Geographies of life and death in Ecuador

Understanding inequalities in material deprivation and mortality in a context with deficient data sources

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DOCTORAL THESIS UPF / 2019

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“When one individual inflicts bodily injury upon another such that death results, we call the deed manslaughter; when the assailant knew in advance that the injury would be fatal, we call his deed murder. But when society places hundreds of proletarians in such a position that they inevitably meet a too early and an unnatural death, one which is quite as much a death by violence as that by the sword or bullet; when it deprives thousands of the necessaries of life, places them under conditions in which they cannot live – forces them, through the strong arm of the law, to remain in such conditions until that death ensues which is the inevitable consequence – knows that these thousands of victims must perish, and yet permits these conditions to remain, its deed is murder just as surely as the deed of the single individual; disguised, malicious murder, murder against which none can defend himself, which does not seem what it is, because no man sees the murderer, because the death of the victim seems a natural one, since the offence is more one of omission than of commission. But murder it remains.”

(Frederik Engels, 1845)

Dedicatoria:

A Susana, mi madre; Maruja, mi abuela; y María, mi tía; las tres mujeres que me enseñaron el valor de compartir y darlo todo por la gente que uno quiere;

a mi padre, que cuando yo era muy pequeño logró que me guste leer; y que me enseñó a ser crítico con todo lo que creía saber o haber aprendido;

a mi hermano Rodolfo, que me enseñó la importancia de hacer lo que te gusta y parece importante en la vida;

a Rambo, Ale, Vero, Ana, Brenda, Vanessa, Hugo, Juli, Laura, Mercè y tanta otra gente que ha sido mi familia durante este largo camino;

a Joaquín y Daniel, mi esperanza de un futuro (y presente) justo y alegre;

este trabajo es tan suyo como mío.

Acknowledgments / Agradecimientos

En estos últimos años, he tenido la inmensa suerte de cruzarme en el camino con muchísimas personas geniales que merecen ser reconocidas. Unas pocas líneas no alcanzan para expresar toda la gratitud y aprecio que tengo por ustedes; así que aquí pondré un pequeño texto y luego me encargaré de expresarlo en persona a cada una de ustedes.

Susana y **Fofo**, sin ustedes no hubiese podido hacer este trabajo. Les agradezco todo el esfuerzo, comprensión y cariño que me han dado siempre. Cada día me siento afortunado por la familia que tengo.

Marc y **Joan**, muchas gracias por guiar mi camino todos estos años. Es un honor poder trabajar tan cercanamente con personas que admiras y respetas mucho.

A Joan le agradezco sus sabios consejos, agudos comentarios y su preocupación tanto a nivel personal como profesional. Este proyecto nació hace muchos años en tu oficina y ahora lo vemos florecer. Como tú dices: “esto es sólo un comienzo”. Espero seguir colaborando y siendo amigos mucho tiempo más.

Marc, en unas líneas no cabe todo el agradecimiento y aprecio que mereces. Te agradezco el estar siempre ahí, en las buenas y en las malas, y en cada punto del trabajo. Cuando decidí empezar la tesis, no podía pensar en otro director más que tú. El tiempo ha probado que tenía razón. He aprendido mucho de ti en estos cinco años, y cada día sigo aprendiendo cosas nuevas contigo. En ti, he descubierto un director, un maestro, un compañero y un amigo. Aún nos quedan muchas cosas por planificar y trabajar juntos. Estoy seguro de que nuestros caminos se seguirán cruzando por mucho tiempo.

Carme, muchas gracias por todo. Tu eres, en gran medida, responsable de que la Agència de Salut Pública de Barcelona (ASPB) sea como un hogar para mí. Gracias por preocuparte por mí y por el proyecto, y actuar cuando tenías que hacerlo. Muchas gracias por siempre ser la que se toma el tiempo para contestar, por siempre dar el comentario o sugerencia adecuado, y en general por estar siempre ahí. Es un verdadero honor para mí haber trabajado con alguien que admiro tanto.

Ana, esta tesis sale a pesar de ti y gracias a ti al mismo tiempo. Gracias por todo el apoyo en la tesis y en la vida; por las semanas de cuidados, y por las demás. Eres una gran amiga y mejor persona. Te agradezco además el haber leído y corregido gran parte de este trabajo.

Brenda, **Miguel**, **Laura** y **Carla**, cuando tuve momentos difíciles, ustedes me acogieron y se convirtieron en mi familia. El piso de Coll i Vehí pronto se convirtió en mi hogar aquí. No puedo expresar el cariño y agradecimiento eterno que les tengo.

Ale, tú me empujaste a empezar esta tesis en un tiempo en el que no estaba nada seguro de hacerlo. Ahora que se termina la tesis, sólo me queda agradecer mucho tu tenacidad y empuje. Rambo y tu han sido una parte fundamental de este camino.

Vero, muchas gracias por compartir tanto a lo largo de este camino. Contigo aprendí el valor del trabajo colaborativo. Eres una gran amiga, maestra y persona. Que haya muchos años más de crecer, equivocarnos y aprender.

Hugo y Juli, muchas gracias por acompañar este camino por tanto tiempo. Con ustedes, nos hemos permitido soñar. Ustedes son una verdadera fábrica de ideas y proyectos. Espero que por mucho tiempo sigamos soñando y haciendo todo por volver esos sueños realidad.

A **Vanessa** y **Mercè**, muchas gracias por estar siempre ahí, por siempre escuchar y dar un consejo apropiado. Gracias por tantos cuidados y por saber bien cuándo hay que desconectar del trabajo y vivir. Espero que las cosas "se nos vayan de las manos" muchas veces más amigas.

A toda la gente de la **ASPB**, muchas gracias por ser tan buenas compañeras y amigas siempre.

A toda la gente que ha pasado por el **SESIS (Clara, Marc, Marta, Laia, Ana, Gloria, Mercè, Vanessa, Xavier, Catherine, Patri, Brenda, Vero, Elena, Hugo, Carme, Lluis, Davide** y muchas otras personas**)**. Esta fue mi primera casa en la ASPB. Gracias

por siempre mostrar interés y contribuir positivamente a este trabajo; y por haber podido ensamblar un espacio seguro donde aprender y ser críticos. He aprendido mucho de cada una de ustedes y espero poder seguir haciéndolo por mucho tiempo.

A todas las personas del **SEQUIA (Anna, Natàlia, Pau, Laura, Marc, Andreu, Laia, Jaume, Esteve, Marc, Sònia, Cristina, Mayla, Marcos, Lidia, Llorenç, Lorena, Neus** y demás personas que han estado ahí**)**, muchas gracias por acogerme y hacerme sentir en casa. Siempre recordaré la alegría que tuve cuando tenía que presentar algunos de los resultados de esta tesis un viernes por la mañana y vi que todas ustedes llegaban solidariamente.

Muchas gracias también a todas las personas que conforman (o han pasado por) el **Grup de Habitatge y Salut** de la ASPB (**Juli, Esther, Carme, Catherine, Ana, Hugo, Patri, Ana, Constanza, Laura** y demás). En este espacio hemos podido aprender y crecer juntas, Las reflexiones sobre la vivienda, el barrio, la energía y la salud que hemos hecho juntos también me han sido de gran utilidad en esta tesis. Respeto y aprecio mucho a cada una de ustedes y espero poder seguir haciendo cosas juntas por muchos años más.

María José y **Marc**, gracias por ser tan comprensivos con el trabajo estos últimos meses. Espero poder retribuir de alguna manera toda su generosidad y paciencia.

También me gustaría agradecer a las personas de **GREDS/EMCONET (Marisol, Irene, Carolina, Emmanuel, Alba, Mireia y Paco)** por su ayuda y amistad.

A **Mónica** y todas las personas de **ABD**, muchas gracias por la oportunidad de trabajar con ustedes un tiempo. Son un equipo genial. Espero poder verlas pronto y darles un gran abrazo.

Quiero dar un agradecimiento especial a **Vero, Juan Mateo, Lucas, Estefy, Richie, Lore, Ale, Fernando** y tantas otras amigas y amigos de Ecuador. A pesar de la distancia, ustedes siempre han estado a mi lado. Sólo les puedo decir que les extraño mucho y que no puedo esperar para darles un gran abrazo y conversar con ustedes largo.

Para terminar, quisiera agradecer también a tantas amigas y amigos que he encontrado en estos años: **Anita, Nico, María, Helena, Esther, Laia, Gema, Marta, K**, **Laia**, **Fede, Andrea, Gloria** y tantas otras personas**.** Sin ustedes, no sé si este trabajo hubiese sido posible. Gracias por estar ahí y compartir tantos momentos. No sé dónde me lleve la vida, pero donde esté yo siempre tendrán un amigo para lo que sea.

Todas estas personas han contribuido directa e indirectamente con este trabajo. Si me he olvidado de alguien, le haré llegar mi agradecimiento en persona mediante un gran abrazo.

Abstract

The aim of this dissertation was to analyse social and geographical inequalities in mortality in Ecuador, correcting the potential deficiencies found in the mortality registry. For this purpose, four studies were developed. In the first study we found that, at the national and provincial levels, the mortality registry of Ecuador performs poorly both in terms of completeness and quality. In most of the studied areas, indicators were poorer for the mortality registry in women. Moreover, quality and completeness were lower in the Amazon, central Andean, and northern Coastal regions where historically excluded groups have traditionally lived. In the second study, after correcting deficiencies in the completeness and quality of the mortality registry in the country, we observed not only changes in the number of deaths, but also in the geographic patterns of mortality risks due to some of the main causes of death in women and men. In the third study, a clear geographical pattern of material deprivation in the country was evidenced. High levels of material deprivation were found in areas in the northern Coastal, central Andean and Amazonic regions. In the final study of the dissertation, unique patterns of specific cause of death mortality were observed in women and men in the country. Moreover, many of the main causes of death in men and women were positively associated with material deprivation.

Resumen

El objetivo principal de esta tesis doctoral fue analizar desigualdades sociales y geográficas en la mortalidad en Ecuador, corrigiendo las potenciales deficiencias que se puedan encontrar en el registro de mortalidad. Para conseguir este fin, se realizaron cuatro estudios. En el primer estudio, se encontró que el registro de mortalidad tiene un pobre desempeño tanto en cobertura como en calidad (a nivel nacional y provincial). Los indicadores analizados fueron peores en el registro de mujeres en la mayoría de las áreas estudiadas. Las áreas con peores indicadores de cobertura y calidad se encontraron en la Costa norte, la Sierra central y en la Amazonía. En el segundo estudio observamos que, después de corregir deficiencias en el registro de mortalidad, no sólo hubo importantes cambios en el número de muertes, sino también en los patrones geográficos de los riesgos de mortalidad por algunas de las principales causas en mujeres y hombres. En el tercer estudio, se evidenció un claro patrón geográfico de la privación material en los cantones de Ecuador. Áreas con altos niveles de privación material se concentraron en la Costa norte, Sierra centro y Amazonía. En el estudio final de la tesis doctoral, se pueden observar distintos patrones geográficos de riesgo de mortalidad según causa y sexo. La privación material a nivel cantonal se asocia positivamente con muchas de las principales causas de mortalidad en mujeres, hombres, o en ambos sexos.

Preface

1. Personal notes on distance and perspective:

In the last 4 years, many people have asked me about the experience of making a dissertation* about Ecuador while living in Barcelona. The answer is always the same. I really think that this work could be done precisely because I was 10,000 kilometres away. The first set of reasons for my answer are practical. I found Marc, Joan, Carme and all my colleagues from the Public Health Agency of Barcelona here. Without their theoretical and methodological assistance, this work would have never existed.

But being in Barcelona contributed in another significative way to the dissertation. Distance has allowed me to reflect and see Ecuador in ways I could not see it when I lived there. More than 10,000 km away, I met amazing people from Ecuador and other Latin American countries. Their points of view and personal histories made me understand many things about our shared country / region. With them, I understood a lot more about colonialism, gender norms and sexism, capitalism (especially extractivist capitalism) and their impacts in our countries. In here, I read more about Ecuadorian history and reflected more on the history of oppressions that generates health inequalities in our country. In here, I re-discovered remarkable authors of Latin American critical epidemiology and collective health and admired the enormous theoretical and practical contributions made by people committed to social change and social justice in our continent. I expect that the ideas and contributions of all these friends and people I admire have permeated and have become an integral part of this work.

Finally, distance made me reflect on my personal story and how it relates to the topics we discuss in this text. Privilege is hard to see when you are immersed in it; and in Ecuador a white-mestizo male from the north of the capital city and with university studies has way too many privileges. Being a migrant in Europe, and – once more – getting to know so many wonderful persons helped me to identify many of those privileges and their relations with the systematic oppressions and human rights violations of entire populations in the country. Ecuador, as many other Latin American nations, has a colonial past and present, based largely on heteropatriarchy and capitalism. This historical context and social systems have systematically oppressed

indigenous, afro-Ecuadorian and montubio populations; people from rural areas; and women in general. The same social systems have allowed white and mestizo populations, and especially men to have freedom and control over material and social resources of the country. The (un)natural consequence of these societal systems and structures is an unequal and unfair society. At a personal level, all these things mean that – in many ways - I was able to reach this point and perform this research because of all the privileges given to me and taken away from many other capable people just because of the colour of their skin, ethnicity or social class. I think it is my responsibility to acknowledge this injustice. The research presented in this dissertation, evidences some of the gigantic inequalities and injustices present in Ecuador. I hope that it joins the voices and views of many other committed researchers and of social movements in Ecuador that for many years have been denouncing this system of oppressions and privileges, trying to achieve a fairer and just society.

2. Structure of the dissertation:

This dissertation is structured in 7 chapters. The first chapter includes the introduction, justification, objectives and hypotheses of the dissertation. The second chapter presents a description the methods used in the studies presented in the following chapters. Chapters 3 thru 6 present the four articles that make up the main body of the text. The first article (chapter 3) presents the evaluation of the performance of the mortality registry in Ecuador at a provincial level (first administrative level). The article has been published in the journal "Population Health Metrics". The second article (chapter 4) proposes a set of methods to correct deficiencies in the mortality registry in order to study social and geographic inequalities in mortality. This article has been accepted and would soon be published in the journal "Epidemiology". The third article (chapter 5) describes the creation and validation of a deprivation index to study health inequalities at a cantonal level (second administrative level) in Ecuador. This was a collaborative work of more than 3 years and was accepted for publication in the journal "Revista de Saúde Pública". Chapter 6 is a final manuscript of a study that analyses geographical patterns of mortality due to 17 causes of death in men and women and their associations with material deprivation in the cantons of Ecuador. Finally, chapter 7 discusses some of the main results of the dissertation and includes the main recommendations and conclusions of the collection of studies presented.

*: Along all this work, I have used the terms "dissertation" and "doctoral thesis" interchangeably.

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Chapter 1: Research introduction, justification, objectives and hypotheses

Key Points:

- The study of geographical and socioeconomic inequalities in mortality has been one of the cornerstones of epidemiological and public health research worldwide.
- Well-functioning civil registration and vital statistics (CRVS) systems provide essential data for the study of health inequalities in many countries. Nevertheless, CRVS systems are still deficient in many countries, and especially in low and middle-income countries.
- The capacity to perform analyses of general mortality and cause of death statistics greatly depends on the completeness and quality of mortality data. Important geographical inequalities in the performance of mortality registries has been observed between and within countries.
- In Ecuador – as in many other countries in Latin America - shocking socio-economic inequalities between geographical regions and by ethnicity/race, social class and gender (among others) have existed for centuries and are still persistent. Thus, it is plausible to assume that great inequalities in health and mortality exist between territories and population groups. Nevertheless, research on health and mortality inequities has been scarce.
- The mortality registry in Ecuador shows important limitations in its completeness and quality. Evaluations of geographical inequalities in the performance of the mortality registry have not been carried out in the country.
- The aim of this dissertation is to analyse social and geographical inequalities in mortality in Ecuador, correcting the potential deficiencies found in the mortality registry.

Capítulo 1: Introducción, justificación, objetivos e hipótesis de la investigación

Puntos Clave:

- El estudio de desigualdades geográficas y socioeconómicas en la mortalidad ha sido una de las bases de la investigación epidemiológica y en salud pública en el mundo.
- En muchos países, los sistemas de registro civil y estadísticas vitales (RCEV) logran proveer datos esenciales para el estudio de desigualdades en salud. Sin embrago, los sistemas de RCEV aún son deficientes en muchos países; y especialmente en los de rentas medias y bajas.
- La capacidad de realizar análisis tanto de mortalidad general, como de mortalidad por causas específicas depende en gran medida de la cobertura y calidad de los datos de mortalidad. Se han observado importantes desigualdades en el desempeño de los registros de mortalidad, tanto entre países como dentro de algunos países.
- Como en otros países de la región, en Ecuador han existido enormes desigualdades socioeconómicas entre áreas geográficas, y según etnia/raza, clase social y género (entre otras) por siglos. Estas desigualdades siguen siendo importantes actualmente en el país. Por este motivo, podríamos intuir la existencia de grandes desigualdades en salud y mortalidad entre territorios y grupos sociales - poblacionales. A pesar de esto, la literatura sobre desigualdades en salud y mortalidad en el país es escasa.
- El registro de mortalidad de Ecuador presenta importantes limitaciones en su cobertura y calidad. No se han realizado estudios sobre desigualdades geográficas en el desempeño del registro de mortalidad en el país.
- El objetivo de esta tesis doctoral es analizar desigualdades geográficas y sociales en la mortalidad en Ecuador, corrigiendo las deficiencias potenciales que se puedan encontrar en el registro de mortalidad del país.

Introduction

1. Studying mortality and inequalities in mortality

The study of mortality, its geographical and social patterns, and its causes has been one of the cornerstones of sociological, demographical, geographical and epidemiological research. Moreover, the description of overall mortality and cause of death statistics is one of the main activities in public health surveillance, as it reflects important aspects of health and health inequalities in a population. In many countries, especially from the global north, mortality data and registries, and analyses have been performed since the nineteenth century (in European cities such as London, registries existed hundreds of years before) [1]. In countries with a history of collecting and analysing health data, mortality registries have been considered one of the most reliable sources of information. For that reason, there has also been a tradition of analysing mortality data in public health research. One of the most notorious examples of this tradition are the studies on social and geographical inequalities in mortality. Farr, Engels, Antonovsky and many other relevant thinkers and researchers are part of this tradition [2–4]. One of the most relevant phenomena noticed by these –and many other – authors studying mortality was that it is not distributed evenly across territories and social groups, and also that there were gradients where the most privileged groups have less mortality risk (general mortality and by specific causes) and higher life expectancies than deprived and oppressed social groups (by socio-economic position, ethnicity, territory, etc). The cumulative evidence on these social inequalities has been one of the foundations of modern social epidemiology and public health overall. Nevertheless, for reasons we will explore in some detail in the following sections, studying inequalities in mortality has been a challenge for many countries in the global south and particularly in Latin America.

2. Geographies of health and mortality

The notion of territory (space, geography) – so important in the beginnings of public health and epidemiological research – was rather absent from the literature and discussion on what are the main causes of health and disease for a great part of the twentieth century [5,6]. The dominant individualism (and reductionism), often characteristic in public health research, not only attributed all differences in health to the

individuals (mainly due to behavioural and genetic characteristics), but also discredited all ecological epidemiological approaches to study health and illness under the assumption of the important and largely cited ecological fallacy. In spite of these dominant views, research on how territories can affect health reappeared and bloomed by the end of the century. Thus, mainly in the global north, theoretical advances on the subject included the description of contextual and collective effects (in contrast to merely compositional effects) on health, or definitions of place (in contrast to space), viewed not only as static but also as a relational dimension [6,7]. These theoretical advances were accompanied by notable methodological innovations such as multilevel analyses, and Bayesian models to smooth rates in small areas; and also by the development of computer technologies that allowed more sophisticated and accurate analyses at the small area level. In this context, analyses on the relationships between space, place and health (especially mortality) were carried out in many countries and cities, yet mostly in high-income countries [8–11].

Meanwhile, in many Latin American countries, the concept of territory was conceptualized as one of the fundamental categories for the study of public health. Far from the static classical view of geography often used in mainstream epidemiological research, scholars in critical epidemiology and social medicine defined territories as places were intertwined complex processes of social production and reproduction take place and where a variety of ecological-societal mechanisms processes, and factors are generated. This means that territories have to be understood as dynamic entities, being historically created, where culture, economy and political conflicts play important roles. Under these scenarios, health and illness profiles of populations and social groups are thus unequally generated [12,13]. These conceptions of territory and health have configured in the region in the past decades much of the research on social determination of health.

3. Mortality and deprivation

In each society, there are a set of material and social resources needed by individuals to achieve the living standards in a given historical time that are considered essential by their social and cultural groups. The lack of these resources has been defined in the literature as material and social deprivation [14]. Deprivation has sometimes been represented with single variables that can be considered “proxies” of the construct

(educational level or income for example). Nevertheless, many authors consider it to be a complex construct with multiple dimensions that can change across contexts and time periods. Under this premise, compound indicators or indexes are more appropriate than one-dimensional indicators.

Indicators of deprivation have been widely used in epidemiology to describe social determinants of health and the impact of contexts on the health of populations [15]. Research showing associations between mortality (general and specific causes) and deprivation is extensive, especially in high income countries [10,14]. Indeed, most of the efforts undertaken to conceptualise and measure material and social deprivation have centred on high-income countries [16,17]. Consequently, only few studies have analysed how multiple types of deprivation shape people's health and health inequities (including mortality and many health outcomes) in middle- and low-income countries [18].

4. The importance of civil registration and vital statistics (CRVS) systems

In most countries, data on deaths and births are collected, validated, compiled and disseminated by CRVS systems. CRVS systems are complex structures that work along and interact with the healthcare and public health systems, judicial systems, and research institutions, within wider social contexts. The governance and characteristics of each CRVS system is unique, but they all share similar objectives and processes [19]. An adequate vital statistics system not only allows governments and scholars to monitor and analyse the health of a population, but it can also be a fundamental tool for the planning and evaluation of public policy [20]. The availability of timely high-quality vital statistics not only allow people to claim and exercise their basic human rights but could also be an essential tool to inform and empower the population [21]. Moreover, some evidence suggests that countries with better vital statistics systems have better health outcomes (even after consideration of income and other socioeconomic factors) [22].

A well-functioning CRVS system should also be a fundamental part of a health equity surveillance system. The final report of the World Health Organization (WHO) Commission on Social Determinants of Health (CSDH 2008) recommended that all countries should: First, register all births, which allows people to exercise their citizenship rights in each country; and second, have adequate mortality data with adequate variables for stratification (by different socio-economic groups, sex, ethnic and racial groups) as part of a standard high-quality health equity surveillance system.

Indeed, the information collected and processed by each nation should allow for the identification of health inequalities and guide public policy oriented to their reduction [23].

5. How can we evaluate the performance of CRVS systems and particularly mortality registries?

Many direct and indirect approaches can be used to monitor the performance of vital statistics in general, and mortality registries in particular. In this doctoral thesis, we will focus on the most widely used indicators related to the completeness and quality of the collected information. Regarding mortality statistics, completeness can be defined as the percentage of deaths registered in the population covered by the mortality registration sub-system [29]. Death distribution methods (DDMs), a set of demographic techniques, are the most widely used tools to estimate adult mortality completeness worldwide [30]. Quality is evaluated with multiple indicators. One of the most widely used is the percentage of garbage codes (GCs) in the registry. GCs can be defined as deaths assigned to codes that provide little or no information for cause of death analysis in public health [31]. Deficiencies in both quality and completeness have been related to the socioeconomic characteristics of the study areas, to the organization and sociocultural adaptation of vital registration systems, and to the availability and training of health professionals in charge of certifying deaths [21]. We will further describe the methods to evaluate the performance of mortality registries in the following chapter of this dissertation.

6. Inequalities in mortality in countries with defective data and other particularities

In many countries, especially high-income ones, mortality registries are usually considered one of the most reliable sources for timely and accurate health statistics. Yet, the situation in many low- and middle-income countries is quite different. The 2015 Lancet Series “Counting Births and Deaths” reported disappointing global progress in CRVS systems worldwide [24]. In 2007, only 31 of the 192 member states of the World Health Organisation (13% of the world’s population) had mortality statistics with completeness estimates over 90%, using a recent version of the international classification of diseases and related health problems (ICD8, ICD9 or ICD10), and with

10% or less of ill-defined codes [25]. Moreover, striking inequalities between countries and regions are seen in death registration. In a study analysing mortality data from all WHO member states, Mathers and colleagues reported three interesting issues: first, coverage of death registration (percentage of the population covered by the mortality registry) ranged from 100% in the WHO Europe Region to less than 10% in the WHO Africa Region; second, completeness ranged from 100% in most high-income countries, to less than 50% in countries such as the Dominican Republic, Haiti, Lebanon and Morocco; and third, the percentage of deaths coded with ill-defined codes ranged from 4% in New Zealand to more than 40% in places like Thailand and Sri Lanka [26].

Inequalities in mortality statistics are not only seen between countries but also within countries, even though studies evaluating within-country differences are still rather uncommon. In Latin America, for example, studies in Brazil and Chile have found wide differences in the completeness and quality of mortality statistics between sub regions in each country [27,28]. These kind of studies are essential for two main reasons: 1) They may help public health authorities to invest more efforts and resources to strengthen the vital statistics system in areas with the greatest deficiencies; and 2) They allow researchers and public health workers to use the available data, adjusting them or taking into account its completeness and potential deficiencies in quality.

7. Can mortality be analysed in contexts were mortality data is defective?

This important question arises when data necessary for the study of mortality is incomplete or defective. Thus, the possible biases induced by low performances of mortality registries and vital statistics systems may discourage many researchers from initiating studies on mortality and its patterns in many countries, especially in middle and low-income countries. Others, despite these great challenges, attempt to find the deficiencies in data and develop methods to try to correct those deficiencies, or rely on other non-official sources of information as surveys. Neither option is perfect, as in the first case the phenomenon is left in the dark; nor in the later, where the results found can have important deficiencies. Therefore, the only "ideal" situation would be the sustainable improvement of CRVS systems in all countries in the world [32].

Until CRVS systems can be improved, and knowing the importance of mortality statistics for monitoring and analysing the health and inequalities of populations and for planning and evaluating public policy [20], several mechanisms for correcting deficiencies

have been developed and applied in many countries. The most ambitious attempt to do this (for its scale and complexity) has been the Global Burden of Disease (GBD) study. Specifically, the GBD attempts to assess and correct deficiencies in the mortality data in more than 200 countries by (along with other procedures) estimating its completeness and correcting deaths for it, and by applying garbage code redistribution protocols to improve quality of the cause of death data [33].

However, the GBD study applies its methods to allow comparisons between countries but not within them. Therefore, at the regional and local levels, much effort is still needed to evaluate and correct current deficiencies in mortality registries of many countries and regions. Subnational studies can be thus vital to help governments and public health institutions to increase their efforts and resources to strengthen vital statistics systems in areas with the greatest deficiencies and also to obtain more accurate statistics helpful for policy design and monitoring. In Brazil, for example, researchers have evaluated and corrected deficiencies in mortality data at a sub-national level, identifying the most vulnerable regions that could be targeted by public policy [34–36].

8. Studying social inequalities in health (including mortality) in Latin America

Social inequalities in health are differences in the health status (including life expectancy and mortality) between groups that are "judged to be unfair, unjust, avoidable, and unnecessary (meaning: are neither inevitable nor unremediable)" [37]. Social inequalities arise from historical processes, social structures and power relations that allow some social groups to have more privileges over others and that determines unequal distributions of social and material resources, and of health and wellbeing.

Latin America has historically been a land of large socio-economic inequalities, and it is still regarded as "the most unequal region in the world". In spite of some notable advances in poverty and inequalities reduction in the beginning of the twenty-first century (2002-2017), not only incomes remain persistently unequal in the region but other resources as education and land are also unequally distributed [38,39]. It is expectable that these inequalities have great impact on the health of populations in the region.

It seems plausible that these rampant and persistent social and economic inequalities in conjunction with a long tradition of social movement struggles and resistance have contributed to the fact that Latin American countries have a rich tradition in the study of the social determination of health. Many epistemological, theoretical and

methodological advances in the field have developed since the first texts critiquing traditional epidemiological analyses circulated in universities in the 1970`s [40]. In spite of those important contributions to the fields of public (collective) health and (critical) epidemiology, the ability of local institutions and researchers to study health inequalities in many Latin American countries has remained rather limited because of diverse factors here summarised: 1) lack of data or data with low quality or completeness; 2) limited financing and resources; 3) limited institutional support for the study of inequalities; 4) limited technical training of scholars and members of institutions in the making of epidemiological investigations; and 5) rejection and opposition to dominant and reductionistic epidemiological paradigms that lead to the notion of a (false) opposition between quantitative and qualitative methods by a part of Latin American academics [41,42].

9. Ecuador as a case example

Ecuador, located in the Andean region of South America, presents many of the challenges that other Latin American countries have when attempting to study inequalities in mortality. Although extreme poverty has been substantially reduced in the last decade, social, geographical, ethnic and gender-based inequalities persist in the country [43]. Like many other Latin American countries, Ecuador inherited a colonialist model grounded in patriarchy, classism and racism that have created a social stratification benefiting social elites that continue to exert strong power and control over land tenure and wealth [43]. Consequently, many women, peasants' communities, indigenous people and Afro-Ecuadorian groups are living in poverty as a collective experience, an issue which has structural and historical origins [44]. It is expected that the prominent socio-economic inequalities that still exist in the country can have great impacts on health, especially in the most vulnerabilised and deprived populations.

9.1. Mortality Registration in Ecuador

In Ecuador, by law, the declaration and registration of all deaths is mandatory. The mortality registry contains all death certificates completed in the country by health professionals or (in their absence) by police or civil authorities or civil registration officials. Death certificates include socio-demographic information such as age and sex, home and death addresses, and causes of death. The National Institute of Statistics and

Censuses (INEC) uses the information in the certificates to determine the underlying causes of death.

In spite of the legal framework present in the country, studying mortality in general and inequalities in mortality in particular is challenging in Ecuador due to important deficiencies in the completeness and quality of the data. Considering completeness and ill-defined codes used, among other indicators, some studies have classified the mortality data in Ecuador as being of either low or medium performance [24,26]. In addition, a study by Phillips and colleagues (see supplementary material) suggests that the quality of mortality statistics in the country – and specially completeness – fell between the 1980s and 2010 [29]. In the latest edition of the Pan American Health Organization "Core Indicators – Health Situation in the Americas", a completeness of 75% was reported at the national level; 9% of the registered deaths were assigned to ill-defined codes, and more than 16% of deaths were "assigned to causes not considered useful for public health purposes" (garbage codes) [45]. As in the case of other similar countries, no studies analysing geographical inequalities in the death registration system have been carried out in Ecuador, but we can hypothesise that less urbanized areas, deprived regions, and places were ethnic groups reside could have a worse registration system.

10. Theoretical, ontological, and epistemological position of this dissertation

Epidemiology is the science that intends to study the health of populations and what determines it. Mainstream epidemiological models are built on some standard ideas on health and the collective as study subjects. Thus, health is majorly seen as a merely biological, behavioural or health care - related phenomenon, while the collective dimension of populations is seen predominantly as the addition of individual characteristics of subjects. From the viewpoint of a critical social epidemiology - especially from eco-social and social production of disease theories [46] – these notions are way too limited. Health is thus seen as a dynamic state of equilibrium were biological, individual and social factors and determinants play different roles at different scales and times. Likewise, populations are seen as more than just a collection of individuals, but as interplays between a dynamic web of contexts, social relations and power structures that determine privilege, exploitation, and different types of oppressions and discrimination. In this sense, if our subject of research is inequalities in mortality and its determinants, we must understand that these inequalities are not a

natural phenomenon, but that they are socially produced through power structures that allow some groups to have more material and health advantages, at the cost of the health and lifespan of other groups.

To acquire an in-depth knowledge on this subject, we must understand that positivism, reductionism, and functionalism (dominant in health sciences) present several limitations ranging from atomism (dissection of the reality into small bits of facts or items) to the illusion of a neutral evidence and a radical separation between researchers and the study subjects. In order to try to overcome these epistemological limitations, this thesis adopts a critical post-positivist epistemological standpoint, recognizing that our theoretical view on health, health equity, and its causes, not only has a key interest in the study subject, but also has guided our methods and interpretation of results. Moreover, even if this thesis is mainly observational in nature, our overall analyses and interpretation of the results try to understand or at least assess the mechanisms involved in these inequalities in order to propose interventions and policies with the capacity of transforming society (scientific realism) [47]. Under this paradigm, public health and epidemiological research should not merely evidence the existence of health inequalities, but also be able to propose viable theories on the key mechanisms involved and how to tackle these inequalities.

10.1. A Conceptual framework to assess determinants of social and geographical inequalities in mortality in Ecuador

Conceptual frameworks on social determinants of health have guided for decades not only research in the field of social epidemiology, but have also aided in the development and evaluation of policies and interventions to tackle health inequities [48–51]. Although no framework can be comprehensive or perfect, they make our theories on the study subject explicit and help us not only to guide our research objectives and methods but also our analyses, and to interpret our findings. Most conceptual frameworks on social determinants of health share two similar characteristics: they consider that wider social and economic determinants and structures are responsible for the conditions in which people live; and they propose that these social and material living conditions can differently impact the health of populations, directly, or by interactions with individual characteristics that impact health.

The conceptual framework proposed in this thesis (figure 1) was adapted from previous ones, mainly the influential model by Solar and Irwin (2010) and the Commission to Reduce Social Inequalities in Health in Spain (2012). In general, our framework follows

the general characteristics of those models, but it is adapted to inequalities in mortality in Ecuador.

If we observe the figure from left to right, the first thing we notice is the presence of structural determinants, that are a combination of historical, social, economic, political, labour and environmental factors. Each dimension is influenced by its own historical development, in which wider systems of oppression (e.g. colonialism and heteropatriarchy) have acted in time to produce unique contexts. As mentioned before, in Ecuador - as in many other Latin American countries – the colonial past (and a post-colonial present) combined with a patriarchal culture and capitalism as economic system of dependency and dispossession, have interacted for many years, allowing privileged oligarchies to set a political-economic system in which markets, laws and policies have favoured inequality, racism, sexism and poverty [44,52]. This political-economic environment interacts with the natural environment, determining or influencing how and where people live and die. In Ecuador, for example, the interaction of physical and social geographies with history determine the uneven distribution of different ethnic groups across the territory of Ecuador.

