SCUOLA DI DOTTORATO
UNIVERSITÀ DEGLI STUDI DI MILANO-BICOCCA

Department of Sociology and Social Research

PhD program: URBEUR - Urban Studies (XXXII Cycle)

Social and Spatial Inequalities in Health in Milan: the Case of Type 2 Diabetes Mellitus

PhD Candidate: David Consolazio

Registration Number: 713211

Tutor: Prof. David Benassi

Co-tutor: Prof. Simone Sarti

Coordinator: Prof. Lavinia Bifulco

ACADEMIC YEAR 2018-2019

To my mum, she would be so proud.

Acknowledgments

This work would have not been possible without the support from many people.

First of all, I would like to thank David Benassi, wise and rigorous but nonetheless always smiling and fun supervisor, and Simone Sarti, with whom I would talk for hours about sociology and also much less serious stuff.

Special thanks go to Marco Terraneo, with whom I had the pleasure to work and learn so much during the last two years, and to Jonathan Pratschke, for his always kind and prompt methodological advices.

A very special thank goes to Antonio Russo and the people from the Epidemiology Unit at the *ATS Città Metropolitana di Milano*: Maria Teresa Greco, Laura Andreoni, Brunella Frammartino, Sara Tunesi, Rossella Murtas, Maria Elena Gattoni, Antonio Riussi, Laura Zettera, Anita Andreano, Monica Sandrini, Federico Gervasi, Angelo Mezzoiuso, Pietro Magnoni, Davide Guido, Adriano Decarli.

What a great time I spent in the lovely city of Maastricht! Many thanks to Hans Bosma, Annemarie Koster, Angelique Vermeiren, Isel van Noppen, the whole Social Medicine Department at Maastricht University and the members of *De Maastricht Studie*. Thanks to my *Vijverdalseweg* family: Romano, Anne-Gabrielle, Daisy, Kitty, Rachael, Silvia, AK, Evelyn, Eleonora, Jochen, Lio, and to my *Raccordement* family: Tiago, Ricardo, Peter, Csongor, Matteo, Clara, Katia. And of course, to Clyde, Anindita, and Isabel.

Muchas Gracias to the Latinos crew in Essex: José, Alba, Nuria, Juan, Matteo, Paola, Jim, and William. *Los quiero mucho… mariposa!*

Though we spent most of the time believing to be still in high school, a huge thank to my PhD mates Jim McNeil, Luca Calafati, William Otchere-Darko, Roei Bachar, Vanessa Turri. Thanks also to all the friends and colleagues in rooms 208 and 205. Thanks to *Casaloca*!

Thanks also to Luca Bottini, Fabio Quassoli, Marianna D'Ovidio, Gabriele Cerati, Emma Garavaglia, Alberto Vitalini.

How could I forget the wonderful people from the *Centro Studi Etnografia Digitale*? Thanks to Alessandro Caliandro, Adam Arvidsson, Stefania Barina, Massimo Airoldi, Guido Anselmi, Valentina Sturiale, Corina Iamandi, Davide Beraldo, Chiara Francesca Russo, Umberto Pellegrini.

Being a southerner, I would need too much space to thank one by one my whole family, so thank you all! Just a special mention for my dad and Paolino, they deserve it.

Thanks to all my closest friends. You know who you are, just wait for your beers.

The most special of all thanks is for Glo... I bothered her so much with sociology and health inequalities that I still wonder how she did accept to marry me during this PhD adventure! Thanks also to Gindo and Fiona, so tender, lazy and always hungry!

I spent three awesome years, and you have been part of them. Thanks.

