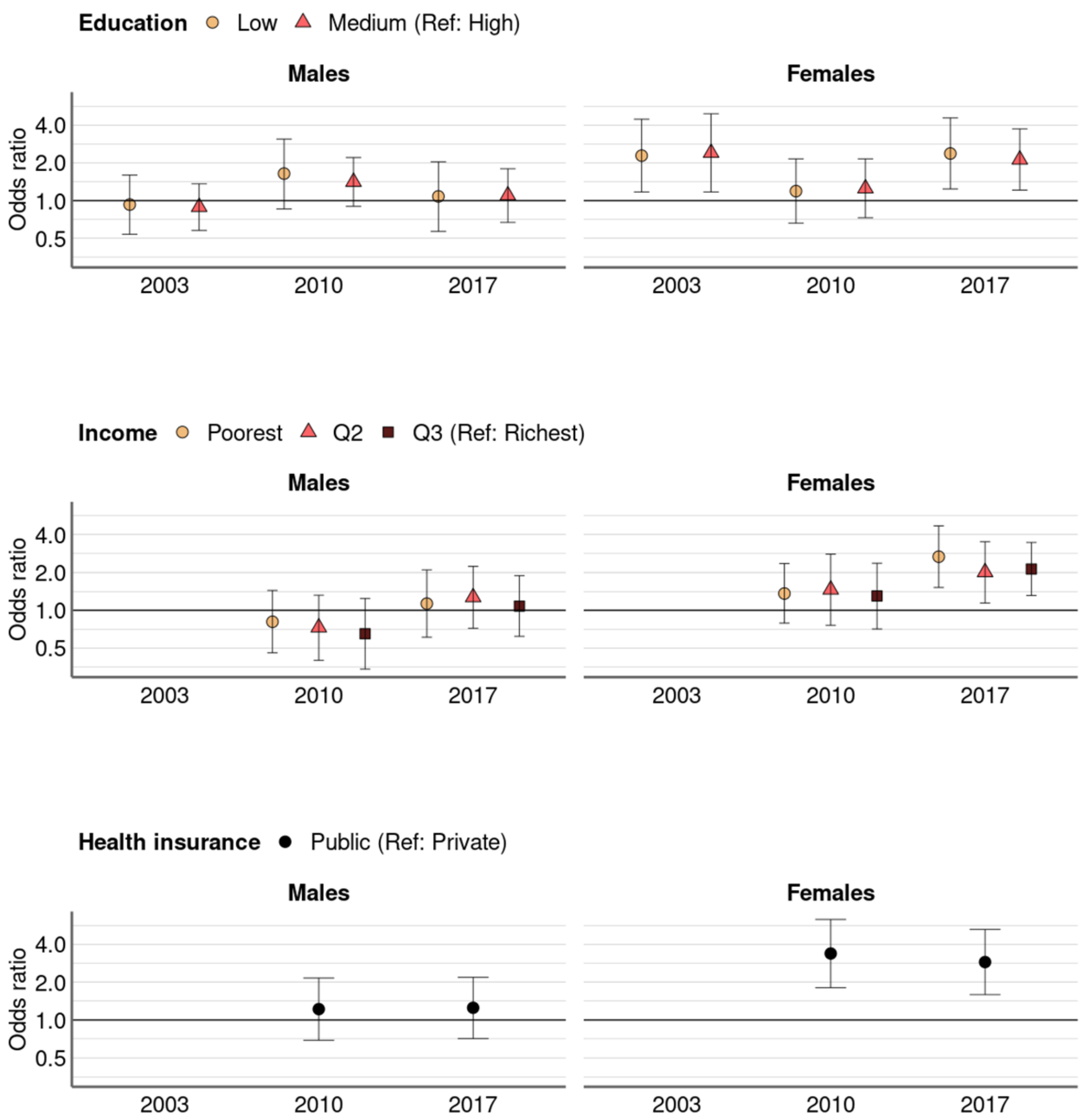
Income: Levels of hypertension did not show any clear differences across income quartiles among males in 2010 or 2017 (2017 estimates Q1: 32% (95% CI: 25-39); Q4: 31% (95% CI: 25-36); p=0.790). Females in the poorest income quartile in 2017 showed higher hypertension prevalence than those in the richest quartile, with respective values of 34% (95% CI: 28-40) and 24% (95% CI: 20-29; p=0.007).

Health insurance: Hypertension prevalence by health insurance status was similar among males in 2010 and 2017. In 2017, hypertension was 32% (95% CI: 29-36) among those with public health insurance and was 31% (95% CI: 23-39) among those with private health insurance (p=0.683). Hypertension prevalence was higher among females with public vs private health insurance in 2010 and 2017. In 2017, hypertension among females with public health insurance was 31% (95% CI: 29-34), compared with 18% (95% CI: 11-26) among those with private health insurance (p=0.003).

Simple measures of SEP inequalities in hypertension (pairwise comparisons)

The age-adjusted ORs for SEP inequalities in hypertension are summarised in Figure 5.3. For brevity, only the results by health insurance status are described here. Results by education and income are presented in a later section using complex measures of inequality (for these SEP indicators, the simple and complex measures showed a similar pattern of inequality).

Figure 5.3: SEP inequalities in hypertension (pairwise comparisons).



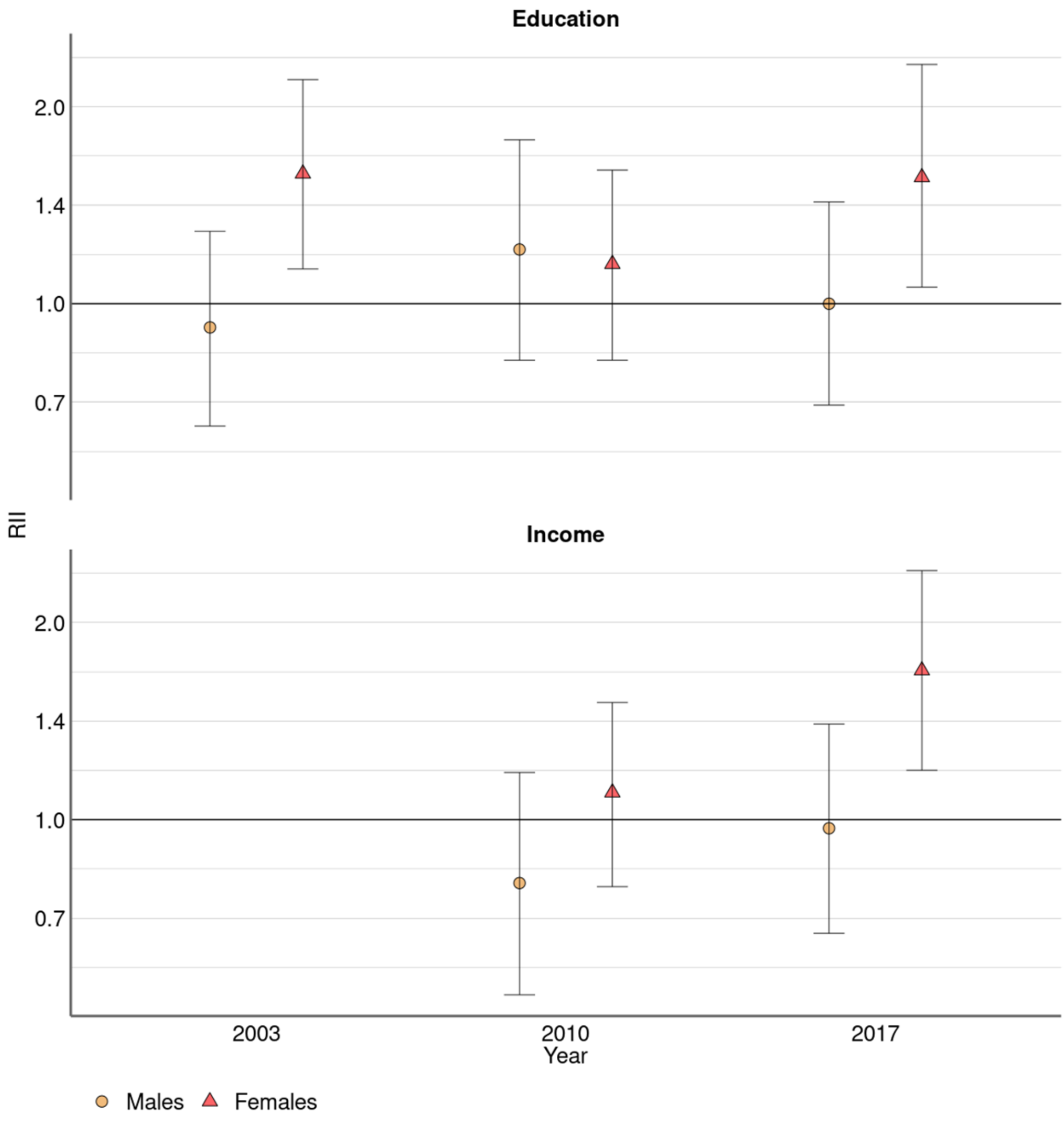
Odds ratios and 95% CIs calculated from age-adjusted logistic regressions. SEP indicators were evaluated in separate models. Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. Income and health insurance measured in 2010 and 2017 only.

Health insurance: Non-statistically significant differences in the odds of hypertension between participants with public vs private health insurance were found among males (OR in 2010: 1.22 (95% CI: 0.69-2.16); OR in 2017: 1.25 (95% CI: 0.71-2.19)). In contrast, females with public vs private health insurance had substantially higher odds of hypertension in both years (OR in 2010: 3.38 (95% CI: 1.81-6.31), OR in 2017: 2.89 (95% CI: 1.59-5.25)).

Complex measures of inequalities in hypertension

Relative SEP inequalities in hypertension estimated using complex measures (RII) are shown in Figure 5.4. The pattern of SEP inequalities was similar using either absolute or relative estimates. For brevity, here I describe only the results based on the relative measure (SII and RII values are provided in full in Appendix 5).

Figure 5.4: SEP inequalities in hypertension estimated using RII.



Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear models (Poisson family and log link) adjusted for the SEP ridit scores (of education or income in separate models) and age. RII can be interpreted as the prevalence ratio between the lowest and highest groups. Income measured in 2010 and 2017 only.

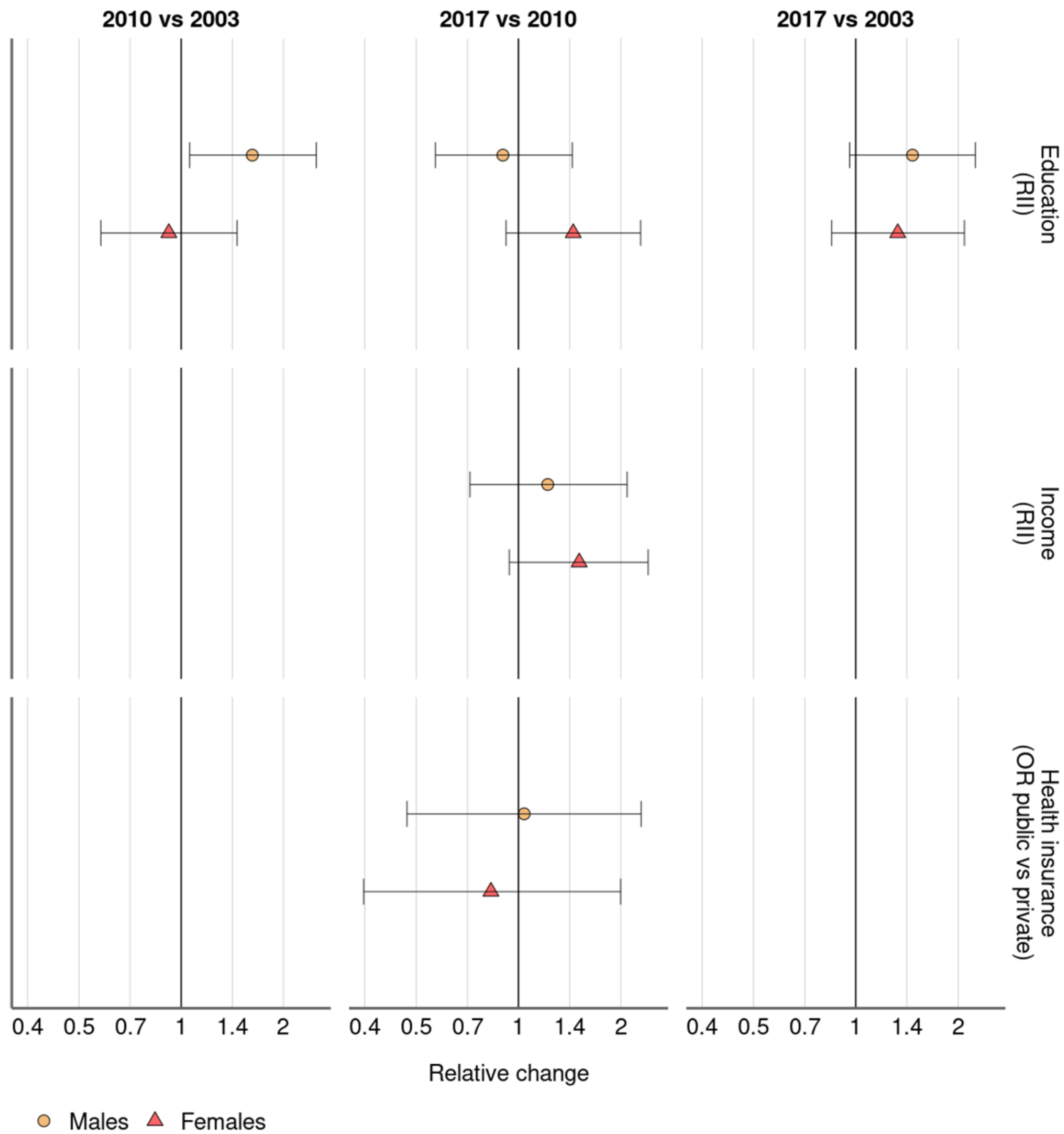
Education: Non-statistically significant relative educational-based inequalities in hypertension were observed among males (RII values were 0.92 (95% CI: 0.65-1.29) in 2003; 1.21 (95% CI: 0.82-1.78) in 2010; 1.00 (95% CI: 0.70-1.43) in 2017). Statistically significant educational-based inequalities were observed among females in 2003 and 2017 (higher levels towards the least educated). The educational-based RII, which can be interpreted as the prevalence ratio between the lowest and highest groups, among females was 1.58 (95% CI: 1.13-2.20) in 2003, 1.15 (95% CI: 0.82-1.60) in 2010 and 1.56 (95% CI: 1.06-2.32) in 2017.

Income: Income-related inequalities were non-statistically significant among males in 2010 (RII: 0.80 (95% CI: 0.54-1.18)) and 2017 (RII: 0.97 (95% CI: 0.67-1.40)). Statistically significant inequalities were found among females in 2017 (higher levels among the poorest) but not in 2010 (RII in 2010: 1.10 (95% CI: 0.79-1.51); RII in 2017: 1.69 (95% CI: 1.19-2.40)).

Changes in SEP inequalities in hypertension over time

Changes over time in relative inequalities in hypertension are shown in Figure 5.5. These estimates were obtained using models on pooled 2003-2010-2017 data that contained the two-way interaction term SEP by survey year. The pattern of changes over time was similar using either absolute or relative estimates. For brevity, here I describe only the results based on the relative measure (a full set of absolute and relative estimates are provided in Appendix 5).

Figure 5.5: Change over time in SEP inequalities in hypertension using relative measures.



Changes over time analysed by the inclusion of the two-way interaction term SEP indicator by survey year to the models while adjusting for age. SEP indicators were evaluated in separate models. Relative Index of Inequality (RII) and odds ratios (ORs) and 95% CIs estimated from generalised linear models. Using the interaction term, the change in RII can be interpreted as the ratio of year-specific RIIs. Income and health insurance measured in 2010 and 2017 only.

Education: As shown in Figure 5.5, the educational-based RII widened over time among males. The increase in RII comparing 2010 with 2003 was statistically significant (RII: 1.62 (95% CI: 1.06-2.50)), reflecting a sharper decrease in hypertension at the highest educational level; the increase in RII comparing 2017 with 2003 almost attained statistical significance (RII: 1.47 (95% CI: 0.96-2.25)). Among females inequalities also widened, but this change did not attain statistical significance. Comparing 2017 with 2003, the relative increase in RII was 33% (RII: 1.33 (95% CI: 0.85-2.09)).

Income: Income-based inequalities also widened over time in both genders but did not reach statistical significance. Between 2010 and 2017, the RII increased by 22% among males (RII: 1.22 (95% CI: 0.72-2.09)) and by 51% (RII: 1.51 (95% CI: 0.94-2.41)) among females.

Health insurance: The odds of hypertension for those with public vs private health insurance were stable among males (OR 2017 vs 2010: 1.04 (95% CI: 0.47-2.30)) and females (OR 2017 vs 2010: 0.83 (95% CI: 0.35-2.00)).

Summary of findings in hypertension

For the sake of brevity, Table 5.3 summarises the age-gender-standardised prevalence levels of hypertension, and the gender-specific RII estimates by educational level, only. The summary table also includes the estimated change in RII over time. A full set of RII and SII estimates by health insurance and income quartile are provided in Appendix 5.

Table 5.3: Summary of educational-based inequalities in hypertension.

	Prevalence by educational level			
ENS	**Low**	**Medium**	**High**	**RII**
Males				
2003	46% (39-54)	39% (34-44)	43% (35-50)	0.92 (0.65-1.29)
2010	40% (28-53)	34% (30-38)	29% (22-37)	1.21 (0.82-1.78)
2017	33% (24-42)	31% (28-35)	30% (24-37)	1.00 (0.70-1.43)
2010 vs 2003				**1.62 (1.06-2.50)**
2017 vs 2010				0.90 (0.57-1.44)
2017 vs 2003				1.47 (0.96-2.25)
Females				
2003	39% (34-44)	36% (33-40)	26% (20-32)	**1.58 (1.13-2.20)**
2010	38% (32-44)	34% (30-38)	29% (24-35)	1.15 (0.82-1.60)
2017	39% (28-52)	30% (28-34)	20% (14-27)	**1.56 (1.06-2.32)**
2010 vs 2003				0.92 (0.58-1.46)
2017 vs 2010				1.45 (0.92-2.29)
2017 vs 2003				1.33 (0.85-2.09)

In bold: statistically significant inequalities (p<0.05). Prevalence estimates were directly age-gender-standardised using data from Census 2017 (age groups: 17-44y; 45-64y; ≥65y). Relative Index of Inequality (RII) and 95% CIs from estimated generalised linear models adjusted for age and education (ridit scores). Changes over time analysed by including a two-way interaction term educational level (ridit scores) by survey year.

5.4.2. Inequalities in hypertension management indicators

Socioeconomic characteristics of the analytical sample

Estimates of undiagnosed, untreated, and uncontrolled hypertension were calculated among the 2,342 males and 3,195 females with survey-defined hypertension (Table 5.4 males; Table 5.5 females). Among the subset of ENS participants with hypertension, the analytical sample showed an increase over time in levels of education and income, and stable levels of public health insurance. In agreement with the results shown in Section 5.4.1 (the socioeconomic characteristics of the ENS general population), the proportion of adults at the lowest educational level (<8y of formal education) was higher among persons with hypertension compared with the general population (e.g. in 2017, respective figures were 27% vs 14% (males) and 40% vs 20% (females)). Participants with hypertension were older compared with the general population (e.g. the percentage of males aged ≥65y in 2017 was 12% in the general population and 33% among those with hypertension; 15% vs 39% among females, respectively). The age distribution of participants with hypertension was older over time (e.g. the percentage of males aged ≥65y increased from 20% to 33% between 2003 and 2017).

Table 5.4: Analytical sample of males with hypertension.

		2003		2010		2017	
Variable		**n**	**%**	**n**	**%**	**n**	**%**
Total	All	771	100	758	100	813	100
Age	17-44y	165	39	116	24	101	19
	45-64y	297	42	346	49	329	48
	≥65y	309	20	296	27	383	33
Educational level	Low	369	34	296	30	285	27
	Medium	313	48	347	52	388	49
	High	86	19	98	17	132	23
	Missing	3	0	17	1	8	1
Income	Poorest	‡		120	19	96	14
	Q2			221	25	162	22
	Q3			143	20	170	22
	Richest			222	28	242	25
	Missing			52	8	143	17
Health insurance	Public	‡		594	80	683	78
	Private			62	10	75	14
	Army			23	1	19	2
	None			47	7	26	4
	Missing			32	2	10	1

n: unweighted sample size. Estimates are weighted for the complex survey design. Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. ‡: Measured in 2010 and 2017 only.

Table 5.5: Analytical sample of females with hypertension.

		2003		2010		2017	
Variable		**n**	**%**	**n**	**%**	**n**	**%**
Total	All	827	100	1,064	100	1,304	100
Age	17-44y	95	25	117	18	79	10
	45-64y	319	43	464	47	546	51
	≥65y	413	33	483	35	679	39
Educational level	Low	523	50	506	37	619	40
	Medium	273	44	423	46	568	50
	High	29	5	94	14	102	10
	Missing	2	0	41	2	15	1
Income	Poorest	‡		196	22	200	24
	Q2			332	26	278	19
	Q3			252	24	334	26
	Richest			200	19	248	13
	Missing			84	9	244	18
Health insurance	Public	‡		909	86	1,174	88
	Private			42	6	52	4
	Army			24	2	29	2
	None			36	3	32	4
	Missing			53	3	17	1

n: unweighted sample size. Estimates are weighted for the complex survey design. Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. ‡: Measured in 2010 and 2017 only.

Descriptive analysis

The *observed* and *age-standardised* estimates for the three management indicators among males are presented in Figures 5.6 and 5.7, respectively. Figures 5.8 and 5.9, show the respective values for females.

Figure 5.6: Hypertension management indicator by SEP among males (observed).

Observed estimates (% and 95% CI). Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. Income and health insurance measured in 2010 and 2017 only.

Figure 5.7: Hypertension management indicator by SEP among males (age-standardised).

Values and 95% CIs were directly age-gender-standardised using the age composition of participants with hypertension in ENS2017 (age groups: 17-44y; 45-64y; 65-74y; ≥75y). Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. Income and health insurance measured in 2010 and 2017 only.

Figure 5.8: Hypertension management indicator by SEP among females (observed).

Observed estimates (% and 95% CI). Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. Income and health insurance measured in 2010 and 2017 only.

Figure 5.9: Hypertension management indicator by SEP among females (age-standardised).

Values and 95% CIs were directly age-gender-standardised using the age composition of participants with hypertension in ENS2017 (age groups: 17-44y; 45-64y; 65-74y; ≥75y). Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. Income and health insurance measured in 2010 and 2017 only.

Below, I describe the age-standardised results for each outcome.

Undiagnosed hypertension by SEP indicators

Among males, inequalities in undiagnosed hypertension were clearer when education or health insurance were used as SEP indicators. Males with lower levels of education showed higher levels of undiagnosed hypertension in 2003, 2010, and 2017 (e.g. in 2017 low: 55% (95% CI: 43-67); high: 34% (95% CI: 22-47); p=0.017). Levels of undiagnosed hypertension were higher among males with public than with private health insurance in 2017 (public: 44% (95% CI: 39-49); private: 25% (95% CI: 20-30); p=0.016).

Among females, however, those with low educational level showed lower levels of undiagnosed hypertension in 2003 (low: 21% (95% CI: 16-27); high: 73% (95% CI: 44-93); p<0.001). Between 2003 and 2017, undiagnosed hypertension decreased sharply among females at the highest educational level and increased slightly at the low and middle levels, resulting in a narrowing of differences. In 2017, 19% (95% CI: 9-32) of females in the highest educational group were undiagnosed vs 25% (95% CI: 18-34) of females in the lowest educational group (p=0.317). No obvious patterns in undiagnosed hypertension by income or health insurance were observed.

Untreated hypertension by SEP indicators

Overall, males showed similar levels of untreated hypertension by education and health insurance. The gap in untreated hypertension by SEP groups was larger among females than males. However, the 95% CIs were wide and only a few estimates reached statistical significance. For example, females with low vs high educational level showed higher levels of untreated hypertension in 2017 (low: 31% (95% CI: 25-38); high: 18% (95% CI: 8-31); p=0.038).

Uncontrolled hypertension by SEP indicators

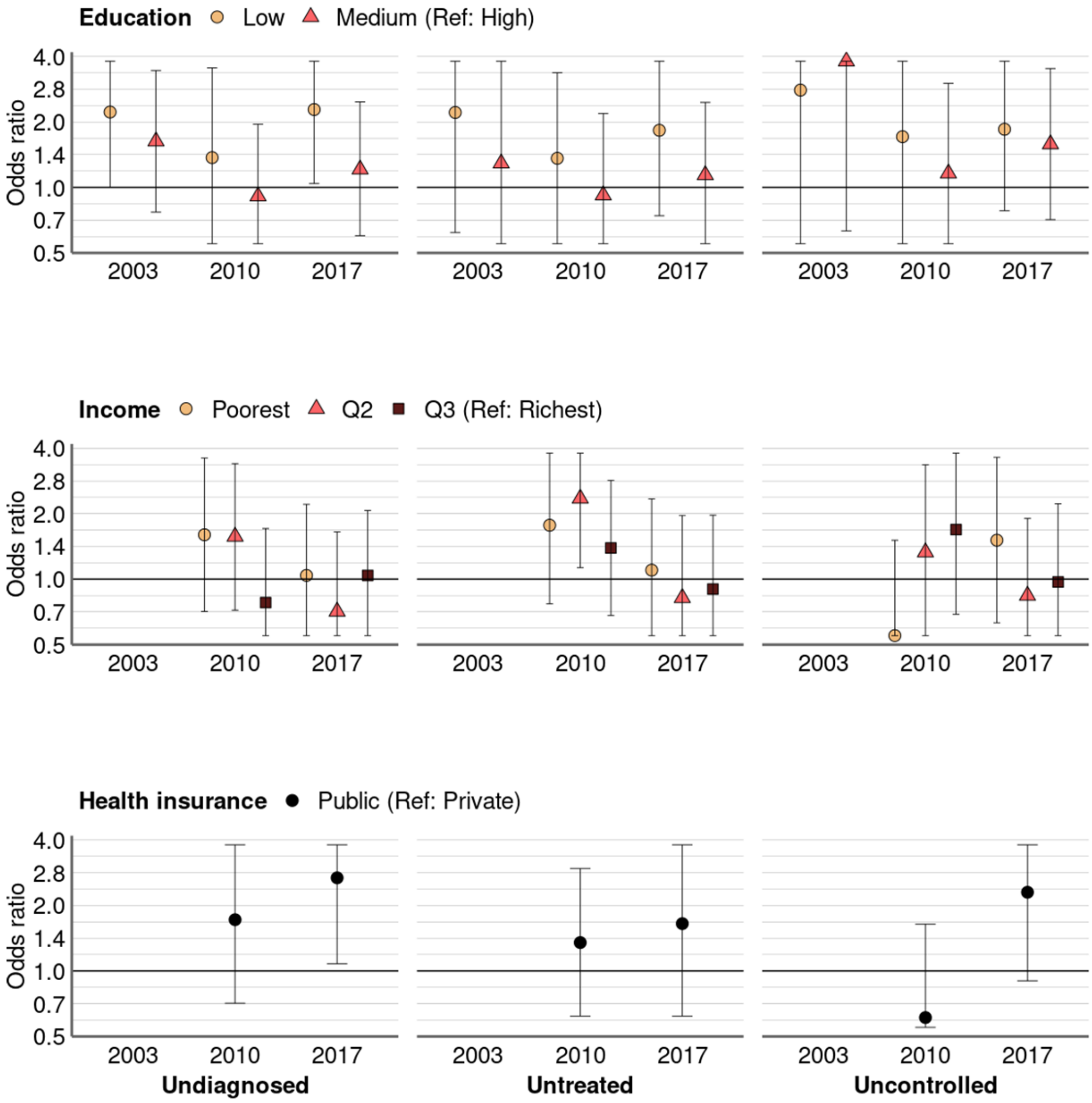
Among males, similar levels of uncontrolled hypertension were found by SEP groups. Among females, levels of uncontrolled hypertension were similar by education in 2003. However, the gap increased over time, driven by a sharp decrease among those in the highest educational group. In 2003, the levels of uncontrolled hypertension were 83% (95% CI: 77-87) in the lowest educational group and 78% (95% CI: 36-98) in the highest educational group (p=0.315). Respective figures in 2017 were 72% (95% CI: 64-79) and 43% (95% CI: 24-63; p=0.003).

Levels of uncontrolled hypertension seemed to decrease over time only among females with private health insurance. In 2010, levels of uncontrolled hypertension were similar, at 67% (95% CI: 61-72) and 63% (95% CI: 47-77) in the public and private health insurance groups, respectively (p=0.526). The corresponding figures in 2017 were 62% (95% CI: 59-65) and 30% (95% CI: 22-38; p=0.001).

Simple measures of SEP inequalities in hypertension management (pairwise comparisons)

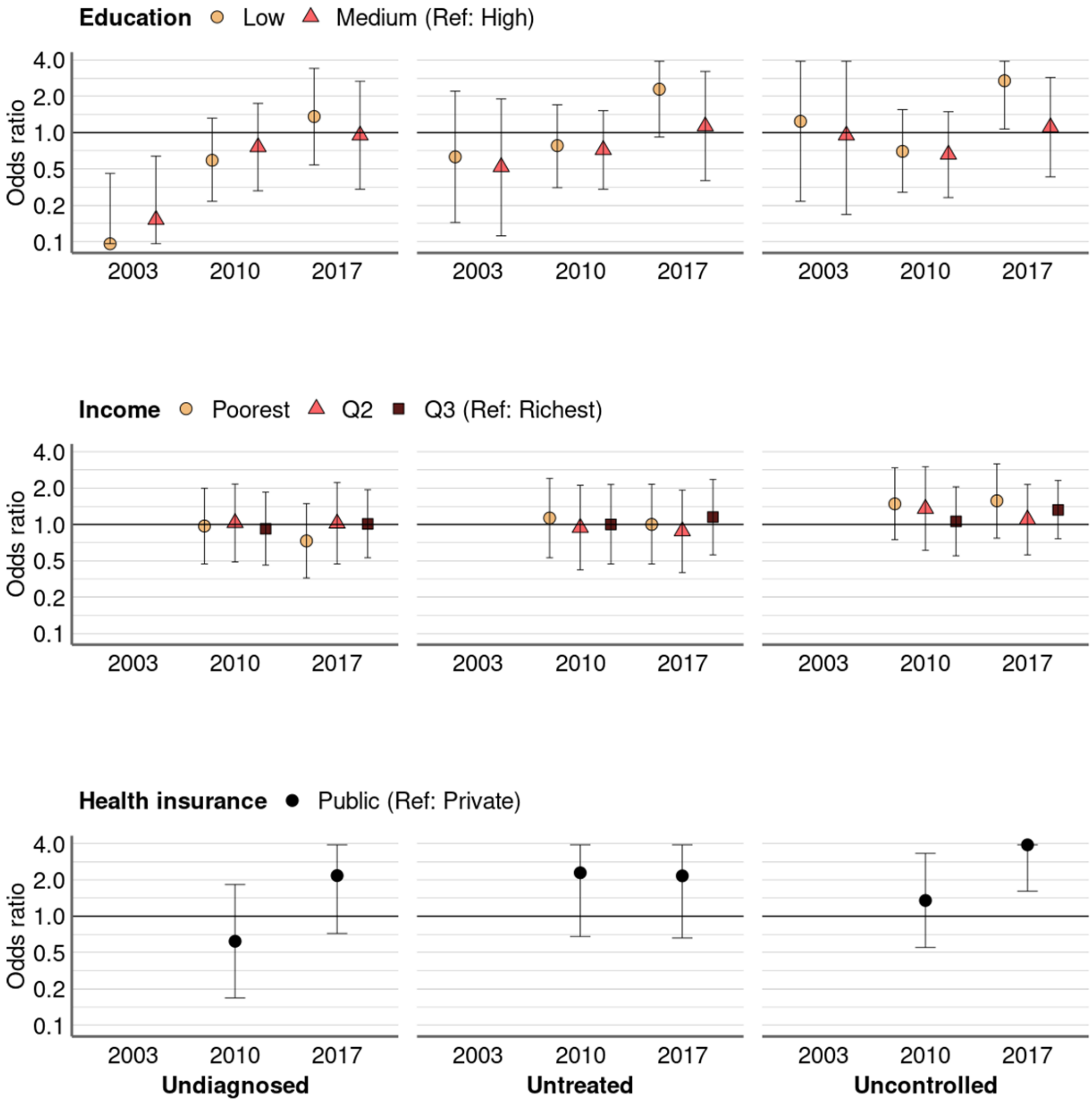
Simple measures of inequalities in hypertension management indicators (estimated using ORs) are presented in Figures 5.10 and 5.11 for males and females, respectively. Results by education showed a dose-response gradient, and so these associations are presented in a later section using complex measures of inequalities. Here I describe results for the simple measures of inequalities (pairwise comparisons) by income and health insurance status only.

Figure 5.10: SEP inequalities in hypertension management indicators among males (pairwise comparisons).



Odds ratios and 95% CIs calculated from age-adjusted logistic regressions. SEP indicators were evaluated in separate models. Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. Income and health insurance measured in 2010 and 2017 only. To simplify the plot, 95% CIs were truncated at the minimum and maximum value of the coefficients. Original values are presented in Appendix 5.

Figure 5.11: SEP inequalities in hypertension management indicators among females (pairwise comparisons).



Odds ratios and 95% CIs calculated from age-adjusted logistic regressions. Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the size of the household. Income and health insurance measured in 2010 and 2017 only. To simplify the plot, 95% CIs were truncated at the minimum and maximum value of the coefficients. Original values are presented in Appendix 5.

Inequalities in undiagnosed hypertension

Income: No clear income-based inequalities in undiagnosed hypertension were found. Among males, the OR for undiagnosed hypertension in 2017 (richest as reference) was 1.04 (95% CI: 0.49-2.21) in the poorest quartile; 0.71 (95% CI: 0.31-1.65) in Q2; and 1.04 (95% CI: 0.52-2.07) in Q3. Respective values among females were 0.73 (95% CI: 0.36-1.49); 1.02 (95% CI: 0.47-2.22); and 1.01 (95% CI: 0.53-1.94).

Health insurance: Males with public health insurance (vs private) showed higher odds of undiagnosed hypertension in 2010 and 2017, however, this association attained statistical significance only in 2017 (OR in 2010: 1.72 (95% CI: 0.71-4.19); OR in 2017: 2.68 (95% CI: 1.08-6.63)). Inequalities in undiagnosed hypertension by health insurance status were not statistically significant among females (OR in 2010: 0.62 (95% CI: 0.21-1.83); OR in 2017: 2.17 (95% CI: 0.72-6.47)).

Inequalities in untreated hypertension

Income: No clear inequalities by income quartile in untreated hypertension were observed. Among males in 2017, the estimated OR (richest as reference) was 1.10 (95% CI: 0.52-2.34) in the poorest group, 0.82 (95% CI: 0.34-1.96) in Q2 and 0.90 (95% CI: 0.41-1.97) in Q3. Among females, the respective figures were 1.00 (95% CI: 0.47-2.15), 0.88 (95% CI: 0.40-1.93), and 1.15 (95% CI: 0.56-2.36).

Health insurance: Inequalities in untreated hypertension by health insurance status were not statistically significant. However, the estimates consistently showed higher odds of untreated hypertension among those with public health insurance. Among males, the estimated OR (public vs private) was 1.35 (95% CI: 0.62-2.96) in 2010 and 1.65 (95% CI: 0.62-4.35) in 2017. Among females, the respective ORs were 2.29 (95% CI: 0.68-7.69) and 2.16 (95% CI: 0.66-7.06). To increase the sample size (and statistical power), I estimated the ORs using the 2010-2017 pooled data combined across gender. After gender adjustment, the estimated OR (public vs private health insurance) almost attained statistical significance (1.65 (95% CI: 0.97-2.81)).

Inequalities in uncontrolled hypertension

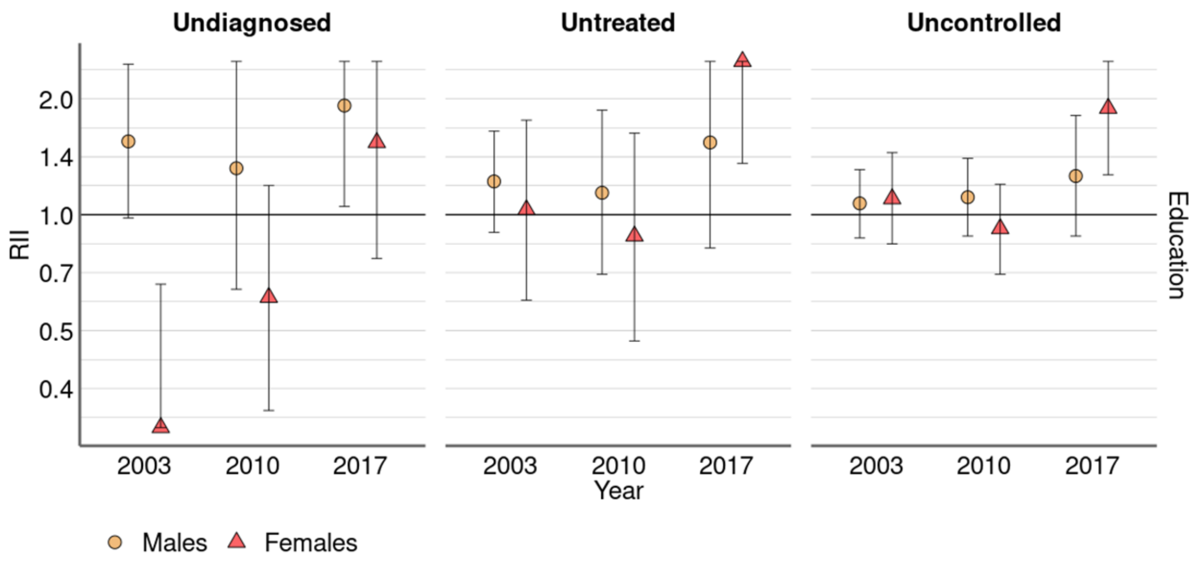
Income: Inequalities in uncontrolled hypertension by income were not significant in either gender. Among males in 2017, the estimated OR for uncontrolled hypertension in the poorest, Q2 and Q3 income quartiles (richest as reference) were 1.51 (95% CI: 0.63-3.63), 0.84 (95% CI: 0.37-1.90) and 0.97 (95% CI: 0.42-2.22), respectively. The respective figures among females were 1.57 (95% CI: 0.77-3.18), 1.10 (95% CI: 0.56-2.14), and 1.32 (95% CI: 0.76-2.32).

Health insurance: Inequalities in uncontrolled hypertension by health insurance status were not statistically significant among males in 2010 (OR for public vs private: 0.61 (95% CI: 0.23-1.64)) but almost attained significance in 2017 (OR: 2.30 (95% CI: 0.90-5.91)). In a similar pattern, these inequalities were non-statistically significant among females in 2010 (OR: 1.35 (95% CI: 0.55-3.31)) whereas in 2017, the odds of having uncontrolled hypertension were significantly higher for those with public rather than private health insurance (OR: 3.90 (95% CI: 1.61-9.46)).

Complex measures of SEP inequalities in hypertension management

Based on the pairwise comparisons, the estimates for education showed a dose-response gradient with the hypertension management outcomes. Estimates for the educational-based RII by year and gender are shown in Figure 5.12. A similar pattern was observed using either the RII or SII. For the sake of brevity, I describe here the estimates for the RII only (estimates for both are provided in Appendix 5).

Figure 5.12: Educational-based inequalities in hypertension management indicators using RII.



Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear models (Poisson family and log link) adjusted for the SEP ridit scores of education and age. RII can be interpreted as the prevalence ratio between the lowest and highest groups. To simplify the plot, 95% CIs were truncated at the minimum and maximum value of the coefficients. Original values are presented in Appendix 5.

Inequalities in undiagnosed hypertension

My analyses for undiagnosed hypertension among males showed non-statistically significant inequalities by education in 2003 and 2010, but inequalities emerged in 2017: the educational-based RII in 2017 was 1.92 (95% CI: 1.05-3.53). Among females, I observed inequalities in 2003, with lower levels of undiagnosed hypertension among those with lower educational levels (RII=0.28 (95% CI: 0.12-0.66)). The magnitude of these inequalities changed towards narrower differences across the educational groups over time (e.g. in 2017: RII=1.54 (95% CI: 0.77-3.07)).

Inequalities in untreated hypertension

Both genders showed the same direction of educational-based inequalities in untreated hypertension (higher levels among the least educated). However, the estimates among males did not reach statistical significance. The educational-based RII among males in 2017 was 1.54 (95% CI: 0.82-2.88). Educational-based inequalities in untreated hypertension were larger among females (RII in 2017: 2.50 (95% CI: 1.36-4.62)).

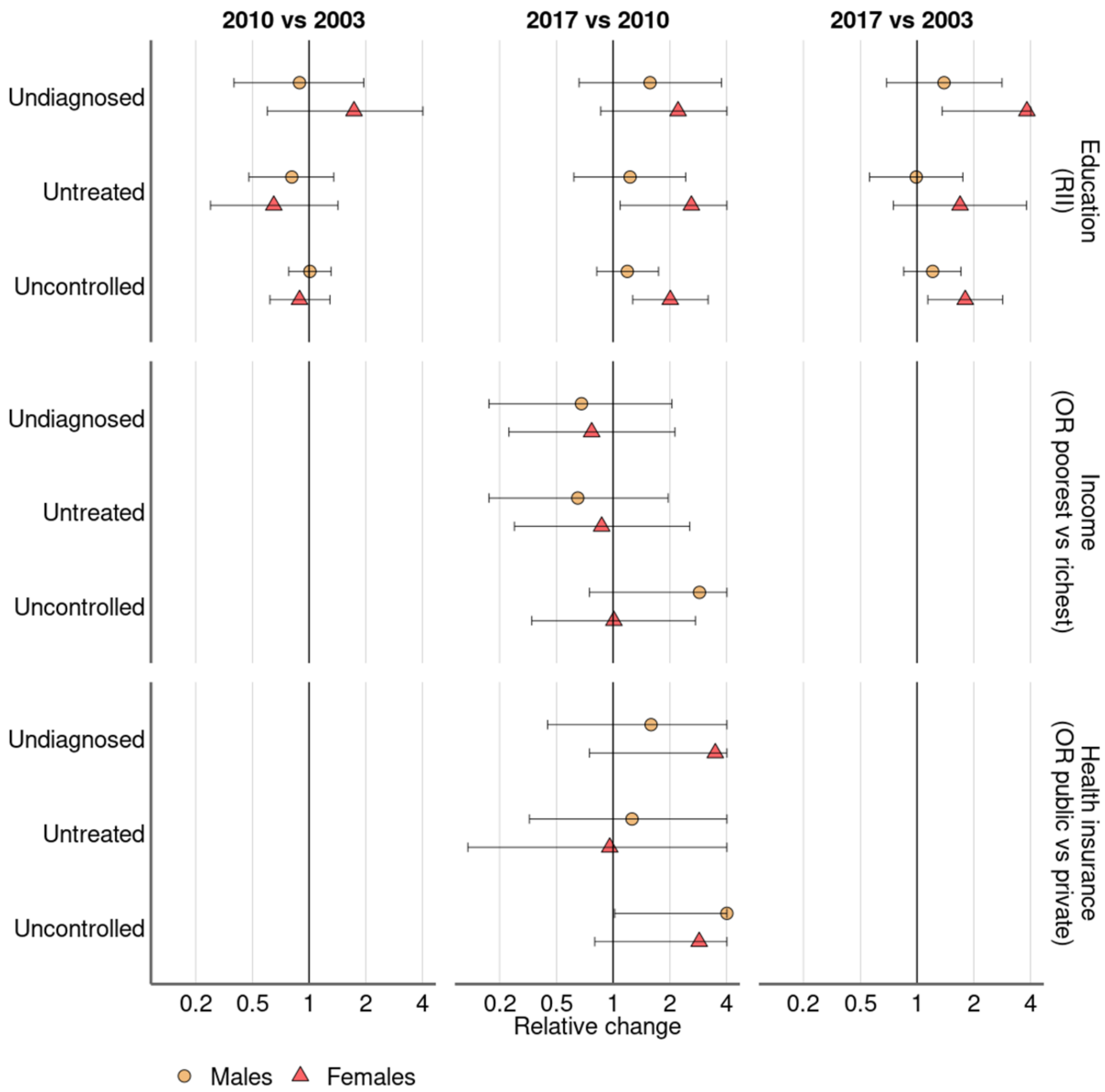
Inequalities in uncontrolled hypertension

Non-statistically significant educational-based inequalities in uncontrolled hypertension were found among males in each survey year and among females in 2003 and 2010. Inequalities in uncontrolled hypertension among females emerged in 2017. The educational-based RII among males in 2017 was 1.26 (95% CI: 0.88-1.81) while the corresponding figure among females was 1.89 (95% CI: 1.27-2.83).

Changes over time in SEP inequalities in hypertension management

Changes over time in relative inequalities in undiagnosed, untreated, and uncontrolled hypertension are shown in Figure 5.13. These estimates were obtained using models on pooled 2003-2010-2017 data that contained the two-way interaction term SEP by survey year. Inequalities by health insurance status and income quartile are shown using simple measures (pairwise comparisons); inequalities by education are shown using a complex measure (RII). The pattern of changes over time was similar using either absolute or relative estimates. For brevity, here I describe only the results based on the relative measure (absolute and relative changes over time are provided in full in Appendix 5).

Figure 5.13: Relative change over time in SEP inequalities in hypertension management indicators.