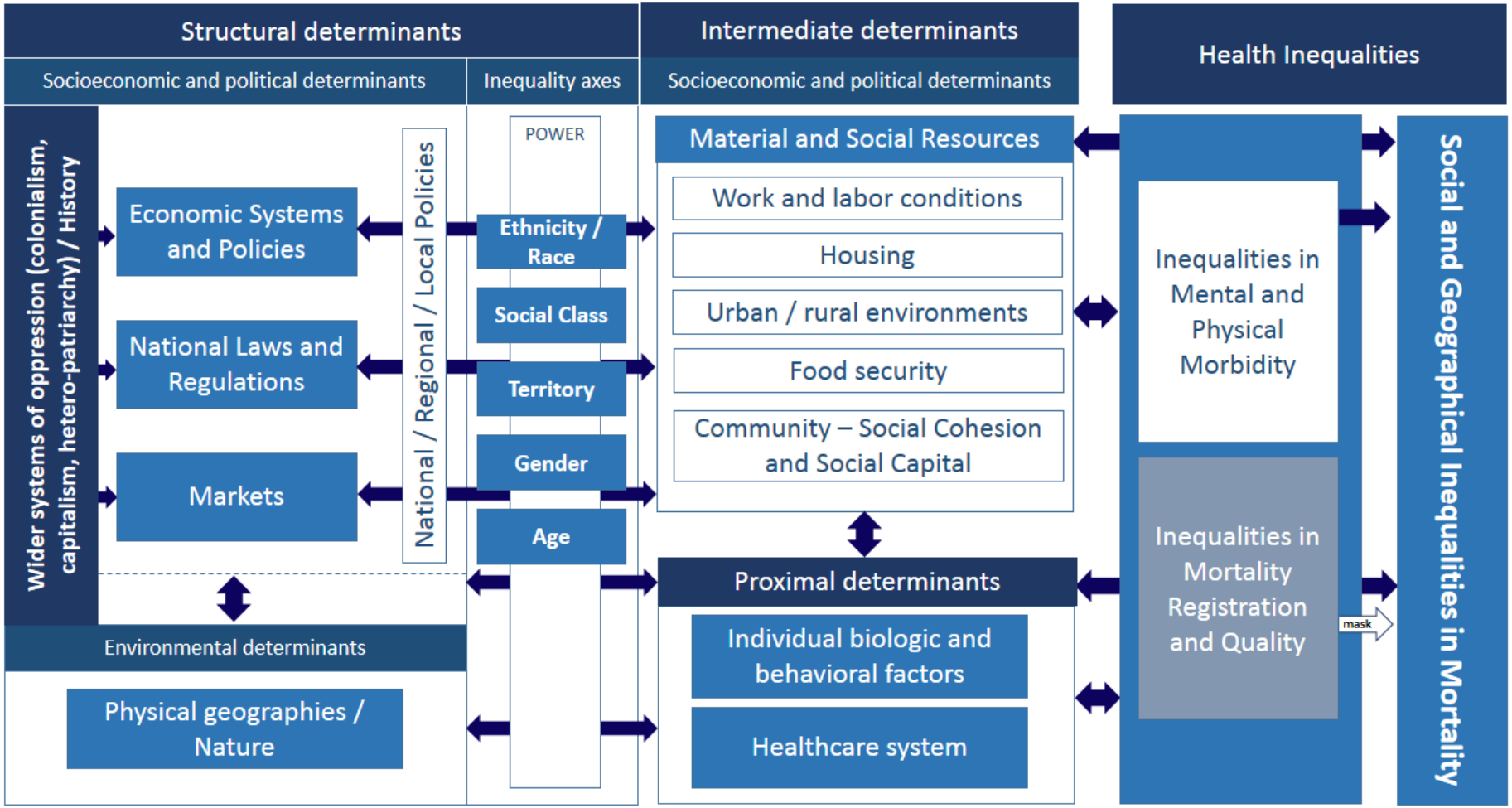
If we move our sight to the centre of Figure 1, we may observe that material and social resources (or how people live) are not equally distributed in the population. Inequality axes such as ethnicity/race, social class, territory, gender, and age among others, greatly define the distribution of these resources among social groups. Furthermore, the intersection of these axes can generate multiple types of oppression in certain groups – leading to different levels of material and social deprivations. In Ecuador, for example, this can be seen in the great inequalities in material resources between geographical areas and ethnic groups [52]. Both material and social resources interact with individual biological and behavioural factors as well as the healthcare system to improve or deteriorate health of individuals and communities. In Ecuador, availability and adequacy of healthcare services is greatly determined by the interaction of physical geographies and historical processes of exclusion. For example, remote places where most of the indigenous, afro-Ecuadorian, and montubio populations live (i.e., in the Amazonic provinces, central Andes and central and northern coastal regions), have limited access to healthcare services and other public services.

Finally, on the right side of the framework, we propose that all the previously discussed situations leading to socio-economic inequalities can generate health inequalities, including inequalities in mortality between social groups and between territories.

Inequalities in data collection and its quality have been included here since they are an essential component to be considered in low- and middle-income countries, and they can hide inequalities presented in the official vital statistics. If, in accordance to what has been observed in other contexts, we assume that completeness and quality of data are greater in deprived areas and where vulnerabilised groups live, it is easy to understand how official vital statistics can wrongly claim that these groups have an equal or better health than privileged groups.

One important issue to be noticed in our framework is that it is assumed not only that the structural and intermediate determinants affect the proximal determinants and health inequalities, but also that there can be a counter flow in which populations can also affect their social, political, economic and ecologic environments (agency).

Figure 1: Conceptual Framework on the Determinants of Social and Geographical Inequalities in Mortality in Ecuador



Justification

A great and growing body of evidence has described the existence of geographical inequalities in mortality, and how contextual characteristics of areas as deprivation can be associated with those inequalities. Yet, most studies have been conducted in high-income countries, while research in middle and low-income countries is still very limited [53]. Ecuador is a country with large and persistent social and economic inequalities across geographical areas and social groups. Therefore, large inequalities in mortality and other health outcomes are expected in the country. The study of these inequalities is important for three main reasons: 1) gaining knowledge of the descriptive characteristics and the potential causes and mechanisms leading to those health inequalities in the country; 2) the design, implementation and evaluation of public policies to tackle inequalities; and 3) empowering populations living in areas with worse health outcomes (and high mortality by specific causes), by obtaining the knowledge to advocate and enforce the improvement of living and working conditions in their areas of residence.

In spite of the great improvements and advantages that could arise from the study of inequalities in mortality in the country, deficiencies in the quality and completeness of the data (among other factors) have not allowed these studies to be made in the country. This can only be done by performing a comprehensive evaluation of the Ecuadorian mortality registry and proposing the right tools and methodologies to correct it. The evaluation of the mortality registry might help to improve the CRVS system of the country, and the methods proposed to correct those deficiencies can be valuable until proper actions are taken to improve the registry. Moreover, the proposed methodologies could be adapted and applied in other countries with similar contexts that wish to study inequalities in mortality.

Objectives

1. General Objective of the thesis

To analyse social and geographical inequalities in mortality in Ecuador, correcting the potential deficiencies found in the mortality registry.

To respond to the global objective of the thesis, four studies were developed, each with unique general and specific objectives.

2. Objectives of the four studies presented

2.1. Study 1

General Objective:

Evaluate the completeness, quality and internal consistency of Ecuador´s mortality registry from 2001 to 2013, describing geographical inequalities (between provinces – first administrative level), and social inequalities (by age and sex) within the country.

Specific Objectives

- Estimate the completeness of the registry in men and women for the provinces of Ecuador and for the whole country between 2001 and 2010 (the inter-censal period).
- Evaluate the quality of the registry in men and women for all the studied areas between 2001 and 2013, by estimating the percentages of garbage codes and the percentages of deaths with unspecified age / sex.
- Evaluate the internal consistency of the registry in men and women for all the studied areas between 2001 and 2013 by estimating the percentage of deaths with reported causes considered impossible in some age–sex combinations
- Classify the provinces of Ecuador in relation with the completeness and quality of the mortality registry in men and women.

2.2. Study 2

General Objective:

Analyse geographic inequalities in mortality due to some of the main specific causes of death in men and women in the provinces of Ecuador (2001–2016) after correction for the deficiencies found in the mortality registry.

Specific Objectives

- Propose a methodological framework for the correction of deficiencies in the mortality registry in order to study mortality due to specific causes of death.
- Correct deficiencies in the quality of mortality data in each of the studied areas in men and women by redistributing garbage codes.
- Correct mortality statistics for deficiencies in completeness in each of the studied areas in men and women.
- Analyse changes in the geographical patterns of mortality due to specific causes after correction of the deficiencies in quality and completeness in the mortality registry in men and women.

2.3. Study 3

General Objective:

Develop a deprivation index for the study of health inequalities in 221 areas of Ecuador (cantons – second administrative level) and describe the geographical pattern of deprivation in Ecuador.

Specific Objectives

- Generate an appropriate definition for deprivation and its dimensions in the context of Ecuador.
- Operationalize deprivation by selecting relevant variables collected periodically and proposing a methodology to generate a deprivation index in the cantons of Ecuador.
- Describe the geographical patterns of deprivation in Ecuador.
- Analyse the association between deprivation in the cantons of Ecuador and all-cause mortality from 2009 to 2011 in men and women.

2.4. Study 4

General Objective:

Explore the association between material deprivation and mortality from 17 specific causes in men and women in the cantons of Ecuador between 2001 and 2014.

Specific Objectives

- Describe the geographical pattern of mortality for the principal 17 causes of death in men and women in the cantons of Ecuador in the study period, after correcting data for deficiencies in the mortality registry.
- Analyse the association between mortality by each studied causes and deprivation at the cantonal level for men and women in the study period.

Hypotheses

- The mortality registry of Ecuador will present greater deficiencies in provinces in the Amazonic, central Andean and central – northern coastal regions (that have greater percentages of indigenous, afro-Ecuadorian and montubio populations).

- The geographical patterns of mortality due to specific causes will change after correction for deficiencies in the mortality registry. These changes will correspond to the pattern of deficiencies in the mortality registry.

- Deprivation in the cantons of Ecuador will have a clear geographical pattern, being higher in cantons in the Amazonic, central Andean and central – northern coastal regions.

- Deprivation and cause-specific mortality will be associated for many causes in men and in women in the cantons of Ecuador.

- The association between deprivation and mortality by the 17 studied causes will be different for men and women.

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Chapter 2: Methodological considerations

Key Points:

- In the following chapter, the methods used in this dissertation to study social and geographical inequalities in mortality in Ecuador are described. The presented methods pretend to be sequential and can be used as an example to study social inequalities in mortality in similar contexts.
- After reviewing available data-sources, the performance of the mortality registry was assessed. Completeness was estimated using death distribution methods. Quality was assessed by estimating the percentage of deaths coded with "garbage codes" or that had no age or sex information. Internal consistency was evaluated by estimating the percentage of deaths registered with causes deemed not plausible for their age-sex group combinations.
- Deficiencies in the mortality registry were corrected by applying a garbage code redistribution protocol and correcting deaths for completeness in each study area.
- To construct a deprivation index to study health inequalities in the cantons of Ecuador, three steps were performed: 1) A context appropriate definition of deprivation was created and its possible dimensions were conceptualized; 2) relevant indicators were selected; and 3) sequential principal component analyses were performed in order to maximize variance of the first component.
- To study mortality patterns and their relationships with deprivation in the cantons of Ecuador, multivariate Bayesian hierarchical Poisson regression models were performed in order to: 1) Obtain smoothed standardized mortality ratios corrected for completeness for seventeen causes of death at the cantonal level in men and women; and 2) to analyse the association between deprivation at the cantonal level and mortality due to the studied causes of death in the country.

Capítulo 2: Consideraciones metodológicas

Puntos Clave:

- En el siguiente capítulo se explican brevemente los métodos usados en esta tesis doctoral para estudiar desigualdades sociales y geográficas en mortalidad en Ecuador. A pesar de incluir particularidades del país, estos métodos pueden ser usados como referencia en países con contextos similares.
- Después de revisar las fuentes de información disponibles en el país, se evaluó el desempeño del registro de mortalidad. Se evaluó la cobertura (completeness) de los datos de mortalidad usando métodos de distribución de muertes (DDMs). La calidad de los datos de mortalidad se valoró estimando el porcentaje de muertes codificadas con "códigos basura", y el porcentaje de muertes sin información de edad o sexo. La consistencia interna se evaluó estimando el porcentaje de muertes codificadas con causas poco plausibles para combinaciones de sexo y edad.
- Las deficiencias encontradas en el registro se corrigieron de dos maneras: 1) aplicando un protocolo de redistribución de códigos basura; y 2) corrigiendo las muertes por la cobertura en las áreas de estudio.
- Se construyó un índice de privación para estudiar desigualdades en salud en los cantones de Ecuador. Para conseguir esto se realizaron tres pasos: primero se conceptualizó la privación y sus posibles dimensiones en el país. Posteriormente se seleccionaron indicadores relevantes disponibles. Finalmente se realizaron análisis de componentes principales seriados, maximizando la varianza del primer componente.
- Para estudiar la relación entre privación y mortalidad en los cantones de Ecuador, se ajustaron modelos Bayesianos jerárquicos multivariantes que permitieron: 1) Obtener razones de mortalidad estandarizadas cantonales, suavizadas y corregidas por cobertura para 17 causas de muerte en hombres y mujeres; y 2) Analizar la asociación entre la privación cantonal y la mortalidad por las 17 causas estudiadas en hombres y mujeres.

Researchers that want to study mortality in general and specifically social and geographical inequalities in mortality in any setting, first have to consider some important questions on how to appropriately perform their research. For example: Which time period to study and why? Do they want to study general mortality or mortality due to specific causes? Which causes are more relevant? Which geographical scale should be used? Do they want to standardize by age? Which standardization method should be used? What statistical methods are best suited for each particular research? Which relevant variables can explain inequalities in mortality?

Moreover, in many low- and middle-income countries researchers also have to consider other important issues: Are mortality and population data available at the geographical scale studied? For which time period are they available? Is data comparable for the whole time period for which data is available? How can we identify the major deficiencies in the available data? Can those deficiencies be corrected? Are the relevant explicative variables for inequalities in mortality in our specific context different? Are those relevant variables available?

In this chapter we will examine how these issues have been addressed in order to study geographical and social inequalities in mortality due to some of the main causes of death in Ecuador. Even though some of the mentioned issues are particular to the Ecuadorian context and of the research being carried out, we believe that these methodological considerations might also be useful to other researchers either in Ecuador or in countries with similar contexts.

1. Data Availability

For the research presented in this dissertation, we have used several publicly available information sources from Ecuador. The main information sources were the National Mortality Registry between 2001 and 2016 (range of years depends on the specific study carried out), and the 2001 and 2010 National Population Censuses. All yearly mortality databases and databases of both censuses (2001 and 2010) are available at the National Institute of Statistics and Censuses (INEC) webpage (https://www.ecuadorencifras.gob.ec/). Other information sources were the National Living Conditions Survey 2014-2015 and provincial population estimates from demographical projections and retro-projections of the 2010 census. In this chapter, we

will focus on the two main sources of information. Additional sources will be described in the studies where they were used (Chapters 3 thru 6).

As we have mentioned earlier, the National Mortality Registry feeds on all individual death certificates issued by health professionals or (in their absence) by police, civil authorities or civil registration officials. INEC collects all death certificates, determines the underlying cause of death, performs basic quality checks and ensembles yearly mortality databases for the country [1]. Mortality databases include socio-demographic information such as age and sex, home and death addresses; and causes of death. Other relevant variables as educational level or ethnic self-identification are also present, but they are either not included in all the yearly mortality databases, or the definitions of the variables has changed during the studied period.

Population censuses have been performed since the 1950's in Ecuador, approximately every 10 years. Censuses collect fundamental demographic and socio-economic information of the population in a given territory and thus are vital for the design of public policy and demographical estimations of population dynamics. Both the 2001 and 2010 studies were de facto population censuses, meaning they count all people present in the national territory in the place where they are at the moment of the census (in opposition to the place of residence). In both cases, information was collected in just one day (November 25, 2001 and November 28, 2010) by thousands of voluntary pollsters - mainly high-school and university students and teachers [2]. For the study of mortality, the main variables used were population counts by age and sex groups in each of the studied areas. We also used diverse variables from the 2010 census related to education, information and communication, housing and urban environment, work and social security, and ethnicity to construct a deprivation index for the study of health inequalities in the cantons of Ecuador (complete description in Chapter 5).

2. Evaluating the mortality registry of Ecuador

Many approaches can be used to monitor the performance of vital statistics in general, and mortality registries in particular. Direct techniques (as capture-recapture methods) and indirect techniques can be employed for these evaluations [3]. The advantages of indirect methods include the use of available data (as censuses), that they are less resource-intensive, and that they allow for international comparisons as they have been applied worldwide. Multi-country evaluations of CRVS systems and cause of death data

have focused mainly on completeness and quality of the system. However, they have also included other aspects as the level of detail of cause of death reporting, data availability or timeliness [4,5]. In order to evaluate the performance of the mortality registry of Ecuador, we focused on completeness, quality and internal consistency of the data. We selected these three aspects of the performance of the mortality registry because they were the most consistently used in the literature and because they were the ones that we needed to correct in order to analyse geographical and social inequalities in mortality in Ecuador.

2.1. Completeness

Completeness can be defined as the percentage of deaths registered in the population covered by the mortality registration system [6]. Death distribution methods (DDMs), a set of demographic methods, are the most widely used to estimate adult mortality completeness worldwide [7]. These methods estimate the average completeness of death registration in the period between two censuses. To estimate completeness, we used the three types of DDMs: synthetic extinct generations (SEG), generalized growth balance (GGB), and the GGB-SEG hybrid. All DDMs compare the age distribution of a population at two points (2001 and 2010 censuses in our study) with the age distribution of the recorded deaths in that population (in the intercensal period). The following table adapted from Murray et al. (2010) summarizes the basic concepts in each method [7]:

Table 1: Description of the 3 DDM method used

GGB	**Hill, 1987**
Base Concept: The mathematical relationship of the demographical balancing equation: **Birth Rate = growth rate + death rate** The slope and intercept of the modeled equation (plotting birth rate versus death rate) along with observed growth rates can be used to obtain the relative coverage of census 1 to census 2, as well as the relative completeness of death registration to census coverage.	
SEG	**Bennett and Horiuchi, 1981 and 1984**
Base Concept: The number of people at age x at time 0 is equal to the number of deaths age x in year 0, plus deaths age x+1 in year 1, plus deaths age x+2 in year 2 and so on until the entire cohort is extinct. SEG uses intercensal age-specific growth rates and current deaths at older ages to estimate future cohort deaths. By comparing estimated future cohort deaths to current cohort size, the completeness of death registration can be estimated.	
GGB-SEG (Hybrid)	**Hill and Choi, 2004**
Base Concept: Use of GGB to estimate coverage of census 2 relative to census 1 and use this coverage to adjust populations prior to use in SEG method.	

Adapted from Murray et al. (2010).

DDMs make the following assumptions: 1) that the population is closed to migration; 2) that the completeness of recording of deaths is constant by age; and 3) that ages of the

living and the dead are reported without error [8]. Moreover, SEG makes the assumption of constant coverage across the two censuses; and GGB-SEG assumes that the relative coverage of censuses is constant by age [7].

DDM methods usually perform well when the data used for estimations is compliant with their assumptions. The three methods are especially sensitive to migration. Adjustment of the methods for migration has been proposed, but has been limited for two main reasons: 1) migration statistics are scarce or incomplete in many countries; and 2) the adaptation of the methods when migration is not known [8] is still not completely developed and accepted [9].

Apart from the potential biases that could happen when data is not compliant with the assumptions of the methods, DDMs have certain limitations that are worth noticing:

1. **Lack of timeliness**: DDM methods depend on information from national censuses and give completeness estimates for the whole intercensal period. This makes completeness estimates inadequate to study rapid or medium-term evolutions in death registry completeness. The next census in Ecuador is planned for 2020. This means that only by then we can get a sense of the completeness of death registration in the current decade (2010-2020).
2. **Uncertainty**: Murray et al. (2010) reported that "…the uncertainty around relative completeness of registration is likely to be at least +/-20% of the estimated level, and perhaps considerably more." This means that the completeness estimates obtained should be taken with care. Also, it is important to assess uncertainty in DDM estimates.

To try to minimize the bias induced by non-compliance with the assumptions of DDMs, researchers have adopted various strategies, many times of subjective kind. One of the main strategies is to use an age range that is more compliant with the assumptions of the methods. To minimize the effect of migration, some authors have preferred to use age ranges which are considered to be less affected by migration (over 60 years old for example). Other authors have used simulated data or comparisons of methods to real data in places in which complete registration is presumed in order to determine the appropriate age ranges to be used [7,9,10]. Hill, You and Choi (2009) conclude that the best strategy is to use GGB-SEG with an age range of 5 to 65 years old. On the other hand, Murray et al. (2010) conclude that the most appropriate strategy is to combine the three types of DDMs using the following age trims: 55 to 80 years old for SEG, 40 to 70

years old for GGB, and 50 to 70 years old for GGBSEG. Other approaches to select the appropriate age trims are based on graphical analyses for each DDM method.

The R DDM package - developed by Tim Riffe, Everton Lima and Bernardo Queiroz - was used in this dissertation to estimate completeness using the 3 DDM methods [11]. The DDM package automatically selects the age interval that best fits the models and minimizes the residuals for each sex and for each method used (more or less like automatizing the use of graphical analyses for GGB). This strategy to minimize bias in DDM estimates was preferred over the use of specific age ranges because: 1) the estimates obtained through the automatic age interval were closer to those observed in previous literature for Ecuador; and 2) neither the estimates obtained through automatic age interval selection, nor estimates obtained using the fixed age ranges seemed to be affected by migratory patterns in Ecuador (as we mentioned, DDM methods are specially affected by migration).

2.2. Quality

Quality of the mortality registry can be assessed in many ways. Authors have proposed different strategies based on the review of sex and age distribution, of cause of death patterns and the review of ill-defined causes / garbage codes (GC) [12,13]. In this dissertation, quality of mortality registration was assessed by two means: 1) estimating the percentage of garbage codes in the registered deaths in each of the study areas; and 2) estimating the percentage of reported deaths with unspecified age or sex.

Garbage codes can be defined as deaths assigned to codes that provide little or no information for cause of death analysis in public health. Naghavi et al. (2010) described four typologies of garbage codes: 1) “Causes that cannot or should not be considered as underlying causes of death”, such as signs and symptoms (R category in the ICD-10) or essential primary hypertension; 2) “Intermediate causes of death”, such as heart failure or peritonitis; 3) “Immediate causes of death that are the final steps in a disease pathway leading to death”, such as cardiac arrest; and 4) “Unspecified causes within a larger cause grouping”, such as diseases where the site is unspecified [14]. We complemented the garbage code list described by Naghavi et al. by comparing it with the Global Burden of Disease (GBD) 2010, 2013 and 2015 cause lists [15,16]. This process allowed us to obtain a consistent list of GBD codes and garbage codes. We then estimated the percentage of garbage codes (total and of each of the 4 types) in each of the studied areas for deaths of men and women. Annual percentages of garbage codes were also

obtained to describe the temporal evolution in each study area. The complete list of garbage codes used in the study is presented in the following table:

Table 2: List of ICD-10* codes considered garbage codes

Garbage Code Type	ICD-10 Codes
Type 1	A31.1, A59, A60.0, A71-A74, A63.0, B00.0, B07, B08.1, B08.8, B30, B35-B36, F32-F33.9, F40-F42.9, F45-F48.9, F51-F53.9, F60-F98.9, G43-G45.9, G47-G52.9, G54-G54.9, G56-G58.9, H00-H04.9, H05.2-H69.9, H71-H80.9, H83-H93, J30, J33, J34.2, J35, K00-K11.9, K14, L04-L08.9, L20-L25.9, L28-L87.9, L90-L92, L94, L98.0-L98.3, L98.5-L98.9, M03, M07, M09-M12, M14-M25, M35.3, M40, M43.6-M43.9, M45.9, M47-M60, M63-M71, M73-M79, M95-M99, N39.3, N40, N46, N60, N84-N93, N97, Q10-Q18, Q36, Q38.1, Q54, Q65-Q74, Q82-Q84, R00-R99, B94.8, B949.9, G80-G83, Y86, Y87.2, Y89, I10, I15, I70, G09, I69, Y85
Type 2	A40-A41, A48.0, A48.3, E85.3-E85.9, E86-E87, G91.1, G91.3-G91.8, G92, G93.1-G93.6, I26, I27.1, I44-I45, I49-I50, I74, I81, J69, J80-J81, J86, J90, J93, J93.8-J93.9, J94, J98.1-J98.3, K65-K66, K71-K72 (except K71.7), K75, K76.0-K76.4, K92.0-K92.2, M86, N14, N17-N19, I31.2-I31.3, K71.0
Type 3	D65, I45-I46, J96
Type 4	C80, C26, C39, C57.9, C64.9, C76, D00-D13, D16-D18, D20-D24, D28-D48, A49.9, B83.9, B99, E88.9 I51, I99, X59, Y10-Y34, A64, B19, B82, C14, C55, C63.9, C75.9, F99, I64, J98.9, K92.9, P96.9, Q89.9, Q99.9, V87.0-V87.1, V87.4-V87.9, V88.4-V88.9, V89, V99, X84, Y09

Adapted from: Naghavi et al. (2010)
***ICD-10**: International classification of diseases – 10th revision

2.3. Internal Consistency

Following previous studies on the subject, the internal consistency of the death registry was assessed by estimating the percentage of deaths with reported causes of death considered impossible in some age–sex combinations [5,6]. These combinations were created for the study by Phillips et al. (2014) by reviewing medical literature and by expert consultation. This internal consistency indicator was also estimated for 20 age groups in order to observe if a specific age pattern existed.

3. Correcting deficiencies in the mortality registry for different causes of death

As we have mentioned in Chapter 1, until CRVS systems can be improved, and knowing the importance of mortality statistics for monitoring and analysing the health and inequalities of populations and for planning and evaluating public policy [17], several mechanisms for correcting deficiencies have been developed and applied in many countries. To study geographical and social inequalities in mortality in Ecuador, we applied a garbage code redistribution protocol and corrected mortality for completeness in each of the studied areas.

3.1. Garbage code redistribution

To correct deficiencies in the quality of the cause of death data in the mortality registry, GCs were redistributed following the GBD-2010 algorithms [18]. Since the GBD-2010 study, GC redistribution protocols have been developed upon the work of Naghavi et al. (2010). In that work, the authors propose a three-step approach to redistribute GCs by: 1) Identifying them; 2) identifying target causes to which GCs can be redistributed; and 3) choosing how GCs are redistributed to target causes. GCs can be redistributed in three ways: 1) proportional redistribution to all target causes; 2) using statistical models to find the adequate proportions in which each GC should be redistributed to its target causes; and 3) through consultation with experts who decide how each GC is redistributed [14]. For GBD-2010, a combination of these three ways was used to create the redistribution algorithm [19].

No GC redistribution method is ideal, and biases can arise from their application. For example, proportional redistribution ignores the distribution of cause-specific mortality in specific geographical areas, age or sex groups. Expert opinion can be valuable but could be biased. For example, experts from low- and middle-income countries could be underrepresented in expert groups. Regression models have the advantage of including uncertainty, but they need reliable covariables in order to work and can be difficult to adapt to subnational contexts. The GBD-2010 redistribution protocol used has few age and sex restrictions. Later GBD studies have developed more complex GC redistribution protocols that include more age and sex restrictions and cause-specific regression models, including different geographical locations. Unfortunately, adapting and applying these protocols at a subnational scale in low- and middle- income countries can be challenging.

3.2. Correction for completeness

In order to correct mortality for completeness, we have followed two strategies. In the first one, we exemplified how correction methods work at a provincial level (first administrative level – 22 areas). In order to do this, we used the harmonic mean (a measure of central tendency not affected by extreme values and appropriate for rates) of the completeness estimates obtained from the three DDM methods to correct the number of deaths in our analyses. To obtain the corrected number of deaths, we divided the registered deaths by the provincial completeness estimates. When we applied indirect age standardization, we also corrected the reference rates (national age specific

mortality rates) by the harmonic mean of the three estimations of national mortality completeness.

When working at a cantonal level (second administrative level – 193 areas), we had to adapt the strategy to correct mortality for completeness. Completeness estimations can be more unstable in smaller areas, and especially in the ones with low population counts or that had higher migration rates [20]. Moreover, the methods used to estimate completeness do not consider uncertainty or the spatial patterns of mortality and completeness that can be present in the country. For these reasons, we decided to include the cantonal completeness estimates (from the three methods) in the Bayesian Poisson models used to estimate smoothed standardized mortality ratios for Ecuador (which will be described in detail latter in this chapter). By doing this, we could: 1) Obtain posterior smoothed estimates of cantonal completeness that take into account the uncertainty of the three completeness measures in each area; and 2) to obtain mortality estimates (SMRs) corrected by completeness directly from the statistical models.

4. Conceptualizing and measuring deprivation in Ecuador

The conceptualization and components of material and social deprivation can change in different contexts. As mentioned in Chapter 1, most of the research on deprivation and health has been carried out in high income countries. For this reason, it was of paramount importance to define and measure deprivation, taking into account the Ecuadorian context.

In Chapter1, we mentioned a definition for deprivation that is commonly found in the literature, mostly in high-income countries. In the Ecuadorian context, deprivation was defined as *a historically and structurally determined collective phenomenon linked to human rights violations; that creates a social stratification based on power structures and relations that privilege certain social groups and oppress others. This stratification has consequences on the capabilities of certain segments of the population to achieve decent living standards, which in turn affects their health.* This definition was constructed after a literature review that included relevant documents from the Latin American Social Medicine movement[21], official documents from the country (e.g., development plans and the national constitution); and conceptual discussions between the authors.

To operationalise our deprivation definition, we performed a comprehensive search for available data in the country. Demographic and socioeconomic indicators were obtained from The National Population Census 2010, while social capital and subjective wellbeing measures were estimated from the national Living Conditions Survey (LCS) 2014–2015. Subsequently, indicators were distributed in seven deprivation dimensions: 1) Education, 2) Information and Communication, 3) Housing and Urban Environment, 4) Work and Social Security, 5) No discrimination, 6) Healthy Environment, and 7) Social Environment and Social Capital. These dimensions emerged from an assessment of the reviewed literature with the available data. A set of 41 indicators fitting into the above-mentioned deprivation dimensions were selected from our information sources. Indicators were selected or constructed so that higher scores (or percentages) represented less deprivation.

As the selected indicators had different measurement units and scales, they were first standardised to obtain new variables, z, with mean 0 and variance 1. Next, bivariate Spearman correlations were obtained, and when the variables showed correlations greater than 0.90, one of them was removed from subsequent analyses (those more in agreement with our deprivation definition were retained).

Sequential principal component analyses (PCA) were performed to maximise the variance of the first component [22]. PCA can be described as "… a multivariate statistical technique used to reduce the number of variables in a data set into a smaller number of dimensions" [23]. PCA has been widely used to construct socioeconomic and deprivation indexes [22,24–28]. The conditions for applying a PCA were assessed using two criteria: 1) Bartlett's test of Sphericity (statistical significance value set at 5%), and 2) sampling adequacy through the Kaiser-Meyer-Olkin test for the whole dataset and for individual variables. A first PCA was carried out with 36 initial indicators. The correlation of each variable with the first component was estimated. Those variables with correlations lower than 0.50 were removed unless they were considered conceptually essential. A final PCA was performed and the first component was used to estimate standardised index values. Finally, the proportion of contribution of each variable to the index was estimated.

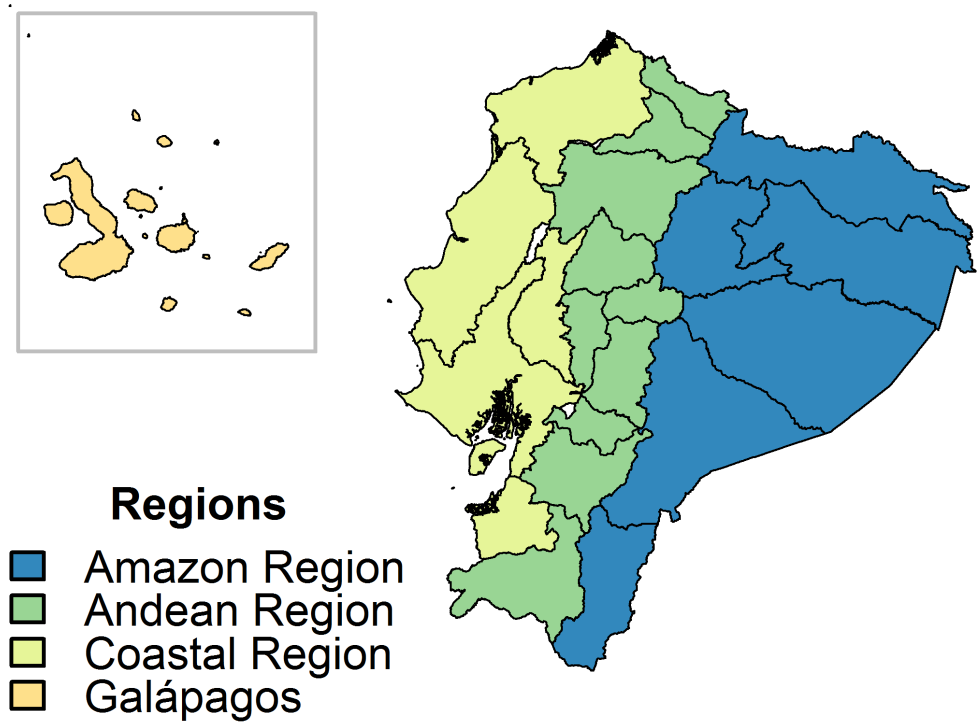
Finally, a Spearman's correlation was performed to determine the correlation between an index obtained with the variables of the first PCA (36 variables) and the final index to assess whether a more parsimonious index could be created without losing important information.

5. Studying the relationship between deprivation and mortality from specific causes of death in Ecuador

5.1. Study areas – geographical scale

For the initial studies of this dissertation, we made the analyses at the provincial level (first administrative level). We selected this geographical scale because it allowed us to test the proposed methods with less bias - especially the estimation of completeness. During the study period, the provinces of Santo Domingo and Santa Elena were created in Ecuador. A stable cartography with 22 provinces was used (joining Pichincha with Santo Domingo, and Guayas with Santa Elena) for the analyses.