Table of Contents

Abstract **1**
Introduction **5**
1. Social and Spatial Inequalities in Health: an Overview **8**
Introduction 8
1.1 Health 10
1.2 Health Differences, Health Inequalities 13
1.3 Explanations for Health Inequalities 15
The Artefact Explanation 16
Natural and Social Selection 16
Materialist or Structural Explanations 16
Cultural/Behavioural Explanations 17
1.4 A Theoretical Framework for Health Inequalities 18
1.4.1 The Fundamental Causes Theory 18
1.4.2 Social Epidemiology 23
1.4.3 The Social Determinants of Health 26
1.5. Spatial Inequalities: Neighbourhood Effects on Health 45
1.5.1 Contextual and Compositional Effects 49
1.5.2 Theoretical and Methodological Issues 51
1.5.3 Neighbourhoods and Health: Mechanisms and Pathways 52
Conclusion 56
2. Type 2 Diabetes Mellitus **60**
Introduction 60
2.1 Type 2 Diabetes Mellitus: an Overview 61
2.1.1 Diabetes Mellitus 61
2.1.2 Types of Diabetes Mellitus 61
2.1.3 Risk Factors for T2DM 63
2.1.4 T2DM Management 67
2.1.5 T2DM Consequences 68
2.2 Trends in Diabetes Prevalence 70
2.2.1 Worldwide 70
2.2.2 The Italian Case 74
2.3 Diabetes and Social Inequalities in Italy 79

2.3.1 Age and Regional Distribution 80
2.3.2 T2DM and Education 82
2.3.3 Diabetes, Education, Quality of Life 85
2.4 Diabetes and Social Inequalities: Mechanisms in Action 89
2.4.1 Socioeconomic and Political Context 90
2.4.2 Structural Determinants and Socioeconomic Position 93
2.4.3 Ecological Determinants 97
Conclusion 99
3. Social and Spatial Inequalities in Type 2 Diabetes Mellitus in Milan: a Multilevel Study 101
Introduction 101
3.1 Background 101
3.1.1 Individual SES 103
3.1.2 Neighbourhood SES 104
3.1.3 Defining Neighbourhood 107
3.1.4 Research Questions 109
3.2 Methods 109
3.2.1 Study Population 110
3.2.2 Measures 110
3.2.3 Statistical Analysis 114
3.2.4 Missing Data 116
3.3 Data Presentation 118
3.4 Results 126
3.5 Discussion 140
3.5.1 Methodological Caveats 143
3.5.2 Limitations 145
3.5.3 Strengths 146
Conclusion 147
4. Quality of Care in Type 2 Diabetes Mellitus Patients 149
Introduction 149
4.1 Background 149
4.1.2 T2DM Quality of Care Indicators: Glycated Hemoglobin (HbA1c) 150
4.1.3 Research Questions 151
4.2 Methods 152
4.2.1 Study Population 152

4.2.2 Measures....152
Glycaemic Control....152
HbA1c Targets....152
Educational Level, Deprivation Index....152
Confounders....153
4.2.3 Statistical Analysis....153
4.3 Results....153
4.4 Discussion....158
Conclusion....162
Conclusion....165
Appendix....169
References....186

Abstract

(English)

This PhD dissertation is aimed at studying health inequalities in the Italian city of Milan. Health inequalities can be defined as differences in people's health across the population and between population groups, which are attributable to individuals' socioeconomic status as a consequence of the uneven distribution of social, economic, cultural, and relational resources that enable people to reach their health potential (Sarti *et al.,* 2011). Moreover, people's health may also be affected by psychosocial and physical characteristics of the local environment in which they live, so that those living in disadvantaged areas may be at a higher risk of being subjected to worse health conditions (Macintyre and Ellaway, 2000; 2003).

Moving from the theoretical and conceptual foundations of the *Fundamental Causes Theory* (Link and Phelan 1995; Phelan *et al.,* 2010) and the *Social Determinants of Health* approach (Solar and Irwin, 2010; Wilkinson and Marmot, 2003) this work intends to provide both an accurate mapping of the distribution of health conditions within the Milanese territory – and its association with individual and contextual socioeconomic status – and to contribute to the debate on the presence of neighbourhood effects on health (Diez-Roux, 2004; Galster, 2012). We thus relied on an interdisciplinary approach, making use of tools and methods from sociology, epidemiology, and geography. A fine-grained study of disease distribution among the neighbourhoods of the city of Milan was missing, and we opted to focus on Type 2 Diabetes Mellitus in light of its typical association with both individual socioeconomic conditions (Agardh et al., 2011) and environmental characteristics (Den Braver et al., 2018).

