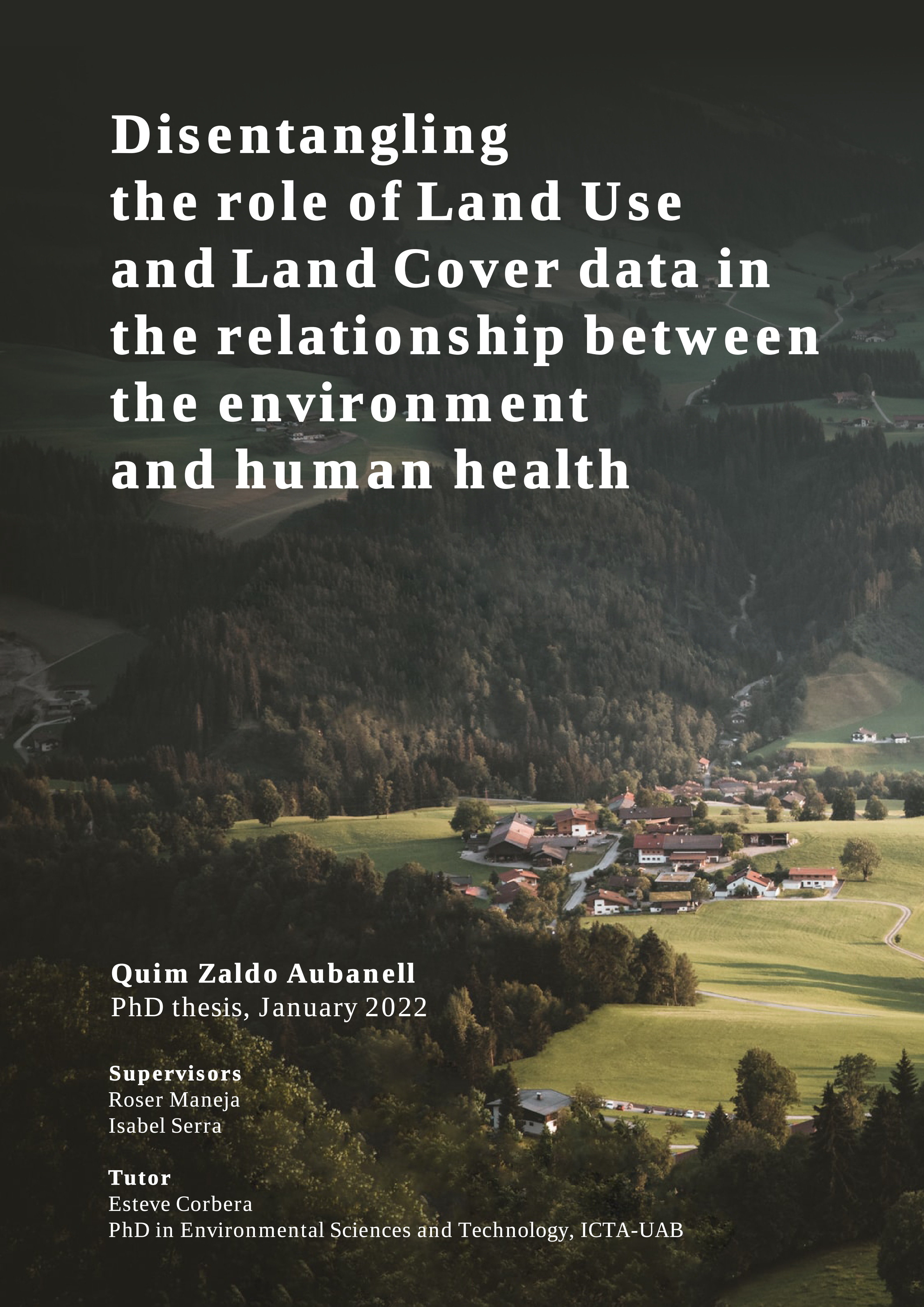
Universitat Autònoma de Barcelona

Disentangling the role of Land Use and Land Cover data in the relationship between the environment and human health

Quim Zaldo Aubanell



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PhD thesis, January 2022

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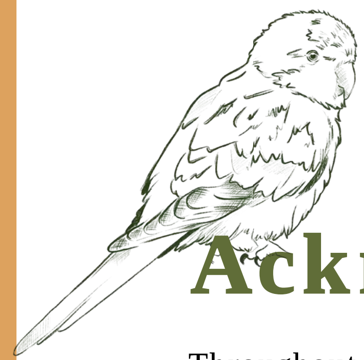


Acknowledgements

Throughout this research, we highlight the relevance of interdisciplinary approaches to address problems and create better solutions holistically. Rather than an empty message, it is the result of consciously applying interdisciplinarity to this research and noticing how much it has flourished as a consequence. From the first step, we were always aware that this journey would not have been possible without the support, insights, work, efforts, and advice of all colleagues accompanying us during these years. From the first people that planted the seed for this research to become a thesis: Dr Martí Boada, Dr Jordina Belmonte, Dr Jordi Bartrolí, Dr Teresa Romanillos and Dr Jordi Serra Cobo. The co-authors who have taken part our publications: Dr Lluís Alsedà, Dr Josep Sardanyés, Dr Marc Saez, Dr Albert Bach, Dr Pablo Knobel, Dr Ferran Campillo I López, Dr Pepus Daunis-i-Estadella, Mr Joan Olievet-Vila and Dr David Pino. The mentoring received from Dr Esteve Corbera, and all the technical support provided by incredible people such as Ms Marta Borrós, Mr Stephen Bell, Mr Miquel Barcelona, Dr Marcel Bach-Pagès and the staff of the Information System for Research in Primary Care (SIDIAP, in Catalan).

In the same vein, I would like to give a special thanks to my directors, Dr Roser Maneja and Dr Isabel Serra; without their guidance, encouragement, and affection, this journey would have been much harder if not impossible to undertake. Likewise, I sincerely thank all my family, those present today and those who have passed away during these years for their untiring support.

I warmly thank all of you.

We all can recall a moment in which we felt alive and energized when we immersed ourselves in a particular landscape. Likewise, it would not be difficult to think about another moment when our surroundings made us feel overwhelmed, insecure, or simply down. The connection between the environment and humans has always existed. Prehistoric civilizations adapted their food sources and activities to the natural tempo. Moreover, in return, the environment met all their necessities: shelter, food, clean air, and water, but also the incommensurable scenario for humans to enjoy, grow, and interact with others. All these were exclusive attributes of the environment. And they still are.

Today, in a post globalized world, many of these attributes may have been taken for granted, and consequently, our connection with the environment is not as easy to see. However, it is still there, like roots, that help us remember who we are, where we belong, and what we need.

Abstract

In the context of Global Change, many researchers have endeavoured to evaluate the consequences of environmental degradation on human health. On the other hand, increasing evidence also points to the positive effects of healthy environments. However, much of the research today simplifies the environment as that which is green, using a metric gathering the "amount of green". Although this *greenness* idea has unequivocally been a doorway to new nuances about the importance of surroundings for human health, the theory has been considered limited and inadequate to elucidate critical subjects of debate in the research field.

The Land use and Land cover (LULC) dataset has proved to be a suitable tool to describe the environment. Unlike other environmental datasets, the LULC dataset measures the biophysical features (the biophysical material over the surface of the Earth, the land cover) and the socioeconomic features (the human activities involved in that specific place, the land use) of the environment, providing a holistic definition. In addition, it is a versatile tool that can help notions of the complex systems theory to be put into practice.

To date, some researchers have used LULC data to describe the environment in health studies. Furthermore, the interest in LULC data is expected to increase in the near future. However, no study linking LULC data with human health data has yet considered that LULC data is of a compositional nature since they are limited by the so-called sum up constant constraint. Considering the room for improvement regarding the environment description and analysis, in this thesis, we investigate *to what extent Land use and Land cover data is a useful tool to assess the effect of the environment on human health outcomes in population-based studies*. To reach our main goal, we have developed three research chapters (RCH). Each RCH is centred around one specific research question and one specific goal that stems from our main goal.

First, in RCH1 we review previous literature relating LULC data to human health and highlight that the relevance of LULC data lies in the use of the LULC categories. The findings of this RCH1 help identify new research gaps on which researchers should focus. We summarise them in 4 key points: 1) most studies still simplify the environment as the "amount of green"; 2) many authors report challenges in dealing with LULC data; 3) there are no apparent clues about how to measure the living environment; and 4) there is a lack of longitudinal studies and thus, of causal inference.

In RCH2 we analyse the LULC data-related limitations and show that they are related to not dealing with the compositional nature of LULC data. We propose the use of the ilr-orthogonal transformation for LULC data. Furthermore, we demonstrate that this transformation is a feasible and straightforward step that allows researchers to conduct traditional environmental epidemiologic analysis while taking into account the compositional nature of LULC data. We test the methodology in a cross-sectional population-based study, examining the impact of LULC broad categories on three human health outcomes. Our investigation shows a considerable improvement regarding the environment description and analysis. Particularly, because the results discussion revolves around the many biophysical and socioeconomic features gathered in the LULC categories.

Finally, in RCH3 we carry out a case study in which we conduct traditional environmental epidemiologic analyses to explore the effect of air pollutant concentration levels and type of agri-food industry on COVID-19 incidence and mortality in Catalonia. Complementing the analyses, we use the methodology developed in RCH2 to screen the effect of the overall LULC which provides extra insights. Thus, we emphasise that the assessment of the effect of LULC data on human health outcomes is helpful and can be performed in complementary analysis. Moreover, as shown in RCH2, the results discussion can leverage the pathway framework to better understand the environment-human health relationship.

All the expertise gathered in the three RCHs can be summarised in what we call the *Complex environment procedure*. This procedure is a practical and applicable tool for traditional environmental epidemiologic analysis to easily assess the effect of LULC categories on health data. Furthermore, this procedure leverages interdisciplinarity science and allow researchers to conceive the environment through a complex lens, and thus, it is a reliable tool to analyse Global Change's challenges.

In a nutshell, the findings of this thesis highlight that LULC data is a reliable and suitable environmental data source that holistically describes the environment, acknowledging its complexity. By analysing the impact of LULC categories on health data, researchers can maintain a parsimonious analysis while qualitatively investigating the impact of many biophysical and socioeconomic features, doing a much complete and robust assessment. This is particularly useful to draw or test hypotheses, complementing traditional analyses and facilitating replicability and comparability among studies. To conclude, this thesis provides valid information for researchers in several research fields, civil society and policymakers.

Resum

Dins un context de Canvi Global, molts investigadors s'han centrat en avaluar les conseqüències de la degradació ambiental per a la salut de les persones. Per altra banda, existeix una evidència creixent que també assenyala els efectes positius dels ambients saludables. Tot i així, molta de la investigació feta fins el moment simplifica el medi ambient considerant-lo "allò que és verd", utilitzant mètriques per mesurar la "quantitat de verd". Tot i que aquesta idea de *verdor* del medi ambient ha estat una font d'inspiració inequívoca facilitadora de noves comprensions sobre la importància dels ambients per a la salut humana, la teoria en si s'ha considerat limitada i inadequada per elucidar temes de debat crucials per al camp d'investigació.

La base de dades sobre Usos i Cobertes del sòl (LULC, en les seves sigles en anglès) ha provat la seva eficàcia com una eina per a descriure el medi ambient. A diferència d'altres bases de dades ambientals, les bases de dades LULC mesuren per igual les característiques biofísiques (el material biofísic que cobreix la superfície de la Terra, les cobertes del sòl) i les característiques socioeconòmiques (les activitats humanes desenvolupades en un territori, els usos del sòl) del medi ambient. A més, és una eina versàtil que pot ajudar a posar en pràctica varis conceptes de la teoria dels sistemes complexes.

Fins ara, vàries investigacions han utilitzat les dades LULC per descriure el medi ambient en estudis sobre salut. L'interès cap a aquestes dades ha anat creixent i s'espera que encara creixi més en un futur proper. Tot i així, no existeix cap estudi que relacioni les dades LULC amb dades sobre salut humana que hagi tingut en compte que les dades LULC són de naturalesa composicional, ja que estan limitades pel que es coneix com la limitació de la suma constant. Considerant l'espai de millora pel que fa a la descripció i l'anàlisi del medi ambient, en aquesta tesi doctoral investiguem *fins a quin punt les dades d'Usos i Cobertes del sòl són una eina útil per analitzar l'efecte del medi ambient en la salut de les persones en estudis poblacionals*. Per aconseguir el nostre objectiu principal, desenvolupem tres capítols de recerca (CR). Cada CR està centrat en una pregunta de recerca específica i un objectiu específic que concreten el nostre objectiu principal.

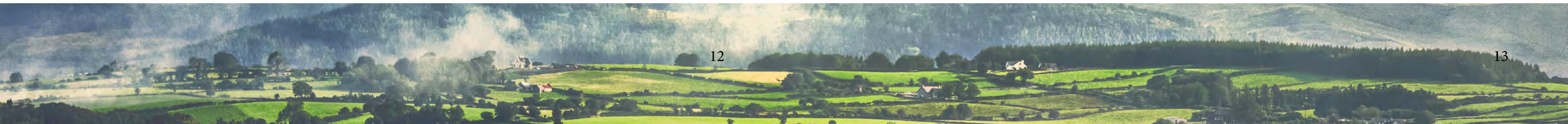
En primer lloc, en el CR1 revisem la literatura prèvia que relaciona les dades LULC amb la salut de les persones i subratllem que la rellevància de les dades LULC recau en l'ús de les categories LULC. Els resultats d'aquest CR1 ajuden a identificar els buits de recerca, on caldria que els investigadors prestessin atenció. Els resumim en quatre punts: 1) la majoria d'estudis encara simplifiquen el medi ambient a través de la "quantitat de verd"; 2) molts autors reporten dificultats a l'hora de lidiar amb les dades LULC; 3) no existeixen pistes aparents sobre com mesurar els ambients vitals; i 4) existeix una manca d'estudis longitudinals i, per tant, d'inferència causal.

En el CR2 analitzem les limitacions relacionades amb les dades LULC i mostrem que aquestes estan relacionades amb el fet de no lidiar amb la seva naturalesa composicional. Proposem la transformació ilr-ortogonal per les dades LULC. I a més, demostrem que aquesta transformació és un pas directe i viable que permet als investigadors dur a terme anàlisis tradicionals d'epidemiologia ambiental, a la vegada que es respecta la naturalesa composicional de les dades LULC. Més endavant, testem aquesta metodologia en un estudi poblacional transversal, examinant l'impacte de diferents categories generals de LULC en tres malalties. La nostra investigació mostra una considerable millora tant en la descripció com en l'anàlisi del medi ambient. Particularment, perquè la discussió dels resultats pot girar al voltant de les diferents característiques biofísiques i socioeconòmiques que es troben en les categories LULC.

Finalment, en el CR3 duem a terme un estudi on analitzem l'efecte dels nivells de pol·lució atmosfèrica i el tipus d'indústries agroalimentàries en la incidència i la mortalitat de la COVID-19 a Catalunya, utilitzant anàlisis tradicionals d'epidemiologia ambiental. Complementant aquest anàlisi, utilitzem la metodologia desenvolupada en el CR2 per explorar l'efecte de les dades LULC de manera general, la qual cosa aporta coneixements extra. Per tant, emfatitzem el fet que l'avaluació de l'efecte de les dades LULC en la salut humana és útil i es pot desenvolupar en anàlisis complementaris. A més, tal i com mostrem en el CR2, la discussió dels resultats pot aprofitar la teoria sobre les vies per a una major comprensió de la relació entre el medi ambient i la salut.

Tot el coneixement acumulat al llarg dels tres CR pot ser resumit en el que anomenem el *Procediment pel medi ambient complex*. Aquest procediment és una eina pràctica i aplicable pels anàlisis tradicionals en epidemiologia ambiental amb la fi d'analitzar l'efecte de les categories LULC en les dades de salut. Així mateix, aquest procediment posa en valor la ciència interdisciplinària i permet concebre el medi ambient a través d'unes lents complexes i, per tant, és una eina confiable per l'avaluació dels desafiaments del Canvi Global.

En resum, les troballes d'aquesta tesi accentuen que les dades LULC són una font ambiental confiable i adequada que permet descriure el medi ambient de manera holística, respectant la seva complexitat. A través de l'anàlisi de l'impacte de les categories LULC en les dades de salut, els investigadors poden mantenir un anàlisi parsimoniós a l'hora que investiguen qualitativament l'impacte de moltes característiques biofísiques i socioeconòmiques, duent a terme un anàlisi robust i complet. Aquesta particularitat és especialment útil per desenvolupar o testar hipòtesis, complementar anàlisis tradicionals i facilitar la rèplica i la comparabilitat entre estudis. Concloent, aquesta tesi proveeix d'informació vàlida a investigadors en diferents camps d'investigació, però també a la societat civil i als polítics.



Resumen

En un contexto de Cambio Global, muchos investigadores se han centrado en evaluar las consecuencias de la degradación ambiental para la salud de las personas. Por otro lado, existe una evidencia creciente que también señala los efectos positivos de los ambientes saludables. Aun así, mucha de la investigación hecha hasta el momento simplifica el medio ambiente considerándolo "aquello que es verde", usando métricas para medir la "cantidad de verde". Aunque esta idea de *verdor* del medio ambiente ha sido una fuente de inspiración inequívoca facilitando nuevas comprensiones sobre la importancia de los ambientes para la salud humana, la teoría por si sola se ha considerado limitada e inadecuada para elucidar temas de debate cruciales para el campo de investigación.

La base de datos sobre Usos y Cubiertas del suelo (LULC, en sus siglas en inglés) ha probado su eficacia como herramienta para describir el medio ambiente. A diferencia de otras bases de datos ambientales, la base de datos LULC mide por igual las características biofísicas (el material biofísico que cubre la superficie de la Tierra, las cubiertas del suelo) y las características socioeconómicas (las actividades humanas desarrolladas en un territorio, los usos del suelo) del medio ambiente. Además, es una herramienta versátil que puede ayudar a poner en práctica varios conceptos de la teoría de los sistemas complejos.

Hasta la fecha, varios investigadores han usado los datos LULC para describir el medio ambiente en estudios sobre salud. El interés hacia estos datos ha ido creciendo y se espera que aún crezca más en un futuro cercano. Aun así, no existe ningún estudio que relacione los datos LULC con datos sobre salud humana que haya tenido en cuenta que los datos LULC son de naturaleza composicional, ya que están limitados por lo que se conoce como la limitación de la suma constante. Considerando el espacio para la mejora en lo que respecta a la definición y el análisis del medio ambiente, en esta tesis doctoral investigamos *hasta qué punto los datos de Usos y Cubiertas del suelo son una herramienta útil para analizar el efecto del medio ambiente en la salud de las personas en estudios poblacionales.* Para alcanzar este objetivo principal, desarrollamos tres capítulos de investigación (CI). Cada CI está centrado en una pregunta de investigación específica y un objetivo específico que concretan nuestro objetivo principal.

En primer lugar, en el CI1 revisamos la literatura previa que relaciona los datos LULC con la salud de las personas y subrayamos que la relevancia de los datos LULC reside en el uso de las categorías LULC. Los resultados de este CI1 ayudan a identificar las lagunas de investigación, en donde los investigadores deberían poner atención. Los resumimos en cuatro puntos: 1) la mayoría de los estudios aún simplifica el medio ambiente a través de la "cantidad de verde"; 2) muchos autores reportan desafíos para lidiar con los datos LULC; 3) no existen pistas aparentes sobre cómo medir los ambientes vitales; y 4) existe una falta de estudios longitudinales y, por lo tanto, de inferencia causal.

En el CI2 analizamos las limitaciones relacionadas con los datos LULC y mostramos que estas están relacionadas con el hecho de no lidiar con su naturaleza composicional. Proponemos la transformación ilr-ortogonal para los datos LULC. Y además, demostramos que esta transformación es un paso directo y viable que permite a los investigadores llevar a cabo análisis tradicionales de epidemiología ambiental, a la vez que se respeta la naturaleza composicional de los datos LULC. Más adelante, testamos la metodología en un estudio poblacional transversal, examinando el impacto de distintas categorías generales de LULC en tres enfermedades. Nuestra investigación muestra una considerable mejora tanto en la descripción como en el análisis del medio ambiente. Particularmente, porque la discusión de los resultados puede girar en torno a las distintas características biofísicas y socioeconómicas que se encuentran en las categorías LULC.

Finalmente, en el CI3 llevamos a cabo un estudio en donde analizamos el efecto de los niveles de polución atmosférica y el tipo de industria agroalimentaria en la incidencia y mortalidad de la COVID-19 en Cataluña, usando análisis tradicionales de epidemiología ambiental. Complementando estos análisis, usamos la metodología desarrollada en el CI2 para explorar el efecto de los datos LULC de manera general, lo cual aporta conocimientos extra. Por lo tanto, enfatizamos el hecho que la evaluación del efecto de los datos LULC en la salud humana es útil y puede desarrollarse en análisis complementarios. Además, tal y como mostramos en el CI2, la discusión de los resultados puede aprovechar la teoría sobre las vías para una mayor comprensión de la relación entre el medio ambiente y la salud.

Todo el conocimiento acumulado a lo largo de los tres CI puede ser resumido en lo que llamamos el *Procedimiento para el medio ambiente complejo*. Este procedimiento es una herramienta práctica y aplicable para los análisis tradicionales de epidemiología ambiental con el fin de analizar el efecto de las categorías LULC en los datos de salud. Asimismo, este procedimiento pone en valor la ciencia interdisciplinaria y permite concebir el medio ambiente a través de unas lentes complejas y, por lo tanto, es una herramienta confiable para la evaluación de los desafíos del Cambio Global.

En resumen, los hallazgos de esta tesis acentúan que los datos LULC son una fuente ambiental confiable y adecuada que permite describir el medio ambiente de manera holística, respetando su complejidad. A través del análisis del impacto de las categorías LULC en los datos de salud, los investigadores pueden mantener un análisis parsimonioso mientras investigan cualitativamente el impacto de muchas características biofísicas y socioeconómicas, haciendo un análisis robusto y completo. Esta particularidad es especialmente útil para desarrollar o testar hipótesis, complementando análisis tradicionales y facilitando la replicabilidad y comparabilidad entre estudios. Para concluir, esta tesis provee de información válida a investigadores en distintos campos de investigación, pero también a la sociedad civil y a los políticos.

1. Introduction

We are living in times of change without precedent in recent history. The so-called Global north has thrived over the last century, evidenced by longer life spans, better access to education, healthcare, information and excellent material comfort (Sage, 2020). However, this progress has come at the expense of the natural systems, expropriating biosphere resources such as freshwater, raw materials, arable land, and living beings' bodies (Costanza et al., 2017; Krausmann et al., 2013), particularly from the so-called Global South (Chichilnisky, 1994). Nowadays, human exploitation of Earth's natural capital has been estimated to be a quarter or more of the potential net primary production (NPP) (Haberl et al., 2007; Krausmann et al., 2013; Smith et al., 2012), with 75% of the planet's ice-free land area being modified (Hooke et al., 2012) and half of the accessible freshwater being expropriated (Gleick and Palaniappan, 2010).