Figure 1: Provincial cartography used in the dissertation

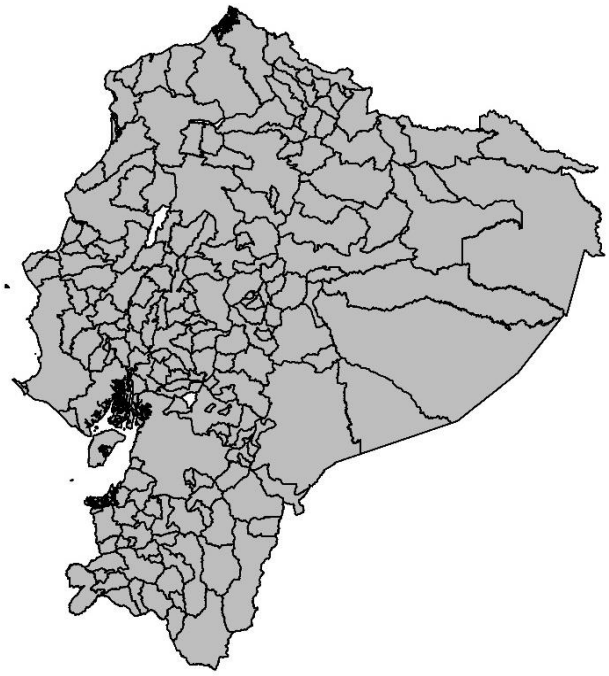


Nevertheless, when we wanted to study the effects of contextual phenomena - as deprivation - on health, the provincial scale is not adequate. Larger geographical scales mask inequalities and, at this level, the identification of clusters is not possible [29]. For this reason, we tried to identify a geographical scale that could properly reflect the territory and that allowed us to perform the research. Cantons (second administrative level) were selected as area of study for three reasons: 1) Cantons are the smallest administrative level with comparable data available. Statistical information in Ecuador is only available at a smaller scale for rural parishes. Information for urban areas is presented only at the cantonal level; 2) each canton has a unique history, social and

natural environment; and 3) Cantons are the smallest administrative level with the capacity to design and implement local policies. Each canton has its own political representation (elected mayor and local elected council members) and budget. People living in a particular canton share a history of common local policies that can affect the distribution of wealth and health.

At the time of the 2010 national population census, Ecuador had 221 cantons with populations ranging from 1,760 to 2,350,278 (median 23,820). As the number of cantons and their borders has changed significantly since 2001, we generated a stable cartography with 193 areas for the analysis of mortality at the cantonal level in Ecuador. Cantons in the Galápagos Islands were excluded as low population and death counts lead to unstable completeness and mortality estimates.

Figure 2: Cantonal cartography used in the dissertation



However, cantons are not a perfect unit of analysis as they are heterogeneous in size and population. Moreover, some of the cantons that had to be joined due to changes in cartography during the study period are quite different geographically and socially. Nevertheless, this has been the best solution until the National Institute of Statistics and Censuses starts to collect and disseminate information in more homogeneous and stable areas.

5.2. Causes of death selected for analyses

For the entire study period, cause of death information was coded using the international classification of diseases and related health problems - 10th Revision (ICD-10). To analyse cause of death data and correct the shortfalls in their quality, deaths were recoded from ICD-10 to Global Burden of Disease (GBD) codes. The GBD cause list is hierarchical and has four levels of diseases and injuries [30]. One of the advantages of using the GBD cause list is that appropriate protocols are available to redistribute ICD codes considered as "garbage" to more appropriate GBD codes. The GBD-2010 cause list was used as reference. Because our database still had ICD-10 codes that were neither assigned to GBD codes nor classified as GCs, we compared our list with the GBD-2013 and GBD-2015 cause lists to obtain a consistent list of cause of death codes and GCs that could be redistributed. Consequently, each ICD-10 code used in the mortality registry was either assigned to a GBD code directly or categorized as a GC and redistributed later to GBD codes.

To select the specific causes of death to be studied, we followed two strategies: 1) to review the causes of death with most registered deaths in both men and women in the country during the study period; and 2) to compare different mortality atlases and research on socioeconomic inequalities in mortality in other countries. With these two assessments, we built a preliminary list and discussed it with the co-authors of the studies presented in this doctoral thesis. A final list with 17 causes of death for women and 17 for men was finally selected and approved. The list includes 3 causes from GBD group A (communicable, maternal, neonatal and nutritional disorders), 11 causes from GBD group B (non-communicable diseases), and 3 causes from GBD group C (injuries). Of the 11 causes from GBD group B, 5 are cancers. We selected the most common fatal neoplasia in the country for men and women (breast cancer is analysed in women and prostate cancer in men). All selected causes (with the exception of cirrhosis of the liver) are level 3 GBD codes. In the following table, we present the cause list used with the number of registered deaths and percentages of death of each cause from 2001 to 2013.

Table 3: Proposed Cause of Death List

Causes	GBD Codes	TOTAL (%) *	WOMEN (%) *	MEN (%) *
All Deaths	All	762,131 (100.00)	330,450 (100.00)	431,681 (100.00)
Lower Respiratory Infections	A.2.3	43,160 (5.66)	20,741 (6.28)	22,419 (5.19)
Tuberculosis	A.1.1	8,821 (1.16)	2,961 (0.90)	5,860 (1.36)
HIV/AIDS	A.1.2	7,924 (1.04)	1,691 (0.51)	6,233 (1.44)
Ischemic Heart Disease	B.2.2	31,545 (4.14)	12,446 (3.77)	19,099 (4.42)
Diabetes Mellitus	B.8.1	30,938 (4.06)	17,361 (5.25)	13,577 (3.15)
Cerebrovascular Disease	B.2.3	29,518 (3.87)	14,407 (4.36)	15,111 (3.50)
Chronic Obstructive Pulmonary Disease	B.3.1	12,988 (1.70)	5,406 (1.64)	7,582 (1.76)
Cirrhosis of The Liver	B.4	22,876 (3.00)	8,174 (2.47)	14,702 (3.41)
Hypertensive Heart Disease	B.2.4	13,714 (1.80)	6,981 (2.11)	6,733 (1.56)
Stomach Cancer	B.1.2	20,400 (2.68)	9,006 (2.73)	11,394 (2.64)
Prostate Cancer (Men)	B.1.9	9,316 (1.22)	0 (0.00)	9,316 (2.16)
Breast Cancer (Women)	B.1.6	5,086 (0,67)	5,086 (1.54)	62 (0.01)
Trachea, Bronchus and Lung Cancers	B.1.5	8,030(1.05)	3,204 (0.97)	4,826 (1.12)
Liver Cancer	B.1.3	7,998 (1.05)	4,332 (1.31)	3,666 (0.85)
Colon and Rectum Cancers	B.1.10	6,225 (0.82)	3,481 (1.05)	2,744 (0.64)
Road Injury	C.1.1	17,173 (2.25)	3,600 (1.09)	13,573 (3.14)
Interpersonal Violence	C.3.2	25,578 (3.36)	2,348 (0.71)	23,230 (5.38)
Self-Harm	C.3.1	10,635 (1.40)	3,069 (0.93)	7,566 (1.75)

***Number of deaths and percentages before garbage code redistribution and correction for completeness**

5.3. Time period – years studied

The studies presented in this dissertation have different time periods that depended on the availability of data when the studies where developed, considering the geographical scale used for each study. We selected 2001 as the staring year because it was the year of the first census we used for the analyses and because changes in cartographical and mortality data were more prominent before this year. When the first study of this dissertation was being developed (2015-2016), the last mortality database available was the one of 2013. Since then, mortality databases from other years have appeared. For study two (provincial level), we could include mortality data until 2016. For study four (cantonal level), we could only include mortality data until 2014 because, since the 2015 national mortality database, the National Institute of Statistics and Censuses of Ecuador censors the information on canton of residence because of new confidentiality policies.

5.4. Population estimates

At the provincial level, population estimates by sex and age groups used for studies were demographical projections and retro-projections from the 2010 census. They were estimated by the National Information System of Ecuador (Spanish acronym: SNI) and

are available online from their web page (http://sni.gob.ec/proyecciones-y-estudios-demograficos).

At the cantonal level, demographical projections were not disaggregated by sex and age groups (only sex or age groups separately). For this reason, we estimated yearly cantonal populations by age and sex using a two-step approach:

- First, using the 2001 and 2010 censuses cantonal population counts by sex and age groups, we performed a probabilistic population projection using the R package "bayesPop" [31]. This package has compiled the methods used by the United Nations (UN) to project national population estimates from available data. For subnational population projections, bayesPop applies the cohort component method; using a set of initial sex and age-specific populations for the subnational study areas. National fertility rates and migration estimates obtained from the UN population projections (2017) are used for the estimations. The complete description of the methods used for probabilistic population projections is not in the scope of this dissertation and can be found elsewhere [31–33]. This population projection allowed us to have cantonal population projections for 2015 and 2020.
- Subsequently, starting from the census (2001 and 2010) and projected (2015 and 2020) populations by sex and age groups, we fitted quadratic equations considering the populations by sex and age and the year. This way we obtained a consistent set of yearly cantonal population estimates by sex and age groups for all the study period.

5.5. Age Standardization

For each study area and selected cause of death in men and women, indirect age standardization was applied using the national mortality rates - after GC redistribution and correction for the harmonic mean of the three national completeness estimates obtained - for the study period in 18 age groups as a reference. Indirect standardization estimates the expected number of deaths in each area by applying reference rates (in this case national mortality rates in each age group) to the population in each age group–area combination. The ratio between observed and expected deaths is called the standardized mortality ratio (SMR). Indirect standardization is useful when age-specific rates in the study areas are considered to be unstable or when age-specific mortality rates are

missing [34]. Moreover, when mapping mortality, this type of age standardization has been preferred to direct standardization as it allows direct comparison of the risks (SMR) between the study regions [35].

5.6. Statistical Analyses

As mentioned, when populations in our study areas are low, or when there are few deaths due to an specific cause, mortality estimations can be unstable and biased. Two main strategies have been used to cope with this problem that presents when analysing small areas. The first one is to aggregate several years of information in order to obtain more stable results [29]. This is not always an acceptable solution, as areas with low populations can still have unstable rates (especially if the studied health condition is uncommon) due to extra-variability from non-measured variables that either have an spatial structure (spatial dependence) or that do not have an spatial structure (non-correlated heterogeneity) [35]. For this reason, several statistical modelling strategies have been developed under the Bayesian statistical paradigm to "smooth" health information in small areas. These models give more robust estimates, as they consider the information not only from individual areas, but also from their neighbouring areas [36]. One of the most widely used approaches for smoothing mortality ratios in small areas, is the use of hierarchical Poisson models that consider both spatial and heterogenous effects [37,38].

The Bayesian hierarchical models used can be univariate (when only one cause of death is included) or multivariate (when several causes are included). The main advantage of multivariate models is that they account for dependence among the studied causes of death while still considering the spatial dependence between the study areas [36]. This means that the estimations of causes with similar risk factors can be more robust, as information for one cause of death is taken also from related causes of death. Building upon previous work in the field of disease mapping, Botella-Rocamora et al.(2015) proposed a multivariate modelling framework (known as M-models) that allows to analyse more causes of death simultaneously in a computationally efficient manner [39]. This modelling strategy was used for our analyses.

Models were run separately for men and women. In our models, in order to consider uncertainty, the three DDM estimations for each study area were introduced, and area means were estimated assuming a normal distribution. In each iteration of the models, the mean of these distributions was used to correct observed deaths. Expected deaths

were estimated using national age-specific mortality rates corrected for national completeness. Cantonal deprivation was introduced as a co-variable in the models. Estimations were obtained using Monte Carlo Markov Chains. Convergence was assessed by visual inspection of the simulated chains; and by inspecting the effective sample size and the potential scale reduction statistic of the model parameters [40].

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Chapter 3 - Evaluation of the mortality registry in Ecuador (2001–2013) – social and geographical inequalities in completeness and quality

Key Points:

- Completeness, quality and internal consistency of the mortality registry in women and men were assessed in the provinces of Ecuador. A classification of provinces based on quality and completeness was also proposed.
- We found substantial inequalities in the performance of the mortality registry between men and women and between geographical areas.
- At the national level, between 2001 and 2010, we estimated a completeness of 65% for women and 68% form men. In both sexes, the worst completeness estimates were seen in Galápagos, the Amazonic provinces and in some of the areas in the Coastal region.
- In all Ecuador during all the study period, 37% of the deaths of women and 34% of the deaths of men were coded with garbage codes. Garbage code percentages were consistently higher for women than for men. In addition, in men and women, the highest garbage code percentages were seen in the Amazonic provinces, in the northern Coastal provinces and in the central Andean region.
- The percentage of deaths with unspecified age or sex, and the percentage of deaths with reported causes of deaths considered impossible in some age–sex combinations were low in all the studied areas.
- The mortality registry could **not** be classified as "acceptable" for both men and women in any of the provinces of Ecuador.
- This study is the first comprehensive evaluation of the mortality registry in the provinces of Ecuador. The results presented can be important to improve mortality statistics, focusing on the areas with the greatest deficiencies.

In this chapter, the preprint of the article published in "Population Health Metrics" is presented. Citation:

Peralta, A., Benach, J., Borrell, C., Espinel-Flores, V., Cash-Gibson, L., Queiroz, B. L., & Marí-Dell'olmo, M. (2019). Evaluation of the mortality registry in Ecuador (2001-2013) - Social and geographical inequalities in completeness and quality. Population Health Metrics, 17(1). https://doi.org/10.1186/s12963-019-0183-y

Capítulo 3: Evaluación del registro de mortalidad de Ecuador (2001 – 2013): desigualdades sociales y geográficas en cobertura y calidad

Puntos Clave:

- Se evaluó la cobertura, calidad y consistencia interna del registro de mortalidad en las provincias de Ecuador. También se propuso una clasificación de las provincias basada en los indicadores obtenidos.
- Se encontraron grandes desigualdades en el desempeño del registro entre hombres y mujeres, y entre las provincias de Ecuador.
- Entre el 2001 y el 2010, a nivel nacional; estimamos una cobertura de registro de mortalidad del 65% en mujeres y del 68% en hombres. Las coberturas más bajas se encuentran en Galápagos, en la región amazónica y en algunas provincias de la costa.
- En todo Ecuador durante todo el periodo de estudio, un 37% de las muertes en mujeres y un 34% de las muertes en hombres se codificaron con códigos basura. Este indicador de calidad es consistentemente más deficiente en mujeres. Las provincias con mayor cantidad de códigos basura se encuentran en la región amazónica, la costa norte y la sierra central.
- En todas las áreas estudiadas, el indicador de deficiencias en consistencia interna fue bajo en el período de estudio.
- El registro de mortalidad no pudo ser considerado “aceptable” en ambos sexos en ninguna de las provincias de Ecuador.
- Este estudio realiza una primera evaluación de diversos aspectos del registro de mortalidad en las provincias de Ecuador. Los resultados presentados pueden ser de gran importancia para mejorar los datos y estadísticas de mortalidad en el país, enfocando recursos y esfuerzos en las áreas con mayores deficiencias.

Peralta A, Benach J, Borrell C, Espinel-Flores V, Cash-Gibson L, Queiroz BL, et al. Evaluation of the mortality registry in Ecuador (2001-2013) - social and geographical inequalities in completeness and quality. Population health metrics. 2019;17(1):3. DOI: 10.1186/s12963-019-0183-y

Chapter 4 - Studying geographic inequalities in mortality due to specific causes in contexts with deficient data sources: lessons from Ecuador

Key Points:

- Deficiencies in data completeness and quality were corrected in order to study mortality due to some of the main causes of death in the provinces of Ecuador in men and women from 2001 to 2016.
- Mortality was corrected using completeness as a correction factor and applying the Global Burden of Disease 2010 garbage code (GC) redistribution protocol. Age-standardized mortality ratios were estimated in the provinces of Ecuador for men and women, before and after application of the correction methods.
- The number of deaths due to ischemic heart disease (IHD) and lower respiratory infections (LRI) greatly increased in the provinces of Ecuador. Overall, GC redistribution added more IHD deaths; and correction for completeness added more LRI deaths. In all Ecuador, after GC redistribution and correction for completeness, deaths from IHD increased by more than 58,000 in women and more than 60,000 in men; and deaths from LRI increased by more than 22,000 deaths in women and more than 21,000 in men.
- Changes in the geographical patterns of cause-specific mortality after corrections of deficiencies in the mortality registry could be evidenced. Provinces in the Amazonic region and Galápagos had large increases in standardized mortality ratios for the studied causes after garbage code redistribution and correction for completeness.
- The new geographical patterns of mortality obtained after correction of the deficiencies were more positively associated with income poverty, which is a sign that corrections could be providing a clearer picture of mortality patterns in the country.

Capítulo 4: Analizando las desigualdades geográficas en mortalidad por causas específicas en contextos con fuentes de información deficientes: lecciones desde Ecuador

Puntos Clave:

- Se corrigieron deficiencias en cobertura y calidad del registro de mortalidad en las provincias de Ecuador entre 2001 y 2016 para estudiar desigualdades geográficas en la mortalidad por algunas de las principales causas de muerte en el país.
- Se corrigió deficiencias en calidad aplicando el protocolo de redistribución de códigos basura (CB) del estudio de carga mundial de enfermedad 2010 (GBD-2010). La cobertura se usó como factor de corrección de la mortalidad. Razones de mortalidad estandarizadas (RME) por edad se estimaron para las causas estudiadas en hombres y mujeres antes y después de aplicar los métodos de corrección.
- El número de muertes por enfermedades isquémicas del corazón (EIC) fue más afectado por la redistribución de CB; y el de muertes por infecciones respiratorias bajas (IRB) se incrementó más por la corrección por cobertura. Los métodos de corrección añadieron, a nivel nacional, más de 118,000 muertes por EIC y más de 41,000 muertes por IRB en ambos sexos.
- Después de aplicar los métodos de corrección, se observaron cambios en los patrones geográficos en la mortalidad por las causas estudiadas. Especialmente se evidenciaron grandes aumentos en las RME en provincias Amazónicas y en Galápagos.
- Los patrones de mortalidad observados en las causas estudiadas después de corregir las deficiencias en el registro se asocian de manera positiva con la pobreza por ingresos. Las correcciones podrían permitir mostrar imágenes más fidedignas de la mortalidad por estas causas en Ecuador.

Este este capítulo presentamos la versión final del artículo aceptado para publicación en la revista "Epidemiology". Referencia bibliográfica:
Peralta A, Benach J, Espinel-Flores V, Gotsens M, Borrell C, Marí-Dell'Olmo M. Studying geographic inequalities in mortality due to specific causes in contexts with deficient data sources: lessons from Ecuador. Epidemiology (In Press. 2019).

Peralta A, Benach J, Espinel-Flores V, Gotsens M, Borrell C, Marí-Dell'Olmo M. Studying Geographic Inequalities in Mortality in Contexts with Deficient Data Sources: Lessons from Ecuador. Epidemiology (Cambridge, Mass). 2020;31(2):290–300. DOI: 10.1097/EDE.0000000000001146

Chapter 5 - Developing a deprivation index to study geographical health inequalities in Ecuador

Key Points:

- A deprivation index to study health inequalities in the cantons of Ecuador was created. In order to accomplish this, a definition of deprivation adapted to the particular context was created, deprivation dimensions were conceptualized, and available indicators for each dimension were selected. Sequential principal component analyses were carried out in order to maximize variance of the first component.
- The final index was constructed with seventeen indicators distributed in five deprivation dimensions: 1) Education, 2) Information and Communication, 3) Housing and Urban Environment, 4) Work and Social Security, and 5) No discrimination. Analyses prioritized material deprivation indicators over social deprivation indicators.
- A clear pattern of deprivation was observed in the country. The most deprived cantons in the country are located in the Amazon, central Andean, and northern and central Coastal regions.
- The index scores are positively associated with all-cause mortality in the study areas, demonstrating the potential utility of the index for public health surveillance, research and public policy planning.

Capítulo 5: Desarrollo de un índice de privación para el estudio de desigualdades geográficas en salud en Ecuador

Puntos Clave:

- Se generó un índice de privación para el estudio de desigualdades en salud en los cantones de Ecuador. Para poder realizarlo, se creó una definición de privación adaptada al contexto de país; se conceptualizaron dimensiones de privación; y se buscaron y seleccionaron indicadores disponibles para cada dimensión. Se realizaron análisis de componentes principales seriados para maximizar la varianza del primer componente.
- El índice final se construyó con diecisiete indicadores distribuidos en cinco dimensiones: 1) Educación, 2) Información y Comunicación, 3) Vivienda y Ambiente Urbano, 4) Trabajo y Seguridad Social, y 5) No discriminación. Los análisis priorizaron a los indicadores de privación material por sobre los de privación social.
- Se encontró un patrón geográfico de privación en Ecuador. Los cantones con mayor privación se localizan en la región Amazónica, en la Sierra central, y en el norte y centro de la Costa.
- Los valores del índice se asocian positivamente con la mortalidad general en las áreas de estudio. El índice creado podría tener un gran número de aplicaciones potenciales para la vigilancia en salud pública, investigación y planificación de política pública en Ecuador.

The following article is the first product of a three-year collaboration with Verónica Espinel-Flores. We both shared every step of the study and preparation of the manuscript. Specifically, we both shared all the tasks of conceptualization, planning, compiling databases, analyses, interpretation of results, writing of the first draft of the article, and preparation of the final version that was accepted for publication. For that reason, we decided to share the first authorship. I will like to thank Veronica for this wonderful shared-learning experience. I think our dissertations are richer after all the collaborative work done together.

Peralta A, Espinel-Flores V, Gotsens M, Pérez G, Benach J, Marí-Dell'Olmo M. Developing a deprivation index to study geographical health inequalities in Ecuador. Revista de saúde pública. 2019;53:97. DOI: 10.11606/s1518-8787.2019053001410

Chapter 6: Material deprivation and leading causes of death by sex in a context of deficient data sources: nation-wide evidence from cantons in Ecuador (2001-2014)

Key Points:

- Studying the relationships between cause-specific mortality and the social and material contextual characteristics of areas is important for research and public policy planning (i.e. to propose possible mechanisms and actions to reduce health inequalities), as well as the generation of knowledge to empower populations. Nevertheless, accomplishing these aims can be challenging in those contexts were data is deficient.
- We analysed the associations between cantonal-level (193 areas) deprivation in continental Ecuador and mortality from seventeen causes of death in men and women between 2001 and 2014.
- Unique geographical patterns of mortality were found for the studied causes of death in both sexes. Many of those causes of death were positively associated with deprivation in both women and men.
- Associations between deprivation and mortality were higher in women than in men.
- The relations between mortality and deprivation rise alarms about persistent health inequalities in the country.
- For many causes of death, the geographical patterns of mortality raise questions about possible connections not only between intermediate determinants of health (that generate deprivation and other social conditions), and proximal risk factors that deteriorate heath; but also with structural determinants (e.g. colonialism, extractivist economies, racism and sexism).

In this chapter, the following manuscript is presented. Citation:
Peralta A, Benach J, Espinel-Flores V, Gotsens M, Borrell C, Martinez-Beneito M, Quijal M, Marí-Dell'Olmo M. Mortality and deprivation in a context with deficient data sources: analysis of 17 causes of death in women and men in the cantons of Ecuador (2001 to 2014). (Unpublished manuscript, 2019).

Capítulo 6: Privación material y las principales causas de muerte por sexo en un contexto con fuentes de información deficientes: evidencia en los cantones de Ecuador (2001 a 2014)

Puntos Clave:

- El estudio de las relaciones entre la mortalidad por causas específicas y características contextuales (materiales y sociales) de áreas geográficas es importante para la planificación de políticas públicas, empoderar a poblaciones y para generar hipótesis sobre posibles mecanismos y acciones que puedan reducir las desigualdades en salud. Sin embargo, realizar este tipo de estudios puede ser un reto en contextos donde existen deficiencias en la calidad y cobertura de datos.
- Este estudio analiza las asociaciones entre privación material a nivel cantonal (193 áreas) en Ecuador continental y la mortalidad por diecisiete causas en mujeres y hombres entre 2001 y 2014.
- Se encontraron patrones geográficos únicos según causa de muerte y sexo. Muchas de las causas de defunción se asociaron positivamente con la privación cantonal tanto en hombres como en mujeres.
- Las asociaciones entre privación material y mortalidad tienden a ser mayores en mujeres.
- Las relaciones entre mortalidad y privación alertan sobre desigualdades en salud importantes y persistentes en Ecuador.
- Los patrones geográficos de la mortalidad por muchas de las causas analizadas generan preguntas sobre las posibles conexiones entre determinantes sociales estructurales como el capitalismo extractivista, el racismo estructural y el machismo; que pueden generar privación y otras condiciones sociales adversas que deterioran la salud de poblaciones - en mayor grado - en ciertas áreas del país.

En este capítulo, se presenta el siguiente manuscrito. Referencia bibliográfica:
Peralta A, Benach J, Espinel-Flores V, Gotsens M, Borrell C, Martinez-Beneito M, Quijal M, Marí-Dell'Olmo M. Mortality and deprivation in a context with deficient data sources: analysis of 17 causes of death in women and men in the cantons of Ecuador (2001 to 2014). (Unpublished manuscript, 2019).

Material deprivation and leading causes of death by sex in a context of deficient data sources: nation-wide evidence from cantons in Ecuador (2001-2014)

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Conflicts of interest: None declared

Sources of funding:

Andrés Peralta and Verónica Espinel were funded by scholarships by the National Secretary of Higher Education, Science, Technology and Innovation of Ecuador (SENESCYT) - Convocatoria Abierta 2013. Joan Benach is recipient of an ICREA Academia award (Generalitat de Catalunya).

Acknowledgments: This article forms part of the doctoral dissertation of Andrés Peralta, at Universitat Pompeu Fabra (UPF) in Barcelona, Spain.

The data used for this study is publicly available from official sources in Ecuador. The complete set of databases and R-scripts can be obtained upon request to the corresponding author.

Abstract

Introduction: Studying the relationships between cause-specific mortality and the social and material contextual characteristics of areas is of vital important in public health. Nevertheless, accomplishing this can be challenging in contexts were data is deficient. The aim of this study was to analyse the associations between cantonal-level (193 areas) deprivation in continental Ecuador and mortality from seventeen causes of death in men and women between 2001 and 2014.

Methods: Ecological study using mortality data from 2001 to 2014 for 193 areas in Ecuador. Completeness was assessed using death distribution methods (DDM) for the intercensal period 2001 to 2010. Quality was assessed by estimating the percentage of garbage codes (GCs) for the entire study period and corrected using a garbage code redistribution protocol. Age-standardized mortality ratios were estimated in the study areas for men and women, using multivariate Bayesian hierarchical models introducing the completeness estimates in order to account for uncertainty. Cantonal-level deprivation was introduced to the models in order to obtain relative risks (RR) and 95% credible intervals (95%CredInt).

Results: Unique patterns of mortality could be observed for different causes of death in women and men. In women, deprivation was positively associated with mortality in 10 of the 17 studied causes. In men, deprivation was positively associated with mortality in 8 of the 17 studied causes. The highest relative risks in both sexes were found for HIV-AIDS (RR 1.38, 95%CredInt 1.27-1.50 in women and RR 1.23, 95%CredInt 1.15-1.31 in men), tuberculosis (RR 1.37, 95%CredInt 1.28-1.46 in women and RR 1.16, 95%CredInt 1.07-1.25 in men) and self-harm (RR 1.23, 95%CredInt 1.15-1.30 in women and RR 1.13, 95%CredInt 1.07-1.19 in men). In general, associations between deprivation and mortality were stronger in women than in men.

Conclusions: We have observed cause and sex specific geographical patterns and relationships between mortality and deprivation. Further research is required to clarify this associations, especially the connexions between racism, sexism, extractivist capitalism and deprivation should be deepened.

Key Words: Mortality; Vital Statistics; Social Determinants of Health; Social Inequity; Poverty; Ecuador, Health Geography.

Introduction

The study of mortality - general and by specific causes of death – has historically been one of the main approaches for the evaluation of the health status of populations. Moreover, studying mortality patterns and their associations with variables representing the social conditions of populations is a fundamental part of a social determinants of health surveillance system[1]. Indeed, for many years it has been known that mortality is not distributed evenly across social groups and territories[2–4]. Nevertheless, performing this type of studies has shown to be challenging in many middle and low-income countries. Limitations in national research capacities[5], and in the completeness and quality of data[6,7] contribute to a large and widening gap in research between the global south and north. Moreover, inequalities in mortality data and statistics are not only seen between countries but also within countries. In Latin America, for example, studies in Brazil, Chile and Ecuador have found wide differences in the completeness and quality of mortality statistics between sub regions in each country[8–10].

Considering that many civil registration and vital statistic systems present deficiencies, several methods to correct data for deficiencies in completeness and quality have been developed and applied in global studies in which countries are the units of analysis[11–13]. In a nutshell, these methods correct deficiencies in quality by applying garbage code redistribution methods, and estimate completeness and correct deaths for those estimates[14]. For example, a recent study performed in Ecuador at a provincial level applied correction methods to study mortality due to specific causes of death finding profound changes not only in the number of deaths but also in the geographical patterns of mortality[15].

Deprivation can be defined as the lack of material and social resources needed by individuals and social groups to achieve the living standards in a given historical time and geographical location considered to be essential by their social and cultural groups[16]. Indicators of deprivation have been widely used in social epidemiology and public health to describe the effects of social determinants of health and contexts on the health of populations[17]. Research showing associations between mortality (general and specific causes) and deprivation is thus extensive, especially in high income countries[16,18]. However, only few studies have analysed how multiple types of deprivation shape people's health and health inequities (including mortality and other health outcomes) in middle- and low-income countries[19]. A recent study in Ecuador

found a clear geographical pattern of high deprivation, and associations between deprivation and all-cause mortality in women and men at a small area level (cantons, second administrative level). In that study, for each standard deviation increase in the cantonal deprivation score, mortality risk increased six percent in women and four percent in men[20]. Nevertheless, to our knowledge, there have been no studies analysing the associations between cause-specific mortality and deprivation in the country.

The main aim of this study was to analyse associations between material deprivation and 17 of the leading causes of death in men and women in Ecuador from 2001 to 2014. Specific objectives included correcting mortality for deficiencies in the mortality registry, estimating age standardized mortality rates for the studied causes in women and men and examining the associations between cause-specific mortality and deprivation.

Methods

A) Study design, units of analysis and information sources

Ecological study that uses mortality data from 2001 to 2014. The units of analysis are the cantons of Ecuador. At the time of the 2010 national population census, Ecuador had 221 cantons with populations ranging from 1,760 to 2,350,278 (median 23,820). As the number of cantons and their borders has changed significantly since 2001, we generated a stable cartography with 193 areas for the analysis of mortality at the cantonal level in Ecuador (see supplementary figure 1). The three cantons from the Galápagos Islands were excluded from the analyses as they presented low population and mortality counts, leading to unstable completeness and mortality estimates.

The main information sources of the study were the National Mortality Registry between 2001 and 2014, the 2001 and 2010 National Population Censuses; and cantonal deprivation scores from a recent study carried out in the country[20]. The National Mortality Registry feeds on all individual death certificates issued by health professionals or (in their absence) by police, civil authorities or civil registration officials. The National Institute of Statistics and Censuses (INEC) collects all death certificates, determines the underlying cause of death, performs basic quality checks and ensembles yearly mortality databases for the country[21]. Mortality databases include socio-demographic information such as age and sex, home and death addresses; and causes of death. Population censuses have been performed since the 1950's in Ecuador,

approximately every 10 years. Both the 2001 and 2010 studies were de facto population censuses, meaning they count all people present in the national territory in the place where they are at the moment of the census (in opposition to the place of residence). In both cases, information was collected in just one day (November 25, 2001 and November 28, 2010)[22]. For the study of mortality, the main variables used were population counts by age and sex groups in each of the studied areas. Both the mortality and census databases are publicly available the INEC webpage[23,24].

B) Cause of death information

For the entire study period, cause of death information was coded using the International classification of diseases and related health problems - 10th Revision (ICD-10). To analyse cause of death data and correct the shortfalls in their quality, deaths were recoded from ICD-10 to Global Burden of Disease (GBD) codes. The GBD cause list is hierarchical and has four levels of diseases and injuries[14]. One of the advantages of using the GBD cause list is that appropriate protocols are available to redistribute ICD codes considered as "garbage" to more appropriate GBD codes. The GBD 2010 cause list was used as reference. Because our database still had ICD-10 codes that were neither assigned to GBD codes nor classified as GCs, we compared our list with the GBD 2013 and GBD 2015 cause lists to obtain a consistent list of cause of death codes and GCs that could be redistributed. Consequently, each ICD-10 code used in the mortality registry was either assigned to a GBD-2010 code directly or categorized as a GC and redistributed later to GBD codes.

To select the specific causes of death to be studied, we followed two strategies: 1) to review the causes of death with most registered deaths in both men and women in the country during the study period; and 2) to compare different mortality atlases and research on socioeconomic inequalities in mortality in other countries[25–30]. A final list with 17 causes of death for women and 17 for men was constructed and approved by the research team; including the following causes of death: lower respiratory infections, tuberculosis, HIV-AIDS, ischemic heart disease, diabetes mellitus, cerebro-vascular-disease, chronic-obstructive pulmonary disease, cirrhosis, hypertensive heart disease, stomach cancer, breast cancer (women only), prostate cancer (men only), respiratory cancer, liver cancer, colon cancer, road injuries, self-harm and interpersonal violence. For each sex, the list includes 3 causes from GBD group A (communicable, maternal, neonatal and nutritional disorders), 11 causes from GBD group B (non-communicable

diseases), and 3 causes from GBD group C (injuries). All selected causes (with the exception of cirrhosis of the liver) are level 3 GBD codes. The list of the specific ICD-10 codes for each of the selected causes can be found in the supplementary material of the GBD-2010 studies[31].

C) Completeness

To estimate completeness, we used the three types of DDMs: synthetic extinct generations (SEG), generalized growth balance (GGB), and the GGB-SEG hybrid. All DDMs compare the age distribution of a population at two points (2001 and 2010 censuses in our study) with the age distribution of the recorded deaths in that population (in the intercensal period). Completeness estimates for male and female mortality in the study areas were estimated using the R DDM package[32], following the methodology described in a recent study in the country[10]. The DDM package automatically selects the age interval that best fits the models and minimizes the residuals for each sex and for each method used. In the cited study, this strategy to minimize bias in DDM estimates was preferred over the use of specific age ranges[33] because: 1) estimates obtained through automatic age intervals were closer to those observed in previous literature for Ecuador; and 2) estimates obtained using both strategies were not related to migratory patterns in Ecuador (DDM methods are specially affected by migration).