Relying on the unprecedented use of administrative healthcare data provided by the Epidemiology Unit of the Health Protection Agency of the Metropolitan City of Milan, linked with data from the most recent Italian census, we performed a multilevel population-based case-control study, aimed at assessing the relative impact of individual and neighbourhood socioeconomic status on the propability of developing the disease. We additionally focused on the management of the disease and on the quality of care in the Milanese diabetic population, making use of specific indicators relative to the adherence to recommended guidelines for blood glucose assessment and to the levels of glycated haemoglobin in blood, a marker of compliance to therapy.

Our results confirmed the presence of a social gradient in the distribution of the disease, with an increasing prevalence in correspondence with lower educational attainment. Moreover, we found evidence of a spatial heterogeneity in the distribution of the disease, which was not entirely explained by individual socioeconomic status: the association between neighbourhood socioeconomic status and the probability of developing Type 2 Diabetes Mellitus remained statistically significant even after accounting for individual-level variables, suggesting a role of the context in shaping risk exposure independently of the clustering of individuals with similar characteristics in the same areas. Concerning blood glucose assessment, it appeared to be slightly influenced by patients' area of residence, but not by their own socioeconomic status, while, conversely, levels of glycated haemoglobin showed no significant territorial variability, but a slight individual socioeconomic status dependency.

In line with the existing literature, we found that individual characteristics still play a major role in explaining risk exposure, but also that the context where people live has a non-negligible effect and should be encompassed in the design of policies aimed at tackling the disease and reducing social inequalities at its onset. Concerning blood glucose assessment and glycated haemoglobin levels, these appeared to be less socially and spatially structured compared to the onset of the disease. Despite playing a role in mitigating disparities in relation to disease management and quality of care, there is evidence that the healthcare system alone is not able to effectively tackle existing inequalities, and that broader actions intervening in the structure that contribute to the generation and perpetuation of social and spatial inequalities are needed.

(Italian)

La presente tesi di dottorato si propone di indagare lo stato delle disuguaglianze di salute nella città di Milano. Si parla di disuguaglianze di salute in presenza di differenze negli stati di salute delle persone all'interno di una popolazione, o tra gruppi di individui, quando queste sono attribuibili alle condizioni socioeconomiche delle persone, in virtù dell'iniqua distribuzione di risorse sociali, economiche, culturali e relazionali che consentono a ciascuno di raggiungere il proprio potenziale di salute (Sarti *et al.*, 2011). In aggiunta, il raggiungimento di uno stato di salute ottimale può essere influenzato anche dalle caratteristiche materiali e psicosociali del contesto di residenza, esponendo coloro che vivono in contesti svantaggiati a maggiori rischi per la loro salute (Macintyre and Ellaway, 2000; 2003).

Muovendo dai presupposti teorici e concettuali della *Fundamental Causes Theory* (Link and Phelan 1995; Phelan *et al.,* 2010) e dall'approccio alla salute basato sui determinanti sociali (Solar and Irwin, 2010; Wilkinson and Marmot, 2003), questo lavoro si pone l'obiettivo di fornire una mappatura della distribuzione delle condizioni di salute all'interno del territorio milanese, contribuendo altresì al dibattito circa la presenza di *neighbourhood effects* sulla salute (Diez-Roux, 2004; Galster, 2012). Il lavoro svolto si basa sull'utilizzo di un approccio interdisciplinare, nel quale si fa ricorso a metodi e strumenti di tipo sociologico, epidemiologico, e geografico. Uno studio dettagliato della distribuzione sociale e territoriale di una patologia nei diversi quartieri della città è ad oggi assente, abbiamo dunque deciso di concentrarci sul Diabete Mellito di Tipo 2 alla luce della sua tipica associazione sia con le condizioni socioeconomiche individuali (Agardh et al., 2011), che con le caratteristiche dell'ambiente di vita (Den Braver et al., 2018).