Changes over time analysed by the inclusion of the two-way interaction term SEP indicator by survey year to the models while adjusting for age. SEP indicators were evaluated in separate models. Relative Index of Inequality (RII) and odds ratio (ORs) and 95% CIs estimated from generalised linear models using Poisson (log link) and binomial (logit link) functions, respectively. Using the interaction term, the change in RII/OR can be interpreted as the ratio of year-specific RIIs/OR's. Income: quartiles of household monthly income equivalised to the size of the household. Income and health insurance measured in 2010 and 2017 only. To simplify the plot, 95% CIs were truncated at the maximum value of the coefficients. Original values are presented in Appendix 5.

Overall, similar patterns in the changes over time in the hypertension management indicators were observed using relative or absolute inequality measures. Changes in income-based inequalities were non-statistically significant. However, a few noticeable changes over time by education (in each management indicator) and by health insurance status (in uncontrolled hypertension) were observed.

Changes over time in SEP inequalities in undiagnosed hypertension

Among males, the estimated RII for undiagnosed hypertension increased over time, but the increase was non-statistically significant (RII 2017 vs 2003: 1.39 (95% CI: 0.69-2.82)), suggesting persistent inequalities. Among females, a significant increase in the RII was observed between 2003 and 2017 (RII 2017 vs 2003: 3.82 (95% CI: 1.36-10.70)), reflecting a narrowing of the gap between the educated groups (undiagnosed hypertension was markedly higher among the most educated in 2003).

Changes over time in SEP inequalities in untreated hypertension

The educational-based RII for untreated hypertension showed a non-statistically significant increase between 2010 and 2017 among males (RII 2017 vs 2010: 1.23 (95% CI: 0.62-2.43)). The corresponding estimate reached statistical significance among females (RII 2017 vs 2010: 2.60 (95% CI: 1.09-6.23)), reflecting widening inequality due to a sharper fall in untreated hypertension among the most educated.

Changes over time in SEP inequalities in uncontrolled hypertension

The educational-based RII for uncontrolled hypertension showed a non-statistically significant change between 2003 and 2017 among males (RII 2017 vs 2003: 1.21 (95% CI: 0.85-1.71)). The corresponding estimate reached statistical significance among females (RII 2017 vs 2003: 1.80 (95% CI: 1.14-2.84)), reflecting a sharper fall in uncontrolled hypertension among the most educated.

Inequalities in uncontrolled hypertension between 2010 and 2017 by health insurance status (public vs private) increased significantly among males (OR 2017 vs 2010: 4.01 (95% CI: 1.02-15.77)). Among females, the change in the odds of having uncontrolled hypertension did not reach statistical significance (OR 2017 vs 2010: 2.86 (95% CI: 0.80-10.21)).

Summary of findings in hypertension management indicators

Table 5.6 summarises the (i) directly age-standardised levels of the hypertension management indicators, and (ii) educational-based RII estimates. A full set of estimates by income quartile and health insurance status are provided in Appendix 5. Overall, higher levels of undiagnosed, untreated, and uncontrolled hypertension were found among the least educated males in each survey year and among females in the most recent survey (2017). Among males, statistical significance was attained only for the RII estimate for undiagnosed hypertension in 2017. Among females, statistical significance was attained for untreated and uncontrolled hypertension in 2017. The direction of inequalities among females shifted from showing significantly higher levels of undiagnosed hypertension among the most educated in 2003 to narrower differences across the educational groups in 2017.

Table 5.6: Summary of educational-based inequalities in hypertension management indicators.

	Prevalence by educational level			
ENS	**Low**	**Medium**	**High**	**RII**
Males				
Undiagnosed hypertension				
2003	56% (48-64)	47% (39-55)	46% (28-66)	1.55 (0.98-2.46)
2010	50% (40-61)	37% (30-46)	37% (23-52)	1.32 (0.64-2.74)
2017	55% (43-67)	39% (31-47)	34% (22-47)	**1.92 (1.05-3.53)**
2010 vs 2003				0.89 (0.40-1.95)
2017 vs 2010				1.57 (0.66-3.76)
2017 vs 2003				1.39 (0.69-2.82)
Untreated hypertension				
2003	72% (66-78)	66% (58-74)	63% (44-80)	1.22 (0.90-1.65)
2010	56% (47-65)	51% (43-60)	59% (40-76)	1.14 (0.70-1.87)
2017	52% (40-64)	42% (33-51)	39% (27-53)	1.54 (0.82-2.88)
2010 vs 2003				0.81 (0.48-1.35)
2017 vs 2010				1.23 (0.62-2.43)
2017 vs 2003				0.99 (0.56-1.75)
Uncontrolled hypertension				
2003	92% (88-95)	94% (87-98)	86% (66-97)	1.07 (0.87-1.31)
2010	88% (81-93)	84% (76-91)	86% (72-94)	1.11 (0.88-1.40)
2017	73% (61-83)	76% (69-82)	63% (49-76)	1.26 (0.88-1.81)
2010 vs 2003				1.01 (0.78-1.31)
2017 vs 2010				1.19 (0.82-1.74)
2017 vs 2003				1.21 (0.85-1.71)

	Prevalence by educational level			
ENS	**Low**	**Medium**	**High**	**RII**
Females				
Undiagnosed hypertension				
2003	21% (16-27)	31% (23-39)	73% (44-93)	**0.28 (0.12-0.66)**
2010	19% (14-25)	26% (20-33)	23% (10-41)	0.61 (0.31-1.19)
2017	25% (18-34)	24% (19-30)	19% (9-32)	1.54 (0.77-3.07)
2010 vs 2003				1.73 (0.60-5.02)
2017 vs 2010				2.21 (0.86-5.66)
2017 vs 2003				**3.82 (1.36-10.70)**
Untreated hypertension				
2003	42% (35-49)	39% (30-49)	68% (34-92)	1.03 (0.60-1.76)
2010	26% (19-35)	30% (24-36)	25% (12-41)	0.88 (0.47-1.63)
2017	31% (25-38)	22% (17-28)	18% (8-31)	**2.50 (1.36-4.62)**
2010 vs 2003				0.65 (0.30-1.42)
2017 vs 2010				**2.60 (1.09-6.23)**
2017 vs 2003				1.69 (0.75-3.80)
Uncontrolled hypertension				
2003	83% (77-87)	78% (70-85)	78% (36-98)	1.10 (0.84-1.45)
2010	66% (58-73)	68% (60-74)	64% (48-78)	0.92 (0.70-1.20)
2017	72% (64-79)	56% (48-63)	43% (24-63)	**1.89 (1.27-2.83)**
2010 vs 2003				0.89 (0.62-1.29)
2017 vs 2010				**2.01 (1.27-3.19)**
2017 vs 2003				**1.80 (1.14-2.84)**

In bold: statistically significant results ($p<0.05$). Values (% and 95% CI) were directly age-gender-standardised using the age composition of participants with hypertension in ENS2017 (age groups: 17-44y; 45-64y; 65-74y; ≥75y). Educational-based Relative Index of Inequality (RII) and 95% CIs from age-adjusted linear models. Changes over time analysed by including the two-way interaction term education (ridit scores) by survey year.

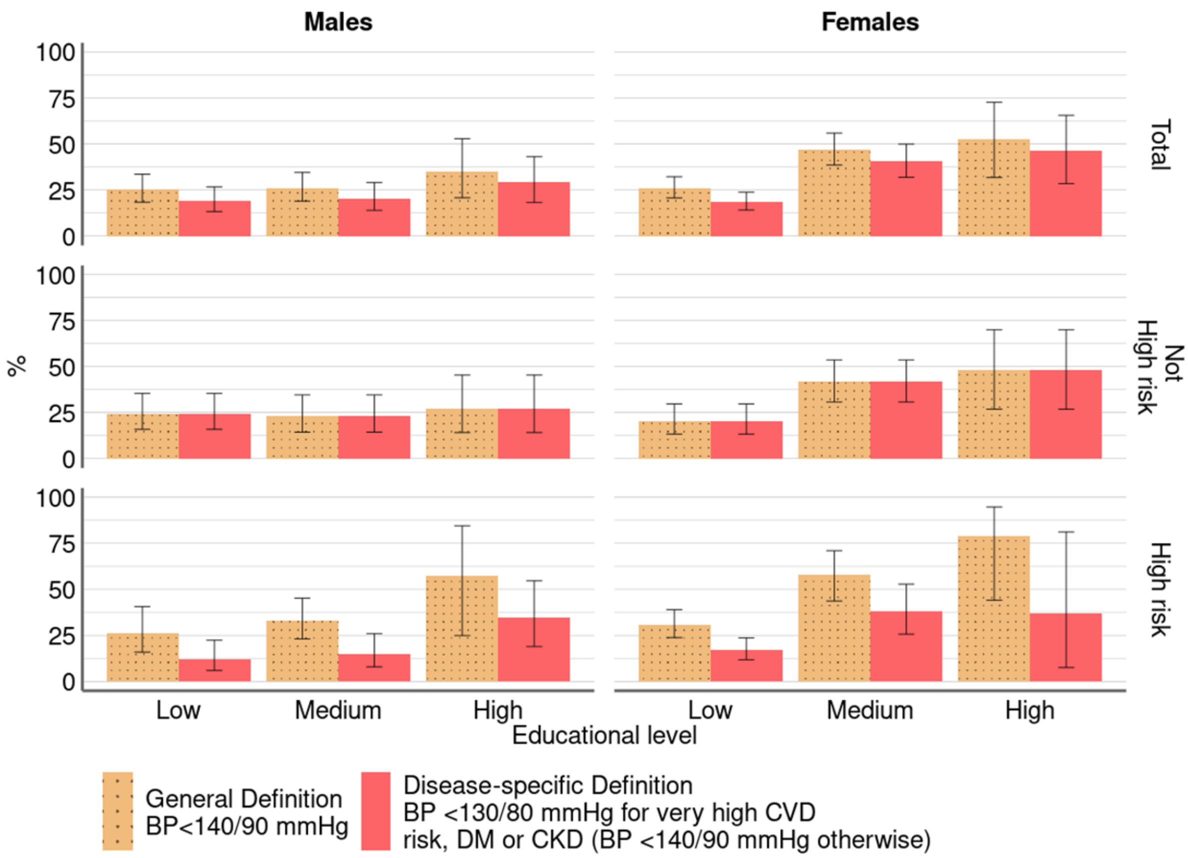
Changes over time in these estimates by education are also shown in Table 5.6. Overall, inequalities did not change significantly over time among males, but they increased among females. Among females, a statistically significant increase in the RII was observed for (i) undiagnosed and uncontrolled hypertension between 2003 and 2017, and for (ii) untreated hypertension between 2010 and 2017. These increases reflected a sharper decrease over time in levels of undiagnosed, untreated, and uncontrolled hypertension among females at the highest educational level.

Controlled hypertension based on two BP goals

The following analysis was performed among those participants with survey-defined hypertension and valid data on the comorbid conditions used to classify adults as being high risk (CKD, or prior diagnosis of stroke, infarction, or DM). The prevalence of high risk (at least one comorbidity) was 42% (95% CI: 33-52), 30% (95% CI: 22-39), and 27% (95% CI: 14-44) in the low, medium, and high educational groups among males. Prevalence of high risk was 54% (95% CI: 46-61), 33% (95% CI: 26-41), and 14% (95% CI: 7-28), respectively among females.

Figure 5.14 shows the difference in the levels of controlled hypertension by BP goals: (i) control (general definition) and (ii) control (disease-specific definition). *Overall levels of controlled hypertension* (i.e. regardless of the comorbid conditions) were higher among males and females with higher than lower levels of education (using both general or disease-specific BP goals). Levels of controlled hypertension were about 5-6 pp lower in absolute terms when using the disease-specific than general BP goal across educational levels among males (*disease-specific*: low: 19%, medium: 21%, high: 29%; *general*: low: 25%, medium: 26%, high: 35%). The equivalent figures among females were 6-8 pp lower (*disease-specific*, low: 18%, medium: 41%, high: 47%; *general* low: 26%, medium: 47%, high: 53%).

Figure 5.14: Controlled hypertension by educational level and disease-specific BP goal.



Very high CVD risk: history of stroke or infarction. DM: self-reported diagnosis. CKD: estimated glomerular filtration rate (eGFR) > 15 and <60 mL/min/1.73m². High risk: Very high CVD risk, DM, or CKD. Observed estimates (% and 95 CI).

Education-based inequalities in levels of controlled hypertension were more pronounced among males and females with than without high-risk. Among those with hypertension and high-risk, controlled hypertension was higher among those with higher educational attainment (regardless of BP goal). The absolute difference in controlled hypertension was larger at the highest than lowest educational level. Among males, the gap at the lowest educational level was 14% (12% *disease-specific* vs % 26 *general*) and at the highest level was 22% (35% *disease-specific* vs 57% *general*). Among females in the lowest educational level, the gap was 14% (17% *disease-specific* vs 31% *general*) and in the highest 42% (37% *disease-*

specific vs 79% *general*). These results suggest that among participants with high risk, those in the highest educational level have a greater proportion of SBP values between 130 mmHg and 140 mmHg or DBP values between 80 mmHg and 90 mmHg (and so are sensitive to the more stringent target), whereas those in the lowest educational level have a greater proportion with SBP values ≥140 mmHg and DBP values ≥90 mmHg (and so are less sensitive to the more stringent target).

Among participants with *not high risk*, the estimated levels of controlled hypertension (<140/90 mmHg) in the lowest and highest educational levels were 24% and 27% among males; and 20% and 48% among females, respectively.

5.4.3. Sensitivity analyses

Multiple imputation to replace missing values in household income

Hypertension: Overall, the estimates from the multiple imputations for replacement of missing values in income showed very similar values to those using complete cases. For example, the complete case income-based OR comparing the poorest vs richest quartiles for survey-defined hypertension among females in the 2010 dataset was 1.36 (95% CI: 0.79-2.36), similar to the estimate using multiply imputed data: 1.39 (95% CI: 0.80-2.41).

Hypertension management indicators: Slightly wider income-based differences were observed with the management indicators as the outcome, but none of the results using multiply imputed data changed the direction, magnitude or statistical significance of the main findings. For instance, the income-based OR comparing the poorest vs richest quartiles for undiagnosed hypertension among males using complete cases in the 2010 dataset was 1.60 (95% CI: 0.71-3.61), modestly higher than the estimate using multiply imputed data: 1.40 (95% CI: 0.65-3.02).

Mutual adjustment for multiple indicators of SEP

Hypertension: The direction of the educational-based inequalities in hypertension was unchanged after adjustment for health insurance. The largest change in the educational-based OR was observed among males in 2010, showing that those in the least vs most educated groups had even higher odds of hypertension after adjustment for health insurance: the OR increased from 1.64 (95% CI: 0.86-3.09) in the unadjusted model to 2.22 (95% CI: 1.12-4.39) in the mutually adjusted model (a relative increase of 35%). Among females, the largest change in the educational-based ORs was observed in 2010 comparing medium vs high educational levels. However, the original null association with education was maintained: the OR decreased from 1.25 (95% CI: 0.73-2.15) in the unadjusted model to 1.00 (95% CI: 0.56-1.80) after adjustment for health insurance (a relative change of -20%).

Hypertension management indicators: The direction of the educational-based inequalities in hypertension management remained constant after adjustment for health insurance, with the magnitude of the ORs slightly increasing in 2010 but slightly decreasing in 2017. In 2010, the largest increase in the educational-based ORs was observed among males for the outcome of uncontrolled hypertension: the odds of uncontrolled hypertension among those in the medium vs highest educational level increased from 1.16 (95% CI: 0.45-3.01) in the unadjusted model to 1.68 (95% CI: 0.54-5.26) in the adjusted model (a relative increase of 45%). In 2017, the largest decrease in the educational-based ORs was observed among males for the outcome of undiagnosed hypertension: the OR comparing the least vs most educated decreased from 2.28 (95% CI: 1.04-4.99) in the unadjusted model to 1.40 (95% CI: 0.63-3.11) in the adjusted model (a relative change of -39%).

5.5. Discussion

In this section, I summarise the main findings and the strengths and limitations of the work presented in this chapter. A lengthier discussion, including comparisons with other studies (particularly in LACCs) and a consideration of the policy implications of the findings, is provided in the Discussion chapter (Chapter 8).

5.5.1. Main findings of SEP inequalities in hypertension

The aim of this second empirical chapter was to examine the gender-specific magnitude of SEP inequalities in hypertension prevalence and in undiagnosed, untreated, and uncontrolled hypertension, and their change over time in Chilean adults since 2003, using individual-level measures of SEP. To the best of my knowledge, this study is the first to present estimates of SEP inequalities in the management of hypertension in Chile and is also one of the first in the context of LACCs.

Chile has experienced a positive population-wide decrease in BP levels, which may be explained partly by a significant rise in the levels of treated- and controlled-hypertension since 2003 (Chapter 4).[111] Education levels have improved and poverty levels have decreased over the last decades, and a reform to the Chilean healthcare system was introduced in 2005 (including the GES-hypertension plan). My analyses showed that, despite these improvements, persisting SEP inequalities in hypertension remain a problem in Chile.

I found higher levels of hypertension among adults with (i) lower levels of education and (ii) public health insurance. Inequalities in hypertension were more pronounced among females. Among females, SEP inequalities in hypertension remained stable over time in relative and absolute terms. Males showed a transient increase in educational-based relative inequalities in hypertension between 2003 and 2010, but stable levels between 2010 and 2017. Results by income were mixed (and null) and inequalities did not change over time.

Two hypotheses related specifically to hypertension prevalence informed this work:

- **H5.1**: Levels of hypertension prevalence are higher in lower SEP groups among both males and females.
- **H5.2**: SEP inequalities in hypertension have persisted over time among both males and females.

My analysis supported the hypothesis about the presence of SEP inequalities in hypertension (**H5.1**) by educational status and income among females but not among males. The hypothesis that SEP inequalities in hypertension have persisted over time (**H5.2**) was supported among females (higher levels among those least educated). Despite the magnitude of educational-based inequalities in hypertension among females being statistically significant only in 2003 and 2017, the direction of the inequalities persisted over time. Due to some evidence of widening inequalities in hypertension (reflecting sharper falls among the most educated), hypothesis H5.2 was not supported among males; inequalities increased significantly between 2003 and 2010 but remained stable between 2010 and 2017.

5.5.2. Main findings of SEP inequalities in hypertension management

Most of the observed inequalities in the management indicators were found with the SEP markers of education and health insurance. According to my results, the observed SEP inequalities in hypertension are magnified by inequalities in hypertension management. This was evident among females in 2017: I reported higher levels of hypertension, as well as higher levels of untreated and uncontrolled hypertension among those in lower than higher educational levels. Educational-related inequalities in undiagnosed, untreated, and uncontrolled hypertension (with higher levels among the least educated) increased over time more among females than males, reflecting a sharper decrease over time among females at the highest educational level.

Inequalities by health insurance status increased over time, reflecting a sharper decrease in levels of undiagnosed and uncontrolled hypertension among those with private vs public health insurance. Inequalities in hypertension management by income were mixed and showed less precise estimates.

I stated three hypotheses related specifically to hypertension management:

- **H5.3**: Levels of undiagnosed, untreated, and uncontrolled hypertension are higher in the lower SEP groups among both males and females.
- **H5.4**: SEP inequalities in undiagnosed, untreated, and uncontrolled hypertension have decreased over time among both males and females.
- **H5.5**: The absolute difference in controlled hypertension using a disease-specific than a general BP goal is larger among those in the lowest than highest educational level among both males and females.

Overall, the hypothesis concerning SEP inequalities in hypertension management (**H5.3**) among both genders was supported. Males showed inequalities in each management indicator, with higher levels of undiagnosed, untreated, and uncontrolled hypertension among those with lower educational level. However, these estimates reached statistical significance only for the outcome of undiagnosed hypertension in 2017. Females showed inequalities in untreated and uncontrolled hypertension (higher levels among those with lower educational level) in 2017. The hypothesis that inequalities in hypertension management have decreased over time (**H5.4**) was not supported: educational-based inequalities over the 15-year period were stable among males and increased among females, reflecting sharper falls in undiagnosed, untreated, and uncontrolled hypertension among the most educated.

Finally, the hypothesis that the difference in controlled hypertension by BP goal was larger among those in the lowest than highest educational level (**H5.5**) was not supported: the gap between general vs disease-specific definitions was larger among those in the highest than lowest educational level.

5.5.3. Strengths and limitations

My analysis of inequalities in hypertension and its management using individual-level measures of SEP has several relevant strengths. First, my results describe the secular changes (2003-2017) in inequalities before and after implementation of one of the major public health reforms in Chile in the last three decades, which included the establishment of Universal Access to Care for hypertension in 2005 (i.e. GES-hypertension plan). It was particularly relevant to evaluate the secular changes in inequalities before and after the 2005 healthcare reform, because equity in health access was one of its key priorities. Secondly, I analysed inequalities using the most commonly used individual-level SEP indicators (e.g. educational status and income) using comparable methods over time, allowing pooled data analysis (increasing statistical power), analyses of secular changes and comparison of findings with nationally-representative HES from other countries (Chapter 8). In this context, I defined outcomes and show the results of analytical techniques that are comparable with other nationally-representative studies of SEP inequalities in hypertension management, like those presented in my systematic review of studies conducted in LACCs (Chapter 2) or by studies conducted elsewhere, such as the US,[215] Korea,[101] China,[216] and India.[217]

However, a few limitations could have affected my results. First, there are limitations inherent to the cross-sectional design of my analyses that reduced the ability to show firm conclusions about causality in the associations between SEP and hypertension outcomes compared with longitudinal studies, although this is less of a concern for results for educational attainment, which is generally achieved by young adulthood.

Secondly, I used indicators of adult SEP only. Some authors suggest evaluating inequalities in adult health outcomes by use of early-life measures of SEP since the use of adult SEP indicators may underestimate the magnitude of inequalities.[40, 218] A large body of evidence shows that early-life SEP and life-course SEP trajectories are associated with cardiovascular outcomes, including hypertension and cardiovascular mortality.[219, 220] Several (not mutually exclusive) models could describe the association between life-course SEP and SEP inequalities in hypertension outcomes, including the (i) *latent effect* model (early-life SEP impacts on adult health outcomes regardless of changes in SEP status over the life-course); (ii) *cumulative life-course SEP* model (outlines a dose-response association between the length of time in lower SEP and adult health outcomes); and (iii) *life-course SEP trajectories* model (different trajectories in SEP status over the life-time influence the impact of early-life SEP on adult health outcomes).[219] However, early life measures of SEP were not available in ENS: to facilitate such analyses, future rounds of the ENS should extend the questionnaire on sociodemographic characteristics to include items on early-life SEP.

Thirdly, my models adjusted for age were stratified by gender in order to account for the potential confounding effects of age and differences in inequalities by gender. In my main analyses, I did not mutually adjust for the other markers of SEP (as mutual adjustment ignores aspects of SEP that are common to all SEP measures and could introduce multicollinearity into the analysis).[214] However, I performed a robustness check to evaluate if the magnitude of educational-based inequalities changed after adjustment for health insurance (the two SEP measures most strongly associated with hypertension outcomes). Reassuringly, my findings regarding the educational-based inequalities remained largely unchanged. Nevertheless, I cannot rule out the possibility of residual confounding by unobserved or imperfectly measured variables.

Fourthly, my results could have been affected by survival bias: it is likely that persons with hypertension in the lowest SEP groups in the Chilean population may have died earlier than those in the highest SEP groups: for example, previous studies have shown higher mortality rates from complications of hypertension among those in the lower vs higher SEP groups.[221] This bias could attenuate the magnitude of SEP inequalities, thereby increasing the likelihood of finding null associations. This potential survival bias is a common shortcoming among studies analysing cross-sectional HES data.

Fifthly, some analyses were potentially underpowered, especially for the outcomes of hypertension management. In order to overcome this issue, at least partially, my results were estimated first without using a strict threshold for statistical significance and were then estimated by pooling data (across survey years and gender) to increase the analytical sample size when appropriate. As I mentioned in Chapter 2, estimates of inequalities that did not reach statistical significance could be misinterpreted as evidence of *true* equality. In this way, it is necessary to evaluate the magnitude of SEP inequalities (and their uncertainties), together with overall patterns across subgroups and over time.

Finally, the inequalities presented in this chapter were based on individual-level SEP indicators. However, an increasing body of evidence has shown the relevance of the social contexts in which people live for several chronic health conditions, including hypertension.[106] Health effects of the social context (contextual factors) have been described as additional to the effects of individual-level SEP. Single-level regression models such as those presented in this chapter are able to adjust for both individual-level SEP and contextual SEP measures in a single equation, but such models cannot be used to estimate how much of the variability in an outcome lies between and within areas. Alternatively, multilevel analyses are an appropriate method to estimate separately the magnitude of the variance in an outcome between and within areas. In Chapter 6, I will extend the analyses of individual-level SEP inequalities presented in this chapter by presenting the results from multilevel models that appropriately estimate contextual factors.

5.6 Conclusion

One of the reasons that the Chilean government implemented the healthcare reform in 2005 (including the GES-hypertension plan) was to address the growing inequalities in health. However, according to my results, SEP inequalities in hypertension, and in undiagnosed, untreated, and uncontrolled hypertension, using different individual-level indicators of SEP, were observed among Chilean adults (especially females) in 2010 and 2017.

My results provide evidence to suggest that levels of undiagnosed, untreated, and uncontrolled hypertension were stable over time among females in the lowest SEP groups, but decreased in the highest SEP groups (e.g. the highest educated and those with private health insurance). These results show that improvements in the management of hypertension over time were not distributed equally by SEP in females, and that inequalities in hypertension are magnified by inequalities in various hypertension management indicators (namely treatment and control).

Chile, therefore, currently needs interventions to improve the management of hypertension and simultaneously decrease SEP inequalities, especially among females. *Proportionate universalism* is an approach that aims to improve levels of health across the population as a whole (universal) but with interventions that are proportionate to the needs and levels of disadvantage.[3] According to this approach, policies to be implemented in Chile should have a stronger intervention among the lowest SEP groups.

Chapter 6: Multilevel analyses of individual-level socioeconomic inequalities in the prevalence and management of hypertension

6.1. Introduction

Positive changes in hypertension outcomes have been observed over the past 15 years among adults in Chile. Hypertension prevalence decreased whilst attainment of its management indicators (i.e. awareness, treatment, and control) improved between 2003 and 2017 (presented in Chapter 4). However, evidence presented in Chapter 5 showed that these improvements were not equally distributed across SEP groups. For example, according to my results, females with lower educational levels in 2017 had higher levels of hypertension and higher levels of untreated and uncontrolled hypertension than those with higher educational levels.

I also showed that, among the three individual-level markers of SEP considered (education, income, and health insurance), educational status was the only indicator of SEP measured across all three ENS that showed statistically significant associations with hypertension and its management indicators. Therefore, I use only educational status as the marker of individual-level SEP in this chapter where I present a further investigation of SEP inequalities in hypertension and its management indicators using a multilevel modelling framework.

As shown in my conceptual model (Figure 3.1), a broader perspective of the conditions of daily life, as captured for example by measures of the socioeconomic environment, is required to better understand individual-level SEP inequalities.[6–8] There is a growing literature reporting associations between aspects of the socioeconomic environment and several health outcomes. Previous literature has shown associations between measures of the socioeconomic environment (e.g. poverty and income inequality) and hypertension.[105, 106, 222] Adjustment for the socioeconomic environment could change or modify some of the observed individual-level SEP inequalities in hypertension outcomes (i.e. whereby adjustment for socioeconomic environment measures reduces or increases the magnitude and statistical significance of individual-level SEP inequalities).[106]

With regards to the analytical strategy, single-level (or fixed effect) regression models allow for adjustment of socioeconomic environment measures. Adjustment for such measures could change or modify the magnitude of individual-level SEP inequalities in hypertension outcomes.[106] However, such models cannot estimate the magnitude of the clustering or area effect (i.e. variability in outcomes are not partitioned across levels of a hierarchy, e.g. individuals within areas). In contrast, multilevel models estimate separately the magnitude of the variance in an outcome *between* and *within* areas.

In addition to adjustment, previous epidemiological research using multilevel analyses has shown that the magnitude of associations between individual-level exposures and health outcomes may change in strength or in direction according to characteristics of the area of residence (i.e. described in the literature as a *cross-level interaction*).[223, 224] For example, evidence from a population-based cohort in the United States (the Stanford Heart Disease Prevention Program) showed that individuals in lower SEP groups (based on an individual-level composite SEP index) living in richer areas had higher mortality rates than those in lower SEP groups living in poorer areas.[223] According to the study authors, this demonstrated that adults of low SEP do not benefit from the availability of higher quality resources and knowledge generally associated with areas (neighbourhoods) that have higher SEP.[223] To date, however, there is scarce evidence regarding the strength of any cross-level interactions between individual-level SEP and contextual socioeconomic measures on hypertension outcomes.

Chilean territory is highly segregated, displaying a clear clustering of socioeconomic levels across the country.[225] Striking differences in socioeconomic measures at the county level are present in Chile. For example, whereas 2% of the 346 Chilean counties in 2020 showed high levels of development (based on indicators of education, health and financial resources), over 60% of counties had a medium-low or low level of development.[226] Previous research conducted in Chile has linked county-level socioeconomic measures with several health outcomes, including mortality, self-rated health, diabetes, mean BP, and mental health.[65, 227–232] This evidence suggests that the area of residence could play an important role in explaining the variation in hypertension outcomes in Chile. Indeed, using a multilevel approach on Chilean data from ENS2003 and ENS2010, Guerrero-Ahumada (2017) reported associations between mean SBP and county-level measures of income, unemployment and deprivation. For example, mean levels of SBP were higher among participants living in poorer counties.[65] However, the variability in hypertension that was attributed to differences between counties was not statistically significant (i.e. hypertension did not appear to cluster significantly within areas).[65] In this chapter, I present further exploration of the variation between counties in hypertension using the most recent ENS (ENS2017) and estimate between- and within-area variations in each of the three key hypertension management indicators.

Analysis framework

There are several ways to analyse the association between educational status (at the individual level), the socioeconomic environment (e.g. measures of income inequality at area level), and hypertension outcomes. When the main exposure of interest is at the individual level, the analysis options to include the variables measuring the socioeconomic characteristics of areas (i.e. contextual factors) in a multilevel model are as follows:

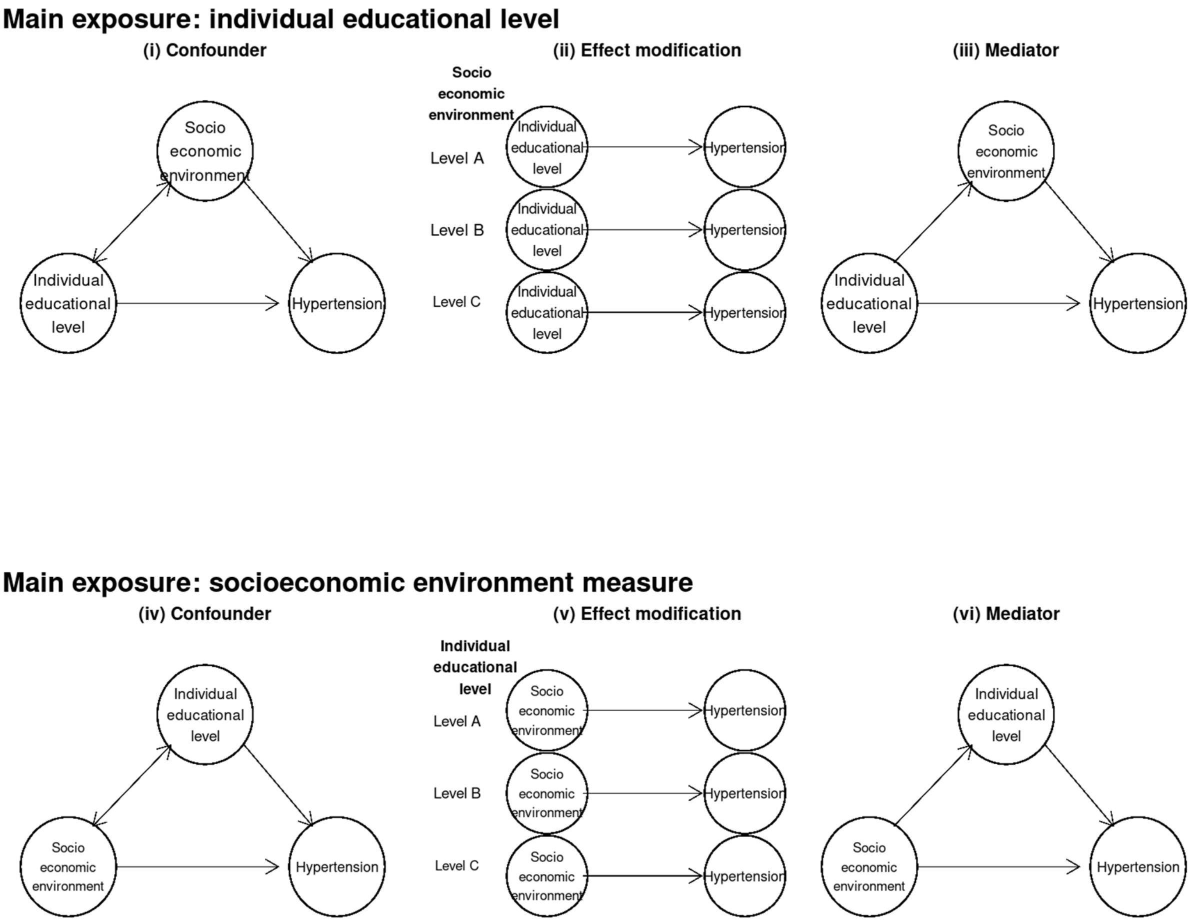
(i) Contextual factors as **confounders** of the associations between individual educational level and hypertension outcomes. Here, the socio-environment measure has a direct effect on hypertension and is associated with individual educational level (they can mutually influence each other). Further, the socio-environment measure is not perceived to be on the causal pathway between individual educational level and hypertension. In this case, failing to adjust for the socio-environment measure can lead to a biased association between individual-level SEP and adult health outcomes. Adjustment for area-level SEP can also be viewed as a strategy to evaluate whether the associations between individual-level SEP and outcomes remain robust when controlling for contextual factors.

(ii) Contextual factors as **moderators** or (effect modifier) of the associations between individual educational level and hypertension outcomes (i.e. *a cross-level interaction*). Here, the direction or magnitude of the association between individual educational level and hypertension varies according to levels of the socio-environment measure. Evidence of effect modification is usually obtained by including an interaction term in the model (individual-level SEP × area-level characteristics) or by stratifying the analysis of individual-level SEP inequalities in hypertension by levels of the socio-environment measure (e.g. least deprived and most deprived areas).

(iii) Contextual factors as **mediators** of the associations between individual educational level and hypertension outcomes. Here, the socio-environment measure is perceived to be on the causal pathway between individual-level SEP and adult health outcomes (e.g. a higher individual-level SEP could increase the chances of moving to a neighbourhood with better socioeconomic resources). This conceptual framework (with individual-level SEP as the main exposure of interest) is less frequently investigated. Most previous studies have instead identified contextual factors as the main exposure of interest and have considered individual-level SEP as a potential mediator of the association.[233]

Research on the association between measures of the socioeconomic environment (the ‘area effect’ as the main exposure of interest) and hypertension outcomes, including individual-level SEP, results in three additional analytical approaches: Individual-level educational status considered as a (iv) confounder, (v) modifier, or (vi) mediator of the association between area-level characteristics and hypertension outcomes.[233, 234] A schematic representation of the six analytical approaches is shown in Figure 6.1.

Figure 6.1: Analytical frameworks for examining individual and area-level measures of SEP on hypertension.



As discussed by Diez Roux (2001), it is crucial to evaluate which of these conceptual models (and the respective analytical approach) is more suitable for each research question and data.[233] Analyses that consider an area-level measure as a confounder (*approach i*) or a mediator (*approach iii*) of individual-level SEP inequalities in hypertension will typically adjust for the contextual factor. The rationale is different for the two approaches: the first reduces confounding bias (*approach i*), and the second estimates only the direct (i.e. not mediated) effect of the individual-level SEP measure (*approach iii*).[233] The same logic applies to *approaches iv and vi*.[233] Longitudinal data, with clear temporality of exposures and outcomes is required to properly evaluate any potential mediation effects. Chaix et al. (2010) argue that *approach iii* (area-level characteristics as a mediator of the association between individual-level exposures and outcomes), is less plausible, and that it is better to implement an analytical strategy that is more consistent with highlighting area-level characteristics as a potential confounder.[235] The literature highlighting the complexity of these associations, therefore also suggests considering potential cross-level interaction effects (*approaches ii and v*) and area-level and individual-level variables that mutually influence each other (confounders and mediators).[233]

Because of the constraints of the cross-sectional nature of ENS data, I did not formally evaluate any mediation effect (*approaches iii and vi*). The options using ENS data are restricted to (a) examine the associations between individual-level educational status and hypertension outcomes whilst considering the socioeconomic environment as a potential confounder or effect modifier (*approaches i or ii*), or (b) examine the associations between the socioeconomic environment and hypertension outcomes whilst considering individual-level educational status as a potential confounder or effect modifier (*approaches iv or v*).

Up-to-date research is therefore needed to assess the extent to which socioeconomic environment measures influence individual-level SEP inequalities in hypertension and its management in Chile; and also to evaluate whether measures of the socioeconomic environment associates with hypertension outcomes.

6.2. Research problem, aim, objectives and hypotheses

Problem

Chilean evidence about educational-based inequalities in hypertension outcomes using a multilevel approach is available for hypertension prevalence in 2003 and

2010 only.[65] Therefore, up-to-date research based on multilevel modelling using ENS2017 data and extending the focus to other hypertension outcomes (i.e. undiagnosed, untreated, and uncontrolled hypertension) is needed.

Aim

The aim of this chapter is to contextualise gender-specific individual-level educational inequalities in hypertension and in hypertension management indicators in Chilean adults in 2003, 2010, and 2017 by considering the role of socioeconomic environment measures using a multilevel analytical approach.

Objectives

The objectives of this empirical work are as follows:

- Estimate the contribution of ENS participants' county of residence to the total variation in hypertension and in each hypertension management outcome.
- Examine whether county-level socioeconomic measures modify the gender-specific associations between individual-level educational status and hypertension outcomes.
- Estimate the gender-specific magnitude of individual-level educational inequalities in hypertension outcomes before and after adjustment for socioeconomic measures at the county level.
- Estimate the gender-specific magnitude of area-level inequalities in hypertension outcomes before and after adjustment for individual-level education.

Hypotheses

The four hypotheses for this analytical chapter are as follows:

- **H6.1**: The county of residence of ENS participants contributes to the variation in hypertension and in each hypertension management outcome. This would indicate, for example, that levels of hypertension are clustered among survey participants residing in the same county.

- **H6.2**: The magnitude of individual-level educational inequalities in hypertension outcomes does not vary according to levels of the socioeconomic environment measures among both males and females.
- **H6.3**: The magnitude of individual educational-based inequalities in hypertension outcomes is attenuated after adjustment for socioeconomic environment measures among both males and females.
- **H6.4**: The magnitude of area-level inequalities in hypertension outcomes is attenuated after adjustment for individual-level educational status among both males and females.

6.3. Methods

Information about the ENS study design, setting and data collection, definitions of hypertension and of undiagnosed, untreated, and uncontrolled hypertension, and the individual-level sociodemographic variables were described previously in Chapters 4 and 5. Here I will describe the specific methods related to measures of the socioeconomic environment.

6.3.1. Data source for the socioeconomic environment measures

In Chile, the smallest administrative units are counties. In 2017, the total number of counties was 346, with a median number of counties per region of 18 (minimum: 4; maximum: 52). The population size by county ranged between 137 and 645,909 (median: 19,770). The county of residence for each ENS participant was used to define the boundaries of the area or cluster. The Ministry of Health provided the county in the ENS datasets based on the participant's address registered during the first interview. The address of ENS participants is not publicly available to protect anonymity, therefore, the smallest geographical cluster identifiable in the ENS is the county.

A single data resource provided data on the county-level measures. The Chilean National Socioeconomic Characterization Survey (CASEN) is one of the main household surveys conducted in Chile. CASEN is conducted every two years, and is the official source for national socioeconomic statistics, including area-levels of income inequality, poverty, and unemployment. CASEN has been carried out by the Ministry of Planning since 1985 to describe the socioeconomic situation, as well as the impact of social programmes on the living conditions of the Chilean population. Similar to ENS, CASEN uses a complex multistage sampling strategy to be representative at national, regional and county levels.[13]

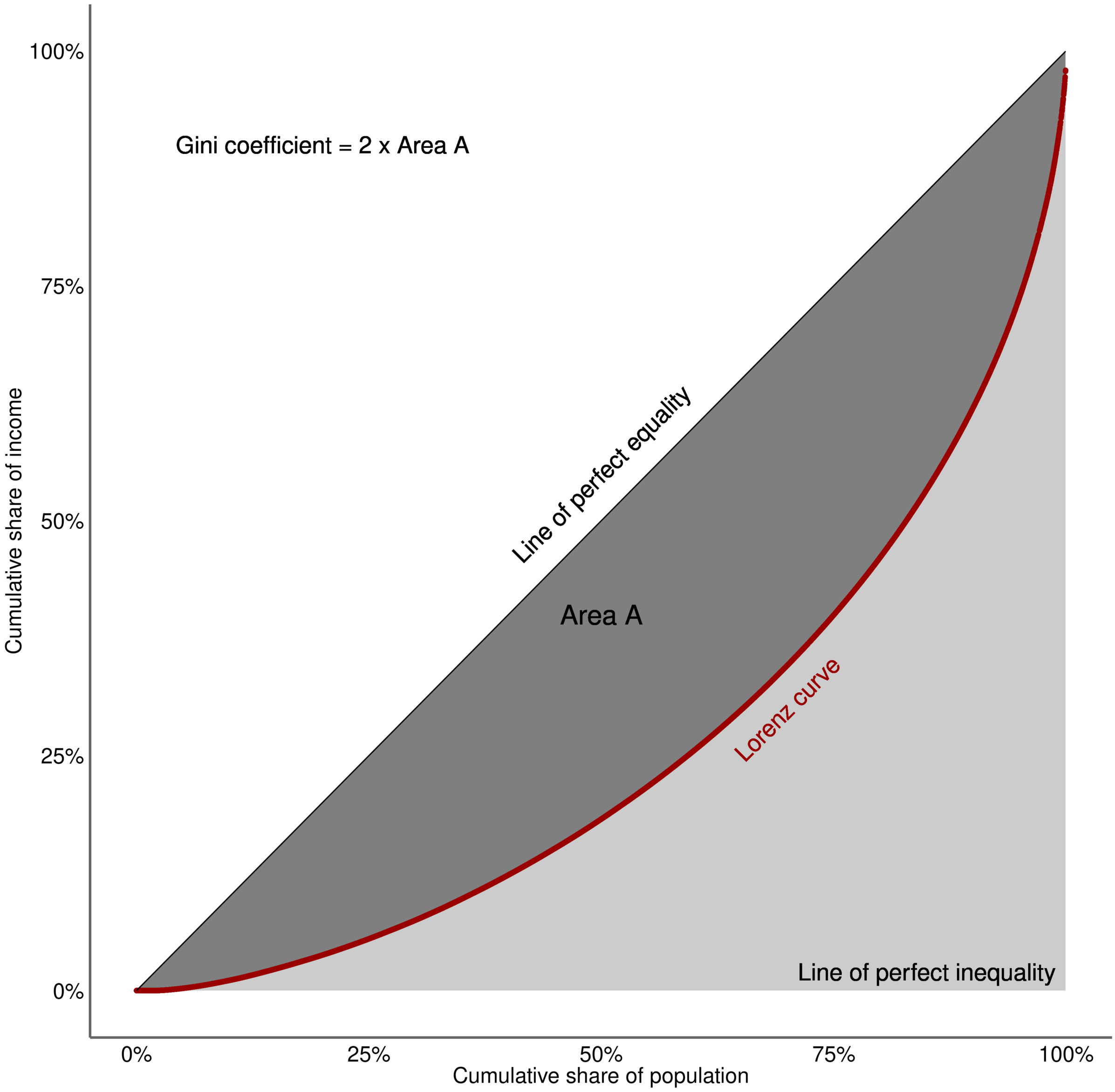
6.3.2. Socioeconomic environment measures

Definitions

Several county-level variables were examined for this empirical work. I selected measures of the socioeconomic environment that had been hypothesised to be relevant to inequalities in hypertension and in hypertension management outcomes. Due to data availability, the three selected area-level measures were income inequality, and rates of poverty and unemployment. These are defined in turn below:

Income inequality (Gini coefficient): As explained in Section 1.2.2, the Gini coefficient is a well-known measure of statistical dispersion and is widely used as an index of income inequality. The Gini coefficient is defined as twice the area between the 45-degree line and the Lorenz curve, where the Lorenz curve is a graph describing the cumulative share of total income versus the cumulative proportion of the population. The Gini coefficient ranges between 0 (i.e. *perfect equality*: everybody has an equal amount of income) and 1 (i.e. *perfect inequality*: all income is owned by one person). Gini coefficients can also be reported as a percentage (range: 0-100%, the scale used in this chapter). Higher Gini values indicate higher levels of income inequality. The Lorenz curve estimated using CASEN 2017 income data is shown in Figure 6.2. The corresponding Gini coefficient for this Lorenz curve was 49%. According to CASEN, income inequality in Chile has slightly decreased over the last several decades (the Gini decreased from 54% in 2003 to 49% in 2017).[13] However, Chile remains one of the most unequal among OECD countries (ranking: 2/38) but is similar to other LACCs.[10]

Figure 6.2: Lorenz curve for income. Chile, CASEN 2017.



Lorenz curve, shown in red, was estimated using monthly household income data from CASEN 2017. Gini coefficient: coefficient: 49%.

Poverty: The poverty rate was defined as the percentage of the population living in households whose income was insufficient to meet the basic needs of their members according to the individual minimum basket for the satisfaction of food and non-food needs (i.e. housing, health, clothing and footwear, transport, household amenities, and education).

Unemployment: The unemployment rate was defined as the percentage of the population aged 15-64y who reported that they had not worked in gainful employment for at least one hour in the previous week and who did not have a job that they were absent from during the reference week.