D) Quality

The quality of mortality registration was assessed by estimating the percentage of GCs in the registered deaths in each of the study areas. To correct deficiencies in the quality of the cause of death data in the mortality registry, GCs were redistributed following the GBD-2010 algorithms[13]. Since the GBD-2010 study, GBD redistribution protocols have been developed upon the work of Naghavi et al. (2010), who proposed a three-step approach to redistribute GCs by: 1) Identifying them; 2) identifying target causes to which GCs can be redistributed; and 3) choosing how GCs are redistributed to target causes. GCs can be redistributed in three ways: 1) proportional redistribution to all target causes; 2) using statistical models to find the adequate proportions in which each GC should be redistributed; and 3) through consultation with experts[34]. For GBD-2010, a combination of these three approaches was used to create the redistribution algorithm[35].

E) Population estimates

We estimated yearly cantonal populations by age and sex for all the study areas using a two-step approach: First, using the censal cantonal population counts by sex and age, groups (2001 and 2010), we performed a probabilistic population projection using the R package "bayesPop". This package has compiled the methods used by the United Nations (UN) to project national population estimates from available data. For subnational population projections, bayesPop applies the cohort component method; using a set of initial sex and age-specific populations for the subnational study areas. National fertility rates and migration estimates obtained from the UN population projections (2017) are used for the estimations. The complete description of the methods used for probabilistic population projections can be found elsewhere[36–38]. This population projections allowed us to have cantonal population counts or estimates for 2001, 2010, 2015 and 2020. Subsequently, we fitted quadratic equations considering the populations by sex and age and the year. These steps allowed us to obtain a consistent set of yearly cantonal population estimates by sex and age groups for all the study period.

F) Age Standardization

For each study area and selected cause of death in men and women, indirect age standardization was applied using the national mortality rates (after GC redistribution and correction for completeness) for the study period in 18 age groups as a reference. To correct the national age-specific age rates for completeness, the harmonic means of the national estimations of the three GGB methods in men and women were used. Indirect standardization estimates the expected number of deaths in each area by applying reference rates (in this case national mortality rates in each age group) to the population in each age group–area combination. The ratio between observed and expected deaths is called the standardized mortality ratio (SMR). Indirect standardization is useful when age-specific rates in the study areas are considered to be unstable or when age-specific mortality rates are missing[39]. Moreover, when mapping mortality, this type of age standardization has been preferred to direct standardization as it allows direct comparison of the risks (SMR) between the study regions[40].

G) Statistical Analyses

When populations in some of the study areas are low, or when there are few deaths, SMR estimations can be unstable and biased. For this reason, several statistical

modelling strategies have been developed under the Bayesian statistical paradigm to obtain more robust estimates, as they consider the possible existence of spatial dependence of the information[41]. One of the most widely used approaches for smoothing mortality ratios in small areas, is the use of hierarchical Poisson models that consider both spatial and heterogeneous effects(e.g. BYM models proposed by Bessag, York and Mollie)[42,43].

The Bayesian hierarchical models used can be univariate (when only one cause of death is included) or multivariate (when several causes are included). The main advantage of multivariate models is that they account for dependence among the studied causes of death while still considering the spatial dependence between the study areas[41]. This means that the estimations for causes with similar risk factors can be more robust, as information for one cause of death nourishes from related causes of death. Building upon previous work in the field of disease mapping, Botella-Rocamora et al. proposed a multivariate modelling framework that allows to analyse more causes of death simultaneously in a computationally efficient manner[44]. This modelling strategy, called M-based modelling, was used for our analyses.

In our models, in order to consider uncertainty of completeness estimates, the three DDM estimations for each study area were included, considering that these three values in each area follow a normal distribution. In each iteration of the models, the mean of these normal distributions was used to correct observed deaths. Cantonal deprivation was introduced as a co-variable in the models. In the cited study, deprivation scores were estimated by applying principal component analysis to seventeen indicators distributed in five proposed deprivation dimensions: 1) Education, 2) Information and Communication, 3) Housing and Urban Environment, 4) Work and Social Security, and 5) No discrimination. The resulting score is a z-score were higher values represent higher levels of material deprivation[20]. Deprivation was estimated for the 221 areas of Ecuador (in 2010), and we had a stable cartography with 193 areas. For this reason, population-weighted means of deprivation scores were estimated for the areas that were joined for this study.

The model has two steps. The first step of the model is the following:

$$O_{ij} \sim Poisson(\lambda_{ij})$$

$$\log(\lambda_{ij}) = \log(E_{ij}) + \log(mu\_c_i) + \alpha_j + \theta_{ij}$$

(step 1)

For each area i and cause j, O_{ij} is the observed number of deaths (after GC redistribution), E_{ij} is the expected number of deaths, and mu_c_i represents the mean of the three completeness estimates in each area, assuming a normal distribution with a fixed standard deviation for all areas. θ_{ij} represents a collection of random effects that jointly specify how within-cause and between-cause dependence is defined. This first step allowed us to estimate sSMR (by exponentiating θ_{ij}) for each area and cause combination, and fixing a posterior completeness mean (mu_c_i) for each area that can be used in the second step, were we analyse the relationship between cause specific mortality and deprivation scores in each area (D_i):

$$O_{ij} \sim Poisson(\lambda'_{ij})$$

$$\log(\lambda'_{ij}) = \log(E_{ij}) + \log(mu\_c_i) + \alpha'_j + \beta_j \cdot D_i + \theta'_{ij}$$

(step 2)

This step allowed us to obtain the cause-specific relative risks (RR) for each unit increment in deprivation (and their 95% credible intervals) by exponentiating β_j. In both steps, the within -cause dependence part of θ for each cause was modelled following the BYM approach that considers both spatial and heterogenous effects. All areas that share part of a border were considered neighbours. An improper uniform prior distribution was assigned to β_j. For the rest of the effects, we assigned prior distributions as recommended by Botella-Rocamora et al.[44].

The posterior distributions were obtained using Monte Carlo Markov Chains. These analyses were carried out calling WinBUGS 1.4.3 through R using the R2WinBUGS package[45–47]. Three chains were iterated up to 200,000 times. The first 20,000 were discarded as bur-in; and 3,000 iterations were saved. Convergence was assessed by visual inspection of the simulated chains; and by inspecting the effective sample size and the potential scale reduction statistic of the model parameters[48].

Models were run separately for men and women. Deprivation and sSMR are geographically represented in septiles, using a diverging blue-red scale. In the case of deprivation, red colours indicate higher deprivation scores; while blue colours indicate lower deprivation scores. In the case of mortality, red colours indicate higher mortality risk and blue colours lower mortality ratios. Posterior means of completeness estimates are geographically represented in quintiles, using a sequential scale were lighter colours represent higher completeness estimates and dark red represent low completeness

estimates. Finally, the probabilities of sSMR being higher than 100 in each area are represented using a fixed scale (Less than 10%, 10 to less than 20%, 20 to less than 80%, 80 to less than 90%, and 90 to 100%) and a diverging colour scheme, were green represents the lowest probabilities and red the highest probabilities. This final representation allows the reader to assess the statistical strength of the sSMR estimates in each area.

Results

Table 1 shows the wide differences in mortality, population, deprivation and mortality registry performance between the study areas. For all studied causes of death in both sexes, there were areas with 0 registered deaths and one-quarter of the areas have less than 15 registered deaths during the study period for all the studied causes. In Supplementary table 1, the distribution of the number of deaths from the studied causes after GC redistribution in the study areas is shown. Changes can be seen in all the studied causes but are more prominent on deaths due to ischemic heart disease in women and men.

Table 1: Description of the main study variables in the 193 study areas in women and men

	Women						Men					
	Min	P25	P50	Mean	P75	Max	Min	P25	P50	Mean	P75	Max
Lower Respiratory Infection (n)	0	12	31	117	85	4,749	0	14	37	125	95	4,882
Tuberculosis (n)	0	1	5	16	12	844	0	3	7	32	27	1,989
Human Immunodeficiency Virus (HIV - AIDS) (n)	0	0	1	10	4	855	0	1	3	36	15	3,064
Ischemic Heart Disease (n)	0	9	19	74	48	2,818	0	13	33	112	81	3,777
Diabetes Mellitus (n)	0	10	22	98	59	4,851	0	6	16	77	45	4,311
Cerebro-Vascular Disease (n)	0	8	23	82	57	3,122	0	9	23	85	63	3,345
Chronic-Obstructive Pulmonary Disease (n)	0	3	7	31	22	1,335	0	5	12	44	31	1,853
Cirrhosis (n)	0	4	11	46	33	2,314	0	7	23	83	59	3,350
Hypertensive Heart Disease (n)	0	3	9	40	28	2,242	0	3	10	38	27	2,172
Stomach Cancer (n)	0	6	18	51	41	1,415	0	10	25	64	58	1,659
Breast Cancer (n)	0	2	6	29	15	1,377	-	-	-	-	-	-
Prostate Cancer (n)	-	-	-	-	-	-	0	7	17	53	38	1,775
Respiratory Cancer (n)	0	1	5	19	12	803	0	3	8	28	17	1,261
Liver Cancer (n)	0	3	8	25	21	830	0	2	7	21	17	669
Colon Cancer (n)	0	1	4	20	11	917	0	1	4	16	10	686
Road Injuries (n)	0	3	7	20	18	615	0	13	29	76	72	2,323
Self Harm (n)	0	2	6	17	14	440	0	8	17	42	37	1,018
Interpersonal Violence (n)	0	1	3	13	11	465	0	7	25	124	97	5,303
Mean Yearly Population[1]	1,241	6,029	12,452	35,973	27,631	1,150,230	1,326	6,068	13,032	35,297	27,326	1,114,658
Garbage Codes (%)	24	34	42	45	55	81	22	32	38	42	51	77
Completeness (%)[2]	16	63	70	69	80	97	29	64	74	73	82	97
Deprivation Score[3]	-3.1	-0.7	0.0	0.0	0.6	3.1	-3.1	-0.7	0.0	0.0	0.6	3.1

(n): Counts of deaths in cantons before garbage code redistribution or correction for completeness.

1: Mean yearly population is the average yearly population in the 14 years of the study period.

2: Posterior mean of the completeness mean estimated by the statistical models used.

3: Higher deprivation scores represent cantons with higher levels of material deprivation.

P25, P50 and P75 are the first quartile, median and third quartile respectively.

Yearly population presents wide variation between areas too, ranging from 1,241 to 1,150,230 in women and from 1,326 to 1,114,658 in men. The performance indicators of the mortality registry reveal an heterogeneous picture too. For example, in the mortality registry of women, half of the studied areas present completeness estimates under 70% and with more than 40% of deaths coded with garbage codes. In Figure 1, we can see that both in women and men, the lowest completeness estimates can be found in the Amazonic and northern Coastal regions mainly, while the highest completeness estimates can be found in the Andean region. Material deprivation scores are higher in cantons in the Coastal region, the central Andean region and some Amazonic areas.

Figures 2 and 3 show the geographical representation of sSMR and the probabilities of sSMR being higher than 100 for the most incident cause of death in each GBD group (lower respiratory infections, ischemic heart disease, road injuries) and the most incident fatal cancer in the country (stomach cancer). Maps for the rest of the studied causes can be found in the Supplementary Appendix (figures 2 thru 18). If we examine lower respiratory infections, in both men and women high sSMR estimates are found mainly in areas located in the southern Amazonic and central Andean regions. It is

worth noticing that Guayaquil, the most populated canton in the country has high sSMR for this cause in both women and men. In contrast, if we look at the geographical distribution of ischemic heart disease, it can be noticed that in for both men and women, high sSMR are located mainly in the Coastal region (especially areas in the central and northern parts of the region). Similar patterns can be seen for other disorders of the circulatory system (cerebro-vascular diseases and hypertensive heart disease) and for diabetes. The analyses of stomach cancer reveal a different pattern. In both women and men, most of the areas with high sSMR are located in the Andean region. A group of areas with high risk of stomach cancer mortality can be observed in the northern Andean region (all the cantons of Carchi province – bordering with Colombia). In the final column of both figures, we can examine mortality due to road injuries. Most of the areas with high sSMR in men and women are located in the Amazonic region. In men, high risk areas are more concentrated in the northern Amazonic region, while in women they extend through all the region.

Figure 1: Geographical representation of deprivation and completeness estimates in the cantons of Ecuador

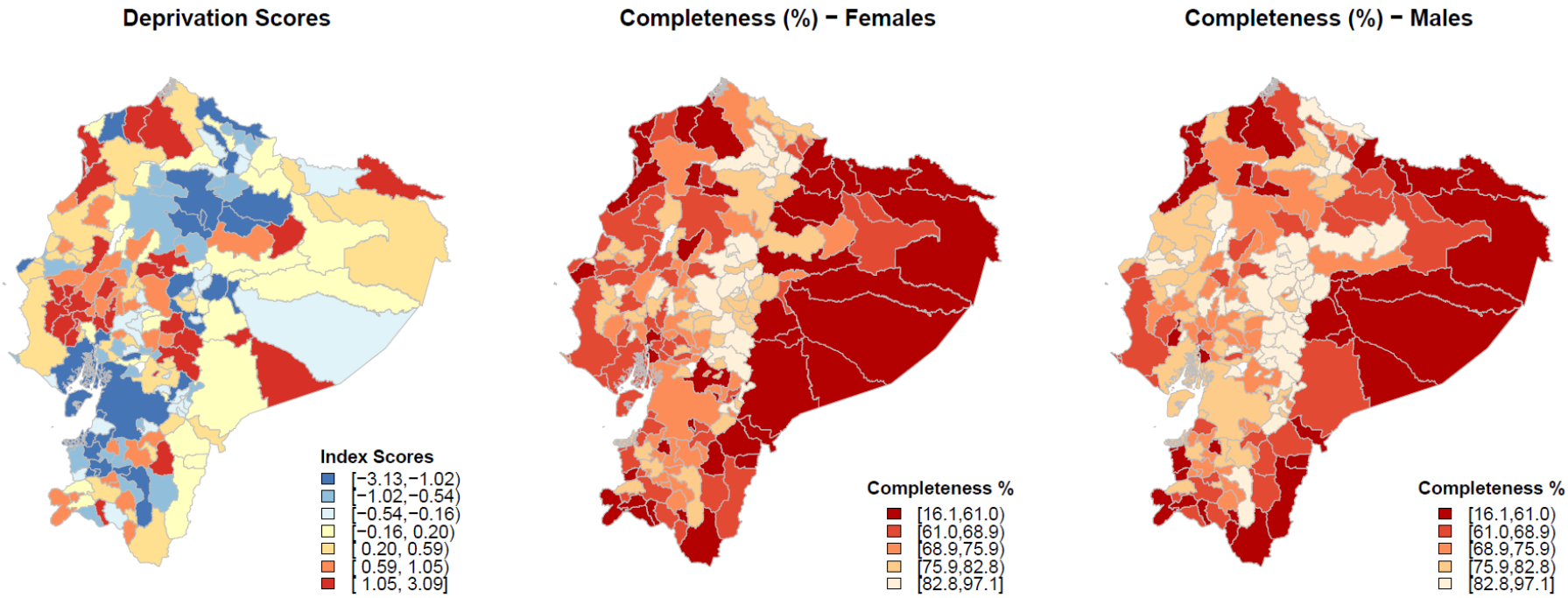
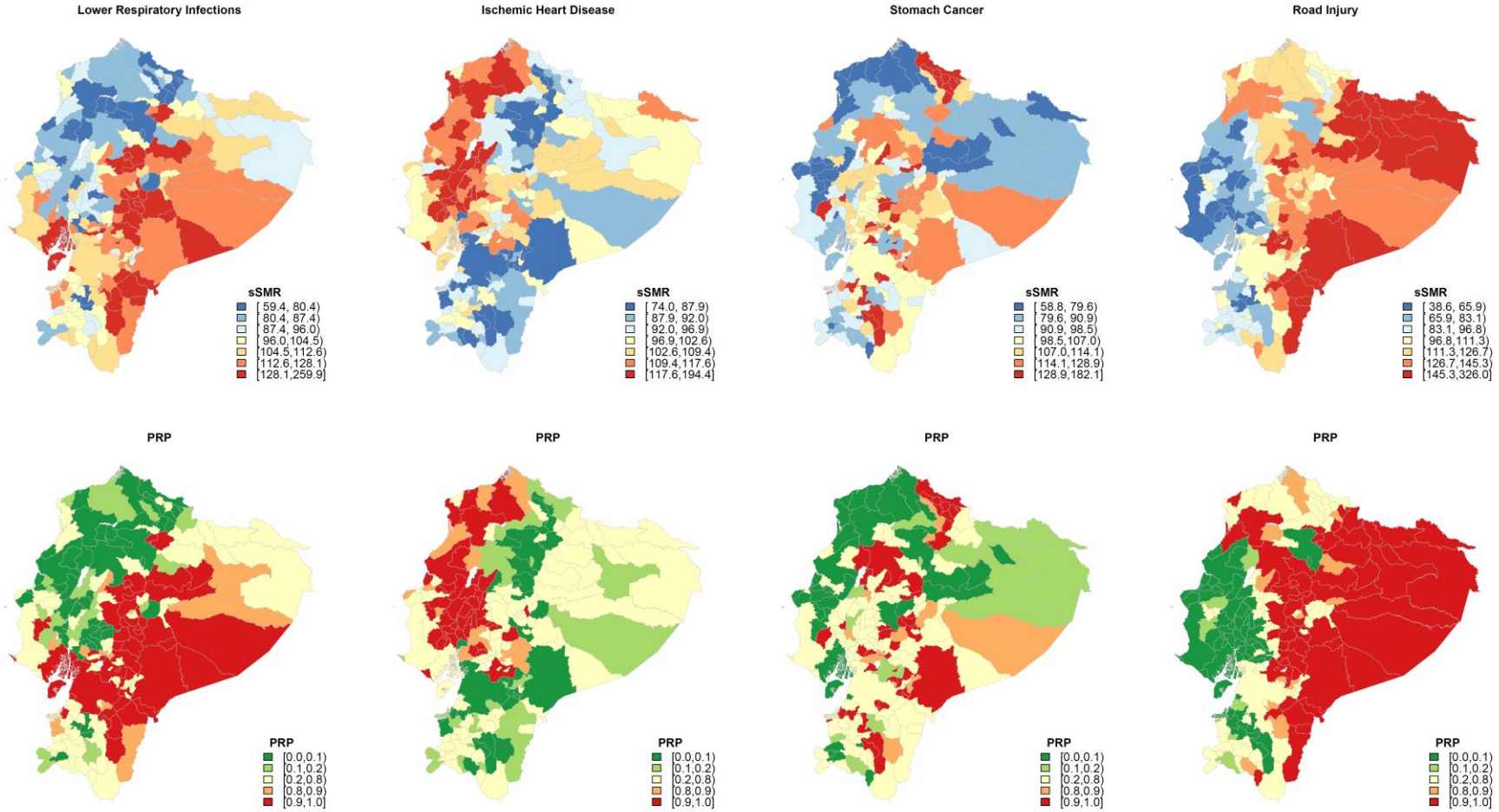
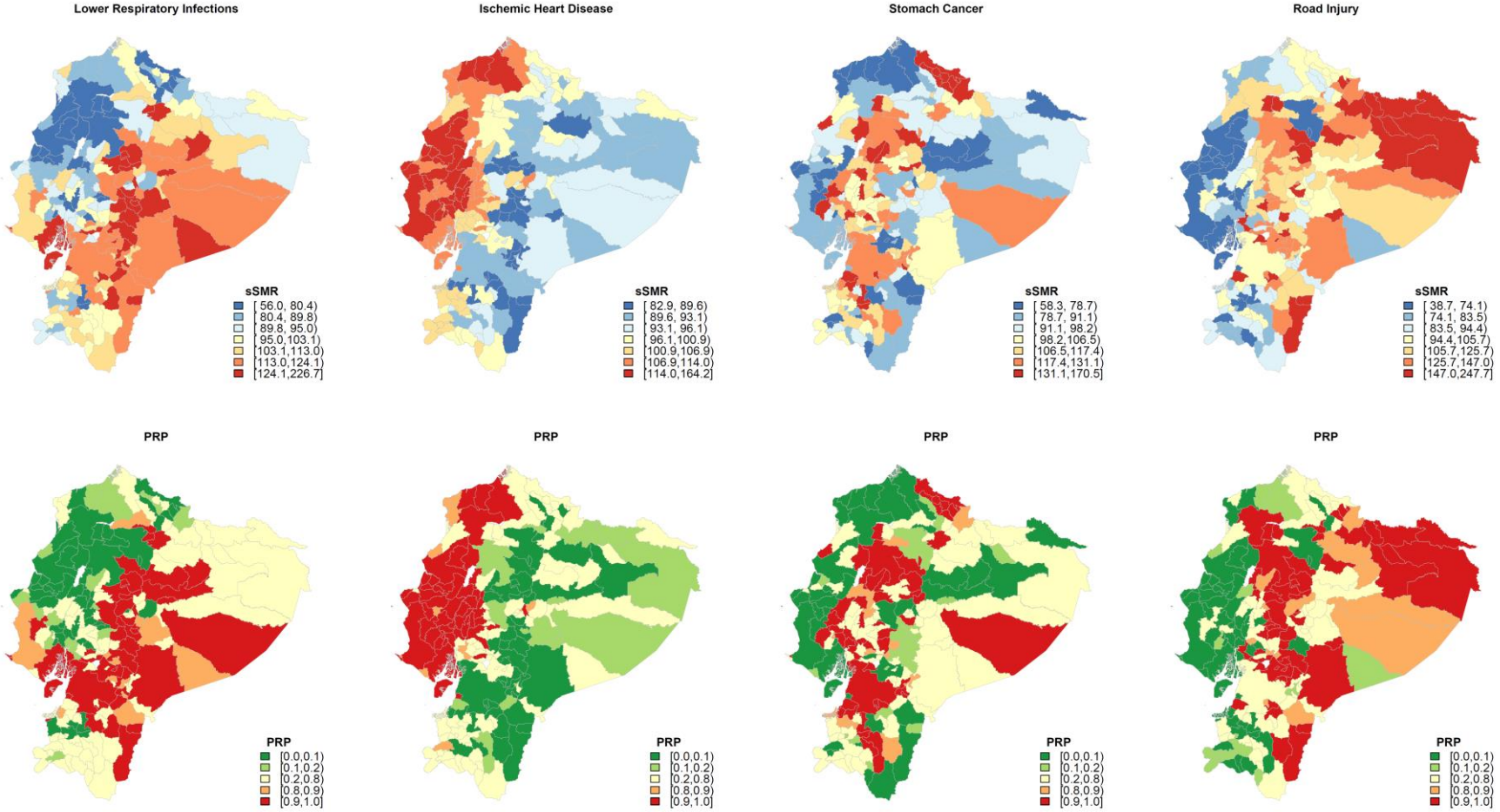


Figure 2: smoothed Standardized Mortality Rates (sSMR) for women – Ecuador – 2001 to 2014



PRP: Probability of sSMR being higher than 100

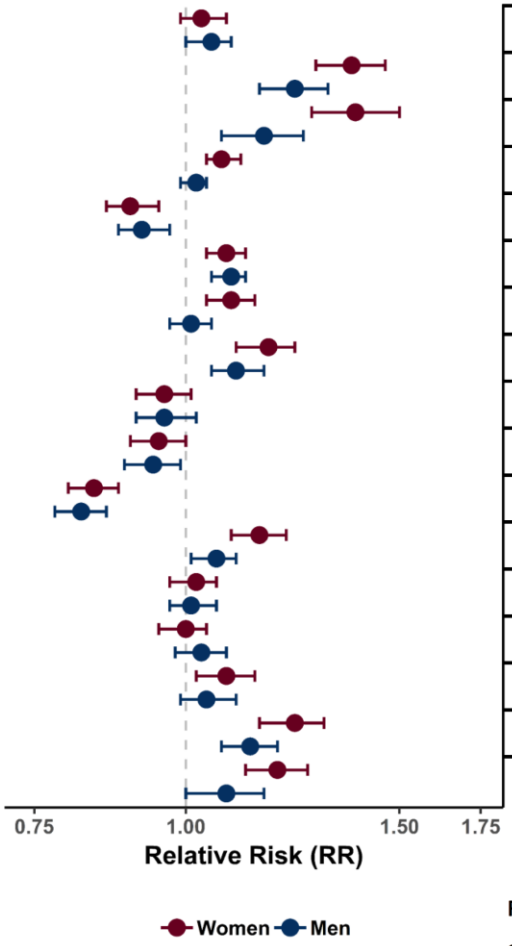
Figure 3: smoothed Standardized Mortality Rates (sSMR) for men – Ecuador – 2001 to 2014



PRP: Probability of sSMR being higher than 100

In the Supplementary Appendix, geographical representations of sSMR for all the studied causes of death can be found next to the geographical representation of deprivation in the study areas. These representations allow visual assessments of similarities and differences between mortality and material deprivation patterns. Figure 4 shows the associations between deprivation and mortality found for the 17 causes of death by sex, and their 95% credible intervals (95%CredInt). In the following lines we will describe the causes of death for which the 95%CredInt does not include the number 1 (considered significative). In women, deprivation was positively associated with mortality in 10 of the 17 studied causes (tuberculosis, HIV-AIDS, ischemic heart disease, cerebro-vascular disease, chronic-obstructive pulmonary disease, cirrhosis, respiratory cancer, road injuries, self-harm and interpersonal violence). For 3 of the 17 causes analysed (diabetes miellitus, stomach cancer and breast cancer), cantonal deprivation was negatively associated with mortality. The highest relative risks in women were found for HIV-AIDS (RR 1.38, 95%CredInt 1.27-1.50), tuberculosis (RR 1.37, 95%CredInt 1.28-1.46) and self-harm (RR 1.23, 95%CredInt 1.15-1.30). In men, deprivation was positively associated with mortality in 8 of the 17 studied causes (lower respiratory infections, tuberculosis, HIV-AIDS, cerebro-vascular disease, cirrhosis, respiratory cancer, self-harm and interpersonal violence). For 3 of the 17 causes analysed, negative associations between cantonal deprivation and mortality were found (diabetes miellitus, stomach cancer and prostate cancer). The highest relative risks in men were found in the same causes of death: HIV-AIDS (RR 1.23, 95%CredInt 1.15-1.31), tuberculosis (RR 1.16, 95%CredInt 1.07-1.25) and self-harm (RR 1.13, 95%CredInt 1.07-1.19). In general, associations between deprivation and mortality were stronger in women than in men.

Figure 4: Associations between mortality and deprivation for women and men – Ecuador – 2001 to 2014



Cause	RR Women	95%CredInt	RR Men	95%CredInt
Lower Respiratory Infections	1.03	0.99 - 1.08	1.05	1.00 - 1.09
Tuberculosis	1.37	1.28 - 1.46	1.23	1.15 - 1.31
Human Immunodeficiency Virus (HIV-AIDS)	1.38	1.27 - 1.50	1.16	1.07 - 1.25
Ischemic Heart Disease	1.07	1.04 - 1.11	1.02	0.99 - 1.04
Diabetes Miellitus	0.90	0.86 - 0.95	0.92	0.88 - 0.97
Cerebro-Vascular Disease	1.08	1.04 - 1.12	1.09	1.05 - 1.12
Chronic-Obstructive Pulmonary Disease	1.09	1.04 - 1.14	1.01	0.97 - 1.05
Cirrhosis	1.17	1.10 - 1.23	1.10	1.05 - 1.16
Hypertensive Heart Disease	0.96	0.91 - 1.01	0.96	0.91 - 1.02
Stomach Cancer	0.95	0.90 - 1.00	0.94	0.89 - 0.99
Breast Cancer / Prostate Cancer	0.84	0.80 - 0.88	0.82	0.78 - 0.86
Respiratory Cancer	1.15	1.09 - 1.21	1.06	1.01 - 1.10
Liver Cancer	1.02	0.97 - 1.06	1.01	0.97 - 1.06
Colon Cancer	1.00	0.95 - 1.04	1.03	0.98 - 1.08
Road Injuries	1.08	1.02 - 1.14	1.04	0.99 - 1.10
Self Harm	1.23	1.15 - 1.30	1.13	1.07 - 1.19
Interpersonal Violence	1.19	1.12 - 1.26	1.08	1.00 - 1.16

RR: Relative Risk

95%CredInt: 95% credible interval

Discussion

We have estimated mortality ratios at a cantonal level for some of the leading causes of death in women and men in Ecuador from 2001 to 2014, correcting deficiencies in the mortality registry. Also, we analysed whether mortality due to these main causes of death is associated with deprivation. Our results show rather unique geographical patterns of sSMR for different causes of death in both women and men. Moreover, most of the studied causes of death were associated with deprivation in both men and women. The highest positive associations between deprivation and mortality were observed in both sexes for tuberculosis, HIV-AIDS and self-harm. Associations between material deprivation and mortality causes were stronger in women than in men.

The analyses of the geographical patterns of mortality and their association with deprivation presented in this article are of vital importance in order to identify high risk areas that can be targeted by public policy, and also to generate hypotheses for further studies that can help to elucidate the potential causes of those patterns and associations [49]. In the next paragraphs we will discuss some of the results obtained, ordered by GBD level 1 categories, emphasising questions or hypotheses that can be studied in further studies.

A) Infectious Diseases

This group includes tuberculosis and HIV-AIDS, the two mortality causes that are more strongly associated with deprivation in both women and men. The relation between tuberculosis and HIV-AIDS mortality, and deprivation has been well-documented worldwide[50–52]. This seems to be the case in Ecuador too. Nevertheless, other social, cultural and behavioural contextual and individual variables should be studied in depth too in the country in order to understand these relationships. It is important to notice and understand the potential causes for the agglomeration of high-risk areas for HIV-AIDS mortality in the Coastal region. In the case of mortality due to lower respiratory infections, the presence of a mild positive association with deprivation in men only should be further studied. A recent study in the country suggests that policies as conditional cash transfers between 2009 and 2014 have reduced respiratory mortality in children under 5[53]. It is plausible that these types of policies have effectively reduced socioeconomic inequalities in mortality due to some causes. However, many other factors including ethnic discrimination, overcrowding and access to basic services among others, should be studied in order to plan and develop effective policies in those

areas with higher mortality risk in the country (especially in the Amazonic and Central Andean regions and Guayaquil).

B) Non-Communicable Diseases

Three of the causes analysed correspond to circulatory system diseases (ischemic heart disease, cerebro-vascular disease and hypertensive heart disease). The similar geographical patterns of mortality seen in these causes point out to similar determinants, risk factors, and aetiologies. The National Survey on Health and Nutrition of Ecuador (ENSANUT-2012) found high prevalences of high blood pressure and metabolic syndrome in coastal provinces in Ecuador[54]. The distribution of these factors however needs to be studied more in depth in the country. For example, ischemic heart disease mortality in women shows a clear positive association with deprivation; which is not the case among men. We may speculate that this phenomenon could be partially explained by gender bias in the diagnostic and early treatment of ischemic heart disease[55] being greater in women that live in more deprived areas. However, the differences in the associations between mortality and deprivation between causes and between sexes remain to be clarified.

Diabetes mortality is a particular case because it presents a similar geographical pattern as circulatory system diseases, but paradoxically cantonal deprivation seems to act as a protective factor in both women and men. ENSANUT-2012 reported higher prevalences of diabetes in urban centres of the Coastal region. Moreover it also found that diabetes prevelences were higher in less deprived populations[54]. Both findings may explain why diabetes is negatively associated with cantonal deprivation in our study.

In both men and women, the risk of death due to chronic-obstructive pulmonary disease was higher in the central Andean and northern Amazonic regions. Nevertheless, mortality due to this cause was only associated with deprivation in the case of women. This might be explained by the higher exposure of women to indoor pollution from the use of solid fuels to cook, a phenomenon observed in many countries[56]. In Ecuador, solid fuel cooking is much more common in rural areas, among indigenous groups and in the most deprived segments of the population[54]. Since women, and specially women from ethnic minority groups, spend more time at home and doing care labour, it seems plausible that they would be more affected by indoor air pollution, while men could be more affected by cigarette consumption. Further studies should analyse these interesting differences in both sexes.

The final cause of death analysed in this group is cirrhosis. As in many other countries, in Ecuador, the leading cause of liver cirrhosis is alcohol consumption[57]. In spite of its public health importance, there are few studies showing geographical patterns of alcohol consumption within the country. The strong association between cirrhosis mortality risk and deprivation in both sexes highlights the importance of public health research and policies oriented towards the prevention of alcohol-related disorders, especially in vulnerabilised populations.

C) Cancers

Among the studied causes of death in this group, only respiratory cancers were positively associated with material deprivation, while breast cancers (women), prostate cancers (men), and stomach cancers were negatively associated with deprivation. In the Latin American context, the burden of both breast and prostate cancer is shown to be higher in urban and less deprived areas[58–60]. Respiratory cancers have tobacco smoking as a main risk factor, but other factors such as occupational exposures, radon exposure, and indoor and outdoor pollution are also important[61]. As mentioned earlier, indoor pollution due to indoor solid fuel use can be contributing to make this inequality higher in women than in men.

Regarding stomach cancer, the geographical pattern seen in Ecuador is consistent with studies from neighbouring countries. For example, in Colombia it has been found that stomach cancer death risks are much higher in Andean regions. It is worth noticing that there is a high-risk cluster in Carchi, an Andean province bordering Colombia. Studies in Colombia have identified the neighbouring areas to Carchi to be also areas of high risk for this type of cancer. Factors as helicobacter pylori infection, high salt and low fruit intake diets, and high exposure to nitrites have been reported as possible contributing factors[62,63].

Mortality risk from neither colon nor liver cancers are associated with cantonal deprivation. Nevertheless, the geographical pattern of mortality risk reveals areas with high sSMR in the northern Amazonic region, especially for liver cancer in both sexes and colon and respiratory cancers in women. These regions have the greatest concentration of oil fields in the country (and some of the oldest ones). In the first years of the twenty-first century, several studies analysed the presence of high levels of cancerogenic substances in the environment, and high levels of other illnesses, including cancer, in communities near oil fields[64–66]. The authors recommended the

implementation of a proper surveillance system in those areas where oil exploitation was being carried out. In spite of some possible methodological limitations, this recommendation seems today as good as it was 15 years ago. A surveillance system of environmental exposures, and health outcomes that includes the motorization of social determinants of health, and other possible risk factors as alcohol and cigarette consumption, viral infections and nutrition could be helpful to elucidate the mortality patterns observed in this region, as well as to improve health of the population by detecting possible risks and taking actions to reduce possible negative health impacts. Moreover, there is also the need to undertake analyses on structural determinants such has colonialism, neoliberalism, racism, sexism, and other related factors, typically neglected in many middle- and low-income countries.