Facendo ricorso all'utilizzo inedito di dati amministrativi del sistema sanitario forniti dall'Unità di Epidemiologia dell'Agenzia di Tutela della Salute della Città Metropolitana di Milano, in combinazione con i dati provenienti dall'ultimo censimento della popolazione italiana, abbiamo condotto uno studio caso-controllo multilivello, con l'obiettivo di esaminare l'impatto relativo delle condizioni socioeconomiche individuali e del quartiere di residenza sul rischio di sviluppare la patologia in esame. Inoltre, grazie all'utilizzo di specifici indicatori relativi all'aderenza alle line guide per il monitoraggio dei livelli di glucosio nel sangue e ai livelli di emoglobina glicata – un indicatore di aderenza al percorso terapeutico – è stato possibile focalizzarsi sulla gestione della patologia e sulla qualità delle cure nella popolazione diabetica milanese.

I risultati hanno confermato la presenza di un gradiente sociale nella patologia, con una più alta prevalenza rintracciabile nelle persone con titolo di studio più basso. È stata inoltre riscontrata un'eterogeneità nella distribuzione territoriale della patologia, la quale non viene tuttavia spiegata unicamente dalle condizioni socioeconomiche individuali: l'associazione tra condizioni socioeconomiche del quartiere di residenza e rischio di sviluppo del Diabete Mellito di Tipo 2 risulta infatti essere statisticamente significativa anche controllando per le variabili individuali, suggerendo un ruolo del contesto di residenza nel plasmare l'esposizione al rischio indipendentemente dalla concentrazione di individui con caratteristiche simili nelle stesse aree. In relazione agli indicatori di qualità delle cure, il monitoraggio dei livelli di glucosio nel sangue è risultato essere leggermente influenzato dal contesto di residenza del paziente, ma non dalle sue condizioni socioeconomiche, viceversa i livelli di emoglobina glicata presenti nel sangue non hanno mostrato una rilevante variabilità territoriale, in presenza tuttavia di una lieve associazione con le condizioni socioeconomiche individuali.

In linea con la letteratura di riferimento, è stato riscontrato che le caratteristiche individuali giocano un ruolo predominate nel determinare l'esposizione, ciononostante il quartiere dove le persone vivono esercita un effetto non trascurabile sulla salute e necessita di essere tenuto in considerazione nello sviluppo di politiche volte a contrastare l'incidenza della patologia e a ridurre le disuguaglianze sociali connaturate alla sua insorgenza. Nonostante alcune tendenze siano emerse in relazione al monitoraggio dei livelli di glucosio nel sangue e ai livelli di emoglobina glicata, questi fenomeni sono risultati essere decisamente meno strutturati da un punto di vista sociale e territoriale rispetto all'insorgenza della patologia. Pur essendo parzialmente in grado di mitigare le disparità in ambito di gestione della patologia e qualità delle cure, è evidente che il sistema sanitario da solo non può essere in grado di porre rimedio alle disuguaglianze sociali esistenti nel Diabete Mellito di Tipo 2, evidenziando il bisogno di interventi più ampi capaci di agire sulla struttura che contribuisce a generare e perpetuare le disuguaglianze sociali e territoriali in relazione alla patologia.