This increasing appropriation of natural resources, the rising human population and technological innovations have resulted in the present times of profound change (Sage, 2020), the so-called **Global Change** (Meyer and Turner, 1992). Many authors recognise this era as a new geological epoch called the *Anthropocene* (Lewis and Maslin, 2020), which is characterized by experiencing changes which historically have occurred over millennia but now take mere decades (Sage, 2020).

At different scales (local/regional/global), the three principal manifestations of the Global Change on the planet can be distinguished as follows:

1. Alteration of biogeochemical cycles.

Biogeochemical cycles represent the fluxes of chemical elements among different parts of the Earth (from non-living to living, from the atmosphere to land to sea). The term "cycles" highlights that matter is always conserved and that these elements move to and from significant pools via various two-way fluxes (Galloway et al., 2014). Compared to pre-industrial times, the human mobilization of carbon, nitrogen and phosphorus from the Earth's crust and atmosphere into the environment has increased 36, 9 and 13 times, respectively (Schlesinger and Bernhardt, 2013). These shifts have resulted in raised temperatures, ocean acidification and deoxygenation (Gruber, 2011) and alterations in ecosystem-climate interactions (Peñuelas et al., 2009; Piao et al., 2019; Richardson et al., 2013).

2. Loss of biodiversity.

The alarming rates and intensity of Global Change drivers overwhelm the abilities of species and ecosystems to adapt, resulting in a widespread biodiversity loss (Vitousek et al., 1986) which has been referred to as the looming sixth mass extinction (Ceballos et al., 2015). The exponential pace of the accelerated biodiversity loss is now estimated to be two or three orders of magnitude greater than natural extinction rates (Rockström et al., 2009), and its consequences are related to an imminent ecological collapse (Salomon, 2008).

3. Land use and cover changes.

Recent estimations suggest that land use and cover change has affected almost a third (gross change of 32%) of the planet's land area in just six decades (1960-2019), and 17% of the total Earth's land surface has changed at least once, four times greater that previously estimated (Winkler et al., 2021). With these estimations, the authors show the spatial extent of land use and cover change from 1960-2019 for six broad land use and cover categories (urban area, cropland, pasture/rangeland, forest, unmanaged grass/shrubland and non-/sparsely vegetated land) (see Figure 1). Globally, a net loss in forest area of 0.8 million km^2 and an expansion in agriculture of 1.0 million km^2 have been identified (Winkler et al., 2021). However, these change dynamics dramatically depend on regional features (for instance, forest areas have declined severely in the tropic whereas they have increased in subtropical, temperate and boreal climate zones (Song et al., 2018)). Likewise, single change events are most evident in developing countries (e.g. deforestation), while multiple change events (e.g. crop-grass rotation) dominate in the Global North (Winkler et al., 2021). These human alterations of Earth's land surface strongly affect carbon sources and sinks (Arneth et al., 2014; Popp et al., 2014), causes habitat loss (Powers and Jetz, 2019) and undermine food production (Lambin and Meyfroidt, 2011).

In parallel, the global urban population has risen dramatically (Cox et al., 2018). Most of this growth has been attributed to rural-to-urban migration (United Nations, 2014). Furthermore, this phenomenon is expected to continue, since 60% of people are projected to reside in cities by 2030 (United Nations, 2014), threatening biodiversity and affecting ecosystem productivity through loss of habitat, biomass, and carbon storage (Seto et al., 2012). Although some effects of moving from rural to urban environments are positive (such as economic growth, development and many beneficial social outcomes (Dye, 2008)), cities are also crowded, polluted and stressful places with little space for nature. These features combined with busy modern lifestyles lead to reduced exposure to natural environments, which has been associated with worse human health (Cox et al., 2018).

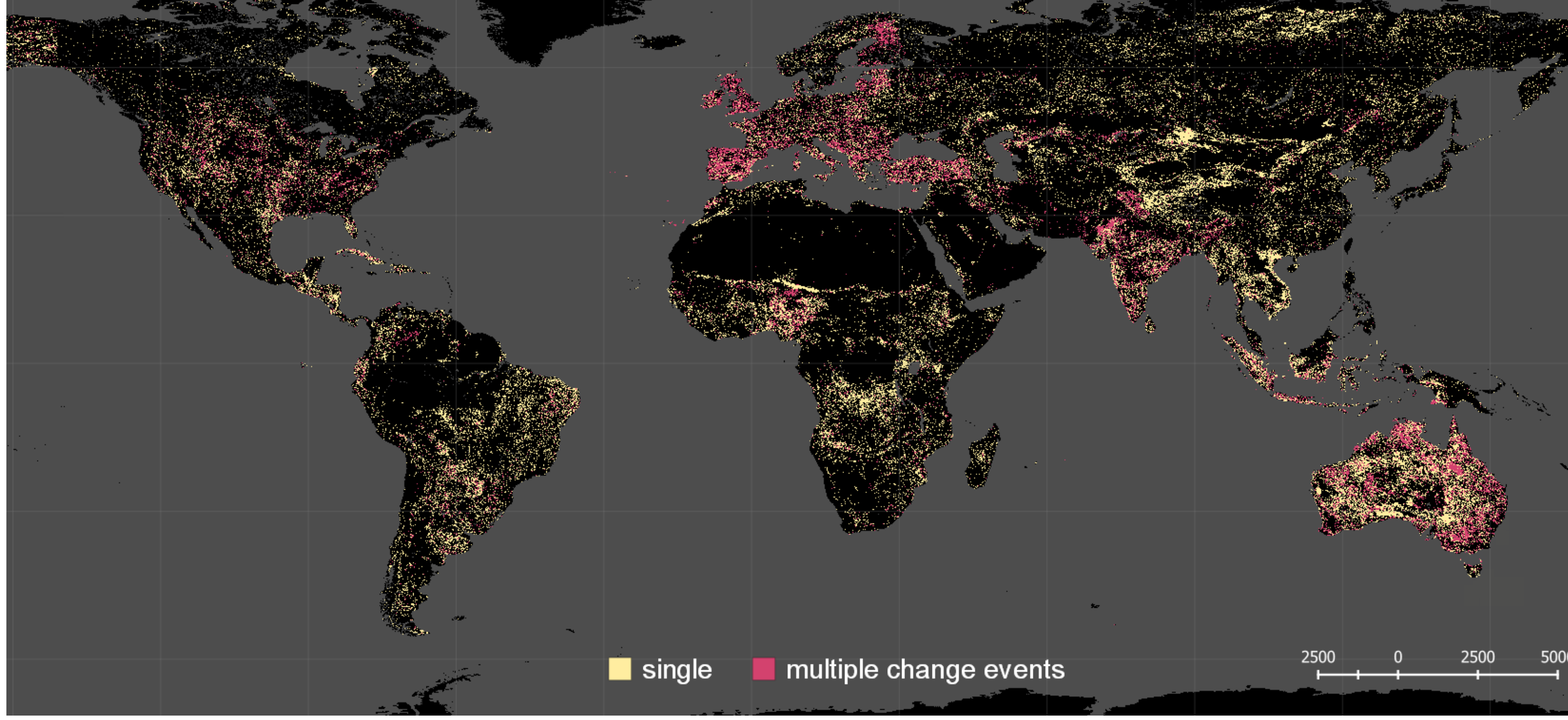


Figure 1. From (Winkler et al., 2021).
The spatial extent of global land use and cover change (1960-2019).

The Global Change's manifestations affect not only all Earth's species but also ecological interactions, co-dependencies, functions, structural complexity, and mechanisms of resilience that characterize living systems and their capacity to provide ecosystem services (Hooper et al., 2005; Oliver et al., 2015; Salomon, 2008). And thus, they affect the overall health of Earth's environments. Likewise, the rapid environmental changes are linked to the emergence and re-emergence of infectious and non-infectious diseases (Destoumieux-Garzón et al., 2018), threatening human and animal health.

In this context of Global Change, this thesis explores the relationship between the environment and human health through Land use and Land cover data. We are conscious that many environmental factors influence human health. Thus, a comprehensive approach is needed for an accurate environment-human health assessment. In this sense, we use the **One Health** concept, which the United Nations define as an integrated approach that recognizes the fundamental relationship between animals, people, plants and the environment. This concept underlines the importance of healthy environments and allows us to identify the many possible environmental factors affecting human health. Moreover, by using the One Health approach, we align ourselves with today's major programmes, policies and legislation and research, which promote communication between multiple sectors and interdisciplinary work to achieve public health outcomes (for instance, the One Health European Joint Programme and the Centers for Disease Control and Prevention's One Health Office) (WHO, 2017).

1.1 The connection between the environment and human health

In the last decades, many researchers have endeavoured to evaluate the **consequences of environmental degradation** for human populations. They have done so, for instance, by exploring the harmful effects of air pollution (Eze et al., 2015, 2014), traffic noise (Shin et al., 2020), light pollution (Falchi et al., 2011), the vulnerability of human health to parasites (Sutherst, 2001) and vector-borne diseases (Sutherst, 2004), invasive species (Donovan et al., 2013), loss of biodiversity (Pongsiri et al., 2009) and climate change impacts (McMichael et al., 2006), among other things.

On the other hand, increasing evidence is also pointing to the **positive effects of healthy environments**, which are listed as follows: psychological (positive effect on mental processes and behaviour); cognitive (positive effect on cognitive ability or function); physiological (positive effect on physical function and/or physical health); disease exposure and regulation (potential to reduce the incidence of infectious disease); social (positive effect at community level); aesthetic, cultural, recreational and spiritual (positive effect on individual well-being); provision of tangible materials (material goods); and increased resiliency (personal and communal ability to withstand impacts and remain healthy) (Sandifer et al., 2015).

Modern research assessing the benefits of the environment for human health derive from the work of Roger Ulrich (1984). He compared two groups of hospitalized patients with different views from their windows and concluded that the group who could see green vegetation recovered better and faster than the group whose windows faced a brick building. Inspired by this revealing study, much of the research today showing positive associations between the environment and human health describe the environment as that which is green, for instance, using percentages of greenspaces (Mitchell and Popham, 2007), average Normalized Difference Vegetation Index (NDVI) (Grigsby-Toussaint et al., 2015), the nearest green space (Dadvand et al., 2014), or the presence of plants (Deng and Deng, 2018). The common denominator of all these widely used practices is the core assumption that the environment can be reduced to a metric gathering the "**amount of green**" (see Figure 2a). Although this greenness idea has unequivocally been a doorway to new nuances about the importance of surroundings for human health, the theory itself has been considered limiting since it is not able to provide answers to the questions which lie at the heart of the debate (Astell-Burt and Feng, 2019; de Vries, 2019a; White et al., 2013). The scientific community have listed these questions as follows:

- What are the environment's specific elements related to the health conditions? (Bach et al., 2020; MacKerron and Mourato, 2013; Wheeler et al., 2015)
- Do they affect individually or as a combination? (Barnes et al., 2019; Kiley et al., 2017)
- Which are the mechanisms through which humans may benefit from the environment? (Markevych et al., 2017)
- Which are the variables that modify this environment-human health relationship? (Prüss-Üstün et al., 2008)

This thesis examines the relationship between LULC data and human health. Thus, we move away from the simplistic approach of the environment as "something green" to a more holistic definition of the environment through LULC data. This approach will enable us to move forward by discussing the above questions, providing new insights into these subjects of debate.

1.2 Land use and land cover data in health studies

Defining the **environment** is not a simple endeavour. Being a widely used term, the definition of the environment usually changes depending on the context and the research field. Nevertheless, as a broad definition, many researchers today would agree that the environment is what surrounds us, and thus, it integrates all things, living beings, processes, forces, and energy within its limits.

In order to understand the environment, the scientific community has traditionally dissected this concept into different parts, which implies that researchers have specialized in acquiring knowledge about specific and discrete parts of the environment. As a result, holistic approaches have not been commonly performed, leading to incomplete analyses. For example, in health-related sciences, the isolated vision that the mind was located in the brain prevented researchers from focusing on the effect of gut biota on mood disorders (Cryan and Dinan, 2012; Farmer et al., 2014). However, today there is a common agreement that the environment needs to be defined through an **interdisciplinary perspective**, moving away from the fragmented classical vision and considering the many environmental elements and their mutual interactions. In this sense, the ecosystem concept, defined as "the place/part of the world where and with which the biotic systems interact" (Gignoux et al., 2011), represents a suitable definition of the environment that integrates this **interaction** concept. So, here, the ecosystem is not seen as a simple "container" but as an entity composed of biotic and abiotic elements (Salomon, 2008) and their interactions.

Despite the merit of some authors in proposing thorough definitions of the ecosystem concept (Gignoux et al., 2011; Keith et al., 2020), many ecosystem definitions are not always coincident and compatible (Jax, 2006; Scheffer et al., 2001). One particularity is that the social context and human intervention are not always accounted for in the ecosystems' definition (Jax, 2006; Salomon, 2008). Nowadays, there is arguably no place on the planet which has not been affected by human intervention (Johnson et al., 1997) (for instance, human industry effects (McKibben, 1990)). Moreover, climate change affects every region globally, with human influence contributing to many observed changes in weather and climate extremes. Thus, the vast majority of the environments worldwide are a mixture of natural and human drivers.

In this context, a less conflictive and more suitable concept to describe the environment is given by the **Land use and Land cover (LULC) data**. Unlike other environmental datasets, the LULC dataset describes the environment measuring both the **biophysical features** (the biophysical material over the surface of the Earth, the land cover) (Grekousis et al., 2015; Meyer and Turner, 1994) and the **socioeconomic features** (the human activities involved in that specific place, the land use) of the environment (Lambin et al., 2001), creating an integrated and holistic vision which constitutes the very nature of the dataset.

The LULC data is characterized by GIS-defined units, as detailed as the fundamental categories composing the LULC dataset and its resolution. Furthermore, the LULC dataset is a versatile tool. It offers an unequivocal a priori definition of what is considered the environment. Furthermore, through its hierarchical organisation, it allows researchers to group certain categories defining a place (for instance, forested areas grouping all types of forest LULC categories, or human-related environments grouping urban LULC categories; see next section). Using this data, one can provide a precise characterization of the environment taking into consideration the different types of environments, which are defined in more or less detail through the LULC categories depending on the purpose of the study (see Figure 2b).

As a periodically updated and reliable source, the LULC dataset is also replicable and feasible in terms of efficiency and cost (Grekousis et al., 2015). In addition, it can capture the driving forces behind a change (economic, demographic, political and environmental), as well as the specific processes of conversion from one LULC category to another (Meyer and Turner, 1994). Thus, the LULC data contains and integrates vital aspects of the Earth's system functioning, gathering biodiversity, soil degradation, ecosystem services and climate change information (Lambin et al., 2001), and is a crucial tool for assessing Global Change effects (Penuelas and Boada, 2003).

To date, some researchers have used LULC data to describe the environment in health studies (Groenewegen et al., 2012; Maas et al., 2009; Mitchell and Popham, 2007; van den Berg et al., 2010; Wheeler et al., 2012). Furthermore, the interest in LULC data is expected to increase in the near future (Grekousis et al., 2015). However, no study linking LULC data with human health data has yet considered that LULC data is of a **compositional nature** since it is limited by the so-called sum up constant constraint (Egozcue and Pawlowsky-Glahn, 2016). A century ago, Pearson (1896) already warned that compositional data should not be used directly in traditional statistical methods since the data exist in the so-called Aitchison geometry (Aitchison and Egozcue, 2005), not the Euclidean one, which all the traditional statistical methods perform. Considering the room for improvement, the pillars of this thesis are built around the idea of acknowledging the compositional nature, and thus, enhancing current methodologies linking LULC data to human health.

1.2.1 The environment as a complex system

The systems derived from human and nature interconnections have been defined as complex systems (Preiser et al., 2018; Schlüter et al., 2019). In this sense, LULC data can help notions of the **complex system theory** to be put into practice since it has proven to be a reliable source to describe complex human-natural systems.

Any complex system is distinguished by being an ensemble of many **elements** which **interact** (Newman, 2011). In parallel, each of the LULC categories contains a set of environmental elements (the biophysical and socioeconomic features) that make up but do not limit its definition. Some of these environmental elements have already been explored in health studies and can be listed as follows, regarding:

a) Living beings: **natural sounds** (Coensel et al., 2011; White et al., 2010), **microbial diversity** (Ege et al., 2011; Jatzlauk et al., 2017), **soil biodiversity** (Wall et al., 2015) and **overall biodiversity** (Aerts et al., 2018; Methorst et al., 2020).

b) Structural aspects: **visual stimuli** (Franco et al., 2017; Jacobs and Suess, 1975), **presence of water** (White et al., 2020), **density** (Han, 2007), **accessibility** (Ekkel and de Vries, 2017) and **walkability** (Zandieh et al., 2017).

c) Biophysical aspects: **soil properties** (Steffan et al., 2018), **temperature** (MacKerron and Mourato, 2013), **humidity** (Dalziel et al., 2018), **heat events** (Soneja et al., 2016), **negative ions** (Perez et al., 2013), **allergenic pollen levels** (Cariñanos and Casares-Porcel, 2011), **volatile organic compounds** (Bach et al., 2021), **air pollution** (Eze et al., 2015, 2014; Guarnieri and Balmes, 2014), **pesticides** (Starling et al., 2014), and **noise** (Shin et al., 2020).

When analysing the distribution of LULC categories, if an adequate level of detail for LULC categories is used, it can be shown that some categories appear more frequently, and some rarely appear. Thus, the use of LULC data can help assess emerging ordered patterns of the complex system, such as **scale invariance** properties. In this way, some authors provided evidence of this scale invariance property in natural and artificial map structures related to biodiversity and pedodiversity (Ibáñez et al., 2021). In another publication, the authors used lacunarity analysis as a scale-dependent measure of heterogeneity based on the principles of fractals (Labib et al., 2020). They presented some evidence of scale-free behaviour of complex systems by producing a "lacunarity curve" across multiple spatial scales and finding a linear relation in loglog scale for all sizes except for larger ones, where finite-size effect was found.

Another property of complex systems is that LULC data exhibits their **hierarchical organization**. This property means that individual elements from higher structural levels are themselves complex systems at lower structural levels (Kwapień and Drozdz, 2012). In this sense, the higher levels of the complex system integrate the lower structures, their causal regularities, symmetry, order and periodic behaviour (Ladyman et al., 2013). However, at the same time, at each stage, entirely new laws, concepts, and generalizations are necessary (Andersen, 1972). Describing the environment using LULC data allows the accuracy of the definition to be adapted to the purposes of the study. For example, a particular area can specifically be called "vineyards", whereas in a higher level of organization, it can be referred to as "permanent crop", and in an even higher level, it can be named "agricultural area".

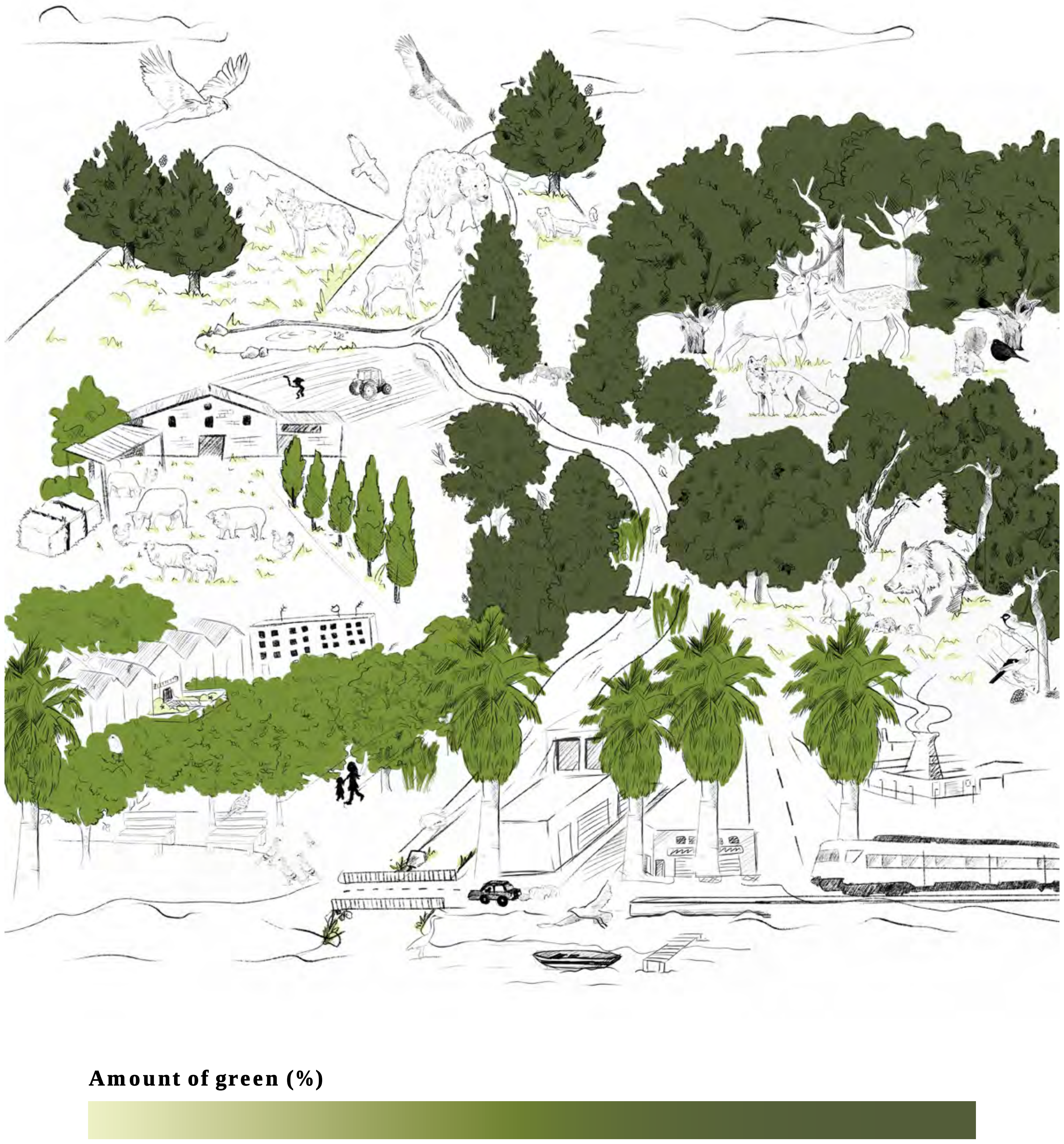


Figure 2a.
Representation of the usual environment description based on the "amount of green".