D) Injuries

The three causes studied in this group are positively associated with material deprivation (with the exception of road injuries in men). International literature, and studies in similar contexts, have consistently related higher mortality and the burden of external injuries with deprivation[67–69]. The geographical pattern of road injury mortality risk is consistent with the results of a recent study in Ecuador[70]. The authors of this study attribute the high mortality risk found in Amazonic provinces to material deprivation, poor access to health services, and poor road infrastructure. We believe that other factors as alcohol consumption, main transportation types, access to public transportation, capacitation of professional and non-professional drivers, road design, safety of circulating vehicles, and access and quality of pre-hospital and hospital care should be considered too as potential contributing factors[71].

Regarding self-harm and interpersonal violence deaths, much could be said. We will only focus on three intertwined aspects that could be linked to the observed pattern of mortality due to these causes in the country: 1) structural racism; 2) extractivist capitalism; and 3) sexism. Starting with the last one, in contexts of an hegemonic inherited colonialist and hetero-patriarchal model, gender roles make men both the main perpetrators and victims of violence, while women are largely victims of violence[72,73]. Moreover, failures to maintain masculine ideals by men have been theoretically linked with suicide attempts and success[74]. In Latin America, most of the victims of homicide are young men, and studies have related male involvement in violence with a culture of hegemonic-dominant masculinity that favours both the exposure to and the participation

in violent actions[75,76]. These phenomena related to sexism, power, and gender roles could explain the results of our study: ratios between deaths of men and women were 7.3:1 for interpersonal violence and 2.5:1 for suicide deaths (after garbage code redistribution).

Self-harm mortality risk is higher in cantons in the central Andean and Amazonic regions, characterized by having the highest proportions of indigenous population. In many international studies, and specifically in South America, higher suicide rates have been reported among indigenous populations[77,78]. Some of the probable causes found in similar contexts in those studies are the loss of control and power over their ancestral territories and means of living, the pressures on their traditions, behaviours and ways of living, and the irruption of farming and extractive industries in indigenous territories. Yet, in recent years, studies in Ecuador have found conflicting evidence. While some studies found that the burden of suicide among indigenous populations was lower than in mestizo/white populations, others found that suicides are among the main causes of death in indigenous populations and especially in people between 20 and 50 years old[79,80].

The northern Amazonic region also has some of the highest sSMR due to interpersonal violence, along with the northern and central Coastal region (areas with high proportions of afro-ecuadorian and montubio populations). Historically, indigenous and black populations in Ecuador have been oppressed and excluded both economically and politically. On the other hand, mestizos and especially white populations have enjoyed full participation in the political and economic processes and have had more control over resources and means of production. Discrimination towards people from minority ethnic groups persists in Ecuador and can intersect with discrimination by gender, health status, age, and rural origin, among other factors[81,82]. These inequalities could be somehow related to the higher risk of violent deaths. Moreover, many of the territories with high violence mortality risk also share the characteristic of having extractive legal and illegal industries (oil and minerals) and/or have suffered intense deforestation in order to increase grasslands and farming lands[83,84]. Besides of the immense environmental consequences of these economic activities, conflicts and violence (by companies, the state and between newcomers and minority ethnic groups) have been a constant characteristic of extractive industries[83,85–87].

The relations and interactions between extractivist capitalism, racism, sexism and deprivation can help us understand the unique geographies of mortality and particularly

mortality from violence and suicide in the country. Much more research is needed in order to understand this complex reality in Ecuador and in many other low and middle-income countries.

Limitations and Strengths

The study presented here has some limitations worth noticing. A first set of limitations relate to DDM methods, which assume that: 1) the studied population is closed to migration; 2) completeness is constant in all age groups; and 3) age misreporting is minimal or non-existent.[33] All these issues could be important, but migratory patterns could be a vital factor in Ecuador during the study period (with substantial internal and external migratory waves).[88,89] Some authors have proposed approaches to adjust some of the DDM methods for migration,[90] but their use is still not widespread. Another important limitation of DDM methods is their high level of uncertainty, especially when the study areas become smaller in population or number of deaths.[33] Moreover, completeness estimates are constant for all the causes of death studied. In this study we have attempted to measure and consider uncertainty in our estimations of mortality but estimates still have to be used with caution. The completeness estimates presented should still be polished to better correct mortality estimates. More work is needed to refine methods to estimate completeness at subnational levels and in countries where data are not completely compliant with the assumptions of DDM methods.

Another limitation of the methods used to study completeness is their lack of timeliness. DDM methods depend on information from national censuses and give completeness estimates for the whole intercensal period. This makes completeness estimates inadequate to study rapid changes in death registry completeness.

The second set of limitations relates to the quality indicator and redistribution protocols used to correct this deficiency. It could be important to assess and adapt the GCs and their redistribution protocols to the local context and time. No GC redistribution method is ideal, and biases can arise from their application. Proportional redistribution ignores the distribution of cause-specific mortality in specific geographical areas, age or sex groups. Expert opinion can be valuable but also could be biased. For example, experts from low- and middle-income countries could be underrepresented in expert groups. Regression models have the advantage of including uncertainty, but they need reliable covariables in order to work properly and can be difficult to adapt to subnational contexts. The GBD-2010 redistribution protocol used in this study has few age and sex

restrictions. It is worth mentioning that the protocols add proportionately more deaths in women, children and older people, a phenomenon especially noticeable in IHD deaths.

Another limitation could be derived from the characteristics of the areas analysed. Although cantons are the smallest area in which data was available, they are still widely heterogeneous in size and population. Moreover, in order to obtain a stable cartography for the study period, some areas that are not necessarily homogenous had to be joined and we could not perform our analyses in the three cantons of the Galápagos Islands. Nevertheless, we think that the use of cantons as units of analysis in this study is fully justified, based on political, economic and cultural aspects that can be unique to each of them. In the future, the National Institute of Statistics and Censuses of Ecuador should collect and disseminate information in more homogeneous and stable areas to allow researchers to analyse contextual effects and health on other scales (e.g., urban areas).

In spite of these limitations, this is the first attempt to estimate mortality risks for a wide variety of specific main causes of death and relate them to material deprivation at a cantonal level in the whole country. Remarkably, this useful research approach remains neglected in many countries around the world. We have used some of the best state of the art methods in order conduct our analyses. We think that the methodological framework that has been proposed will be of great utility in future studies in the country and elsewhere. The geographical patterns of specific cause of death mortality in both sexes should encourage the development of new research, and guide public policy aimed at reducing mortality inequalities in the country. We think this study is an important first step that can generate hypotheses and help to develop the research field in Ecuador.

Concluding Remarks

The study of the geographies of mortality and their causes is a challenge in contexts where data completeness and quality are low. We have used some of the best available methods to correct mortality for deficiencies in data, estimated mortality risks for 17 causes in men and women and analysed their relationship with cantonal deprivation. Unique patterns of mortality have been observed by cause and sex. Moreover, many of the analysed causes of death were positively associated with material deprivation. We believe that these relationships and its mechanisms require further research. Especially, research can go beyond the exploration of connexions between intermediate determinants of health and proximal risk factors that deteriorate health, but should also focus on understudied broader structural determinants such as colonialism, extractivist

economies, racism and sexism. For this purpose, it is especially important that the quality and completeness of data improves dramatically. Given the importance of generating accurate and ready to use mortality statistics, all stakeholders in the country, including the National Institute of Statistics and Censuses and the National Ministry of Health, should lead a process of continuous improvement of vital statistics in Ecuador.

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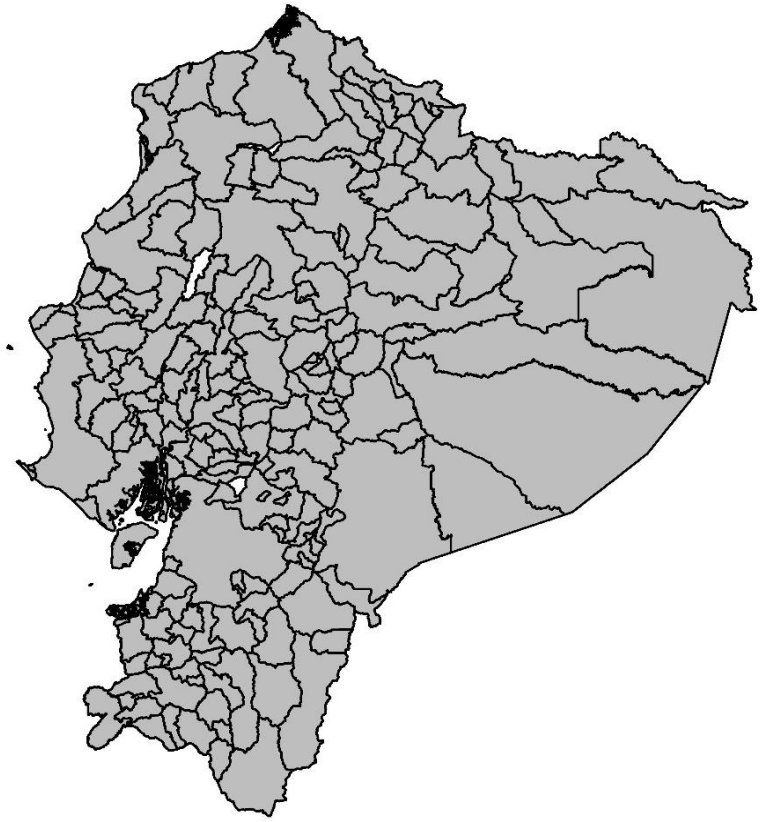
Supplementary Material

Supplementary figure 1: Cantonal cartography used in the study

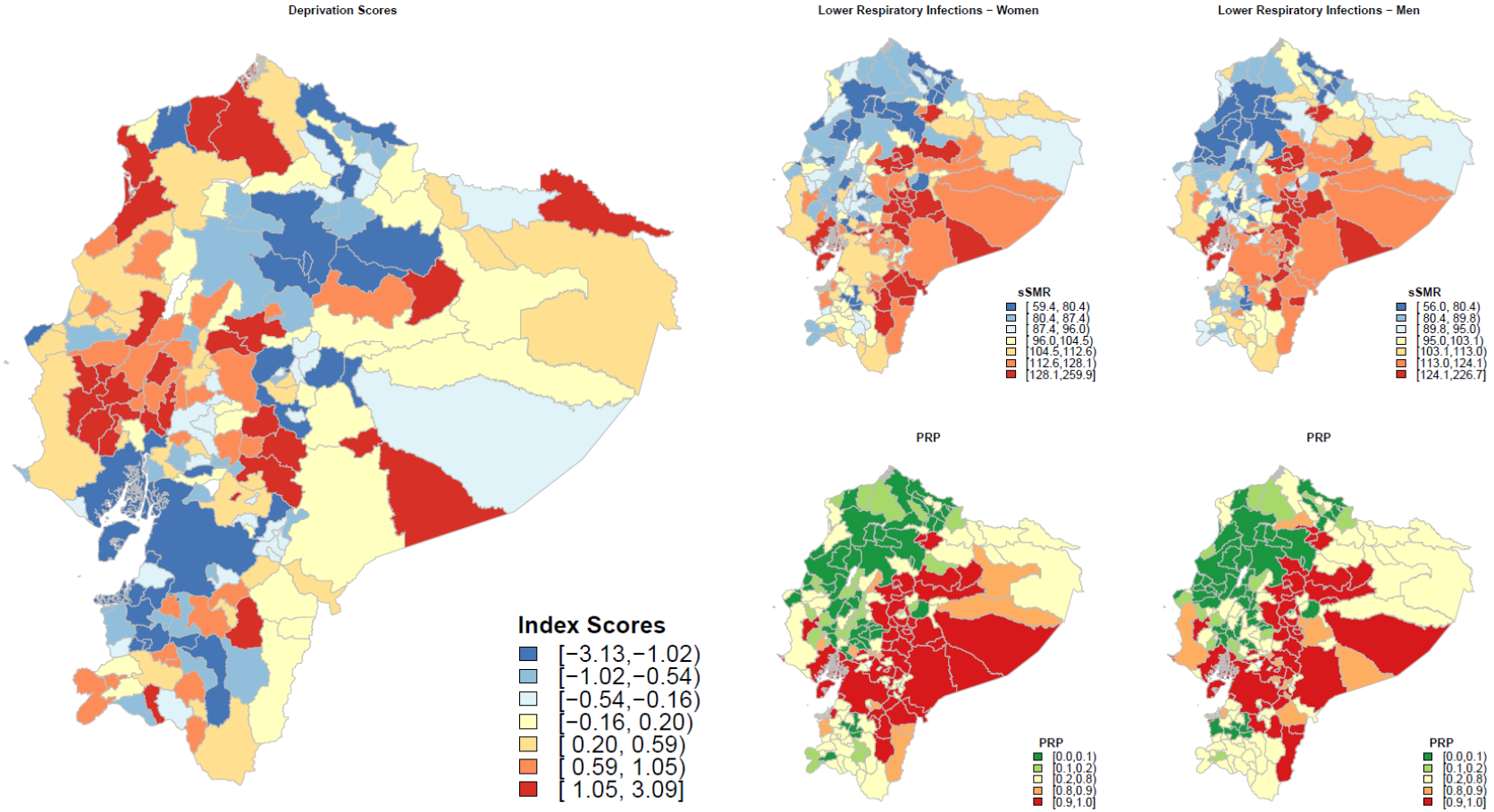


Supplementary table 1: Description of the number of deaths in the study areas in women and men after garbage code redistribution

	Women						Men					
	Min	P25	P50	Mean	P75	Max	Min	P25	P50	Mean	P75	Max
Lower Respiratory Infection (n)	3	22	45	141	103	5,049	1	24	51	152	122	5,242
Tuberculosis (n)	0	4	9	22	19	869	0	5	13	40	35	2,025
Human Immunodeficiency Virus (HIV - AIDS) (n)	0	2	5	16	12	911	0	3	10	43	25	3,129
Ischemic Heart Disease (n)	5	44	82	221	168	7,109	5	51	104	266	208	8,575
Diabetes Mellitus (n)	0	15	31	107	71	4,921	0	10	23	87	55	4,393
Cerebro-Vascular Disease (n)	4	19	45	129	101	4,424	3	21	50	135	110	4,879
Chronic-Obstructive Pulmonary Disease (n)	1	8	17	49	35	1,666	2	12	23	63	49	2,154
Cirrhosis (n)	2	12	25	71	56	2,590	1	18	41	113	95	3,728
Hypertensive Heart Disease (n)	1	10	20	69	52	3,440	1	10	21	69	53	3,482
Stomach Cancer (n)	0	8	21	54	44	1,461	0	10	27	68	60	1,700
Breast Cancer (n)	0	3	8	32	16	1,398	-	-	-	-	-	-
Prostate Cancer (n)	-	-	-	-	-	-	0	8	20	55	40	1,804
Respiratory Cancer (n)	0	4	11	28	21	862	0	6	17	38	28	1,331
Liver Cancer (n)	0	4	11	29	24	884	0	5	10	26	20	714
Colon Cancer (n)	0	4	9	28	19	1,021	0	4	9	25	17	799
Road Injuries (n)	0	5	11	33	26	895	0	20	39	103	97	2,491
Self Harm (n)	0	4	10	23	20	544	2	12	24	56	51	1,244
Interpersonal Violence (n)	0	3	8	20	16	563	0	11	34	146	116	5,717

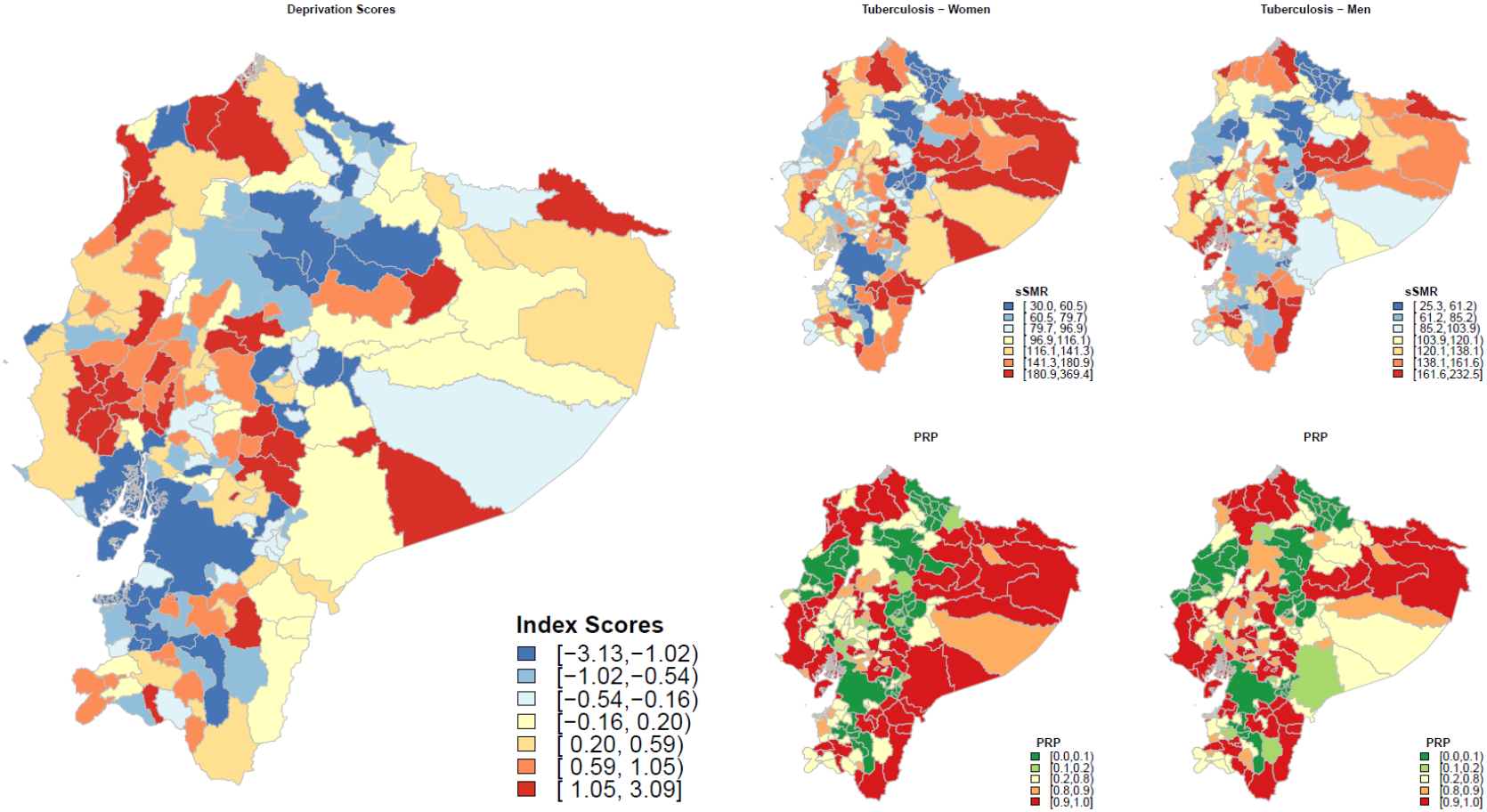
(n): Counts of deaths in cantons after garbage code redistribution.

Supplementary Figure 2: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – lower respiratory infections – Ecuador – 2001 to 2014



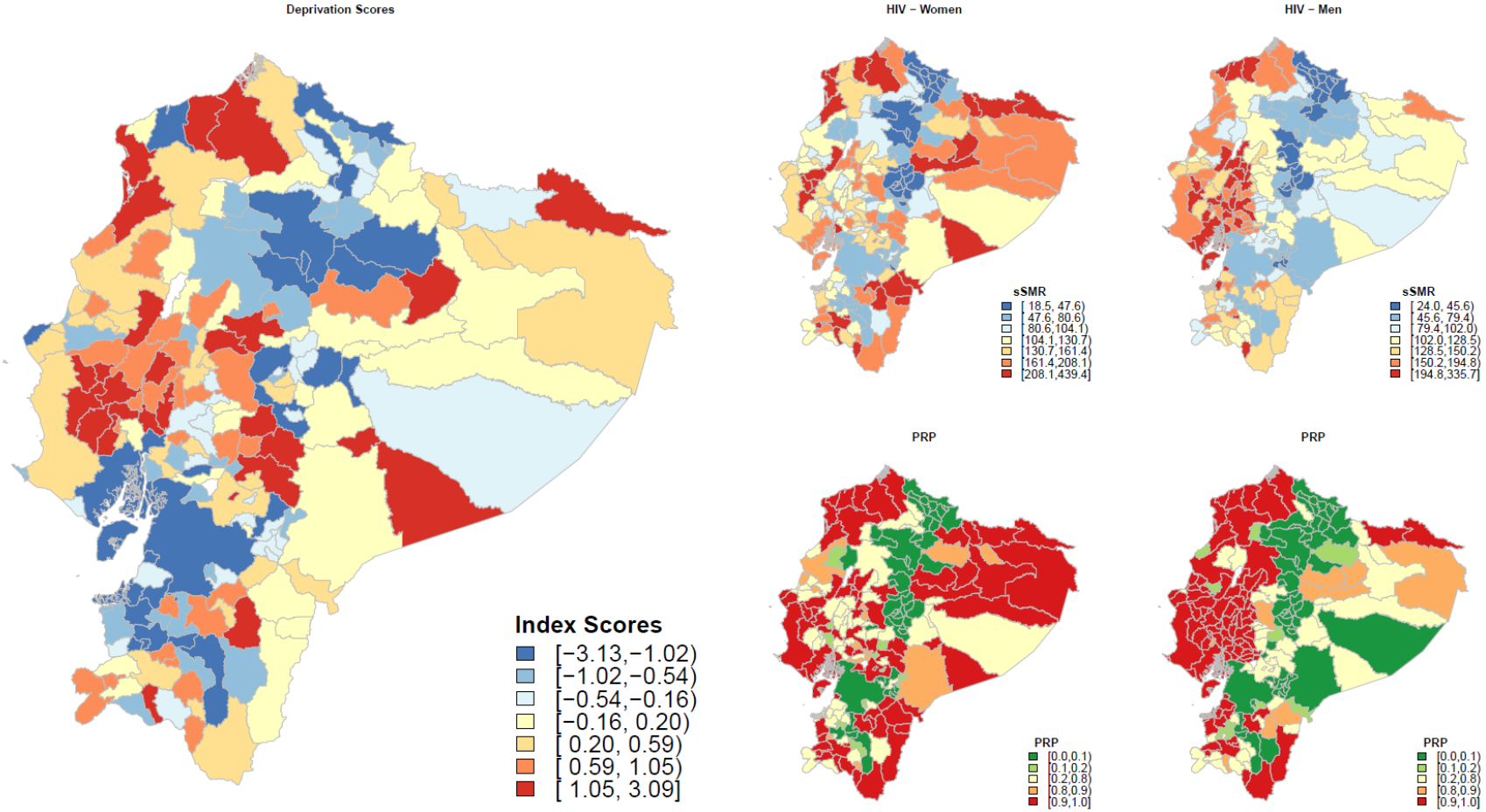
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 3: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – tuberculosis – Ecuador – 2001 to 2014



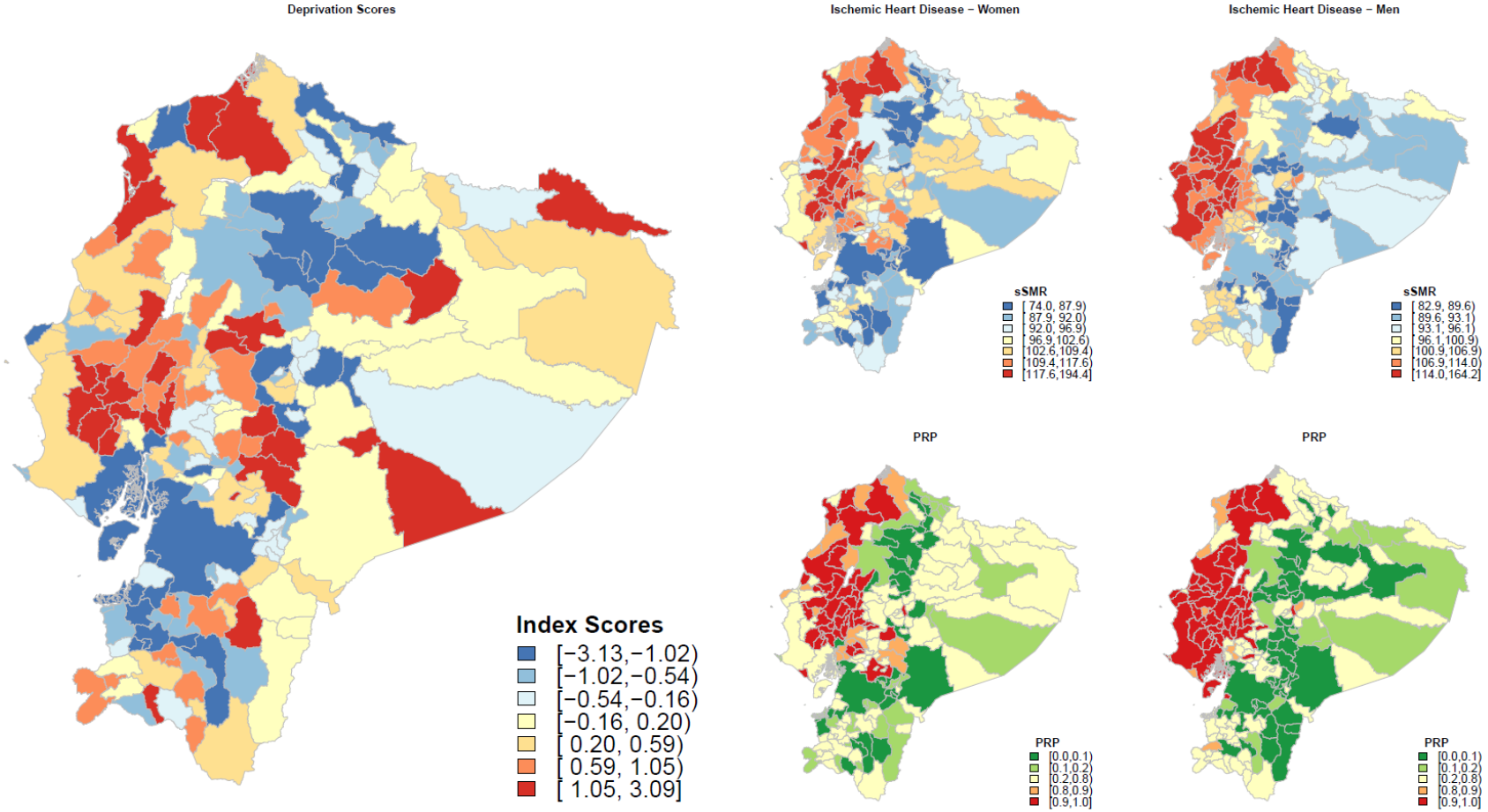
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 4: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – HIV/AIDS – Ecuador – 2001 to 2014



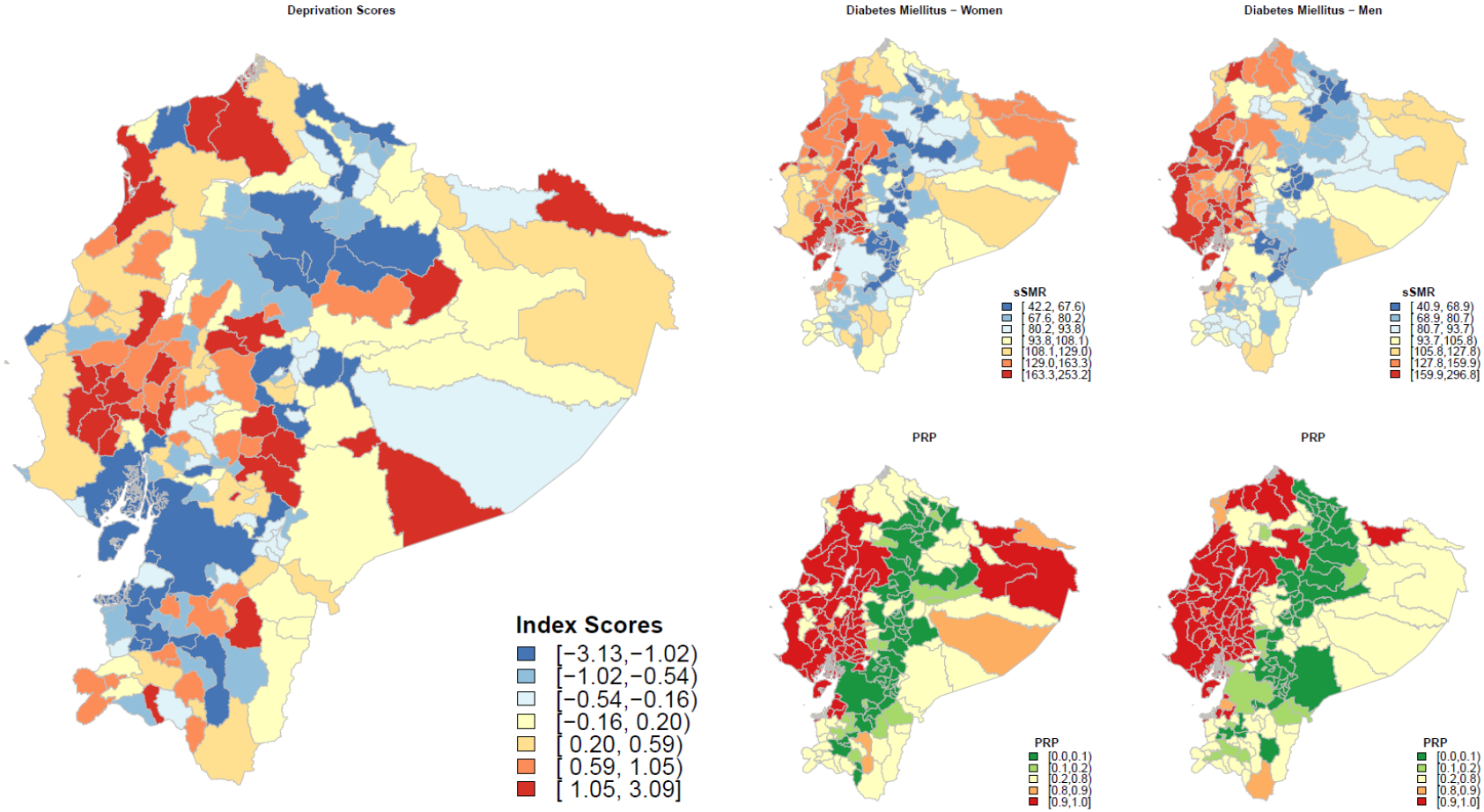
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 5: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – ischemic heart disease – Ecuador – 2001 to 2014



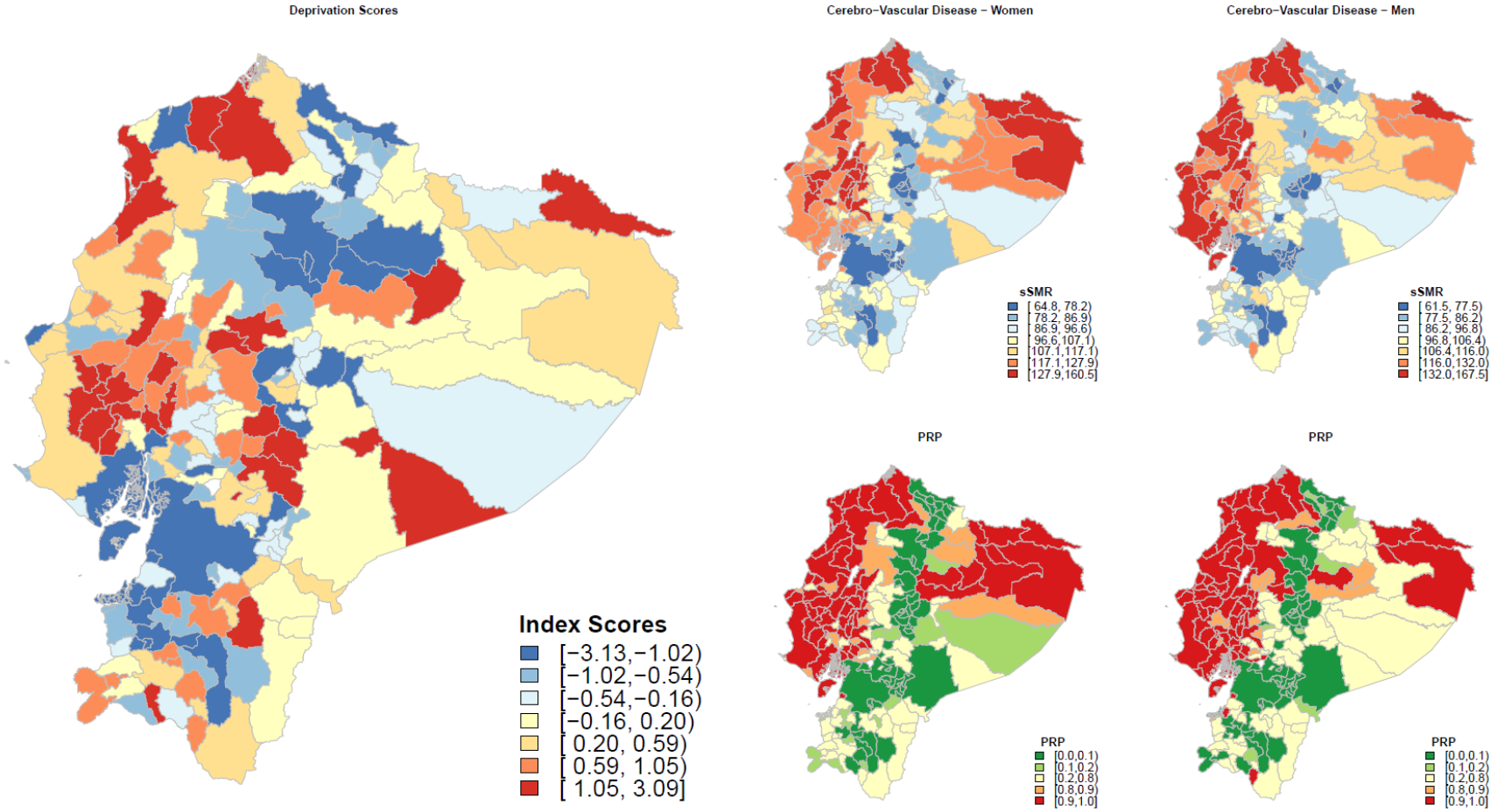
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 6: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – diabetes miellitus – Ecuador – 2001 to 2014