Introduction

Health is one of the most desirable aims to pursue in life as well as the prerequisite to achieve life goals and live a satisfactory life. Being both the means to reach specific targets and a target in itself, there are probably few other concepts with such a centrality in human life. It is thus surprising that sociology as a discipline has long neglected to explore the relationship between society and its individuals' health and disease conditions in a systematic way. This may have happened as a consequence of an implicit misconception of health as an individual phenomenon, rooted in people's biology, genetic, behaviours, choices, lifestyles, dispositions, and the like. Individual attitudes surely play an important role in shaping health and disease outcomes; however, they do not act in a social vacuum. They are socially embedded, just like the economy, the market, gender and family roles, deviance and criminality, migration, or any other social phenomenon. Health is a social phenomenon, and as such can be analysed through the lens and with the tools of social sciences. Given the intertwinement of strictly individual and broader societal factors in influencing health conditions, several disciplines had to interact with each other to begin to understand how health phenomena are socially patterned, lending and borrowing each other methods, techniques, theoretical models and paradigms. This led to the birth of various strands of research under the labels of *health sociology*, *sociology of health and illness*, *medical sociology*, *social epidemiology*, *social medicine*, as well as others. Sometimes improperly used as synonyms and sometimes overlapping, these fields of research focus from time to time on the social structuring of morbidity and mortality rates, on health and illness in relation to social institutions, on patient-practitioner relationships, and so on, sharing the common objective of studying the relationship between society and health (Cockerham, 2007; Conrad, 2005; Timmermans and Haas, 2008). From the 1960s onward, in the Anglo-Saxon context a consistent flow of research on *the social determinants of health*, begun to systematically assess to what extent socioeconomic conditions are able to structure health and disease outcomes. Since then, many studies were able to demonstrate the existence of *social inequalities in health* – or, more commonly, *health inequalities* – not merely as global differences in morbidity and mortality rates or access to care between poor and rich countries, but also as an uneven distribution of health conditions between individuals belonging to different social groups within the same society (Link and Phelan 1995; Phelan *et al.*, 2010; Solar and Irwin, 2010; Wilkinson and Marmot, 2003). Our work here fits precisely in this direction, being aimed at assessing how social conditions are associated with the onset and the

management of a specific disease – Type 2 Diabetes Mellitus – in a specific setting – the Italian city of Milan. To do that, we rely on administrative healthcare data provided by the Epidemiology Unit of the Health Protection Agency of the Metropolitan City of Milan – which have never been used for this scope before – together with data from the most recent Italian census. Type 2 Diabetes Mellitus is a chronic disease with increasing incidence and prevalence worldwide, leading some to refer to it as a new global epidemic (Lam and LeRoith, 2012; Zimmet *et al.*, 2001). Being its onset triggered by unhealthy lifestyles (overweight/obesity, unhealthy diet, lack of physical activity), Type 2 Diabetes Mellitus has been often studied to explore the pathways linking individual agency to the broader context in which it takes place, examining the extent to which a disease with such an individually-shaped risk profile can be instead strongly socially structured. The focus on the Milanese case is of particular interest for at least two reason. First, it allows studying social inequalities in health in a wealthy city of a high-income country with universal healthcare coverage, which is known to be one of the most efficient in the world. Finding that disparities in health conditions originate and persist in such a context would highlight that much still needs to be done to tackle health inequalities, as well as that a top-performing healthcare system alone cannot be conceived as a proper remedy to the issue. Second, we are interested in examining the distinct role of individual and neighbourhood socioeconomic status in shaping the health profile of a population, contributing to the debate about the presence of compositional and contextual effects for health phenomena. As many other diseases, Type 2 Diabetes Mellitus is not driven exclusively by individual-level risk factors, but also by contextual ones, in the way in which the psychosocial and physical environment in which people spend their lives can foster or inhibit the onset of the disease. Nowadays, *ad hoc* statistical techniques permit to disentangle the relative contribution of each level of exposure, overcoming the intrinsic methodological limits present at the origins of the *neighbourhood effects* debate within the urban studies literature. We thus believe that our work could be of interest both in light of the unprecedented information about the case study itself and as a methodological contribution to the wider literature in which is inserted. Concerning the first, to our knowledge no one attempted to map the distribution of Type 2 Diabetes Mellitus – or any other specific health outcome – within the territory of Milan before, nor to put the disease in relation to individual and neighbourhood socioeconomic conditions simultaneously in such a systematic way. Regarding the latter, beyond the specific case analysed, the study could add a piece of knowledge to the never-ending debate about the presence of relevant place effects on health and social outcomes in general.

In line with the tradition of studies focusing on the social and spatial distribution of health status, our research is the product of an interdisciplinary approach. Someone may like to define it as a study in the field of *social epidemiology, epidemiological sociology*, *urban sociology*, *urban health* or whatever other cross-disciplinary label. Our work draws its origins from the encounter between theories and methods – among all – from sociology, epidemiology, and geography, with a specific attention on the urban setting. However, we believe that it is far more interesting to focus on its contents and its findings rather than trying to locate it within a proper specific discipline.