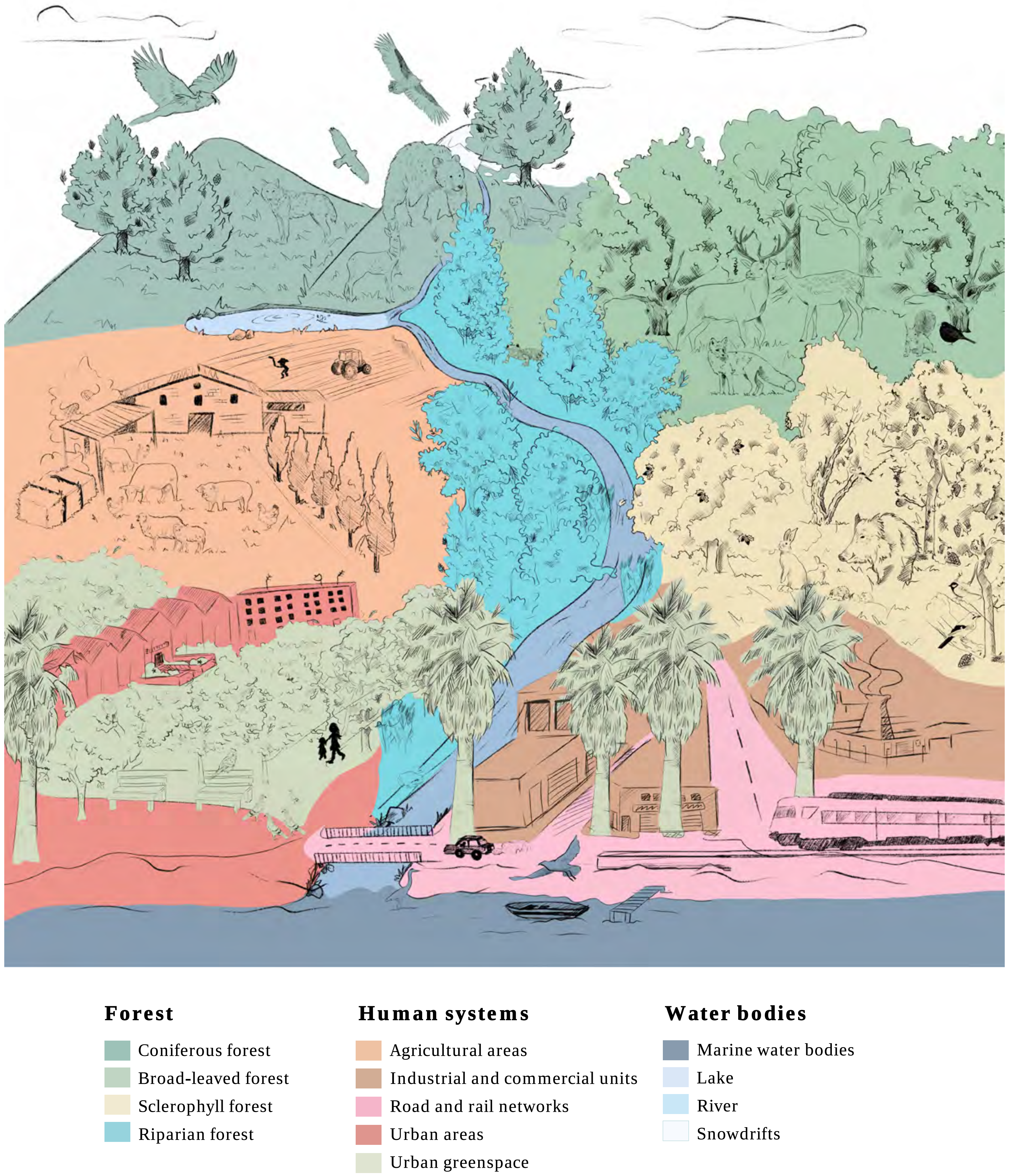


Figure 2b.
Representation of a more complex vision of the environment in which different types of environments are distinguished through the LULC categories.

1.3. Area of research

This thesis covers the Catalonia region (Spain) and leverages health data of the entire Catalan population using a population-based approach. The Catalonia region is located in the temperate northern hemisphere, in the northeast of Spain. It is geographically confined by the Pyrenees mountains (in the north) and the Mediterranean Sea (in the south), and is next to Mediterranean Europe (east) and the continental Spanish peninsula (west). These location characteristics, along with the diverse topography, grants it a certain uniqueness that results in three bioclimatic regions in the territory: the Mediterranean, Euro-Siberian, and boreo-alpine (Boada and Gomez, 2012). Consequently, a wide variety and richness of landscapes can be found throughout the Catalan region (see Figure 3), one of the territories within the European continent with the most variety of landscapes (The Landscape Observatory and the Cartographic and Geologic Institute of Catalonia, 2019). This particularity makes Catalonia a suitable scenario for this research.

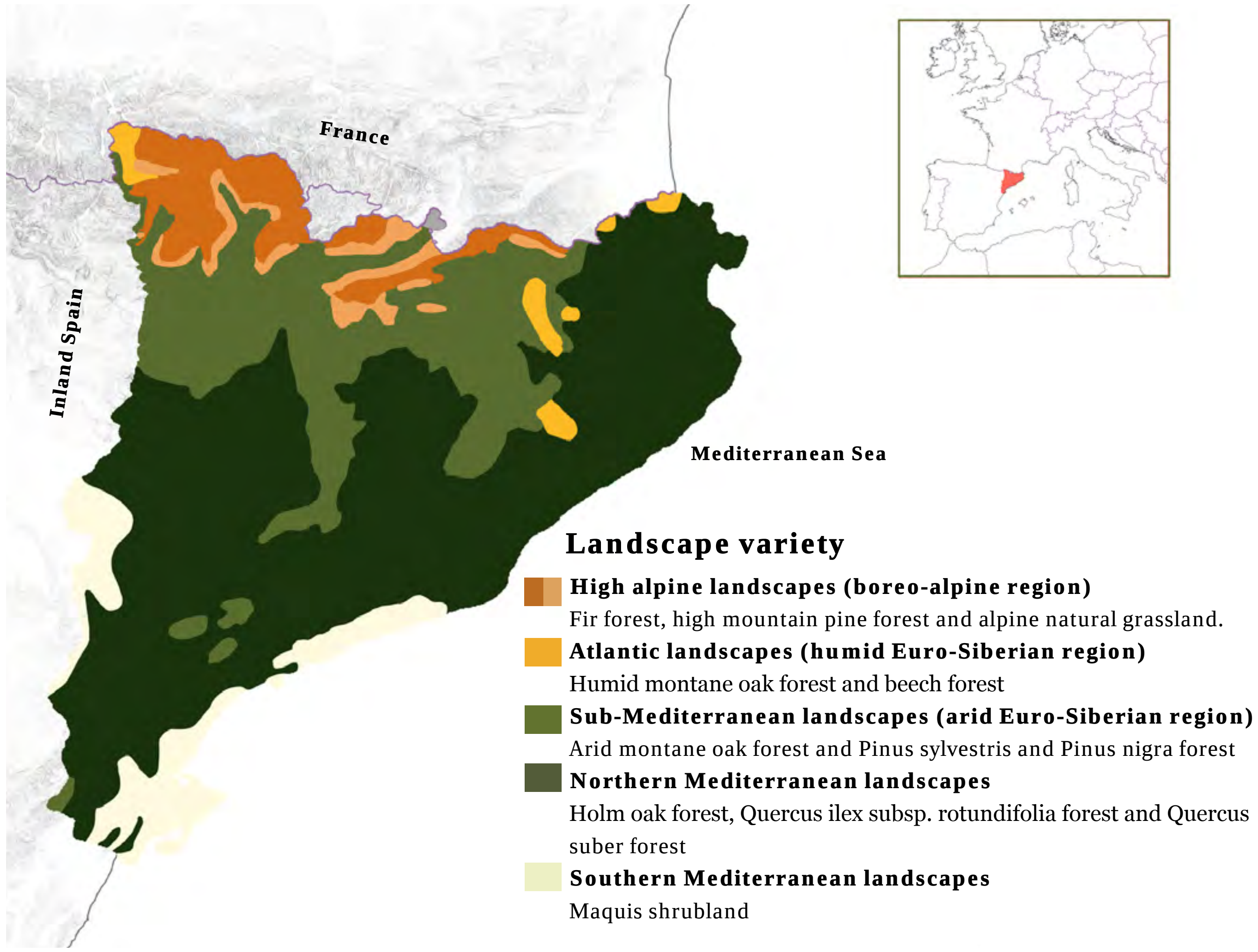


Figure 3.
Landscape variety in Catalonia (Spain). Elaborated by Joan M. Roure Nolla (2002) from Rivas Martínez, S.'s cartography (1987).

2. Goals, research questions and chapters

Throughout this thesis, we show our concern over the impacts of Global Change on human health. Although the impacts on human health of all three Global Change manifestations are tackled to some extent in this thesis, we are specifically focused on the third principal manifestation, and thus, we examine the relationship between **land use and land cover data and human health**. In particular, our main goal is ***to investigate to what extent Land use and Land cover data is a useful tool to assess the effect of the environment on human health outcomes in population-based studies.***

2.1 Research questions and specific goals

To achieve our main goal, we divide it into three more minor research questions (RQ), each of them leading to one specific goal (SG) (see Figure 4, below).

RQ1: *How has LULC data commonly been employed in studies relating LULC data to human health outcomes?*

SG1. To review existing methodologies and widely used practises in studies relating LULC data with human health.

RQ2: *How can LULC data be used to better assess its effect on human health?*

SG2. To propose a methodology that takes into account the compositional nature of LULC data for population-based health studies.

RQ3: *Is LULC data useful to assess the territorial distribution of COVID-19 incidence and mortality during the first pandemic wave in Catalonia (2020)?*

SG3 To explore the effect of LULC data on COVID-19 incidence and mortality in Catalonia.

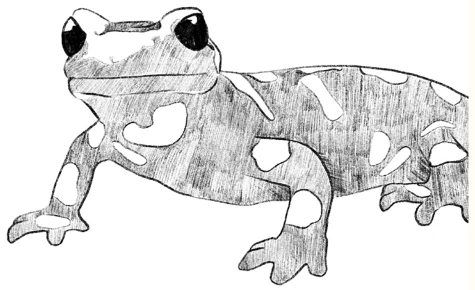
2.2 Research chapters

To tackle both the main goal and the three specific goals of the present research, we have developed three research chapters (RCH). Each research RCH is centred around one specific goal and, thus, responds to one specific research question (see Figure 4).

RCH1: To answer the first research question (RQ1), we conducted a review of 41 articles relating LULC data with human health outcomes. This research highlights the principal methodologies along with the analysis methods. Furthermore, it summarizes the main limitations in the field and concludes with four recommendations for future research. The results of the RCH1 have been published in the Environmental Research Journal (https://doi.org/10.1016/j.envres.2020.110578)

RCH2: Progressing from the findings of RHC1 and responding to the RQ2, in the RCH2, we explore the compositional nature of LULC data and propose a methodology that takes it into account. The proposed methodology is tested, assessing the independent effect of each LULC category on the prevalence of type 2 diabetes mellitus, asthma, and anxiety in Catalonia. Moreover, the results are discussed, providing a conceptual framework in which many previously studied environmental elements are considered, and pathways connecting the environment and human health are discussed. This research has been published in Science of the Total Environment (https://doi.org/10.1016/j.scitotenv.2021.150308)

RCH3: Presented as a case study, the RCH3 shows the potential of the proposed methodology in RCH2. This research uses traditional environmental epidemiology analyses to explore the effect of air pollutant concentration levels and type of agri-food industry on COVID-19 incidence and mortality in Catalonia at the area level while controlling for relevant demographic, socioeconomic and comorbidity covariables. The novelty is presented with the complementary analyses that screen the effect of the overall LULC data using the proposed methodology in RCH2. The results of this research have been published in the International Journal of Environmental Research and Public Health (https://doi.org/10.3390/ijerph18073768)



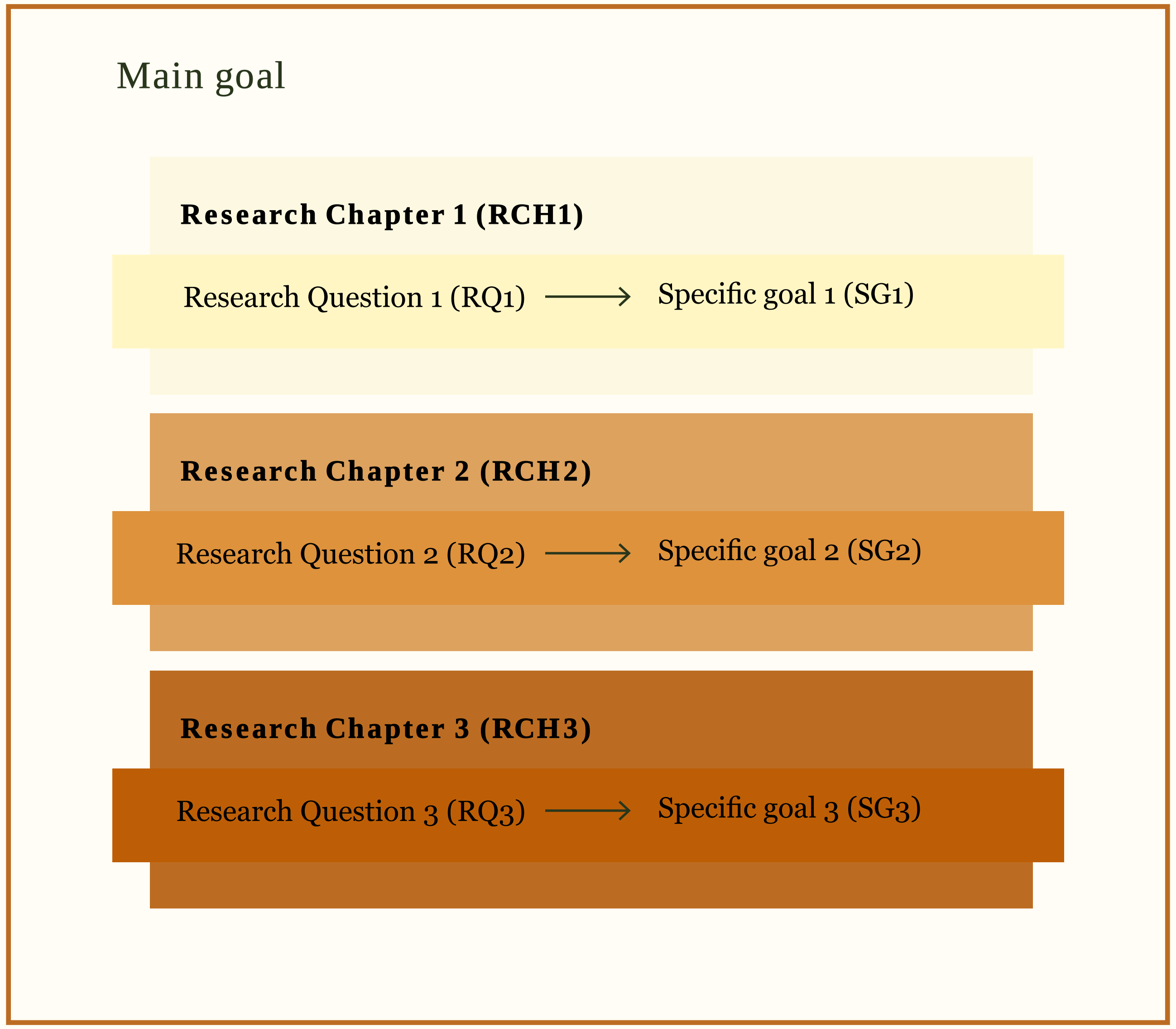


Figure 4.
Diagram of the main goal and its derived research questions (RQ). Each RQ is associated with a specific goal (SG) and structured within each research chapter (RCH).

3. Research Chapters

3.1 Research Chapter 1: Reviewing the reliability of Land Use and Land Cover data in studies relating human health to the environment

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Review article

Reviewing the reliability of Land Use and Land Cover data in studies relating human health to the environment

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ABSTRACT

Background: In recent years, research has been increasingly devoted to understanding the complex human health-environment relationship. Nevertheless, many different measurements have been applied to characterize the environment. Among them, the application of Land Use and Land Cover (LULC) data is becoming more noticeable over time.
Aims: This research aims to analyse the reliability of Land Use and Land Cover data (LULC) data as a suitable describer of the environment in studies relating human health to the environment. With a specific focus on the methodologies using LULC data, we also examine the study designs and analytical methods that have been commonly performed so far.
Materials and Methods: We gathered studies relating human health outcomes to Land Use and Land Cover (LULC) data. A Boolean search limited to reviews was conducted in February 2019 using *Web of Science Core Collection* search engines. Five reviews were selected as our preliminary starting set of literature and from those, two backward snowballing searches were conducted. The first backward snowballing search used the reference lists of the first 5 reviews and revealed 17 articles. From these, the second search gathered 24 new articles also fulfilling the inclusion criteria established. In total, 41 articles were examined.
Results: Our main results reported that Land Use and Land Cover (LULC) data national level data was preferred over LULC international level data. However, this tendency seems to be strongly related to the specific aims of the articles. They essentially defined the living environment either through buffer zones, using the administrative boundaries wherein the individuals reside, or using the specific location of the individuals assessed. As for the characterization of the environment, authors performed 4 principal methodologies: extracting the percentage of green space, computing the "Land Use mix", recording the type of land cover, and using the percentage of tree canopy. Besides, all the articles included measurements in urban contexts and most of them evaluated the accessibility of individuals to their surroundings. Furthermore, it was clearly stated that the complexity of the topic and the challenging data leads authors to carry out advanced statistical methods and mostly cross-sectional designs with no causal relations.
Discussion and Conclusions: Land Use and Land Cover (LULC) data has been demonstrated to be a versatile tool supporting both local-focused studies with few individuals involved and broad territorial-scoped studies with huge populations. Promising synergy has been highlighted between Electronic Health Records (EHR) and LULC data in studies dealing with massive information and broader scopes with regards to the assessment of territorial realities. As this emerging topic matures, investigators should (1) elucidate subjects of ongoing debate such as the measurement of the living environment and its characterization; (2) explore the whole potential of LULC data, using methodologies that encompass both their biophysical and socioeconomic information; (3) perform innovative designs that are able to establish causal relationships among the studied variables (for example, Cellular Automata models), and (4) expand the current set of studied health outcomes leveraging comprehensive and trustworthy health data sources such as EHR.

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3.2 Research Chapter 2: Environmental heterogeneity in human health studies. A compositional methodology for Land Use and Land cover data

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Environmental heterogeneity in human health studies. A compositional methodology for Land Use and Land cover data

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HIGHLIGHTS

- Compositional methodology spotting independent effect of LULC categories
- Important effect measure modification of socioeconomic status, age group and sex
- Environmental heterogeneity as a key factor in environment-health studies
- Compositional methodology as a suitable tool assessing environmental heterogeneity

GRAPHICAL ABSTRACT

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ABSTRACT

The use of Land use and Land cover (LULC) data is gradually becoming more widely spread in studies relating the environment to human health. However, little research has acknowledged the compositional nature of these data. The goal of the present study is to explore, for the first time, the independent effect of eight LULC categories (agricultural land, bare land, coniferous forest, broad-leaved forest, sclerophyll forest, grassland and shrubs, urban areas, and waterbodies) on three selected common health conditions: type 2 diabetes mellitus (T2DM), asthma and anxiety, using a compositional methodological approach and leveraging observational health data of Catalonia (Spain) at area level.

We fixed the risk exposure scenario using three covariates (socioeconomic status, age group, and sex). Then, we assessed the independent effect of the eight LULC categories on each health condition. Our results show that each LULC category has a distinctive effect on the three health conditions and that the three covariates clearly modify this effect.

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Type 2 diabetes mellitus
Asthma
Anxiety

This compositional approach has yielded plausible results supported by the existing literature, highlighting the relevance of environmental heterogeneity in health studies. In this sense, we argue that different types of environment possess exclusive biotic and abiotic elements affecting distinctively on human health.

We believe our contribution might help researchers approach the environment in a more multidimensional manner integrating environmental heterogeneity in the analysis.

1. Introduction

In the last decades, the study of the relationship between the environment and human health has increasingly captured the scientific community's attention worldwide. As a result, growing evidence is starting to highlight the potential benefits that the environment might provide to human health (Barnes et al., 2019; Sandifer et al., 2015; Stier-Jarmer et al., 2021; Taylor and Hochuli, 2015). Until now, different metrics assessing the environment have been showcased (Bach et al., 2020); from measurements of the landscape proportion, the Normalized Difference Vegetation Index (NDVI), to the Simpson's patch diversity and percentages of tree canopy and green spaces (Cushman et al., 2008; Donovan et al., 2013; Frank et al., 2006; Hanski et al., 2012; Sarkar et al., 2013). Among these metrics, Land use and Land cover (LULC) data are gradually becoming more widely spread (Zaldo-Aubanell et al., 2021b).

LULC data is usually a low-cost and high resolution resource, which is regularly updated (Grekousis et al., 2015). Unlike other environmental data, LULC data encompasses both biophysical (e.g., temperature, humidity, biodiversity, and soil features) and socioeconomic (e.g., political, economic, and cultural) environmental information (Boada and Gomez, 2012). Moreover, LULC data is versatile and can distinguish between different types of environments, which is particularly relevant since different types of environments are suggested to have specific elements that might promote distinct benefits to human health (Astell-Burt and Feng, 2019; de Vries, 2019; Wheeler et al., 2015; White et al., 2013; Zaldo-Aubanell et al., 2021b).

Many researchers have used LULC data to describe the environment (Groenewegen et al., 2012; Maas et al., 2009a; Mitchell and Popham, 2007; van den Berg et al., 2010; Wheeler et al., 2012). However, little research has acknowledged the compositional nature of such data (Aitchison, 2009; Pearson, 1896).

The compositional nature of LULC data can be observed in the analysis of proportions of specific LULC categories composing geographical regions (Leininger et al., 2013). Each observation is a vector of proportions which has the peculiarity of being constrained, so the sum of all its parts is a constant (Aitchison and Egozcue, 2005). Thus, the vector of proportions is a D-part composition, with D components, and the "sample space" is not the real Euclidean space associated with unconstrained data (Aitchison, 2009). Therefore, D-part compositions only provide information about the relative magnitudes of the compositional components (Aitchison and Egozcue, 2005; Hron et al., 2012), and this information is completely gathered in D-1 ratios between the components.

Some researchers have avoided the singularity constraint of LULC data by classifying the percentages of LULC categories according to quantile division (Bixby et al., 2015; Lachowycz and Jones, 2014; Mitchell and Popham, 2008; Mytton et al., 2012; Wu et al., 2015). These methods represent a step forward to the proper use of LULC data. However, consideration of the compositional nature of LULC data might be a critical factor as this has been demonstrated to respect scale invariance and the relative scale issues that are completely ignored when raw data (e.g., proportions or percentages) is used (Müller et al., 2018). To our knowledge, no other study relating LULC data to human health has yet used a compositional approach for the analysis, except for one study assessing the potential contribution of LULC categories to explain the geographical distribution of both COVID-19 incidence and mortality in Catalonia (Spain) (Zaldo-Aubanell et al., 2021a).

The aim of this study is to explore, for the first time, the independent effect of eight LULC categories (agricultural areas, bare land, coniferous forest, broad-leaved forest, sclerophyll forest, grassland and shrubs, urban areas, and waterbodies) on three selected common health conditions (type 2 diabetes mellitus (T2DM), asthma and anxiety) using a compositional methodological approach. This study leverages observational health data of Catalonia (Spain) at area level (the Basic Health Areas; BHAs).

2. Materials and methods

2.1. Environmental heterogeneity: Land use and Land cover (LULC) dataset

We described the environmental heterogeneity of each Basic Health Area (BHA) according to relevant literature (Astell-Burt and Feng, 2019; Hanski et al., 2012; Wheeler et al., 2015). First, we reclassified the prior 23 LULC categories of the Land Use and Land Cover map of Catalonia (Spain) from 2012 into eight major categories: agricultural areas, bare land, coniferous forest, broad-leaved forest, sclerophyll forest, grassland and shrubs, urban areas, and water bodies (see Table S1 and Fig. S2 in Supplementary materials). Then, we calculated the vector of proportions of each reclassified LULC category for each BHA.