Derivation of social-environmental variables

The contextual measures were estimated at the county level at three-time points: 2003, 2009, and 2017. To derive values of the Gini coefficient by county and year, I used monthly household income (including government benefits), equivalised to the size of the household (i.e. divided by the number of individuals living in the household). I used data from CASEN instead of ENS to estimate county levels of the Gini coefficient as the samples for CASEN were representative at the national, regional and county levels, whereas the samples for ENS were representative at the national and regional levels only. I estimated weighted Gini coefficients using the *Reldist* package in R. To estimate the percentage of the population living in poverty, I used the original CASEN poverty classification, based on poverty lines (cut-offs of income values) from the official CASEN reports.[13]

Levels of income inequality (Gini coefficients, %), poverty (%), and unemployment (%) by county and year were estimated, accounting for the complex sampling design of CASEN. I merged CASEN variables with the ENS datasets using county and year as the matching variables.

6.3.3. Statistical analyses

As in previous chapters, I restricted analyses to adults aged ≥17y (ensuring comparability across the three ENS surveys). Chapters 4 and 5 showed differences between males and females in the levels of hypertension outcomes and in the patterns of individual-level SEP inequalities. Accordingly, all analyses in this chapter were gender specific and were conducted on complete cases using Stata (version 16). P-values <0.05 were classified as statistically significant (two-tailed), but I also interpret P-values as continuous values in order to avoid using an arbitrary cut-point.[192]

I. Descriptive analyses

Using counties as the unit of analysis (194, 147, and 157 counties in ENS 2003, 2010, and 2017, respectively), I describe the distribution of the three socioeconomic environment measures. Descriptive statistics included the minimum, mean, median, and maximum values and Pearson correlations.

I estimated the prevalence of survey-defined hypertension (BP ≥140/90 mmHg or use of antihypertensive medication) and levels of undiagnosed, untreated, and uncontrolled hypertension by quartiles of the area-level variables. Both *observed* and *age-standardised* estimates were calculated using the same procedures as described in Chapter 5.

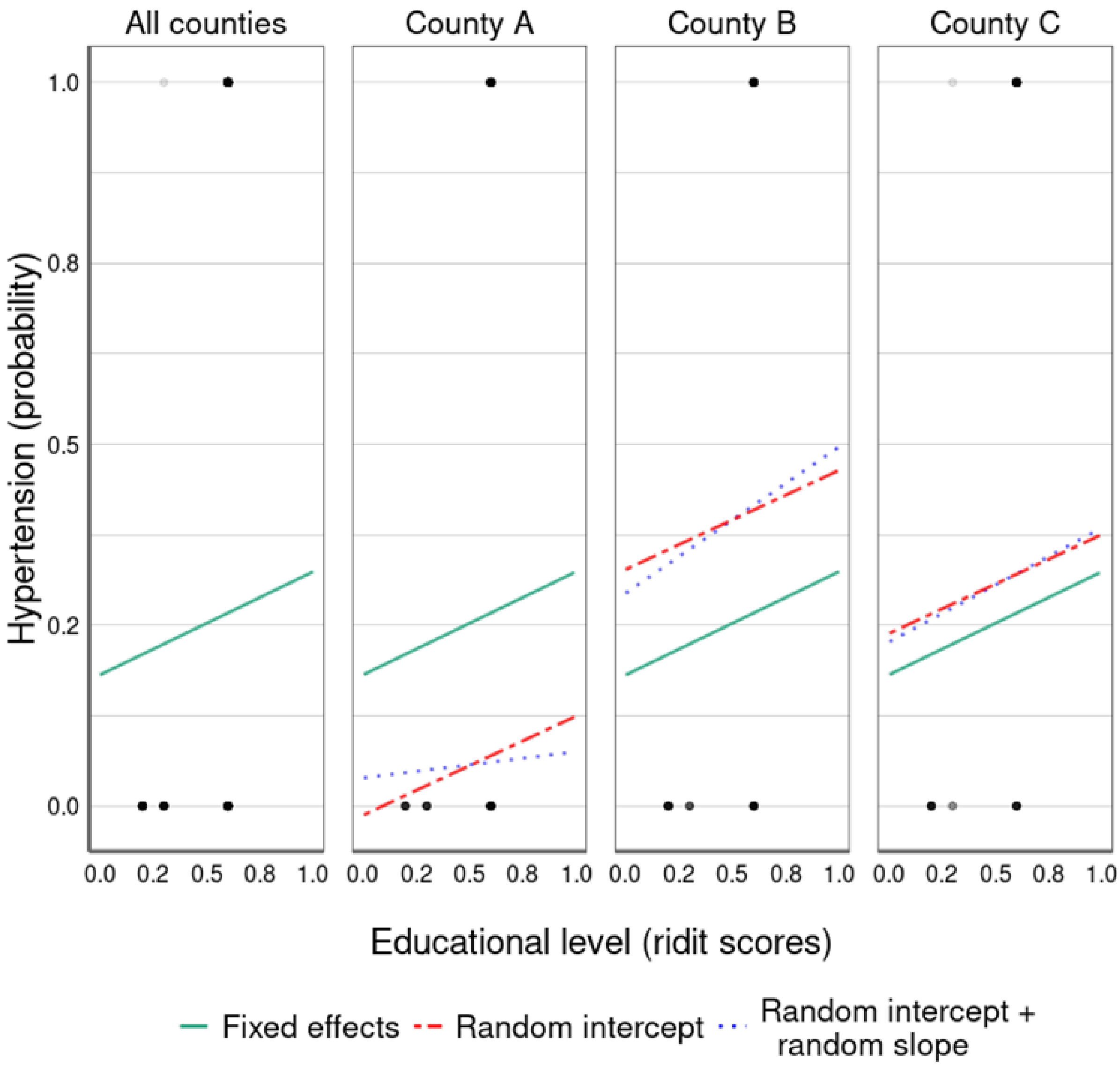
P-values from the Pearson's chi-squared test were used to evaluate differences in the age-gender standardised levels of hypertension outcomes between the lowest (Q1) and the highest quartiles (Q4) of each area-level variable.

II. Multilevel modelling

To allow for the hierarchical clustering of ENS participants within counties, I conducted multilevel regression analyses appropriate for binary outcomes. Multilevel models can include both *fixed effects* (i.e. fixed intercept and fixed slope of explanatory variables) and *random effects* (i.e. variance of the fixed effects [intercepts or slopes] between clusters). For the empirical work presented here, I built a two-level equation: ENS participants (Level 1) nested within counties (Level 2).

Multilevel models allow for variation in (i) intercepts only or (ii) in intercepts and slopes, in Level-1 equations within units in Level-2 (counties). *Random intercepts* mean that the values of the intercept vary randomly across clusters, whereas *random slopes* mean that the slope of the individual-level exposure in Level-1 equations varies randomly across clusters. Figure 6.3 illustrates these concepts using the predicted probability of hypertension (vertical axis) by educational level (ridit scores, horizontal axis) according to different models: (i) fixed-effect models; (ii) random-intercept multilevel models, and (iii) random-intercept-and-random-slope multilevel models. The intercept and slope in the fixed-effect model (green-solid line) are constrained to be the same across counties. In the random intercept model (red-dashed line), the value of the intercept varies between counties whilst the value of the slope is constrained to be the same across counties. Finally, in the random-intercept-and-random-slope model (blue-dotted line), both the intercept and slope vary between counties (e.g. both the intercept and slope appear to be highest in County B in this illustrative example).

Figure 6.3: Illustrative example of fixed-effects model and random-effects models for hypertension by individual educational level (ridit scores).



Fictional data. Points: observed values 1 (hypertensive) or 0 (non-hypertensive). The more observed points fall on top of each other, the darker the point. Lines: Models predicting the probability of hypertension according to educational level (ridit scores). Fixed effects: single-level model; Random intercept: intercept varies across counties, slope is fixed. Random intercept + random slope: both intercept and slope vary between counties.

In order to evaluate if the hypertension outcomes vary between counties, and so provide a basis for using a multilevel rather than a single-level regression model, I first built the simplest multilevel model (known as an *empty* or *unconditional model*), with a random intercept but with no explanatory variables (Step 1). Secondly, those hypertension outcomes observed to vary randomly between counties were further analysed to evaluate a potential cross-level interaction effect (Step 2). I also evaluated the potential confounding effect of the contextual SEP measures on the individual-level SEP inequalities (Step 3). Finally, I evaluated the potential confounding effect of individual-level SEP on the inequalities according to the socioeconomic environment measure (Step 4). I briefly describe each of these steps below.

Step 1: Intraclass correlation (ICC)

Multilevel models can estimate differences in hypertension outcomes *between counties* and between participants *within counties*. The sum of both individual and county-level differences constitutes the total variation in hypertension outcomes that is explained by the model. I estimated the percentage of the total variance in each outcome that was explained at the county level (*differences in hypertension outcomes between counties*) using an *empty* or *unconditional* model (which accounts for the influence of the county as a random intercept only). This indicator (percentage of total variance at Level-2) is known in the literature as the intraclass correlation coefficient (ICC) and ranges from 0% to 100%. The expression of an *empty* multilevel model is presented in Equation 6.1.

Equation 6.1:

$$logit(P_{ij}) = \gamma_{00} + \mu_{0j}$$

In the equation, $logit(P_{ij})$ corresponds to the logit transformation of the outcome probability (P) for person i residing in county j. The model equation is composed of the *fixed effect* (γ_{00}, the intercept of the intercepts) and the *random effect* of the intercept (μ_{0j}, how the intercept changes between j counties).

I present the values of the ICC and accompanying 95% CIs that were estimated using survey year-specific multilevel logistic regression models.[218, 236, 237] At the county level, even small values of the ICC (e.g. 1%) could reflect a relevant area-level impact on the health status of many people. Higher values of the ICC indicate higher variability in outcomes between counties. An estimate of zero for the ICC implies similarity between counties in outcomes (i.e. the absence of a clustering effect). There is no strict cut-off value to define values of the ICC that are ‘low’ or ‘high’. However, for the purposes of this study, models that produced an estimate for the lower bound of the 95% CI for the ICC higher than 1% were further evaluated using multilevel modelling. I chose this cut-off based on slightly lower values of the ICC (between 2% and 3%) reported by previous multilevel studies on hypertension.[218, 236, 237]

Step 2: Cross-level interaction

I evaluated the statistical significance of a *cross-level interaction* between individual-level educational status (represented in the model by ridit scores) and the continuous socioeconomic environment measure in the multilevel models. Models allowed for random variation in both intercepts and slopes: to estimate cross-level interactions, a two-way interaction term between a Level-1 (individual educational level) variable and a Level-2 variable (e.g. county-level income inequality) was included in the fixed effects part of the model along with the respective main effects. A simple multilevel model to estimate the outcome probability (P) (e.g. binary outcome of survey-defined hypertension) in individual i residing in county j, including the individual-level explanatory variable X and area-level explanatory variable Z, is presented in Equation 6.2.

Equation 6.2:

$$log(P_{ij}) = \gamma_{00} + \gamma_{10}X_{ij} + \gamma_{01}Z_j + \gamma_{11}X_{ij}Z_j + \mu_{0j} + \mu_1 X_{ij}$$

In the equation, $log(P_{ij})$ corresponds to the log transformation of the outcome probability (P). Note the difference with Equation 6.1 where I specified a logit transformation. I opted to use multilevel logistic regressions (*logit* function) in Step 1 to compare ICC values with previous publications; in Step 2 I used a multilevel Poisson model (*log* function) to compare coefficients with the results (estimates of individual-level inequalities) presented earlier in Chapter 5. An additional reason for using Poisson rather than logistic regression was based on their statistical properties: when binary outcomes are relatively common (i.e. a prevalence greater than 10%), logistic regression models usually overestimate the magnitude of associations (e.g. prevalence ratio) compared with Poisson regression models.[168]

The model equation set out in Equation 6.2 can be divided into two main segments: (i) *fixed effects*: $\gamma_{00} + \gamma_{10}X_{ij} + \gamma_{01}Z_j + \gamma_{11}X_{ij}Z_j$ and (ii) *random effects*: $\mu_{0j} + \mu_1 X_{ij}$. The cross-level interaction term is represented by $\gamma_{11}X_{ij}Z_j$ in which the coefficient γ_{11} indicates the extent to which the estimated slope at the individual-level (e.g. educational level) varies with Z_j, the socioeconomic environment measure (e.g. poverty rate). A null value for the cross-level interaction term suggests that the main effects are sufficient, i.e. that the association between the individual-level SEP measure and the outcome is similar across all levels of the socioeconomic environment measure.

The Level-1 part of the equation included a term to adjust for age (as a continuous variable) and a term for the two-way interaction (e.g. *educational ridit scores* x *county-level socioeconomic measure*). The equation included the random intercept for the county and the random slope for individual-level education: these are shown in Equation 6.2 as μ_{0j} and $\mu_1 X_{ij}$, respectively. According to the literature, multilevel models including cross-level interaction terms as fixed effects should also include a random slope for the individual-level SEP variable to achieve better estimates of the fixed effects for both Level-1 variables and for the cross-level interaction term.[238] In the results section, I report the exponential coefficient of the cross-level interaction term.

Step 3: Confounding effect of socioeconomic environment measures

In Step 3, I built the same multilevel regression models as in Step 2 but excluded the cross-level interaction term $\gamma_{11}X_{ij}Z_j$. In this way, models were further explored to examine a potential confounding effect: so as to permit estimation of individual-level educational-based inequalities independently of the socioeconomic environment measure. Using the same analytical technique as presented in Chapter 5, I built a single-level (*fixed-effect*) regression model to estimate the magnitude of age-adjusted individual-level inequalities in a baseline model (i.e. without adjustment for the socioeconomic environment measure). I then estimated the change in the magnitude of the individual educational-based inequalities from the multilevel models (adjusting for age and socioeconomic environment measure) relative to the corresponding single-level models (no adjustment for socioeconomic environment measure) as follows:

Equation 6.3:

$$100 \times \frac{Multilevel\ model - Single\ level\ model}{Single\ level\ model}$$

Step 4: Inequalities by measures of the socioeconomic environment

Although my main interest was to estimate the magnitude of individual-level inequalities in hypertension outcomes (before and after adjustment for area level SEP), using similar age-adjusted multilevel models as described above, I also estimated the magnitude of area-level inequalities (reported as prevalence ratios) in hypertension outcomes before and after adjustment for individual-level educational status.

Relative and absolute measures of inequality

Individual educational-based inequalities were assessed using complex measures of inequality. Poisson models with a log link function were used to compute the RII (Equation 6.2) and Gaussian models with an identity link function were used to calculate the SII.

Models were survey year- and gender-specific. As in previous chapters, performing analysis by survey year enabled investigation of changes in inequalities over time. As in Chapter 5, I decided *a priori* to run separate models for the three area-level variables instead of estimating a single model that mutually adjusted for all area-level variables to avoid multicollinearity.[214]

6.3.3. Sensitivity analyses

Inequalities adjusted for lagged values of the socioeconomic environment measures

There is a long-standing debate about the use of lagged rather than contemporary values when assessing associations between measures of the socioeconomic environment and health outcomes.[218] This discussion relies on the hypothesis that contextual factors require a certain amount of time before having an impact on health outcomes. For example, Blakely et al. (2000) argued that levels of contextual income inequality measured 15 years before are better than the contemporaneous measure when evaluating contextual income-based inequalities in self-reported health.[239] Recent research has evaluated the lagged effect of contextual income inequality levels on hypertension and found similar results about the benefits of using lagged rather than contemporaneous contextual exposures.[218]

Accordingly, I performed a sensitivity analysis to examine if lagged values of the socioeconomic environment measures had a greater impact on the magnitude of individual-level educational inequalities in the hypertension outcomes than those estimated using contemporaneous values. Data from CASEN 1990, 1996, 2000, 2003, 2009, and 2017 were used to estimate the lagged values of the three county-level variables. I repeated the multilevel analyses as described above (Steps 2 and 3), using lagged rather than contemporaneous values of the socioeconomic environment measures. I estimated the relative change in the education-based RII by comparing lagged vs contemporary values (expressed as a percentage). I reported RIIs only if there was no strong evidence of a cross-level interaction between individual educational level and the socioeconomic environment measures.

6.4. Results

My description of the results is divided into four parts. First, I describe the socioeconomic environment measures and the number of ENS participants by survey year. Secondly, I describe the age-gender standardised levels of hypertension outcomes by quartiles of the socioeconomic environment measures. Thirdly, I report the results of the four steps of the multilevel analyses for hypertension: (i) estimates of the intraclass correlation (ICC); (ii) estimates of the cross-level interaction terms; (iii) estimates of the individual-level educational-based inequalities after adjustment for the socioeconomic environment measures; and (iv) estimates for the associations between the socioeconomic environment measures and hypertension before and after adjustment for individual-level education. Finally, I present the results of the sensitivity analysis, comparing associations using lagged versus contemporaneous values of the socioeconomic environment measures.

6.4.1. Descriptive analyses of the socioeconomic environment measures

A total of 3,416; 4,820; and 5,369 participants aged ≥17y with valid BP and medicine data were nested in 194, 147, and 157 counties in ENS 2003, 2010, and 2017, respectively. The description of socioeconomic environment measures and the number of participants included in the analysis is presented in Table 6.1. Over time, mean levels of income inequality, poverty, and unemployment decreased at the county level. For example, the median poverty rate decreased from 21% in 2003 to 9% in 2017.

Table 6.1: Socioeconomic environment measures and number of participants within counties by year.

Feature by year	Min	Mean	Median	Max
Participants (n)				
2003	2	18	11	119
2010	2	34	19	291
2017	3	35	22	303
Income inequality (Gini, %)				
2003	25	46	46	81
2010	32	44	43	66
2017	25	37	36	57
Poverty (%)				
2003	0	22	21	42
2010	0	16	15	41
2017	0	10	9	43
Unemployment (%)				
2003	31	46	46	64
2010	28	46	46	65
2017	21	41	41	58

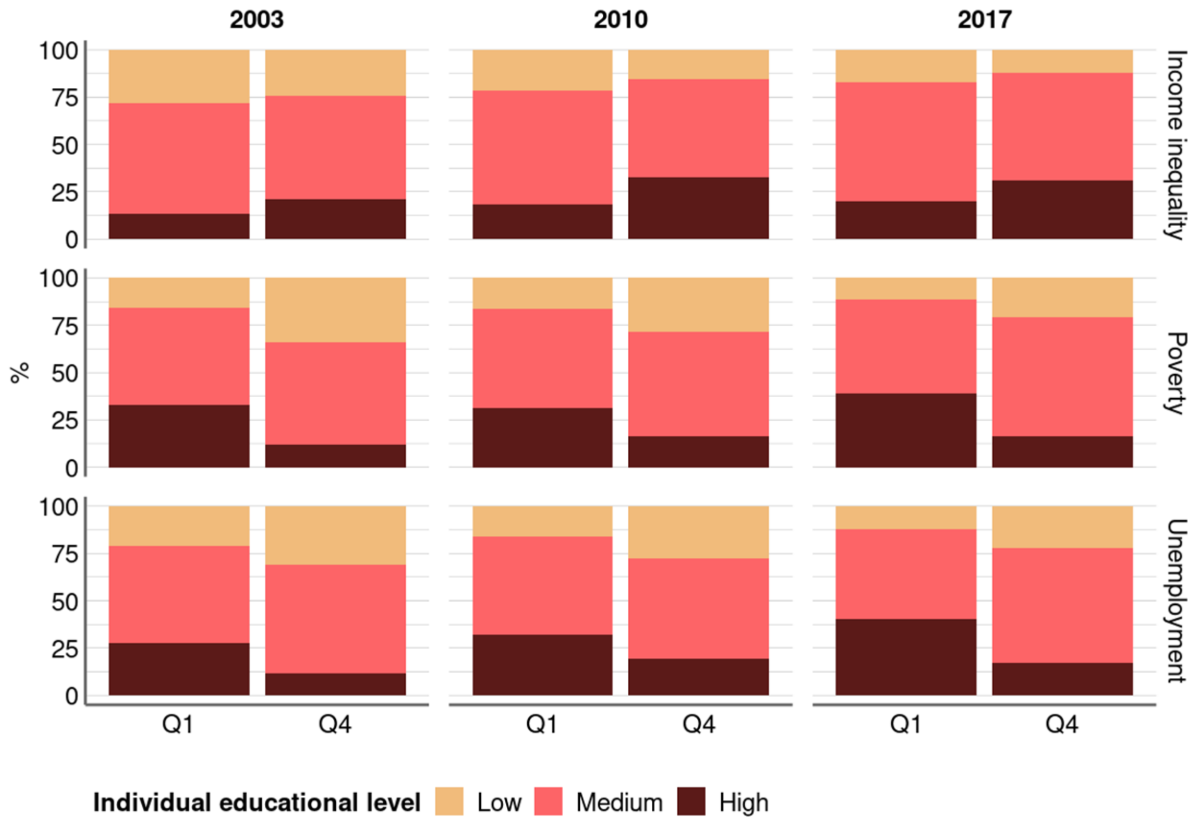
Table 6.2 shows the Pearson correlations between the three socioeconomic environment measures by ENS survey year. In 2003, 2010, and 2017, levels of income inequality showed a very weak correlation with the rates of poverty and unemployment (not statistically significant in 2003 and 2010 but almost significant in 2017), whereas levels of unemployment and poverty were positively and highly correlated ($p<0.001$ every year). Similar correlations were obtained using CASEN 2003-2010-2017 (results not shown).

Table 6.2: Correlation matrix of contextual indicators.

Socioeconomic environment measure by year	Income inequality	Poverty
2003 (n=194)		
Income inequality	1	
Poverty	0.038 (p=0.601)	1
Unemployment	-0.002 (p=0.978)	0.827 (p<0.001)
2010 (n=147)		
Income inequality	1	
Poverty	-0.002 (p=0.977)	1
Unemployment	-0.114 (p=0.171)	0.763 (p<0.001)
2017 (n=157)		
Income inequality	1	
Poverty	-0.137 (p=0.086)	1
Unemployment	-0.089 (p=0.267)	0.643 (p<0.001)

Figure 6.4 show the estimated distribution of individual educational level (%) by socioeconomic environment measures (in Q1 and Q4). Briefly, the proportion of participants at the lowest educational level was higher among counties with the highest (Q4) than the lowest (Q1) levels of poverty and unemployment. On the other hand, counties with the highest levels of income inequality showed a higher proportion of participants at the highest educational level.

Figure 6.4: Distribution of individual educational level by socioeconomic environment measures.



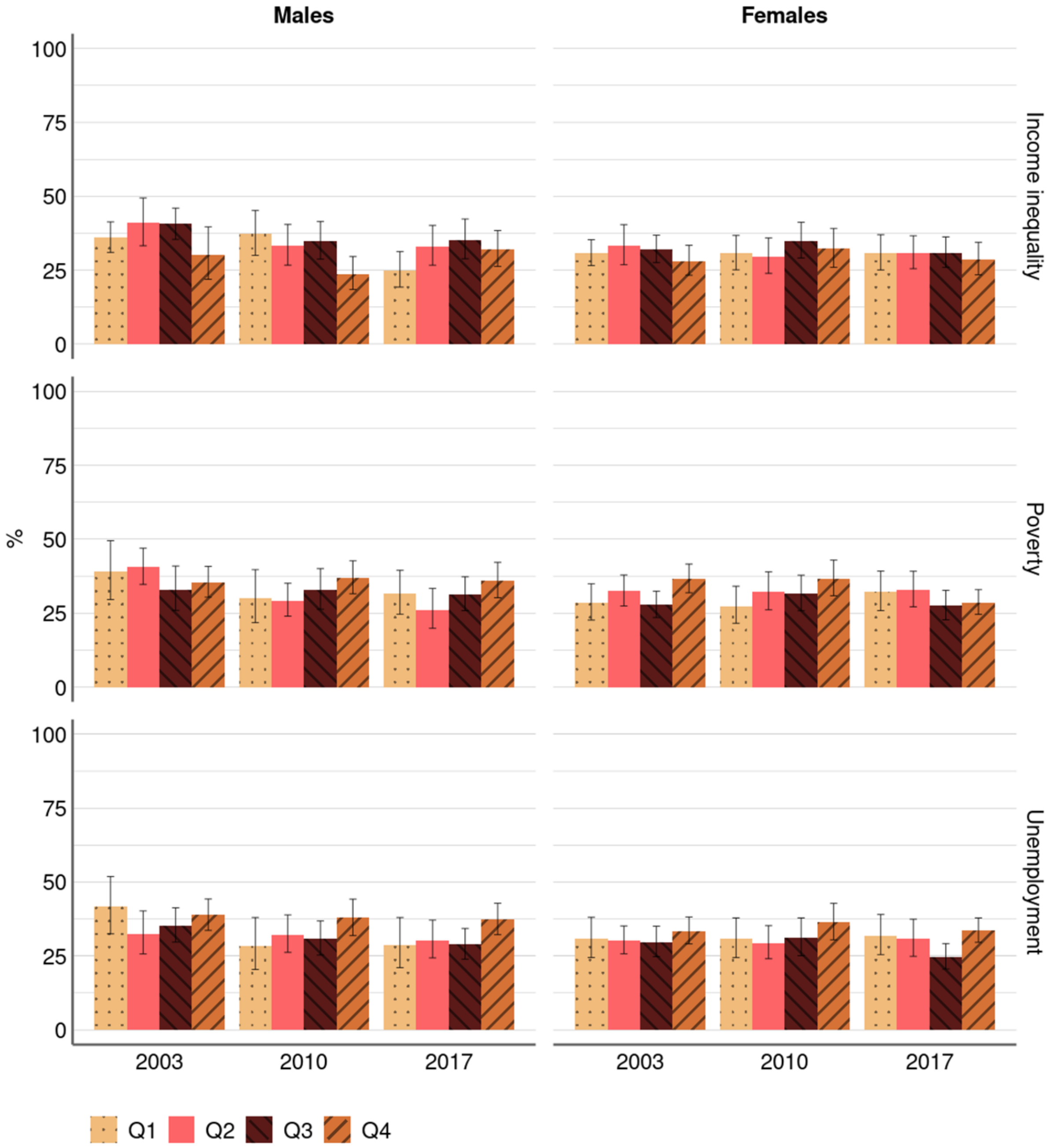
Socioeconomic environment measures categorised in quartiles. Q1: lowest quartile (e.g. counties with the lowest poverty levels) and Q4: highest quartile (e.g. counties with the highest poverty levels).

6.4.2. Descriptive analyses of hypertension outcomes

Survey-defined hypertension

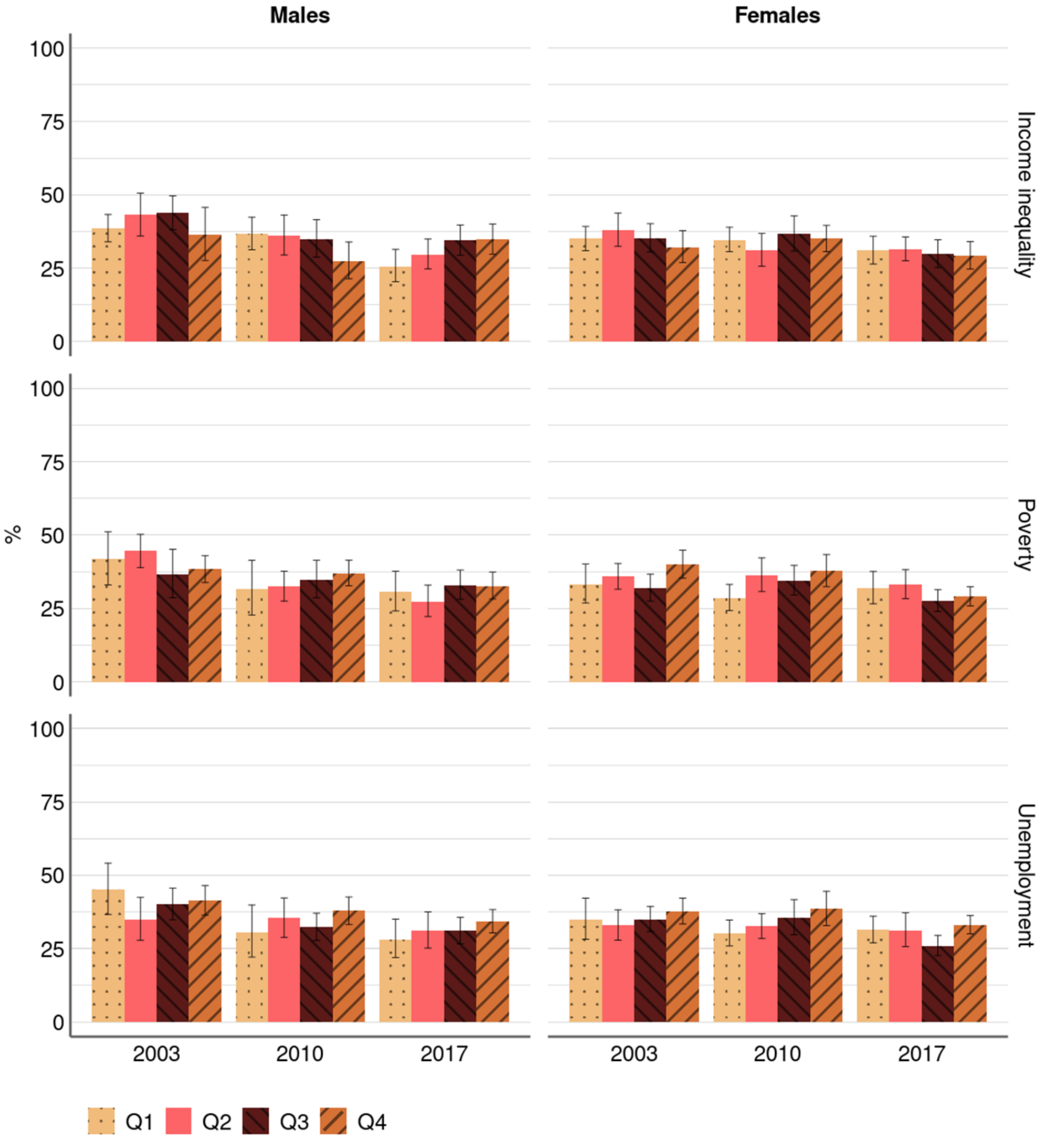
Figures 6.5 and 6.6 show the estimated gender-specific *observed* and *age-standardised* levels of survey-defined hypertension, respectively. For brevity, here I focus on differences in the age-standardised estimates between the lowest (Q1) and highest (Q4) quartiles.

Figure 6.5: Hypertension prevalence by quartiles of the socioeconomic environment measures (observed).



Observed estimates (% and 95% CI). Socioeconomic environment measures categorised in quartiles. Q1: lowest quartile (e.g. counties with the lowest poverty levels) and Q4: highest quartile (e.g. counties with the highest poverty levels).

Figure 6.6: Hypertension prevalence by quartiles of the socioeconomic environment measures (age-standardised).



Values and 95% CIs were directly age-gender-standardised using data from Census 2017 (age groups 17-44y, 45-64y and ≥65y). Socioeconomic environment measures categorised in quartiles. Q1: lowest quartile (e.g. counties with the lowest poverty levels) and Q4: highest quartile (e.g. counties with the highest poverty levels).

Overall, results by quartiles of **income inequality** among males showed similar levels of hypertension in Q1 and Q4 in 2003 (Q1: 39%, Q4: 36%, p=0.646); in 2010, levels of hypertension were higher in Q1 than in Q4 (Q1: 37%, Q4: 27%, p=0.026); and in 2017, levels of hypertension were higher in Q4 than in Q1 (Q1: 26%, Q4: 35%, p=0.015). Among females, similar levels of hypertension were observed in Q1 and Q4 in all three years (e.g. in 2017, Q1: 31%, Q4: 29%, p=0.588).

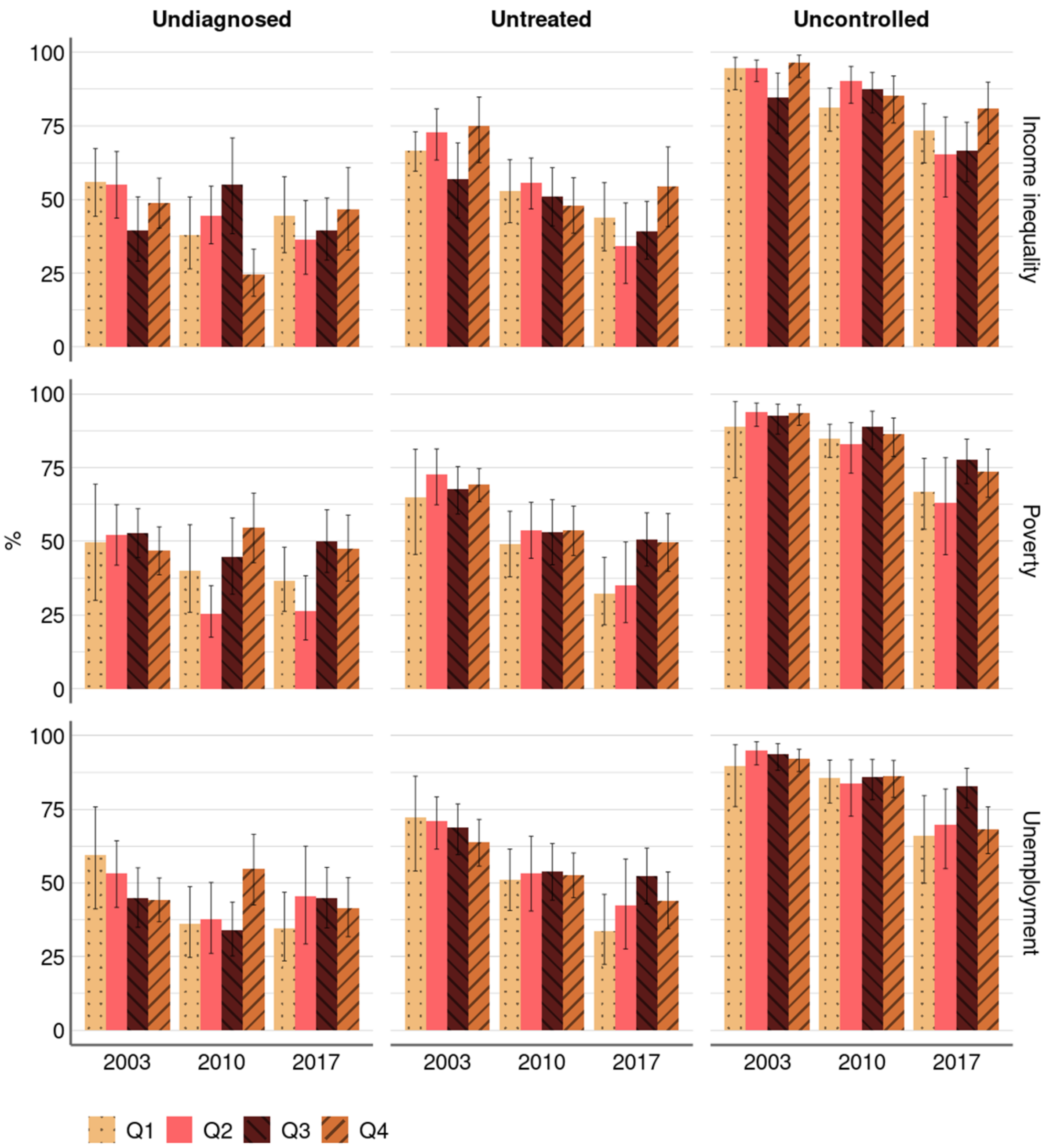
I found similar levels of hypertension in the lowest and highest **poverty** quartiles among males in all three years (e.g. in 2017, Q1: 31%, Q4: 33%, p=0.604). Among females, in 2010, higher levels of hypertension were observed in Q4 than in Q1 (Q1: 29%, Q4: 38%, p=0.008), whilst levels were similar in 2017 (Q1: 32%, Q4: 29%, p=0.368).

Among males, hypertension levels by **unemployment** were similar in Q1 and Q4 in all three years (e.g. in 2017, Q1: 28%, Q4: 34%, p=0.116). Among females, levels of hypertension were higher in Q4 than in Q1 in 2010 (Q1: 30%, Q4: 39%, p=0.019). Levels were similar in Q1 and Q4 in 2003 and in 2017 (e.g. in 2017, Q1: 31%, Q4: 33%, p=0.536). A full set of observed and age-standardised levels of hypertension by socioeconomic environmental measures are provided in Appendix 6.

Hypertension management indicators

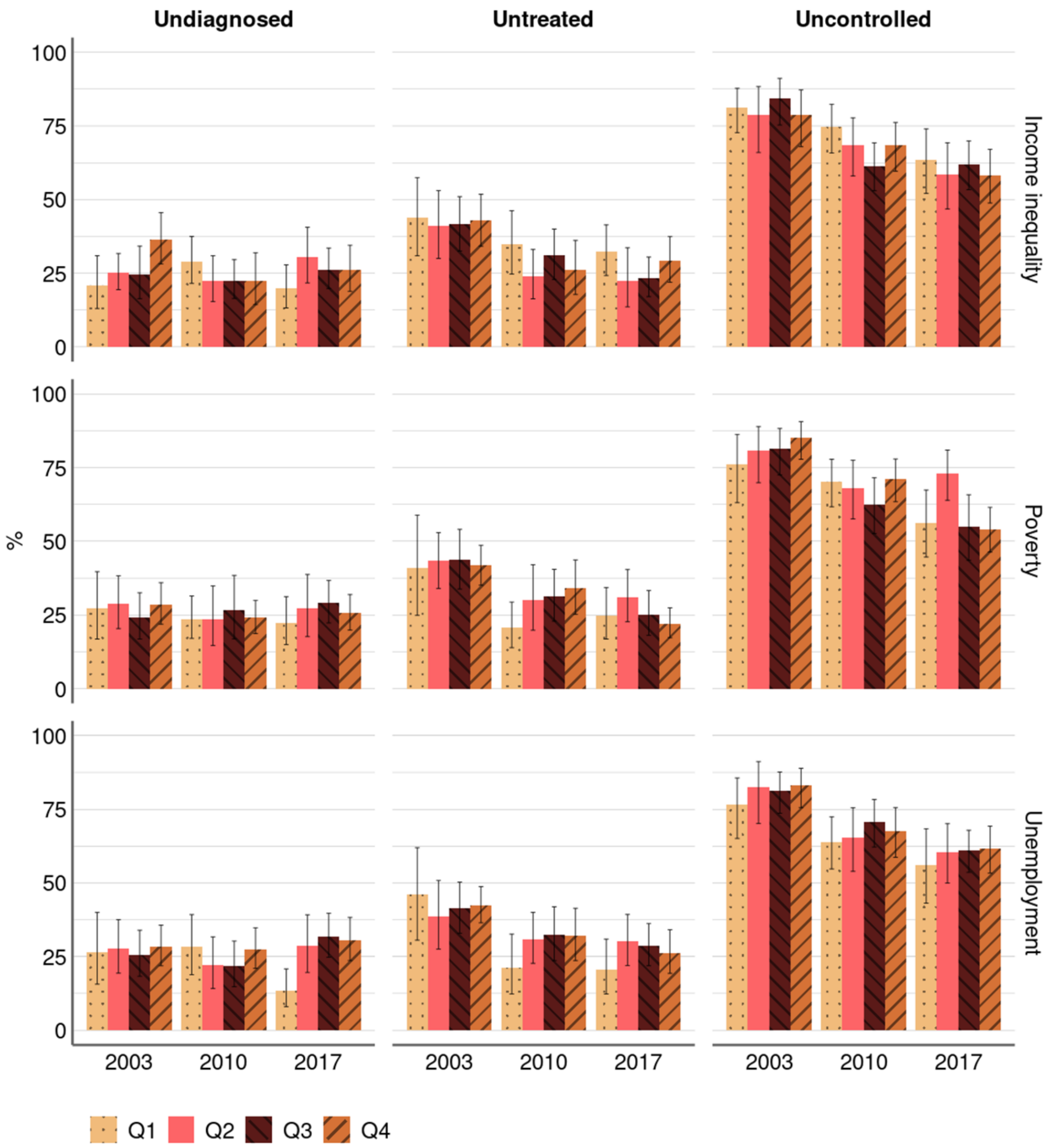
For the sake of brevity, here I briefly describe the differences between the lowest and highest quartiles (Q1 and Q4) in *age-standardised* levels of undiagnosed, untreated, and uncontrolled hypertension by the three socioeconomic environment measures. I provide a full set of *observed* and *age-standardised* levels in Appendix 6. Figures 6.7 and 6.8 show the *age-standardised* levels of undiagnosed, untreated, and uncontrolled hypertension by the three socioeconomic environment measures for males and females, respectively.

Figure 6.7: Hypertension management outcomes by quartiles of the socioeconomic environment measures among males (age-standardised).



Values and 95% CIs were directly age-gender-standardised using the age composition of participants with hypertension in ENS2017 (age groups: 17-44y; 45-64y; 65-74y; ≥75y). Socioeconomic environment measures categorised in quartiles. Q1: lowest quartile (e.g. counties with the lowest poverty levels) and Q4: highest quartile (e.g. counties with the highest poverty levels).

Figure 6.8: Hypertension management outcomes by quartiles of the socioeconomic environment measure among females (age-standardised).



Values and 95% CIs were directly age-gender-standardised using the age composition of participants with hypertension in ENS2017 (age groups: 17-44y; 45-64y; 65-74y; ≥75y). Socioeconomic environment measures categorised in quartiles. Q1: lowest quartile (e.g. counties with the lowest poverty levels) and Q4: highest quartile (e.g. counties with the highest poverty levels).

Overall, despite wide 95% CIs, the descriptive results show that the levels of hypertension management improved over time in both the lowest and highest quartiles of the socioeconomic environment measures among both genders. However, the estimates suggested a greater decrease over time in levels of undiagnosed, untreated, and uncontrolled hypertension among males residing in the lowest quartile (i.e. those counties with the lowest levels of income inequality, poverty, and unemployment). Focusing on 2017, the only difference between Q1 and Q4 in levels of hypertension management that reached statistical significance was found among females using unemployment as the contextual measure: higher levels of undiagnosed hypertension were observed in Q4 compared with Q1 (Q1: 14%, Q4: 31%, p=0.001).

6.4.3. Multilevel analyses

Step 1: Intraclass correlation (ICC)

Intraclass correlation for survey-defined hypertension

The ICC estimates the proportion of the total variance in survey-defined hypertension that can be attributed to differences between counties. The estimated ICC from the empty multilevel logistic regression models for hypertension in 2003, 2010, and 2017 were 3.9% (95% CI: 1.4-10.8), 7.6% (95% CI: 4.2-13.5), and 4.5% (95% CI: 2.0-9.9), respectively.

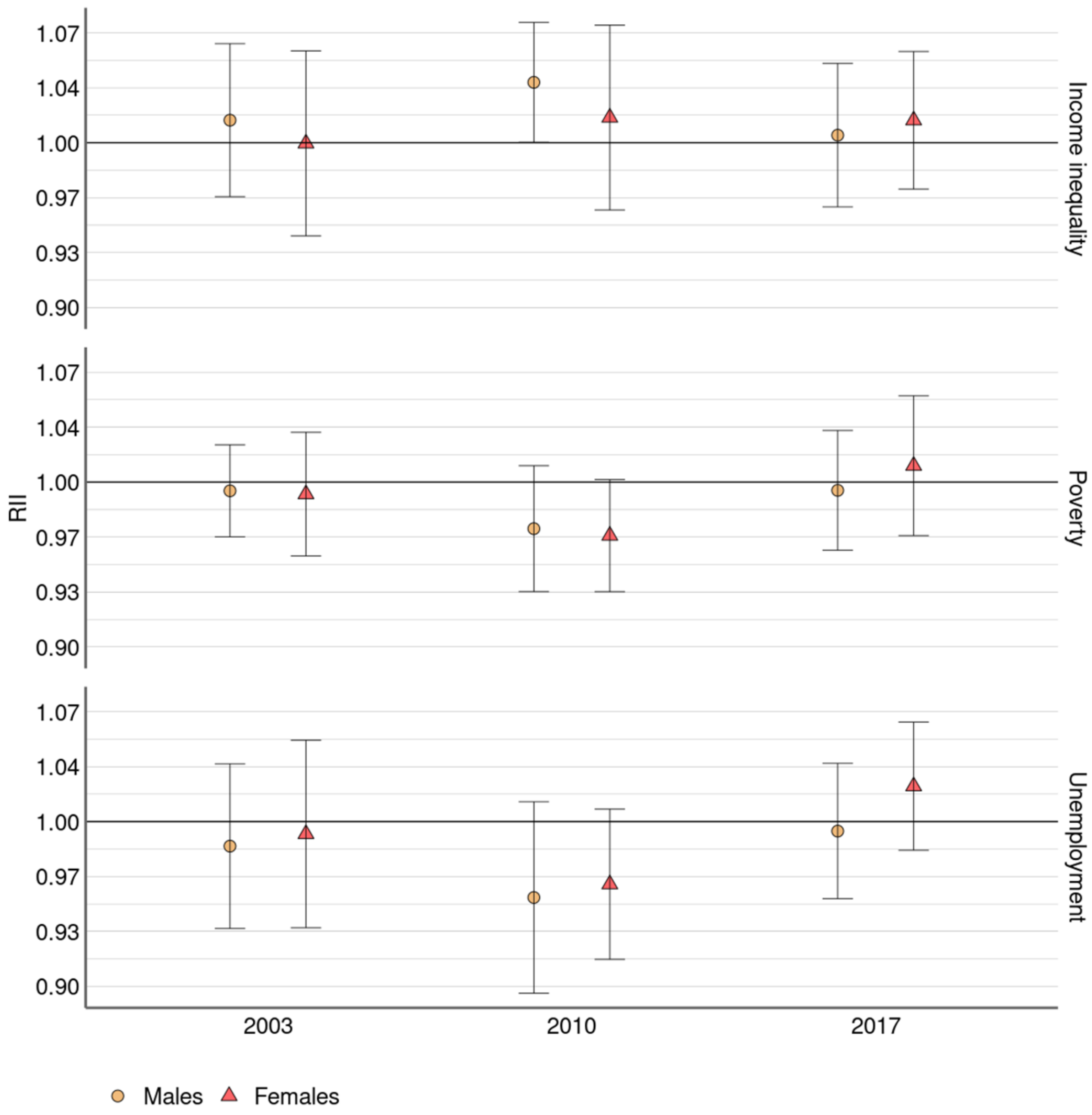
Intraclass correlation for hypertension management indicators

The estimates of the lower bound of the 95% CI for the ICC from the empty multilevel logistic regression models for undiagnosed, untreated, and uncontrolled hypertension in 2003, 2010, and 2017 were each in the region of 0%, indicating a similarity between counties in the estimated probability of a participant with survey-defined hypertension being undiagnosed, untreated or having uncontrolled blood pressure (i.e. the absence of a clustering effect). Hence, no further multilevel analyses for the three indicators of hypertension management were performed.