This PhD thesis is structured as follows. The first chapter is dedicated to the presentation of the theoretical and conceptual frameworks from which the research takes place. Starting from the definitions of the concepts of health and health inequalities, we subsequently review the most relevant theoretical contributions explaining the pathways and the mechanisms linking socioeconomic conditions to health and disease outcomes, both at the individual and the environmental level. The second chapter provides an overview on Type 2 Diabetes Mellitus, its risk factors, management, and consequences. We show how the incidence and the prevalence of the disease have been changing in the last forty years worldwide, and how the disease is differently distributed among the Italian regions and according to some socioeconomic indicators, to have a first account of its social patterning. The third chapter is the core of this work, with the multilevel population-based case-control study aimed at assessing the probability of developing Type 2 Diabetes Mellitus in relation to individual and neighbourhood socioeconomic status in the Milanese population in 2018. Finally, the fourth chapter focuses on quality of care among people with Type 2 Diabetes Mellitus, again in relation to individual and neighbourhood socioeconomic status, making use of specific indicators of disease control and compliance to therapy.

Chapter 1

Social and Spatial Inequalities in Health: an Overview

Introduction

In his *The Birth of the Clinic*, Foucault (1973) drawn a distinction between *medicine of the species* and *medicine of social spaces*. The first concept refers to what is normally conceived as medicine, that is the pathogenic classification of disease, diagnosing and treating patients and finding cure. In this framework, the human body is studied in order to bring physiological processes under medical control, in a context where medicine's thinking is dominated by the search for cure and drugs as *magic bullets* (Dubos, 1959) to shoot into human bodies to restore order. On the other hand, the medicine of social spaces is concerned with preventing diseases, rather than curing them, focusing not so much on the individual body, but rather on contextual characteristics that affect people's health, such as public hygiene, medical care and policies. We can find traces of this conception back in the Greek physician Hippocrates' *On Airs, Waters, and Places*, where the author describes human well-being as influenced by a set of environmental factors, as well as – much later – in *On the miners' sickness and other miners' diseases*, one of the first systematic studies concerning the relationship between living habits and health, in which Paracelsus demonstrated that specific diseases common among miners were depending on their working conditions. Studies of this kind, aiming at assessing the social and ecological – instead of individual – foundations of health outcomes, can be considered pioneering contributes to what has been then called s*ocial epidemiology*. The idea that social conditions play an important role in affecting health outcomes is anything but recent. Durkheim's sociological classic *Suicide* (1897) was intended to explain different rates of suicide among various groups of population, suggesting that this act is not attributable merely to free choice, since there are social factors determining it. The four types of suicide he outlined – egoistic, altruistic, anomic, and fatalistic – are all dependent upon the relationship between individual and society. Even before, physicians such as Villermé (1830) and Virchow (1848a) identified social class and working conditions as crucial determinants of health and disease. As the increased risk of disease among the poor was progressively made clear by several studies, policies in developed countries started to aim at improving physical environments, sanitation, nutrition, and work conditions (Rosen, 1979), leading to a considerable increase in life expectancy and a dramatic decline in the incidence of several diseases, such as diphtheria,

measles, typhoid fever, tuberculosis, and syphilis (Link and Phelan, 1995). The fact that by the twentieth century in modern welfare states many of the factors linking socioeconomic status to disease were addressed, led some scientists to forecast a large reduction – or even the disappearing – of social disparities in health. Kadushin (1964), for instance, argued that Americans from the lower classes were no more likely to develop disease than those from the middle or upper classes, a statement that turned out to be absolutely wrong considering the evidence from research subsequently developed on the issue, which documented an enduring association between socioeconomic conditions and health.