The 2012 Land Use and Land Cover map of Catalonia is a tool generated with automated image classification of a 30-m resolution (minimum area representing 30x30m). Images are obtained thought Landsat satellite (Landsat-5, Landsat-7, Landsat-8, and Sentinel-2) using both their sensors (Thematic Mapper (TM), Enhanced Thematic Mapper Plus (ETM+), Operational Land Imager (OLI) and Multispectral Imager (MSI)), and complementary information such as the Urbanistic Map of Catalonia and the graph of the Catalonia infrastructures network. The map also incorporates the cartographic database of forest fires from the Ministry of Agriculture, Livestock, Fisheries and Food of Catalonia, and the LIDAR database from the *Institut Cartogràfic i Geològic de Catalunya* (ICGC) (https://territori.gencat.cat/ca/01_departament/12_cartografia_i_toponimia/bases_cartografiques/medi_ambient_i_sostenibilitat/usos-del-sol/).

2.2. Health data

The prevalence rates of T2DM, asthma, and anxiety for each BHA were obtained from the Catalan Health Department and the Catalan Agency for Health Quality and Evaluation (AQuAS). The health data corresponded to 2014, they were aggregated by age group and sex, and were provided for each Basic Health Area (BHA), the fundamental territorial unit through which the Catalan Healthcare System is articulated (see Fig. S2 in Supplementary materials).

The data did not distinguish between type 1 diabetes and type 2 diabetes. However, almost 95% of all diagnosed cases of diabetes are estimated to be type 2 in adults (Centers for Disease Control and Prevention, 2011). Therefore, we assumed a well representation of individuals with T2DM in our data as previously described (Astell-Burt et al., 2014a).

2.3. Covariates

Three covariates (age group, sex, and socioeconomic status (SES)) were used for segmentation to fix the risk exposure scenario and assess the independent effect of the eight LULC categories.

We considered six age groups: paediatric (named 1 in the figures and the tables; <15 years), teenagers and young adults (2; 15–44 years), adult (3; 45–64 years), senior (4; 65–74 years), old (5; 75–84 years) and very old (6; >84 years). Besides, sex was categorised as male or female.

Furthermore, SES information was obtained using the 2015 Composed Socioeconomic Index (CSI) (Colls et al., 2020) from the Catalan Health Observatory. The CSI is a deprivation index calculated for each BHA and used in assessing resources for Primary Health. The CSI is a continuous variable (0 to 100) that includes the following information: economic income, level of education, professional occupation, life expectancy, premature death rate, and evitable hospitalizations rate (Colls et al., 2020). We used a quintile division of this index, creating five categories: very high ($CSI \le 34.75$), high ($34.75 > CSI \le 42.60$), medium ($42.60 > CSI \le 48.99$), low ($48.99 > CSI \le 56.37$) and very low SES ($56.37 > CSI \le 100$).

2.4. Data analysis

2.4.1. Compositional ilr-transformation

The use of raw compositional data to directly conduct common statistical analyses raises the problem of singularity, which was already warned as problematic over a century ago (Pearson, 1896). Instead, we propose a proper transformation of compositional data, moving the compositions isometrically from the simplex with the Aitchison geometry to the standard real space with the Euclidean geometry (Egozcue and Pawlowsky-Glahn, 2016; Hron et al., 2012). The transformation creates new coordinates in the Euclidean geometry and thus allow for popular statistical methods to be applied (Müller et al., 2018). In this case, regression modelling.

Since regression models are meaningful only when the compositional covariates are expressed on an orthonormal basis, a feasible alternative to raw data (e.g., proportions and percentages) is to use the isometric logratio (ilr) transformation (Hron et al., 2012). In particular, this could be the set of pivot logratios (PLRs), which are a succession of ilr-coordinates where the numerator in the ratio is always a single component and the denominator all those other components "to the right" in the ordered list of components (Greenacre and Grunsky, 2019).

For a better interpretation of the regression coefficients, Müller et al. (2018) suggest moving from the orthonormal to the orthogonal coordinates (see Eq. (1)). So, in a regression with non-compositional response and compositional regressors, an additive increment of one unit in the ilr-orthogonal variable ($z^{(l)*}$) is equal to a two-fold multiplicative increase in the relative dominance of the original composition variable x, if the base-2 logarithm is used (Müller et al., 2018) (see Eq. (2)). This transformation follows:

$$z_i^{(l)*} = \log_2 \frac{x_i^{(l)}}{\sqrt[D-i]{\prod_{j=i+1}^{D} x_j^{(l)}}}, i = 1, \ldots, D-1 \tag{1}$$

$$\Delta z_i^{(l)*} = \log_2 \left(2 \times \frac{x_i^{(l)}}{\sqrt[D-i]{\prod_{j=i+1}^{D} x_j^{(l)}}} \right) = \log_2(2) + \log_2 \frac{x_i^{(l)}}{\sqrt[D-i]{\prod_{j=i+1}^{D} x_j^{(l)}}} = 1 + \log_2 \frac{x_i^{(l)}}{\sqrt[D-i]{\prod_{j=i+1}^{D} x_j^{(l)}}} \quad i = 1, \ldots, D-1 \tag{2}$$

In our study, we used the transformation suggested by Müller et al. (2018) (Eq. (1)) to transform the vector of proportions of the eight LULC categories describing the environmental heterogeneity for each BHA.

We observed some zeroes derived from the lack of some LULC categories in specific BHAs. To simplify and given that the minimum resolution of our LULC data was 30 × 30 m, we opted for simple imputation of these zeroes. Thus, we replaced the zeroes by the minimum value of 900 m^2 to create a vector of positive components $w \in S^D$ that then was closured $r = \mathcal{C}(w)$. We assumed that it was plausible to consider that each LULC category could be represented in at least one area of 30 × 30 m within each BHA. For instance, agriculture areas might take the form of urban agriculture in heavily urbanised BHA. Forested areas might also be present, shaping street trees. Even waterbodies might be represented in small pools of water.

2.4.2. Statistical analysis

Before the analyses, and to avoid potential interaction problems derived from possible associations, we used a Chi-square testing for significant differences between socioeconomic levels and the presence of LULC categories.

We fitted four different regressions to our data: Binomial, Poisson, Negative Binomial, and Beta regression. Similar results were found for all regressions, although Negative Binomial and Beta regression showed higher confidence intervals. As expected, the best-fit model according to AIC was for Negative Binomial regression. However, we noted no important differences in the estimates derived from the four regressions. Thus, we finally modelled our data using the Binomial regression with logit link, as it best represented the nature of the assessed health conditions (see Eq. (4)). Furthermore, this model was the most feasible in terms of simplicity and interpretability. The population size of each BHA was used as weights when fitting the model.

$Y_i \sim Bernoulli(p_i)$ for $i = 1, \ldots, n$.

$$Logit(\mu_i) = \log\left(\frac{p_i}{1-p_i}\right) = \beta_0 + \sum_{i=1}^{n} \beta_i \times X_i^* \tag{4}$$

where Y_i was the binary (Bernoulli) response variable; p_i was the probability of successes $P(Y_i = 1)$, in this case, 1 stands for a diagnosed case; μi was the expected value of each Y_i which was equal to the probability of successes p_i; β_0 was the intercept, and β_i denoted the logistic regression coefficients for the design ilr-matrix X^* of covariables i.

The role of the covariates 'age group', 'sex', and 'socioeconomic status' has been extensively used to describe health status (Beyer et al., 2018; Frank et al., 2004; Mobley et al., 2006; Richardson and Mitchell, 2010; Van den Berg et al., 2016). We used these covariates for segmentation to fix the risk exposure scenario. In total, sixty segmentations were performed. Then, we assessed the independent effect of the eight ilr-transformed LULC categories on each health condition, as previously described in Müller et al. (2018).

Additionally, we also show the estimated coefficients of all explanatory variables (sex, age group, socioeconomic status, and ilr-transformed LULC categories) for each selected health condition derived from ordinary general models using non-segmented data (see Table S3 in Supplementary materials).

We conducted the statistical analyses using the R language environment for statistical computing, R version 3.6.2 (12 December 2019) (R Core Team, 2019).

3. Results

Before conducting any regression analysis, and to avoid potential interaction problems derived from possible associations, we used a Chi-square to test for significant differences between socioeconomical levels and LULC categories. The Chi-squared test showed no significant evidence to reject the hypothesis that SES was not related with LULC categories: $X^2(28, N = 369) = 28.403, p = 0.443$. Therefore, we assumed no significant relationship between socioeconomic levels of BHAs and the presence of any particular LULC category.

Hereunder, we show the independent effect of each ilr-transformed LULC category on the segmented health conditions (see Figs. 2, 3, and 4;

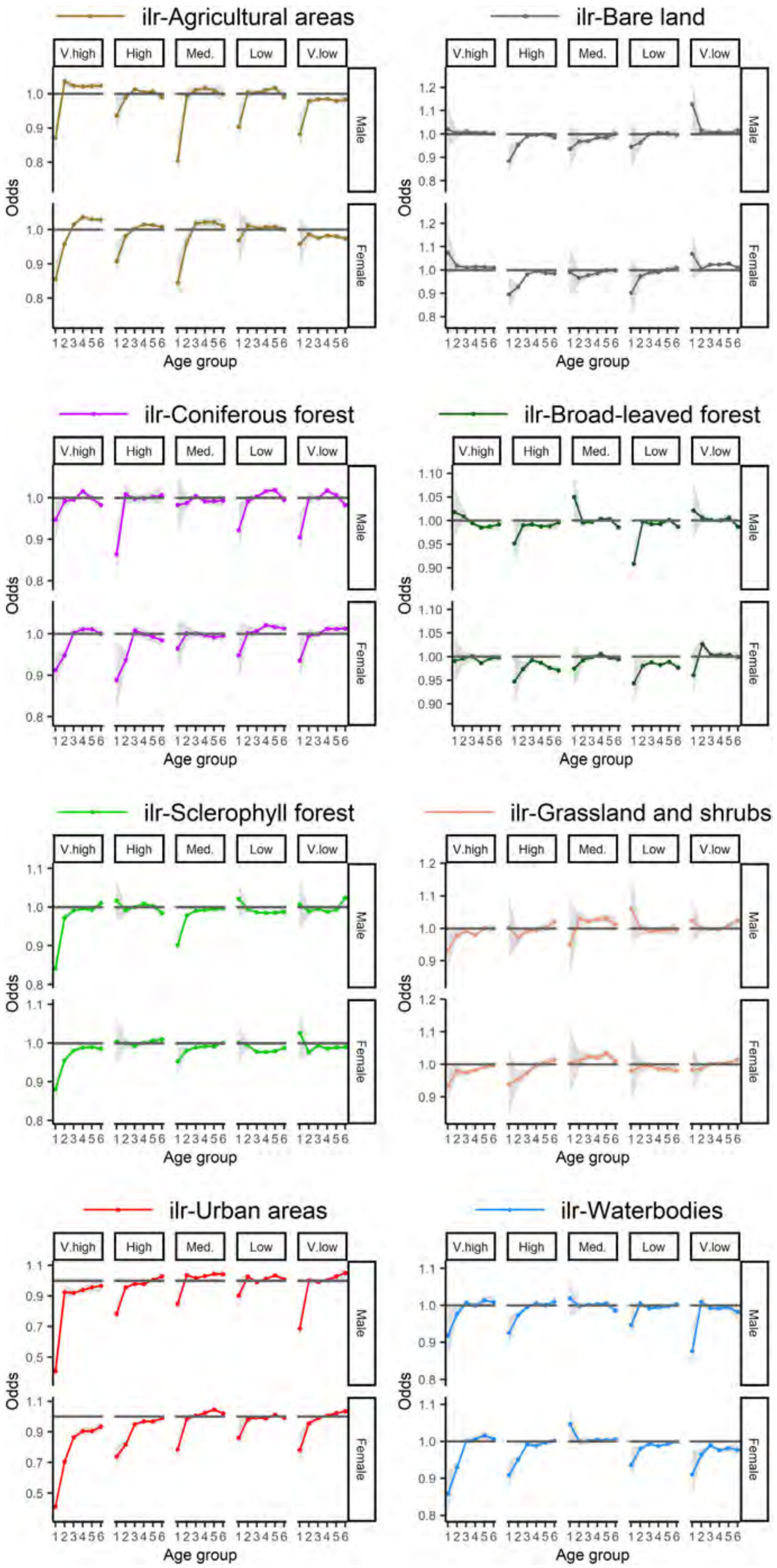

Fig. 2. Odds ratios (in colour) and 95% CI (grey bands). Associations between the prevalence of T2DM and ilr-LULC categories. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

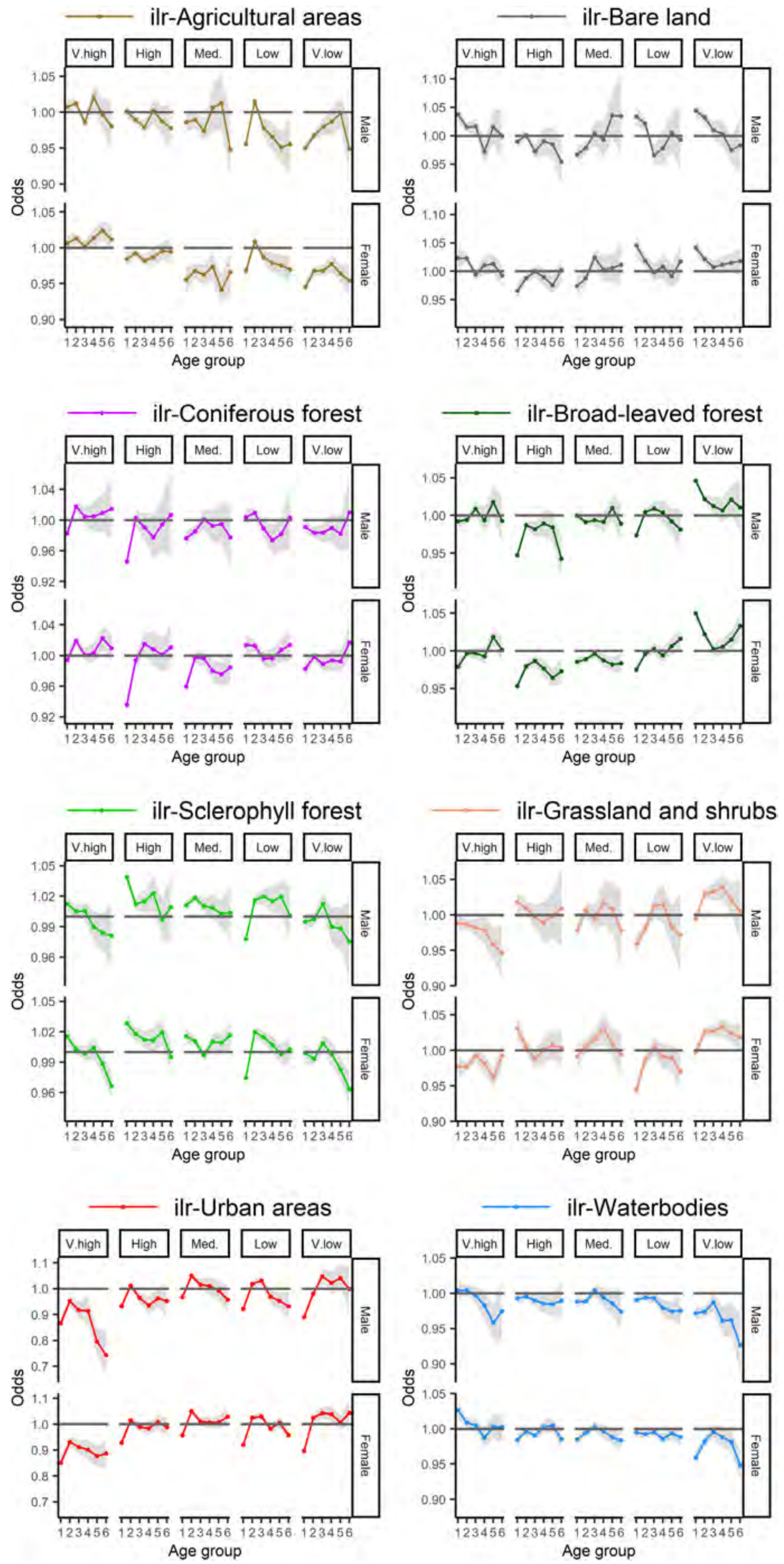

Fig. 3. Odds ratios (in colour) and 95% CI (grey bands). Associations between the prevalence of asthma and ilr-LULC categories. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

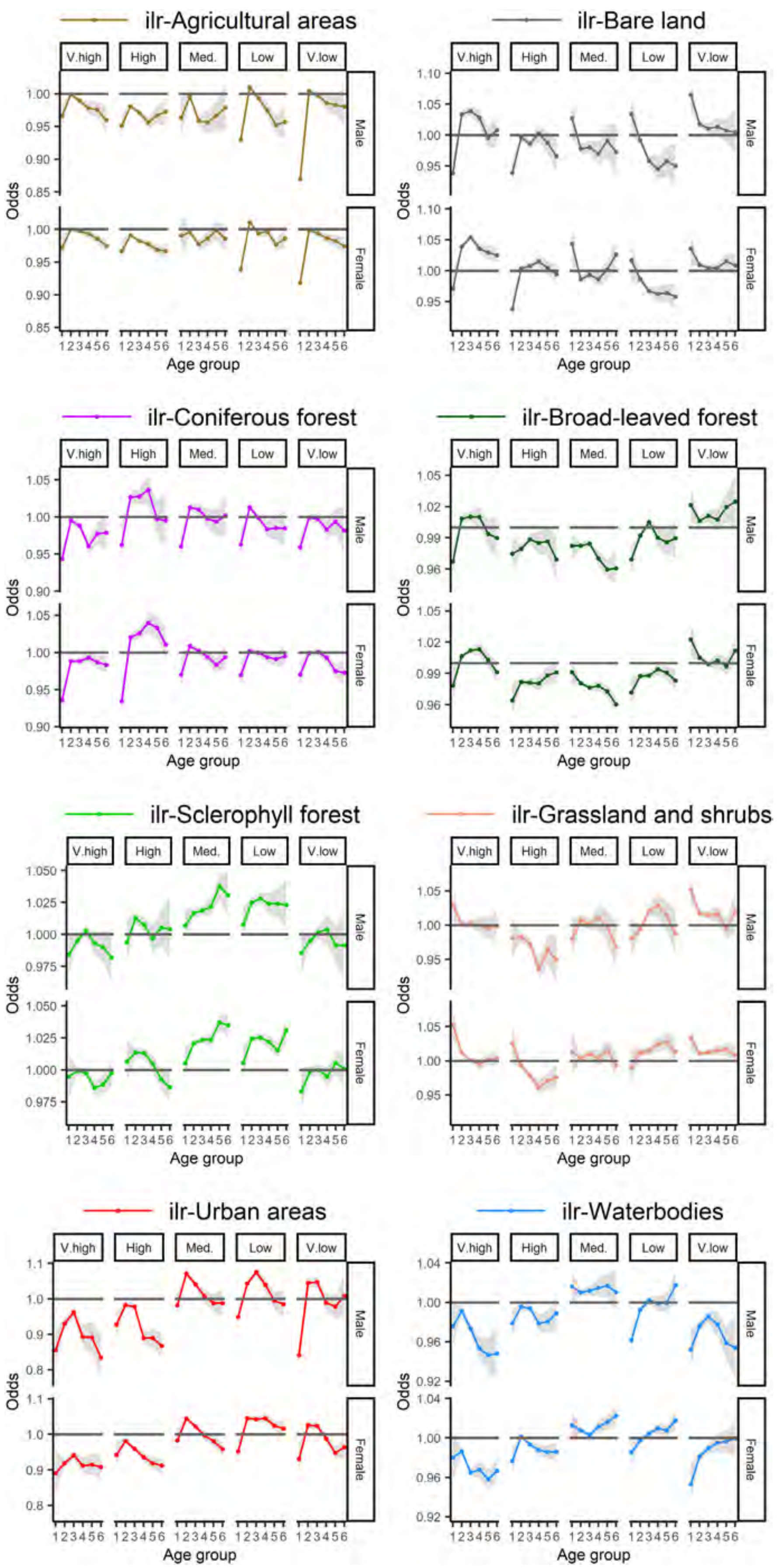

Fig. 4. Odds ratios (in colour) and 95% CI (grey bands). Associations between the prevalence of anxiety and ilr-LULC categories. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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coloured lines). Since we used data representing the entire population of Catalonia, inference information gathered in the *p*-values has little relevance. However, we also provide the 95% Wald confidence intervals (95% CI), reporting the precision of the estimations (Figs. 2, 3, and 4; grey bands).

3.1. T2DM

As shown in Fig. 2, most groups for ilr-agricultural areas showed an increased risk of T2DM, with some exceptions on paediatric (1), some young-adults (2), and very low SES groups.

For ilr-bare land areas, very high and very low SES groups were associated with an increased risk of T2DM, while all the rest were mainly associated with a reduced risk.

For ilr-coniferous forest, younger groups showed a reduced risk, although the majority of other groups showed an increased risk.

In the case of ilr-broad-leaved and ilr-sclerophyll forest, the majority of the estimates showed a reduced risk while some age groups, especially paediatric (1), showed the opposite effect.

As to the effect of ilr-grassland and shrubs areas, higher average risk was observed for medium SES groups, although low SES paediatric (1) male group showed the highest risk.

For ilr-urban areas, we found an increasing risk for more impoverished areas, especially for older groups.

Finally, results for ilr-waterbodies suggested a reduced risk for more impoverished areas with some exceptions in high and very high SES paediatric (1) and young adult (2) groups and low and very low SES young-adult (2) male groups.

3.2. Asthma

For ilr-agricultural areas, our results show a reduced risk for lower SES groups (see Fig. 3).

For ilr-bare land areas, most groups showed an increased risk, especially females. However, high SES groups and other age groups within each SES group showed the opposite effect.

Results for ilr-coniferous forest differed between sex groups. In general, males showed a predominant reduced risk (except for very high SES groups). On the contrary, females showed a predominant increased risk for very high, high, and low SES groups, while medium and very low groups were associated with a reduced risk.

For ilr-broad-leaved forest, results suggest an increased risk for lower SES groups. Furthermore, for ilr-sclerophyll forest, results show a predominant increased risk for all groups, except for older groups of very high and very low SES, and younger groups of low and very low SES.

Results for ilr-grassland and shrubs and ilr-urban areas suggest a progressively increased risk across SES variable.

Lastly, for ilr-waterbodies, most groups showed a predominant reduced risk of asthma, especially very low SES groups.

3.3. Anxiety

As shown in Fig. 4, we found a predominant decreased risk for most groups for ilr-agricultural areas.

For ilr-bare land, very high and very low SES groups showed a predominant increased risk of anxiety, while medium and low SES showed the opposite trend. In contrast, results for high SES groups differed between sexes. Males showed a predominant decreased risk and females showed a predominant increased risk.

As to the effect of ilr-coniferous forest, we observed a predominant reduced risk for most groups. However, some groups of high, medium and low SES showed an increased risk in both sexes. Following the same trend, we found a predominant reduced risk for ilr-broad-leaved forest except for some very high and very low SES groups.