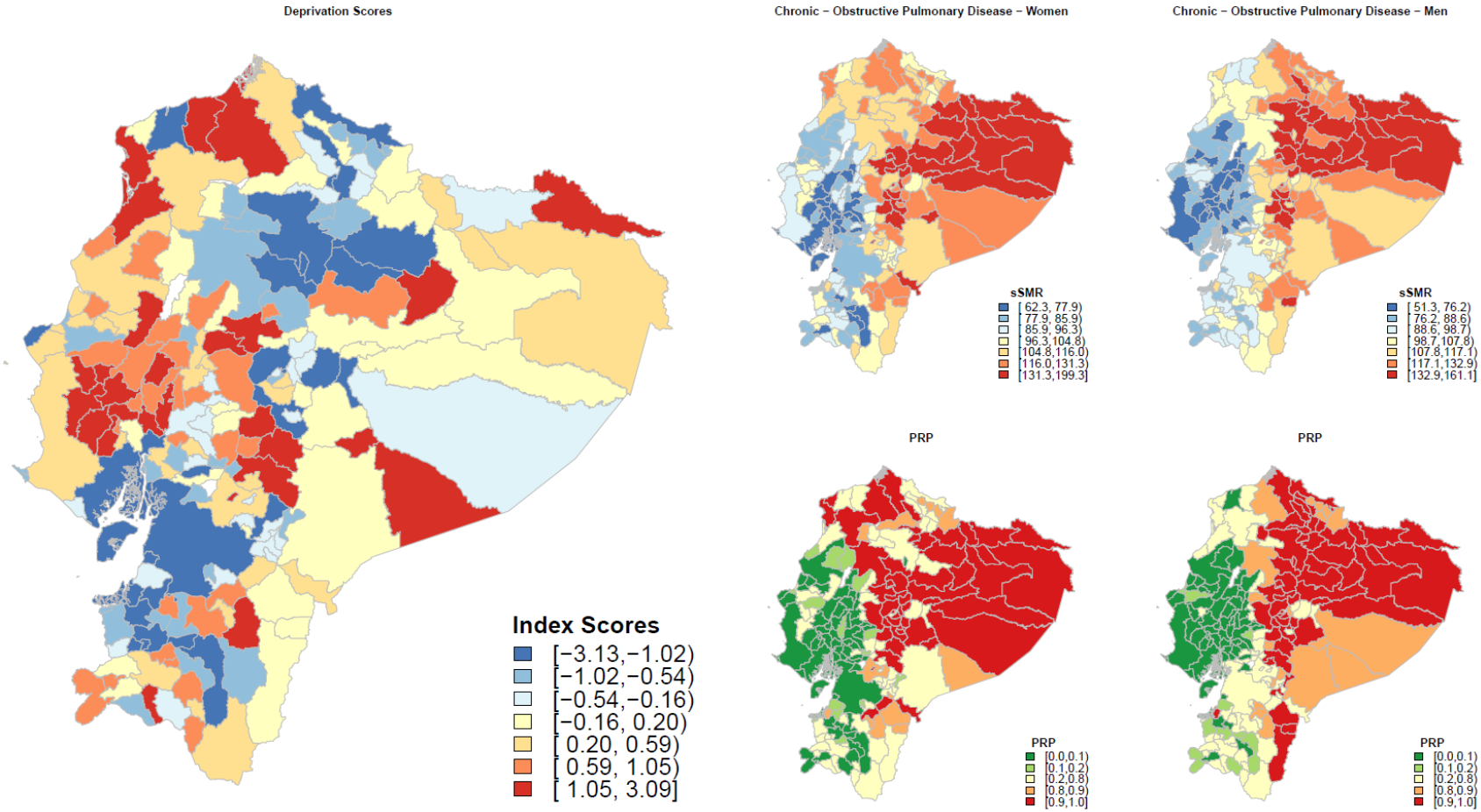
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 7: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – cerebro-vascular disease – Ecuador – 2001 to 2014



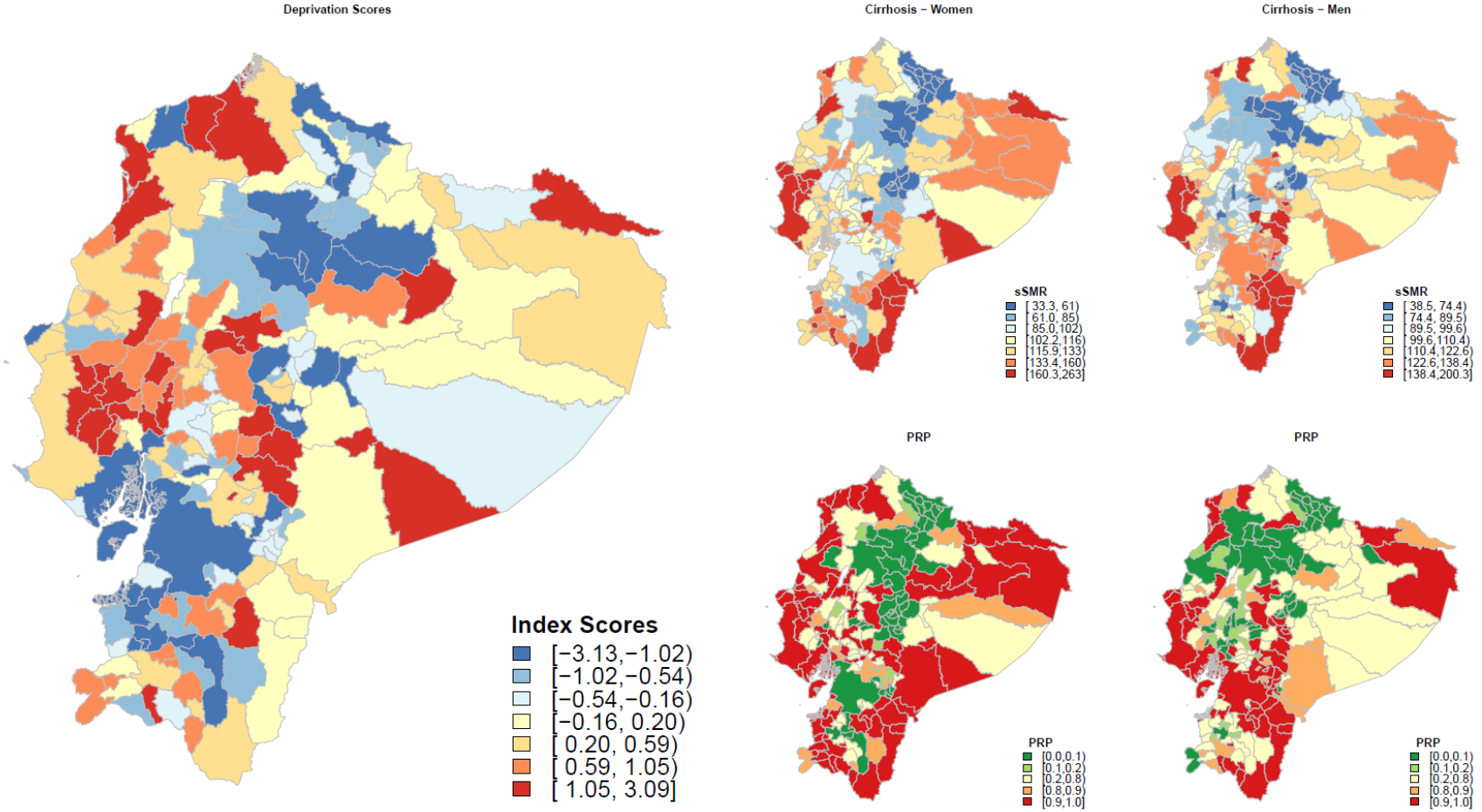
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 8: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – chronic-obstructive pulmonary disease– Ecuador – 2001 to 2014



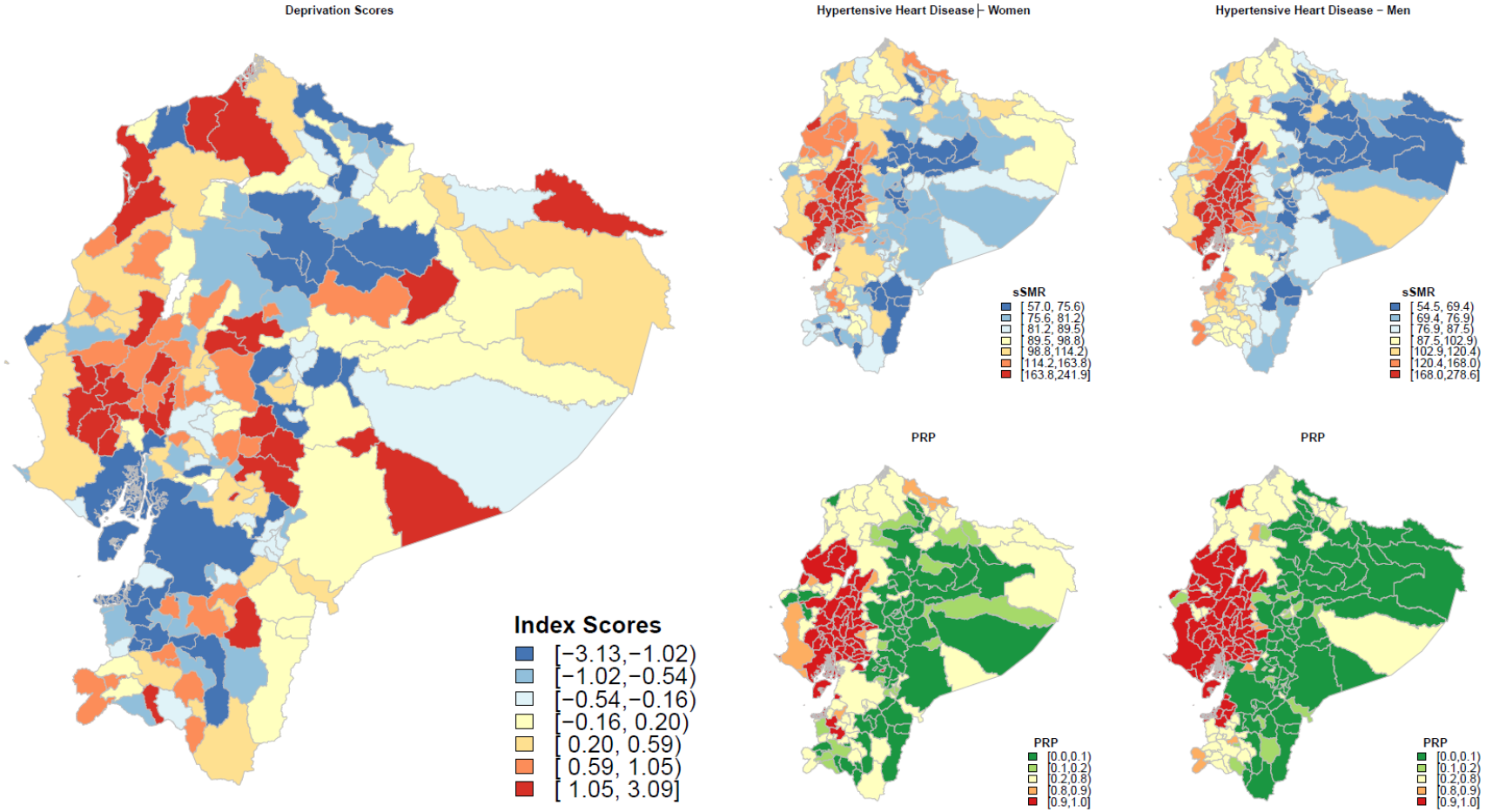
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 9: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – cirrhosis – Ecuador – 2001 to 2014



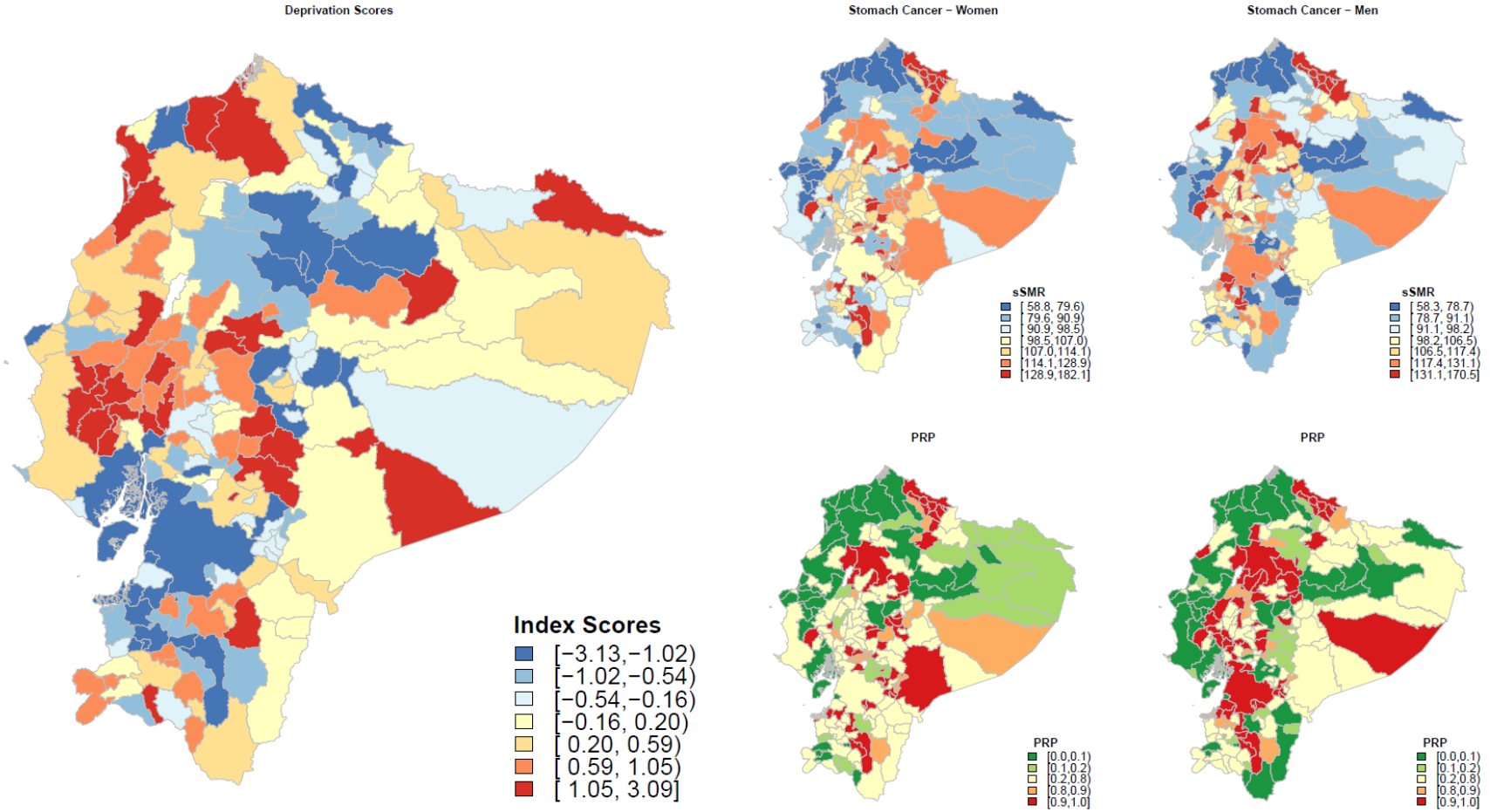
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 10: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – hypertensive heart disease– Ecuador – 2001 to 2014



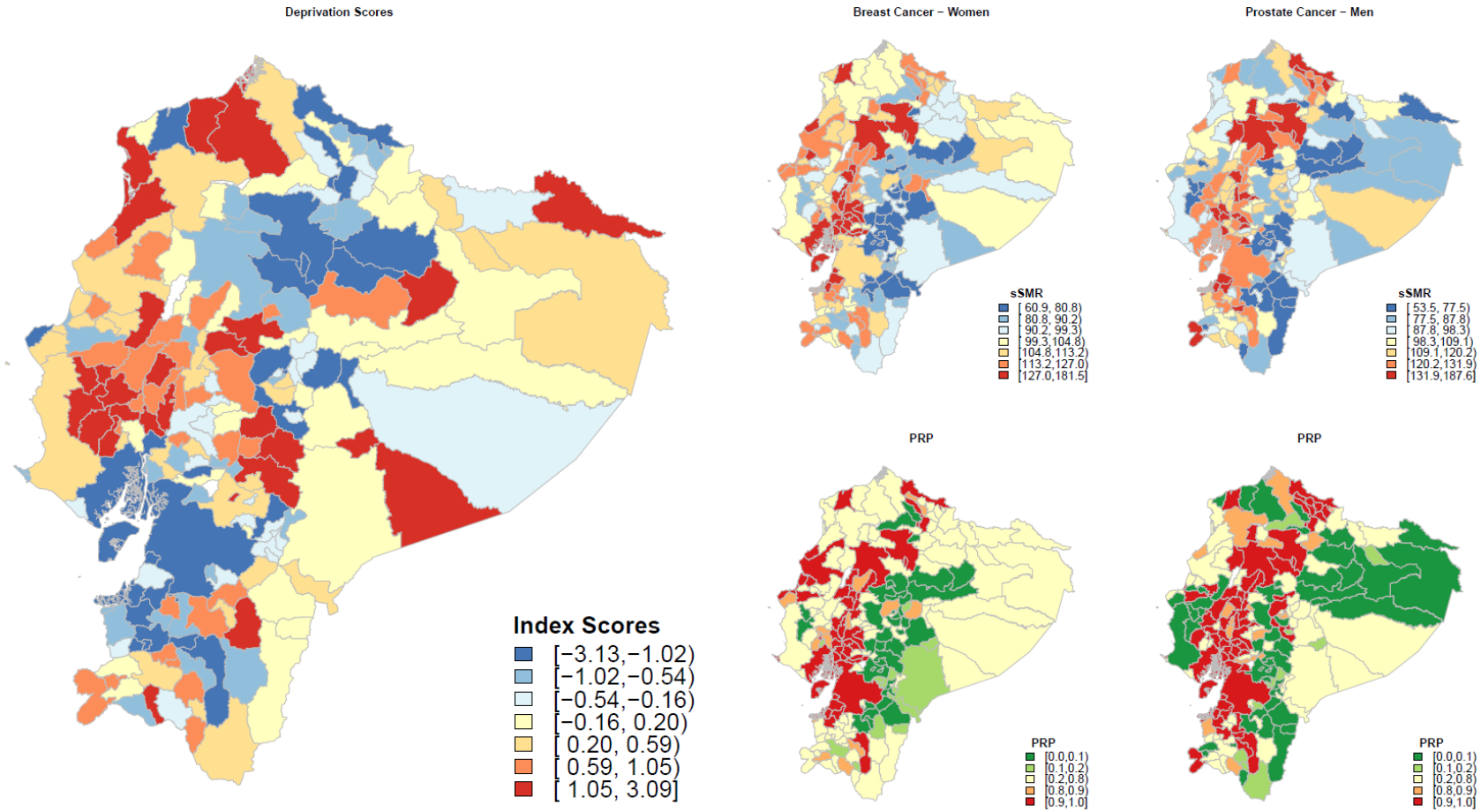
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 11: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – stomach cancer– Ecuador – 2001 to 2014



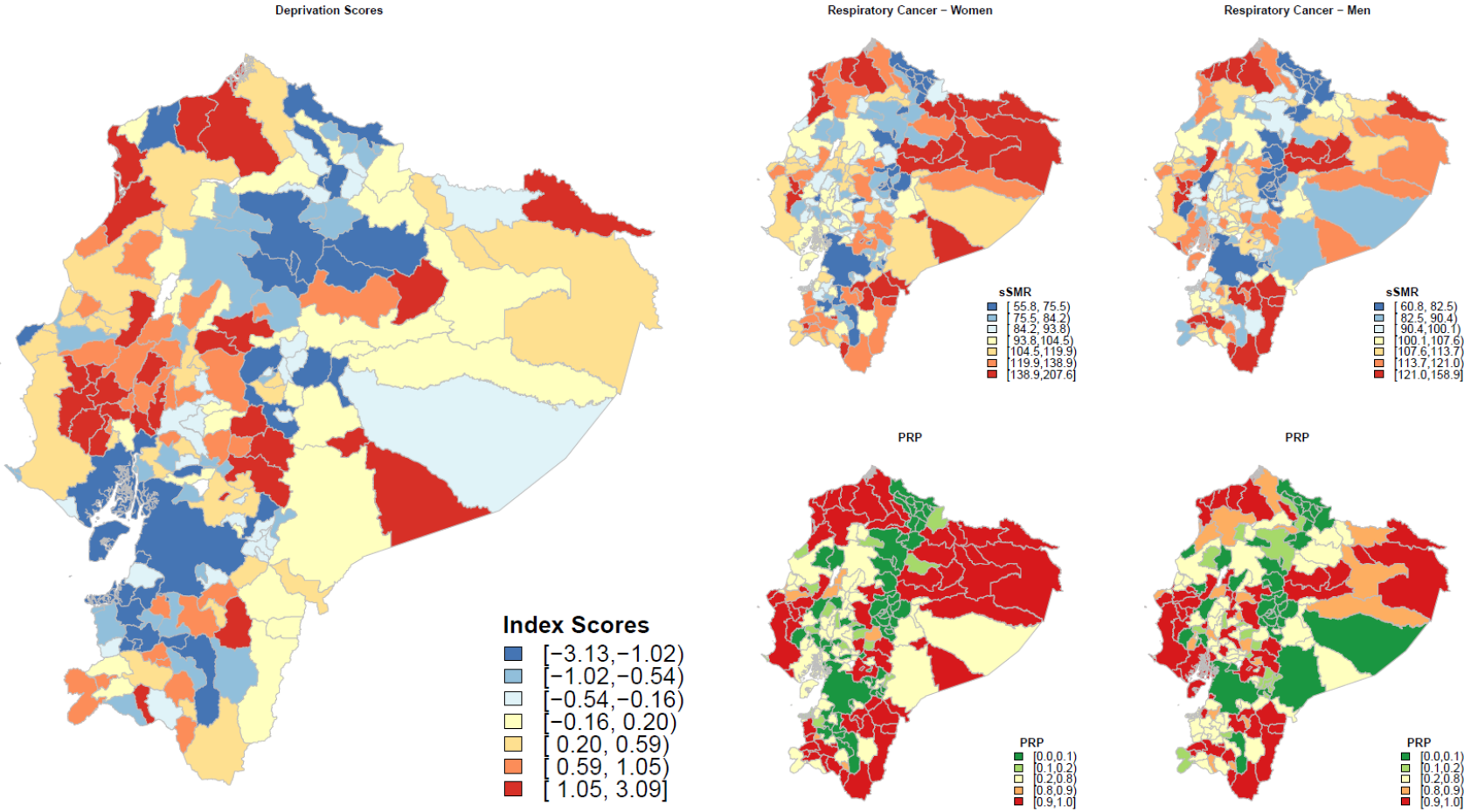
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 12: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – breast and prostate cancers – Ecuador – 2001 to 2014



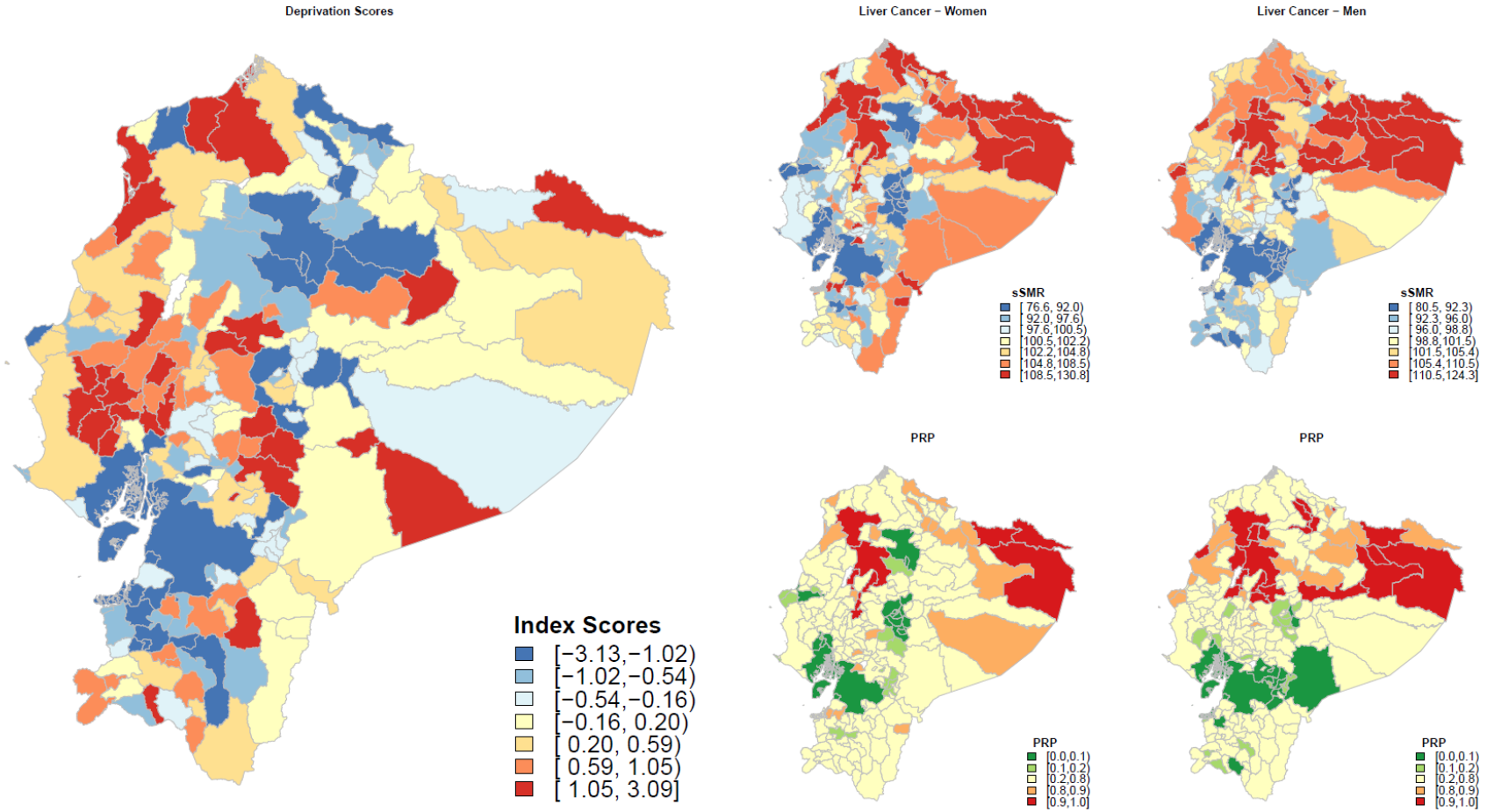
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 13: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – respiratory cancers – Ecuador – 2001 to 2014



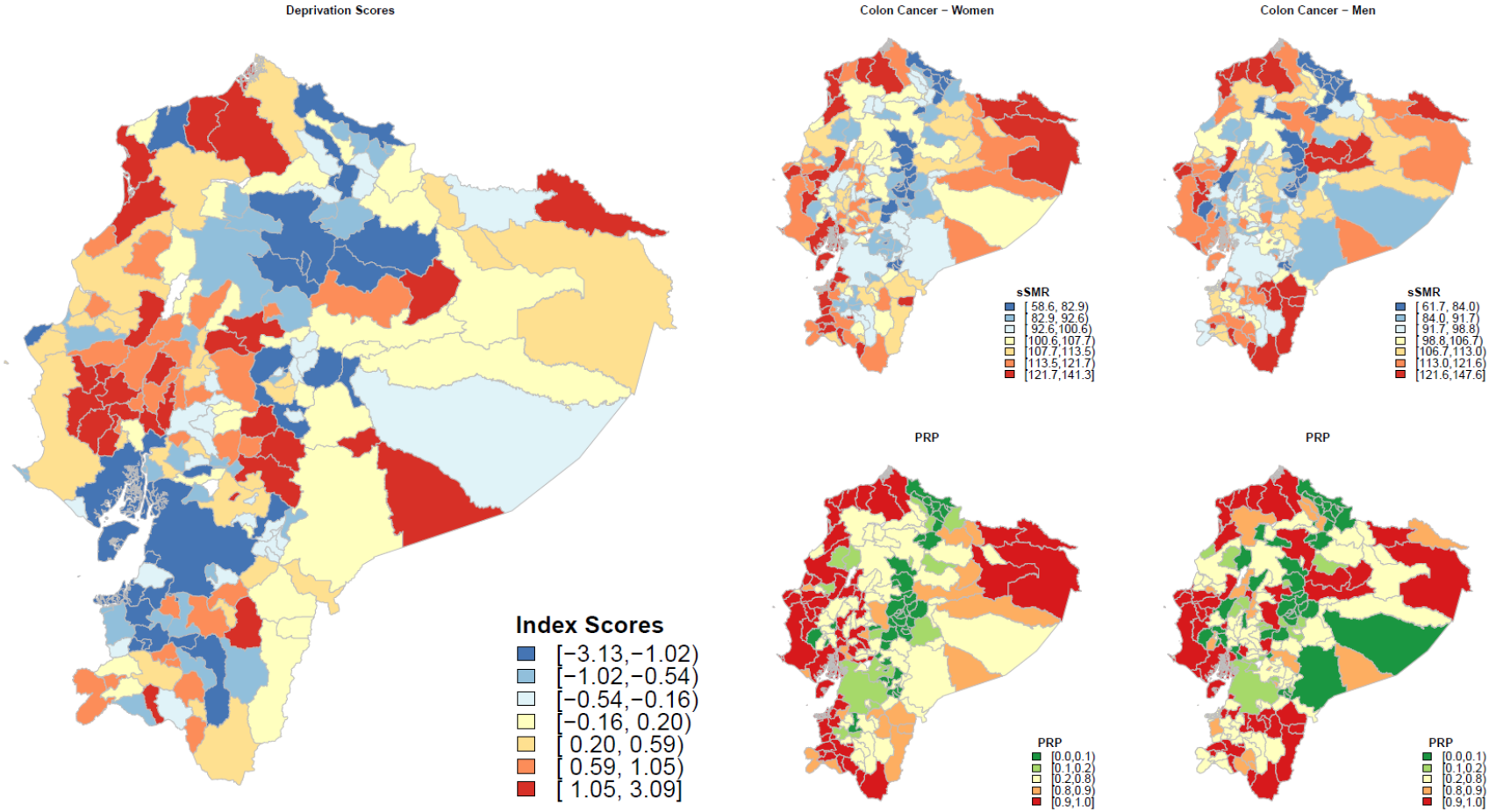
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 14: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – liver cancer – Ecuador – 2001 to 2014



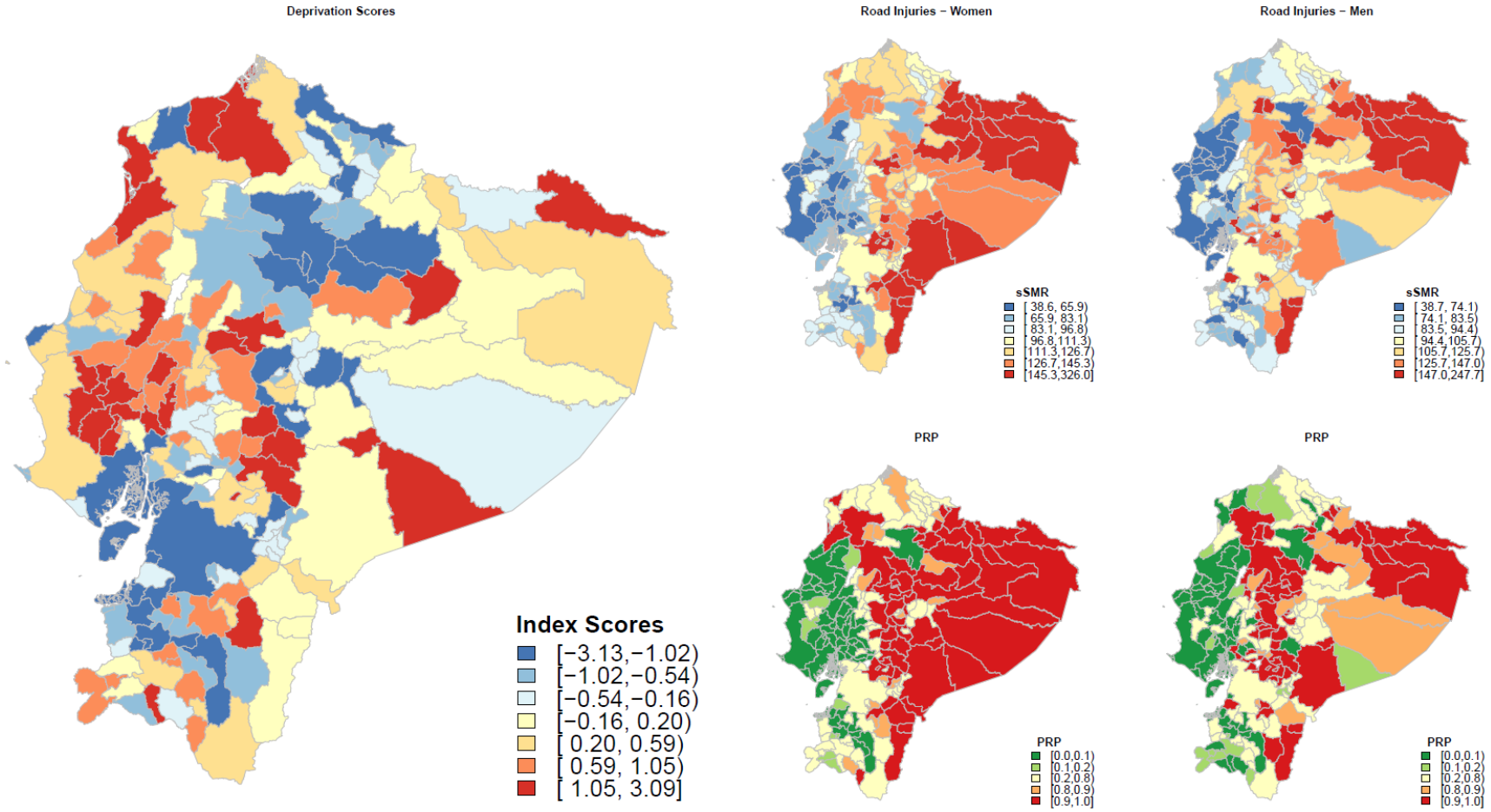
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 15: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – colon cancer – Ecuador – 2001 to 2014