In this chapter, we sought to outline a theoretical framework for the systematic study of this relationship, starting from definitions of health and health inequalities that take into account the social characterization of individuals' well-being. As we will see, this perspective does not intend to deny the individual determinants of health, such as genetic, personal choices, and behaviours. Rather, it considers health outcomes as a function of a set of different characteristics, questioning approaches that tend to overemphasize individually-based risk factors, claiming the need to contextualize them, focusing more on social and ecological factors. Such a choice could be more efficient in providing broad-based societal interventions able to produce substantial health benefits for individuals and groups (Link and Phelan 1995, Phelan *et al.*, 2010). The field of health inequalities – or social inequalities in health – is by its nature a multidisciplinary one, born from the convergence of medical and social sciences. Each of these disciplines provides specific theories and methods, in a way that sometimes in the most recent contributions in the literature it is difficult to discern from which specific field a study draws its origin. This is the reason why in this chapter we did not limit ourselves to present a framework through which understanding health inequalities, paying attention also to the historical development that accompanied the growing interest in studying health through new lens. Since the first attempts to shed light on the influence of social conditions on health, research on the issue has grown consistently, and together with it, the development of theoretical models accounting for the empirical evidence reached. Our purpose here was not to review all the conceptualizations of health inequalities available to date, but rather to show some specific models that stand out for their ability to synthetize the relationship between the factors involved, drawing on the findings from decades of empirical research on the issue. Therefore, we start discussing the possible explanations of health inequalities as identified by Black and colleagues, in what is probably the first systematic study of health inequalities in Europe, the so-called *Black Report* (Black *et al.*, 1980). Then, to understand the order and the

direction of the causal factors involved in the process of development of health inequalities, we relied on a description of *The Fundamental Causes Theory*, as proposed by Link and Phelan (Link and Phelan 1995, Phelan *et al.*, 2010). A detailed description of each health determinant was left to the presentation of the conceptual framework outlined by Solar and Irwin (2010), which is based on an accurate review of the most relevant efforts to systematize the current knowledge about the social determinants of health, such as Dahlgren and Whitehead's (1991) and Diderichsen's (Diderichsen *et al.*, 1998; 2001) models. Given the interest in analysing health inequalities not merely as a product of individual characteristics – such as education, occupation, and income – but also as a consequence of the surrounding physical and pyschosocial environment in which people live, we summarize the literature on the role of contextual effects on health as well. Driven by the development of new analysis techniques, researchers have increasingly put attention on the role of small-area characteristics – typically the neighbourhood – on health, trying not only to quantify them, but also to unveil the mechanisms through which the place of living may affect the distribution of health within a population. Despite this growing interest, the literature on the ecological shaping of health inequalities is not flourishing as the one concerning the more general social shaping. To date, Macintyre's list of factors (Macintyre *et al.*, 1993) and Galster's (2012) list of mechanisms determining territorial inequalities in health conditions are the most detailed theoretical contributions on the issue, whereas most of the literature is aiming at improving methodological approaches (Kawachi and Berkman, 2003).

1.1 Health

The definition of health is a debated topic, with several disciplines depicting the issue through the lens of their specific frameworks, instruments and objectives. Obviously, the most intuitive and immediate definition is the biomedical one, conceiving health as the absence of any disease or injury and putting it in relation with the concept of 'normality' of human body. However, it has been argued that such a definition fails in embracing the complexity and multidimensionality of a concept that cannot be conceived in a dichotomous and deterministic way, without considering the whole set of factors and circumstances contributing to define each individual's health conditions. Beyond the objective assessment through a medical diagnosis, the impact of a disease may lead to a variety of different situations according to personal characteristics, social, cultural, and economic resources, as well as the broader context in which someone lives. The extent to which objective physical conditions are able to affect what people can do in their life cannot be neglected while attempting to provide an exhaustive definition of