Results for ilr-sclerophyll forest showed an increased risk for lower SES groups, although the results for very low SES groups were somewhat inconclusive. For ilr-grassland and shrubs, inconclusive results were observed for very high SES groups and an increased risk was observed for lower SES groups. Likewise, ilr-urban areas showed an increased risk for lower SES groups.

Finally, ilr-waterbodies showed a reduced risk for most of groups. However, we found some exceptions for medium SES groups and some age groups of low SES.

4. Discussion

Our study has stepped forward to detect the independent contribution of eight LULC categories to the prevalence of three assessed health conditions (T2DM, asthma and anxiety). We propose a compositional approach that shows the estimated odds ratio after segmenting the data according to the SES status, age group, and sex. Moreover, this methodology has allowed us to discuss the possible set of particular elements of each LULC category related to the studied health conditions.

4.1. Human health conditions

For this study, we used the major pathways framework suggested by Markevych et al. (2017), and hypothesised that each selected health condition was related to the environment through specific pathways.

4.1.1. Type 2 diabetes mellitus

T2DM has been associated with obesity and sedentary behaviour (low physical activity) (Colagiuri et al., 2010). Thus, the relationship between the environment and T2DM may partly occur through the instoration pathway (Markevych et al., 2017). In particular, the capacity of LULC categories to promote physical activity. In addition to this, research is also associating long-term air pollution exposure (Eze et al., 2015, 2014), as well as traffic noise (Shin et al., 2020) with increased risk of T2DM. Thus, T2DM might arguably be related to the environment through the mitigation pathway (Markevych et al., 2017).

Urban areas showed an increased risk of T2DM for medium to lower SES groups. This effect could be explained due to the fact that higher SES groups, which tend to be more physically active during leisure time (Marielle et al., 2012), are also associated with a higher presence of greenspaces in their neighbourhoods (Astell-Burt et al., 2014b). This might lead to higher levels of physical activity in higher SES groups (Frank et al., 2007; Richardson et al., 2013). Contrarily, lower SES groups, which are less able to afford gym fees (Giles-Corti and Donovan, 2002) and have little access to open public spaces (Koohsari, 2011), tend to walk in more unsupportive build environments (Adkins et al., 2017), which lack certain land-use types such as green spaces and recreation centres (Zandieh et al., 2017). These factors might arguably lead to less opportunities for physical activity in deprived neighbourhoods, increasing the risk of T2DM in lower SES groups. In fact, higher risk of T2DM and many lifestyle-related risk factors have been reported for people living in deprived neighbourhoods (Astell-Burt et al., 2014a; Feng and Astell-Burt, 2013; Williams et al., 2012). Moreover, deprived neighbourhoods are more associated with polluted areas (Bolte et al., 2010), higher perceived noise and lower perceived safety, cleanliness and aesthetic quality of their neighbourhoods (Mouratidis, 2020). In this sense, the increased risk of T2DM for poorer groups could also be explained through the mitigation pathway (Markevych et al., 2017), since both air pollution exposure and traffic noise have been related to increased risk of T2DM (Eze et al., 2015; Shin et al., 2020).

Broad-leaved forest, which generally has low undergrowth, cool temperatures, and smooth slopes, was predominantly associated with lower levels of T2DM. Likewise, sclerophyll forest, which tend to be close to urban settlements, showed a generally decreased risk of T2DM. This suggests that, despite its undergrowth densely populated with shrubs and some lianas, people might be attracted to perform physical activity on the sclerophyll forest principal routes and paths. Regarding the coniferous forest, it might not always be accessible to people to perform physical activity (at least the high mountain forest, which is established on higher altitudes of the mountains). This might explain the predominant increased risk of T2DM observed for most groups.

Regarding waterbodies, we found a heterogeneous effect, suggesting that effect measure modification of SES and age group appeared to be especially important.

In agricultural areas, results showing increased risk of T2DM could be explained through the pesticides exposure pathway (Lee et al., 2011; Turyk et al., 2009). In a previous study, researchers found five pesticide types positively associated with incident diabetes (Starling et al., 2014). In this regard, epidemiological evidence suggests an association between exposure to organochlorine pesticides and T2DM (Evangelou et al., 2016).

4.1.2. Asthma

The relationship between the environment and asthma may occur mainly through the mitigation and instoration pathways (Markevych et al., 2017). Air quality is crucial (Toure et al., 2019), not only regarding the allergenic pollen levels that might aggravate this respiratory disease (Cariñanos and Casares-Porcel, 2011), but also concerning air pollution (Guarnieri and Balmes, 2014). In addition, other studies have explored the connection between air quality and heat events (Soneja et al., 2016) and microbial diversity (Ege et al., 2011).

A higher prevalence of asthma is directly related to the higher presence of allergenic elements in the air (D'Amato et al., 2007). We found that waterbodies show a generally reduced risk of asthma for all SES groups. This could be because waterbodies might arguably be associated with little presence of allergenic elements due to the lack of vegetation, and because the allergenic elements might be trapped in the waterbodies. In fact, Spanish researchers found that living next to the coast may protect against sensitization to pollens and *Alternaria* (Moral Gil et al., 2008).

Although a set of allergenic species might be distinguished for each LULC category, the differences across SES groups for LULC categories associated with vegetation suggest that the presence of allergenic species might not be the only relevant predictor. For broad-leaved forest and grassland and shrubs, we found a higher risk in lower SES groups. On the other hand, sclerophyll forest showed a predominant increased risk, bare land showed higher predominant risk for females, and coniferous forest showed a reduced predominant risk for males.

For urban areas, we found increased levels of asthma for lower SES groups. Some research has suggested that air polluted environments are associated with a higher prevalence of respiratory illnesses such as asthma (Annesi-Maesano et al., 2007; D'Amato et al., 2002). Furthermore, lower SES groups are known to be in worse health status and associated with more polluted areas (Bolte et al., 2010; de Vries et al., 2003; Su et al., 2011). Contrarily, the increased levels of greenspaces in richer SES neighbourhoods might lower air pollutant concentrations (Kroeger et al., 2014).

In addition, the higher risk of asthma found in lower SES urban areas would also be explained since lower SES groups have been linked with increased susceptibility to heat-associated health effects (Gronlund, 2014). In addition, extreme heat events have been linked with increasing risk of hospitalization for asthma (Soneja et al., 2016).

We found agricultural areas to be generally associated with a reduced risk of asthma for all SES groups except for very high SES groups. Some authors highlight microbial diversity and specific microbial exposure as protective factors against asthma and atopy (Bach, 2018; Jatzlauk et al., 2017). In this regard, farm environments that promote higher microbial exposure would be associated with decreased risk of asthma (Ege et al., 2011). As previously highlighted (Farfel et al., 2010; Shankardass et al., 2007), the results for very high SES groups are compatible with the so-called "hygiene hypothesis". However, other studies (Eum et al., 2019) state that complexity in the prevalence of asthma symptoms calls for a more comprehensive framework for its understanding.

4.1.3. Anxiety

Anxiety could be mainly linked to the environment through the restoration pathway (Markevych et al., 2017). The restorative role of natural environments has been associated to the visual (Franco et al., 2017; Jacobs and Suess, 1975) and auditory stimuli (Coensel et al., 2011), to the openness of natural spaces (Han, 2007) and to species richness (Aerts et al., 2018). Many studies have highlighted the potential of the natural environment to increase feelings of restoration (White et al., 2013), and reduce stress levels (Morita et al., 2007) and heart rate (Lee et al., 2014).

Our results suggest that agricultural areas seem foster mental restoration, leading to a main decreased risk of anxiety. Agricultural areas may represent more diverse landscape configuration, such as the forest-agriculture mosaic, which can increase bird richness (Atauri and De Lucio, 2001). Concerning this, recent research has highlighted the positive association between bird diversity and people's wellbeing (Methorst et al., 2020). Moreover, the openness of agricultural scenarios might also promote restoration for individuals (Han, 2007).

Likewise, we found that environments with more waterbodies were associated with decreased anxiety levels in the majority of groups. Some authors have underscored the importance of water sounds for mental health (White et al., 2010). Others have hypothesised the independent beneficial effect on health for waterbodies (Nutsford et al., 2016), even without a full exposure but with only observation of water elements photographs (White et al., 2010).

The beneficial effect of waterbodies might also be linked to evolutionary and cultural theories such as the Biophilia effect (Browning et al., 2014), which highlights the significance of water for the biological, wellbeing and survival needs (Han, 2007; Orians and Heerwagen, 1992; Ulrich, 2016, 2014). In addition, some research points out to the role of negative ions that are present in water environments, especially by the sea (Jiang et al., 2018), in lowering depression scores (Perez et al., 2013).

Regarding forested LULC categories, only broad-leaved forests, arguably the most walkable of the forest types, showed decreased risk of anxiety for most of the SES groups. On the other hand, we found increased anxiety levels for lower SES groups in urban areas. As described above, important differences between deprived and non-deprived neighbourhoods seem to be essential elements modifying the effect of urban areas on anxiety levels. These differences include the built environment, presence of greenspaces (Astell-Burt et al., 2014b), accessibility to public open spaces (Koohsari, 2011), and other important factors mentioned above such as noise, light and air pollution. Likewise, results showing a higher risk for sclerophyll forest and grassland and shrubs might be explained by differences in quality of spaces across SES groups.

4.2. The role of covariates: SES, age group, and sex

The three covariates studied (SES, age group, and sex) have widely been described as important modifiers of nature effects (Markevych et al., 2017). Considering this, we have segmented our data accordingly. Thus, the three covariates did not play a role in the residuals of our models. Nevertheless, we can compare the effects of the covariates when comparing the estimated odds ratios across different groups (Figs. 2, 3, and 4).

We found SES to be the most important covariate as to the effect of the LULC categories on the selected health conditions. As previously reported (Knobel et al., 2021a), we found a dissimilar risk between the highest and lowest SES groups. This effect measure modification could be explained because lower SES groups might be more likely to benefit from a health promotion intervention (Bolte et al., 2010; de Vries et al., 2003; Markevych et al., 2017; Su et al., 2011), such as being exposed to particular LULC categories. Lower SES groups have been described to be less mobile (Maas et al., 2006; Schwanen et al., 2002), to have less health status (Markevych et al., 2017), and to live in more polluted areas (Bolte et al., 2010). In this sense, lower SES groups show stronger associations with their environment (Dadvand et al., 2014; Maas et al., 2009b). On the contrary, higher SES groups might be more capable of changing the environment they live in in order to be less exposed to particular harmful conditions (Bell et al., 2010; Markevych et al., 2017). In addition, other factors such as better social environments, health care accessibility and use, residential environment preferences, and even better general behaviour and lifestyle might also be key factors linking higher SES groups with better general health (Adler and Newman, 2002).

Regarding the age group, many of the estimates showed a more intense effect on very old (6) age group than on young-adult (2), adult (3), senior (4) and old (5). Likewise, we found a recurrent intensified effect for the paediatric (1) group compared to the rest of groups. This effect was found to go either in the same direction as the rest of the age groups (e.g., prevalence of T2DM for high SES groups for ilr-broad-leaved forest; Fig. 3), or in the opposite direction (e.g., prevalence of anxiety for low SES groups for ilr-bare land; Fig. 4).

On the one hand, elderly people are undoubtedly the groups with less moving capacity. This makes elders more strongly associated with their surroundings (Maas et al., 2006). On the other hand, paediatric people have unique characteristics that differ from adults (Ortega-García et al., 2019). Additionally, the paediatric group might be underrepresented in at least two of the health conditions considered; T2DM and anxiety. Type 1 diabetes, more associated with paediatric groups (Soltész, 2003), is an autoimmune disorder genetically mediated, while type 2 is more of a life style induced disorder (Joshi and Shrestha, 2010). Regarding anxiety, the anxiety diagnostic criteria in children might also differ from adults. Children have particular features (for instance, difficulties in communication, cognition and emotions) that create unique challenges when distinguishing between normal and pathological anxiety (Beesdo et al., 2021).

Lastly, in line with other studies (Richardson and Mitchell, 2010), we found sex to be an important variable modifying the effect of LULC categories on the three selected health conditions.

4.3. Future research

The compositional methodology used in this study has allowed us to raise many hypotheses linking LULC categories to the three assessed human health conditions. Although these hypotheses have been supported by previous studies, they should be tested further with specific study designs in future studies.

4.3.1. Complex pathways linking the environment to human health

To simplify the results interpretations, we have assumed that anxiety was related to the environment mainly through the restoration pathway. In contrast, we assumed that T2DM and asthma were related to the environment mainly through two pathways (instoration and mitigation pathways). However, it is possible that, in reality, many other pathways intertwine (Hartig et al., 2014; Markevych et al., 2017). For instance, some of the results found for T2DM needed a broad scope to be interpreted, such as the pesticide exposure for T2DM.

Moreover, differences in preferences (Han, 2007; Kiley et al., 2017; Lyons, 1983) between the different tested groups, the amount of knowledge about the environment (Aerts et al., 2018), and even the environmental quality of the LULC categories (Knobel et al., 2021b; Wheeler et al., 2015) might be important factors modifying the LULC – human health relationship. Therefore, more studies with accurate information about the variables mentioned above should be conducted to relate specific health conditions with specific LULC categories.

4.3.2. Further exploration of LULC categories

We aimed to test the independent effect of broad LULC categories on human health. However, we believe that important characteristics might have remained unstudied in these general classifications. One example is the coniferous forest category, which gathered three forest types: low land pine tree forest, the montane pine tree forest, and high mountain forest. Each of them possessing individual and exceptional features. In this sense, we argue that using a combination of other existing datasets and GIS techniques to construct a more exhaustive classification of the different ecosystems or types of environment would result in better analyses. In the same direction, authors could make use of the present framework to conduct further research testing for differences within agricultural areas (irrigated, non-irrigated), urban (residential, sprawl, industrialized, urban greenspaces) or waterbodies (inland, marine), among other examples.

4.4. Limitations

4.4.1. Unit of analysis

We have used the Basic Health Area (BHA) as our unit of analysis to describe the living environment for individuals. However, other research encompassing LULC data and human health has used different unit of analysis, from census areas to different buffer radii (Zaldo-Aubanell et al., 2021b). In this sense, further research is needed to test our results and approach using different units of analysis.

4.4.2. Cross-sectional design

We followed a cross-sectional design. Thus, limitations derived from this methodology must be carefully considered. Although cross-sectional designs leverage population-based data and are useful to detect differences between areas, they do not allow for causal inference to be established (Wu et al., 2020).

Furthermore, we did not consider possible spatial autocorrelations derived from data. In this sense, robust spatio-temporal methodologies should be needed allowing for the establishment of causal inference.

5. Conclusions

There is a recurrent call for new methodologies that detect the independent effect of different types of environment on human health. We have proposed an innovative methodology using a compositional approach. We have defined eight types of environment using a classification of Land use and Land cover data and have tested their individual contribution on explaining three selected health conditions using observational data. In this regard, the proposed methodology has shown to be an acceptable and a feasible way to address the compositional nature of LULC data, facilitating the interpretation of the estimates through the Log2 ilr-transformation.

Our approach has led us to plausible results supported by the existing literature while has enabled us to push forward the debate on the relevance of environmental heterogeneity in health studies. We have proposed a detailed conception of the environment that goes beyond *green* and *natural*. In addition, we have discussed how different types of environment possess exclusive elements (humidity, temperature, type of flora and fauna, accessibility, walkability, openness, presence of water, sounds, air compounds and air quality, heat, and noise, light contamination, and even chemical exposure) affecting distinctively on human health. Furthermore, we have found the relationship between the environment and human health to be clearly modified by socioeconomic status, age group, and sex. Lastly, we have highlighted that other important ideas such as the preferences (or agreeableness) for specific types of the environment of certain groups and quality of the environments might be important factors and should be considered in future research.

We believe that our contribution might help researchers approach the environment in a more multidimensional scope, allowing environmental heterogeneity to be brought into the analysis.

CRediT authorship contribution statement

Quim Zaldo-Aubanell: Conceptualization, Formal analysis, Investigation, Data curation, Writing – original draft. **Isabel Serra:** Conceptualization, Methodology, Formal analysis, Data curation, Writing – original draft, Supervision. **Albert Bach:** Writing – review & editing, Visualization. **Pablo Knobel:** Writing – review & editing. **Ferran Campillo i López:** Resources, Writing – review & editing. **Jordina Belmonte:** Writing – review & editing. **Pepus Daunis-i-Estadella:** Methodology, Validation. **Roser Maneja:** Resources, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2021.150308.

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3.3 Research Chapter 3 : Community Risk Factors in the COVID-19 Incidence and Mortality in Catalonia (Spain). A Population-Based Study

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Community Risk Factors in the COVID-19 Incidence and Mortality in Catalonia (Spain). A Population-Based Study

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Abstract: The heterogenous distribution of both COVID-19 incidence and mortality in Catalonia (Spain) during the firsts moths of the pandemic suggests that differences in baseline risk factors across regions might play a relevant role in modulating the outcome of the pandemic. This paper investigates the associations between both COVID-19 incidence and mortality and air pollutant concentration levels, and screens the potential effect of the type of agri-food industry and the overall land use and cover (LULC) at area level. We used a main model with demographic, socioeconomic and comorbidity covariates highlighted in previous research as important predictors. This allowed us to take a glimpse of the independent effect of the explanatory variables when controlled for the main model covariates. Our findings are aligned with previous research showing that the baseline features of the regions in terms of general health status, pollutant concentration levels (here NO_2 and PM_{10}), type of agri-food industry, and type of land use and land cover have modulated the impact of COVID-19 at a regional scale. This study is among the first to explore the associations between COVID-19 and the type of agri-food industry and LULC data using a population-based approach. The results of this paper might serve as the basis to develop new research hypotheses using a more comprehensive approach, highlighting the inequalities of regions in terms of risk factors and their response to COVID-19, as well as fostering public policies towards more resilient and safer environments.

Keywords: COVID-19; air pollutants; cardiovascular diseases; psychological disorders; cancer; agri-food industry; land use and land cover data

1. Introduction

The COVID-19 pandemic, caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has become a leading health concern worldwide. As of 31 May 2020, there were 5,939,234 confirmed cases and 367,255 deaths globally [1]. The severity and mortality have been related to aging and pre-existent health conditions, including respiratory and cardiovascular diseases, as well as psychological disorders and cancer [2,3]. Nevertheless, the geographic COVID-19 distribution within countries or regions has been uneven [4]. Socioeconomic status has also been pointed out as a community determining factor, but inconsistently for both richer and poorer populations [5,6]. In the same direction, inconclusive results have been found regarding population density [6–8]. Previous studies have reported the association between population physical distancing and COVID-19 spreading dynamics [9–11], as well as other weather conditions such as humidity and temperature [12]. These links might lie behind the local outbreaks of the pandemic in certain agri-food sectors such as meat and leather and fur industries [13,14]. However, other studies have recently pointed out that COVID-19 incidence correlates to ultraviolet radiation, rather than temperature-humidity [15,16].

Air pollution remains one of the main threats for human health worldwide and can also play a relevant role in the COVID-19 crisis mainly in two ways: increasing the severity of the virus' clinical effects in chronically exposed populations and, probably to a lesser extent, promoting the virus' airborne dispersion [17–19]. On one hand, according to the World Health Organization (WHO), there are 4.2 million deaths every year mostly due to cardiorespiratory diseases as a result of exposure to outdoor air pollution [20]. Recent studies have shown that ambient air pollution may be linked to the lethality of COVID-19 in Asia, Europe and America [21–26]. Thus, regions chronically exposed to nitrogen dioxide (NO_2) and particulate matter ($PM_{2.5}$ and PM_{10}) seem to be more susceptible to the virus. Still, many of those studies do not include well identified health covariates [27–29] and are focused only on mortality. On the other hand, some authors have studied the role of particulate matter in the spreading of SARS-CoV-2 [12,30–32], principally in industrialised areas [33].

Air pollution and aerosol formation and distribution have been widely linked to Land Use and Land Cover (LULC) [34–36], with an especial concern regarding particulate matter ($PM_{2.5}$ and PM_{10}) [37–39]. In this sense, urbanised and industrial areas are associated with worse air quality than other LULC categories such as agricultural or forested areas [39]. LULC information is useful open source data which is associated with other factors like population density, biodiversity and economic activities [40], and has been identified as a suitable describer of the environment in studies relating the environment to human health [41]. For the aforementioned, research encompassing the associations between COVID-19 and LULC data appears to be relevant, since this spatial data (LULC) leverage socioeconomic and biophysical information of the environment.

In Catalonia (Spain), there was a heterogenous distribution of both COVID-19 incidence and mortality in the early stages of the pandemic. This suggests that differences in baseline risk factors across regions might have modulated the outcome of the pandemic. The purposes of this study are to:

1. Analyse the associations between both COVID-19 incidence and mortality and long-term exposure to pollutant concentration (NO_2 and PM_{10}), while adjusting for demographic information, socioeconomic status and general health status (cardiovascular diseases, psychological disorders and all-cause cancer);
2. Explore the potential links between agri-food industry and COVID-19 incidence and mortality as observed from the outbreaks in these particular industries;
3. Screen, for the very first time, the potential use of the overall Land Use and Cover data on describing the geographical COVID-19 incidence and mortality.

2. Materials and Methods

2.1. COVID-19 Cases and Deaths

The number of patients infected with SARS-CoV-2 (cases) and deaths attributed to COVID-19 in Catalonia were gathered until 18 May 2020, after the first peak decreased and the incidence of new cases started to stabilise.

The number of cases was obtained from the RSAcovid19 records from the Catalan Health Department. We collected both the positive cases (patients positively diagnosed by a PCR—Polymerase Chain Reaction—or rapid diagnostic test) and suspicions cases (patients who presented symptoms compatible with COVID-19 and were classified as a possible case, even though they were diagnosed neither by a PCR nor by a rapid diagnostic test). All of them were active cases under the control of Epidemiologic Surveillance Service in Catalonia and were attributed to their residential Basic Health Area (BHA), the fundamental territorial unit through which Catalan Healthcare System is articulated and the unit of analysis of this paper. In total, 372 BHA compose the Catalan territory.

The number of registered deaths due to COVID-19 was obtained from the Catalan Agency for Health Quality and Evaluation (AQuAS) and the Central Register of Insured Persons of the Catalan Health Department. These data included not only people who were positively diagnosed by a laboratory test but also people who presented symptoms compatible with the illness. These open data are updated several times per day, so analyses and figures might change depending on the date. Furthermore, death observations might be modified by the Mortality Register of Catalonia once all death certificates have been collected [42].

Both data sets were provided already segmented by sex (male and female). Incidence and mortality rates were calculated using the number of cases and the number of deaths divided by the total amount of population within each BHA. Figures S1 and S2 show the COVID-19 incidence and mortality rates, respectively (see Supplementary Information Section).

2.2. Comorbidities

During the first wave of the pandemic in Catalonia, COVID-19 tests were not conducted on every person showing symptoms. Rather, people with more severe symptoms or having pre-existent health conditions were more likely to be tested and thus, finally diagnosed. To control for the general health status of each BHA, we created three groups of principal health conditions explored by previous literature: cardiovascular diseases; psychological disorders and all-cause cancer. Pre-existent respiratory conditions could not be considered as the health dataset was incomplete.