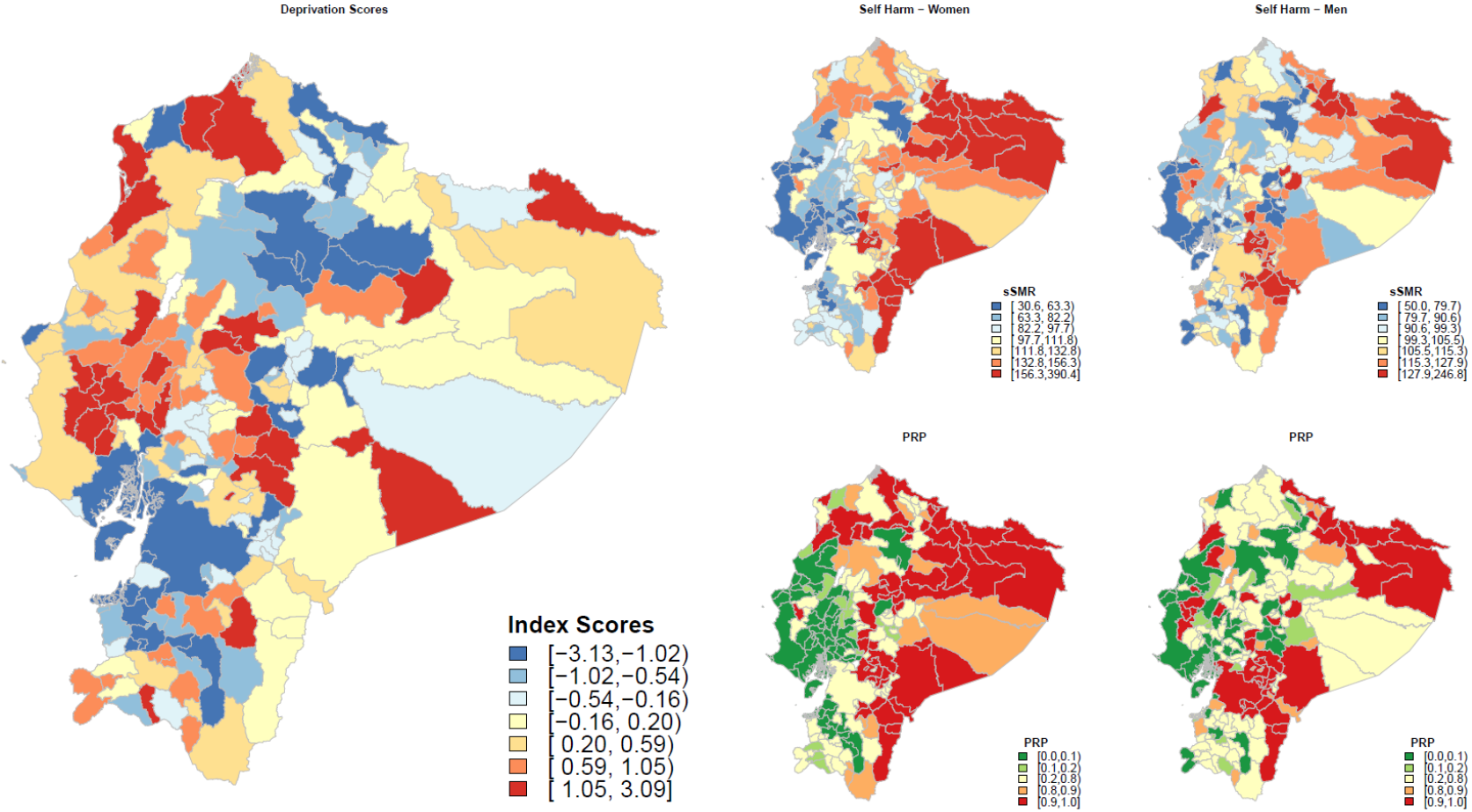
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 16: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – road injuries – Ecuador – 2001 to 2014



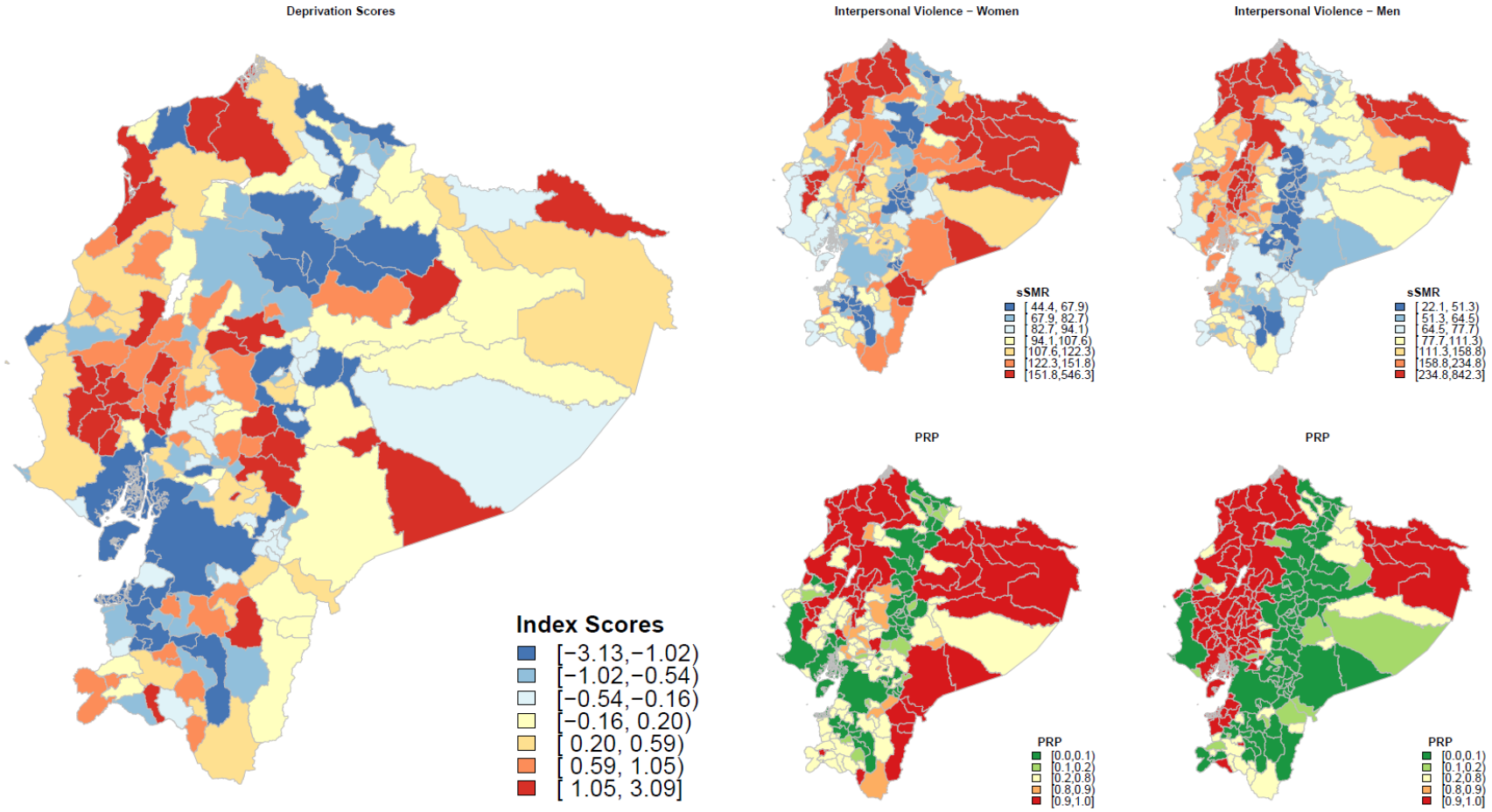
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 17: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – self harm – Ecuador – 2001 to 2014



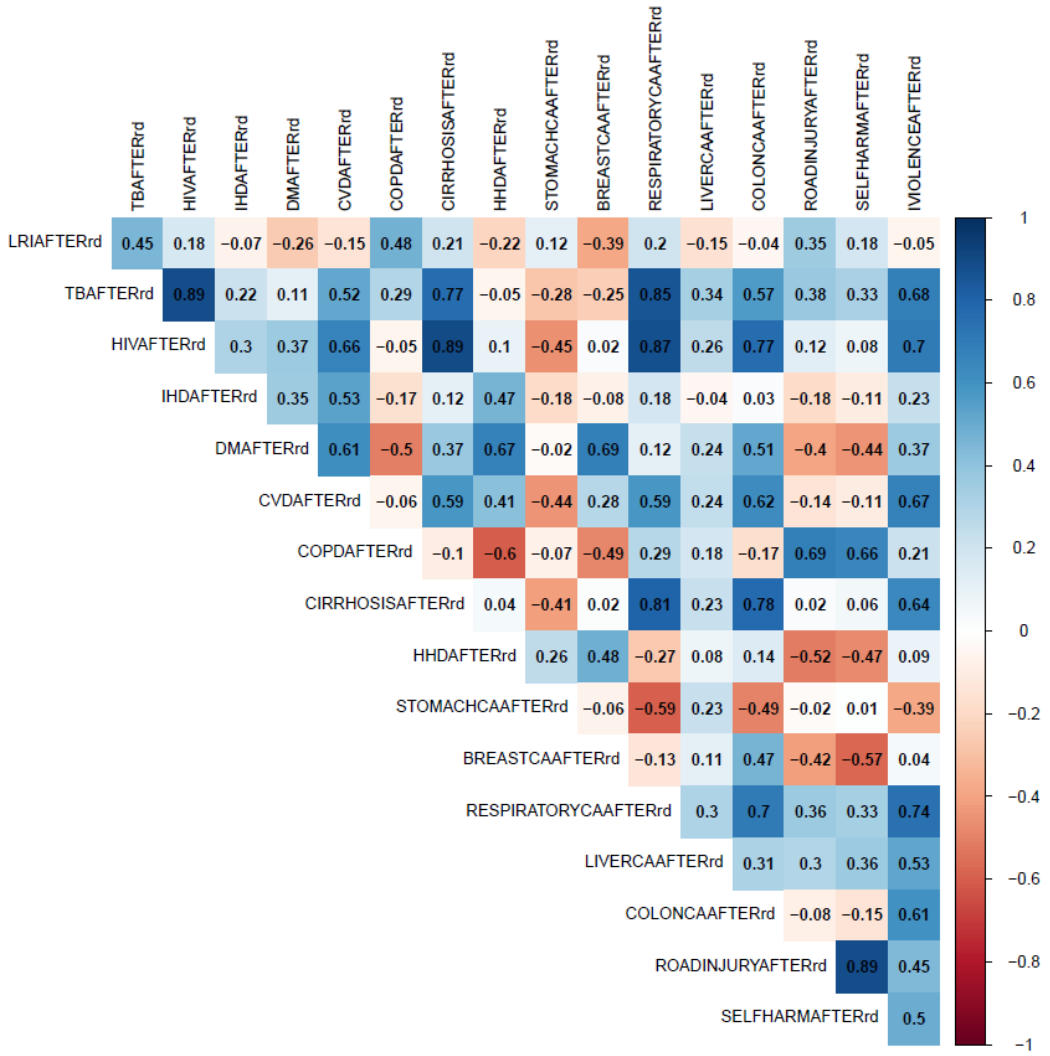
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 18: Deprivation and smoothed Standardized Mortality Ratios (sSMR) – interpersonal violence – Ecuador – 2001 to 2014



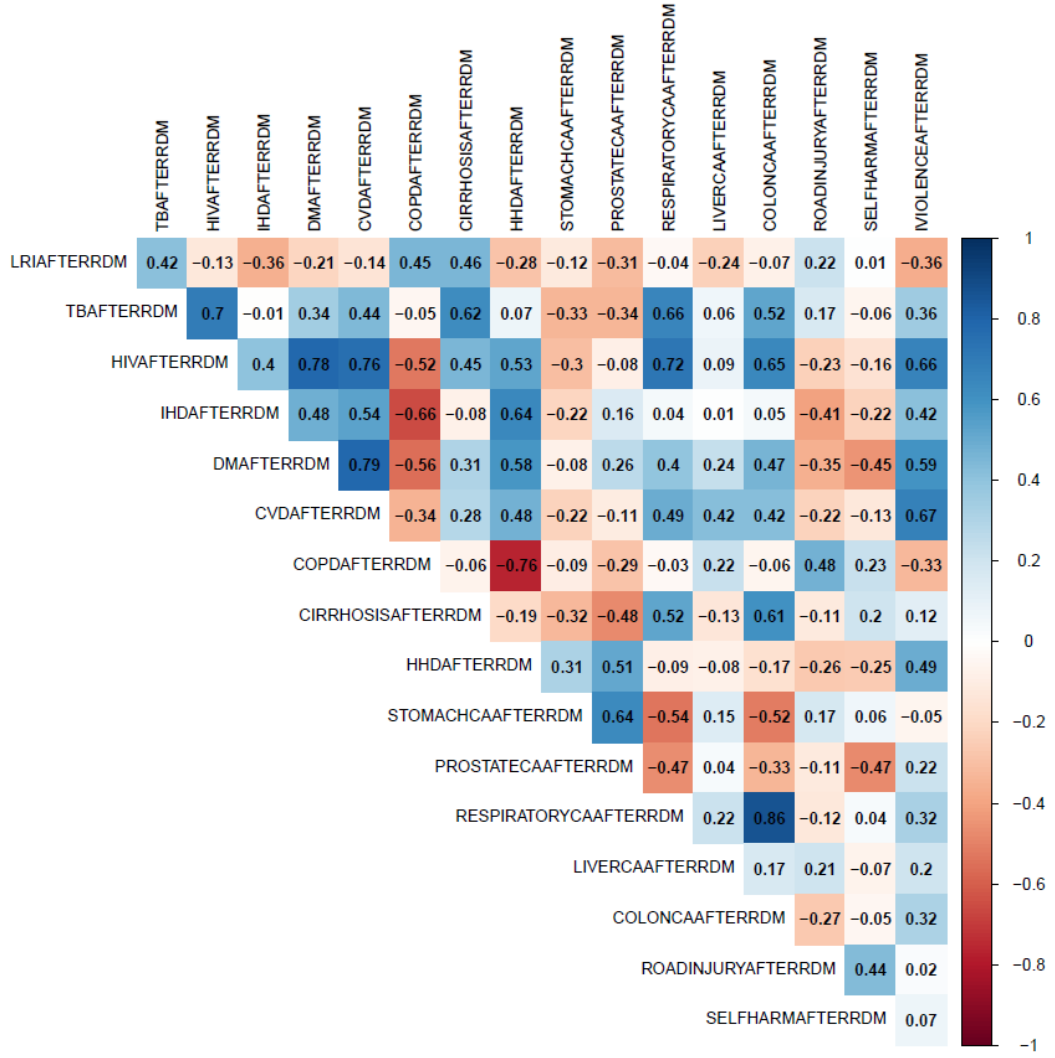
PRP: Probability of sSMR being higher than 100
Index Scores: Higher index scores represent higher levels of material deprivation

Supplementary Figure 19: Correlation matrix between the studied causes of death – women



All bivariate correlations are Spearman correlations.

Supplementary Figure 20: Correlation matrix between the studied causes of death – men



All bivariate correlations are Spearman correlations.

Chapter 7: Discussion and conclusions

Key Points:

- In this final chapter, we discuss some of the main findings of the studies presented in this dissertation.
- In order to do this, we first review some of the main points that have already been discussed in previous chapters.
- After that, we discuss four topics that were not addressed in the articles but that have emerged when discussing the studies as a whole.
- Subsequently, the main limitations and strengths of the dissertation are mentioned.
- Afterwards, research and policy recommendations are presented.
- Finally, the main conclusions of the dissertation are stated.

Capítulo 7: Discusión y conclusiones

Puntos Clave:

- En este capítulo final, discutimos los principales resultados de los estudios presentados.
- Comenzamos recordando algunos de los temas que han sido discutidos en capítulos anteriores.
- Posteriormente, tratamos cuatro puntos que son fruto de las reflexiones en torno al conjunto de estudios presentados vistos como un todo.
- Después de esto, mencionamos las principales limitaciones y fortalezas de esta tesis doctoral.
- A continuación, hacemos recomendaciones de investigación y política pública que se desprenden de las investigaciones realizadas.
- Finalmente, presentamos las principales conclusiones de la tesis doctoral.

In this dissertation, we have found important geographical inequalities in material deprivation and not only in mortality but also in the performance of the mortality registry in Ecuador. Moreover, mortality risks for many of the main causes of death in men and women are positively associated with deprivation. In this chapter, we will discuss the main results of the dissertation, reflect on some important ideas that can arise from the presented studies, mention some of the main limitations and strengths of this work, and point out some major recommendations for research and policy derived from the results presented.

1. Discussion on the main results of the thesis

We will start the discussion by mentioning the main results of each of the studies presented in the dissertation. Then, we will outline some of the ideas that have been already discussed in each study, deepening some of the topics that needed further comments, and mentioning other ideas or hypotheses that have appeared after reviewing the four articles that have been presented.

1.1. The mortality registry in Ecuador presents great deficiencies and inequalities by sex and geographical region.

We evaluated the completeness, quality and internal consistency of the mortality registry in the provinces of Ecuador from 2001 to 2013. Our results showed that there were substantial inequalities in the registry by sex, geographical area and age. Completeness was lower for women in 20 of the 22 studied areas. Analysis of the quality of the mortality registry showed that the percentage of garbage codes (GC) was higher for women in 19 of the 22 study areas and in all of Ecuador. As mentioned in chapter 3, inequalities in the mortality registry quality and completeness between men and women have scarcely been studied worldwide; yet some differences in completeness and ill-defined causes between women and men have already been reported in few other Latin American countries [1]. We have proposed some potential explanations for these inequalities: 1) Gender bias in the diagnosis of various conditions has been reported for many conditions in other countries [2,3], which could also be an important issue in Ecuador. 2) As more men die from external causes (which require investigation of the death and autopsy), their deaths could be registered more frequently and with more correct diagnoses. This has been proposed as an explanation for the sex differences in the mortality registry quality observed in Belo Horizonte, Brazil [4]. 3) In

other contexts, maternal deaths have been found to be greatly underreported and misclassified [5,6]. In Ecuador, legal restrictions for the access to safe abortions and penalties toward women and health providers may explain some of the underreporting or misclassification of deaths in women [7]. Considering that maternal and abortion related mortality are related to discriminations due to socioeconomic position, race/ethnicity and age in many parts of the world [8], we can hypothesise that more deaths from women living in deprived areas and from minority ethnic groups are either not being reported or are being misclassified.

Moreover, we think that other possible explanations for the sex differences in the mortality registry performance should be studied in the country. Regarding completeness, we think would be useful to consider the incentives for death registration in a context of immense inequalities between men and women. In most countries, the main incentive families have to register the death of a relative is related to the necessity of having proof of death for legal purposes (mainly inheritances) or for insurance purposes [9]. In Ecuador, there are big inequalities in the control of resources and wealth between both sexes. For example, in married couples, women share only 28% of the financial wealth and 44% of the wealth coming (mainly) from land, housing and businesses [10]. This unequal distribution of wealth and assets could give greater incentives for the registration of deaths of men and less incentives for the registration of deaths of women and especially poor women. We think this hypothesis deserves further exploration in Ecuador and in other contexts.

Other important results of this study relate to the unequal geographies of the mortality registry performance in the country. Galápagos and the Amazonic provinces had lower completeness estimates, and garbage coding was more common in the Amazonic provinces, in the central Andean region and in the northern coastal region. The pattern of completeness and garbage coding is rather similar to the pattern of socio-economic deprivation in Ecuador [11,12]. Moreover, some of the provinces with the worst completeness and/or quality indicators are also those with the highest proportions of ethnic groups that historically have been excluded and impoverished (indigenous, afro-ecuadorian, and montubio) [13]. When analysing the temporal evolution of the quality of the mortality registry, these areas show little or no improvements. The particular geographical patterns observed for both quality and completeness highlight the necessity to study more in depth the relationships between historical oppressions, structural social determinants and poor registration of vital events in the country. It is

also important to elucidate the mechanisms by which these inequalities in the performance are generated. One possible explanation could be that, in many of these areas, access to healthcare services and professionals to certify deaths is more limited. The observed correlations between quality of cause of death information and the percentage of deaths certified by health professionals support this hypothesis. Nevertheless, this is not a completely satisfactory answer since it doesn't fully explain the deficiencies in completeness and/or quality found in certain provinces. Moreover, high percentages of GCs were found in certain areas where most of the deaths were certified by medical doctors, suggest that health professionals need more capacitation to improve quality of registered deaths.

Finally, this study found that the mortality registry could not be classified as acceptable for both sexes in any of the study areas. This means that, beyond the enormous inequalities found in the country, problems with mortality data can be found all over the country. It is necessary that all stakeholders in Ecuador, including the Ministry of Health, the National Institute of Statistics and Censuses, academic sectors, and other social groups work together to substantially improve vital statistics. We believe that several factors should be considered and studied in order to fully understand inequalities in the mortality registry and to improve the system. These include but are not limited to: 1) How material deprivation limits the capacities and/or motivation of citizens to exercise the right / duty to certify deaths. 2) How is the coordination between the health and healthcare systems, the civil registration and vital statistics systems, and the judicial system. 3) How broader structural determinants at national and international levels relate to the poor performance of the mortality registry. These topics will be covered afterwards in this chapter, as we will propose a framework to understand how deficiencies and inequalities in its performance are generated.

1.2. Methods to correct deficiencies in the mortality registry allowed us to study geographical patterns of specific causes of death in the country. Mortality patterns observed in the country change.

In this study, we applied a garbage code redistribution protocol and adjusted mortality for completeness in the provinces of Ecuador. Substantial changes were seen in the number of deaths due to the selected causes after GC redistribution and correction for completeness. Furthermore, changes were noted in the geographical patterns of mortality due to specific causes. As expected by the geographical patterns of

completeness and quality indicators of the mortality registry, provinces in the Amazonic region and Galápagos had large increases in standardized mortality ratios (SMR) for the studied causes after GC redistribution and correction for completeness.

When GCs were redistributed, the changes seen in the number of deaths depended strongly on the cause of death studied, being greater in ischemic heart disease (IHD). Marked changes in mortality due to IHD after GC redistribution have been reported in several countries [14–16]. We have mentioned two possible reasons for these changes: 1) Many deaths worldwide are still coded with vague conditions that could be related to IHD, such as "heart failure" (ICD-10 code I50) [17]. Redistribution protocols redistribute heart failure deaths to IHD in large proportions. 2) A large number of deaths are coded with GCs that cannot be easily related to IHD, such as senility or many of the ICD-10 "R" codes. The GC redistribution protocol used in this study redistributes these GCs in lower proportions to IHD; however, many deaths with these GCs contribute greatly to increase IHD deaths. Other GCs substantially contributing to the increase in the number of IHD deaths were I10 (essential hypertension), R54 (senility) and R99 (other ill-defined and unspecified causes of mortality). In contrast, for the other causes of death studied, fewer GCs redistributed to the target codes.

At the national level, we could compared our estimates with the Global Burden of Disease study (GBD) estimates and the World Health Organization global health estimates (GHE) for the study period [18–21]. For both men and women, our estimates of respiratory cancers, lower respiratory infections (LRI) and IHD were higher than those of the GBD and GHE. Stomach cancer estimates from the three studies were very similar. For road injuries, our estimates were similar to the GHE results, but GBD estimated higher numbers of deaths. These differences can be explained by: 1) Differences in the redistribution algorithms and target code lists of GHE, GBD-2010, and newer GBD versions. Especially differences due to the use of regression models to assign redistribution weights, and age and sex limitations can greatly affect estimates. 2) The use of other information sources as police records to adjust road injuries. 3) Differences in the completeness estimates used to correct mortality. For example, GHE estimated a completeness of 81% in 2016 in Ecuador, and GBD-2017 completeness estimates were over 70% for the entire study period (65% for women and 68% for men in our study).

After correction of deaths for completeness and redistribution of GCs, there were also important changes in the geographical patterns of mortality. Compared with the median

of the 22 areas, SMRs in many Amazonic provinces, some provinces in the northern Coastal region and Galápagos markedly increased, especially in women. The new geographical patterns of mortality observed after correction for completeness and GC redistribution were rather similar to the patterns of socioeconomic deprivation in Ecuador [11,22]. Moreover, the associations between SMR for many of the studied causes in men and women changed from being negatively to being positively associated with income poverty. The observed associations were closer to what has been observed in global mortality studies [23].

In a context with deficient data sources, it is hard to study mortality in general and inequalities in mortality particularly. Thus, deficiencies in mortality data in certain areas could be masking important geographical inequalities. Evidence in this study points out in this direction. Nevertheless, correction methods are far from perfect and results need to be taken with caution.

1.3. A method to estimate a deprivation index for the cantons in Ecuador was created. There is a clear pattern of material deprivation in the country.

This study presented a method to estimate a deprivation index for the cantons of Ecuador that captures several deprivation dimensions. The index was composed of 17 variables available from public sources. The final index included indicators related to multiple forms of oppression in a medium-income country with a colonial history such as Ecuador. A clear geographical pattern of deprivation could be observed in the country. The index is positively associated with all-cause mortality in the study areas.

The creation of multiple deprivation measures is important to enhance research on geographical inequalities in health. Nevertheless, these measures are still scarce in low- and middle-income countries. In this study, as in others that have constructed deprivation indexes in other contexts[24], material deprivation indicators (related to education, work and housing) were prioritised by the analyses. Furthermore, it is important to observe the relatively large contribution to the index of indicators that have been considered more sensitive in detecting deprivation in low- and middle-income countries (e.g., the presence of pipes in the dwelling, literacy, water supply)[25]. It would be important to explore social deprivation measures in the country, as it could be and important determinant of health. Nevertheless, current data availability and the geographical scale at which data is available make this task difficult in Ecuador.

Our index examines the contribution of other possible sources of deprivation in the Ecuadorian context. The relative contribution to the index of indicators of access to mobile phones and particularly to the internet may help to explain an emerging digital divide in the country. Consequently, it is possible that "offline" groups may be marginalised from new forms of political, social and economic participation, thereby reproducing or even accelerating social inequalities[26,27]. Also, the indicator of poverty perception was retained in the construction of the index. In this regard, subjective wellbeing measures have proved to be associated with a range of health outcomes in both high-income countries and low- and middle-income countries[28]. This fact highlights the importance of developing specific definitions, dimensions and methodologies to construct deprivation indexes in Latin American contexts.

Women not in paid work showed a different direction in the correlation with the deprivation index and made the lowest contribution to its construction. Nevertheless, we retained this indicator based on the conceptual premise that it may provide information on gender inequalities based on the sexual division of work. The unequal use of time between men and women in Ecuador could affect health, as occurs in other countries[29]. Women in Ecuador devote considerably more unpaid hours than men to housework, childcare, and elder care, making them dependent in the income of their partner or family[30]. Deprivation measures have been criticized because they can often be gender insensitive [31]. We think researchers should work more on gender-sensitive measures of deprivation, as the experiences and consequences of it can have great variations by gender; which can have important implications for public policy. Our study has made a first effort to include gendered indicators in order to study deprivation. Nevertheless, much more work is needed to theorize and generate methods that can capture the gender relative aspects of deprivation in Ecuador and elsewhere.

The overall geographical pattern of material deprivation observed in Ecuador is highly consistent with the distribution of geographical inequalities in historically discriminated areas and oppressed social groups in the country. For example, this pattern is clearly observed in the Amazon, central Andean highlands and north-central coastal regions of Ecuador, which are predominantly inhabited by indigenous, Afro-Ecuadorian and montubio populations [32]. As in the other studies of this dissertation, a geographical pattern related to historical discriminations and structural racism in the country has emerged. Previous work on the country has already described similar patterns of poverty, relating them to unequal access to education, healthcare, and inequalities in

work and employment conditions between areas, between men and women and between ethnic groups [32].

To illustrate the potential public health uses of the index, we used standardized mortality ratios (SMR) for all-cause mortality in Ecuador (2009–2011) as a common indicator of health inequalities. We observed that the most deprived cantons were more likely to have higher SMR, showing a gradient. This gradient has been extensively observed in a large number of studies in different countries and settings, but mainly in high-income countries[33,34]. These first results of associations between all-cause mortality and material deprivation also generated the need to analyse if the same was true for specific causes of death in women and men in Ecuador.

1.4. Unique geographical patterns of mortality risk were found for individual causes of death in both sexes. Many of the studied causes of death in the country have clear positive associations with material deprivation.

In this final study, we estimated mortality ratios at a cantonal level for some of the leading causes of death in women and men in Ecuador from 2001 to 2014, after correcting deficiencies in the mortality registry. Also, we analysed whether mortality due to these main causes of death was associated with material deprivation. Our results showed rather unique geographical patterns of smoothed standardized mortality ratios (sSMR) by cause of death and sex. Moreover, many of the studied causes of death were positively associated with deprivation in women, men or in both sexes. The highest associations between deprivation and mortality were observed in both sexes for tuberculosis, HIV-AIDS and self-harm. Associations between material deprivation and most mortality causes were stronger in women than in men.

In chapter 6, we have discussed some of the main hypotheses and questions raised by the geographical patterns of mortality observed and by the associations between mortality risk and cantonal material deprivation. Analyses of the relationship between deprivation and mortality have a long history, mostly in high-income countries [35,36]. Our results suggest that health inequalities related to deprivation in Ecuador are not related to just few causes. Deprivation could be impacting health through several potentially different mechanisms and producing diverse health impacts.

In contexts where mortality Atlases have been constructed routinely, etiological hypotheses can be continuously generated and - sometimes - tested in order to

understand and reduce health inequalities [37–40]. In this first exploration of small-area mortality risks in Ecuador, we have been able to identify possible explanations for inequalities related to historical oppressions, structural and intermediate social determinants, material deprivation, and many other contextual and individual risk factors. For us, it is important to emphasize that this study can be a starting point that may open the research field in the country and allow future analyses related to the proposed - or new - possible explanations that have been described.

The analyses of the geographical patterns of mortality and their association with material deprivation presented in this article are of vital importance in order to identify high risk areas that can be targeted by public policy, and also to generate hypotheses for further studies that may help to elucidate the potential causes and mechanisms involved in these inequalities [38].

2. Reflections on specific topics related to the thesis

In the following pages, we will briefly discuss some topics that have appeared after reviewing the four studies presented in this doctoral thesis. These small sections contain thoughts, opinions and original theoretical work. We think that these reflections enhance and complement previous discussions, helping to provide a more integrating perspective of this work as a whole.

2.1. Are inequalities in mortality related to deficiencies in health information systems?

In our conceptual framework (chapter 1), we observe that differential material and social resources obtained by social groups – determined by structural determinants and power relations – may generate both inequalities in health and inequalities in mortality registration completeness and quality. Based on the results we have presented, we believe there is now some new evidence pointing out into that direction. The low quality of health information systems could be a significant "marker" of deeper social inequalities in Ecuador.

Geographical patterns of material deprivation, performance of the mortality registry and mortality risk for many of the studied causes of death are rather similar. Many of the areas with worse indicators share the significant characteristic of having high percentages of population from ethnic minorities in the country. We think that structural racism can be, at least partially, responsible for these similar spatial patterns. Hicken et

al. (2018) highlights three important features when describing structural racism and health inequalities: 1) "cultural racism can render the linkages between structural factors and racial health inequalities invisible"; 2) structural racism erases "historical processes that could clarify the link between racialized groups and health"; and 3) "structural racism[…]is often maintained through inaction" [41]. We hypothesize that deficiencies found in the mortality registry and their particular geographies might be linked to all these characteristics. Power structures can only be maintained if the very large inequalities generated by wider systems of oppression are downsized or accepted as "normal" by great proportions of the population. If racialized populations have greater risks of mortality (or other health problems), it is probable that institutions will not act to make these inequalities visible. As this institutional oblivion is generalized, a vicious circle is generated in which oppressed populations have less access to benefits and services that can contribute to improve their living conditions, and therefore improve their health; and as their worse health conditions or higher mortalities are not well reported and remain invisible, the state has no pressure to identify and act on those social and health inequalities, therefore perpetuating them. We believe a similar rationale could be described regarding the structural sexism derived from the strong heteropatriarchal system that has historically existed in the country. For this reason, it is important for researchers to adopt critical theories and methodologies that recognize, analyse and interpret social, racial/ethnic and gender-based discriminations, in order to take action towards their elimination (e.g. public health critical race methodology, and specially intersectionality theory) [42–44].