Step 2: Cross-level interaction

In the present study, cross-level interaction terms estimate how the values for the coefficient (i.e. slope) for the individual-level SEP variable vary with values of the area-level variable.[237] For the binary outcome of survey-defined hypertension, the estimates for the cross-level interaction terms (on the relative scale: RII) are shown in Figure 6.9. Most 95% CIs included the null value of 1, indicating that the magnitude of individual-level educational-based inequalities in hypertension did not significantly vary by county levels of income inequality, poverty or unemployment.

Figure 6.9: Cross-level interaction term between socioeconomic environment measures and individual educational level (ridit scores) for hypertension.



Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear two-level models using Poisson (log link) function. Multilevel models: 1st level= age (continuous) + individual educational ridit + socioeconomic environment measure + interaction term (individual educational ridit X socioeconomic environment measure); 2nd level= county (random intercept) + random slope for educational ridit. Income inequality: Gini coefficient (%).

However, there was an exception to this general pattern: the cross-level interaction term among males in 2010 between individual educational level and county levels of income inequality reached statistical significance (RII: 1.04 (95% CI: 1.00-1.08); p=0.048): indicating wider educational-based inequalities among those living in counties with higher levels of income inequality. Furthermore, the cross-level interaction term among females in 2010 between individual educational level and county levels of poverty nearly attained statistical significance (RII: 0.97 (95% CI: 0.93-1.00); p=0.062): indicating narrower educational-based inequalities among females living in counties with higher levels of poverty. The full set of cross-level interaction estimates are provided in Table 6.3.

Table 6.3: Cross-level interaction term between socioeconomic environment measures and individual educational level (ridit scores) in hypertension.

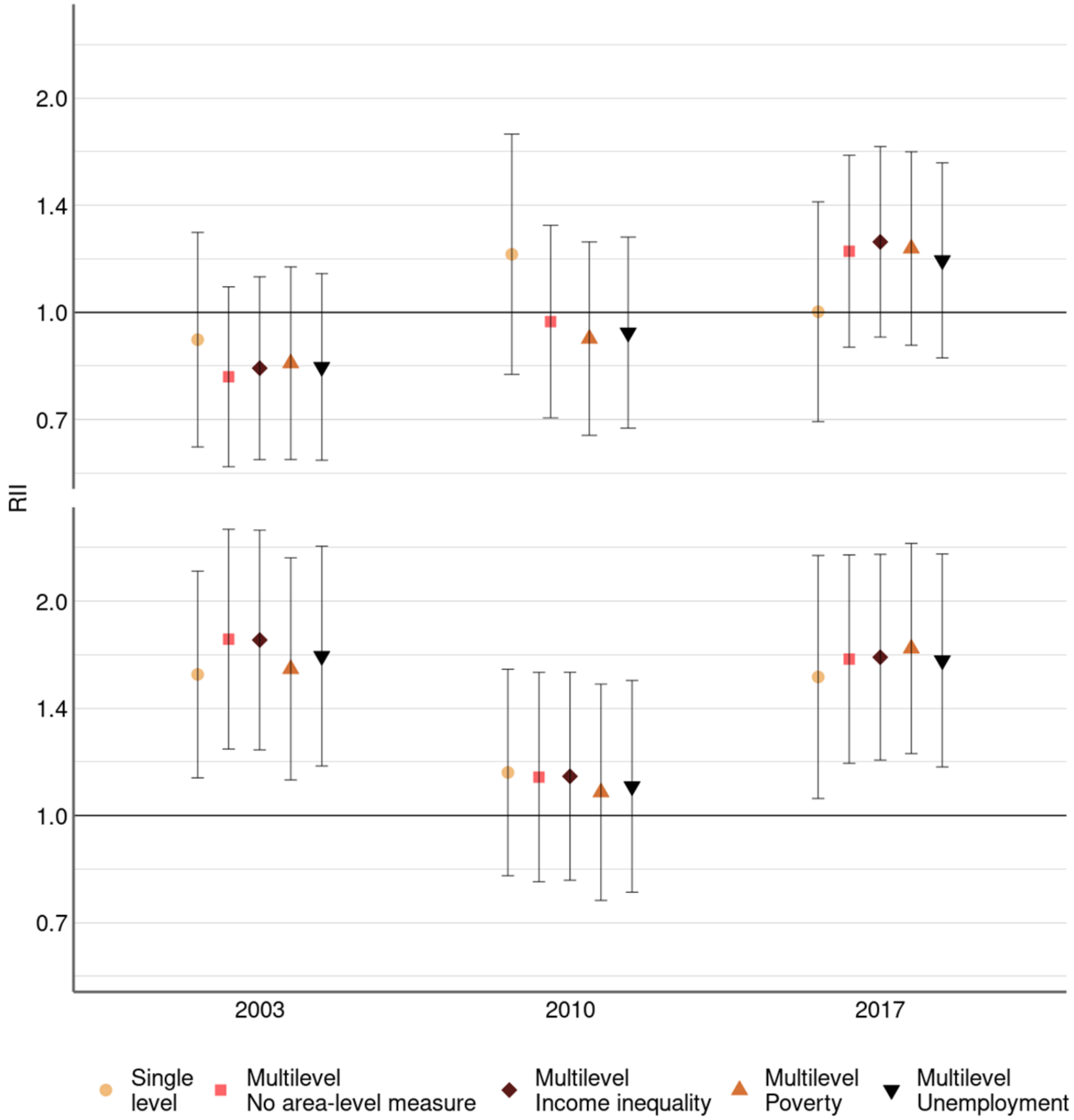
	Males		Females	
	RII Interaction	**P-value**	**RII Interaction**	**P-value**
Income inequality				
2003	1.01 (0.97-1.06)	0.562	1.00 (0.94-1.06)	0.989
2010	**1.04 (1.00-1.08)**	**0.048**	1.02 (0.96-1.08)	0.592
2017	1.00 (0.96-1.05)	0.837	1.01 (0.97-1.06)	0.520
Poverty				
2003	0.99 (0.97-1.02)	0.710	0.99 (0.95-1.03)	0.702
2010	0.97 (0.93-1.01)	0.146	0.97 (0.93-1.00)	0.062
2017	0.99 (0.96-1.03)	0.786	1.01 (0.97-1.06)	0.643
Unemployment				
2003	0.98 (0.93-1.04)	0.557	0.99 (0.94-1.05)	0.795
2010	0.95 (0.90-1.01)	0.119	0.96 (0.92-1.01)	0.101
2017	0.99 (0.95-1.04)	0.781	1.02 (0.98-1.06)	0.278

Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear two-level models using Poisson (log link) function. Multilevel models: 1st level= age (continuous) + individual educational ridit + socioeconomic environment measure + interaction term (individual educational ridit X socioeconomic environment measure); 2nd level= county (random intercept) + random slope for educational ridit. Income inequality: Gini coefficient (%).

Step 3: Confounder effect of socioeconomic environment measures

Figure 6.10 shows the estimates of the relative (RII) individual-level educational-based inequalities in hypertension from both single-level models and multilevel models. Overall, the results from the multilevel analyses were similar for each socioeconomic environment measure (suggesting minimal confounding). For brevity, I outline the results from multilevel analyses on the RII before and after adjustment for county levels of income inequality.

Figure 6.10: Individual educational-based RII for hypertension: single-level versus multilevel models by gender.



Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear two-level models using Poisson (log link) function. Single-level model: age (continuous) + individual educational ridit. Multilevel models: 1st level= Single-level variables + socioeconomic environment measure (continuous, separate models); 2nd level= county (random intercept) + random slope for educational level. The RII adjusted for income inequality for males in 2010 was not reported as the results suggested a strong cross-level interaction.

Among males, weak associations between individual-level educational status (entered as a ridit scores) and hypertension remained after adjustment for county levels of income inequality, poverty, and unemployment. In 2003, the educational-based RII decreased from 0.92 (95% CI: 0.65- 1.30) in the single-level model to 0.83 (95% CI: 0.62- 1.12) after adjustment for county levels of income inequality (relative change: -9%). In 2017, the figures before and after adjustment for county levels of income inequality were 1.00 (95% CI: 0.70- 1.43) and 1.26 (95% CI: 0.92- 1.71), respectively (relative change: 25%).

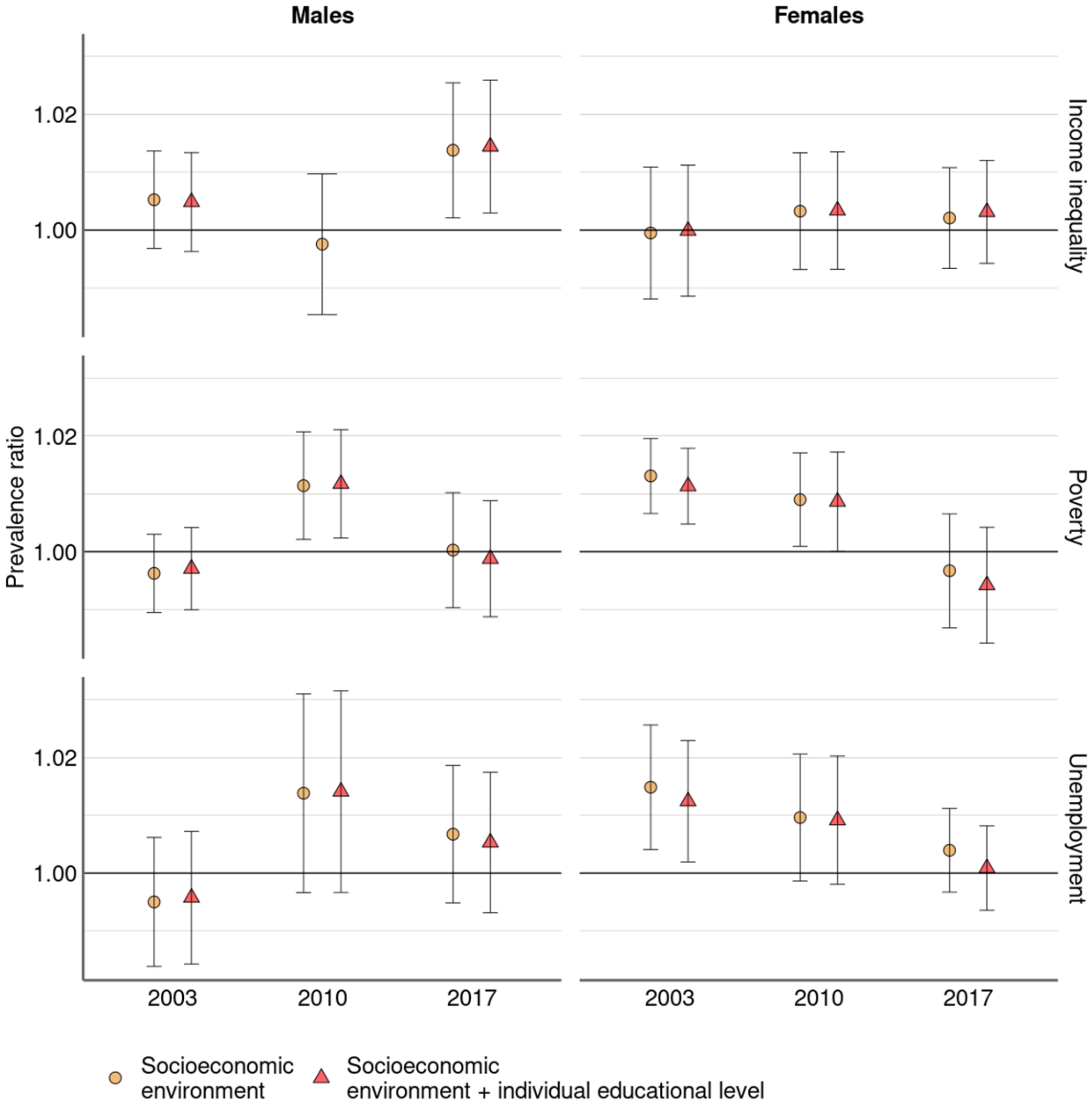
Among females, the observed educational-based inequalities using the single-level regression model did not change in direction or magnitude after adjustment for socioeconomic environment measures. Results for 2003 and 2017 showed consistently higher levels of hypertension among females at the lowest educational level. For instance, in 2017 the estimated educational-based RII slightly increased from 1.56 (95% CI: 1.06- 2.32) in the single-level model to 1.67 (95% CI: 1.20- 2.33) in the multilevel model after adjustment for county levels of income inequality (relative change: 7%).

The direction and magnitude of the individual educational-based inequalities in hypertension after adjustment for the measures of the socioeconomic environment were similar using either relative (RII) or absolute (SII) measures of inequality (a full set of estimates of RII and SII values is provided in Appendix 6).

Step 4: Associations with socioeconomic environment measures

Figure 6.11 shows the relative inequalities (measured as prevalence ratio (PR)) of hypertension prevalence by socioeconomic environment measures before and after adjustment for individual educational level. Overall, changes in the PR before and after adjustment for individual educational level were minimal. I found a strong association between income inequality and hypertension among males in 2017: a one-unit increase in county levels of income inequality (%) was associated with a significant (but modest) increase in the prevalence ratio of hypertension before and after adjustment for individual educational level among males in 2017 (PRs before and after adjustment for individual educational level were identical: 1.02 (95% CI: 1.00-1.03)).

Figure 6.11: Inequalities by socioeconomic environment measures.



Prevalence ratio (PR) and 95% CIs estimated from generalised linear two-level models using Poisson (log link) function. Multilevel models: 1st level= age + socioeconomic environment measure (continuous, separate models); 2nd level= county (random intercept). Socioeconomic environment + individual educational level model also included educational ridit in the 1st level and a random slope for educational level in the 2nd level. The PR adjusted for income inequality and individual educational level among males in 2010 was not reported as the results suggested a strong cross-level interaction.

Similarly, levels of poverty were positively associated with hypertension prevalence among males in 2010 and among females in 2003 and 2010. Unemployment was positively associated with hypertension among females in 2003 and in 2010. Results almost reached 5% statistical significance in 2010. Inequalities by poverty and unemployment seemed to decrease among females over time. A full set of values is provided in Appendix 6.

Summary of findings

The main results of the multilevel models used to estimate the individual educational-based inequalities in hypertension before and after adjustment for measures of the socioeconomic environment are summarised in Table 6.4.

Table 6.4: Individual educational-based inequalities in hypertension: multilevel analyses.

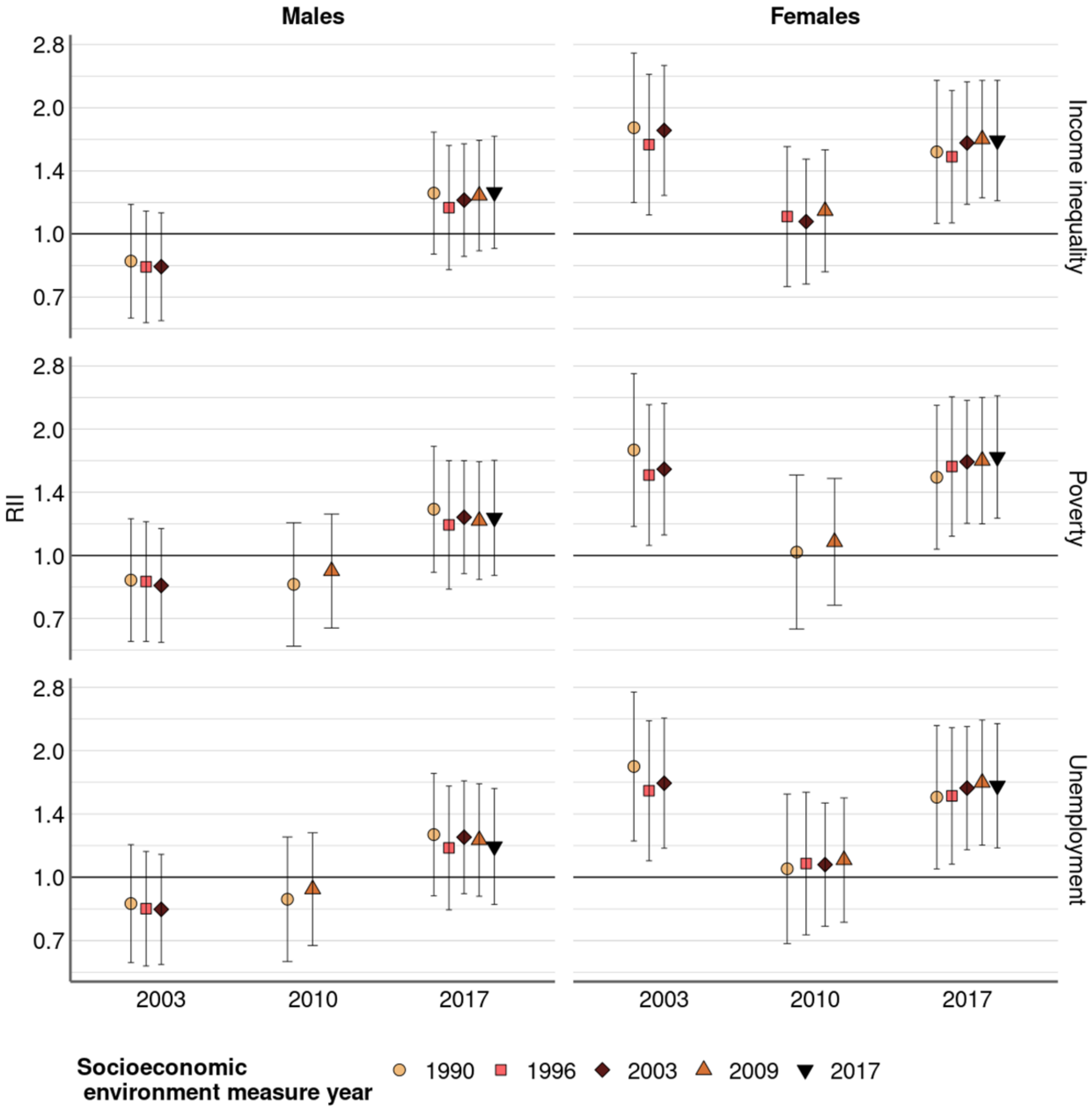
	RII Males	RII Females
2003		
Single-level	0.92 (0.65-1.30)	**1.58 (1.13-2.20)**
No area-level measure	0.81 (0.61-1.09)	**1.77 (1.24-2.52)**
Income inequality	0.83 (0.62-1.12)	**1.76 (1.24-2.52)**
Poverty	0.85 (0.62-1.16)	**1.61 (1.12-2.30)**
Unemployment	0.84 (0.62-1.13)	**1.67 (1.17-2.39)**
2010		
Single-level	1.21 (0.82-1.78)	1.15 (0.82-1.60)
No area-level measure	0.97 (0.71-1.33)	1.13 (0.81-1.59)
Income inequality	#	1.13 (0.81-1.59)
Poverty	0.92 (0.67-1.26)	1.08 (0.76-1.53)
Unemployment	0.94 (0.69-1.28)	1.10 (0.78-1.55)
2017		
Single-level	1.00 (0.70-1.43)	**1.56 (1.06-2.32)**
No area-level measure	1.22 (0.89-1.66)	**1.66 (1.18-2.32)**
Income inequality	1.26 (0.92-1.71)	**1.67 (1.20-2.33)**
Poverty	1.23 (0.90-1.68)	**1.72 (1.22-2.41)**
Unemployment	1.18 (0.86-1.62)	**1.65 (1.17-2.33)**

Values in bold indicate statistically significant results ($p<0.05$). Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear models using Poisson (log link) function. Single-level model: age (continuous) + individual educational ridit. ‡Multilevel models: Single-level variables + socioeconomic environment measure (continuous variable in separate models); 2nd level= county (random intercept) and random slope of the individual educational ridit. #: The RII adjusted for income inequality for males in 2010 was not reported as the results suggested a strong cross-level interaction.

6.4.4. Sensitivity analyses

Figure 6.12 shows the educational-based RII for hypertension using lagged values for the socioeconomic environment measures (SII values are provided in Appendix 6). In general, the direction and magnitude of the RII did not change when I adjusted for the lagged rather than contemporaneous values.

Figure 6.12: Individual educational-based RII: multilevel models adjusted for lagged socioeconomic environment measures.



Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear two-level models using Poisson (log link) function. Single-level model: age (continuous) + individual educational ridit. Multilevel models: 1st level= Single-level variables + socioeconomic environment measure (continuous, separate models); 2nd level= county (random intercept) and random slope of the individual educational ridit. Some RIIs were not reported as the results suggested a strong cross-level interaction.

6.5. Discussion

In this brief discussion, I discuss the main findings in relation to the hypotheses tested, and cover the strengths and limitations specific to the empirical work presented in this chapter. In the Discussion of the thesis as a whole (Chapter 8), I provide comparisons with other studies from LACCs and elsewhere, outline potential explanations for the main findings, and discuss the main policy implications.

6.5.1. Main findings

The aim of this third empirical chapter was to contextualise gender-specific individual-level educational inequalities in hypertension and in hypertension management indicators in Chilean adults in 2003, 2010, and 2017 by considering the role of socioeconomic environment measures using a multilevel analytical approach.

I outlined four testable hypotheses in this chapter:

- **H6.1**: The county of residence of ENS participants contributes to the variation in hypertension and in each hypertension management outcome. This would indicate, for example, that levels of hypertension are clustered among survey participants residing in the same county.
- **H6.2**: The magnitude of individual-level educational inequalities in hypertension outcomes does not vary according to levels of the socioeconomic environment measures among both males and females.
- **H6.3**: The magnitude of individual educational-based inequalities in hypertension outcomes is attenuated after adjustment for socioeconomic environment measures among both males and females.
- **H6.4**: The magnitude of area-level inequalities in hypertension outcomes is attenuated after adjustment for individual-level educational status among both males and females.

Contribution of the county to the variation in hypertension outcomes

I first evaluated the contribution of counties to the estimated variance of hypertension outcomes using estimates of the ICC. Hypothesis (**H6.1**) was partially supported: variability in survey-defined hypertension was partially explained at the county level. Roughly 4-8% of the variance in hypertension was attributed to the variation between counties (this modest proportion is in line with similar multilevel analyses). However, negligible between-county variance was observed in the three key management indicators in each survey year: hence a single-level individual analysis (as done in Chapter 5) was appropriate for estimating the corresponding individual-level SEP inequalities. Survey-defined hypertension therefore was the only outcome explored further using multilevel regression models.

Cross-level interaction between individual educational level and socioeconomic environment measures

Secondly, I evaluated potential gender-specific cross-level interaction effects to estimate whether the magnitude of the individual-level educational-based inequalities in hypertension varied with county levels of income inequality, poverty, and unemployment. Overall, the cross-level interaction terms did not attain statistical significance among males or females. The only exception was found among males in 2010: the relative educational-based inequalities (higher prevalence of hypertension among the least versus most educated) were more prominent among males living in the counties with higher levels of income inequality. Apart from this finding, **H6.2** was supported: in general, the gender-specific magnitude of inequalities by educational level did not change by levels of socioeconomic environment measures.

Inequalities by individual educational level adjusted for socioeconomic environment measures

Thirdly, I evaluated the hypothesis that the gender-specific magnitude of educational-based relative and absolute inequalities in hypertension would change after adjustment for socioeconomic environment measures (**H6.3**). A change in estimates would indicate that area-level characteristics confound at least in part the observed inequalities by individual-level educational status. My findings did not support H6.3: overall, for both genders and each contextual factor, adjustment of county-levels of income inequality, poverty, and unemployment did not change the magnitude or direction of the individual-level educational-based inequalities in hypertension.

Inequalities by socioeconomic environment measures

Over and above the findings used to test the main hypotheses of this chapter, the multilevel models showed that Chilean counties with higher levels of contextual income inequality showed higher levels of hypertension prevalence among males in 2017. Levels of hypertension were positively associated with poverty among males in 2010 and among females in 2003 and in 2010. Unemployment also showed a positive association with hypertension among females living in areas with higher unemployment in 2003 and in 2010. I found weak evidence supporting inequalities in hypertension management outcomes by socioeconomic environment measures. Between 2003 and 2017, counties with lower levels of contextual income inequality, poverty, and unemployment showed a steeper decrease in levels of hypertension and undiagnosed, untreated, and uncontrolled hypertension. Inequalities by socioeconomic environment income inequality, poverty, and unemployment did not change after adjustment for individual educational level among males and females, providing no support to hypothesis **H6.4**.

6.5.2. Strengths and limitations

This is the first study using Chilean data to assess the association between hypertension and hypertension management outcomes and socioeconomic environment measures (area levels of income inequality, poverty, and unemployment). I used multilevel regression modelling, which is an appropriate model to account for any county-level clustering of survey participants and to simultaneously study contextual and individual-level socioeconomic determinants of hypertension outcomes.[237] However, several limitations specific to the analyses presented in this chapter could have affected my results and their interpretation.

First, measurement bias in the socioeconomic environment measures could have affected my results. However, this bias should be minimal as the county of residence was registered by trained interviewers and the county levels of income inequality, poverty, and unemployment were estimated using standard methods on the best data available. Descriptive statistics of the county levels of income inequality, poverty, and unemployment (including their correlation) based only on the ENS data (presented in Tables 6.1 and 6.2) are likely unrepresentative of Chile (CASEN is preferred for these purposes). However, the correlations between the area-level variables were similar using CASEN and ENS data.

Secondly, my results could also have been affected by temporal bias since ENS data does not contain information on how long survey participants had resided at their current address.[218, 240] Moreover, previous research suggests that lagged rather than contemporaneous values of contextual factors are more predictive of health outcomes.[218] However, results from my sensitivity analysis showed that individual-level educational-based inequalities in hypertension were similar in direction and in strength using lagged or contemporaneous values.

Thirdly, I used county to define the area of residence of ENS participants. There is no consensus about which geographical scale might be the most optimal to analyse hypertension-related outcomes using health examination survey data. In Chile, data at the county level are frequently used to characterise the population, and indicators of the economic and social context are widely available at this geographical unit. Also, previous research in Chile has linked socioeconomic environment measures (at the county level) with several health outcomes, including mortality, self-rated health, BP levels, and mental health.[65, 227–229, 231, 232] Furthermore, at the present time, the county is the smallest geographic unit available in the ENS datasets.

Finally, as in all observational studies, other unmeasured or unknown individual characteristics and aspects of the socioeconomic environment not included in the present study (e.g. food environment, green spaces) may have biassed my results to some extent.

6.6 Conclusion

Using multilevel models, the contribution of counties to the estimated variance of hypertension outcomes showed that the binary outcome of hypertension was the only hypertension outcome partially explained at the county level. Contextual factors such as income inequality were considered as potential confounders or modifiers of the associations between individual-level educational status and hypertension. Among both genders adjustment of county-levels of income inequality, poverty, and unemployment did not change the magnitude or direction of the individual-level educational-based inequalities in hypertension (suggesting weak or no confounding). At the same time, among females (especially in 2003 and 2017), higher levels of income inequality, poverty, and unemployment significantly increased the prevalence of hypertension after adjustment for individual-level education: highlighting the independent role of the socioeconomic environment in which people live on an individual-level health outcome.

Chapter 7: Differences in all-cause and cardiovascular mortality rates by hypertension status and by socioeconomic position

7.1. Introduction

Hypertension, labelled by some authors as *the silent killer*, is one of the most important preventable causes of disability, premature mortality (i.e. deaths among younger age groups of the population) and cardiovascular disease in Chile and worldwide.[25, 27, 28, 178] 7.7-10.4 million deaths annually worldwide are attributed to high BP: of those over 88% occur among LMICs.[28] Appropriate management of hypertension (e.g. reducing levels of BP below recommended levels) can reduce the risk of death from cardiovascular disease and in this way, having access to diagnosis and to the recommended antihypertensive treatment plays an important role in preventing or reducing the risk of premature mortality.[180] Differences between population subgroups in hypertension management are worrisome, as successful control of BP helps to reduce the long-term risk of CVD events and premature death.[51]

Moreover, higher hypertension prevalence (as presented in chapter 5) as well as higher mortality rates have been reported in lower SEP groups.[181, 241] Previous epidemiological evidence suggests that being in a low SEP group is comparable to widely recognised risk factors for higher risk of mortality, including raised BP, obesity, diabetes, tobacco and alcohol consumption, and low physical activity.[181] Several studies have analysed the socioeconomic gradient in mortality using a diversity of analytical approaches.[241, 242] Some studies have assessed how much of the socioeconomic gradient in mortality was explained (i.e. mediated) by healthy lifestyle behaviours. For example, Stringhini et al. (2017) using prospective cohorts from HICs reported higher mortality rates among participants with low versus high occupational positions (Hazard Ratio (HR): 1.46; 95% CI: 1.39–1.53).[181] This association remained significant in models that adjusted mutually for smoking, diabetes, physical inactivity, hypertension, obesity, and high alcohol intake (HR 1.26; 95% CI: 1.21–1.32).[181]

In the last decade, the Chilean Ministry of Health (MINSAL) and its Department of Statistics and Health Information (DEIS) pushed for improvements in enhancing the value of health examination surveys such as ENS by linkage to other health statistics databases, including linkage to mortality registry data. National data linkage to mortality registries has enabled the ENS data to be analysed as a longitudinal study. Analyses of linked mortality data can allow investigation of differences in mortality rates across the wide range of variables gathered at the ENS interview and health examination. MINSAL recently released ENS survey data linked with mortality data, and to the best of my knowledge, no research has been published to date using these prospective data. Following my conceptual model (Chapter 3), the analyses in this chapter explore the associations between educational level, hypertension, and mortality, whilst adjusting for potential confounders and evaluating potential effect modification between hypertension status and education on both all-cause and cardiovascular mortality rates.

7.2. Research problem, aim, objectives and hypotheses

Problem

There is no information available on the differences in all-cause and cardiovascular mortality rates in the Chilean adult population by hypertension nor by individual educational level.

Aim

Using the ENS-Mortality linked data, to evaluate gender-specific associations between (i) hypertension status and (ii) individual-level educational status on all-cause and cardiovascular mortality.

Specific objectives

- Estimate the gender-specific rates of all-cause and cardiovascular mortality by hypertension status.
- Estimate the gender-specific rates of all-cause and cardiovascular mortality by individual educational level.
- Evaluate the age-adjusted gender-specific association between all-cause and cardiovascular mortality by hypertension and by individual educational level using regression models.
- Examine whether hypertension status modifies the gender-specific associations between individual educational level and all-cause and cardiovascular mortality.

Hypotheses

- **H7.1**: Hypertension is associated with all-cause and cardiovascular mortality after age adjustment among both males and females. Survey participants with (i) treated and controlled hypertension, (ii) treated but uncontrolled hypertension, or (iii) untreated hypertension, have higher all-cause mortality rates than normotensive participants. Survey participants with hypertension have higher cardiovascular mortality rates than those without hypertension.
- **H7.2**: Educational level is associated with all-cause and cardiovascular mortality after age adjustment among both males and females. Survey participants with lower levels of education have higher rates of all-cause and cardiovascular mortality than those with higher education levels.
- **H7.3**: The association between educational level and mortality is moderated to some extent by hypertension status among both males and females. Evidence of statistical interaction would show that the magnitude of individual-level educational inequalities in mortality varies by hypertension status (e.g. educational-based inequalities in mortality being wider among those with untreated hypertension than among normotensive participants).

7.3. Methods

The ENS study design, setting and data collection, and definitions of hypertension and individual-level educational status, were described previously in Chapters 4 and 5. Here I describe the specific methods related to the ENS2003-2010 cohorts and to the analysis of ENS-Mortality linked data.

7.3.1. Ethical considerations

The ethics committee of the Pontificia Universidad Católica de Chile (PUC) approved the study protocol for this chapter (ID: 211116004, see Appendix 7). ENS2003 and ENS2010 participants authorised in their signed informed consent to use their data in future public health research. However, the informed consent procedures for ENS2003 and ENS2010 did not explicitly request authorisation for the link between ENS data and the national mortality registry. The Chilean Government decided in 2019 to make the mortality-linked ENS2003 and ENS2010 databases publicly available. This was done under the Chilean legal system and the umbrella of *public health functions*: according to Chilean law, MINSAL has the right and responsibility to use data and create links between data sets when there is an overall public health benefit. MINSAL linked both databases in compliance with the confidentiality safeguards using the national ID number of each ENS participant. The ENS-Mortality linked data were publicly released without sensitive data (e.g. without participants' national ID number or residential address): these are the data I analysed for this PhD.

7.3.2. Data source for the longitudinal outcomes

DEIS mortality dataset

The vital statistics system in Chile is centralised in the Health Statistics and Information Department (DEIS) of the Chilean Ministry of Health, involving the coordination of three public organisations: (i) the National Institute of Statistics, (ii) the Civil Registry and Identification Service, and (iii) the Ministry of Health. Chilean law enforces the registration of a death certificate in order to proceed with the burial. In this way, almost 100% of deaths have a medical death certificate. Chile has a long experience with vital statistics data collection and it is recognised to have high-quality information.[243] Currently, death certificates have high levels of completeness (roughly 99% of certificates include information on the cause of death) and they contain a low proportion of ill-defined cause of death codes (<10%).[243, 244] A systematic effort is performed by DEIS to validate each death certificate. Nosologists code the causes of death according to the International Classification of Diseases, 10th revision (ICD-10) code.[245] The date and main cause of death were obtained from DEIS data. The last date of ascertaining mortality status by DEIS was November 11th, 2019 (ENS2003) and December 12th, 2018 (ENS2010).

Study Sample

For this observational longitudinal study of the Chilean non-institutionalised population, I used data from the ENS2003-2010 linked with DEIS mortality data. ENS survey participants with missing data for hypertension status were excluded from the analytical sample. Six participants with a non-valid date of death were also excluded (one and five participants from ENS2003 and ENS2010, respectively). After these exclusions, 8,230 participants were included in the statistical analyses. The length of follow-up was up to 16.3 years in ENS2003 and up to 9.2 years in ENS2010. I did not include data from the ENS2017 because of the short period of follow-up (≤2 years).

7.3.3. Definitions of survival time and cardiovascular death

I calculated survival time as the number of days between the nurse ENS interview (when BP was measured) and the date of death or the end date of the study (the aforementioned last date of ascertaining mortality status by DEIS). Cardiovascular disease deaths were coded by a specific list of ICD-10 codes for the underlying cause of death (Table 7.1).[246]

Table 7.1: ICD-10 codes for cardiovascular mortality.

Cardiovascular causes of death	ICD-10
Coronary heart disease: ischemic heart disease; angina pectoris; acute and subsequent myocardial infarction	I20–I25, excluding I25.0
Stroke: cerebral infarction; intracerebral haemorrhage; subarachnoid haemorrhage	I60–I69
Hypertensive heart disease: essential hypertension, hypertensive heart disease, hypertensive renal disease	I10–I15
Atherosclerosis and unspecified heart disease: general and unspecified atherosclerosis; unspecified cardiovascular disease; unspecified heart disease	I25.0, I51.6, I51.9, I70.9
Heart failure: congestive heart failure; left ventricular failure; unspecified heart failure	I50
Cardiac arrest: cardiac arrest; ventricular tachycardia; ventricular fibrillation	I46, I47.2, I49.0
Inflammatory heart disease: cardiomyopathy; acute and subacute endocarditis; myocarditis; pericarditis	I51.4, I51.5, I30–I33, I38–I43
Other: pulmonary embolism; valvular and conduction disorders; aortic aneurysm; rheumatic heart disease	I01–I09, I26–I28, I34–I37, I44–I49, I51–I52, I70–I99

Cardiovascular causes of death as defined by Murray et al.[246]

7.3.4. Events and exposures

Two main events were analysed separately: (i) all-cause deaths and (ii) cardiovascular deaths. The main exposures were (i) hypertension and (ii) educational status. In Chapters 4-6 of this thesis, I defined four different hypertension outcomes: a binary outcome of survey-defined hypertension (BP ≥140/90 mmHg or use of antihypertensive medication) and three hypertension management indicators (awareness, treatment, and control). In this chapter, hypertension is treated as an exposure rather than the outcome.

For analyses of all-cause mortality, I defined hypertension status in four categories and educational level in three categories. Hypertension status was defined using four mutually exclusive categories: (i) normotensive (<140/90 mmHg, not on antihypertensive medication); (ii) treated and controlled (<140/90 mmHg); (iii) treated, but uncontrolled (≥140/90 mmHg); and (iv) untreated (≥140/90 mmHg). All analyses presented in this chapter are based on the general population (normotensive as reference category). Educational level (years of formal education) was analysed as a three-category variable (low: <8y, medium: 8-12y, high: >12y).

Due to the fewer number of events (see below), cardiovascular mortality analyses are reported by the binary exposures of *survey-defined hypertension* (BP ≥140/90 mmHg or use of antihypertensive medication) vs no hypertension, and low educational level (<8y of formal education) vs more education.

7.3.5. Statistical analyses

I restricted analyses to adults aged ≥17y. To produce estimates that represent the non-institutionalised, civilian Chilean population, I accounted for the complex sampling design of the ENS. In Chapters 4-6, I reported differences by gender in levels of hypertension outcomes and also in educational-based inequalities in hypertension outcomes. Accordingly, all analyses presented in this chapter were gender specific. P-values were evaluated as a continuous variable (ranging from 0 to 1) and so were not interpreted using strict and arbitrary values. However, I defined as statistically significant those tests with an estimated p-value <0.05. Statistical analyses were based on complete cases and were conducted using R (version 4.0.4) and Stata (version 16).

I. Descriptive analyses

The baseline characteristics of the analytical sample were described separately for ENS2003 and ENS2010 and by hypertension status. I described both ENS cohorts by age (in three categories: 17-44y; 45-64y; ≥65y), gender, and educational level (low, medium, high).

II. Survival analyses

The analysis of survival data requires specific statistical methods that can analyse time-to-event data in the presence of censoring. In the case of the ENS cohort, this means that the main outcome of interest is the time between the participant's nurse ENS interview and the date of death (survival time). Participants that were known to have survived by the end of the follow-up are right-censored (and are assigned the total length of time of the follow-up): such cases were "still alive", as the failure event had not occurred by the final date of ascertaining mortality status by DEIS. In the analyses of cardiovascular mortality, persons who died of causes other than cardiovascular disease were censored at the date of death.

Survival analyses for all-cause and cardiovascular mortality are organised into three sections: (i) mortality rates; (ii) Kaplan-Meier plots; and (iii) Cox proportional hazards regression models. I describe each section in turn below.

Mortality rates

First, I calculated the number of deaths and follow-up time in person-years by ENS cohort (2003, 2010), age at ENS interview (17-44y; 45-64y; 65y+), gender, educational level, and hypertension status. Secondly, I estimated all-cause and cardiovascular mortality rates (deaths per thousand person-years of follow-up) with their accompanying 95% Cis.

Kaplan-Meier survival plots

Survival analysis techniques were used to summarise differences in the all-cause and cardiovascular mortality rates across various subgroups of the population. Kaplan-Meier survival plots and log-rank tests evaluated differences in survival in univariate analysis (i.e. evaluating only one exposure at a time) and are useful when the exposure of interest is categorical.

First, Kaplan–Meier plots are useful for estimating (using a non-parametric approach) the survival function (i.e. the estimated probability that a survey participant will survive past a certain time point). These plots are composed of horizontal lines reflecting the proportion of survivors according to the time of follow-up, considering the population that survived or was censored. To meet the specified aims set out earlier, I used Kaplan-Meier survival plots to examine differences in survival probabilities stratified by ENS cohort, hypertension status, and educational level. I stratified analyses by age group (i.e. 45-64y and ≥65y) to adjust, at least partially, for age differences in hypertension or educational level. In order to simplify the presentation of the plots, the youngest age group (17-44y) was excluded, as the number of deaths was small across all categories of hypertension and education.

Secondly, equality of survivor functions across two or more groups was tested using the log-rank test.[247] This non-parametric test, which makes no assumption about the shape of the distribution, is useful to compare the survival distributions of two or more groups. The log-rank test compares the expected (i.e. no difference in mortality rates across the groups over time) versus the observed number of deaths at each observed time that a death occurs.

Cox proportional hazards regression models

For the multivariable analysis, I built Cox proportional hazards (PH) regression models to evaluate differences in mortality risk over the follow-up period. Cox models evaluate how exposures, such as hypertension status or educational level, are associated with the incidence of death (hazard) at a particular point in time. In this way, for a binary exposure, the hazard rate (HR) is the ratio of hazards between two groups (e.g. the hazard among participants with hypertension versus those without hypertension). I used Cox PH models to evaluate the independent associations of educational level and hypertension status with all-cause mortality after adjustment for age.[248] For analyses of cardiovascular mortality, using Cox models, I evaluated the age-adjusted association with binary indicators for survey-defined hypertension and education. A simple equation for the Cox model is presented in Equation 7.1.

Equation 7.1:

$$h(t) = h_0(t) * exp(\beta_1 X_1 + \ldots + \beta_k X_k)$$

In Equation 7.1, t represents the survival time and h(t) is the hazard function depending on a set of exposures (X1,.., Xk). Hazards are dependent on time. The coefficients (e.g. β_1) measure the magnitude (effect size) of the exposure and mortality association. $h_0(t)$ is the baseline hazard (the value of the hazard when all exposures in the model are equal to zero or set to the reference category). $h_0(t)$ is time-varying. The exponential of the coefficients corresponds to the HR. The interpretation of HRs can be summarised as follows:

- HR > 1: higher hazard of death (reduced survival time) in the exposed group compared with the reference group (e.g. higher mortality rate among participants with versus without hypertension).
- HR = 1: no difference in mortality rate between the two groups.
- HR < 1: lower hazard of death (increased survival time) in the exposed group compared with the reference group (e.g. lower mortality rate among participants with treated but uncontrolled hypertension versus normotensive participants).

Cox models assume HRs to be constant over time (hazards of the event may change over the follow-up period, but the estimated HR is constrained to be constant). In this way, the estimated HR is constrained to be independent of time t. For example, an estimated HR of 2 comparing participants with and without hypertension indicates that the relative likelihood of death is twice as high for participants with hypertension at any given point in time during the follow-up period. Time-dependent HRs (e.g. adults with hypertension showing higher mortality rates than adults without hypertension only during the first few years of the follow-up period) violate the PH assumption. Such violations require alternative modelling choices (e.g. stratified Cox models or including a covariate by time interaction term). I assessed the appropriateness of the PH assumption for the variables in the models using the Schoenfeld test and the corresponding Schoenfeld residual plots.[249] The

Schoenfeld test and plots are used to evaluate the existence of a non-zero slope in a generalised linear regression of the scaled Schoenfeld residuals (i.e. the difference between the observed and expected values at each failure time) on functions of time. A non-zero slope indicates a violation of the PH assumption.

Models that showed no violation of the PH assumption were reported using age-adjusted HRs by hypertension and educational level. HRs were obtained by exponentiation of the estimated logarithm of the hazard ratios (the βs in Equation 7.1).

Analyses were stratified by cohort year. I also analysed the ENS2003-2010 pooled data to obtain a general estimate and increase the statistical power. Survey year was also included in age-adjusted models when using pooled data.

Further models were built to evaluate if the estimated association between individual-level education and mortality varied to some extent by hypertension status. The Wald test was used to evaluate the null hypothesis that model fit was not improved by including the interaction term (i.e. $p<0.05$ as evidence of effect modification).[250] Educational-based HRs stratified by hypertension were estimated for the models with a statistically significant interaction term.

7.4. Results

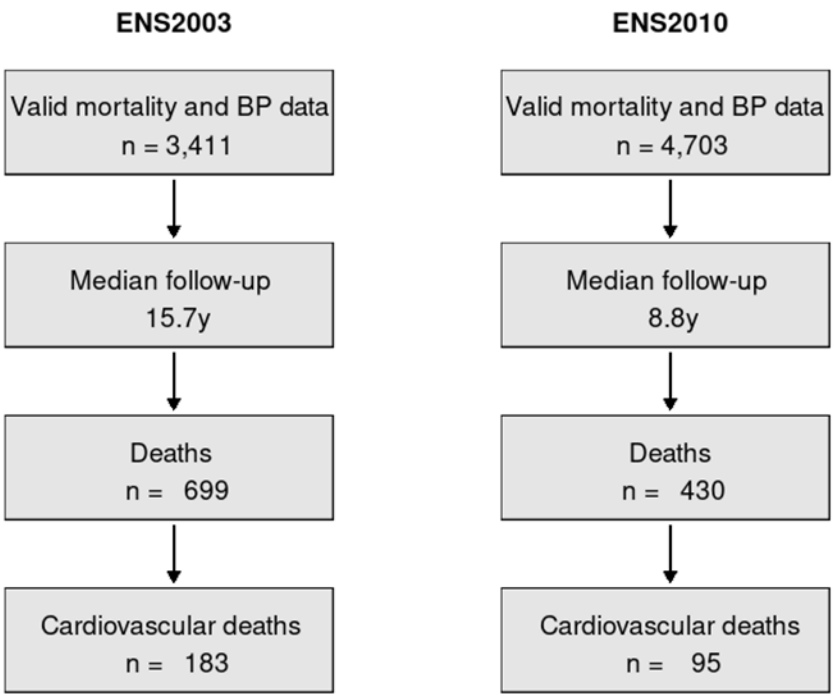
In this section, I first describe the ENS2003 and ENS2010 analytical samples by hypertension status, followed by the survival analyses. I divide the report of the survival analyses into two main parts: (i) all-cause mortality and (ii) cardiovascular mortality. Within each outcome, I first present analyses of the mortality rates by gender, age group, hypertension, and educational level. Secondly, I present the survival analyses across groups using Kaplan-Meier survival plots and report the results of log-rank tests. Finally, I outline the results from the Cox regression models.