The percentages of people presenting cardiovascular diseases (congestive heart failure, hypertension, ischemic cardiomyopathy and patients who suffered cerebrovascular accident), psychological disorders (depression, schizophrenia, intellectual disability, conduct disorder, attention deficit disorder and psychosis), and all-cause cancer were obtained from historical observational data from 2014 provided by the Catalan Health Department and the Catalan Agency for Health Quality and Evaluation (AQuAS). We lacked more recent data to control for the general health status of BHAs. However, the health outcomes assessed were prevalent illnesses with generally slight changes from one year to another. The data was aggregated by BHA and sex (male and female).

2.3. Demographic and Socioeconomic Data

Some authors have highlighted the prominent impacts of COVID-19 on elderly people, especially in nursing homes [43]. Others have also focused their studies in the importance of sex [44]. We controlled for sex and elderly people by calculating the percentage of people over the age of sixty-five in each BHA and distinguishing the COVID-19 cases and deaths between males and females. In addition, socioeconomic data were extracted from the Catalan Health Observatory. We used the Composed Socioeconomic Index (CSI) [45], that is calculated for each BHA. This index is used in the assessment of resources for Primary Health, which includes a set of socioeconomic variables: economic income, education, professional occupation, life expectancy, premature death rate and preventable hospitalizations rate. This is a continuous variable measured from 0 to 100 (0 being the poorest and 100 the richest). Previous works have suggested dividing such data into septiles [3]. However, after testing the model, we opted for using quintiles from a very low (E; CSI $\geq$ 0 and <20) to a very high (A; CSI $\geq$ 80) socioeconomic status (SES).

2.4. Air Pollution

Long-term exposure to air pollutants was assessed using the modelling of the NO_2 and PM_{10} annual average ($\mu g/m^3$) in Catalonia, corresponding to the 2016 assessment from the General Direction of Environmental Quality and Climate Change of the Catalan Government.

We calculated the annual weighted average for each BHA through GRASS GIS (GRASS Development Team, 2017. Geographic Resources Analysis Support System (GRASS) Software, Version 7.2. Open Source Geospatial Foundation. Electronic document: http://grass.osgeo.org (accessed on 23 May 2020)) (see Figures S3 and S4 of Supplementary Information Section showing the annual weighed average of NO_2 and PM_{10} ($\mu g/m^3$) for each BHA (2016)).

Besides air pollution data from 2016, we created a dataset for the period 2018–2019 (the most up-to-date period with data available). We combined three data sources (pollution data from the Catalan Government; Smart Citizen, a citizen science project from the European Community's H2020; and pollution data from the European Environment Agency). Then, we calculated the annual average for each pollutant in each BHA containing sensors, which yielded 63 BHAs with values for NO_2 and 91 with values for PM_{10}. After controlling for possible differences between both periods (2016 and 2018/2019) and finding no significant differences, we chose the modelling of the NO_2 and PM_{10} annual average for 2016 because it provided information for all Catalonia. Results of the two independent t-tests assessing significant differences between pollutant concentration levels (NO_2 and PM_{10}) in 2016 and in 2018/2019 are provided in the Results section.

Other air pollutants have been widely used to assess pollution levels. Previous research hypothesised that long-term exposure to O_3 and $PM_{2.5}$ adversely affects the respiratory and cardiovascular systems, increasing mortality risk and also exacerbating the severity of COVID-19, worsening the prognosis of the disease [46,47]. In this sense, O_3 levels has been found to be associated with COVID-19 confirmed cases [48] and $PM_{2.5}$ to be a highly significant predictor of the number of confirmed COVID-19 cases, deaths and hospital admissions [48,49]. Although assessment of the independent effect of the abovementioned pollutants would have been of interest, we only used NO_2 and PM_{10} data, as they were provided for all Catalan territory.

2.5. Agri-Food Industry

Agri-food industry geographic information was extracted from Catalan Agri-food industry Records (http://agricultura.gencat.cat/ca/serveis/registres-oficials/agroalimentacio/registre-industries-agraries-alimentaries-catalunya/ (accessed on 1 June 2020)). The industries are classified depending on their industrial sector: slaughter of livestock, conservation and elaboration of meat products; preparation and conservation of fish, crustaceans and molluscs; preparation and preservation of fruits and vegetables; manufacturing of vegetables and animal oils and fats; manufacturing of milk products; manufacturing of grain mill products, starches and starch products; manufacturing of bakery and pasta products; manufacturing of other food products; manufacturing of products for animal feeding; manufacturing of beverages; forest industries; and other agricultural industries.

We split the category "other agricultural industries" into two main subtypes: "Leather and fur industry" (industries based on preparation, tanning and dyeing animal skins) and "Garden industry" (industries based on seed conditioning and handling, substrate production and ornamental plant conservation), as we considered that these two sectors

were poorly represented in the above classification. The total number of industries of each type was collected within each BHA.

2.6. Land Use and Land Cover Data

To describe the environment of each BHA we used the most updated and detailed Land Use and Land Cover data of Catalonia, the Land Use and Cover map for 2017. This is a tool generated with automated image classification of a 30-m resolution. The images are obtained thought Landsat satellite (Landsat-5, Landsat-7, Landsat-8 and Sentinel-2) using both their sensors Thematic Mapper (TM), Enhanced Thematic Mapper Plus (ETM+), Operational Land Imager (OLI) and Multispectral Imager (MSI), and complementary information such as the Urban Map of Catalonia and the graph of the Catalonia infrastructures network. It also incorporates the cartographic database of forest fires from the Ministry of Agriculture, Livestock, Fisheries and Food of Catalonia, and the LIDAR database from the Institut Cartogràfic i Geològic de Catalunya (ICGC) (http://territori.gencat.cat/ca/01_departament/12_cartografia_i_toponimia/bases_cartografiques/medi_ambient_i_sostenibilitat/bases_miramon/territori/mapa-dusos-i-cobertes-del-sol/index.html (accessed on 30 May 2020))

As Table 1 shows, we reclassified the 25 Land Use and Land Cover (LULC) categories into four broader categories: urban areas; industrial, commercial and transport units; agricultural areas; and forest and semi-natural areas. In this classification, categories referring to water bodies (inland and marine waters) and bare land were not considered due to their low significance.

Table 1. Reclassification of the 25 LULC categories of the Land Use and Cover Map of Catalonia (2017) into four broader categories.

Urban Areas	Industrial, Commercial and Transport Units	Agricultural Areas	Forest and Semi-NATURAL Areas
Discontinuous urban fabric	Industrial or commercial units	Permanently irrigated land	Lowland natural grasslands
Continuous urban fabric	Road and rail networks and associated land	Non-irrigated arable land	Montane natural grasslands
		Unirrigated Fruit tress	Alpine natural grasslands
		Irrigated Fruit trees	Transitional woodland/shrub
		Vineyards	Wetland vegetation
		Rice fields	Coniferous forest
		Citrus trees	Broad-leaved forest
			Sclerophyll forest

When proportions of land use and cover composing geographical regions are analysed, each observation is a vector of proportions of specific LULC categories [50]. This characteristic raises the problem of singularity (a constant sum constraint) as the vectors (also called compositions) describe the relative contribution of each part (the components) on the whole. So the information is present in the ratios of the components rather than in each component [51–53]. Following Müller et al. (2018) [54], we avoided the singularity constraint by applying an isometric logratio (ilr) transformation to the four LULC variables. This transformation moves the compositions isometrically from the simplex with the Aitchison geometry to the standard real space with the Euclidean one [53]. As recommended [54], we used a Log2 transformation, as it facilitated the understanding of the estimates. With this transformation, a unit additive increment in the ilr-transformed variable is equal to a two-fold multiplicative increase in the relative dominance of the original composition variable x, as a base-2 logarithm is used. In other words, this means that the relative dominance of a specific LULC category is doubled in comparison to the geometric mean of all the rest LULC variables [54].

2.7. Statistical Analysis

To assess the associations between COVID-19 incidence and mortality and the explanatory variables, we fitted a generalised linear model, in the binomial family, with a logit link. This model fit was selected as the dependent variable followed a Binomial distribution.

$$Y_i \sim Bernoulli(p_i) \text{ for } i = 1, \ldots, n.$$

$$Logit(\mu_i) = \log\left(\frac{p_i}{1-p_i}\right) = \beta_0 + \sum_{i=1}^{n} \beta_i \times X_i,$$

where Y_i was the binary (Bernoulli) response variable; p_i was the probability of successes $P(Y_i = 1)$, in this case, 1 stands for a confirmed COVID-19 case or death; μ_i is the expected value of each Y_i which is equal to the probability of successes p_i; β_0 is the intercept, and β_i denotes the logistic regression coefficients for the design matrix X of covariables i.

Logistic regression analyses with 95% Wald confidence intervals (95% CI) were performed to assess the association between both incidence and mortality rate of COVID-19 (number of confirmed COVID-19 cases or deaths within a given BHA/total number of people living within such BHA) and the rest of covariates, while adjusting for demographics, socioeconomic and comorbidity covariates. The model was fitted using population size of each BHA as weights. We built a main model using the demographics, socioeconomic and comorbidity covariates and then, human activity covariates, as well as land use and cover covariates, were included in the model separately (see Table 2).

Table 2. Covariates tested in the model. All the variables were calculated within each BHA, the unit of analysis.

Covariate (Units)	Description
Demographics, socioeconomic status, and comorbidity (Main model)	
Sex: Females	Categorical variable comparing females to males, used as a reference level.
Percent > 65 (%)	Percentage of people aged above 65 years.
SES A SES B SES D SES E	Socioeconomic status categorised with 5 levels, comparing very high, high, low and very low (A, B, D, E) socioeconomic status to normal (C), used as the reference level. Data from 2014.
Cardiovascular diseases (%)	Group variable. Percentage of people with congestive heart failure, hypertension, ischemic cardiomyopathy or who suffered cerebrovascular accident in 2014.
Psychological disorders (%)	Group variable. Percentage of people with depression, schizophrenia, intellectual disability, conduct disorder, attention deficit disorder or psychosis in 2014.
All-cause cancer (%)	Group variable. Percentage of people with any type of cancer in 2014.
Human activity	
NO_2 ($\mu g/m^3$) *	Nitrogen dioxide annual weighed average in 2016.
PM_{10} ($\mu g/m^3$) *	Particulate matter with diameter of 10 µm annual weighed average in 2016.
Meat industry *	Number of industries based on slaughtering of livestock, conservation and elaboration of meat products in 2020.
Fish industry *	Number of industries based on preparation and conservation of fish, crustaceans and molluscs in 2020.
Vegetable industry *	Number of industries based on preparation and preservation of fruits and vegetables in 2020.
Animal oils and fats *	Number of industries based on manufacturing of vegetable and animal oils and fats in 2020.
Milk products *	Number of industries based on manufacturing of milk products in 2020.
Grain mill industry *	Number of industries based on manufacturing of grain mill products, starches and starch products in 2020.
Bakery industry *	Number of industries based on manufacturing of bakery and pasta products in 2020.
Other food products *	Number of industries based on manufacturing of other food products in 2020.
Animal feeding *	Number of industries based on manufacturing of products for animal feeding in 2020.
Beverage industry *	Number of industries based on manufacturing of beverages in 2020.
Forest industry *	Number of forest industries in 2020.
Leather and fur industry *	Number of industries based on preparation, tanning and dyeing animal skins in 2020.
Garden industry *	Number of industries based on seed conditioning and handling, substrate production and ornamental plant conservation in 2020.
Land use and Land cover	
ilr-Urban areas *	Isometric logratio (ilr) transformation of the percentage of urban areas in a given BHA. Numerical variable.
ilr-Industrial areas *	Isometric logratio (ilr) transformation of the percentage of industrial, commercial and transport unit areas in a given BHA. Numerical variable.
ilr-Agricultural areas *	Isometric logratio (ilr) transformation of the percentage of agricultural areas in a given BHA. Numerical variable.
ilr-Forested areas *	Isometric logratio (ilr) transformation of the percentage of forested and semi-natural areas in a given BHA. Numerical variable.

Table 2. *Cont.*

* Variables were included in the model separately.

Statistical analysis were conducted using the R language environment for statistical computing, R version 3.6.2 (12 December 2019) [55].

3. Results

Homogeneity of groups in terms of pollutant concentration levels was assessed using two independent t-tests (Table 3) for the specific BHA which we had available information (63 BHA, for NO_2; and 91 BHA, for PM_{10}). Based on the t-tests outcomes, no significant differences were noted between the annual average of pollutants in 2016 and in 2018/2019 for neither pollutant (NO_2; t = 0.792, p = 0.428, and PM_{10}; t = −1.559, p = 0.119).

Table 3. Independent t-tests between mean pollutant concentration levels in 2016 and in 2018/2019.

Variables	Mean ± SD		Statistical Results		
	2016 Concentration Levels	2018/2019 Concentration Levels	df	t	p-Value
NO_2	20.23 ± 12.163	21.37 ± 10.700	246	0.792	0.428
PM_{10}	21.52 ± 4.397	20.72 ± 5.241	351.37	−1.559	0.119

The adjusted odds ratio (OR) with 95% confidence intervals for the association between COVID-19 incidence and mortality and the explored covariates are shown in Table 4 and also represented in Figure S6 (see Supplementary Information section).

Table 4. Associations between COVID-19 incidence and mortality and the rest of covariates. The main model controlled for demographics, socioeconomics and comorbidity covariables. Human activity covariates as well as land use and cover covariates were included in the model separately.

	Incidence of COVID-19				Mortality of COVID-19			
	Adjusted Main Model		Unadjusted		Adjusted Main Model		Unadjusted	
Covariates	**Odds Ratio (95% CI)**	***p*-Value**	**Odds Ratio (95% CI)**	***p*-Value**	**Odds Ratio (95% CI)**	***p*-Value**	**Odds Ratio (95% CI)**	***p*-Value**
Main Model								
Sex: Female	1.772 (1.7577–1.7870)	***	1.723 (1.7087–1.7366)	***	1.034 (0.9974–1.0724)	-	0.990 (0.9551–1.0257)	-
Percent > 65	1.006 (1.0047–1.0072)	***	1.018 (1.0171–1.0189)	***	1.023 (1.0171–1.0281)	***	1.052 (1.0481–1.0562)	***
SES A (very high)	1.199 (1.1832–1.2150)	***	1.171 (1.1568–1.1848)	***	1.547 (1.4556–1.6434)	***	1.523 (1.4414–1.6093)	***
SES B (high)	1.126 (1.1116–1.1402)	***	1.153 (1.1387–1.1674)	***	1.241 (1.1696–1.3166)	***	1.346 (1.2702–1.4271)	***
SES D (low)	0.967 (0.9542–0.9800)	***	0.998 (0.9849–1.0114)	-	0.914 (0.8573–0.9754)	*	1.015 (0.9517–1.0815)	-
SES E (very low)	0.956 (0.9432–0.9688)	***	0.994 (0.9806–1.0067)	-	0.908 (0.8511–0.9677)	**	1.011 (0.9493–1.0778)	-
Cardiovascular diseases	1.003 (1.0020–1.0049)	***	1.016 (1.0153–1.0173)	***	1.007 (1.0006–1.0136)	*	1.038 (1.0336–1.0423)	***
Psychological disorders	1.148 (1.1418–1.1545)	***	1.057 (1.0517–1.0627)	***	1.312 (1.2809–1.3435)	***	1.255 (1.2282–1.2827)	***
All-cause cancer	1.021 (1.0153–1.0258)	***	1.084 (1.0805–1.0883)	***	1.102 (1.0774–1.1272)	***	1.239 (1.2205–1.2584)	***
Human activity								
NO_2	0.999 (0.9989–0.9996)	***	1.002 (1.0014–1.0020)	***	1.013 (1.0118–1.0151)	***	1.017 (1.0154–1.0182)	***
PM_{10}	1.003 (1.0015–1.0038)	***	1.009 (1.0077–1.0098)	***	1.048 (1.0421–1.0541)	***	1.050 (1.0451–1.0559)	***
Meat industry	1.002 (1.0012–1.0019)	***	1.001 (1.0006–1.0014)	***	0.995 (0.9926–0.9965)	***	0.992 (0.9900–0.9938)	***
Fish industry	0.993 (0.9911–0.9951)	***	0.982 (0.9799–0.9840)	***	0.964 (0.9536–0.9755)	***	0.929 (0.9177–0.9412)	***
Vegetable industry	0.988 (0.9867–0.9885)	***	0.985 (0.9839–0.9856)	***	0.941 (0.9340–0.9478)	***	0.923 (0.9154–0.9300)	***
Animal oils and fats	0.982 (0.9812–0.9836)	***	0.980 (0.9789–0.9813)	***	0.909 (0.8988–0.9189)	***	0.888 (0.8781–0.8991)	***
Milk products	1.000 (0.9982–1.0013)	-	1.001 (0.9995–1.0024)	-	0.973 (0.9650–0.9806)	***	0.975 (0.9675–0.9822)	***
Grain mill industry	0.948 (0.9441–0.9523)	***	0.944 (0.9397–0.9478)	***	0.777 (0.7502–0.8047)	***	0.753 (0.7266–0.7811)	***
Bakery industry	0.984 (0.9809–0.9873)	***	0.977 (0.9740–0.9801)	***	0.974 (0.9589–0.9891)	**	0.938 (0.9236–0.9517)	***
Other food products	0.984 (0.9829–0.9861)	***	0.977 (0.9752–0.9783)	***	0.933 (0.9244–0.9412)	***	0.910 (0.9019–0.9178)	***
Animal feeding	0.998 (0.9967–0.9994)	**	0.999 (0.9975–1.0001)	-	0.970 (0.9630–0.9768)	***	0.967 (0.9605–0.9739)	***
Beverage industry	0.999 (0.9994–0.9996)	***	0.999 (0.9994–0.9996)	***	0.998 (0.9970–0.9983)	***	0.997 (0.9963–0.9978)	***
Forest industry	1.004 (1.0011–1.0077)	*	0.990 (0.9869–0.9931)	***	0.945 (0.9278–0.9632)	***	0.907 (0.8911–0.9240)	***
Leather and fur industry	1.070 (1.0624–1.0779)	***	1.078 (1.0702–1.0856)	***	1.110 (1.0776–1.1441)	***	1.115 (1.0823–1.1489)	***
Garden industry	0.922 (0.9122–0.9329)	***	0.922 (0.9119–0.9321)	***	0.717 (0.6715–0.7649)	***	0.709 (0.6649–0.7560)	***
Land use and cover								
ilr-Urban areas	1.006 (1.0048–1.0076)	***	1.013 (1.0114–1.0136)	***	1.050 (1.0440–1.0569)	***	1.062 (1.0566–1.0669)	***
ilr-Industrial areas	0.990 (0.9884–0.9921)	***	0.991 (0.9892–0.9926)	***	1.039 (1.0304–1.0477)	***	1.036 (1.0281–1.0442)	***
ilr-Agricultural areas	0.982 (0.9806–0.9835)	***	0.977 (0.9762–0.9786)	***	0.936 (0.9303–0.9422)	***	0.925 (0.9200–0.9300)	***
ilr-Forested areas	1.014 (1.0131–1.0158)	***	1.012 (1.0111–1.0136)	***	0.991 (0.9856–0.9971)	**	0.987 (0.9816–0.9925)	***

- non-statistically significant; * p-value < 0.05; ** p-value < 0.005; *** p-value < 0.0005.

In the main model using demographic, socioeconomic and comorbidity covariables, BHAs with more percentage of people aged above 65 years, of A (very high) and B (high) socioeconomic status (SES) showed a positive association with both COVID-19 incidence and mortality. In these cases, estimates for mortality were greater than for incidence. Contrarily, BHAs of D (low) and E (very low) SES were associated with decreased levels of COVID-19 incidence and mortality. However, when tested alone (without adjusting for the rest of covariates), they showed a non-significant effect.

All three comorbidity variables were positively associated with both COVID-19 incidence (OR 1.003 95% 1.0020–1.0049 for cardiovascular diseases; OR 1.148 95% 1.1418–1.1545 for psychological disorders; and OR 1.021 95% 1.0153–1.0258 for all-cause cancer) and mortality (OR 1.007 95% 1.0006–1.0136 for cardiovascular diseases; OR 1.312 95% 1.2809–1.3435 for psychological disorders; and OR 1.102 95% 1.0774–1.1272 for all-cause cancer). Again, the estimates for mortality were found higher than for incidence in all three comorbidity variables.

Finally, sex (comparing females to males) showed a positive significant effect on the incidence of COVID-19 (OR 1.772 95% 1.7577–1.7870) and a non-significant effect on the mortality (OR 1.034 95% 0.9974–1.0724). It also showed a non-significant effect on COVID-19 mortality when tested unadjusted.

We found a positive association between COVID-19 mortality and the annual average of both pollutants (NO_2 and PM_{10}). Our model showed that, when the rest of covariates held constant, an increase of 10 $\mu g/m^3$ in NO_2 and PM_{10} annual average multiplied the odds of COVID-19 mortality by 1.138 (95% 1.1245–1.162) and by 1.598 (95% 1.5104–1.6936), respectively. Regarding COVID-19 incidence, PM_{10} also showed a positive association with COVID-19 incidence (OR 1.003 95% 1.0015–1.0038), while NO_2 showed a negative association when tested adjusted for the rest of covariates (OR 0.999 95% 0.9989–0.9996).

As to the type of agri-food industries, we found several types that showed a reduced risk of both COVID-19 incidence and mortality (fish industry, vegetable, animal oils and fats, grain mill, bakery, other food products, animal feeding, beverage industry and garden industry). Milk products showed a non-significant effect on COVID-19 incidence and a negative effect on COVID-19 mortality. In addition, meat and forest industry showed a positive effect on the incidence of COVID-19 (OR 1.002 95% 1.0012–1.0019 for meat industry and OR 1.004 95% 1.0011–1.0077 for forest industry) but a negative effect on the mortality (OR 0.995 95% 0.9926–0.9965 for meat industry and OR 0.945 95% 0.9278–0.9632 for forest industry. However, unlike forest industry, meat industry showed a positive significant effect when tested unadjusted, as well. Finally, leather and fur industry were the only type of agri-food industry that were associated with increased levels of both COVID-19 incidence (OR 1.070 95% 1.0624–1.0779) and of COVID-19 mortality (OR 1.110 95% 1.0776–1.1441).

Regarding LULC data, we found a decreased risk of COVID-19 incidence for ilr-Industrial areas and ilr-Agricultural areas. In other words, when the relative dominance of industrial areas and agricultural areas were doubled in a given BHA with respect to the rest of LULC categories, the odds for COVID-19 incidence was expected to be reduced by a 0.010% (95% 0.0079–0.0116) and 0.018 % (95% 0.0165–0.0194), respectively. On the other hand, for ilr-Urban areas and ilr-Forested areas the odds for COVID-19 incidence was expected to be increased by 0.006% (95% 0.0048–0.0076) and 0.014% (95% 0.0131–0.0158), respectively. As for the COVID-19 mortality, ilr-Urban and ilr-Industrial areas showed positive significant effects (OR 1.050 95% 1.0440–1.0569, and OR 1.039 95% 1.0304–1.0477, respectively), while ilr-Agricultural and ilr-Forested areas showed negative significant effects (OR 0.936 95% 0.9303–0.9422 and OR 0.991 95% 0.9856–0.9971, respectively)

Main Model Adjustment

For illustrative purposes, the main model adjustment is shown for COVID-19 cases and deaths instead of the incidence and mortality rate. We noted no important differences between the expected values for males and for females for the main model. Thus, we assessed the model with the total number of cases and deaths (females + males).