2.2. Geographical inequalities in mortality risk and wider systems of oppression: the example of violence mortality in Ecuador

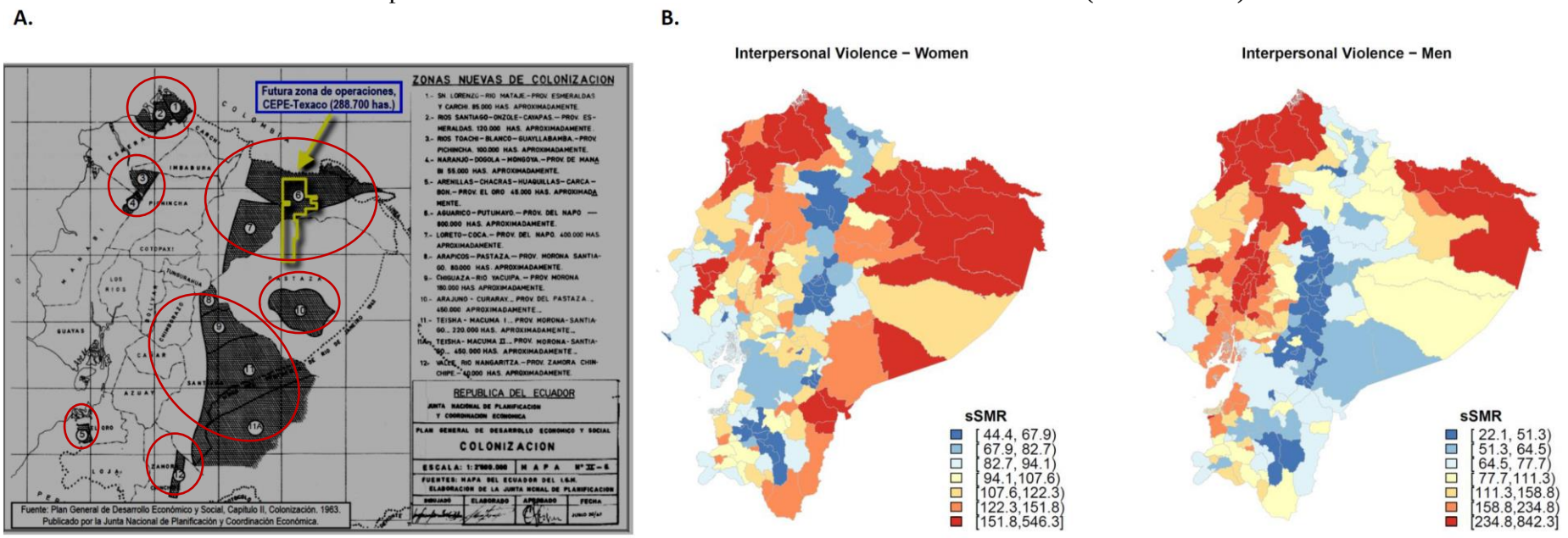
Sometimes, it can be hard to talk about wider systems of oppression and their relations with health as they can be perceived as abstract and distant concepts. For this reason, we reviewed an example derived from the findings of this dissertation to illustrate this specific point. Particularly, we covered it briefly in chapter 6, when we discussed some possible causes for the patterns of the mortality risks for interpersonal violence and some cancers in Ecuador. In no way this example pretends to fully explain all the connections and mechanisms potentially involved, as we understand this is a complex problem. Instead, our aim is to provide some insights on a complex problem and

recommend further lines of research on a topic traditionally neglected in Ecuador and in many other countries in the region.

Since the late 19th century, the Ecuadorian government had ambitions of colonizing vast areas of land in the country, replacing forests with agricultural lands. Special laws in 1899, 1954 and 1973 gave great land incentives to people and companies that settled in many areas of the country, and especially in the Amazonic region [45]. The Ecuadorian state failed to recognize the land rights or even the existence of several indigenous and afro Ecuadorian populations in the areas it offered to settlers. In the 1950`s and 60`s, as the existing petroleum wells that were exploited in the Coastal region of Ecuador declined their production, the Ecuadorian state strengthened both the settlement strategies and concessions to international oil companies to explore new petroleum reserves[46]. In Figure 1A, we show a map created by the national board of planification in 1963 that displays the settlement (colonization) plan of the government of Ecuador [45]. When mapping the mortality risks due to diverse causes, the similarities of some of the geographical patterns with the 1963 settlement planification map strikingly caught our eye. For example, Figure 1B shows the map of mortality risk due to interpersonal violence in women and men in the cantons of Ecuador between 2001 and 2014. It can be observed that both maps in Figure 1B share patterns with the 1963 map presented in Figure 1A. In the next few lines we will try to describe some context that could connect both figures.

By the 1970's, a pipeline connecting the northern Amazon with the northern coastal region (where a refinery was built) allowed petroleum to become Ecuador's leading export product, and it has been this way since then [45,47]. It is estimated that more than 350,000 people settled in the northern Amazonic region of Ecuador from 1972 to 1992. Several indigenous groups inhabited those lands previously. The environmental and social conflicts that derived from colonization and extractivist industries in the northern Amazonic region has been documented in various investigations [45,48,49]. Moreover, important potential health impacts from oil extraction and large health inequalities between settlers and indigenous populations have been reported [50–53]. In the northern coastal region of Ecuador (Esmeraldas), the petrochemical industry has also coexisted with illegal mining [54]. Since the beginning of the 21st century, oil and mining have also been promoted in the southern Amazonic region in areas previously inhabited by indigenous populations and that gather an enormous biodiversity [49].

Figure 1: A. Settlement (colonization) plan made by the government of Ecuador in 1963. B. Smoothed standardized mortality ratios (sSMR) for interpersonal violence in women and men in the cantons of Ecuador (2001 to 2014)



A. Original map created by the national board of planification in 1963 – reproduced from Southgate et al. 2009 [45]. Areas planned for colonization are marked in dark grey and surrounded by red circles. The yellow polygon marks the future operation area of the oil company Texaco.

High mortality risks due to interpersonal violence – as well as self-harm and some cancers - are particularly observed in some areas that share some characteristics: 1) indigenous and afro – Ecuadorian populations have traditionally lived there; 2) the state has purposely settled populations from other parts of the country in those areas; 3) extractive industries have been operating in some of the mentioned areas for many years, and in others they are beginning exploitation or explorations to begin operations; 4) deforestation has replaced formerly biodiverse ecosystems into croplands or grasslands. These shared characteristics point out towards the socio-geographical spatialization of shared oppressions from colonialism (i.e., a racist state that doesn`t recognize indigenous/black people's rights, denying them of control over their own land and resources) and extractivist capitalism (i.e., extractive industries which settle on previously inhabited land and obtain large benefits while generating large environmental, social and health – related impacts). In the example of violence, we can add another level with the case of heteropatriarchy. In Latin America, most of the victims of homicide are young men, and studies have related male involvement in violence with a culture of hegemonic-dominant masculinity that favours both the exposure to and the participation in violent actions[55,56]. In Ecuador, between 2001 and 2014, the ratio of deaths due to interpersonal violence between men and women was 7.3:1.

The association of interpersonal violence mortality risk with material deprivation also points out towards inequalities generated by historical oppressions in the country. We are aware that many other factors (as gun availability and illegal drug trafficking) must be analysed in order to fully understand interpersonal violence mortality. However, we believe that these shared characteristics warrant attention and deserve further research on how the mentioned wider systems of oppression may affect health and mortality in Ecuador and other countries with similar contexts. In order to do so, different research paradigms, theories and methodologies should be explored to fully understand these complex relationships and the mechanisms by which they are acting.

2.3. Improving correction methods or improving the civil registration and vital statistics (CRVS) system?

The straight answer to this important question is that the improvement of the CRVS system should be a priority. First, as we have mentioned before, evidence supports the hypothesis that, even after adjusting for socioeconomic variables, countries with good

CRVS systems have better health outcomes [57]. Moreover, as we have seen all over this dissertation, both the methods to evaluate deficiencies in mortality data and to correct those deficiencies present great problems. No matter how sophisticated correction methods become, they will never be able to replace a well-functioning and high quality CRVS system. Other countries in Latin America like Costa Rica, Colombia and Brazil have shown that the performance of the system can greatly improve with political commitment, appropriate financing and adequate policies [58]. In the next section, focusing on mortality registration, we will try to propose some of the factors that need to be considered in order to improve the system and reduce the inequalities we have found in Ecuador.

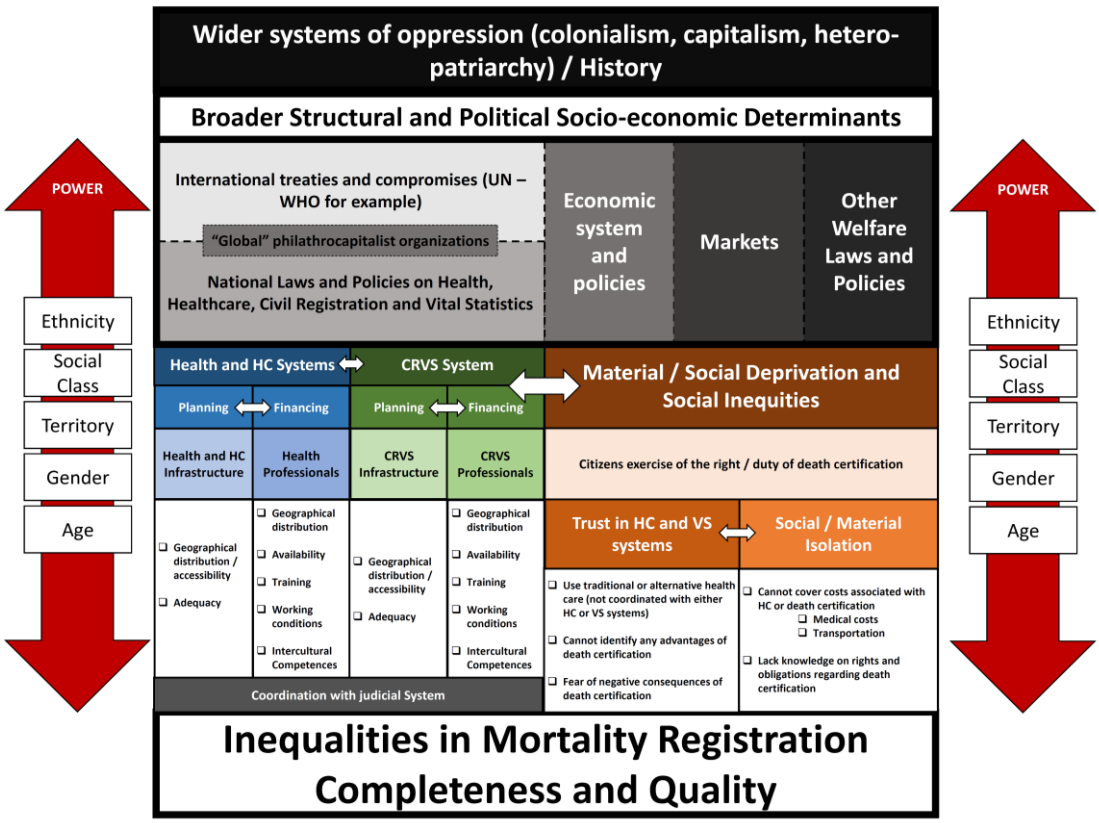
2.3.1. A framework for the improvement of the mortality registry in Ecuador

Throughout this thesis, we have seen that inequalities in both mortality and mortality registration are socially determined. After considering the studies presented in chapters 3 thru 6, and the literature published on CRVS systems, a conceptual framework for understanding and acting on inequalities in mortality registration was created (Figure 2). In the next few lines, the framework and its major components will be briefly described. The conceptual framework starts with the same principle of the conceptual framework presented in chapter 1, that considers that both health inequalities and inequalities in the mortality registry have structural social determinants which are embedded in wider systems of exploitation, domination and oppression; and that are configured according the particular historical and geographical circumstances of each context. The broader structural and political determinants leading to deficiencies and inequalities in CRVS systems, and specifically in mortality registries include: 1) legal and financial determinants directly related to death registration and vital statistics. These determinants include international treaties and commitments with international institutions as the United Nations / World Health Organization that require states to report health statistics [59]. These commitments, along with national laws and policies on health, healthcare, civil registration and vital statistics configure much of the legal framework and financing for mortality registration in each country. Global philanthrocapitalist organizations (as the Gates Foundation) have been included between national and global regulations, as their impact in the financing and priority settings of international and national health

organizations has exponentially grown in the past decades [60]. We will briefly discuss this particular issue in the next section (2.4).

At the same level as the national and international laws and policies that have direct relations with mortality registration, we can find other structural determinants of each territory as the economic system and policies, markets, and other welfare laws and policies. These three structural determinants relate greatly to the living conditions of the population, but can also have great impacts on the financing, planning, infrastructure and professionals needed for death registration. The dotted lines between the structural determinants presented here represent that all these components are interrelated and that they affect -in different ways- all the components shown on the bottom of the graph.

Figure 2: Conceptual framework for understanding and acting on inequalities in mortality registration



At intermediate and proximal levels, on the left side we find a an "institutional" component, that includes the health and healthcare systems and the CRVS system; and in the right side the material and social living conditions of the population. Both sides are interconnected and dependent on each other. On the "institutional" part of the framework, we find that both systems presented require specific planning and financing

at different scales to develop the planned policies and strategies. The planning and financing of each system shapes the local infrastructures needed and the geographical distribution, availability, training, working conditions and intercultural/gender competences of professionals involved in death registration. These two systems have been included because death registration requires an optimal functioning and correct coordination between both of them. A well-functioning health and healthcare system is able to "capture" most of deaths in an area and gives correct information for assigning adequate causes of death. A well-functioning CRVS system collects information from the health and health care system, and adequately performs the steps of validation, registration, certification, information sharing, compilation, assessment of quality, and the generation and dissemination of vital statistics [61]. The coordination of both systems with the judicial system is also included, as it is especially important to have adequate information on deaths from external causes. Geographical variations in the performance and coordination of these systems can greatly impact inequalities in the completeness and quality of mortality data.

Opposing the "institutional" intermediate and proximal determinants, we find the material and social living conditions of people, and the social and geographical inequalities found in those living conditions. We believe that those particular conditions in a particular territory can greatly impact on how inhabitants exercise the right / duty of reporting deaths. On one side material and social deprivation, and historic discriminations due to race/ethnicity, social class and gender can greatly impact on the level of trust that people in an area may have on institutions. For example, culturally incompetent health services and lack of coordination between traditional health practitioners and the institutionalized allopathic health system might make it hard for some indigenous people to access health services, even if they have severe health problems [62]. If those people die (in home or attended by a traditional health provider) and incentives for death registration are absent, it seems highly plausible that families will not notify it. Other example for this institutional mistrust can be related to contexts with high levels of violence, where people might avoid notifying deaths for fear of retaliations. Moreover, social and material deprivation can lead itself to isolation of families, leading to a lack of notification of certain deaths. For example, even if healthcare and death certification are free, some families might not be able to cover transportation costs needed to access healthcare or to report the death of a relative.

All the mentioned components might contribute to generate social and geographical inequalities in mortality registration. Moreover, as discussed along this dissertation, all these components are not distributed equally. Power relations related to ethnicity, gender, social class and age (among other axes of inequality) play an important role on how these components are distributed in space and across social groups [63]. Indeed, these power relations act on many levels simultaneously. For that reason, we have included these axes of inequality vertically on both sides of the graph.

We believe that the framework presented here can help us to identify in a comprehensive manner how deficiencies and inequalities in the mortality registry are generated and also to help to propose policies and interventions that can improve mortality data with a focus on equity.

2.4. Philanthrocapitalism and vital statistics sovereignty in low and middle-income countries

In the past decades, the funding of public health research and surveillance has deeply changed globally. Thus, funding has shifted from governments and international institutions to philanthrocapitalist organizations linked to big global corporations. The paradigmatic example of global health research financed by philanthrocapitalist foundations is the Institute of Health Metrics and Evaluation (IHME) and their well-known project, the Global Burden of Disease (GBD) study. IHME defines itself as "*an independent population health research center at UW Medicine, part of the University of Washington, that provides rigorous and comparable measurement of the world's most important health problems and evaluates the strategies used to address them*"[64]. In 2007, the Bill & Melinda Gates Foundation donated 279 million US dollars to IHME. This represents more than double of the budget for "health systems, information and evidence" or more than four times the budget for "equity, social determinants, gender equality and human rights" of the World Health Organization for the 2018-2019 period [65]. For many years, global philanthrocapitalist organizations have been questioned for potential conflicts of interest, as many of them - including the Bill & Melinda Gates Foundation – have major financial relationships with major actors in food and pharmaceutical industries [60,66]. Moreover, the role of this private foundations and their strategies to impose research and expenditure priorities have also raised many criticisms [60,67].

After 2007, IHME became one of the biggest and most influential global health research institutions in the world. The most recent methodologies to study global burden of disease (and thus to study mortality) have been developed and applied in the GBD studies. For example, the GBD studies have developed or refined the methodologies to estimate mortality in countries with defective vital statistics systems (adjustment for completeness and GC redistribution protocols among others)[68].

GBD studies have shown big inequalities in the burden of disease around the globe. Nevertheless, some criticisms rise when we analyse its funding and practices:

1) States and local communities do not control (or even have any knowledge about) the information developed, analyses and research priorities.
2) Research methodologies are developed and used mainly in few high-income countries. Instead of strengthening local research capacities, local CRVS systems may be weakened and become dependent on IHME to obtain national health statistics. The most recent GBD study (2017) even estimates its own population and fertility estimates [20].
3) Even though GBD studies evidence great global inequalities, their research papers rarely discuss inequalities or the root causes generating them. Historical processes and systems of exploitation, domination and oppression such as colonialism, neoliberal capitalism and heteropatriarchy are almost never present in the GBD published papers.
4) Potential conflicts of interest from the roots of IHME financing are rarely discussed in mainstream publications.

Even though significant scientific research has been produced in the mentioned institution and other research centres financed by global philanthrocapitalist organizations, we believe that these criticisms should be appropriately addressed and understood. Moreover, we also believe that it is vital for local and national institutions to have the capacity to develop and adapt methods to appropriately study mortality and burden of disease locally, establishing priorities that are adapted to local contexts and necessities.

3. Strengths and Limitations

3.1. Limitations

This doctoral thesis has some limitations worth mentioning. These limitations have been mentioned throughout the dissertation and many of them were included in the presented articles. Therefore, we will organize them as clearly and concise as possible. We have grouped these limitations on two categories: 1) limitations derived from data sources in Ecuador; and 2) limitations from the methods used for the presented research.

3.1.1. Limitations derived from data sources in Ecuador

The statistical system in Ecuador presents several limitations related to data completeness, quality and availability that restrain researchers who want to study inequalities in mortality. We must first recognize that all data used for this dissertation was publicly available from official data sources. Nevertheless, we have to mention some of the limitations that arise from deficiencies in the data.

As we reviewed in chapter 3, the mortality registry in Ecuador presents several deficiencies in completeness and quality. These deficiencies conditioned potential biases in analyses of mortality in the country. Even if state of the art methods are used to correct deficiencies in data, analyses of mortality are still prone to be inaccurate or systematically biased.

Another limitation of mortality and other statistical data in Ecuador is related to the geographical scale for which data is available. As we have mentioned, the smallest area at which most comparable data is available in the country are cantons (second administrative level). We already mentioned some of the limitations related to the heterogeneity of cantons in relation to size, populations and number of deaths. Moreover, much of the data that comes from national surveys in the country is only representative at the provincial level (first administrative level), an even larger geographical scale. Capturing contextual effects in areas such as these can be difficult, and thereby within area inequalities can be masked. Additionally, the lack of data at smaller scales makes research of small-area effects (in urban areas for example) impossible. Part of improving the national statistical system will go through the standardization and use of more stable areas at diverse geographical levels – including small-areas, or the use of modern and accessible geocoding technologies that allow to process information at different scales while preserving anonymity and other ethical standards.

3.1.2. Limitations derived from the methods used for research

A first set of limitations derived from the methods used in the presented studies relates to the methods used to evaluate the performance of the mortality registry and correct deficiencies found in it. Even though they are some of the most widely used methods worldwide, they present several limitations worth mentioning. Regarding completeness, we used death distribution methods, a set of methods that have three important assumptions: 1) that the studied population is closed to migration; 2) that completeness is constant in all age groups; and 3) that age misreporting is minimal or non-existent [69]. All these issues could be relevant, but migratory patterns could be a vital factor in Ecuador during the study period (with substantial internal and external migratory waves) [70,71]. Some authors have proposed approaches to adjust some of the DDM methods for migration[72], but their use is still not widespread. Another important limitation of DDM methods is their high level of uncertainty [69]. Moreover, completeness estimates are constant for all the causes of death studied. Additionally, the methods used to study completeness lack of timeliness. DDM methods depend on information from national censuses and give completeness estimates for the whole intercensal period. This makes completeness estimates inadequate to study rapid changes in death registry completeness. Also, we must mention that the methods used to estimate completeness are adequate for adult mortality. Additional methods should be employed in order to obtain adequate completeness estimates, especially in children. When correcting mortality in the whole population, this could be a relevant issue to be considered. Another limitation of the correction of mortality for completeness is uncertainty. In the second study presented in this dissertation (chapter 4), uncertainty was not considered. In the fourth study (chapter 6) we proposed a novel model that can account for uncertainty. Nevertheless, we think that a lot of work is still needed in order to fully account for it.

Regarding the evaluation and correction of deficiencies in quality of mortality data, it could be important to assess and adapt garbage codes and their redistribution protocols to the local context and time. No garbage code redistribution method is ideal, and biases can arise from their application. Proportional redistribution ignores the distribution of cause-specific mortality in specific geographical areas, age or sex groups. Expert opinion can be valuable but can also be biased. For example, specialists from low- and

middle-income countries could be underrepresented in expert groups. Regression models have the advantage of including uncertainty, but they need reliable covariables in order to work and can be difficult to adapt to subnational contexts. The GBD-2010 redistribution protocol used in this dissertation has few age and sex restrictions and therefore adds proportionately more deaths in women, children and older people, a phenomenon especially noticeable in ischemic heart disease deaths.

A second set of limitations are related to the construction of the deprivation index used in this dissertation (study 3, chapter 5). The deprivation index constructed is based on data available through the Census and Living Conditions Survey (LCS). Although these sources provide many interesting and useful indicators, important information that could be relevant to describe material deprivation (e.g. work and labour conditions and access to public services, among many others) is not available. In addition, the information from the LCS is only representative at the provincial level. This could mask inequalities between cantons and could thus be responsible for the minor contribution of LCS variables to the final index. Finally, and related to the LCS limitations, it is worth mentioning that our index could not capture conceptually relevant social deprivation dimensions that could be related to health and mortality.

To end this list of limitations, we have to mention a possible bias introduced by the methods used to analyse the associations between cause-specific mortality and deprivation. We observed that associations were consistently higher in women than in men. In studies conducted in other parts of the world, associations between material deprivation and mortality have been found to be higher in men [73,74]. Nevertheless, these studies were performed in European urban contexts so comparisons should be made with caution. Nevertheless, there is a possibility that - when correcting mortality for deficiencies in the mortality data – methods could be enhancing associations between deprivation and mortality. The mortality registry in Ecuador shows poorer indicators in women. Moreover, the geographical patterns of high material deprivation and poor performance of the mortality registry are similar. If both the performance indicators of mortality data are related to sex and deprivation, after correcting these deficiencies, we could be pushing mortality estimates to be more associated with deprivation in women. This issue should be studied more in depth in further studies in the country.

3.2. Strengths

Despite the presented limitations, the dissertation has some important strengths worth mentioning:

- A set of methods to study social and geographical inequalities has been generated and presented. This sequential process includes the evaluation of completeness and quality of data, correction of deficiencies found in the data, identification and/or estimation of relevant covariables for the study of inequalities in mortality (material deprivation), and finally the evaluation of geographical and social inequalities in mortality. We believe the methods used in this dissertation could be replicated in Ecuador and in other countries with similar contexts. Moreover, these methods can be critically analysed and modified in order to deepen the study of inequalities in mortality in the country. Certainly, there is still a lot more of work needed in order to understand health and mortality inequalities in Ecuador. We are convinced that this dissertation is an important first step in that direction.
- We performed the first comprehensive evaluation of the mortality registry in Ecuador. Moreover, for the first time in the country, inequalities in the performance of the registry by sex and geographical region were analysed using methods and indicators that are state of the art and that allow comparisons with other countries. This evaluation is a crucial first step, necessary for any researcher that studies mortality in the country. Moreover, the design of the evaluation, allowed us to propose relevant policy recommendations related to sex and geographical inequalities in the performance of the mortality registry.
- A set of methods to correct deficiencies in mortality data were adapted and performed at a subnational level in the country. We have identified and adapted some of the best methods used worldwide to correct completeness and quality deficiencies in mortality data. These methods allowed us to obtain a better picture of the number of deaths and mortality risk patterns for some of the main causes of death in the country. Beyond the use of solid methods, we believe this process has great importance, as it allows institutions and researchers in Ecuador to apply them, establishing their own priorities, according to the necessities of the country. Therefore, we feel this is a first, modest but important, step towards

recovering/creating research sovereignty in the country (especially in the field of social epidemiology).

- We have created a deprivation index for the study of health inequalities in the country that, to the best of our knowledge, is the first multiple deprivation measure constructed for public health purposes at a second administrative level (cantons) in Ecuador. We have adapted some of the best available methods found in the international literature to construct the index. Moreover, we have described the set of methods used, so that other researchers and public institutions can adapt and reproduce them. The development of this kind of social indexes is vital for identifying and understanding the role of the context in diverse health outcomes and health inequalities. Moreover, they can be of paramount importance for local stakeholders that aim to design and implement policies and to allocate material and social resources to tackle health inequalities.
- The estimation of smoothed standardized mortality ratios for the main causes of death in women and men at a cantonal level in Ecuador also presents several strengths. We performed methods that allow to simultaneously accomplish three goals: 1) correct mortality for completeness, considering uncertainty in the three estimations obtained through DDM methods; 2) estimate mortality risks for each studied cause taking into account not only heterogeneity (or independence) between areas, but also the possible existence of spatial dependence and dependence between the studied causes of death; and 3) analyse associations between material deprivation and mortality risks for all the studied causes. The specific models used for this purpose are novel and could be adapted for other uses both in Ecuador and in countries with similar contexts. Additionally, the geographical patterns of mortality risk and associations with material deprivation in the country can be important for future research and for the design and implementation of public policies.
- A central strength of this dissertation is that it has the capacity to generate many new questions and hypotheses for future research. In mainstream biomedical research, descriptive ecological research has many times wrongly been neglected and criticized. We believe this is a crucial mistake, generated by a commercial publishing system that values novelty over importance for public health; and that that needs to be reviewed and changed. Throughout this dissertation important

research necessities, questions and hypotheses have emerged. The inequalities observed in the country need much more research. Yet, without these first descriptive studies, we might not even know some of the relevant questions worth exploring in the country. Results from the presented studies are relevant for policy, but also to establish future research agendas in Ecuador, prioritizing investigations relevant to understand and reduce inequalities in the country.

- Finally, we want to highlight the perspective undertaken by the presented studies as a global strength. The rejection of some of the characteristics of a mainstream reductionist biomedical research model has allowed us to begin to explore and discuss how intermediate and structural social determinants of health could be generating the inequalities observed in the presented studies. Moreover, we have gone a step beyond, proposing hypotheses on how wider systems of exploitation, domination and oppression (colonialism, heteropatriarchy and capitalism) could be the "causes of the causes of the causes" finally responsible for the wide inequalities observed in the country. We believe that this line of research is new and important in a country with a colonial past (and present) as Ecuador.

4. Recommendations for research and policy

4.1. Recommendations for research

- Methods for evaluating the performance of the mortality registry should be enhanced.

As we have reviewed in this doctoral thesis, methods for evaluating the completeness, quality and internal consistency of mortality data currently present several deficiencies. Regarding death distribution methods, we believe it is imperative to: 1) generate and expand on methods that take into account migration; 2) consider uncertainty when estimating the completeness of mortality data; and 3) generate or adapt necessary methods in order to obtain better completeness estimates at the small-area level. Regarding evaluation of quality, we believe it is fundamental to: 1) conceptualize in a better way the meaning and implications of "garbage codes" and each of its sub-types; 2) consider differences between different types of garbage coding and their implications for policy; 3) adapt the lists of garbage codes, considering the unique contexts of each country. Finally, we believe that the lists of causes considered improbable for specific age-sex combinations should be adapted to each specific context and also that

appropriate mechanisms to correct data for deficiencies in internal consistency should be generated.

The great inequalities observed in the mortality registry performance warrant further research. Differences in completeness and quality in the mortality between men and women have not been studied in depth. The possible explanations proposed for this phenomenon should be studied in detail in order to fully understand the mechanisms involved and to propose strategies and policies to reduce this inequality. Geographical inequalities in the performance of the mortality registry also require further studies. Many interesting questions are generated by the spatial patterns we have observed. For example: Do geographical inequalities in the completeness and quality of the mortality registry relate to material deprivation? By which mechanisms are these inequalities generated? Are deaths of people from minority ethnic groups registered less and/or with lower quality? All these questions should be studied more in depth. For this purpose, a combination of research paradigms, theories and methods (qualitative and quantitative) should be employed.

- Methods to correct deficiencies should be enhanced and adapted to each specific context.

We have seen that methods to correct deficiencies in the mortality registry present several limitations that should be addressed and improved. Regarding correction for completeness, it is important to consider uncertainty in completeness estimates when we correct mortality ratios. Regarding corrections for quality, we think there are several important points worth mentioning. First, garbage code redistribution protocols should be adapted to specific contexts and to the main causes of mortality in each country. Second, redistribution protocols should have specific age and sex restrictions to avoid adding too many deaths to certain age groups. The newer redistribution protocols from the GBD project already have cause specific redistributions with more restrictions. Efforts to create new redistribution protocols or to adapt those existing ones can be important to avoid overcounting deaths from certain causes in some age groups. Third, we think efforts should be made to make this type of methods more accessible and applicable to researchers from all over the world. GBD protocols change quickly, and many times it is hard for researchers from all over the world and especially low and middle-income countries to be able to apply them. In this sense, we think that important steps have to be taken towards the democratization of methodologies; with a much

bigger participation from researchers from all over the world in spaces that are not private, but rather real "globally" public for the common good. It is important for researchers from each country, who know the specific local contexts better, to be able to set priorities and have control over the methods being used to study mortality in their countries without being relegated or subject to the mainstream research controlled by only few researchers or powerful groups in the globe. Finally, we must emphasize again that correction methods should only be considered as interim replacements that are useful while national CRVS systems improve substantially. Researchers should clearly recognize that no correction method replaces a well-functioning CRVS system and they should let both decision makers at local, national and international levels, and the general public that more efforts should be undertaken to improve the systems and not towards just making more sophisticated methods.

- Deprivation, its geographical patterns, and its health effects should be studied more in depth in the country.

We have proposed a methodology to generate a deprivation index to study health inequalities in the country. As we have mentioned, the definition, measurement and health impacts of deprivation can have particularities in the Latin American and Ecuadorian contexts. In future research, it can be important to: 1) refine the definition of deprivation in the country; 2) discuss more in depth what are the essential dimensions of deprivation in the Ecuadorian context; 3) find or generate new indicators that can better describe the mentioned dimensions; and 4) explore new methods to generate deprivation indexes in the country. Moreover, we think it would be vital to understand, conceptualize and operationalize deprivation indexes that are both gender sensitive, age sensitive [75], and that consider the living conditions and cultures of ethnic groups in Ecuador.

- The questions and hypotheses raised by the unique geographical patterns of cause-specific mortality and their association with deprivation should be studied.

Many questions were raised by the results presented in the fourth article of this doctoral thesis (chapter 6). Just to mention a few: 1) Why are the associations between material deprivation and mortality higher in women? 2) What explains the cluster of HIV-AIDS mortality risk observed in the Coastal region of Ecuador? 3) Why is the mortality risk from circulatory system diseases higher in many cantons in the Coastal region of Ecuador? 4) What can be done in order to reduce the great social and gender-based

inequalities in mortality risk due to chronic-obstructive pulmonary disease observed in the country? 5) What explains the high mortality risk from stomach cancer in the northern Andean region of Ecuador? 6) What can explain the high mortality risks from external causes in the Amazonic region of Ecuador? 7) What are the sources of environmental risk factors that can be related to certain high-risk areas of mortality due to cancers and other illnesses in the country? 8) How do structural determinants and wider systems of oppression shape mortality risk inequalities due to self harm and interpersonal violence? We think all the presented questions and hypotheses warrant further research. Moreover, we think that in order to better understand the observed mortality inequalities in the country, the scientific research generated by these questions should: 1) be transdisciplinary or at least interdisciplinary, allowing for people from diverse backgrounds to interact and generate new ways of understanding and interpreting the reality; 2) embrace interculturality, not only prioritizing the demands and necessities of all multiple ethnic groups in the country, but fully acknowledging their cultures, worldviews and letting them be completely involved in all the research process; 3) incorporate elements from diverse theoretical positions (intersectionality, feminist theories, post-colonial theories, and critical race theory just to mention a few) and from different schools of thought towards health inequalities (European social epidemiology and Latin American social medicine/critical epidemiology); and 4) use diverse scientific approaches and methods (quantitative and qualitative), including essential contributions from the fields of history, geography and political sciences, among many others.

4.2. Policy recommendations

The results presented in this dissertation made us think on many possible policies that could be implemented in the country both to reduce health inequalities and inequalities in the mortality registry. We will briefly mention them in this section:

- The National Institute of Statistics and Censuses and the Ministry of Health, with the active participation of the academia, social movements, and civil society, should generate a continued process to substantially improve vital statistics in the country. We have identified the geographic areas that have the greatest deficiencies in completeness, quality, or both. These areas should be the priority for interventions. Moreover, interventions directed towards the improvement of quality and towards the improvement of completeness should be

created and implemented in each province according to the needs found in the evaluation of the mortality registry.

- There is a clear geographical pattern of material deprivation in Ecuador. Moreover, the association between material deprivation and mortality for many causes of death in both women and men points out to significant health processes and effects related to these inequalities across the country. Therefore, policies and interventions to reduce health inequalities in the country should focus on reducing these vast socio-economic inequalities in the country.
- Geographical patterns of mortality risks and associations with material deprivation suggest that sexism and racism could play an important role in producing health inequalities in Ecuador. Consequently, policies and interventions to reduce health inequalities should focus on fighting and reducing the impacts of structural and cultural sexism and racism.
- Mortality risks due to certain cancers, self harm and violence suggest that there could be several impacts from certain economic activities performed by large-scale industries in Ecuador. The risks derived from extractivist industries should be evaluated, establishing adequate surveillance systems in the areas where companies operate. These surveillance systems should evaluate environmental risks, social determinants of health and other health related behaviours and exposures that can affect health and health inequalities. If health impacts of these industries are suspected, the precautionary principle should be applied. Moreover, proper health, environmental and social impact assessments should be a compulsory requirement for any new extractivist industry in the country. When economic activities may harm humans, cultures or the environment, outweighing the social and economic gains for communities, it is the duty of the Ecuadorian state to protect the inhabitants of the country by denying the necessary operating licences.

5. Conclusions

- At the national level, the mortality registry of Ecuador performs poorly both in terms of completeness and quality. Large geographical inequalities were observed in mortality data. In most of the studied areas, indicators were poorer for the mortality registry in women. Moreover, quality and completeness were lower in the Amazon, central Andean, and northern Coastal regions where historically excluded groups have traditionally lived.

- After correcting deficiencies in the completeness and quality of the mortality registry in the country, we observed not only changes in the number of deaths, but also in the geographic patterns of mortality risks due to some of the main causes of death in women and men.

- There is a clear geographical pattern of material deprivation in the country. High levels of material deprivation were found in areas in the northern Coastal, central Andean and Amazonic regions.

- Unique patterns of specific cause of death mortality were observed in women and men in the country. Moreover, some of the main causes of death in men and women were positively associated with material deprivation. Socioeconomic inequalities in mortality are not limited to certain causes in the country.

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