7.4.1. Description of the cohort

Sample description.

As shown in Figure 7.1, 3,411 and 4,703 participants with valid mortality, BP and medicine data were included in the analyses. The median length of follow-up was 15.7 years and 8.8 years in the ENS2003 and ENS2010 cohorts, respectively. During the follow-up, the total observed number of all-cause deaths was 699 in ENS2003 and 430 in ENS2010. The corresponding numbers of cardiovascular deaths were 183 and 95.

Figure 7.1: Flow diagram of participants, median follow-up, and number of deaths. ENS2003–2010 cohorts.



Sample with valid mortality status, blood pressure (BP) levels, and antihypertensive medication status.

The baseline characteristics of the analytical sample according to hypertension status (four categories) and ENS cohort are reported in Table 7.2. The gender distribution was different across the hypertension categories. For example, in the ENS2003 cohort, females represented roughly two-thirds of those with treated and controlled hypertension and only one-third of those who were untreated. Overall, in both cohorts, normotensive adults and those with untreated hypertension were younger than those with treated and controlled hypertension or with treated but uncontrolled hypertension. Normotensive adults showed the highest percentage of participants at the highest educational level. Compared with the ENS2003 cohort, participants in the ENS2010 cohort showed a higher proportion of participants at the highest educational level. The age distribution among normotensive participants was similar in the two cohorts. Participants with survey-defined hypertension were older in the ENS2010 than the ENS2003 cohort.

Table 7.2: Baseline characteristics. ENS2003-ENS2010 cohorts.

	2003				2010			
	Normotensive	**Treated and controlled**	**Treated but uncontrolled**	**Untreated**	**Normotensive**	**Treated and controlled**	**Treated but uncontrolled**	**Untreated**
All (n)	1,816	198	542	855	2,943	458	640	662
Gender (%)								
Males	47	26	37	66	48	30	44	62
Females	53	74	63	34	52	70	56	38
Age (%)								
17-44y	78	25	10	43	76	15	8	34
45-64y	19	49	41	41	21	56	42	49
≥65y	3	26	49	16	3	29	50	18
Educational level (%)								
Low	17	42	54	36	12	34	43	28
Medium	60	45	40	49	58	51	43	54
High	23	13	6	15	30	14	14	18

n: unweighted sample size. Estimates are weighted for the complex survey design. Totals may not sum to 100% due to rounding.

7.4.2. Survival analyses

All-cause mortality

Mortality rates

The number of deaths and person-time at risk are presented in Table 7.3 (ENS2003) and Table 7.4 (ENS2010). After accounting for the complex survey design of the ENS, during 51,000 and 40,300 person-years at risk, 375 and 281 deaths were observed in the ENS2003 and ENS2010 cohorts, respectively.

Table 7.3: All-cause mortality rates. ENS2003 cohort.

Variable	n	Deaths	Person-years	Mortality per 1,000 person-years
All	3,411	375	51.0	7.4 (6.5-8.3)
Gender				
Males	1,556	177	25.0	7.1 (6.0-8.3)
Females	1,855	198	26.0	7.6 (6.4-9.1)
Age				
17-44y	1,445	33	33.3	1.0 (0.6-1.7)
45-64y	1,092	112	13.7	8.1 (6.6-10.1)
≥65y	874	230	4.0	58.1 (51.6-65.4)
Educational level				
Low	1,360	250	11.6	21.6 (18.7-25.0)
Medium	1,623	111	29.1	3.8 (3.0-4.8)
High	420	13	10.2	1.3 (0.7-2.4)
Hypertension status				
Normotensive	1,816	111	34.8	3.2 (2.5-4.1)
Treated and controlled	198	28	2.1	13.4 (9.0-20.1)
Treated but uncontrolled	542	128	3.7	34.4 (28.5-41.6)
Untreated	855	109	10.4	10.4 (8.4-12.9)

n: unweighted sample size. Deaths and follow-up time were calculated with normalised sample weights.

Table 7.4: All-cause mortality rates. ENS2010 cohort.

Variable	n	Deaths	Person-years	Mortality per 1,000 person-years
All	4,703	281	40.3	7.0 (6.0-8.2)
Gender				
Males	1,867	146	19.4	7.5 (5.9-9.8)
Females	2,836	135	20.9	6.5 (5.4-7.9)
Age				
17-44y	2,195	15	24.0	0.6 (0.3-1.3)
45-64y	1,598	80	12.1	6.6 (5.0-9.0)
≥65y	910	186	4.2	44.5 (36.6-54.4)
Educational level				
Low	1,265	162	7.2	22.5 (18.2-28.1)
Medium	2,519	90	22.7	3.9 (3.1-5.2)
High	903	28	10.3	2.7 (1.6-5.2)
Hypertension status				
Normotensive	2,943	61	27.9	2.2 (1.6-3.0)
Treated and controlled	458	55	2.9	18.6 (11.9-30.8)
Treated but uncontrolled	640	110	3.9	28.1 (22.1-36.0)
Untreated	662	56	5.5	10.2 (7.2-14.7)

n: unweighted sample size. Deaths and follow-up time were calculated with normalised sample weights.

As Tables 7.3 and 7.4 show, the crude (i.e. non-age adjusted) all-cause mortality rates (per 1,000 persons-years) were slightly lower in the ENS2010 than the ENS2003 participants. Mortality rates among females compared with males were slightly higher in the ENS2003 but slightly lower in the ENS2010. Mortality rates increased with age at ENS interview and were highest among the least educated. Mortality rates were higher among those with treated but uncontrolled hypertension and were lowest among the normotensive participants.

Kaplan-Meier survival plots and log-rank tests

The contributions of hypertension status and educational level to the risk of all-cause mortality (descriptive analyses) were independently assessed using Kaplan-Meier survival curves and log-rank tests. In the ENS2003 cohort, analyses by hypertension status (Figure 7.2) showed differences in the survival curve between normotensive participants versus those with treated but uncontrolled hypertension among those aged 45-64y (log-rank test: p=0.006) and among those aged ≥65y (p=0.048), showing the lowest survival probabilities among those with treated but uncontrolled hypertension. Differences in survival by hypertension status in the ENS2010 cohort were non-statistically significant (log-rank test: all p>0.1).

Figure 7.2: All-cause mortality Kaplan-Meier curve by hypertension status. ENS2003-2010 cohorts.

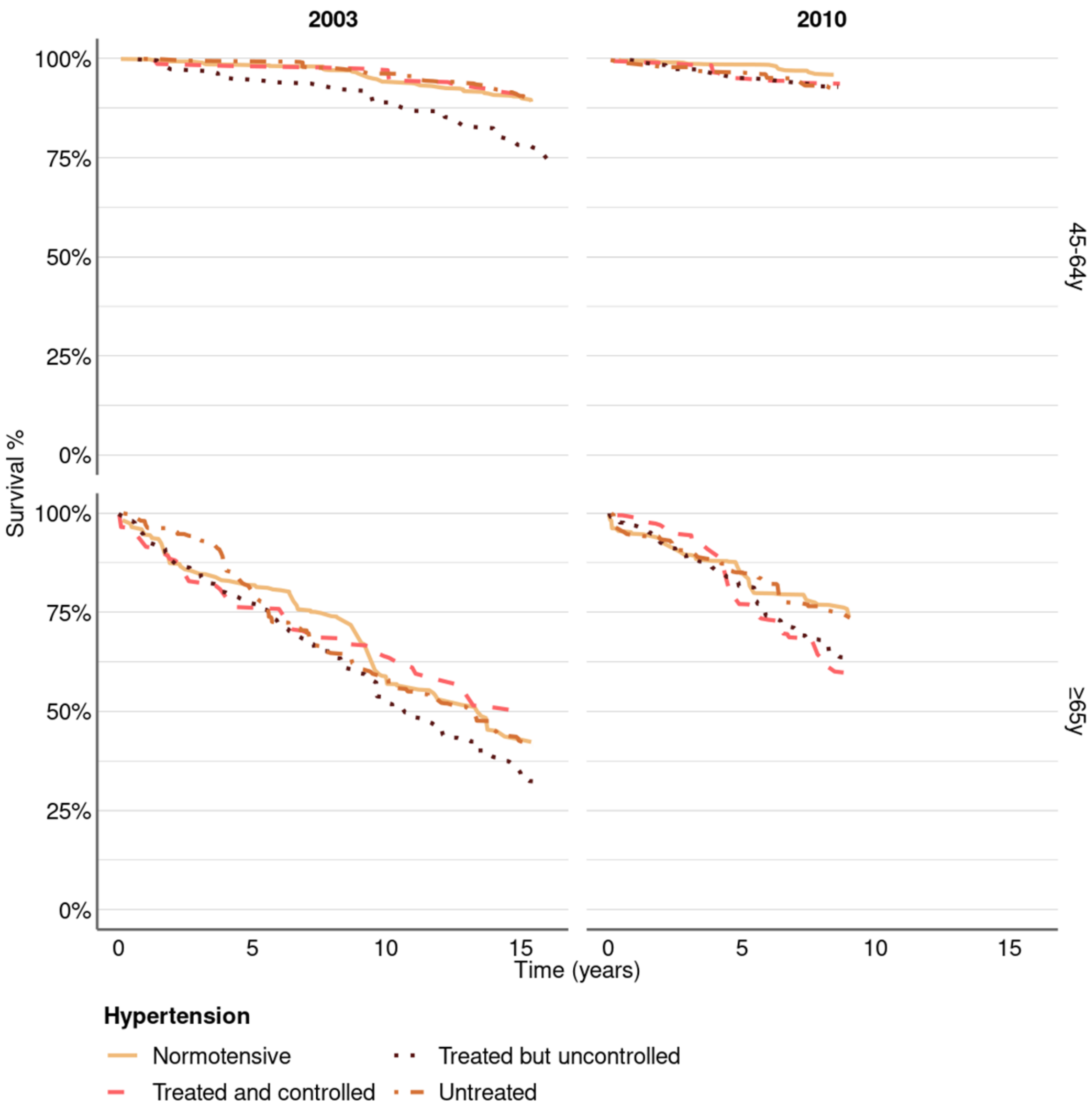
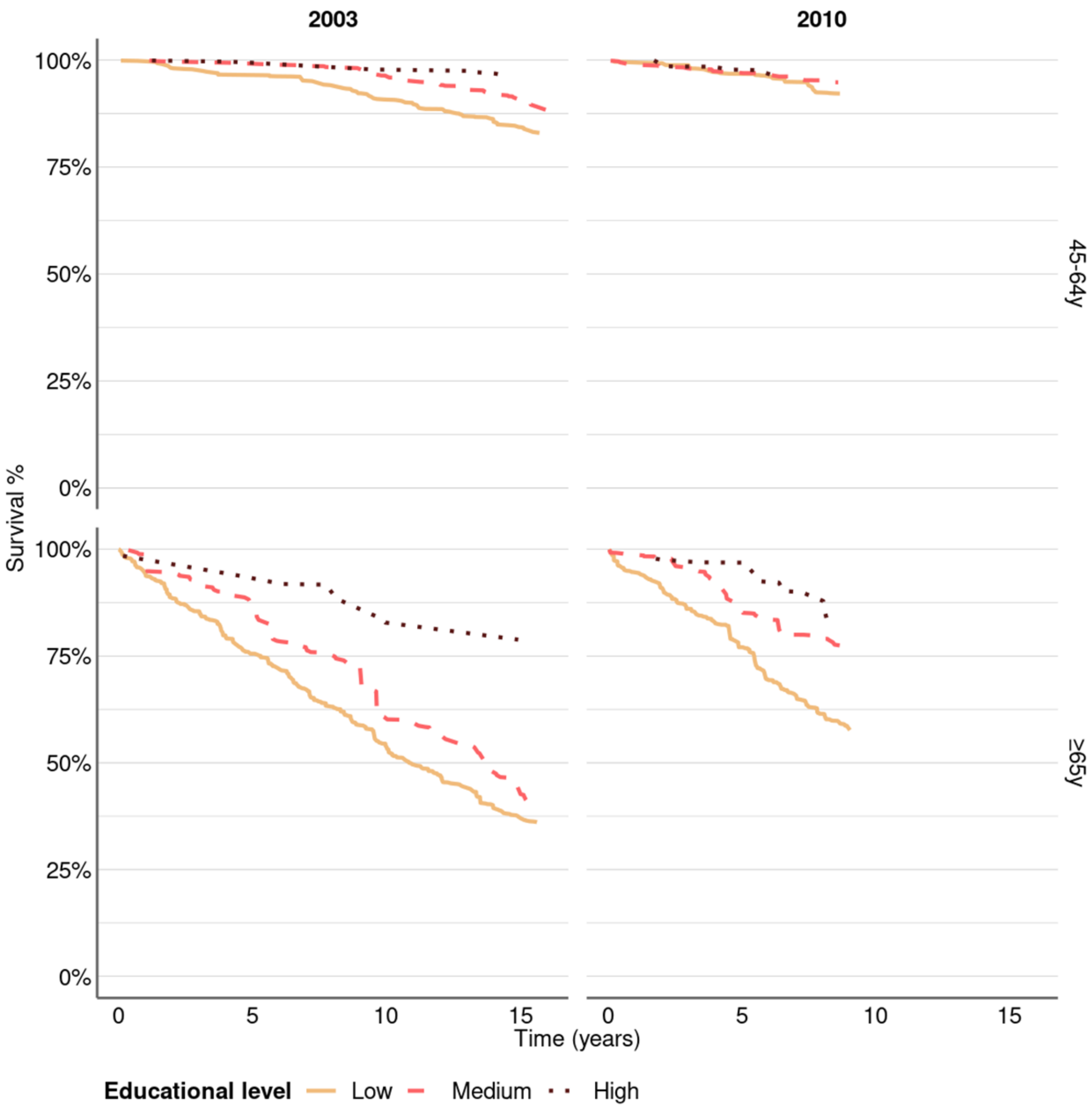


Figure 7.3 shows the Kaplan-Meier survival curves by educational level. Lower survival probability was observed among those with lower versus higher educational levels in both older age groups in the ENS2003 cohort. This difference was

statistically significant among those aged 45-64y and was marginally significant among those aged ≥65y (log-rank test: 45-64y p=0.006; ≥65y p=0.078). Differences by educational level in the ENS2010 cohort were only statistically significant among those aged ≥65y (log-rank test: 45-64y p=0.141; ≥65y p=0.001).

Figure 7.3: All-cause mortality Kaplan-Meier curve by educational level. ENS2003-2010 cohorts.



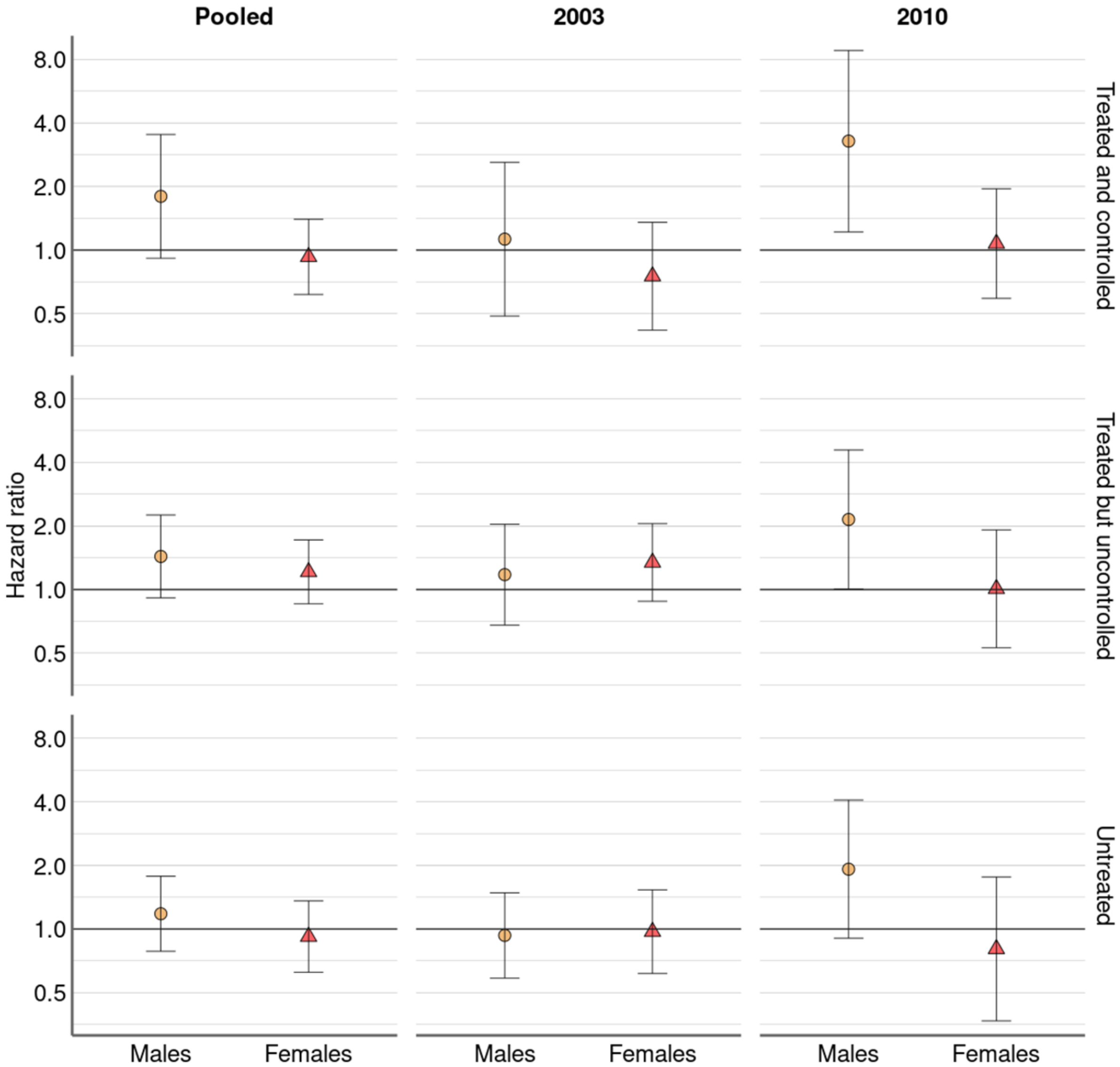
Cox proportional hazards regression models

Cox PH regression models were used to estimate the independent association of hypertension status and educational level, in turn, on the risk of all-cause mortality. Cox regression modelling enables further adjustment for other independent variables (e.g. confounders), including statistical control for differences in age across the exposure categories (e.g. those in the highest educational group were younger than those in the lowest educational group). As described earlier, one of the main assumptions of Cox regression modelling is the proportionality of hazards over time. I confirmed the PH assumption using plots of the scaled Schoenfeld residuals and statistical test for Cox regression models stratified by ENS cohort and with adjustment for (i) age and hypertension status, and (ii) age and educational level.

The gender-specific residuals related to both exposures (hypertension status and educational level) showed evidence of proportionality of hazards over time: the plots suggested no systematic departures from the horizontal line ($p>0.05$ for all; Schoenfeld residual plots provided in Appendix 7).

Age-adjusted hazard ratios (HRs) by hypertension status, stratified by ENS cohort and gender are shown in Figure 7.4. Most of the estimated HRs by hypertension status were non-statistically significant. The exceptions to this pattern were found among males using the ENS2010 cohort: Males with (i) treated and controlled hypertension or with (ii) treated but uncontrolled hypertension, were observed to have higher mortality risk of all-cause mortality than normotensive participants (HR treated and controlled hypertension: 3.28 (95% CI: 1.22-8.82); HR treated but uncontrolled hypertension: 2.15 (95% CI: 1.01-4.57); HR untreated hypertension: 1.92 (95% CI: 0.90-4.08)).

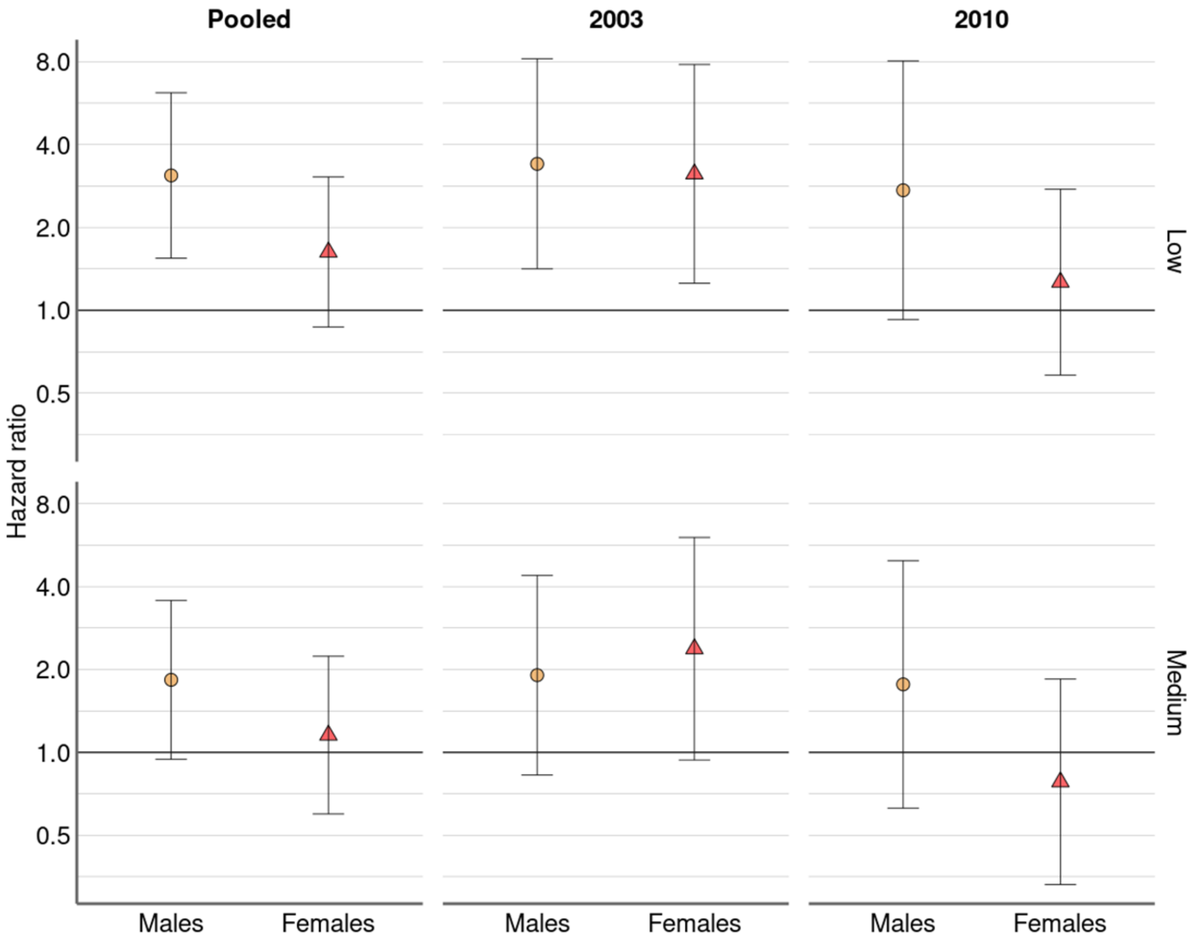
Figure 7.4: Relative hazards of death (all-cause) by hypertension status. ENS2003-2010 cohorts.



Reference category: normotensive. Age-adjusted Hazard Ratios (HRs) and 95% CIs from Cox regression models. Models run on ENS2003-2010 pooled data were additionally adjusted for survey year.

As shown in Figure 7.5, participants at the lowest educational level showed a higher mortality risk than those at the highest educational level. Based on the ENS2003 cohort, this difference was statistically significant for both males (HR: 3.40 (95% CI: 1.41-8.18)) and females (HR: 3.13 (95% CI: 1.25-7.81)).

Figure 7.5: Relative hazards of death (all-cause) by educational level. ENS2003-2010 cohorts.



Reference category: high educational level (>12y). Age-adjusted Hazard Ratios (HRs) and 95% CIs from Cox regression models. Models run on ENS2003-2010 pooled data were additionally adjusted for survey year.

Interaction term between education and hypertension

I evaluated a potential interaction effect between education and hypertension on the risk of all-cause mortality, in models that were stratified by ENS cohort and gender. Overall, these interaction terms did not reach statistical significance. The only interaction term that almost reached statistical significance was found among females using the ENS2003-2010 pooled data (p=0.06).

To investigate this further, I ran regression models stratified by hypertension status among females using the ENS2003-2010 pooled data. Results showed that the educational-based HRs were higher in (i) normotensive and (ii) treated but uncontrolled hypertension status. The stratum-specific HRs comparing those with low versus high education were as follows: normotensives: 2.77 (95% CI: 1.06-7.25); treated and controlled hypertension: 0.63 (95% CI: 0.22-1.77); treated but uncontrolled hypertension: 3.74 (95% CI: 0.62-22.32); and untreated hypertension: 0.69 (95% CI: 0.14-3.36).

Summary of findings for all-cause mortality

All-cause mortality HRs by hypertension and educational levels are summarised in Table 7.5.

Table 7.5: Relative hazards for all-cause mortality by hypertension status and educational level. ENS2003-2010 cohorts.

	Males			Females		
Exposure	**Pooled**	**2003**	**2010**	**Pooled**	**2003**	**2010**
Hypertension status						
Treated and controlled	1.80 (0.91-3.52)	1.13 (0.49-2.60)	**3.28 (1.22-8.82)**	0.93 (0.62-1.40)	0.75 (0.42-1.35)	1.07 (0.59-1.95)
Treated but uncontrolled	1.43 (0.91-2.25)	1.18 (0.68-2.04)	**2.15 (1.01-4.57)**	1.21 (0.86-1.72)	1.34 (0.88-2.05)	1.01 (0.53-1.92)
Untreated	1.18 (0.78-1.78)	0.93 (0.59-1.48)	1.92 (0.90-4.08)	0.92 (0.62-1.36)	0.97 (0.62-1.53)	0.81 (0.37-1.76)
Educational level						
Low	**3.09 (1.55-6.17)**	**3.40 (1.41-8.18)**	2.73 (0.93-8.04)	1.63 (0.87-3.05)	**3.13 (1.25-7.81)**	1.27 (0.58-2.76)
Medium	1.83 (0.94-3.56)	1.91 (0.83-4.39)	1.77 (0.63-4.97)	1.15 (0.60-2.23)	2.38 (0.94-6.03)	0.78 (0.33-1.84)

Reference categories: (i) normotensive and (ii) high educational level (>12y). Values in bold indicate statistically significant hazard ratios (HRs) (p<0.05). Age-adjusted HRs and 95% CIs estimated using Cox regression models. Models run on ENS2003-2010 pooled data were additionally adjusted for survey year.

Cardiovascular mortality

Mortality rates

As shown in Table 7.6 and Table 7.7, 98 and 64 cardiovascular deaths were observed in the ENS2003 and ENS2010 cohorts, respectively. Crude (non-age adjusted) cardiovascular mortality rates were slightly lower in the ENS2003 compared with the ENS2010 cohort. Mortality was slightly higher among males than females in the ENS2003 cohort, but similar in the ENS2010 cohort. Similar patterns to those observed for all-cause mortality were observed with cardiovascular mortality: mortality rates increased with age and were higher among the least versus more educated participants. Mortality rates were higher among those with survey-defined hypertension compared with their non-hypertensive counterparts in both cohorts.

Table 7.6: Cardiovascular mortality rates. ENS2003 cohort.

Variable	n	Deaths	Person-years	Mortality per 1,000 person-years
All	3,411	98	51.0	1.9 (1.5-2.4)
Gender				
Males	1,556	51	25.0	2.0 (1.6-2.7)
Females	1,855	47	26.0	1.8 (1.3-2.7)
Age				
17-44y	1,445	4	33.3	0.1 (0.0-0.7)
45-64y	1,092	24	13.7	1.7 (1.2-2.7)
≥65y	874	71	4.0	18.0 (14.0-23.0)
Educational level				
Low	1,360	62	11.6	5.4 (4.2-7.0)
Medium or high	2,043	35	39.4	0.9 (0.6-1.4)
Survey-defined hypertension				
No hypertension	1,816	15	34.8	0.4 (0.3-0.7)
Hypertension	1,595	84	16.3	5.2 (4.0-6.7)

n: unweighted sample size. Deaths and follow-up time were calculated with normalised sample weights. Cardiovascular mortality based on ICD-10 codes.[246]

Table 7.7: Cardiovascular mortality rates. ENS2010 cohort.

Variable	n	Deaths	Person-years	Mortality per 1,000 person-years
All	4,703	64	40.3	1.6 (1.2-2.3)
Gender				
Males	1,867	32	19.4	1.6 (1.0-2.9)
Females	2,836	32	20.9	1.6 (1.0-2.4)
Age				
17-44y	2,195	2	24.0	0.1 (0.0-0.8)
45-64y	1,598	20	12.1	1.7 (0.9-3.3)
≥65y	910	42	4.2	10.0 (6.8-16.0)
Educational level				
Low	1,265	38	7.2	5.2 (3.4-8.5)
Medium or high	3,422	26	33.0	0.8 (0.5-1.4)
Survey-defined hypertension				
No hypertension	2,943	5	27.9	0.2 (0.1-0.6)
Hypertension	1,760	59	12.3	4.8 (3.4-7.0)

n: unweighted sample size. Deaths and follow-up time were calculated with normalised sample weights. Cardiovascular mortality based on ICD-10 codes.[246]

Kaplan-Meier survival plots and log-rank tests

The contribution of survey-defined hypertension and educational level to cardiovascular mortality was initially assessed using Kaplan-Meier survival curves and log-rank tests. Kaplan-Meier curve analyses by survey-defined hypertension (Figure 7.6) showed different survival curves in the ENS2003 cohort among adults aged 45-64y and ≥65y (log-rank test 45-64y p=0.018; ≥65y p=0.038), showing lower survival probabilities among those with hypertension. Survival curves by hypertension were statistically different in the ENS2010 cohort among adults aged 45-64 (lower survival probabilities among those with hypertension), but showed similar mortality risk among those aged ≥65y (log-rank test: 45-64y p=0.004; ≥65y=0.138).

Figure 7.6: Cardiovascular mortality Kaplan-Meier curve by survey-defined hypertension. ENS2003-2010 cohorts.

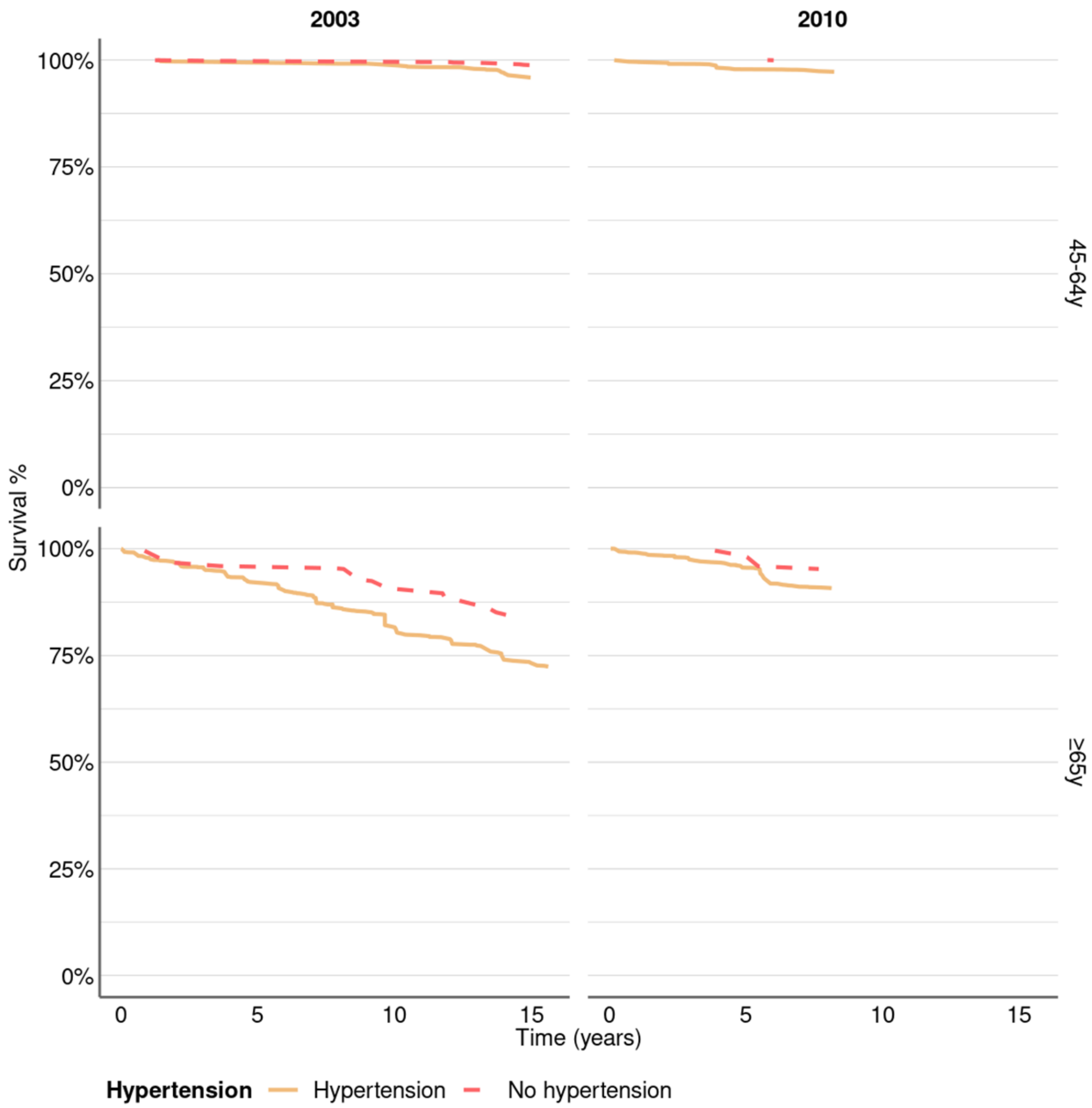
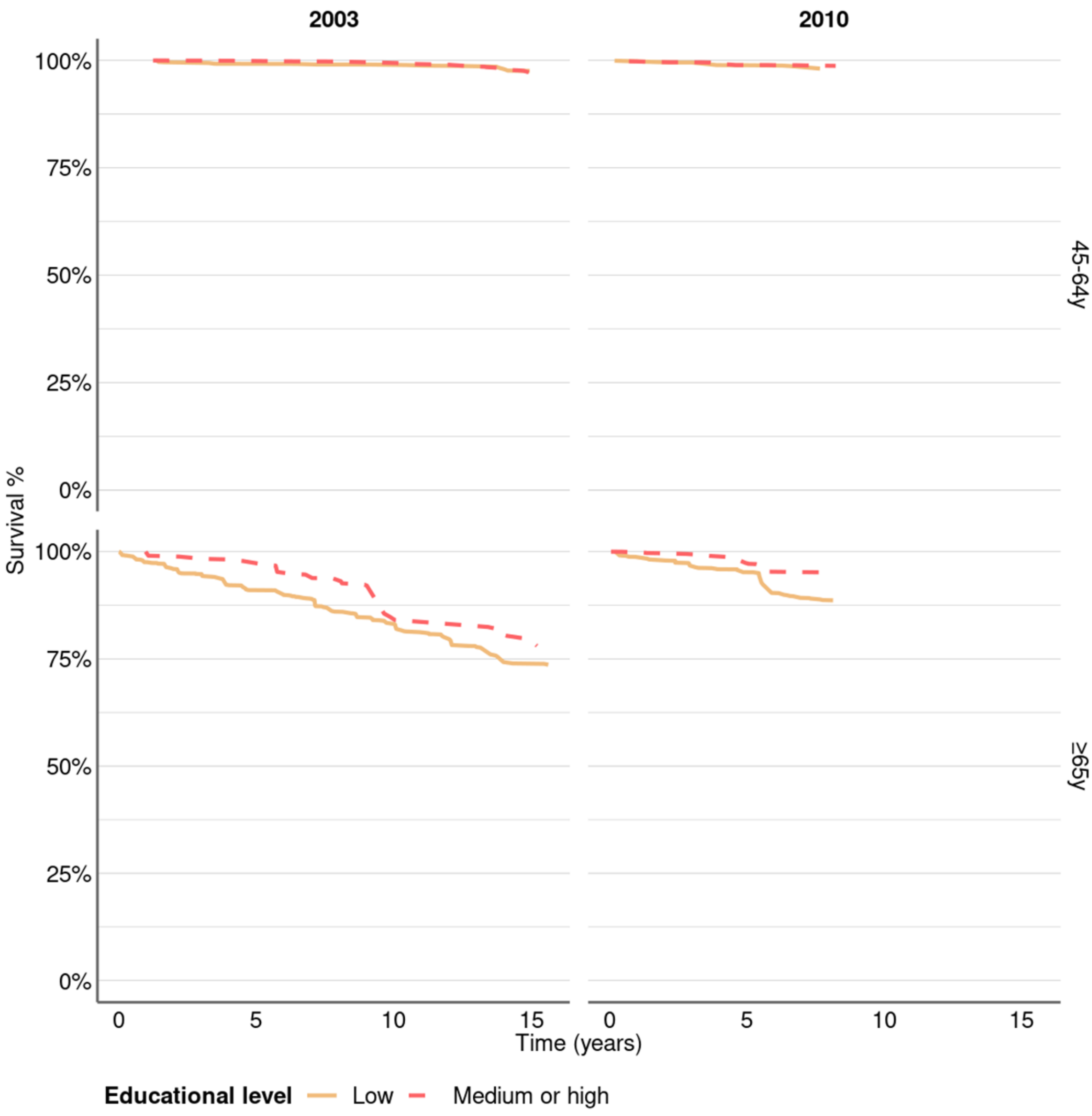


Figure 7.7 shows similar survival curves by educational level in both the 45-64y and ≥65y age groups in the ENS2003 cohort (log-rank test: 45-64y p=0.681, ≥65y=0.314). In the ENS2010 cohort similar curves by education were found among

adults aged 45-64y (log-rank test: 45-64y p=0.625). The difference in survival curves was marginally significant among those aged ≥65y in the ENS2010 cohort, showing lower survival probabilities among adults with lower versus higher educational levels (log-rank test: p=0.059).

Figure 7.7: Cardiovascular mortality Kaplan-Meier curve by educational level. ENS2003-2010 cohorts.

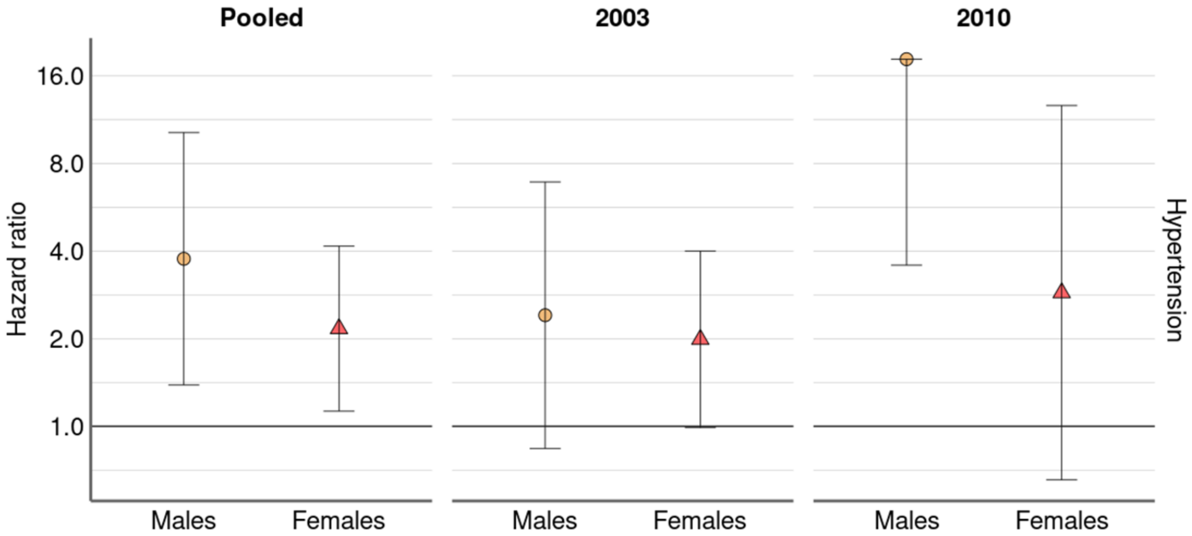


Cox proportional hazards regression models

Evaluation of the PH assumption based on plots of the scaled Schoenfeld residual and statistical test for Cox regression models for cardiovascular mortality are provided in Appendix 7. The residuals related to both main exposures, survey-defined hypertension and educational level, showed no evidence of non-proportional hazards over time (p>0.9 for the majority of models). The one model which did show evidence of non-proportional hazards over time (males in ENS2003 cohort) is discussed later.

Age-adjusted HRs by survey-defined hypertension and by ENS cohort and gender are shown in Figure 7.8. Combining the ENS2003-2010 data across genders, higher cardiovascular mortality risk was observed among participants with survey-defined hypertension (HR: 2.78 (95% CI: 1.58-4.89)). Similar findings were observed in gender-specific analyses. In the ENS2003-2010 pooled data, the age-adjusted HR for survey-defined hypertension was 3.76 (95% CI: 1.39-10.19) among males and 2.16 (95% CI: 1.13-4.15) among females. In cohort specific analyses, the age-adjusted HR for survey-defined hypertension among males in ENS2010 was more than six times higher than among males in the ENS2003 cohort (ENS2003 HR: 2.41, ENS2010 HR: 18.20). However, this finding needs to be interpreted with caution: the estimated HR for the ENS2010 cohort had a wide 95% CI and clearly overlapped with the estimate for the ENS2003 cohort.

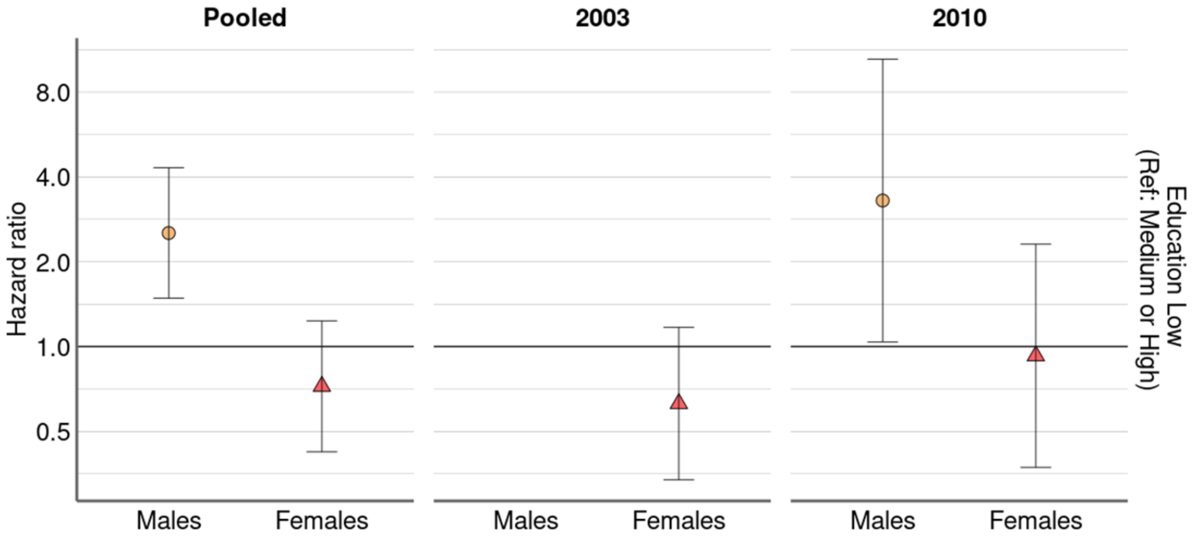
Figure 7.8: Relative hazards of cardiovascular death by survey-defined hypertension. ENS2003-2010 cohorts.



Reference category: no hypertension. Age-adjusted Hazard Ratios (HRs) and 95% CIs from Cox regression models. Models run on ENS2003-2010 pooled data were additionally adjusted for survey year. To simplify the plot, upper 95% CIs were truncated at the maximum value of the coefficients. Original values are presented in the summary table.

Age-adjusted HRs by educational level and by ENS cohort and gender are shown in Figure 7.9. Higher cardiovascular mortality risk was observed among males with lower versus medium or higher levels of education in the ENS2003-2010 pooled data (HR: 2.53 (95% CI: 1.48-4.31)). Educational-based HRs among females did not reach statistical significance (e.g. HR in the ENS2003-2010 pooled data: 0.72 (95% CI: 0.42-1.23)).

Figure 7.9: Relative hazards of cardiovascular death by educational level. ENS2003-2010 cohorts.



Reference category: medium or high educational level (≥8y). Age-adjusted Hazard Ratios (HRs) and 95% CIs from Cox regression models. Models run on ENS2003-2010 pooled data were additionally adjusted for survey year. Model for males in ENS2003 violated PH assumption.

Notably, among females in the ENS2003 cohort, I observed a higher risk of all-cause mortality among those at the lowest education level (HR: 3.13 (95% CI: 1.25-7.81), Figure 7.5). In contrast, the risk of cardiovascular mortality was non-significantly lower (HR: 0.63 (95% CI: 0.34-1.17), Figure 7.9).