Figure 1 shows a scatter plot were the observed number of COVID-19 cases (on the left) and deaths (on the right) are plotted against the expected number of COVID-19 cases and deaths predicted by the model. Those BHA which fulfilled the criterion that the difference between the observed rate and the fitted rate was either >0.03 or <0.03 (for COVID-19 cases), and >0.004 or <0.004 (for COVID-19 deaths) were identified as outliers.

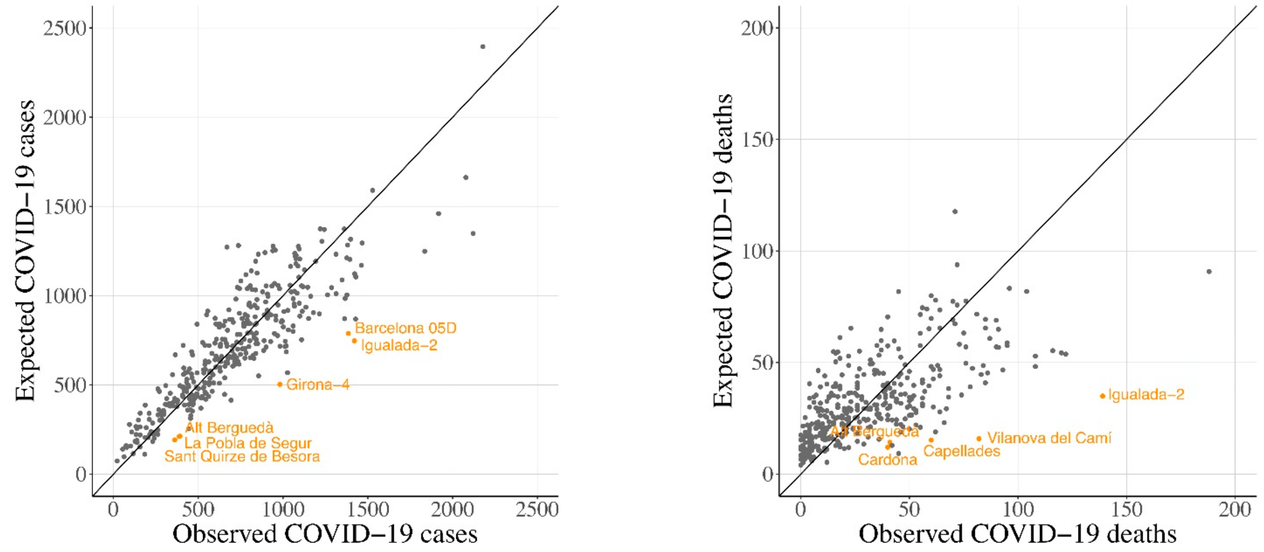

Figure 1. Scatter plot of the observed number of COVID-19 cases (**left**) and deaths (**right**), and the expected value predicted by the main model, logarithmic transformation has been performed.

The outliers coincide with either northern BHAs with high amounts of forest and semi-natural areas, low population and high incidence and mortality cases, or with regions from Central Catalonia where incidence and mortality were also high ("Barcelona 05D", "Girona-4", "Alt Berguedà", "la Pobla de Segur", "Sant Quirze de Besora" and "Igualada-2" for COVID-19 cases, Figure 1 left; and "Cardona", "Alt Berguedà", "Capellades", "Vilanova del Camí" and "Igualada-2" for COVID-19 deaths, Figure 1 right). As a matter of fact, two of the observed outliers ("Vilanova del Camí" and "Igualada-2") were BHAs in which the early outbreaks of the pandemic occurred.

Additionally, Figures 2 and 3 show the observed number of COVID-19 cases and deaths (on the left) and the expected number of cases and deaths (on the right) for each BHA predicted by the main model. In purple, there are represented those BHAs where the expected value was overestimated (difference between observed cases or deaths and expected cases or deaths < Q1) by the main model. On the other hand, in orange there are represented those BHAs where the expected value was underestimated (difference > Q3) by the main model. In green, those BHAs where the difference between the observed value and the expected fell within the Q1 and the Q3 are plotted.

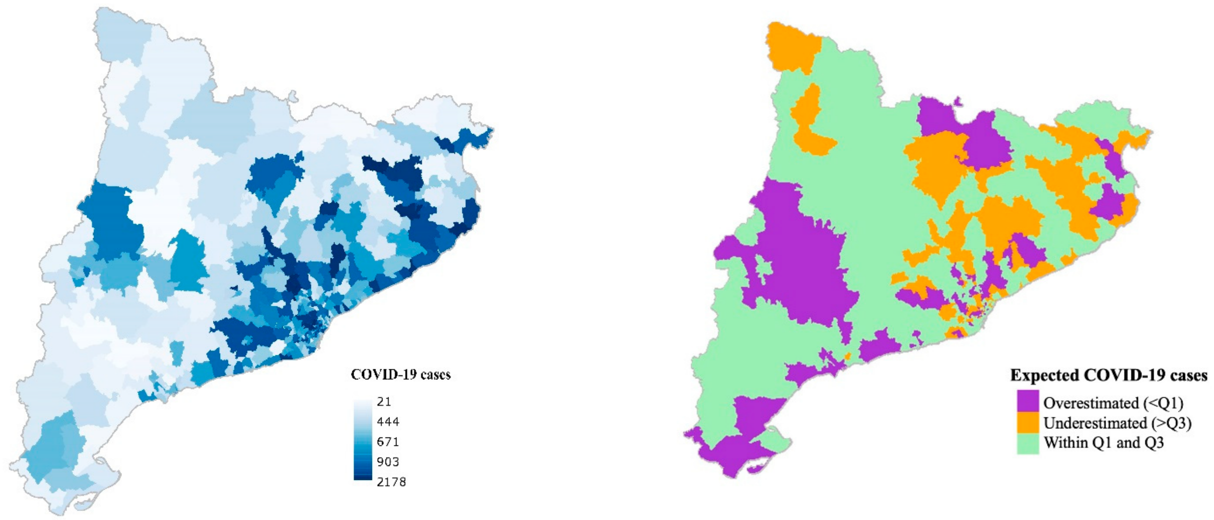

Figure 2. Number of observed COVID-19 cases (**left**) and the quartile distribution of the number of expected COVID-19 cases predicted by the main model (**right**).

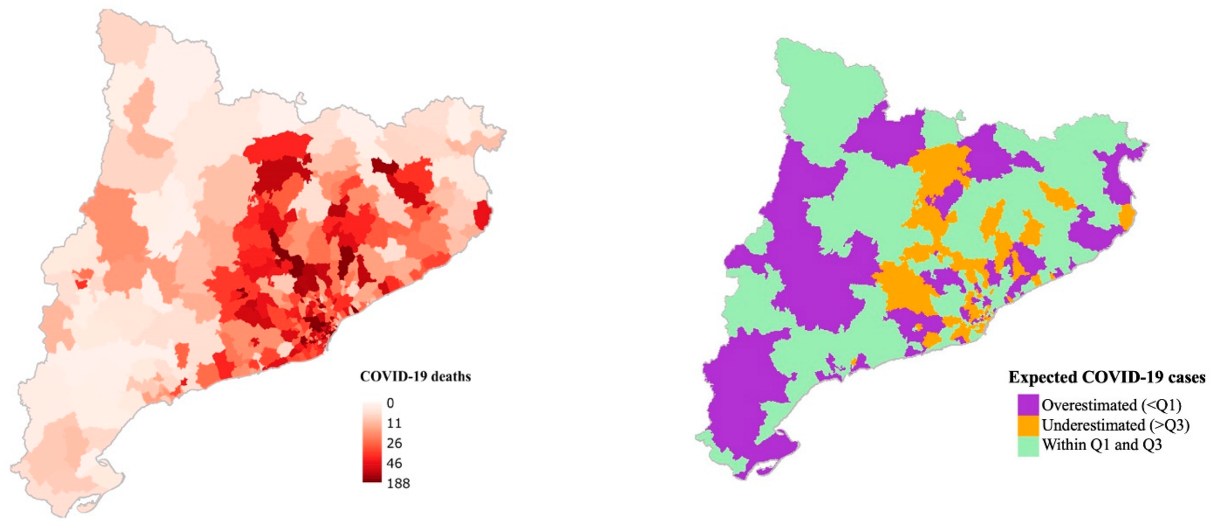

Figure 3. Number of observed COVID-19 deaths (**left**) and the quartile distribution of the number of expected COVID-19 deaths predicted by the main model (**right**).

4. Discussion

This cross-sectional study aimed to evaluate the associations between COVID-19 incidence and mortality and long-term exposition to air pollution (NO_2 and PM_{10}) while adjusting for demographic (sex, percentage of people aged above 65 years), socioeconomic (quintile division of the Composed Socioeconomic Index) and comorbidity data (percentage of people presenting cardiovascular disease, psychological disorders and all-cause cancer). Additionally, for the first time, the contribution of agri-food industry type and the overall Land Use and Land Cover data was also explored to explain the geographical distribution of COVID-19 incidence and mortality, leading to novel results.

4.1. Demographics

Registered cases of COVID-19 in Catalonia have a clear female predominance (165,597 cases in females compared to 95,317 cases in males). Compared to other nations, the proportion of women in the incidence rate is only surpassed by Wales (63.46% vs. 64.18%), while being still slightly higher than the Netherlands (62.45%), Scotland (62.01%), Northern Ireland (61.94%), or Sweden (59.37%) [56]. Mortality was also higher among females

(50.41%), but below what has occurred in Finland (52.00%) and the Republic of Ireland (50.50%) [56]. Catalonia has a positive small prevalence of female population (50.9%). In addition, this predominance positively increases for people older than 65 years (57.0%), while being reversed in 0–24-year-old children (around 48.6%) [57]. With older people being the most affected by COVID-19 and the younger the least (in the early stages of the pandemic), women might be expected to carry most of the burden. In addition, research has highlighted women as composing the majority of the healthcare workforce in the US, and also with roles requiring more close and prolonged contact with patients [58]. Furthermore, for employed women or single parents, gender disparities may even be accentuated, as women are disproportionally responsible for the bulk of domestic tasks, including not only childcare but also eldercare [59]. These factors might explain our results showing women having 77.2% more risk of COVID-19 infection than males.

However, other countries with comparable age-gender pyramids (younger male population and older female population), such as Italy or the United States [60], have not experienced this phenomenon, following the global trend of male predominance [61,62].

However, we did not find greater risk of COVID-19 mortality for females, as the number of deaths for females and males was not significantly different (6098 and 5998, respectively).

Recent studies have pointed out that older age is as a major individual risk factor for severity of the COVID-19 infection and mortality [58,63]. We detected this effect in the adjusted and non-adjusted models for both COVID-19 infection and mortality. Nevertheless, the effect of age was reduced when adjusted for the rest of covariates.

4.2. Socioeconomics

Previous studies have suggested that socioeconomically deprived groups were associated with a higher risk of confirmed COVID-19 infection [64]. At the beginning of the outbreak, some authors suggested that working class people might be more exposed to the virus, as they were associated with the use of public transport [65]. However, other reports encouraged its use as the incidence of COVID-19 attributed to public appeared to be very low [66], even though safety countermeasures should be taken into account [67]. Regarding deprived people, some authors suggest that this group might face several disadvantages which make physical distancing a difficult issue [68]. That is, besides showing greater mobility due to the impossibility of working from home, lower-income population might tend to visit denser places (grocery stores, religious establishments, etc.), and spend longer times than upper class populations [69]. In Catalonia, some studies observed higher incidence of COVID-19 in poorer areas of Barcelona city [70].

Despite all the research showing a greater impact of COVID-19 on lower SES classes, our results seem to point to the other way around. We found higher incidence and mortality ratios for higher SES BHAs compared to medium SES. This effect was significant before and after adjusting for the rest of the covariates. In addition, although a non-significant effect was found for low (D) and very low (E) SES BHAs when tested unadjusted, when adjusting them into the model, they showed a significant negative association with both COVID-19 incidence and mortality. It is possible that differences between SES classes in Catalonia were not as noticeable as they were in other regions (in the UK, for example [64]). However, it is also possible that the Composed Socioeconomic Index used to measure the SES at area level might be weak measurement to detect individual-based characteristics. Nevertheless, as shown elsewhere [69], using a more detailed unit of analysis (e.g., census area) or completing SES information with individual-based information [64] might result in better estimations as to the impact of SES on COVID-19 incidence and mortality.

4.3. Comorbidities

Chronic medical conditions have been linked to disproportionate morbidity due to SARS-CoV-2 virus [58]. Regarding previous literature on SARS-CoV, some authors have reported that cardiovascular comorbidities might be the most important components for

predicting adverse outcome, increasing the risk of death by twice as much as other risk factors [71]. In a recent meta-analysis [72], the proportion of cardia-cerebrovascular disease in patients with COVID-19 was found to be 16.4%. A proportion much higher than what is found in the general population [72]. In this sense, many researchers acknowledge the consistent association between cardiovascular disease and SARS-CoV-2 [2,73–75].

In another sense, some researchers have reported that people diagnosed with psychological disorders had significantly higher odds of COVID-19 infection than people without a psychological disorder, with the strongest effect for depression and schizophrenia [76]. In the same way, these authors reported that the death rate for patients with both a recent diagnosis of psychological disorder and COVID-19 infection was higher than patients with COVID-19 infection but with no psychological disorder [76].

Other research also states the role of cancer in aggravating the prognostics of COVID-19 [73]. In this regard, people with ongoing cancer treatments have shown higher risk because their immune system is compromised [77].

Our results are aligned with previous literature showing increased risk for both COVID-19 infection and mortality for those areas with more percent of people suffering from cardiovascular disease, psychological disorders and all-cause cancer. Similar to previous literature, we used these variables to control for the general health status of the BHAs, building our main model. They all showed a positive significant association with both COVID-19 infection and mortality before and after adjustment. This research adds evidence that these comorbidity variables are significant predictors.

Additionally, other relevant comorbidities such as obesity [78] or respiratory illnesses (e.g., COPD [79] and asthma [2]) have also been found to be positively associated with both infection and mortality for COVID-19. Our study was not able to control for these variables as we lacked the information. However, future studies might also use respiratory illnesses to describe the general health statutes of the unit of analysis.

4.4. Air Pollution

The major route of transmission for COVID-19 is through small droplets and aerosols of different sizes exhaled by an infected person when breathing, talking, coughing or sneezing [29,80,81]. Additionally, some research suggests the rapid spread of the SARS-CoV-2 could be explained by air pollution-to-human transmission (e.g., airborne transmission) [17–19]. Considering that the data used in this paper was historical (2016), we could not assess the relationship between short-term exposition to high levels of air pollutants (e.g., PM_{10}) and the COVID-19 incidence or mortality and hence, provide evidence neither supporting these hypotheses nor against them.

In our opinion, the principal pathway linking air pollution to increased levels of COVID-19 incidence and mortality is the worse health status of more exposed populations [29,82,83].

Long-term exposure to air pollution has been widely linked to cardiovascular diseases, respiratory illnesses, psychological disorders and cancer [84–86]. We believe that this might explain the association between more polluted areas and more severe and lethal forms of COVID-19 [26,80]. In this sense, areas more chronically exposed to higher air pollution levels would presumably be in worse health status and thus, showing increasing levels of COVID-19 mortality. Regarding the incidence of the virus, the positive association between increased pollutant levels and increased incidence levels of COVID-19 (at least for PM_{10}) would be explained as during the early stages of the pandemic, people with pre-existent health conditions, or with more severe symptoms, were more likely to be tested, and thus, to finally be diagnosed as a new case.

As shown elsewhere [87], NO_2 and PM_{10} effects on COVID-19 mortality remained significant after adjusting for socioeconomic, demographic and health-related variables. When adjusted in the model, NO_2 showed a negative association with COVID-19 infection levels. In this sense, other relevant research conducted in Catalonia [88] highlights an association between NO_2 and COVID-19 incidence, but the association was only found in more polluted BHAs. Our approach of using this data for all Catalonia without stratifying for more polluted areas might prevent us from detecting the aforementioned effect.

4.5. Forest, Meat, and Leather and Fur Industry

Our results show a significant positive effect of forested areas on COVID-19 incidence. Although forest industries might apparently be more abundant in BHAs with more forested areas, its positive effect was only found when it was adjusted, showing a significant negative effect when tested alone. We hypothesise that, rather than a positive independent effect for forest industry on COVID-19 incidence, possible associations with some main model covariates might have contributed to changing the direction of the effect.

In Catalonia, there is a huge production of pork meat, with a degree of self-sufficiency of 228.73%, that has been constantly growing in recent decades [89]. While swine breeding is concentrated in Lleida region and Central Catalonia, most slaughterhouses and pork meat industries are located in Central Catalonia and Girona region [89]. Working conditions in slaughterhouses and meat industries such as low temperatures, high humidity, overcrowding, physical effort and other things may contribute to amplifying virus viability and transmission [90]. These conditions might also be found in other types of industries with high working density, making them prone-to-infection industries. However, apart from forest industries, we only found animal-related industries, namely the meat industry and the leather and fur industry, to be related with COVID-19 incidence and mortality (only the leather and fur industry).

In other coronavirus infections such as MERS, there was a high prevalence of infection in slaughterhouse workers compared to the general population [91]. COVID-19 transmission has been reported in the meat and poultry industry [13] and slaughterhouses are now considered a new front line in the COVID-19 pandemic [92]. In the same direction, local outbreaks in the fur industry have also been reported, particularly in the mink furriery [93,94]. The fact that this particular economic activity is significantly increasing both the incidence and the mortality rate in our model makes it plausible that this kind of industry poses a unique and independent risk for COVID-19 transmission.

In a recent study from the Netherlands [94], the authors reported that minks are susceptible for SARS-CoV-2. In addition, that infected animals are able to transmit the virus among each other. The authors also claim that although mink farms are present in other countries in Europe, China and the US, only the Netherlands has reported SARS-CoV-2 infections in these animals. In our study, we did not identify the animal species of the leather and fur industries we assessed. However, and given the results shown, more attention and research should be placed upon this specific industry.

In this sense, it is advised that COVID-19 pandemic should trigger a profound transformation of industrial animal agriculture by improving living conditions and increasing their space through extensive farming, diversify the protein source industry to increase far more sustainable plant-based market shares, and empowering the ecological transition of animal farmers [95].

4.6. Land Use and Cover

LULC data has been shown to be a suitable describer for the environment surrounding individuals in studies linking the environment to human health [41]. Unlike other environmental data sets, they combine both the biophysical (e.g., temperature, humidity, soil features) and socioeconomic (e.g., political, economic, cultural) drivers of a territory [40,96]. Given the uneven geographical distribution of the virus in Catalonia, we wanted to screen whether environmental composition of the BHAs (seen as urban, industrial, agricultural and forested areas) might be related with the impact of COVID-19.

Urban areas and industrial, commercial and transport units are known to be more associated with air pollution, aerosol emission, human mobility and higher population density [97]. These factors might be the reasons behind the increased risk of COVID-19 mortality shown by the two ilr-transformed LUC categories, and an increased risk of COVID-19 infection for urban areas. Industrial areas showed a negative association with the incidence of COVID-19. This suggests that rather than the extension of the LULC category, the type of industry might be more relevant (as appreciated for agri-food industries).

On the other hand, agricultural areas and forested areas are more related to better air quality [34,38,98,99], which might lead to higher general health status. That, in turn, might explain the negative association for both categories with COVID-19 mortality. However, despite people remaining under lockdown during most of the period analysed in this paper, agricultural tasks were considered essential services. These tasks mainly include individual work and are frequently done outdoors. Additionally, agricultural areas tend to be less populated which increases social distancing. We hypothesise that these aspects might have prevented regions with higher agricultural areas to easily register COVID-19 cases.

Although forest and semi-natural areas showed a decreased risk of COVID-19 mortality, the increased risk for COVID-19 incidence was somewhat a surprising result. Forested areas are widely known for their air purification role [38]. Furthermore, vegetation can also lessen other determinant variables for aerosol dispersion such as wind speed. In the same direction, areas with an increased amount of forest are associated with less population density and hence, more physical distancing. In Catalonia, the BAHs with the highest amount of forest and semi-natural areas tend to be sparsely populated. Moreover, many of these BAHs held second residences, mainly belonging to people living in the Metropolitan Area of Barcelona, who may have commuted to the countryside as soon as the emergency state was declared [100]. In these regions, few cases can be translated into high incidence rates, which might explain the increased risk of COVID-19 infection for higher levels of forested areas.

During the first wave of the pandemic, people remained at home, decreasing human interactions. In future studies, LULC data might be leveraged encompassing variables such as population density, air quality, biodiversity and economic activities to further validate LULC data in scenarios with mobile people.

4.7. Limitations

We implemented a cross-sectional design, so we could not escape from many of the limitations of ecological regression analysis highlighted elsewhere [46]. One of the major constraints is that, when using these designs, causal inference cannot be spotted. Nevertheless, these studies do leverage data for an entire population (Catalonia in our case) and are able to make conclusions at the area level (e.g., BHAs), which might be useful for policy-making [46]. Furthermore, the associations detected in this paper can provide justification for ongoing or future research.

We did not study the evolution of the epidemic taking place later than the 18 May 2020. As for age groups, we only controlled for the percentage of elder people (>65 years). However, the advance of the epidemic has shown that many other age groups are vulnerable and should be considered in further analyses.

Controlling for other pre-existent health conditions such as obesity or respiratory illnesses and incorporating a greater variety of human mobility data (in scenarios with mobile people) such as the public transport network may enhance future research.

Although we controlled for significant differences for the pollutant concentration levels between 2016 and 2018/2019, accounting for the most recent modelling of the NO_2 and PM_{10} annual average ($\mu g/m^3$) in Catalonia may have improved the analysis as well. Furthermore, controlling for other air pollutants such as O_3 or $PM_{2.5}$, which have been described as relevant in previous research, might enhance future research.

In the same direction, the incapability for acquiring more updated data led us to use different datasets from different years for all the assessed covariates. However, the estimations found are consistent with previous research, which adds evidence as to the independent effect of the covariates assessed.

5. Conclusions

Recent literature has highlighted the importance of controlling for covariates in studies linking air pollution to COVID-19. We used a main model with demographic, socioeconomic and comorbidity covariates highlighted from previous research as important predictors. This allowed us to take a glimpse of the independent effect of each explanatory variable when controlled for the main model covariates. Our findings are aligned with previous research showing that the baseline features of the regions in terms of health status, pollutant concentration levels (NO_2 and PM_{10}), type of agri-food industry and type of land use and land cover have modulated the impact of the COVID-19 at a regional scale. A warning is made regarding future pandemics caused by respiratory infectious diseases. Thus, actions that improve air quality, diversify economic activities and enhance overall public health should be considered, not only to weaken the intensity of the current coronavirus, but for other virus-related problems expected to come.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/ijerph18073768/s1, Figure S1: COVID-19 incidence rate, data from the beginning of the epidemic to the 18th of May 2020, Figure S2: COVID-19 mortality rate, data from the beginning of the epidemic to the 18th of May 2020, Figure S3: NO_2 annual weighed average in $\mu g/m^3$ at BHA level (2016), Figure S4: PM_{10} annual weighed average in $\mu g/m^3$ at BHA level (2016), Figure S5: Reclassification of the 25 categories of the Land Use and Land Cover map of Catalonia (2017) into the 4 broader categories, Figure S6: Odds ratios and 95% CI. Associations between COVID-19 incidence (in blue) and mortality (in red) and the rest of covariates. The main model controlled for demographics, socioeconomics, and comorbidity covariables. Human activity covariates as well as land use and cover covariates were included in the model separately.