Evidence of non-proportional hazards

As the Cox PH model for the ENS2003 cohort estimating educational-based HRs among males showed evidence of non-proportional hazards, I re-ran this analysis on a smaller analytical sample by excluding deaths within the first five years of follow-up (those with <5y of follow-up). Schoenfeld residual plots for this model suggested no systematic departure from the horizontal line (log-rank test: p=0.263). The educational-based HR for those with ≥5y of follow-up was 1.34 (95% CI: 0.66-2.70).

Interaction term between educational and hypertension

As expected, due to the low number of cardiovascular deaths (especially in the ENS2010 cohort), the vast majority of the [education by hypertension] interaction terms did not reach statistical significance. The only exception was observed among males using the ENS2003-2010 pooled data (p for interaction=0.015). Based on this model, the educational-based gap in mortality risk was higher among participants without hypertension. Results from stratified models showed that among participants without hypertension, the estimated HR comparing low versus medium or high educational levels was 4.65 (95% CI: 0.66-32.78). The corresponding HR among participants with hypertension was 2.32 (95% CI: 1.34-4.01).

Summary of findings for cardiovascular mortality

Cardiovascular mortality HRs by hypertension and educational levels are summarised in Table 7.8.

Table 7.8: Relative hazards for cardiovascular mortality by survey-defined hypertension and educational level. ENS2003-2010 cohorts.

	Males			Females		
Exposure	**Pooled**	**2003**	**2010**	**Pooled**	**2003**	**2010**
Hypertension	**3.76 (1.39-10.19)**	2.41 (0.84-6.90)	**18.20 (3.57-92.71)**	**2.16 (1.13-4.15)**	1.99 (0.99-4.00)	2.87 (0.65-12.61)
Low educational level	**2.53 (1.48-4.31)**	1.34 (0.66-2.70)#	**3.30 (1.04-10.47)**	0.72 (0.42-1.23)	0.63 (0.34-1.17)	0.93 (0.37-2.31)

Reference categories: (i) no hypertension and (ii) medium/high educational level (≥8y). Values in bold indicate statistically significant hazard ratios (HRs) (p<0.05). Age-adjusted HRs and 95% CIs estimated using Cox regression models. Models run on ENS2003-2010 pooled data were additionally adjusted for survey year. Cardiovascular mortality based on specific ICD-10 codes (Table 7.1).[246]
#: Original Cox PH model showed evidence of non-proportional hazards; therefore this analysis used a smaller analytical sample by excluding deaths within the first five years of follow-up.

7.5. Discussion

In this brief discussion, I first summarise the main results of the survival analyses by hypertension and educational status using the Chilean ENS-mortality cohort. Secondly, I describe the strengths and limitations of both the data and my analytical approach. In the Discussion of the entire thesis (Chapter 8), I will provide a more detailed comparison with previous epidemiological studies, including the few conducted in LACCs. In Chapter 8, I will also outline the implications of my results for public policies in Chile and discuss possible future analyses.

7.5.1. Main findings

The aim of this fourth empirical chapter was to evaluate gender-specific associations between (i) hypertension status and (ii) individual-level educational status on all-cause and cardiovascular mortality. To the best of my knowledge, this study is the first based on this nationally-representative population-based cohort. In particular, I outlined three testable empirical hypotheses:

- **H7.1**: Hypertension is associated with all-cause and cardiovascular mortality after age adjustment among both males and females.
- **H7.2**: Educational level is associated with all-cause and cardiovascular mortality after age adjustment among both males and females.
- **H7.3**: The association between educational level and mortality is moderated to some extent by hypertension status among both males and females.

Mortality risk by hypertension status

Analysis of the ENS2003-2010 cohorts provided evidence to support the association between hypertension and all-cause mortality risk (**H7.1**) among males. Compared with those in the normotensive category (BP <140/90 mmHg and not on antihypertensive medication) at the time of the ENS nurse interview, higher all-cause mortality risk was observed among males in the ENS2010 cohort with (i) treated and controlled hypertension and (ii) treated and uncontrolled hypertension. My analyses among females did not provide evidence in support of hypothesis H7.1: all-cause mortality risk was not associated with hypertension status among females. My results for cardiovascular mortality support hypothesis H7.1: I observed higher cardiovascular mortality risk among both males and females with rather than without survey-defined hypertension.

Mortality by educational level

Among males, estimated risks of all-cause and cardiovascular mortality were higher among participants at the lowest versus highest educational levels, giving support to hypothesis **H7.2**. Among females in the ENS2003 cohort, I observed a higher risk of all-cause mortality among those at the lowest education level, yet conversely with a lower risk of cardiovascular mortality.

Interaction effect between hypertension status and educational level

In the majority of cases, the gender-specific hypertension by educational interaction terms did not reach statistical significance. The educational-based HRs, therefore, were generally similar across hypertension categories and so hypothesis **H7.3** was not supported in the present study.

7.5.2. Strengths and limitations

Use of the ENS-mortality cohort data provided several strengths to this empirical study. The linkage between ENS and mortality registry data created a nationally-representative cohort that included several high-quality baseline measurements (e.g. standardised BP measurement and a detailed medication inventory). There was also a reasonably long period of follow-up of over 15 years on average for the ENS2003 cohort and over nine years for the ENS2010 cohort. By using high-quality data sets, ENS and mortality data (including the main cause of death and the exact date of death), I could provide in the present study nationally-representative estimates of the associations of hypertension and educational status (as recorded at the time of the ENS interview and health examination) with all-cause and cardiovascular mortality. The fact that linkage was done using a unique national identity number by DEIS-MINSAL gave reliable and up-to-date information on the mortality status for the vast majority of ENS participants.

Since 2019, the COVID-19 pandemic has resulted in over 33,500 deaths, and has changed mortality patterns in Chile. For example, the number of cardiovascular deaths among men in 2020 was lower than expected, a shortfall that was possibly associated with competitive risks for COVID-19 infection.[251] However, the analyses of mortality presented in this chapter were not affected by COVID-19 as the study end date (last date of ascertaining mortality status by DEIS) preceded the COVID-19 pandemic.

There were a number of limitations to this present study that should be borne in mind when interpreting the results. First, the cross-sectional design of the ENS meant that information on both hypertension and educational status were collected only at the ENS interview/nurse visit. Baseline measurements are not able to entirely represent the hypertension status or the educational level of ENS participants over their lifetime. It is likely that during the follow-up period, those ENS participants with untreated or uncontrolled hypertension may have received antihypertensive medication and had their BP successfully controlled. After the health examination, ENS participants are sent a letter with their BP results and are recommended to share them with their physician. Moreover, an unknown number of ENS participants who were observed to be using antihypertensive treatment at the time of the survey may have stopped their treatment at some point during follow-up. Evidence suggests that adherence to treatment for chronic conditions such as hypertension drops dramatically over time.[252] Additionally, mean levels of SBP rise with age (although BP levels at the population level are decreasing over time). The overall impact of any unobserved change in hypertension status on the associations with mortality shown in the present study is unknown and cannot be estimated using ENS data.

Thirdly, analyses comparing Kaplan-Meier curves across the hypertension status and educational groups were probably confounded by differences in age even after stratifying by (broadly defined) age groups. Within each age stratum, age was distributed differently according to educational levels and hypertension status (higher median age at lower than higher educational levels and among those with hypertension compared with those without hypertension, results not shown). In addition, these analyses used combined data for males and females, which masked differences in mortality rates by gender. Although potential effects of residual confounding cannot be ruled out, the use of gender-specific and age-adjusted Cox regression models reduced to some extent any bias in the associations between hypertension status, educational level, and mortality risk.

Fourthly, some analyses were likely underpowered, especially those analyses for cardiovascular mortality and those estimating educational-based hazard ratios within each category of hypertension status to examine possible interaction. An increased type II error (i.e. lack of statistical power to detect true differences in mortality rates) in these analyses cannot be ruled out. Particularly, the difference in cardiovascular mortality risk by hypertension status among males comparing ENS2003 with ENS2010 is likely explained by a low statistical power in ENS2010. Because of this limitation, I combined categories of hypertension and education for the specific analyses of cardiovascular mortality in order to increase sample sizes and potentially decrease the type II error. Nevertheless, the merging of categories may mask important differences in risk between the groups.

Fifthly, although my models adjusted for age and were stratified by gender, I cannot rule out potential residual confounding by (i) imperfect measurement of confounders (e.g. age was based on self-reported date of birth, thus susceptible to recall or information bias) or by (ii) additional confounders not included in the analysis (e.g. severity of hypertension and ethnicity). Residual confounding is a common limitation in all observational studies. In addition, I evaluated whether the association between educational level and mortality risk was moderated to some extent by hypertension status (using interaction terms). However, other analytical approaches were also possible. For example, studies exploring the association between educational level and mortality could consider hypertension status as a mediator. Other analytical approaches could further adjust for, or consider a different set of, potential mediators including biological factors or health behaviours However, the set of analyses presented in this chapter were mainly descriptive and did not attempt to establish causal associations.

Finally, my analyses of cardiovascular mortality could have been affected by a few cases with *ill-defined* or *pending* causes of death (causes that did not provide helpful information to classify them as cardiovascular deaths or not). These cases (excluded from my analyses) decreased the number of events and, consequently, the power of the analyses. However, I estimated this bias to be infrequent in analyses of the ENS2003 cohort analyses as only 17 of the 701 deaths (2.4%) had ill-defined ICD-10 codes. This bias was slightly more frequent in the ENS2010 cohort: although only seven of the 452 deaths (1.5%) had ill-defined ICD-10 codes and 38 (8.4%) had pending causes of death.

7.6 Conclusion

This is the first nationally-representative population-based longitudinal study in Chile, providing powerful evidence about the associations between hypertension and education on the risk of all-cause and cardiovascular mortality. The linkage between ENS and mortality databases increased the value of both ENS and mortality datasets, providing an important prospective health outcome to the ENS data, and changing its original cross-sectional design into a prospective one with huge potential for further epidemiological insights into the distribution of mortality across population subgroups.

Chapter 8: Discussion

8.1. Introduction

In the introduction to my thesis, I presented background information on hypertension as a chronic disease condition, indicators of hypertension management, and socioeconomic inequalities in hypertension worldwide and in Chile (Chapter 1). In Chapter 2, I presented a systematic review of what is currently known about SEP inequalities in hypertension management in LACCs. Based on the first two chapters, I defined the framework that informed the four empirical chapters (Chapter 3). The four analytical aims of my thesis were as follows:

- To quantify gender-specific secular changes in hypertension prevalence and in diagnosed, treated, and controlled hypertension; to quantify the impact of lowering BP thresholds on these hypertension outcomes; and to estimate levels of controlled hypertension using a disease-specific BP goal (Chapter 4).
- To examine the gender-specific magnitude of SEP inequalities in hypertension prevalence and in undiagnosed, untreated, and uncontrolled hypertension, and their change over time in Chilean adults since 2003, using individual-level measures of SEP (Chapter 5).
- To contextualise gender-specific individual-level educational inequalities in hypertension and in hypertension management indicators in Chilean adults in 2003, 2010, and 2017 by considering the role of socioeconomic environment measures using a multilevel analytical approach (Chapter 6).
- To evaluate gender-specific associations between (i) hypertension status and (ii) individual-level educational status on all-cause and cardiovascular mortality (Chapter 7).

In each empirical chapter, I described the main strengths and limitations of the work presented. To complement those sections, here I compare my results with evidence from LACCs; provide explanations for my main findings and discuss potential policy implications.

8.2. Key findings

8.2.1. Hypertension prevalence and management

Hypertension prevalence: I used nationally-representative valid BP and medication data from 13,605 adults (aged ≥17y) who participated in ENS 2003, 2010, and 2017. My analyses showed a decrease from 2003 to 2017 in levels of survey-defined hypertension (BP <140/90 mmHg or use of antihypertensive medication) from 37% to 31% for males, and from 31% to 30% for females (Table 4.2). After age-and survey year-adjustment in the 2003-2010-2017 pooled data, my analyses showed significantly lower odds of hypertension among females than males (Section 4.4.3).

Hypertension management: Levels of hypertension awareness, treatment, and control improved substantially among males between 2003 and 2017 (awareness: from 46% to 58%; treatment: from 24% to 57%; control: from 6% to 28%, all as a percentage of those with survey-defined hypertension, Table 4.2). Among females, levels of awareness remained stable, while treatment and control levels increased between 2003 and 2017 (awareness: 73% and 74%; treatment: from 55% to 74%; control: from 20% to 40%). After adjustment for age and survey year in the 2003-2010-2017 pooled data, levels of attainment of each hypertension management indicator were higher among females than males (Section 4.4.3).

JNC 7 vs 2017 ACC/AHA guidelines: The 2017 ACC/AHA guidelines lowered the raised (clinic-based) BP threshold to define hypertension from 140/90 mmHg to 130/80 mmHg, with the aim of identifying patients at early stages of cardiovascular disease and so reduce cardiovascular morbidity and mortality.[36] Based on my analyses, hypertension prevalence in 2017 would be about 17 pp higher in absolute terms if the BP threshold were lowered from <140/90 mmHg to <130/80 mmHg (Figure 4.5; 2017 ACC/AHA: 48%; JNC 7: 31%). This higher prevalence is due to the inclusion of adults not on treatment but with levels of SBP 130 mmHg to 139 mmHg or with DBP levels 80 mmHg to 89 mmHg.

BP target goal: A number of guidelines for hypertension, including the JNC 7, 2017 ACC/AHA, and GES-hypertension guidelines in Chile, recommend a more aggressive BP goal (BP <130/80 mmHg instead of BP <140/90 mmHg) for patients with hypertension and comorbid conditions (the GES-hypertension guidelines, for example, identify prior infarction or stroke, diabetes mellitus, or chronic kidney disease as comorbidities).[36, 37, 54] Applying a more stringent definition lowers levels of controlled hypertension. Based on my analyses of ENS2017 data, among all persons with hypertension, levels of controlled hypertension using a disease-specific (BP <130/80 mmHg for those with very high CVD risk (prior infarction/stroke), DM or CKD, BP <140/90 mmHg otherwise) vs a general BP goal (BP <140/90 mmHg) were 5 pp (23% vs 28%) and 7 pp (32% vs 39%) lower in absolute terms among all male and female participants, respectively (Figure 4.6).

The lower level of controlled hypertension is due to the more aggressive 130/80 mmHg BP target for those with very high CVD risk, DM, or CKD. Among this high-risk subset, levels of controlled hypertension using the disease-specific vs general BP goal were 17 pp lower among both genders (males: 19% vs 36%; females: 27% vs 44%).

8.2.2. Educational-based inequalities in the prevalence and management of hypertension

My discussion here will focus on individual educational level as the main SEP indicator of interest. Without underestimating the importance of other SEP measures such as income, and health insurance status, educational level captures and gives the structure to the most relevant aspects of many SEP indicators: it shapes the opportunities for employment, working conditions, income, wealth, and health insurance. Although it is generally completed in young adulthood, it can also reflect socioeconomic circumstances such as the family and home environment in early life.[87]

Educational-based inequalities in hypertension prevalence: I observed higher levels of hypertension among adults with lower vs higher levels of education (Table 5.3). A number of findings, however, were gender-specific: educational-based inequalities in hypertension were observed among females, but not among males. In 2017, the age-standardised prevalence of survey-defined hypertension was 33% and 30% among males in the low and high educational groups, respectively. The corresponding estimates among females were 39% and 20%. Educational-based inequalities in hypertension were stable over time among females (Figure 5.5). Among males, educational-based inequalities in hypertension showed a transitory increase between 2003 and 2010 but were stable between 2010 and 2017.

Educational-based inequalities in hypertension management: Inequalities observed in hypertension are magnified to some extent by inequalities in hypertension management indicators. For example, females in lower educational groups showed higher levels of hypertension, as well as higher levels of untreated and uncontrolled hypertension (Table 5.6). Among females in 2017, age-standardised levels of untreated hypertension were 31% and 18% for those in the low and high educational groups; the respective figures for uncontrolled hypertension were 72% and 43%. Among males in 2017, age-standardised levels of undiagnosed hypertension were 55% and 34% for those in the low and high educational groups, respectively.

With regards to secular changes in inequalities over time, I found emerging educational-based inequalities in 2017 among females (Table 5.6) in untreated- (RII: 2.50, 95% CI: 1.36-4.62) and in uncontrolled-hypertension (RII: 1.89, 95% CI: 1.27-2.83). Over the 15-year period, the educational gap of each hypertension management indicator increased over time more for females than for males, reflecting the sharper decrease over time in the levels of undiagnosed, untreated, and uncontrolled hypertension among females at the highest educational level.

Educational-based inequalities in levels of controlled hypertension (BP target goals): Education-based inequalities in levels of controlled hypertension were more pronounced among participants with than without high-risk comorbidities (higher among those with higher than lower educational levels). The absolute difference in levels of controlled hypertension using the aforementioned disease-specific vs general BP goal was larger in the highest vs lowest educational group (Figure 5.14). In the subset of males at high risk, the gap in levels of controlled hypertension was 14% at the lowest educational level (12% disease-specific vs 26% general) and 22% at the highest level (35% disease-specific vs 57% general). Among females at high risk at the lowest educational level, the gap in levels of controlled hypertension was 14% (17% disease-specific vs 31% general); the corresponding gap at the highest educational level was 42% (37% disease-specific vs 79% general).

8.2.3. Multilevel analyses of individual-level educational inequalities in hypertension

Multilevel analytical approaches allow for estimation of individual-level inequalities in adult health outcomes after adjustment for measures of the socioeconomic environment, potentially highlighting the robustness of associations. In multilevel modelling, the intra-cluster correlation coefficient (ICC) represents the percentage of total variance in an outcome that is explained at the higher level (in this case, at the county level). Higher values of the ICC indicate higher variability in outcomes between areas.

County-level variance: In my analyses, the contribution of counties (second-level variable) to the estimated variance of hypertension outcomes (first-level variables) showed that the binary outcome of hypertension was the only hypertension outcome partially explained at the county level. Based on the estimates of the ICC, roughly 4-8% of the variance in hypertension was attributed to the variation between counties (Section 6.4.3). The ICC estimates in the models for the three hypertension management indicators were very low (0% in most models), indicating an absence of a clustering effect at the county level in undiagnosed, untreated, and uncontrolled hypertension.

Cross-level interaction: The inclusion of cross-level interaction terms allows investigation of whether the magnitude of associations between individual-level exposures and health outcomes change in strength or direction according to characteristics of the area (e.g. measures of the socioeconomic environment, such as the county levels of income inequality (Gini coefficient), poverty, and unemployment as used in my study). In my analyses, I found weak evidence of cross-level interaction effects (Table 6.3) suggesting that any individual-level educational inequalities in hypertension did not change by levels of socioeconomic environment measures.

Educational-based inequalities: Adjustment of county-levels of income inequality, poverty, or unemployment in multilevel regression models did not change the magnitude or direction of the individual-level educational-based inequalities in hypertension (Figure 6.10), using either relative or absolute complex measures of inequality.

Socioeconomic environment measures: Based on multilevel analyses, adjustment for individual-level educational status had a minor effect on the magnitude of the associations between measures of the socioeconomic environment and hypertension (Figure 6.11).

A one-unit increase in county levels of income inequality (%) was associated with a significant increase in the prevalence ratio of hypertension before and after adjustment for individual educational level among males in 2017. Similar findings using poverty as the measure of socioeconomic environment were observed among males in 2010 and among females in 2003 and in 2010. Using unemployment, I observed similar findings among females in 2003 and in 2010.

8.2.4. Differences in all-cause and cardiovascular mortality rates by hypertension status and by educational level

ENS survey data (2003 and 2010) was linked to national mortality data to enable follow-up over a 15-year period. No research has been published to date using these data. Using Cox regression modelling, I evaluated associations between (i) hypertension status and (ii) individual-level educational status, on the outcomes of all-cause and cardiovascular mortality.

All-cause mortality: Mortality rates were 7.4 and 7.0 per 1,000 person-years in the 2003 and 2010 cohorts, respectively (Tables 7.3-7.4). Compared with normotensive participants (BP <140/90 mmHg and not on antihypertensive medication), age-adjusted Cox models showed a higher risk of death among males in the 2010 cohort with hypertension (Table 7.5, HR treated and controlled hypertension: 3.3, 95% CI: 1.2-8.8; HR treated but uncontrolled hypertension: 2.1, 95% CI: 1.0-4.6; and HR untreated hypertension: 1.9, 95% CI: 0.9-4.1). Mortality risk showed no variation by hypertension status among females.

Overall, the all-cause mortality rate was higher among participants at the lowest vs highest educational levels in the 2003 cohort (HR males: 3.4, 95% CI: 1.4-8.2; HR females: 3.1, 95% CI: 1.3-7.8). The corresponding figures almost attained significance in the 2010 cohort among males (HR: 2.7, 95% CI: 0.9-8.0) but not among females.

Cardiovascular mortality: Cardiovascular mortality rates were 1.9 and 1.6 per 1,000 person-years in the 2003 and 2010 cohorts, respectively (Tables 7.6-7.7). The age-adjusted Cox models showed a higher risk among males with vs without survey-defined hypertension in analyses pooled over the two cohorts (Table 7.8, HR males: 3.8, 95% CI:1.4-10.2; HR females: 2.2; 95% CI: 1.1-4.2).

Using the pooled 2003-2010 data, the risk of death from cardiovascular disease was significantly higher among males in the lowest (vs medium or highest) educational level (HR: 2.5, 95% CI: 1.5-4.3). A similar finding was observed among males in the 2010 cohort (HR: 3.3, 95% CI: 1.0-10.5).

Notably, among females in the 2003 cohort, I found a higher risk of all-cause mortality among those at the lowest education level. In contrast, the risk of cardiovascular mortality was lower.

8.3. Comparisons with previous studies and explanations of my findings

8.3.1. Hypertension prevalence and management

Hypertension prevalence: According to my results, levels of hypertension in Chile are similar to those recently described for LMICs[110] and for HICs[253] based on cross-sectional nationally-representative health examination surveys. According to Geldsetzer et al. (2019), based on pooled individual-level population-based data from 44 LMICs, the prevalence of hypertension was about 30% for most LACCs (although it ranged from 10% in Ecuador to 42% in Grenada).[110] Zhou et al. (2021) recently reported global levels of hypertension, attainment of its management indicators, and secular changes, in people aged 30-79y included in population representative studies from 1990 to 2019 with BP measurement and treatment data.[254] In that study, the Chilean population in 2017 showed a slightly higher (age-standardised) prevalence of hypertension (males: 40%; females: 34%) than the worldwide mean prevalence (males: 35%; females: 32%) but showed similar or slightly lower levels compared with LACCs (males: 40%; females: 37%).[254]

In recent decades, the prevalence of hypertension worldwide has remained stable, reflecting a decrease in prevalence in HICs (including Chile) and an increase in LMICs (and in most LACCs).[33] The decrease in (survey-defined hypertension) prevalence could result from a decrease in BP levels and/or a decrease in treatment levels. As levels of treatment among those with hypertension have increased over time, the decrease in hypertension prevalence presented in my study is explained more by the decrease in mean BP levels at the population level (over the 15-year period, mean SBP decreased by 4.4 and 5.8 mmHg among males and females, respectively: Section 4.4.5). The decline in hypertension prevalence in Chile was potentially driven by the population-level decrease in a number of risk factors which buffered the expected increase in high levels of BP due to rises in levels of obesity and diabetes. For instance, levels of salt intake,[255] and tobacco consumption have all decreased over time in the Chilean population.[24, 256] Since 2011, average levels of salt in bread have gradually reduced and *stop signs* were introduced in

2012 on packaged foods high in energy, sodium, sugars, and/or saturated fats, which contributed to a healthier food industry reformulation in Chile.[70, 257]

Despite the decrease in the prevalence of hypertension over time, the number of patients using the cardiovascular programme in the public system (which combines hypertensive and diabetics patients) since 2003 and the total number of patients with hypertension using the GES-hypertension programme benefits (in the public and private health system) since 2005 has increased steadily.[258] This increase in the burden of patients with hypertension is partially explained by population ageing, but also by the increase in levels of diagnosis and treatment.[111]

Hypertension management: Despite the favourable improvements in levels of the hypertension management indicators over time, current levels remain suboptimal. My analyses show that in 2017 (i) only two-thirds of participants with hypertension were diagnosed; (ii) only two-thirds were treated; and (iii) only one-third had controlled blood pressure (Table 4.2).

The levels of diagnosed, treated, and controlled hypertension presented in Chapter 4 are consistent with the crude estimates for Chile reported by Zhou et al. (2021).[254] Whilst suboptimal, the age-standardised estimates reported by Zhou et al. (2021) showed that current levels of attainment of each hypertension management indicator were higher in Chile compared with the estimates worldwide and for LACCs.[254]

Several explanations have been presented for the global improvement in levels of hypertension awareness, treatment, and control, including increases in BP screening at the primary care and community levels, securing better treatment availability, reducing treatment costs, improving treatment adherence, and preventing clinical inertia.[259] As discussed in Chapter 1, the GES was launched in Chile in 2005 with a wide marketing strategy and helped to disseminate evidence-based guidelines with simplified recommendations nationwide. In 2014, the law was enforced with an additional regulation (FOFAR initiative), which, for the publicly insured, warranted medicines free-of-charge for hypertension, diabetes, and dyslipidaemia. Although I could not directly assess the impact of these programmes with the ENS data, it is likely that they had at least some positive impact through the improvements in treatment and control levels presented in my study.

Although levels of hypertension awareness, treatment, and control have increased in HICs over the last two decades, recent evidence from the United States, based on NHANES data, showed a decrease in levels of controlled hypertension between 2015 and 2018.[260] The authors of that study also reported decreasing levels of awareness, treatment, and control among those treated; and they suggest that these unfavourable changes were related to a worsening quality of care in the diagnosis and management of hypertension.[260] This unfavourable trend in the United States reinforces the need to strengthen efforts to continue improving levels of BP control in Chile and worldwide.

Gender differences in hypertension management: Compared with the levels achieved by HICs, levels of diagnosed, treated, and controlled hypertension in Chile were higher among females but lower among males.[254] Potentially, these gender differences arise from unequal levels of healthcare services utilisation: females have more frequent contact with primary care settings than males.[261] This would lead to a higher frequency of BP measurement, increasing the possibilities of being diagnosed and treated for hypertension. A focus of primary health-care services on maternal and child health, gender norms concerning care-seeking, and health-care facility opening hours were identified by Geldsetzer et al. (2019) as possible reasons for males having lower levels of hypertension management indicators than females.[110] In addition, the lower blood pressure levels among women versus men and inherent biological differences might also contribute to higher control rates.[262]

A gender disparity in levels of hypertension management, with better care levels among females than males, has been systematically reported among HICs, LACCs and LMICs,[34, 110, 253, 263] however, the observed gender gap was wider in Chile than in other HICs.[34, 253] For example, current levels of controlled hypertension were 43% and 26% higher in relative terms among females than males in Chile and in HICs, respectively.[34] Several reasons can be suggested to explain the larger gender gap in hypertension management observed in Chile compared to other HICs.

It may be the case that other HICs may have implemented BP screening programmes with higher coverage among males, have better working conditions that facilitate GP visits during working hours, and have fewer barriers related to gender norms in care-seeking. Longer opening hours of primary care facilities can increase access to healthcare resources and potentially reduce gender gaps in hypertension management. Compared to other HICs, Chile has shorter opening hours (e.g. Chile: Monday-Friday, 8am-5pm; England and Canada: Monday-Friday, 8am-6.30pm; Germany: Monday-Friday, 8am-6pm).

Although differences by gender exist, I observed a greater improvement over time in the attainment of the hypertension management indicators among males than females, albeit from a lower base. My analyses showed that the Chilean health objective 2010-2020 of increasing the level of controlled hypertension by 50% in relative terms[264] has been achieved among males, but is only at the halfway point among females, since the relative increases in controlled hypertension from 2010 to 2017 were 100% and 25% for males and females, respectively. The steeper (relative) increase in levels of controlled hypertension among males should be viewed alongside the lower levels of BP control observed for males vs females in each ENS survey.

JNC 7 vs 2017 ACC/AHA guidelines: As mentioned above, the 2017 ACC/AHA guidelines recommended lowering the BP (clinic-based) threshold to define hypertension from 140/90 mmHg to 130/80 mmHg, in order to identify patients at early stages of cardiovascular disease and so reduce cardiovascular morbidity and mortality through improved levels of treatment and control.[36] The recommendation to lower BP thresholds was prompted by the findings of SPRINT (Systolic Blood Pressure Intervention Trial) which found significant reductions in the primary composite outcome (myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes) and in overall mortality among adults in the intensive treatment group (BP target < 120 mmHg) versus those in the standard treatment group (BP target < 140 mmHg). The SPRINT trial was halted six months early as the data showed that more intensive vs less intensive treatment showed clear benefits in reducing cardiovascular events, overall mortality risk, and cognitive impairment.[36] However, there is a growing debate about the merits of reducing the BP threshold according to the 2017 ACC/AHA guideline, including concerns about the expected implementation costs.[265, 266] The lower BP thresholds suggested by the 2017 ACC/AHA guideline were not implemented in the hypertension guidelines in Chile that were updated in 2018, nor by the UK or EU guidelines.[75, 267, 268] Nevertheless, these guidelines (or new ones with lower BP thresholds) are likely to be discussed, and potentially implemented, in future Chilean guidelines.

BP target goal: As mentioned above, a number of guidelines for hypertension, including the JNC 7, 2017 ACC/AHA, and GES-hypertension guidelines in Chile, recommend a more aggressive BP goal (BP <130/80 mmHg instead of BP <140/90 mmHg) for patients with hypertension and comorbid conditions.[36, 37, 54] Several studies have shown benefits of using a more stringent BP target goal among adults with hypertension and high-risk comorbidities, including a decrease in CVD events, MI, and stroke.[269] In my analyses of ENS2017, among participants with hypertension and at least one comorbid condition (stroke/infarction, DM, CKD), levels of controlled hypertension were 17 pp lower using the disease-specific vs general BP goal. Similar changes in BP control levels were reported in analyses of NHANES 1999-2006: among participants with hypertension and CKD, the proportion with controlled BP was 32% using the disease-specific definition and 48% using the general definition: highlighting the large proportion of uncontrolled BP amongst this high-risk group, especially using the more stringent BP control goal.[189]

8.3.2. Educational-based inequalities in the prevalence and management of hypertension

Educational-based inequalities in hypertension prevalence: My main findings of higher levels of hypertension among adults with lower vs higher levels of education are consistent with previous studies. Educational inequalities in hypertension are well known among HICs and are now being found in LMICs including LACCs.[40, 87, 99, 113, 270–272] Worldwide, according to a meta-analysis of socioeconomic inequalities in hypertension, the odds of hypertension among those at the lowest educational level were twice those at the highest educational level.[87] Guerrero-Ahumada (2017), using ENS2003 and ENS2010, previously showed educational-related inequalities in hypertension, with increased odds among adults with a lower level of education.[65]

Daily life conditions, such as the SEP indicators I evaluated in my research, can act as social determinants of inequalities in hypertension through the unequal exposure to risks and protective factors related to each social position.[3] Multiple interrelated routes of embodiment of these social determinants into adult health outcomes such as hypertension have been supported by the empirical literature. These include social gradients in (i) health knowledge, literacy and health behaviours, (ii) work conditions, health care and income, and (iii) psychosocial resources.[87, 162, 242, 273–275]

First, several studies have examined SEP inequalities in the major risk factors of hypertension worldwide and in Chile, showing a higher prevalence of unhealthy lifestyle behaviours (e.g. physical inactivity, obesity, high salt intake) among those in the lowest SEP groups.[83, 84, 84–86, 271, 276]

Secondly, stress and unfavourable working conditions are higher among lower SEP groups and these could explain at least part of the social gradient in hypertension.[277, 278]

Thirdly, SEP inequalities in health care disadvantage lower SEP groups with limited access to healthcare resources than those in higher SEP groups.[279] Mills et al. (2016) identified barriers at the levels of the healthcare system, healthcare provider, and patient that may contribute to disparities in hypertension and BP control: these include lack of access to care, costly medications, overburdened healthcare providers, lack of treatment guideline adherence and low patient health literacy.[34] Recent evidence from Chile showed SEP inequalities in health care use, suggesting greater use of preventive medicine at the primary stage among those with higher resources.[201, 280]

Fourthly, socio-psychological resources, including social capital, locus of control and social support, are associated with indicators of SEP and are also identified as protective factors for hypertension.[87] Using Chilean data, Riumallo-Herl, Kawachi, and Avendano (2014) showed that lower levels of functional social capital (measured as social support and trust) were associated with higher hypertension prevalence.[281] Likewise, in my Master's thesis, I showed an inverse association between social trust and BP control among those with treated hypertension.[124]

Educational-based inequalities in hypertension by gender: Consistently, research from LACCs and worldwide has shown gender-based differences in levels of SEP inequalities in hypertension and its management indicators.[40, 65, 87, 99] For instance, Leng et al. (2015) reported in their meta-analysis that SEP inequalities in hypertension were more prominent among females, although inequalities were less consistent among males.[87] Several explanations can help to understand gender differences in SEP inequalities in hypertension: (i) those with higher SEP have fewer barriers to accessing medical care; (ii) females have more frequent contact with health care services than males; (iii) females are more affected by SEP inequalities than males regarding health care services; and (iv) social gradients in healthy lifestyles (e.g. obesity, insufficient physical activity, and alcohol use) are steeper among females than males.[84, 87, 91, 164, 282] This could be related to the idea that females in higher SEP groups have more access to health information and are more likely to adhere to healthy lifestyles than males in all SEP groups.[87]

Educational-based inequalities in indicators of hypertension management: Because hypertension is often asymptomatic, higher levels of knowledge about health conditions, health-related behaviours and more social and psychosocial resources (associated with higher levels of education) are particularly relevant for the diagnosis, treatment, and control of hypertension.[159] Despite the positive improvements in higher levels of educational attainment and the decrease in hypertension prevalence between 2003 and 2017 in Chile, the benefits did not substantially change the magnitude of inequalities in hypertension outcomes over the 15-year period of this study. One of the main findings of my study was the emerging educational-based inequalities in 2017 among females in untreated and in uncontrolled hypertension, reflecting faster rates of improvement among the most educated females. To some extent, this evidence supports the *inverse equity* *hypothesis*, which suggests that newly introduced health interventions will bring more benefits to the socially privileged population and that the magnitude of socioeconomic inequalities in health and in healthcare will only fall once the needs of the most advantageous are met.[279, 283]

However, these emerging SEP inequalities in hypertension management occurred simultaneously with favourable changes in other health and healthcare indicators in Chile. As reported by Frenz et al. (2014), the odds of *unmet health need* (lack of a health care visit for a health problem occurring in the last 30 days) were higher among adults with lower vs higher SEP in 2000, fortunately this association approached the null in 2009.[284] Núñez et al.'s (2020) findings were less optimistic: SEP inequalities in dental visits, laboratory exams, speciality visits, hospitalizations (concentrated on the richest households), emergency services and preventive medicine (highly concentrated among poor individuals) did not change during the time analysed (1990-2015).[285]

Educational-based inequalities in levels of controlled hypertension (BP target goals): Among those with hypertension, the gap in the level of controlled hypertension comparing the disease-specific and general BP targets was wider among those in the highest educational group. This finding suggests that a higher proportion of the most educated have SBP values between 130 mmHg and 140 mmHg or DBP values between 80 mmHg and 90 mmHg, and so are sensitive to the more stringent target. Put another way, a higher proportion of the least educated have SBP values ≥140 mmHg and DBP values ≥90 mmHg, and so are less sensitive to the more stringent target. This is consistent with the SEP gradient in BP levels distribution reported elsewhere.[286] The suboptimal levels of controlled hypertension I observed among participants with high-risk comorbidities at lower educational levels may justify concern and further research.

8.3.3. Multilevel analyses of individual-level SEP inequalities in hypertension

County-level variance: Only a few studies using comparable methods have reported levels of the ICC in multilevel analyses of hypertension. In these studies, the estimates of the ICC (2-7%) were similar to those presented in my study (4-

8%).[218, 236, 237] It is worth noting that even relatively low ICC values, and weak associations between contextual factors and hypertension, could still reflect a relatively large impact of area-level characteristics on the risk of hypertension at the population level.[218, 237, 287] Although Chile is characterised by its socioeconomic-geographic segregation, my results showed that this segregation at the county-level is more relevant in explaining variability in hypertension than in explaining variability in the hypertension management outcomes.

As described by Diez-Roux and Mair (2010), geographical clustering of individual-level SEP and SEP inequalities in health outcomes are closely related characteristics of *physical* (e.g. food and recreational resources) and *social environments* (e.g. safety, social capital).[7] Both physical and social environments can independently influence health outcomes such as hypertension through shaping health behaviours and inducing stress. As described in Chapter 5, individual-level SEP and measures of the socioeconomic environment (e.g. income inequality) can be associated in different ways with the risk of hypertension, including *cross-level interactions, mediation and confounding* effects.[7]

Cross-level interaction: Literature on cross-level interactions between individual-level SEP and socioeconomic environmental measures in multilevel analyses of hypertension using health survey examination data is scarce. However, similar to my findings, several empirical studies of cardiovascular-related outcomes have not detected cross-level interactions between individual-level SEP and socioeconomic environmental measures.[236, 288–290] These findings suggest that the magnitude of individual educational-based inequalities are similar across levels of the socioeconomic environment.

Educational-based inequalities: Only a few multilevel modelling studies have evaluated change in the magnitude of individual-level SEP inequalities in hypertension outcomes before and after adjustment for measures of the socioeconomic environment.[106, 291, 292] Mixed results have been reported. Some studies observed minor changes (suggesting weak if any area-level confounding),[291, 292] whereas others observed a decrease in the magnitude of individual-level SEP inequalities.[106] Interpretation of research findings depends on how the individual- and area-level variables are incorporated into the conceptual model.[293] As discussed in the Introduction to Chapter 6, I interpret the minor change in the magnitude of individual-level SEP inequalities after adjustment for socioeconomic environmental measures as suggesting minimal confounding effect.

Socioeconomic environment measures: Multilevel modelling studies have analysed the influence of a variety of area-level exposures on levels of BP or the risk of hypertension.[105, 106, 218, 224, 236, 281, 291, 294] In the LACCs context, Lucumi et al. (2017) used data from the Colombian national health survey 2007 to analyse inequalities in hypertension prevalence by area-levels of income inequality (Gini coefficient).[218] Odds of hypertension were found to be higher among those living in areas with higher levels of income inequality: these remained statistically significant even after adjusting for individual-level indicators of education, wealth, and for other area-level exposures, such as poverty and economic development.[218] According to Lynch et al. (2004), three pathways can help to explain the association between contextual levels of income inequality and the risk of hypertension. These pathways were: (i) individual income (individual-level income explains the association between income inequality and health), (ii) psychosocial (health behaviours and stress), and (ii) neomaterial (physical resources).[295] Income inequality by itself is a stressful factor and decreases social capital,[296] increasing the risk of hypertension and acting as a barrier to access healthy resources (e.g. healthy food, green spaces). As mentioned in Chapter 1, despite the decrease over time, unfortunately, levels of income inequality in Chile continue to be one of the highest in the world.

8.3.4. Differences in mortality rates by hypertension outcomes and by socioeconomic position

All-cause mortality: Higher risk of all-cause mortality among people with hypertension than those without has been reported systematically in the last few decades.[179, 181, 297] Similar findings to those presented in my study were reported by Zhou et al. (2018) using NHANES III (1988-1994) linked with death certificate records from the National Death Index.[51] In that 19y follow-up study, Zhou et al. (2018) showed higher risk of all-cause mortality among those with treated but uncontrolled hypertension (HR: 1.62, 95% CI: 1.35-1.95) and among those with untreated hypertension (HR: 1.40, 95% CI: 1.21-1.62), than in those without hypertension.[51]

To the best of my knowledge, my PhD is the first study in the LACCs context to have analysed national HES data linked with mortality data. Among LACCs, data from population-based prospective cohorts have highlighted the relevance of hypertension in explaining all-cause mortality.[297–299] For example, based on 10-year follow-up of participants in the PURE study (including over 24,000 participants from Argentina, Brazil, Chile, and Colombia), mortality risk was higher among those with than those without hypertension (HR: 1.34; 95% CI: 1.18-1.53).[297]

Several explanations for the higher risk of mortality among adults with treated but uncontrolled hypertension have been hypothesised, including higher levels of non-adherence to BP-lowering treatment and resistant hypertension (high blood pressure that does not respond well to aggressive medical treatment).[300, 301] Moreover, these adults may have a higher frequency of other risk factors associated with mortality. Based on my own analyses, adults with treated but uncontrolled hypertension had higher prevalence of diabetes and obesity than normotensive participants had (e.g. the prevalence of obesity was 39% and 13% among males with treated but uncontrolled hypertension and among normotensive, respectively). Similarly, higher risk of all-cause mortality among adults with treated and controlled hypertension could also be related to higher levels of risk factors, such as diabetes. For example, based on my results, the highest diabetes prevalence (fasting blood sugar >7 mmol/L or self-reported diabetes diagnosis) across hypertension status categories in the 2010 cohort was found among males with treated and controlled hypertension (43% among participants with treated and controlled hypertension, 27% among participants with treated but uncontrolled hypertension, 12% among participants with untreated hypertension, and 3% among normotensive participants).

Research using NHANES data linked with mortality registries has systematically reported higher risk of all-cause mortality among adults with the lowest levels of educational attainment.[302–306] The higher frequency of unhealthy behaviours was observed to partially explain higher mortality among those with lower education.[305, 307] Rogers et al. (2013) suggested that the observed educational difference in mortality risk was partially *mediated* by income, marital status (not being married), structural social capital (not being involved with clubs and organisations), smoking, excessive drinking, insufficient exercise, obesity, hypercholesterolemia, and hypertension.[305] As mentioned by Rosengren et al. (2019), in addition to the strong mediating effects of these health behaviours, those with lower levels of educational attainment are potentially exposed to several barriers to accessing health services due to the mediating effect of income, including barriers in purchasing treatment for hypertension.[307]

Cardiovascular mortality: Several studies have also reported a higher risk of cardiovascular mortality among those with hypertension.[51, 297, 308–310] Using NHANES III (1988-1994) linked with death certificate records, Zhou et al. (2018) reported a higher risk of cardiovascular mortality among participants with hypertension (patients with treated but uncontrolled hypertension HR: 1.77, 95% CI: 1.34-2.35; patients with untreated hypertension HR: 2.23, 95% CI: 1.66-2.99).[51]

Among females in the 2003 cohort, I observed higher risk of all-cause mortality among those at the lowest education level, yet this same group of females had a lower risk of cardiovascular mortality than their more educated counterparts. Accordingly, the social gradient in all-cause mortality among females will be most apparent for non-cardiovascular causes of death (including non-specific/ill-defined causes). In support of the role of ill-defined causes, analyses of national mortality registries in Chile showed that the proportion of deaths with ill-defined codes was higher among females than males.[251]

8.4. Strengths and limitations

One strength of my thesis is the provision of recent estimates for hypertension prevalence and its management indicators, including an assessment of secular changes over time. This study is the first to provide estimates of SEP inequalities in hypertension prevalence using the most recent Chilean health examination survey ENS (2017) and is the first to analyse SEP inequalities across a range of hypertension management indicators. Also, my thesis is the first to present results from analysing the ENS 2003 and 2010 cohorts linked with mortality data. With these data, I presented estimates of all-cause and cardiovascular mortality rates by key exposures (educational level and hypertension status).

A key strength of my study is the policy relevance of the research and communication of the findings to key stakeholders. My analyses of SEP inequalities in hypertension, its management indicators, and mortality were presented to the Department of Non-communicable Diseases of the Ministry of Health of Chile in February and March 2022. The Head of the Department at the time requested a copy of my thesis and invited me to perform future research with them. Departmental staff were particularly interested in my findings related to the suboptimal levels of hypertension management among males; SEP inequalities in hypertension among females; and the main findings from the analysis of ENS-mortality-linked data.

More specific strengths of the study include the use of standard definitions of hypertension outcomes (including objective measures of BP and a nurse-led drug inventory), robust data on mortality via linkage by MINSAL, and standard analytical methods, allowing like-for-like comparisons across HES surveys in Chile over time and with HES data from other countries. Finally, my systematic review and the discussion of my main findings prioritised evidence from LACCs, providing a local context to my results.

Another strength of my study was the importance given to the role of gender in this area of research. Analyses adjusting for gender may mask gender-specific inequalities. Indeed, many of my key findings were gender specific (e.g. SEP inequalities in uncontrolled hypertension among females but not among males).

My study was subject to several limitations. Some findings were likely attenuated toward the null as a result of limited power, especially those stratified by gender and survey year on indicators of hypertension management (based on smaller sample sizes). HES conducted in LACCs are characterised by lower sample sizes. Unlike HICs, such as England and the United States, which collect HES data continuously (and thus data can be pooled across years to maximise sample size), surveys in LACCs (including Chile) are generally conducted approximately once every five years. However, in my study, I considered that non-significant differences (P>0.05) do not necessarily imply equality in the results between SEP groups: it simply means that the null effect is statistically consistent with the results observed from the data (which have been stratified by gender and collected only every 5 years). Consequently, I focused primarily on the pattern of results, not on specific p-values, and, where appropriate, combined data (by gender or survey years) to increase sample size and statistical power. The focus on the direction and strength of associations (and not just p-value thresholds) applies to all chapters of my PhD but also applies to HES analyses in general.

Other key limitations of my study are related to the cross-sectional nature of the Chilean health surveys. The cross-sectional nature of the data restricts causative conclusions about SEP inequalities in hypertension outcomes. In Chapters 4, 5 and 6, I discussed in detail the main limitations of the data and the analyses related to hypertension outcomes, SEP markers and county-level measures of the socioeconomic environment. This cross-sectional limitation was minimised to some extent in the analyses of mortality. However, as in all observational studies, my main findings may have been affected by unmeasured or residual confounding.