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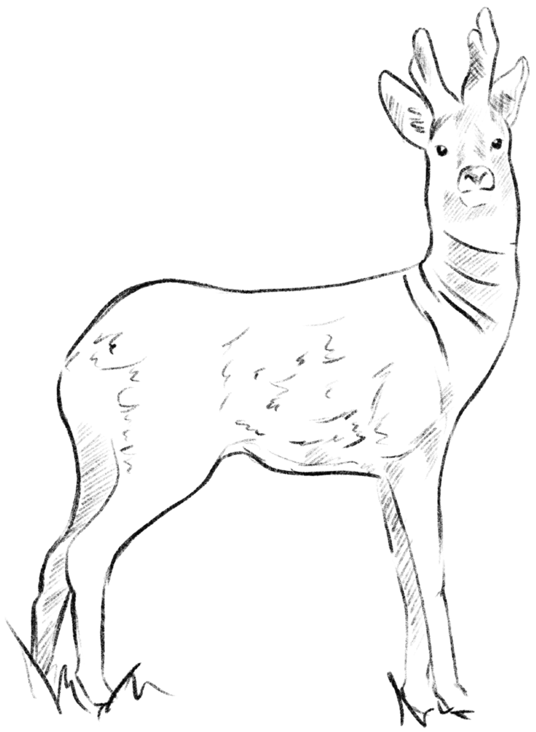

4. Discussion

This section discusses how the results derived from this dissertation contribute to this specific research field. The main contributions are structured according to the three research questions (RQ). In addition, a Future Research subsection shows two pieces of research that could stem from the findings of this thesis.

4.1 Main contributions

In general, all three research chapters conducted contribute to achieving our main goal. First, we reviewed previous literature relating LULC data to human health. Then, we performed an in-depth analysis of the LULC data-related limitations stated in the field and proposed and tested a methodology to take into account the compositional nature of LULC data. Finally, we showcased a case study screening the effect of LULC data on the incidence and mortality of COVID-19 in Catalonia during the first wave of the pandemic (2020).

Furthermore, in all three chapters, we have defined a process in which LULC data can be easily used and analysed to detect the independent effect of different types of environments on the human health assessed data. We have called this process the *Complex environment procedure*, and we present it as our main contribution 4.

4.1.1 Main contribution 1

RQ1: *How has LULC data commonly been employed in studies relating LULC data to human health outcomes?*

In RCH1, we showed that the LULC dataset is increasingly used in health studies. However, most of the reviewed studies linking LULC data to human health use a simplistic approach regarding the description of the environment (using the dataset to detect percentages of greenspaces (Bixby et al., 2015; Mitchell and Popham, 2008; Roe et al., 2013). We only found one article (MacKerron and Mourato, 2013) focused on the effect of the percentages of LULC categories.

In our review, we also showed that the relevance of the LULC dataset lies in the use of the LULC categories, which are able to characterise the environment holistically, measuring both the biophysical and the socioeconomic features. Different types of environment have previously been suggested to affect human health distinctively (Astell-Burt and Feng, 2019; de Vries, 2019b; Wheeler et al., 2015; White et al., 2013). Thus, for a more robust and complete analysis of the effect of the environment on human health, we stress that LULC categories should be considered in the analysis.

In a nutshell, the findings of this thesis have provided evidence of the principal drawbacks of the state-of-the-art methods and widely use practices. They can be summarised as follows:

1. Most studies still describe the environment simplistically as the “amount of green”.
2. Many authors report challenges in dealing with LULC data.
3. There are no apparent clues about how to measure the living environment.
4. There is a lack of causal inference between LULC data and human data derived from a lack of longitudinal studies.

These four key points help identify new considerations on which researchers should focus on.

4.1.2 Main contribution 2

RQ2: *How can LULC data be used to better assess its effect on human health?*

As we showed in RCH1, many authors reported challenges when dealing with LULC data. In order to solve these challenges, some original practices were displayed. For instance, using quantile divisions (Lachowycz and Jones, 2014; Mitchell and Popham, 2008; Mytton et al., 2012; Wu et al., 2015), or creating equal interval groups (Richardson and Mitchell, 2010). However, in RCH2, we argued that the challenges arise because no research linking LULC data to human health data considered the compositional nature of LULC data.

We showed that when a vector of proportions of specific LULC categories is calculated for a geographical region, this vector will always have the sum up constant constraint since the categories will sum up 1 (Aitchison and Egozcue, 2005; Leininger et al., 2013). To properly use LULC data in the analysis, we proposed the isometric log-ratio (ilr)-orthogonal transformation defined by (Müller et al., 2018), moving the compositions (vector of proportions of LULC data) from the Aitchison geometry to the Euclidean geometry. In the RCH2, we demonstrate that the ilr-orthogonal transformation is a feasible and straightforward step that allows researchers to conduct traditional environmental epidemiologic analysis offering a considerable improvement regarding of the environment description and analysis.

Since the ilr-orthogonal transformation was tested in both RCH2 and RCH3, we also demonstrate that LULC categories can be brought into the analysis without giving rise to challenges such as multicollinearity (Dumuid et al., 2020). Hence, the focus of the result discussion is on the many biophysical and socioeconomic features gathered in LULC category definitions and the pathways linking their effect on human health, offering a much more complete analysis.

For instance, RCH2 identified a predominantly reduced risk of type 2 diabetes mellitus (T2DM) for the broad-leaved forest. Among all the forest types used in the analyses, the broad-leaved forest usually has smooth slopes, comfortable temperatures and is more accessible. So, the reduced effect might be explained by the fact that environmental

elements mentioned above can promote physical activity (Coombes et al., 2010; Ho et al., 2021). Another example was given for urban areas, which showed an increased risk of asthma for poorer areas. This effect could be explained by the built environment features of poorer areas, such as increased pollution levels (Bolte et al., 2010; de Vries et al., 2003; Su et al., 2011). Finally, for waterbodies, results showed a predominantly reduced risk of anxiety which could align with the theories on the beneficial effect of water for mental health (Han, 2007; Orians and Heerwagen, 1992; Ulrich, 2016, 2014) (due to, for example, the negative ions in the atmosphere (Jiang et al., 2018; Perez et al., 2013), water sounds (White et al., 2010) and even the blue colours (Wan et al., 2020)).

In line with this, in RCH2, we also showed that the pathway framework proposed by (Markevych et al., 2017) could be leveraged since it comes in handy to discuss the effects of the biophysical and socioeconomic features of the types of environments on the health conditions. In this sense, we hypothesised that T2DM could be related to the environment through the instoration pathway (or the capacity of different environments to promote physical activity) and the mitigation pathway (regarding air pollution and traffic noise exposure). Likewise, asthma could be related to the environment through the instoration pathway (regarding microbial exposure) and the mitigation pathway (regarding air quality). Finally, anxiety could be related to the environment through the restoration pathway.

Although it can be argued that the selection of the pathway is not always easy, and in many cases, many pathways intertwine (Hartig et al., 2014), we showed that the use of the pathway framework is helpful to contextualize results derived from the analyses.

One significant note from our population-based approach is the following. As we analysed data representing the entire population of Catalonia (both environmental and health data), inference information gathered in the p-values has little relevance. This particularity, highlighted in RCH2, emphasizes the fact that studies using an observational approach over an entire population are running the model to describe a particular situation at a given time. Thus, they should consider confident intervals just for the precision of the estimations.

Finally, when using LULC data, we selected a level of accuracy in the LULC categories low enough to allow representativity of all categories and high enough to allow the running of regression modelling. Arguably, the higher the level of accuracy in LULC categories used in the analysis, the better, but this might imply conducting other analytical techniques which are highly nonlinear (for instance, black boxes techniques), which was out of the scope of this research. Instead, we based our contributions on enhancing standard practices in the field of environmental epidemiology, such as statistical regression analysis.

4.1.3 Main contribution 3

RQ3: *Is LULC data useful to assess the territorial distribution of COVID-19 incidence and mortality during the first pandemic wave in Catalonia (2020)?*

RCH3 provides a practical example to apply all the expertise derived from the first two RCHs. Thus, RCH3 can be better understood as a case study. Here, we investigated the effects of air pollutant concentration levels and type of agri-food industry on COVID-19 incidence and mortality in Catalonia at the area level. Completing the analysis, we screened the effect of four broad LULC categories on COVID-19 incidence and mortality. This complimentary analysis provided extra insights, which helped us to discuss the territorial distribution of the COVID-19 impacts.

For instance, we showed that increased air pollution, aerosol emission, human mobility and higher population density of urban areas and industrial, commercial and transport units (Hidalgo et al., 2008) could explain the increased risk of COVID-19 mortality. Likewise, the negative association between industrial, commercial and transport units and COVID-19 incidence might suggest that rather than the extension of LULC category per se (which was the variable measured in this complementary analysis), the type of industry might be more relevant (as appreciated in the results for agri-food industry types). In the same way, the reduced risk of COVID-19 incidence and mortality for agricultural areas might be explained because those regions are arguably associated with smaller populations, which increases social distancing. Finally, forested areas' landscape architecture and functionality, associated with a purified atmosphere (Liu et al., 2015), might explain the reduced risk of COVID-19 mortality shown in forested areas.

In this RCH, we also showed that the results discussion could also leverage the pathway framework mentioned in RCH2. In particular, the mitigation pathway, which highlights nature's capacity to reduce harm. In this sense, the presence of forest could be a protective factor reducing the risk of COVID-19 lethality, as COVID-19 mortality has been related to long-term exposure to air pollution (Domingo et al., 2020), and forested areas and green spaces have been associated with lower levels of air pollutant concentration (Nowak et al., 2014).

4.1.4 Main contribution 4

The findings and knowledge derived from the three RCHs can be summarized in the main contribution number 4. Throughout our research, we wanted our contributions to fit inside the standard structure of traditional environmental epidemiologic analysis linking LULC data to human health. Thus, the outline procedure which was followed consisted of three main phases: the environment description (LULC data), the analysis of LULC data and health data (statistical regression) and the result discussion (from the regression coefficients assessed in regression modelling). Following this same structure, we summarized the knowledge acquired in this thesis in what we will call the *Complex environment procedure*. This procedure is carried out for each of the aforementioned

phases, proposing certain features that enhance the assessment of the relationship between LULC data and human health in population-based studies (see Figure 5).

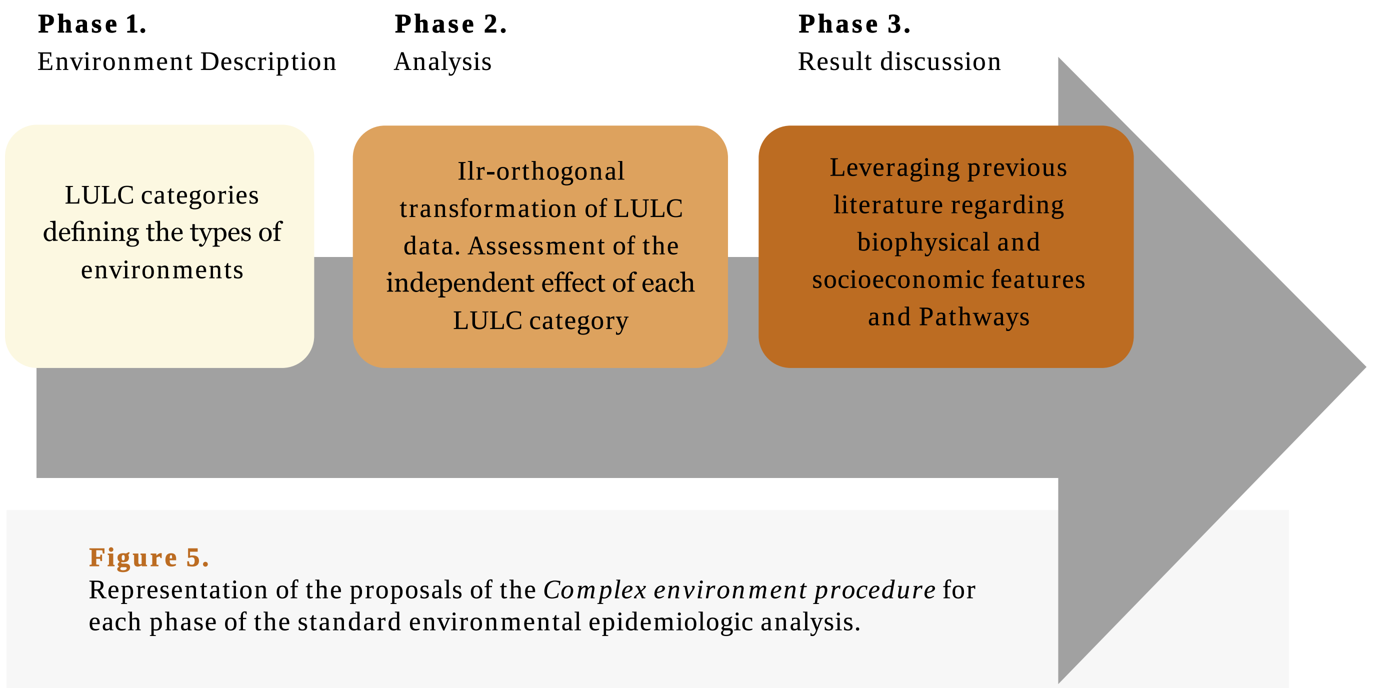

Figure 5.
Representation of the proposals of the *Complex environment procedure* for each phase of the standard environmental epidemiologic analysis.

Through the *Complex environment procedure*, we move away from the simplistic conception of the environment as something "green". Instead, we conceive it as a complex entity that integrates many biophysical and socioeconomic features that interact in a certain way that define but do not limit each type of environment (LULC categories). From this holistic notion of the environment as a central pillar, for the first phase (environment description), we propose that the environment is defined using LULC categories with a level of accuracy determined by the study's research question. One option is using broader types of environments, which can be accomplished by grouping the fundamental LULC categories of the LULC dataset. For instance, in RCH2, we reclassified the prior 23 LULC categories of the Land Use and Land Cover map of Catalonia (Spain) from 2012 into eight major groups of categories: agricultural areas, bare land, coniferous forest, broad-leaved forest, sclerophyll forest, grassland and shrubs, urban areas, and water bodies. In RCH3, we reclassified the prior 25 categories of the LULC map of Catalonia (2017) into four broader groups of categories: urban areas, industrial, commercial and transport units, agricultural areas and forest and semi-natural areas. In both cases, we wanted to broadly assess the effect of major LULC categories on health conditions as this was adequate for our research questions.

Another option is using more detailed types of environments. The most specific types of environments are inevitably restricted to the fundamental categories and the level of resolution of the LULC map. However, if necessary, researchers could create their LULC map beforehand by combining specific GIS information that better suits the purpose of their study. As pointed out elsewhere (Winkler et al., 2021), although LULC data is of the highest importance, sometimes LULC datasets are not available to fulfil specific research purposes.

In RCH1, we showed that a clear environment definition is not usually provided. Thus, defining the environment through LULC categories ensures that the environment is easily described beforehand. Hence, a set of biophysical and socioeconomic features is created for each type of environment, which helps keep track of all the definitions through the study and allows comparability and replicability.

For the second phase, the analysis of LULC and health data, we propose that the vector of proportions of LULC categories is transformed using the ilr-orthogonal transformation proposed by (Müller et al., 2018), which takes into account the compositional nature of LULC data. Using the transformed data in the analysis, we show that the independent effect of each LULC category on the health data can be assessed.

Finally, after the data modelling, the results discussion of traditional environmental epidemiologic studies commonly revolves around the values of the estimated coefficients. If a simple characterisation of the environment is used (for instance, the amount of green), the debate only exists at the level of the magnitude of the effect, meaning if it was high or low. Alternatively, the estimated coefficient can be compared with other studies that have used the same methods. However, using the *Complex environment procedure*, we demonstrate that a more complete result discussion is possible, allowing comparability with previous literature relating specific biophysical or socioeconomic features to human health and leveraging the pathway framework (Markevych et al., 2017) to better contextualize the results.

Using the *Complex environment procedure*, we prove that LULC data can suitably and reliably describe the environment since, unlike other environmental datasets, they can provide a holistic definition, incorporating the nature-human interconnections. We also show that this perspective aligns with the notion of the environment as a complex system (e.g., the environmental elements, interactions, scale invariance properties and hierarchical structure (Ladyman et al., 2013)). Thus, the findings of this thesis may especially motivate researchers in the field of complex system theory.

Furthermore, through the *Complex environment procedure*, we demonstrate that a more thorough analysis of the relationship between the environment and human health can be carried out, which is especially useful to draw or test hypotheses. Moreover, researchers can easily apply this procedure to complement their existing analysis, providing insightful information about the possible effects of biophysical and socioeconomic features of the types of environments on the analysed health data.

4.1.5 Additional notes

Some authors have stated that multidisciplinary science is required to understand and predict Global Change's challenges and that a unifying framework for complexity facilitates this collective endeavour (Wiesner and Ladyman, 2019). In the same way, in socioecology, some authors have pointed out that a complex systems approach for socio-ecological systems is crucial to sustainability research and practice (Epstein et al., 2020; Lu et al.,

2019; Reyers et al., 2018) and supports solution-oriented research for *Anthropocene* problems (Verburg et al., 2016).

Through the procedure presented in this dissertation, we have proved that a thorough exploration of the environment-human health relationship is possible. This procedure leverages interdisciplinarity science and allows the conception of the environment through a complex lens. Thus, it stands out as a reliable tool to analyse Global Change's challenges and *Anthropocene* problems.

Regarding the environment-human health relationship, some authors have highlighted that this relationship is complex and deserves a distinctive assessment (Arora, 2021; Arora et al., 2020). In order to acknowledge the complexity of the environment-human health relationship in this research, we have put into practice the One health approach, which is based on the principle that human health is not isolated from but is dependent on animals, plants and the environment's health.

The outcomes of this thesis are aligned with the seventeen Sustainable Development Goals (SDGs) from the 2030 Agenda of the United Nations (A New Era in Global Health, 2017), and tangentially, cover the majority of them. Specially, we cover the SDG number 3: Good health and well-being, ensuring healthy lives and promoting well-being at all ages; SDG number 13: Climate action, taking urgent action to combat climate change and its impacts; and SDG number 15: Live on land, protecting, restoring and promoting sustainable use of terrestrial ecosystems, sustainably managing forests, combating desertification, halting and reversing land degradation and halting biodiversity loss.

Furthermore, we hope that the contributions outlined in this thesis serve as the basis for policy-making, and they might help raise awareness of the importance of nature conservation, fostering a new perspective based on sustainability in which nature is not only a set of natural assets at human disposal but the home of all Earth's living beings, humans included.

4.2 Future research.

In carrying out this research, we have uncovered two relevant new pieces of research that stem from the findings of this thesis.

4.2.1. Explore the impact of the living environment characterization

In this thesis, we considered the living environment of individuals to be the same geographical units of analysis as health data were derived from (the Basic health areas). However, some research advocates using circular or radial buffer around individuals' neighbourhood centroids (i.e. ZIP code, census tract) or home addresses (Reid et al., 2018). Moreover, others generate more complex shapes based on road-network distances (Higgs et al., 2012). Both the use of administrative zones (as in our case with BHA) and the selection of buffer areas are related to two significant problems: the modifiable area unit problem (MAUP) and the uncertain geographic context problem (UGCoP) (Reid et al., 2018). The former states that the spatial units of analysis chosen (the spatial resolution of the dataset and areal units of the spatially aggregated data) affect the analyses' results (Kwan, 2009). The latter states that the valid geographical unit affecting health may differ from the unit of analysis used (Kwan, 2012).

Our research provides the grounds to further develop this subject by analysing the impact of the buffer size (and thus, the impact of the living environment characterization) on human health conditions. This analysis will leverage knowledge from the complex system theory by investigating how LULC data information is distributed within buffer areas and assessing the distribution pattern in terms of entropy, considering the information within the buffer and the information between buffers. Following this approach, this research might also characterize the scale invariance property of geographical systems and reveal possible clusters of LULC distributions.

4.2.2. Longitudinal study designs

In the absence of longitudinal data for our studies, we conducted cross-sectional designs, which have proven beneficial to leverage data from vast populations and make conclusions at the area level. However, they do not allow inference about individual-level associations and causal inference (Wu et al., 2020). Likewise, most of today's research exploring the relationship between the environment and human health follows the above-mentioned cross-sectional designs.

Longitudinal analysis is considered to allow for causal inference between the studied variables. Moreover, it allows repeated observations of the same individuals over time, permitting comparability (Saez et al., 2019). Thus, moving to longitudinal designs would be highly advisable.

In order to explore the connection between LULC data and human health using a much robust analysis, we count on longitudinal health data (period 2011-2019) at the smallest administrative area in Catalunya, the census area. This data come from the Catalan Health Institute and represents almost 80% of the Catalan territory. In this future study, we will use Bayesian modelling, accounting for both spatial and temporal autocorrelation, to detect the causal relationship of LULC data on health outcomes over time. The analysis will use available environmental data such as LULC data and complement the environment description using quality-related environmental data such as biodiversity-related spatial data.

5. Conclusions

In this research, we have endeavoured to explore to what extent Land use and Land cover data are a useful tool to assess the effect of the environment on human health outcomes in population-based studies. Having finished the three research chapters, we can conclude with the following statements:

- The LULC data is a **reliable** and **suitable** environmental data source to describe the environment **holistically**, taking into account its **complexity**.
- **Biophysical** and **socioeconomic** features can be distinguished by describing the environment through LULC data, defining but not limiting the **LULC categories**.
- Unlike other environmental datasets, the LULC data leverages the **hierarchical organization** property of complex systems, adapting the level of accuracy in the definition of LULC categories according to the study purposes.
- Using the LULC categories in the analysis results in a more **complete** and **robust** assessment of the impact of the **types of environments** on human health, taking advantage of both the **previous literature** and the **pathway framework**.
- By analysing the impact of LULC categories on health data, researchers can maintain a **parsimonious analysis** while qualitatively investigating the impact of **many biophysical** and **socioeconomic features**.
- The proposed **ilr-orthogonal transformation** is a feasible and straightforward way to use LULC data information in the analysis by acknowledging its **compositional nature**.
- Researchers can easily apply the ***Complex environment procedure*** developed in this thesis to **draw** or **test hypotheses** and **complement** their studies by analysing the effect of LULC categories on the assessed health data. Furthermore, applying the ***Complex environment procedure*** can facilitate **replicability** and **comparability** among studies relating LULC data to human health data.
- LULC data is **steadily being used** among researchers analysing the impact of the environment on human health. Thus, the findings of this research are particularly adequate for researchers aiming to perform a more comprehensive analysis. Likewise, researchers in the field of **complex system theory** can benefit from the findings of this research. In particular, LULC data's advantages in analysing the environment as a complex system.

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