8.5. Policy implications

Policy implications related to hypertension prevalence and management in Chile

Overall, suboptimal levels of diagnosed, treated, and controlled hypertension among Chilean adults (especially among males) highlight the need to increase investment in health and to continue developing and strengthening universal health care programmes for hypertension. Continuous efforts to reduce the prevalence of hypertension should continue to be a priority in Chile and worldwide. Using Geoffrey Rose's concepts of *high-risk* vs *population-based* strategies[311] and the example of hypertension, strategies that target individuals at high risk of hypertension offer limited hope to substantially reduce the incidence of hypertension. Many of these high-risk individuals could be identified based on proximal factors (e.g. high BMI, heavy smoking, physical inactivity, and excessive salt consumption). However, as Rose suggests, the impact of interventions that target high-risk individuals will be small compared with the total number of cases arising from the larger share of the population with a medium-risk or average-risk profile.

Population-based prevention strategies (i.e. lowering the risk at the population level) will have a larger impact on the total number of incident cases of hypertension.[311] As described in Chapter 1, the Chilean State has implemented various reforms over the last two decades in order to improve the health profile of the population. These ongoing efforts in Chile were reinforced by participation in the WHO Global Heart Initiative in 2016.[312] This initiative, which aimed to reduce the worldwide burden of cardiovascular disease, included a package of population-wide and targeted health services interventions to standardise treatment, BP measurement and research efforts, and implement innovations in hypertension care. Strengthening and implementing more population-based interventions (e.g. taxation on unhealthy foods) and individual-level interventions (e.g. wider BP screening among younger males) that address both behavioural risk and protective factors are needed to increase levels of controlled hypertension.[257] The WHO developed a list of costly-effective high-risk and population-based interventions to tackle NCDs to be implemented globally (known as the *best buys*).[313] Several high-risk strategies to improve the health profile of adults with hypertension included within these best buys have been implemented in Chile since the mid-'80s through cardiovascular programmes and the GES plan.

As the Chilean population grows and the population ages, the increasing number of people (in absolute terms) requiring interventions will continue to be a tremendous challenge for health systems worldwide. Strategies focusing on those at highest risk require healthcare systems to have enough capacity: this is a challenging aspect for most health systems worldwide, especially among LMICs and LACCs.[314] In order to prevent and successfully control hypertension, it is necessary to strengthen and implement more cost-effective population-based interventions,[313] including the WHO best buys targeting tobacco use, alcohol consumption, unhealthy diet, and physical inactivity.[313]

The Chilean health objective 2010-2020 of increasing levels of controlled hypertension was defined in relative terms (a 50% increase).[264] However, articulating national public health targets in absolute terms may be warranted. Substantial progress in levels of hypertension management in relative terms may be the result of a minor improvement from a low baseline. In contrast to Chile, countries such as England and the US have defined public health targets on hypertension outcomes in absolute terms.[315, 316]

Policy implications related to SEP inequalities in hypertension

The implementation of high-risk and population-based interventions should consider the impact on SEP inequalities. Some authors suggest that high-risk interventions (targeting *downstream* or *proximal* determinants) typically widen socioeconomic inequalities, with examples of increasing SEP inequalities from interventions in antihypertensive treatment and adherence.[317] Population-based interventions can decrease or increase SEP inequalities depending on the type of the intervention (*structural* interventions: changing the context where health behaviours occur can reduce SEP inequalities; *agentic* interventions: relying on individuals to modify health behaviours can increase SEP inequalities).[317]

Several types of interventions (e.g. strengthening communities, improving living and working conditions, and promoting healthy macro-policies) can help to reduce SEP inequalities in hypertension.[318] These interventions can be implemented in society using a range of approaches. Four such approaches described by Benach et al. (2012) are as follows: (i) targeted interventions on the worst-off groups only: people in the lowest SEP groups are the only target of these interventions (e.g. initiatives only implemented in the most deprived neighbourhoods); (ii) universal policy with an additional focus on gap: universal intervention benefiting the population as a whole but with extra efforts targeting those in lower SEP; (iii) redistributive policy: universal intervention on the causes of the health problems that occur more frequently among lower SEP; and (iv) proportionate universalism: Marmot's concept of *"universal (interventions), but with a scale and intensity that is proportionate to the level of disadvantage"*.[319]

Chile has implemented programmes targeting SEP inequalities in health, including a special focus on equality within the GES plan (for all) and in the Cardiovascular Programme (for public health users), and by implementing the inter-sectoral *Equity Commission, Social Determinants of Health and Health in All Policies*. In order to decrease current educational-based inequalities in hypertension prevalence and its management indicators in Chile, universal policies should proportionately target risk factors for hypertension, especially among females at the lowest educational level.

Policy implications related to socioeconomic environment measures, individual-level SEP inequalities and hypertension

To decrease SEP inequalities in hypertension, focussing only on the diagnosis of hypertension and the treatment of hypertension through BP-lowering medicine is likely not enough.[40] Policies should address wider structural determinants of hypertension, particularly policies promoting universal access to the resources needed to engage in healthy behaviours. Such policies should aim to tackle the obesogenic environment and restrict marketing that promotes the consumption of tobacco, alcohol and junk food.[320] To reduce the burden of hypertension further, it is necessary to reinforce and implement new interventions targeting area-level factors such as air pollution and proximity to green spaces.[293, 321]

Policies affecting mortality rates by educational level and hypertension

Reinforcing and implementing cost-effective interventions to tackle NCDs (e.g. WHO best buys) will help to reduce the risk of premature mortality in Chile. As high SBP is the leading cause of attributable deaths worldwide (19.2% of all deaths in 2019) and in Chile (19.3% of all deaths in 2019).[28] Policies to reduce levels of hypertension, improve attainment of each hypertension management indicator, and reduce SEP inequalities in hypertension outcomes, will have a favourable effect on reducing mortality rates overall, and reducing SEP inequalities in the risk of death.

Several educational reforms were implemented in Chile in the past few decades. However, socioeconomic inequalities in the quality of education and in access to tertiary education remain large.[11] Further efforts to improve the quality of education, and to widen access to tertiary education would help to decrease hypertension levels and rates of all-cause and cardiovascular mortality.[322, 323].

The modelling study by Alvarado et al. (2009) offers some insights into how both the overall mortality burden and inequalities in the distribution of mortality could be reduced by reductions in risk factor levels (e.g. high cholesterol, high BP, smoking, diabetes and obesity).[324] A maximum reduction in cardiovascular mortality could be achieved by reducing risk factor levels in all SEP groups; a maximum reduction of SEP inequalities in cardiovascular mortality could be achieved if those in lower SEP groups reduced risk factor levels at a faster pace than those of higher SEP.[324]

8.6. Future research

In future research, the secular changes in hypertension and its management indicators presented in my study could be updated using data from the next Chilean health survey (initially planned for 2022 but now expected in 2023 or 2024). ENS2010 and ENS2017 increased the amount of information collected on hypertension compared to ENS2003. To further improve hypertension surveillance in Chile: the next Chilean health survey should maintain and expand the set of hypertension questions and measurements included in ENS2017. With respect to future Chilean health surveys, I suggest i) including questions on barriers to accessing hypertension care, ii) including questions on self-reported adherence to treatment, iii) implementing new measurements for blood pressure monitoring and treatment adherence (e.g. ABPM, electronic adherence monitoring), and iv) including questions related to SEP in early life. My future analyses of secular changes in hypertension and its management indicators will also take into account other factors that could be associated with these changes: including biological factors (e.g. obesity) and health behaviours (e.g. salt intake).

As mentioned above, resistant hypertension can be another contributing factor to SEP inequalities in levels of uncontrolled hypertension and in the higher risk of mortality among those with treated but uncontrolled hypertension.[325] Accordingly, in future research, I will analyse SEP inequalities in resistant hypertension and examine differences in the risk of mortality among participants with and without resistant hypertension. I will also investigate outcomes such as levels of controlled hypertension by type of hypertensive drug.

Previous literature has highlighted inequalities in hypertension outcomes by ethnicity: race-ethnic groups versus non-Hispanic whites have shown higher levels of hypertension prevalence and higher levels of undiagnosed, untreated and uncontrolled hypertension.[203, 260, 276] This is an interesting topic that is under-researched in Chile. Ethnicity information was collected in ENS 2017 but not in ENS 2003 or 2010. Consequently, ENS2017 (and probably future versions of ENS) provide an opportunity to explore inequalities by ethnicity. In future research, using ENS data, I will assess the association between ethnicity and levels of hypertension prevalence and its management indicators.

In future analyses, I will explore SEP inequalities in non-cardiovascular mortality and use multilevel Cox models to examine county-level variations in mortality. I will also explore how gender-specific age-adjusted associations between SEP and mortality change after adjustments for potential mediators (e.g. biological factors and/or health behaviours).

Also, at the time of writing, I am currently validating and harmonising data which links the ENS with data from hospitalisation registries. Similar to the work presented in Chapter 7, using these data, my future analyses will examine the associations between SEP, hypertension status and (i) time to first hospitalisation, (ii) time to at least one cardiovascular-related hospitalisation, and (iii) the length of hospital stay.

Finally, the COVID-19 pandemic brought several challenges to researching SEP inequalities in hypertension and in all-cause and cardiovascular mortality. The changes post COVID-19 reported in Chile and worldwide in the (i) patterns of mortality and (ii) management of chronic health care services are likely to have had an impact on the results from data collected since the end of 2019.[326] Recent evidence suggests that the COVID-19 pandemic may have increased the magnitude of SEP inequalities in hypertension management in the US through the widespread use of virtual healthcare platforms that potentially widen socioeconomic differences in healthcare access.[327] Emerging impacts of COVID-19 on SEP inequalities in hypertension management are likely to occur in Chile and globally. In Chile, evidence has shown SEP inequalities in COVID-19 incidence and mortality.[229, 328] Therefore, going forward, my research on socioeconomic inequalities in the prevalence and management of hypertension, and the risk of all-cause and cause-specific mortality, will need to consider the potential effects of COVID-19 in the short-, medium- and long-term.

8.7. Conclusions

Hypertension continues to be one of the most important health challenges, being a major risk factor for cardiovascular morbidity and mortality worldwide. Over the past 15 years in Chile, hypertension prevalence has slightly decreased, and its management indicators (diagnosed, treated, and controlled hypertension) have improved but they remain suboptimal, particularly among males.

Higher levels of hypertension among the least versus most educated females persisted over time. Inequalities in untreated and uncontrolled hypertension among females emerged in 2017, indicating faster rates of improvement among the most educated females. Educational-based inequalities in all-cause mortality were observed for both genders; adults with hypertension had a higher risk of cardiovascular mortality.

The results of my work can help stakeholders, including the Chilean Ministry of Health, to design and implement further interventions targeting risk factor reduction to reduce the incidence of hypertension and programmes to increase levels of diagnosed, treated, and controlled hypertension, especially among males. With regards to inequalities, although Chile introduced Universal Access to Care for hypertension (GES-hypertension) in 2005 to improve the quality of care and tackle inequalities in hypertension outcomes, my worrisome findings, especially for females, show there is room for improvement.

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Appendices

Appendix 4: Secular changes in the prevalence and management of hypertension among adults in Chile (Chapter 4)

Figure A4.1: Invitation letter from the Ministry of Health

SUBSECRETARÍA DE SALUD PÚBLICA
DIVISIÓN PREVENCIÓN Y CONTROL DE ENFERMEDADES
DEPTO. ENFERMEDADES NO TRANSMISIBLES

INVITATION LETTER

March 11, 2022

Mr. Álvaro Passi, PhD (c)

Department of Public Health,
School of Medicine,
Pontificia Universidad Catolica de Chile,
Santiago, Chile.

Department of Epidemiology and Public Health,
University College London,
London, UK.

Dear Mr. Passi,

On behalf of the Chilean Health Ministry, I am writing to invite you to participate in updating the Chilean cardiovascular risk charts.

Cardiovascular diseases (CVD) are one of the main causes of death in Chile, which are due to the combination of different risk factors such as high blood pressure, diabetes mellitus, smoking, overweight, excessive alcohol consumption and sedentary lifestyle. This is why, starting in 2009, the Ministry of Health has promoted cardiovascular risk evaluations.

Cardiovascular risk is estimated in Chile with the Framingham risk charts adapted to the Chilean population. These charts need to be recalibrated with the data reported in the National Health Strategy of 2016-2017, considering that the tables used presently were adjusted with the population of 2003. On the other hand, in 2019 the World Health Organization published new tables for 21 global regions. Making a comparison between these two estimators will be relevant in making the decision of which one to use.

Due to your experience in the study of cardiovascular Risk factors and mortality, including you PhD research at UCL, we would like to request your collaboration in the evaluation of the risk charts that will be recalibrated, comparing them with the previous ones and with those of the World Health Organization. This work will be started in March and we expect that in April we can convene an expert panel to decide which risk chart to use.

Hoping you can collaborate with us,

Yours sincerely,

[redacted]

MINISTERIO DE SALUD - DIVISIÓN DE PREVENCIÓN Y CONTROL DE ENFERMEDADES - JEFE DEPTO. ENFERMEDADES NO TRANSMISIBLES

MELANIE PACCOT B., MD
HEAD OF THE DEPARTMENT OF
NON-COMMUNICABLE DISEASES

Figure A4.2: PhD study protocol approval by the Ethics committee of the Pontificia Universidad Católica de Chile (PUC) (ID: 200205003)

PONTIFICIA
UNIVERSIDAD
CATÓLICA
DE CHILE

ACTA DE APROBACIÓN
COMITÉ ÉTICO DE CIENCIAS DE LA SALUD UC
Re- acreditado por SEREMI de Salud
Resolución Exenta Nº012321 del 07 de junio de 2017

NUEVO ESTUDIO

Fecha y N° de Sesión: 16 de abril de 2020, Sesión N°5.

Investigador Responsable: Alvaro Passi Solar

ID Protocolo: 200205003

Título del Proyecto: Socioeconomic inequalities in the management of hypertension: analyses of the Chilean National Health Surveys 2003, 2010 and 2017

Facultad/Unidad Académica: Facultad de Medicina, Pontificia Universidad Católica de Chile

Académico Responsable: Alvaro Passi Solar

Financiamiento: CONICYT (indicar) Becas doctorado extranjero 2017

Miembros del Comité que participaron en la aprobación del estudio:

Dra. Claudia Uribe Torres, Presidente.

Dra. Colomba Cofré Dougnac, Vice-Presidente.

Mg. Andrea Villagrán Torres, Secretaria Ejecutiva.

Sr. Jorge Muñoz Castillo, Abogado miembro externo.

Dr. Gustavo Kaltwasser González, Miembro externo.

Srta. Alyssa Garay Navea, Representante de la comunidad.

Dra. Katia Abarca Villaseca, Departamento Infectología.

Table A4.1: Hypertension prevalence, awareness, treatment, and control by gender, age, and urban-rural residence.

Variable	Exposure	2003	2010	2017
Prevalence				
Gender	All	34 (32-36)	32 (30-34)	31 (28-33)
	Males	37 (34-41)	32 (29-36)	31 (28-35)
	Females	31 (28-34)	32 (29-35)	30 (28-33)
Age	17-44y	18 (15-20)	12 (9-14)	8 (7-11)
	45-64y	54 (48-59)	52 (47-56)	48 (43-52)
	≥65y	80 (75-84)	82 (78-86)	79 (76-83)
Residence	Urban	33 (31-36)	31 (29-34)	30 (28-32)
	Rural	40 (35-46)	39 (31-47)	38 (33-43)
Awareness				
Gender	All	58 (54-62)	66 (61-70)	66 (62-70)
	Males	46 (39-52)	57 (50-64)	58 (52-64)
	Females	73 (68-77)	74 (69-78)	74 (69-78)
Age	17-44y	48 (40-57)	52 (40-64)	48 (36-60)
	45-64y	58 (52-64)	67 (60-74)	72 (66-77)
	≥65y	72 (67-76)	72 (66-78)	66 (60-71)
Residence	Urban	58 (54-63)	66 (61-71)	66 (62-71)
	Rural	59 (49-68)	62 (49-74)	63 (56-70)
Treatment				
Gender	All	38 (34-43)	56 (52-61)	65 (61-69)
	Males	24 (20-30)	44 (39-50)	57 (50-63)
	Females	55 (49-61)	68 (63-73)	74 (68-78)
Age	17-44y	18 (12-25)	29 (21-40)	30 (21-42)
	45-64y	40 (34-47)	56 (50-62)	68 (62-74)
	≥65y	62 (56-67)	75 (70-80)	75 (70-80)
Residence	Urban	38 (34-43)	56 (52-61)	65 (60-70)
	Rural	39 (31-48)	57 (48-65)	66 (58-73)
Control				
Gender	All	13 (10-16)	23 (20-27)	34 (30-38)
	Males	6 (4-10)	14 (11-19)	28 (23-34)
	Females	20 (16-25)	32 (27-37)	40 (34-45)
Age	17-44y	10 (6-16)	17 (10-27)	21 (13-32)
	45-64y	15 (11-20)	27 (23-32)	44 (37-50)
	≥65y	13 (10-17)	22 (17-28)	26 (22-31)
Residence	Urban	12 (9-16)	23 (19-27)	34 (30-39)

Variable	Exposure	2003	2010	2017
	Rural	15 (9-24)	26 (20-33)	32 (26-39)

Prevalence: BP ≥140/90 mmHg or use of antihypertensive medication; Awareness: prior diagnosis of hypertension; Treatment: use of antihypertensive medication; and Control: BP <140/90 mmHg. Levels of hypertension estimated among all adults. Levels of awareness, treatment, and control estimated among persons with hypertension. Estimates (95% CI) were not age-standardised.

Table A4.2: Age-adjusted differences (pairwise comparisons) in hypertension and its management indicators of care by gender and urban-rural residence.

Variable	Pooled	2003	2010	2017
Prevalence				
Female vs Male	0.73 (0.63-0.84)	0.59 (0.47-0.73)	0.82 (0.62-1.08)	0.81 (0.64-1.03)
Rural vs Urban	1.25 (1.03-1.52)	1.3 (0.97-1.75)	1.23 (0.84-1.8)	1.19 (0.87-1.63)
Awareness				
Female vs Male	2.26 (1.82-2.81)	2.91 (2.02-4.19)	2.04 (1.4-2.97)	1.97 (1.34-2.89)
Rural vs Urban	0.92 (0.7-1.21)	1.07 (0.7-1.62)	0.84 (0.46-1.52)	0.87 (0.6-1.27)
Treatment				
Female vs Male	2.53 (2.07-3.09)	3.28 (2.42-4.45)	2.58 (1.84-3.63)	1.98 (1.35-2.91)
Rural vs Urban	1.03 (0.8-1.33)	1.11 (0.71-1.75)	0.99 (0.64-1.55)	0.98 (0.64-1.5)
Control				
Female vs Male	2.35 (1.83-3.02)	3.68 (2.11-6.39)	2.82 (1.81-4.39)	1.73 (1.18-2.51)
Rural vs Urban	1.14 (0.89-1.46)	1.33 (0.72-2.47)	1.31 (0.91-1.88)	0.93 (0.66-1.31)

Odds ratios (95% CI) calculated from age-and survey year-adjusted logistic regressions. Models that pooled data across genders (rural vs urban) were further adjusted for gender

Table A4.3: Age-adjusted change over time in hypertension prevalence, awareness, treatment, and control by gender.

Variable	2010 vs 2003	2017 vs 2010	2017 vs 2003
Prevalence			
All	0.75 (0.62-0.90)	0.75 (0.62-0.90)	0.56 (0.46-0.67)
Males	0.63 (0.48-0.83)	0.77 (0.58-1.01)	0.48 (0.37-0.63)
Females	0.90 (0.70-1.15)	0.73 (0.58-0.92)	0.65 (0.52-0.83)

Variable	2010 vs 2003	2017 vs 2010	2017 vs 2003
Awareness			
All	1.25 (0.96-1.63)	0.96 (0.74-1.26)	1.21 (0.94-1.55)
Males	1.45 (0.98-2.14)	0.97 (0.65-1.44)	1.40 (0.97-2.03)
Females	1.03 (0.73-1.45)	0.95 (0.67-1.35)	0.98 (0.69-1.38)
Treatment			
All	1.91 (1.46-2.51)	1.31 (1.01-1.69)	2.51 (1.88-3.34)
Males	2.17 (1.48-3.18)	1.45 (0.99-2.13)	3.15 (2.07-4.81)
Females	1.70 (1.22-2.38)	1.17 (0.82-1.66)	1.99 (1.40-2.82)
Control			
All	2.07 (1.48-2.90)	1.74 (1.35-2.26)	3.61 (2.56-5.09)
Males	2.29 (1.25-4.20)	2.21 (1.41-3.45)	5.06 (2.76-9.27)
Females	1.97 (1.34-2.90)	1.48 (1.07-2.06)	2.93 (1.98-4.32)

Odds ratios and 95% CIs estimated from age-adjusted logistic regressions.

Table A4.4: Hypertension prevalence and management: JNC 7 and 2017 ACC/AHA guidelines by gender in 2017.

Gender	Status	JNC 7	ACC/AHA
All	Normotensive	69 (67-71)	52 (50-55)
	Treated and controlled	10 (9-12)	6 (5-7)
	Treated but uncontrolled	10 (8-11)	14 (12-16)
	Untreated	11 (9-12)	28 (25-30)
Males	Normotensive	69 (65-72)	47 (43-50)
	Treated and controlled	9 (7-11)	4 (3-6)
	Treated but uncontrolled	9 (7-11)	14 (11-16)
	Untreated	14 (11-16)	36 (32-39)
Females	Normotensive	70 (67-72)	58 (55-61)
	Treated and controlled	12 (10-14)	8 (6-10)
	Treated but uncontrolled	10 (9-12)	14 (13-17)
	Untreated	8 (6-10)	20 (17-23)

Seventh Joint National Committee (JNC 7) (i) normotensive (BP <140/90 mmHg, not on antihypertensive medication); (ii) treated and controlled (BP <140/90 mmHg); (iii) treated, but uncontrolled (BP ≥140/90 mmHg); and (iv) untreated (≥140/90 mmHg). Categories using the 2017 American College of Cardiology/American Heart Association guidelines (ACC/AHA) used 130/80 mmHg instead of 140/90 mmHg.

Appendix 5: Individual-level socioeconomic inequalities in the prevalence and management of hypertension (Chapter 5)

Table A5.1: Hypertension outcomes by SEP indicator (observed): males.

Variable	Exposure	2003	2010	2017
Prevalence				
Education	Low	58 (52-64)	57 (47-67)	61 (52-69)
	Medium	31 (27-36)	29 (25-34)	29 (25-33)
	High	32 (24-40)	21 (16-28)	22 (17-29)
Income	Poorest		32 (24-41)	30 (23-39)
	Q2		34 (26-42)	36 (28-46)
	Q3		30 (23-38)	32 (25-40)
	Richest		37 (31-45)	30 (24-37)
Health insurance	Public		35 (31-39)	34 (30-38)
	Private		23 (15-33)	24 (16-35)
Undiagnosed				
Education	Low	54 (46-63)	43 (31-56)	49 (39-60)
	Medium	58 (49-66)	43 (34-53)	41 (32-50)
	High	47 (29-66)	43 (28-60)	36 (23-51)
Income	Poorest		47 (31-64)	44 (30-60)
	Q2		47 (33-61)	35 (21-53)
	Q3		31 (20-44)	44 (31-58)
	Richest		37 (26-50)	43 (33-54)
Health insurance	Public		43 (35-52)	44 (38-51)
	Private		32 (17-53)	23 (11-41)
Untreated				
Education	Low	70 (64-76)	47 (36-58)	38 (29-49)
	Medium	79 (72-85)	60 (52-68)	46 (37-56)
	High	78 (52-92)	58 (42-73)	43 (29-58)
Income	Poorest		56 (40-72)	48 (33-63)
	Q2		62 (50-74)	41 (26-57)
	Q3		51 (39-62)	40 (28-54)
	Richest		48 (37-58)	47 (35-59)
Health insurance	Public		55 (48-61)	44 (38-50)
	Private		53 (33-71)	33 (17-54)
Uncontrolled				
Education	Low	92 (87-95)	85 (74-92)	75 (67-82)
	Medium	97 (93-98)	87 (81-91)	74 (66-81)

Variable	Exposure	2003	2010	2017
	High	90 (67-98)	84 (68-92)	64 (47-79)
Income	Poorest		75 (57-87)	79 (65-88)
	Q2		88 (79-93)	67 (53-79)
	Q3		90 (83-94)	70 (57-81)
	Richest		85 (76-92)	71 (58-81)
Health insurance	Public		84 (78-88)	73 (67-78)
	Private		90 (79-96)	54 (32-75)

Observed estimates (% and 95% CI). Educational level: low (<8 years); medium (8-12 years); high (>12 years). Income: quartiles of household monthly income equivalised to the composition of the household. Income and health insurance measured in 2010 and 2017 only.

Table A5.2: Hypertension outcomes by SEP indicator (observed): females.

Variable	Exposure	2003	2010	2017
Prevalence				
Education	Low	53 (47-60)	57 (50-64)	62 (55-67)
	Medium	25 (22-29)	28 (24-32)	27 (24-31)
	High	10 (6-17)	19 (13-26)	12 (8-17)
Income	Poorest		28 (23-34)	32 (26-39)
	Q2		39 (32-47)	31 (24-39)
	Q3		32 (26-38)	34 (30-40)
	Richest		32 (25-39)	24 (19-29)
Health insurance	Public		34 (31-38)	31 (28-34)
	Private		16 (9-26)	16 (10-23)
Undiagnosed				
Education	Low	21 (16-26)	21 (16-27)	28 (22-34)
	Medium	29 (22-37)	27 (21-35)	25 (19-32)
	High	68 (35-90)	34 (19-53)	27 (11-51)
Income	Poorest		27 (19-37)	24 (15-35)
	Q2		27 (18-39)	28 (18-43)
	Q3		26 (18-35)	28 (20-37)
	Richest		27 (18-38)	28 (19-38)
Health insurance	Public		25 (20-30)	28 (23-33)
	Private		33 (14-60)	16 (6-34)
Untreated				

Variable	Exposure	2003	2010	2017
Education	Low	41 (34-47)	26 (19-33)	29 (22-36)
	Medium	48 (38-58)	33 (27-40)	25 (19-33)
	High	66 (32-89)	42 (23-64)	26 (10-50)
Income	Poorest		37 (27-47)	29 (19-43)
	Q2		29 (20-41)	24 (14-37)
	Q3		32 (24-43)	28 (20-37)
	Richest		31 (18-47)	26 (17-36)
Health insurance	Public		31 (26-37)	27 (22-33)
	Private		15 (5-40)	16 (6-35)
Uncontrolled				
Education	Low	83 (78-88)	69 (63-75)	74 (68-79)
	Medium	76 (67-84)	64 (55-72)	52 (43-60)
	High	76 (37-95)	72 (57-84)	48 (28-69)
Income	Poorest		70 (61-78)	64 (50-76)
	Q2		69 (55-81)	58 (45-70)
	Q3		64 (53-73)	63 (54-71)
	Richest		63 (51-73)	56 (45-66)
Health insurance	Public		67 (61-72)	63 (57-68)
	Private		61 (39-80)	29 (14-52)

Observed estimates (% and 95% CI). Educational level: low (<8 years); medium (8-12 years); high (>12 years). Income: quartiles of household monthly income equivalised to the composition of the household. Income and health insurance measured in 2010 and 2017 only.

Table A5.3: Hypertension outcomes by SEP indicator among males (age-standardised).

Variable	Exposure	2003	2010	2017
Prevalence				
Education	Low	46 (39-54)	40 (28-53)	33 (24-42)
	Medium	39 (34-44)	34 (30-38)	31 (28-35)
	High	43 (35-50)	29 (22-37)	30 (24-37)
Income	Poorest		36 (29-43)	32 (25-39)
	Q2		34 (27-41)	34 (28-41)
	Q3		31 (24-39)	32 (26-39)
	Richest		38 (32-45)	31 (25-36)

Variable	Exposure	2003	2010	2017
Health insurance	Public		35 (31-39)	32 (29-36)
	Private		35 (27-43)	31 (23-39)
Undiagnosed				
Education	Low	56 (48-64)	50 (40-61)	55 (43-67)
	Medium	47 (39-55)	37 (30-46)	39 (31-47)
	High	46 (28-66)	37 (23-52)	34 (22-47)
Income	Poorest		46 (33-58)	44 (30-58)
	Q2		46 (33-60)	35 (21-52)
	Q3		30 (19-43)	41 (29-54)
	Richest		35 (25-47)	45 (35-56)
Health insurance	Public		43 (34-51)	44 (39-49)
	Private		28 (14-47)	25 (20-30)
Untreated				
Education	Low	72 (66-78)	56 (47-65)	52 (40-64)
	Medium	66 (58-74)	51 (43-60)	42 (33-51)
	High	63 (44-80)	59 (40-76)	39 (27-53)
Income	Poorest		54 (39-67)	48 (34-62)
	Q2		60 (49-71)	40 (26-56)
	Q3		50 (40-61)	41 (28-55)
	Richest		44 (33-55)	47 (35-58)
Health insurance	Public		52 (46-58)	44 (39-49)
	Private		44 (30-59)	38 (33-44)
Uncontrolled				
Education	Low	92 (88-95)	88 (81-93)	73 (61-83)
	Medium	94 (87-98)	84 (76-91)	76 (69-82)
	High	86 (66-97)	86 (72-94)	63 (49-76)
Income	Poorest		74 (59-86)	79 (65-89)
	Q2		87 (77-93)	69 (55-80)
	Q3		89 (82-94)	68 (54-80)
	Richest		87 (79-93)	73 (62-82)
Health insurance	Public		83 (77-88)	73 (69-76)
	Private		91 (78-97)	60 (55-64)

Values and 95% CIs were directly age-gender-standardised using data from Census 2017 (age groups: 17-44y; 45-64y; ≥65y). Educational level: low (<8 years); medium (8-12 years); high (>12 years). Income: quartiles of household monthly income *equivalised to the composition of the household. Income and health insurance measured in 2010 and 2017 only.*

Table A5.4: Hypertension outcomes by SEP indicator among females (age-standardised).

Variable	Exposure	2003	2010	2017
Prevalence				
Education	Low	39 (34-44)	38 (32-44)	39 (28-52)
	Medium	36 (33-40)	34 (30-38)	30 (28-34)
	High	26 (20-32)	29 (24-35)	20 (14-27)
Income	Poorest		37 (32-41)	34 (28-40)
	Q2		36 (29-44)	33 (27-39)
	Q3		34 (29-40)	33 (29-38)
	Richest		31 (25-38)	24 (20-29)
Health insurance	Public		36 (33-39)	31 (29-34)
	Private		20 (14-28)	18 (11-26)
Undiagnosed				
Education	Low	21 (16-27)	19 (14-25)	25 (18-34)
	Medium	31 (23-39)	26 (20-33)	24 (19-30)
	High	73 (44-93)	23 (10-41)	19 (9-32)
Income	Poorest		25 (17-36)	25 (18-34)
	Q2		24 (17-33)	27 (17-39)
	Q3		24 (17-33)	28 (20-38)
	Richest		25 (15-36)	27 (18-38)
Health insurance	Public		23 (18-28)	27 (24-31)
	Private		36 (16-61)	17 (12-22)
Untreated				
Education	Low	42 (35-49)	26 (19-35)	31 (25-38)
	Medium	39 (30-49)	30 (24-36)	22 (17-28)
	High	68 (34-92)	25 (12-41)	18 (8-31)
Income	Poorest		32 (23-43)	29 (21-37)
	Q2		27 (19-36)	22 (15-31)
	Q3		31 (22-41)	29 (21-39)
	Richest		25 (16-36)	26 (17-36)
Health insurance	Public		28 (23-34)	27 (24-30)
	Private		19 (5-45)	17 (13-22)
Uncontrolled				
Education	Low	83 (77-87)	66 (58-73)	72 (64-79)

Variable	Exposure	2003	2010	2017
	Medium	78 (70-85)	68 (60-74)	56 (48-63)
	High	78 (36-98)	64 (48-78)	43 (24-63)
Income	Poorest		71 (62-80)	66 (55-77)
	Q2		69 (55-80)	57 (44-70)
	Q3		66 (57-74)	62 (52-70)
	Richest		58 (47-67)	53 (43-63)
Health insurance	Public		67 (61-72)	62 (59-65)
	Private		63 (47-77)	30 (22-38)

Values and 95% CIs were directly age-gender-standardised using data from Census 2017 (age groups: 17-44y; 45-64y; ≥65y). Educational level: low (<8 years); medium (8-12 years); high (>12 years). Income: quartiles of household monthly income equivalised to the composition of the household. Income and health insurance measured in 2010 and 2017 only.

Table A5.5: SEP inequalities by hypertension outcome (pairwise comparisons): males.

Variable	Exposure	2003	2010	2017
Prevalence				
Education	Low	0.93 (0.54-1.60)	1.64 (0.86-3.09)	1.08 (0.57-2.04)
	Medium (Ref: High)	0.89 (0.58-1.36)	1.41 (0.90-2.20)	1.10 (0.67-1.79)
Income	Poorest		0.81 (0.46-1.44)	1.13 (0.61-2.10)
	Q2		0.73 (0.40-1.32)	1.27 (0.72-2.24)
	Q3 (Ref: Richest)		0.65 (0.34-1.24)	1.08 (0.62-1.89)
Health insurance	Public (Ref: Private)		1.22 (0.69-2.16)	1.25 (0.71-2.19)
Undiagnosed				
Education	Low	2.22 (1.00-4.93)	1.37 (0.53-3.54)	2.28 (1.04-4.99)
	Medium (Ref: High)	1.63 (0.77-3.45)	0.91 (0.42-1.95)	1.21 (0.60-2.47)
Income	Poorest		1.60 (0.71-3.61)	1.04 (0.49-2.21)
	Q2		1.57 (0.72-3.40)	0.71 (0.31-1.65)
	Q3 (Ref: Richest)		0.78 (0.36-1.71)	1.04 (0.52-2.07)
Health insurance	Public (Ref: Private)		1.72 (0.71-4.19)	2.68 (1.08-6.63)
Untreated				
Education	Low	2.21 (0.62-7.92)	1.36 (0.55-3.37)	1.83 (0.74-4.50)
	Medium (Ref: High)	1.29 (0.37-4.47)	0.92 (0.39-2.19)	1.14 (0.53-2.46)
Income	Poorest		1.77 (0.77-4.04)	1.10 (0.52-2.34)
	Q2		2.35 (1.13-4.89)	0.82 (0.34-1.96)

Variable	Exposure	2003	2010	2017
	Q3 (Ref: Richest)		1.39 (0.68-2.85)	0.90 (0.41-1.97)
Health insurance	Public (Ref: Private)		1.35 (0.62-2.96)	1.65 (0.62-4.35)
Uncontrolled				
Education	Low	2.80 (0.44-18.00)	1.71 (0.53-5.54)	1.85 (0.78-4.38)
	Medium (Ref: High)	3.80 (0.63-23.06)	1.16 (0.45-3.01)	1.58 (0.71-3.52)
Income	Poorest		0.55 (0.20-1.51)	1.51 (0.63-3.63)
	Q2		1.33 (0.53-3.36)	0.84 (0.37-1.90)
	Q3 (Ref: Richest)		1.69 (0.69-4.15)	0.97 (0.42-2.22)
Health insurance	Public (Ref: Private)		0.61 (0.23-1.64)	2.30 (0.90-5.91)

Odds ratios and 95% CIs calculated from age-and survey year-adjusted logistic regressions. SEP indicators were evaluated in separate models. Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the composition of the household. Income and health insurance measured in 2010 and 2017 only.

Table A5.6: SEP inequalities by hypertension outcome (pairwise comparisons): females.

Variable	Exposure	2003	2010	2017
Prevalence				
Education	Low	2.28 (1.17-4.45)	1.19 (0.66-2.15)	2.37 (1.24-4.55)
	Medium (Ref: High)	2.40 (1.17-4.92)	1.25 (0.73-2.15)	2.12 (1.21-3.73)
Income	Poorest		1.36 (0.79-2.36)	2.67 (1.52-4.69)
	Q2		1.46 (0.76-2.80)	2.01 (1.14-3.52)
	Q3 (Ref: Richest)		1.30 (0.71-2.37)	2.13 (1.31-3.47)
Health insurance	Public (Ref: Private)		3.38 (1.81-6.31)	2.89 (1.59-5.25)
Undiagnosed				
Education	Low	0.12 (0.03-0.46)	0.59 (0.27-1.32)	1.36 (0.54-3.41)
	Medium (Ref: High)	0.19 (0.05-0.64)	0.76 (0.33-1.75)	0.95 (0.34-2.67)
Income	Poorest		0.97 (0.47-1.99)	0.73 (0.36-1.49)
	Q2		1.03 (0.49-2.16)	1.02 (0.47-2.22)
	Q3 (Ref: Richest)		0.92 (0.46-1.85)	1.01 (0.53-1.94)
Health insurance	Public (Ref: Private)		0.62 (0.21-1.83)	2.17 (0.72-6.47)
Untreated				
Education	Low	0.63 (0.18-2.21)	0.78 (0.35-1.70)	2.29 (0.92-5.72)
	Medium (Ref: High)	0.52 (0.14-1.90)	0.72 (0.34-1.52)	1.13 (0.40-3.22)
Income	Poorest		1.13 (0.53-2.41)	1.00 (0.47-2.15)
	Q2		0.94 (0.42-2.11)	0.88 (0.40-1.93)

Variable	Exposure	2003	2010	2017
	Q3 (Ref: Richest)		1.00 (0.47-2.14)	1.15 (0.56-2.36)
Health insurance	Public (Ref: Private)		2.29 (0.68-7.69)	2.16 (0.66-7.06)
Uncontrolled				
Education	Low	1.24 (0.27-5.81)	0.70 (0.32-1.55)	2.69 (1.07-6.77)
	Medium (Ref: High)	0.95 (0.21-4.35)	0.66 (0.29-1.49)	1.11 (0.43-2.87)
Income	Poorest		1.48 (0.75-2.94)	1.57 (0.77-3.18)
	Q2		1.35 (0.61-3.01)	1.10 (0.56-2.14)
	Q3 (Ref: Richest)		1.06 (0.55-2.05)	1.32 (0.76-2.32)
Health insurance	Public (Ref: Private)		1.35 (0.55-3.31)	3.90 (1.61-9.46)

Odds ratios and 95% CIs calculated from age-and survey year-adjusted logistic regressions. SEP indicators were evaluated in separate models. Educational level: low (<8y), medium (8-12y), high (>12y). Income: quartiles of household monthly income equivalised to the composition of the household. Income and health insurance measured in 2010 and 2017 only.

Table A5.7: SEP inequalities in hypertension estimated using RII (males).

Variable	Exposure	2003	2010	2017
Prevalence	Education	0.92 (0.65-1.29)	1.21 (0.82-1.78)	1.00 (0.70-1.43)
Uncontrolled		1.07 (0.87-1.31)	1.11 (0.88-1.40)	1.26 (0.88-1.81)
Undiagnosed		1.55 (0.98-2.46)	1.32 (0.64-2.74)	1.92 (1.05-3.53)
Untreated		1.22 (0.90-1.65)	1.14 (0.70-1.87)	1.54 (0.82-2.88)
Prevalence	Income		0.80 (0.54-1.18)	0.97 (0.67-1.40)
Uncontrolled			0.91 (0.73-1.14)	1.12 (0.84-1.50)
Undiagnosed			1.17 (0.67-2.06)	1.10 (0.64-1.88)
Untreated			1.27 (0.87-1.85)	1.05 (0.64-1.71)

Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear models (Poisson family and log link) adjusted for the SEP ridit scores (of education or income in separate models), survey year and age. RII can be interpreted as the rate ratio between the lowest and highest groups. Income measured in 2010 and 2017 only

Table A5.8: SEP inequalities in hypertension estimated using RII (females).

Variable	Exposure	2003	2010	2017

Variable	Exposure	2003	2010	2017
Prevalence	Education	1.58 (1.13-2.20)	1.15 (0.82-1.60)	1.56 (1.06-2.32)
Uncontrolled		1.10 (0.84-1.45)	0.92 (0.70-1.20)	1.89 (1.27-2.83)
Undiagnosed		0.28 (0.12-0.66)	0.61 (0.31-1.19)	1.54 (0.77-3.07)
Untreated		1.03 (0.60-1.76)	0.88 (0.47-1.63)	2.50 (1.36-4.62)
Prevalence	Income		1.10 (0.79-1.51)	1.69 (1.19-2.40)
Uncontrolled			1.12 (0.83-1.50)	1.27 (0.88-1.83)
Undiagnosed			0.94 (0.48-1.84)	0.75 (0.39-1.44)
Untreated			1.12 (0.61-2.08)	1.10 (0.56-2.15)

Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear models (Poisson family and log link) adjusted for the SEP ridit scores (of education or income in separate models), survey year and age. RII can be interpreted as the rate ratio between the lowest and highest groups. Income measured in 2010 and 2017 only

Table A5.9: SEP inequalities in hypertension estimated using SII (males).

Variable	Exposure	2003	2010	2017
Prevalence	Education	-0.01 (-0.14-0.13)	0.12 (0.00-0.25)	0.04 (-0.09-0.16)
Undiagnosed		0.24 (0.00-0.47)	0.12 (-0.18-0.42)	0.26 (0.02-0.50)
Untreated		0.15 (-0.06-0.37)	0.09 (-0.15-0.34)	0.18 (-0.07-0.42)
Uncontrolled		0.06 (-0.13-0.25)	0.09 (-0.11-0.29)	0.17 (-0.08-0.41)
Prevalence	Income		-0.05 (-0.17-0.07)	0.03 (-0.08-0.14)
Undiagnosed			0.06 (-0.17-0.30)	0.04 (-0.19-0.26)
Untreated			0.13 (-0.08-0.33)	0.02 (-0.20-0.24)
Uncontrolled			-0.08 (-0.27-0.11)	0.08 (-0.13-0.29)

Slope Index of Inequality (SII) and 95% CIs estimated from generalised linear models (Gaussian family and identity link) adjusted for the SEP ridit scores (of education or income in separate models), survey year and age. SII can be interpreted as the rate difference between the lowest and highest groups. Income measured in 2010 and 2017 only.

Table A5.10: SEP inequalities in hypertension estimated using SII (females).

Variable	Exposure	2003	2010	2017
Prevalence	Education	0.14 (0.04-0.23)	0.06 (-0.05-0.17)	0.17 (0.07-0.28)

Variable	Exposure	2003	2010	2017
Undiagnosed		-0.35 (-0.62–0.09)	-0.13 (-0.30-0.05)	0.11 (-0.06-0.29)
Untreated		0.01 (-0.23-0.24)	-0.05 (-0.24-0.14)	0.25 (0.08-0.42)
Uncontrolled		0.08 (-0.13-0.29)	-0.06 (-0.24-0.13)	0.38 (0.16-0.60)
Prevalence	Income		0.03 (-0.07-0.12)	0.15 (0.05-0.25)
Undiagnosed			-0.02 (-0.20-0.16)	-0.08 (-0.26-0.10)
Untreated			0.04 (-0.16-0.24)	0.02 (-0.17-0.21)
Uncontrolled			0.07 (-0.12-0.27)	0.14 (-0.08-0.36)

Slope Index of Inequality (SII) and 95% CIs estimated from generalised linear models (Gaussian family and identity link) adjusted for the SEP ridit scores (of education or income in separate models), survey year and age. SII can be interpreted as the rate difference between the lowest and highest groups. Income measured in 2010 and 2017 only.

Table A5.11: Relative change over time in SEP inequalities in hypertension outcomes (males).

Variable	Exposure	2010 versus 2003	2017 versus 2010	2017 versus 2003
Prevalence	Education	1.62 (1.06-2.50)	0.90 (0.57-1.44)	1.47 (0.96-2.25)
	Income		1.22 (0.72-2.09)	
	Health insurance (OR public vs private)		1.04 (0.47-2.30)	
Undiagnosed	Education	0.89 (0.40-1.95)	1.57 (0.66-3.76)	1.39 (0.69-2.82)
	Income		0.98 (0.45-2.14)	
	Health insurance (OR public vs private)		1.59 (0.45-5.70)	
Untreated	Education	0.81 (0.48-1.35)	1.23 (0.62-2.43)	0.99 (0.56-1.75)
	Income		0.84 (0.46-1.54)	
	Health insurance (OR public vs private)		1.26 (0.36-4.41)	
Uncontrolled	Education	1.01 (0.78-1.31)	1.19 (0.82-1.74)	1.21 (0.85-1.71)
	Income		1.24 (0.86-1.79)	

Variable	Exposure	2010 versus 2003	2017 versus 2010	2017 versus 2003
	Health insurance (OR public vs private)		4.01 (1.02-15.77)	

Changes over time analysed by the inclusion of the two-way interaction term SEP indicator by survey year to the models while adjusting for age. SEP indicators were evaluated in separate models. Relative Index of Inequality (RII) and Odds ratio (ORs) and 95% CIs estimated from generalised linear models. Using the interaction term, the change in RII can be interpreted as the ratio of year-specific RIIs. Income and health insurance measured in 2010 and 2017 only.

Table A5.12: Relative change over time in SEP inequalities in hypertension outcomes (females).

Variable	Exposure	2010 versus 2003	2017 versus 2010	2017 versus 2003
Prevalence	Education	0.92 (0.58-1.46)	1.45 (0.92-2.29)	1.33 (0.85-2.09)
	Income		1.51 (0.94-2.41)	
	Health insurance (OR public vs private)		0.83 (0.35-2.00)	
Undiagnosed	Education	1.73 (0.60-5.02)	2.21 (0.86-5.66)	3.82 (1.36-10.70)
	Income		0.81 (0.32-2.06)	
	Health insurance (OR public vs private)		3.48 (0.75-16.27)	
Untreated	Education	0.65 (0.30-1.42)	2.60 (1.09-6.23)	1.69 (0.75-3.80)
	Income		0.98 (0.40-2.41)	
	Health insurance (OR public vs private)		0.96 (0.17-5.28)	
Uncontrolled	Education	0.89 (0.62-1.29)	2.01 (1.27-3.19)	1.80 (1.14-2.84)
	Income		1.11 (0.69-1.77)	
	Health insurance (OR public vs private)		2.86 (0.80-10.21)	

Changes over time analysed by the inclusion of the two-way interaction term SEP indicator by survey year to the models while adjusting for age. SEP indicators were evaluated in separate models. Relative Index of Inequality (RII) and Odds ratio (ORs) and 95% CIs estimated from generalised linear models. Using the interaction term, the change in RII can be interpreted as the ratio of year-specific RIIs. Income and health insurance measured in 2010 and 2017 only.

Table A5.13: Absolute change over time in SEP inequalities in hypertension outcomes (males).

Variable	Exposure	2010 versus 2003	2017 versus 2010	2017 versus 2003
Prevalence	Education (SII)	0.13 (-0.02-0.29)	-0.08 (-0.23-0.07)	0.05 (-0.1-0.21)
	Occupation (SII)	0.09 (-0.17-0.34)	0.02 (-0.21-0.25)	0.11 (-0.15-0.37)
	Health insurance (β public vs private)		0 (-0.12-0.11)	
	Income (SII)		0.08 (-0.09-0.24)	
Undiagnosed	Education (SII)	-0.07 (-0.42-0.29)	0.18 (-0.17-0.54)	0.11 (-0.21-0.44)
	Occupation (SII)	-0.16 (-0.59-0.27)	-0.04 (-0.54-0.47)	-0.2 (-0.67-0.28)
	Health insurance (β public vs private)		0.09 (-0.17-0.35)	
	Income (SII)		-0.01 (-0.33-0.32)	
Untreated	Education (SII)	-0.08 (-0.37-0.21)	0.11 (-0.2-0.42)	0.03 (-0.25-0.31)
	Occupation (SII)	-0.04 (-0.39-0.31)	-0.01 (-0.45-0.43)	-0.05 (-0.44-0.33)
	Health insurance (β public vs private)		0.05 (-0.21-0.31)	
	Income (SII)		-0.09 (-0.39-0.21)	
Uncontrolled	Education (SII)	0.01 (-0.22-0.24)	0.12 (-0.16-0.41)	0.14 (-0.12-0.4)
	Occupation (SII)	0.11 (-0.05-0.27)	0.09 (-0.36-0.55)	0.2 (-0.23-0.63)
	Health insurance (β public vs private)		0.25 (0-0.5)	
	Income (SII)		0.17 (-0.11-0.45)	

Changes over time analysed by the inclusion of the two-way interaction term SEP indicator by survey year to the models while adjusting for age. SEP indicators were evaluated in separate models. Slope Index of Inequality (SII) and Linear regression coefficient (β) and 95% CIs estimated from generalised linear models using Gaussian family and identity link. Using the interaction term, the change in SII can be interpreted as the absolute difference of year-specific SIIs. Income and health insurance measured in 2010 and 2017 only.

Table A5.14: Absolute change over time in SEP inequalities in hypertension outcomes (females).

Variable	Exposure	2010 versus 2003	2017 versus 2010	2017 versus 2003
Prevalence	Education (SII)	-0.03 (-0.17-0.1)	0.09 (-0.04-0.22)	0.05 (-0.07-0.17)
	Occupation (SII)	-0.03 (-0.34-0.27)	-0.04 (-0.31-0.22)	-0.08 (-0.38-0.23)
	Health insurance (β public vs private)		-0.03 (-0.13-0.06)	
	Income (SII)		0.13 (-0.01-0.26)	
Undiagnosed	Education (SII)	0.16 (-0.15-0.47)	0.2 (-0.04-0.45)	0.36 (0.07-0.66)
	Occupation (SII)	0.19 (-0.46-0.83)	-0.45 (-1.02-0.12)	-0.26 (-0.94-0.41)
	Health insurance (β public vs private)		0.22 (-0.06-0.5)	
	Income (SII)		-0.06 (-0.31-0.19)	
Untreated	Education (SII)	-0.07 (-0.37-0.23)	0.3 (0.05-0.55)	0.22 (-0.06-0.51)
	Occupation (SII)	0.07 (-0.57-0.7)	-0.14 (-0.71-0.43)	-0.07 (-0.72-0.58)
	Health insurance (β public vs private)		0 (-0.24-0.23)	
	Income (SII)		-0.03 (-0.3-0.25)	
Uncontrolled	Education (SII)	-0.1 (-0.36-0.17)	0.41 (0.14-0.68)	0.32 (0.03-0.6)
	Occupation (SII)	-0.02 (-0.49-0.46)	0.44 (-0.16-1.05)	0.43 (-0.19-1.05)
	Health insurance (β public vs private)		0.25 (-0.03-0.53)	

Variable	Exposure	2010 versus 2003	2017 versus 2010	2017 versus 2003
	Income (SII)		0.06 (-0.24-0.35)	

Changes over time analysed by the inclusion of the two-way interaction term SEP indicator by survey year to the models while adjusting for age. SEP indicators were evaluated in separate models. Slope Index of Inequality (SII) and Linear regression coefficient (β) and 95% CIs estimated from generalised linear models using Gaussian family and identity link. Using the interaction term, the change in SII can be interpreted as the absolute difference of year-specific SIIs. Income and health insurance measured in 2010 and 2017 only.

Appendix 6: Multilevel analyses of individual-level socioeconomic inequalities in the prevalence and management of hypertension (Chapter 6)

Table A6.1: Hypertension outcomes by quartiles of the socioeconomic environment measures (observed): males.

Variable	Exposure	2003	2010	2017
Prevalence				
Income inequality	Q1	36 (31-41)	37 (30-45)	25 (19-31)
	Q2	41 (33-49)	33 (27-40)	33 (27-40)
	Q3	41 (35-46)	35 (29-41)	35 (29-42)
	Q4	30 (22-40)	24 (18-30)	32 (26-38)
Poverty	Q1	39 (30-49)	30 (22-40)	32 (25-39)
	Q2	41 (35-47)	29 (24-35)	26 (20-33)
	Q3	33 (26-41)	33 (26-40)	31 (26-37)
	Q4	35 (30-41)	37 (32-43)	36 (30-42)
Unemployment	Q1	42 (32-52)	28 (20-38)	29 (21-38)
	Q2	33 (26-40)	32 (26-39)	30 (24-37)
	Q3	35 (30-41)	31 (25-37)	29 (24-34)
	Q4	39 (34-44)	38 (32-44)	37 (32-43)
Undiagnosed				
Income inequality	Q1	62 (46-76)	37 (25-51)	44 (32-58)
	Q2	59 (48-69)	49 (38-60)	37 (26-51)
	Q3	45 (32-58)	55 (40-70)	38 (29-49)
	Q4	54 (43-64)	25 (17-34)	48 (35-62)
Poverty	Q1	56 (35-75)	42 (24-63)	38 (26-52)
	Q2	55 (43-66)	26 (18-36)	27 (16-41)
	Q3	59 (48-69)	46 (33-59)	51 (41-62)
	Q4	50 (41-59)	55 (45-65)	48 (36-60)
Unemployment	Q1	63 (43-79)	36 (19-57)	33 (21-48)
	Q2	57 (44-68)	44 (30-59)	47 (32-62)
	Q3	49 (38-60)	33 (25-44)	45 (35-55)
	Q4	49 (40-58)	56 (46-66)	42 (32-52)
Untreated				
Income inequality	Q1	79 (72-84)	52 (40-63)	44 (31-57)
	Q2	78 (67-85)	63 (53-72)	33 (21-46)
	Q3	70 (56-81)	55 (43-67)	39 (30-50)
	Q4	79 (68-87)	53 (42-64)	58 (45-70)
Poverty	Q1	72 (52-86)	54 (40-68)	32 (20-47)

Variable	Exposure	2003	2010	2017
	Q2	78 (69-85)	58 (47-68)	35 (23-50)
	Q3	76 (67-83)	55 (44-65)	54 (44-64)
	Q4	76 (70-82)	56 (46-65)	50 (38-61)
Unemployment	Q1	81 (62-92)	56 (42-68)	30 (18-45)
	Q2	75 (66-82)	57 (45-69)	45 (31-61)
	Q3	74 (63-83)	55 (45-65)	53 (42-63)
	Q4	73 (66-80)	55 (45-65)	44 (34-54)
Uncontrolled				
Income inequality	Q1	96 (89-98)	80 (68-88)	73 (62-82)
	Q2	96 (91-98)	91 (83-95)	68 (54-80)
	Q3	88 (77-94)	87 (79-92)	64 (52-74)
	Q4	97 (93-99)	85 (76-92)	82 (71-90)
Poverty	Q1	92 (71-98)	85 (72-93)	69 (54-80)
	Q2	94 (88-97)	84 (75-90)	64 (47-78)
	Q3	94 (89-97)	88 (78-94)	79 (71-86)
	Q4	95 (92-97)	86 (77-91)	73 (64-81)
Unemployment	Q1	92 (75-98)	86 (72-94)	65 (47-79)
	Q2	94 (88-98)	85 (74-92)	71 (57-82)
	Q3	95 (89-97)	86 (78-91)	83 (74-89)
	Q4	94 (90-96)	86 (77-91)	69 (61-76)

Observed estimates (% and 95% CI). Socioeconomic environment measures categorised in quartiles. Q1: lowest quartile (e.g. counties with the lowest poverty levels) and Q4: highest quartile (e.g. counties with the highest poverty levels).

Table A6.2: Hypertension outcomes by quartiles of the socioeconomic environment measures (observed): females.

Variable	Exposure	2003	2010	2017
Prevalence				
Income inequality	Q1	31 (27-35)	31 (25-37)	31 (25-37)
	Q2	33 (27-40)	30 (24-36)	31 (26-37)
	Q3	32 (28-37)	35 (29-41)	31 (26-36)
	Q4	28 (23-33)	32 (26-39)	29 (23-34)
Poverty	Q1	28 (23-35)	27 (22-34)	32 (26-39)
	Q2	32 (27-38)	32 (26-39)	33 (27-39)
	Q3	28 (24-32)	31 (26-38)	27 (23-33)

Variable	Exposure	2003	2010	2017
	Q4	37 (32-42)	37 (31-43)	29 (25-33)
Unemployment	Q1	31 (24-38)	31 (24-38)	32 (25-39)
	Q2	30 (26-35)	29 (24-35)	31 (25-37)
	Q3	30 (25-35)	31 (25-38)	25 (21-29)
	Q4	33 (29-38)	36 (30-43)	34 (30-38)
Undiagnosed				
Income inequality	Q1	21 (13-32)	32 (23-43)	20 (13-28)
	Q2	29 (21-38)	23 (16-33)	30 (21-42)
	Q3	24 (16-36)	24 (17-33)	28 (19-38)
	Q4	36 (27-45)	23 (15-34)	26 (19-35)
Poverty	Q1	25 (16-37)	23 (16-31)	23 (15-34)
	Q2	31 (22-43)	24 (16-35)	28 (18-42)
	Q3	23 (15-32)	28 (18-42)	28 (21-37)
	Q4	29 (21-37)	28 (22-35)	26 (20-32)
Unemployment	Q1	25 (16-38)	25 (17-37)	13 (8-20)
	Q2	27 (18-38)	21 (14-31)	29 (20-41)
	Q3	27 (18-39)	25 (17-33)	33 (26-41)
	Q4	28 (21-37)	31 (23-42)	31 (22-42)
Untreated				
Income inequality	Q1	44 (32-56)	38 (27-50)	30 (20-42)
	Q2	46 (32-61)	25 (18-34)	22 (13-35)
	Q3	45 (35-54)	36 (26-48)	25 (17-36)
	Q4	47 (36-58)	27 (18-38)	30 (23-38)
Poverty	Q1	40 (24-58)	19 (13-28)	26 (17-37)
	Q2	46 (36-56)	34 (22-48)	33 (21-47)
	Q3	46 (35-58)	34 (25-45)	24 (17-33)
	Q4	49 (40-58)	37 (29-47)	22 (17-27)
Unemployment	Q1	45 (29-62)	20 (12-31)	20 (13-30)
	Q2	40 (28-53)	30 (22-39)	31 (21-44)
	Q3	46 (36-56)	39 (27-52)	29 (22-37)
	Q4	50 (42-58)	37 (28-47)	27 (18-39)
Uncontrolled				
Income inequality	Q1	81 (73-87)	75 (66-82)	61 (47-74)
	Q2	79 (65-88)	68 (56-78)	59 (47-69)
	Q3	81 (68-90)	61 (50-71)	63 (54-71)
	Q4	80 (68-88)	68 (59-77)	58 (49-67)
Poverty	Q1	74 (58-85)	72 (62-80)	55 (44-66)
	Q2	80 (68-88)	69 (56-79)	73 (64-81)

Variable	Exposure	2003	2010	2017
	Q3	81 (71-88)	61 (48-72)	55 (43-67)
	Q4	85 (77-91)	71 (64-78)	55 (47-62)
Unemployment	Q1	74 (59-85)	67 (57-76)	57 (44-69)
	Q2	82 (69-90)	64 (50-76)	60 (46-72)
	Q3	80 (71-87)	72 (62-79)	63 (55-70)
	Q4	84 (76-90)	69 (59-77)	62 (53-70)

Observed estimates (% and 95% CI). Socioeconomic environment measures categorised in quartiles. Q1: lowest quartile (e.g. counties with the lowest poverty levels) and Q4: highest quartile (e.g. counties with the highest poverty levels).

Table A6.3: Hypertension outcomes by quartiles of the socioeconomic environment measures (age-standardised): males.

Variable	Exposure	2003	2010	2017
Prevalence				
Income inequality	Q1	39 (34-43)	37 (31-42)	26 (20-31)
	Q2	43 (36-51)	36 (30-43)	30 (25-35)
	Q3	44 (38-50)	35 (29-42)	34 (29-40)
	Q4	36 (28-46)	27 (21-34)	35 (30-40)
Poverty	Q1	42 (33-51)	31 (23-41)	31 (24-38)
	Q2	45 (39-50)	32 (28-38)	27 (22-33)
	Q3	37 (29-45)	35 (29-41)	33 (28-38)
	Q4	38 (34-43)	37 (33-41)	33 (28-37)
Unemployment	Q1	45 (37-54)	30 (22-40)	28 (22-35)
	Q2	35 (28-42)	35 (29-42)	31 (25-38)
	Q3	40 (35-46)	32 (28-37)	31 (27-36)
	Q4	41 (36-46)	38 (33-43)	34 (30-38)
Undiagnosed				
Income inequality	Q1	56 (44-67)	38 (26-51)	45 (32-58)
	Q2	55 (44-66)	45 (35-55)	36 (25-50)
	Q3	40 (29-51)	55 (38-71)	40 (29-51)
	Q4	49 (40-57)	25 (17-33)	47 (33-61)
Poverty	Q1	50 (30-69)	40 (26-56)	37 (26-48)
	Q2	52 (42-62)	26 (17-35)	26 (17-38)
	Q3	53 (44-61)	45 (32-58)	50 (39-61)
	Q4	47 (39-55)	55 (43-66)	48 (37-59)

Variable	Exposure	2003	2010	2017
Unemployment	Q1	59 (41-76)	36 (25-49)	35 (24-47)
	Q2	53 (42-64)	38 (26-50)	46 (29-63)
	Q3	45 (35-55)	34 (25-44)	45 (35-55)
	Q4	44 (37-52)	55 (43-67)	42 (32-52)
Untreated				
Income inequality	Q1	67 (60-73)	53 (42-64)	44 (33-56)
	Q2	73 (63-81)	56 (47-64)	34 (22-49)
	Q3	57 (44-69)	51 (41-61)	39 (30-49)
	Q4	75 (63-85)	48 (39-57)	55 (41-68)
Poverty	Q1	65 (46-81)	49 (38-60)	32 (22-45)
	Q2	73 (62-81)	54 (44-63)	35 (22-50)
	Q3	68 (59-75)	53 (42-64)	51 (42-60)
	Q4	69 (63-75)	54 (45-62)	50 (40-59)
Unemployment	Q1	72 (54-86)	51 (41-61)	33 (22-46)
	Q2	71 (62-79)	53 (40-66)	42 (28-58)
	Q3	69 (60-77)	54 (44-63)	52 (43-62)
	Q4	64 (56-72)	53 (45-60)	44 (35-54)
Uncontrolled				
Income inequality	Q1	95 (87-98)	81 (73-88)	73 (62-83)
	Q2	94 (90-97)	90 (83-95)	65 (51-78)
	Q3	85 (72-93)	87 (79-93)	67 (56-76)
	Q4	97 (91-99)	85 (76-92)	81 (69-90)
Poverty	Q1	89 (72-97)	85 (78-90)	67 (54-78)
	Q2	94 (89-97)	83 (73-90)	63 (45-78)
	Q3	93 (86-97)	89 (81-94)	78 (70-85)
	Q4	93 (89-96)	86 (79-92)	74 (65-81)
Unemployment	Q1	90 (76-97)	86 (77-92)	66 (50-80)
	Q2	95 (90-98)	84 (73-92)	70 (55-82)
	Q3	94 (88-97)	86 (78-92)	83 (75-89)
	Q4	92 (88-95)	86 (79-92)	68 (60-76)

Values and 95% CIs were directly age-gender-standardised using data from Census 2017 (age groups 17-44, 45-64 and 65+ years). Socioeconomic environment measures categorised in quartiles. Q1: lowest quartile (e.g. counties with the lowest poverty levels) and Q4: highest quartile (e.g. counties with the highest poverty levels).

Table A6.4: Hypertension outcomes by quartiles of the socioeconomic environment measures (age-standardised): females.

Variable	Exposure	2003	2010	2017
Prevalence				
Income inequality	Q1	35 (31-39)	35 (31-39)	31 (26-36)
	Q2	38 (32-44)	31 (26-37)	31 (28-36)
	Q3	35 (31-40)	37 (31-43)	30 (25-35)
	Q4	32 (27-38)	35 (31-40)	29 (25-34)
Poverty	Q1	33 (27-40)	29 (24-33)	32 (27-38)
	Q2	36 (32-40)	36 (31-42)	33 (28-38)
	Q3	32 (28-37)	35 (30-40)	28 (24-31)
	Q4	40 (35-45)	38 (32-43)	29 (26-32)
Unemployment	Q1	35 (28-42)	30 (26-35)	31 (27-36)
	Q2	33 (28-38)	33 (28-37)	31 (26-37)
	Q3	35 (31-39)	36 (30-42)	26 (23-30)
	Q4	38 (33-42)	39 (33-45)	33 (30-36)
Undiagnosed				
Income inequality	Q1	21 (13-31)	29 (22-38)	20 (13-28)
	Q2	25 (19-32)	22 (15-31)	31 (22-41)
	Q3	25 (16-34)	23 (16-30)	26 (20-34)
	Q4	37 (28-46)	22 (14-32)	26 (19-35)
Poverty	Q1	27 (17-40)	24 (17-31)	22 (15-31)
	Q2	29 (20-38)	24 (15-35)	27 (18-39)
	Q3	24 (17-33)	27 (17-38)	29 (22-37)
	Q4	29 (22-36)	24 (19-30)	26 (20-32)
Unemployment	Q1	27 (16-40)	28 (19-39)	14 (8-21)
	Q2	28 (19-38)	22 (14-32)	29 (20-39)
	Q3	26 (18-34)	22 (15-30)	32 (25-40)
	Q4	28 (22-36)	27 (21-35)	31 (24-38)
Untreated				
Income inequality	Q1	44 (31-57)	35 (25-46)	32 (24-41)
	Q2	41 (30-53)	24 (16-33)	22 (14-34)
	Q3	42 (33-51)	31 (23-40)	23 (17-30)
	Q4	43 (34-52)	26 (18-36)	29 (22-37)
Poverty	Q1	41 (25-59)	21 (14-29)	25 (17-34)
	Q2	43 (34-53)	30 (20-42)	31 (23-40)
	Q3	44 (34-54)	31 (23-40)	25 (18-33)
	Q4	42 (35-49)	34 (25-44)	22 (17-27)

Variable	Exposure	2003	2010	2017
Unemployment	Q1	46 (31-62)	21 (12-33)	20 (12-31)
	Q2	39 (28-51)	31 (23-40)	30 (22-39)
	Q3	41 (33-50)	32 (24-42)	29 (22-36)
	Q4	43 (36-49)	32 (24-41)	26 (19-34)
Uncontrolled				
Income inequality	Q1	81 (73-88)	75 (66-82)	64 (52-74)
	Q2	79 (66-88)	68 (58-78)	58 (47-69)
	Q3	84 (75-91)	61 (53-69)	62 (53-70)
	Q4	79 (68-87)	68 (60-76)	58 (49-67)
Poverty	Q1	76 (63-86)	70 (62-78)	56 (45-67)
	Q2	81 (70-89)	68 (58-77)	73 (64-81)
	Q3	81 (72-88)	62 (53-72)	55 (44-66)
	Q4	85 (78-91)	71 (63-78)	54 (46-62)
Unemployment	Q1	76 (65-86)	64 (55-72)	56 (43-68)
	Q2	82 (70-91)	65 (54-76)	60 (50-70)
	Q3	81 (74-88)	71 (62-78)	61 (54-68)
	Q4	83 (76-89)	68 (59-76)	62 (53-69)

Values and 95% CIs were directly age-gender-standardised using data from Census 2017 (age groups 17-44, 45-64 and 65+ years). Socioeconomic environment measures categorised in quartiles. Q1: lowest quartile (e.g. counties with the lowest poverty levels) and Q4: highest quartile (e.g. counties with the highest poverty levels).

Table A6.5: Individual educational-based RII for hypertension: single-level versus multilevel models (males).

Area	2003	2010	2017
Single-level	0.92 (0.65- 1.30)	1.21 (0.82- 1.78)	1.00 (0.70- 1.43)
Multilevel No area-level measure	0.81 (0.61- 1.09)	0.97 (0.71- 1.33)	1.22 (0.89- 1.66)
Multilevel Income inequality	0.83 (0.62- 1.12)	0.96 (0.71- 1.32)	1.26 (0.92- 1.71)
Multilevel Poverty	0.85 (0.62- 1.16)	0.92 (0.67- 1.26)	1.23 (0.90- 1.68)
Multilevel Unemployment	0.84 (0.62- 1.13)	0.94 (0.69- 1.28)	1.18 (0.86- 1.62)

Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear two-level models using Poisson (log link) function. Multilevel models: 1st level= age (continuous) + individual educational ridit + socioeconomic environment measure + interaction term (individual educational ridit X socioeconomic environment measure); 2nd level= county (random intercept) + random slope for educational ridit. Income inequality: Gini coefficient (%). Educational ridit was calculated using educational levels in reverse order (higher ridit-score for the lowest educational level).

Table A6.6: Individual educational-based RII for hypertension: single-level versus multilevel models (females).

Area	2003	2010	2017
Single-level	1.58 (1.13- 2.20)	1.15 (0.82- 1.60)	1.56 (1.06- 2.32)
Multilevel No area-level measure	1.77 (1.24- 2.52)	1.13 (0.81- 1.59)	1.66 (1.18- 2.32)
Multilevel Income inequality	1.76 (1.24- 2.52)	1.13 (0.81- 1.59)	1.67 (1.20- 2.33)
Multilevel Poverty	1.61 (1.12- 2.30)	1.08 (0.76- 1.53)	1.72 (1.22- 2.41)
Multilevel Unemployment	1.67 (1.17- 2.39)	1.10 (0.78- 1.55)	1.65 (1.17- 2.33)

Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear two-level models using Poisson (log link) function. Multilevel models: 1st level= age (continuous) + individual educational ridit + socioeconomic environment measure + interaction term (individual educational ridit X socioeconomic environment measure); 2nd level= county (random intercept) + random slope for educational ridit. Income inequality: Gini coefficient (%). Educational ridit was calculated using educational levels in reverse order (higher ridit-score for the lowest educational level).

Table A6.7: Individual educational-based SII for hypertension: single-level versus multilevel models (males).

Area	2003	2010	2017
Single-level	-0.01 (-0.14- 0.13)	0.12 (0.00- 0.25)	0.04 (-0.09- 0.16)
Multilevel No area-level measure	-0.05 (-0.17- 0.06)	0.04 (-0.05- 0.12)	0.07 (-0.02- 0.17)

Area	2003	2010	2017
Multilevel Income inequality	-0.04 (-0.16- 0.08)	0.03 (-0.05- 0.12)	0.08 (-0.02- 0.18)
Multilevel Poverty	-0.04 (-0.16- 0.08)	0.03 (-0.06- 0.11)	0.08 (-0.02- 0.18)
Multilevel Unemployment	-0.04 (-0.16- 0.08)	0.03 (-0.06- 0.11)	0.07 (-0.03- 0.16)

Slope Index of Inequality (SII) estimated from generalised linear two-level models using Gaussian (identity link) function. Single-level model: age (continuous) + individual educational ridit. Multilevel models: 1st level= Single-level variables + socioeconomic environment measure (continuous, separate models); 2nd level= county (random intercept) and random slope of the individual educational ridit.

Table A6.8: Individual educational-based SII for hypertension: single-level versus multilevel models (females).

Area	2003	2010	2017
Single-level	0.13 (0.04- 0.23)	0.06 (-0.05- 0.17)	0.17 (0.07- 0.28)
Multilevel No area-level measure	0.16 (0.07- 0.25)	0.08 (-0.01- 0.16)	0.17 (0.10- 0.25)
Multilevel Income inequality	0.16 (0.07- 0.25)	0.08 (0.00- 0.16)	0.17 (0.10- 0.25)
Multilevel Poverty	0.14 (0.04- 0.23)	0.07 (-0.02- 0.16)	0.18 (0.10- 0.25)
Multilevel Unemployment	0.14 (0.05- 0.23)	0.07 (-0.01- 0.16)	0.17 (0.10- 0.25)

Slope Index of Inequality (SII) estimated from generalised linear two-level models using Gaussian (identity link) function. Single-level model: age (continuous) + individual educational ridit. Multilevel models: 1st level= Single-level variables + socioeconomic environment measure (continuous, separate models); 2nd level= county (random intercept) and random slope of the individual educational ridit.

Table A6.9: Inequalities by socioeconomic environment measures using RII (males).

Area	Adjustment	2003	2010	2017
Income inequality	After adjustment	1.01 (1.00-1.01)	1.00 (0.98-1.01)	1.02 (1.00-1.03)

Area	Adjustment	2003	2010	2017
Income inequality	Before adjustment	1.01 (1.00-1.02)	1.00 (0.98-1.01)	1.02 (1.00-1.03)
Poverty	After adjustment	1.00 (0.99-1.00)	1.01 (1.00-1.02)	1.00 (0.99-1.01)
Poverty	Before adjustment	1.00 (0.99-1.00)	1.01 (1.00-1.02)	1.00 (0.99-1.01)
Unemployment	After adjustment	1.00 (0.98-1.01)	1.02 (1.00-1.04)	1.01 (0.99-1.02)
Unemployment	Before adjustment	0.99 (0.98-1.01)	1.02 (1.00-1.03)	1.01 (0.99-1.02)

Before and after individual educational level adjustment. Prevalence ratio (PR) and 95% CIs estimated from generalised linear two-level models using Poisson (log link) function. Multilevel models: 1st level= age + socioeconomic environment measure (continuous, separate models); 2nd level= county (random intercept). Socioeconomic environment + individual educational level model also included educational ridit in the 1st level and a random slope for educational level in the 2nd level.

Table A6.10: Inequalities by socioeconomic environment measures using RII (females).

Area	Adjustment	2003	2010	2017
Income inequality	After adjustment	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (0.99-1.01)
Income inequality	Before adjustment	1.00 (0.99-1.01)	1.00 (0.99-1.01)	1.00 (0.99-1.01)
Poverty	After adjustment	1.01 (1.01-1.02)	1.01 (1.00-1.02)	0.99 (0.98-1.00)
Poverty	Before adjustment	1.01 (1.01-1.02)	1.01 (1.00-1.02)	1.00 (0.99-1.01)
Unemployment	After adjustment	1.01 (1.00-1.03)	1.01 (1.00-1.02)	1.00 (0.99-1.01)
Unemployment	Before adjustment	1.02 (1.00-1.03)	1.01 (1.00-1.02)	1.00 (1.00-1.01)

Before and after individual educational level adjustment. Prevalence ratio (PR) and 95% CIs estimated from generalised linear two-level models using Poisson (log link) function. Multilevel models: 1st level= age + socioeconomic environment measure (continuous, separate models); 2nd level= county (random intercept). Socioeconomic environment + individual educational level model also included educational ridit in the 1st level and a random slope for educational level in the 2nd level.

Table A6.11: Individual educational-based inequalities (RII) after adjustment for lagged socioeconomic environment measures (males).

Variable	Area year	2003	2010	2017
Income inequality	1990	0.86 (0.63-1.18)	0.88 (0.63-1.25)	1.25 (0.89-1.75)

Variable	Area year	2003	2010	2017
	1996	0.83 (0.61-1.13)	1.17 (0.85-1.61)	1.15 (0.82-1.62)
	2003	0.83 (0.62-1.12)	0.99 (0.72-1.36)	1.20 (0.88-1.64)
	2009	0.81 (0.61-1.09)	0.97 (0.71-1.32)	1.23 (0.91-1.67)
	2017	0.83 (0.61-1.12)	0.96 (0.69-1.32)	1.26 (0.92-1.71)
Poverty	1990	0.87 (0.62-1.22)	0.85 (0.61-1.20)	1.29 (0.91-1.82)
	1996	0.87 (0.62-1.20)	1.06 (0.76-1.48)	1.18 (0.83-1.68)
	2003	0.85 (0.62-1.16)	0.90 (0.65-1.26)	1.23 (0.90-1.68)
	2009	0.82 (0.60-1.10)	0.92 (0.67-1.26)	1.21 (0.88-1.67)
	2017	0.83 (0.61-1.13)	0.92 (0.67-1.27)	1.23 (0.90-1.69)
Unemployment	1990	0.87 (0.63-1.20)	0.89 (0.63-1.25)	1.26 (0.90-1.77)
	1996	0.84 (0.61-1.15)	1.11 (0.82-1.51)	1.17 (0.84-1.65)
	2003	0.84 (0.62-1.13)	0.96 (0.70-1.32)	1.25 (0.91-1.70)
	2009	0.83 (0.61-1.11)	0.94 (0.69-1.28)	1.23 (0.90-1.67)
	2017	0.82 (0.60-1.11)	0.93 (0.68-1.27)	1.18 (0.86-1.63)

Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear two-level models using Poisson (log link) function. Single-level model: age (continuous) + individual educational ridit. Multilevel models: 1st level= Single-level variables + socioeconomic environment measure (continuous, separate models); 2nd level= county (random intercept) and random slope of the individual educational ridit.

Table A6.12: Individual educational-based inequalities (RII) after adjustment for lagged socioeconomic environment measures (females).

Variable	Area year	2003	2010	2017
Income inequality	1990	1.79 (1.19-2.70)	1.05 (0.69-1.59)	1.57 (1.06-2.32)
	1996	1.63 (1.11-2.40)	1.10 (0.75-1.61)	1.53 (1.06-2.20)
	2003	1.76 (1.23-2.52)	1.07 (0.76-1.51)	1.65 (1.18-2.30)
	2009	1.75 (1.24-2.48)	1.13 (0.81-1.59)	1.68 (1.22-2.32)
	2017	1.75 (1.23-2.50)	1.13 (0.80-1.59)	1.67 (1.20-2.32)
Poverty	1990	1.78 (1.17-2.71)	1.02 (0.67-1.55)	1.54 (1.04-2.28)
	1996	1.55 (1.06-2.29)	1.03 (0.68-1.54)	1.63 (1.11-2.39)
	2003	1.61 (1.12-2.30)	1.07 (0.76-1.52)	1.67 (1.19-2.34)
	2009	1.63 (1.15-2.32)	1.08 (0.76-1.53)	1.68 (1.19-2.38)
	2017	1.64 (1.14-2.35)	1.12 (0.79-1.58)	1.72 (1.23-2.40)
Unemployment	1990	1.84 (1.22-2.76)	1.05 (0.69-1.58)	1.55 (1.05-2.30)
	1996	1.61 (1.09-2.36)	1.08 (0.73-1.59)	1.56 (1.07-2.27)

Variable	Area year	2003	2010	2017
	2003	1.67 (1.17-2.39)	1.07 (0.76-1.50)	1.63 (1.16-2.29)
	2009	1.61 (1.12-2.31)	1.10 (0.78-1.55)	1.68 (1.19-2.37)
	2017	1.63 (1.12-2.37)	1.12 (0.80-1.58)	1.65 (1.17-2.32)

Relative Index of Inequality (RII) and 95% CIs estimated from generalised linear two-level models using Poisson (log link) function. Single-level model: age (continuous) + individual educational ridit. Multilevel models: 1st level= Single-level variables + socioeconomic environment measure (continuous, separate models); 2nd level= county (random intercept) and random slope of the individual educational ridit.

Table A6.13: Individual educational-based inequalities (SII) after adjustment for lagged socioeconomic environment measures (males).

Variable	Area year	2003	2010	2017
Income inequality	1990	-0.04 (-0.16-0.09)	0.01 (-0.09-0.10)	0.10 (-0.01-0.20)
	1996	-0.04 (-0.16-0.08)	0.08 (-0.01-0.17)	0.06 (-0.04-0.16)
	2003	-0.04 (-0.16-0.08)	0.04 (-0.04-0.13)	0.07 (-0.02-0.17)
	2009	-0.05 (-0.17-0.06)	0.03 (-0.05-0.12)	0.08 (-0.02-0.18)
	2017	-0.05 (-0.17-0.07)	0.03 (-0.06-0.12)	0.08 (-0.02-0.18)
Poverty	1990	-0.03 (-0.16-0.10)	0.00 (-0.09-0.09)	0.10 (0.00-0.21)
	1996	-0.03 (-0.15-0.10)	0.06 (-0.04-0.15)	0.07 (-0.03-0.18)
	2003	-0.04 (-0.16-0.08)	0.03 (-0.06-0.12)	0.08 (-0.02-0.18)
	2009	-0.05 (-0.17-0.06)	0.03 (-0.06-0.11)	0.08 (-0.02-0.17)
	2017	-0.04 (-0.16-0.08)	0.03 (-0.06-0.11)	0.08 (-0.02-0.18)
Unemployment	1990	-0.04 (-0.17-0.09)	0.01 (-0.08-0.10)	0.10 (0.00-0.20)
	1996	-0.04 (-0.16-0.09)	0.07 (-0.02-0.15)	0.06 (-0.04-0.16)
	2003	-0.04 (-0.16-0.08)	0.04 (-0.05-0.13)	0.08 (-0.02-0.18)
	2009	-0.04 (-0.16-0.07)	0.03 (-0.06-0.11)	0.08 (-0.02-0.18)
	2017	-0.05 (-0.16-0.07)	0.03 (-0.06-0.11)	0.07 (-0.03-0.16)

Slope Index of Inequality (SII) estimated from generalised linear two-level models using Gaussian (identity link) function. Single-level model: age (continuous) + individual educational ridit. Multilevel models: 1st level= Single-level variables + socioeconomic environment measure (continuous, separate models); 2nd level= county (random intercept) and random slope of the individual educational ridit.

Table A6.14: Individual educational-based inequalities (SII) after adjustment for lagged socioeconomic environment measures (females).

Variable	Area year	2003	2010	2017
Income inequality	1990	0.18 (0.08-0.28)	0.06 (-0.04-0.16)	0.16 (0.07-0.25)
	1996	0.14 (0.04-0.24)	0.08 (-0.01-0.17)	0.17 (0.08-0.25)
	2003	0.16 (0.07-0.25)	0.06 (-0.03-0.14)	0.17 (0.10-0.25)
	2009	0.16 (0.07-0.25)	0.08 (0.00-0.16)	0.18 (0.10-0.25)
	2017	0.16 (0.07-0.25)	0.08 (-0.01-0.16)	0.17 (0.10-0.25)
Poverty	1990	0.19 (0.09-0.30)	0.07 (-0.04-0.17)	0.16 (0.07-0.25)
	1996	0.13 (0.04-0.23)	0.07 (-0.03-0.16)	0.17 (0.08-0.25)
	2003	0.14 (0.04-0.23)	0.06 (-0.03-0.15)	0.17 (0.10-0.25)
	2009	0.14 (0.05-0.23)	0.07 (-0.02-0.16)	0.18 (0.10-0.25)
	2017	0.14 (0.04-0.23)	0.07 (-0.02-0.16)	0.18 (0.10-0.25)
Unemployment	1990	0.19 (0.09-0.29)	0.06 (-0.03-0.16)	0.16 (0.07-0.25)
	1996	0.14 (0.04-0.24)	0.07 (-0.02-0.17)	0.16 (0.08-0.25)
	2003	0.14 (0.05-0.23)	0.06 (-0.02-0.14)	0.17 (0.09-0.25)
	2009	0.13 (0.04-0.22)	0.07 (-0.01-0.16)	0.18 (0.10-0.25)
	2017	0.13 (0.04-0.23)	0.07 (-0.02-0.16)	0.17 (0.10-0.25)

Slope Index of Inequality (SII) estimated from generalised linear two-level models using Gaussian (identity link) function. Single-level model: age (continuous) + individual educational ridit. Multilevel models: 1st level= Single-level variables + socioeconomic environment measure (continuous, separate models); 2nd level= county (random intercept) and random slope of the individual educational ridit.

Appendix 7: Differences in all-cause and cardiovascular mortality rates by hypertension status and by socioeconomic position (Chapter 7)

Figure A7.1: PhD study protocol approval by the Ethics committee of the Pontificia Universidad Católica de Chile (PUC) (ID: 211116004)

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DE CHILE

Santiago, 29 de noviembre de 2021

De acuerdo a lo declarado por la investigador **Alvaro Passi Solar**, en la plataforma de evaluación ética UC, la Unidad de Ética y Seguridad en Investigación, deja constancia que el proyecto, titulado: **“Mortality by hypertension outcomes and by individual level socioeconomic position: The Chilean National Health Survey Mortality study"**, ID 211116004, es declarado exento de evaluación ética y seguridad pues no se investigará con personas, datos personales y/o sensibles, ni participarán en él seres vivos o se utilizará materiales, tangibles o intangibles, especialmente protegidos en la investigación científica y no se considera actividades de riesgo o agentes que puedan poner en riesgo a los sujetos que participan, realizan, y/o intervienen en la investigación, así como al medio ambiente.

Le saluda atentamente,

[redacted]

Alejandra Santana Lopez
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Figure A7.2: Schoenfeld's residual plot for all-cause mortality. ENS2003-2010 cohorts.

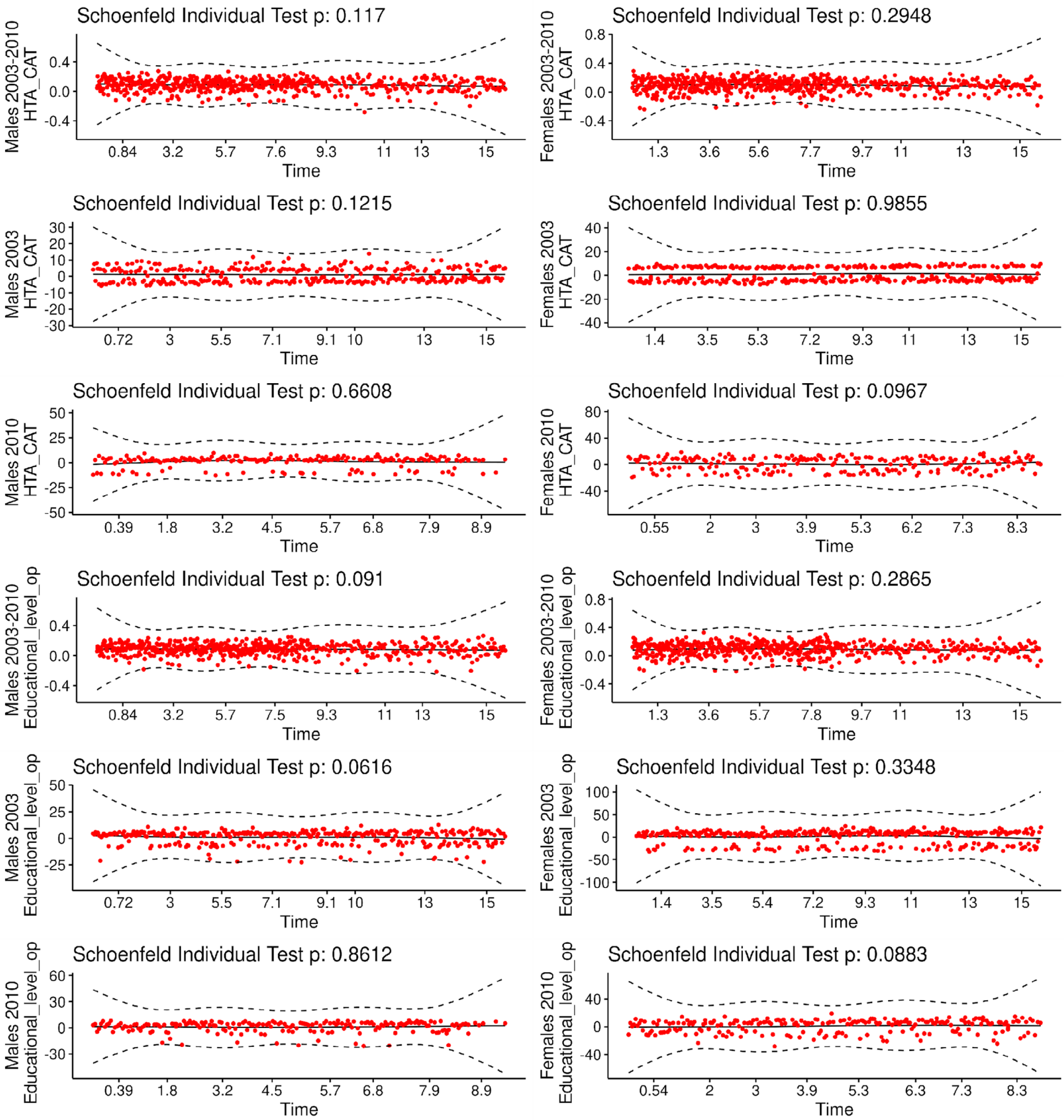

Figure A7.3: Schoenfeld's residual plot for cardiovascular mortality. ENS2003-2010 cohorts.

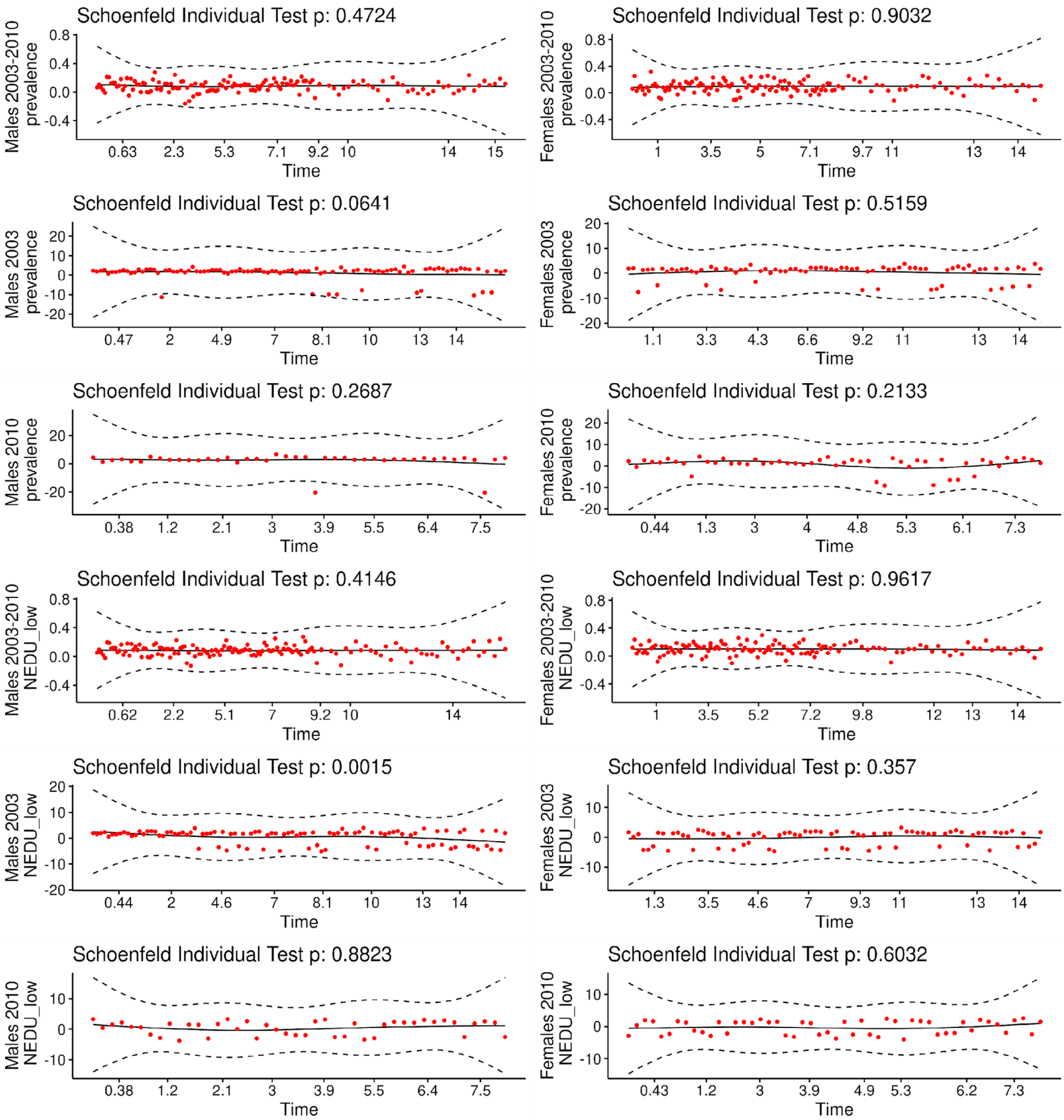

Figure A7.4: Schoenfeld's residual plot for cardiovascular mortality among males excluding early deaths (5y). ENS2003 cohort.