health. In this perspective, health and objective physical conditions are not synonymous, but rather the latter are just a part – a very relevant one – of the first, which is in turn a broader concept that needs to be defined according to a wider set of factors. Adopting this perspective, the World Health Organization (WHO) in its constitution defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO, 1948). Despite this definition has been criticized for being too broad and indefinite (Huber *et al.*, 2011), it encouraged researchers and institutions to expand the conceptual framework they used to referred to when studying health, going beyond the biomedical model and its boundaries (Jadad and O'Grady, 2008). Following this tendency, health can be defined not only in a negative, but also in a positive way, namely without considering just the presence of pathologies or limitations, but also the range of possibilities that an individual faces in the course of his life in order to carry out daily activities and live a satisfactory life. This contributed to frame the concept of health in terms of quality of life, related to physical, but also psychological, social and relational well-being (Ingrosso, 2006). Differently from the traditional medicine approach, this new conceptualization pay attention to the social dimension and meaning of health, that is subjected to a variety of nuances depending not just on the physical condition of the body, but also on the way in which the individual perceives his status in relation to what he can do and be. An emblematic example of this different characterization of the concept in the two fields comes from the distinction between *disease* and *illness*, as outlined by Eisenberg (1977). While the first is a biological condition, a biomedical phenomenon identifiable through a medical diagnosis, the latter deals with the social meaning of this condition, being a subjective and relational phenomenon. Thus, while the biomedical model assumes the universality of diseases and their invariability in relation to time and space, a social constructionist perspective of health (Brown, 1995; Conrad and Barker, 2010) emphasizes how the meaning and experience of health and illness are shaped by cultural and social systems, being strictly dependent on the context and the conditions in which people live. Obviously, this does not pretend to lessen the role of the medical conceptualization of health, labelling it as inappropriate. Rather, the idea is that each definition fits to the specific needs of the situation in which it needs be applied. The discrete distinction is crucial in the medical context in order to discern if a person is healthy or sick, so to proceed or not with the specific treatment he needs, while it would be reductive if applied with regard to the design of policies aiming at improving health conditions. In such a perspective, the concept of health needs to be defined in relation to a wide set of characteristics related not only with the presence or absence

of any pathology, but more broadly with the possibility for an individual to live his life actively, with the smallest degree of limitations possible. The connection between health conditions and ordinary life and the role played in society is present also in Cockerham, who describes health as the ability to carry out daily activities, and as "a prerequisite for the adequate functioning of any individual or society" (Cockerham 2007, 8), which is in turn in line with the definition of health as 'the ability to function' (Dubos 1978; Herzlich 1973). In this view, health is not only an aim to be pursued in order to reach a desirable state of being, but also a means, or better a precondition, through which individuals could reach other valuable aims in their life. Here, there is a strong contact point with Sen's capability approach (1983; 1985), in which he focuses not just on the valuable elements for individuals in order to get a healthy and satisfactory life (the so-called *functionings*), but also on the ability to achieve them (the *capabilities*). Thus, this approach offers a rich set of dimensions useful to define and evaluate health, even though Sen has not provided an exhaustive list of these *capabilities*, but just a general framework to approach the issue. However, this task has been performed by Nussbaum, who identified what she refers to as "central human capabilities" (Nussbaum 2003, 13), which are: *life*, *bodily health*, *bodily integrity*, *senses*, *imagination and thought*, *emotions*, *practical reason*, *affiliation*, *other species*, *play*, *control over one's environment*. In accordance with this conceptualization, Blaxter (1990) articulated a definition of health, which summarizes the contributions mentioned here, developing an efficient conceptualization shaped in a sociological way, including both objective and subjective components, considering the negative as well as the positive range, being relative and multidimensional. Specifically, each element involved in this conceptualization is conceived as follows:

- *Objective/Subjective*. The assessment of the state of health in relation to the biomedical model, in which "disease is defined as deviations of measurable biological variables from the norm, or the presence of defined and categorized forms of pathology" (Blaxter 1990, 3) should be just a part of the general evaluation of a person's condition. The objective indicators of the presence of a pathology or a state of infirmity are not enough to establish if a person is healthy or not; health should be considered also in relation to how a person feels, meaning how he perceives his condition independently of a medical diagnosis.
- *Negative/Positive*. Health can be classified in a negative way, such as being free of symptoms of illness or not having a disease or a disability diagnosed, as well as in positive one, meaning being physically fit and in a state of psychological and social well-being.

- *Relative*. What an individual conceives as health is not an invariant condition, being strictly dependent on the belonging to a specific social group, on gender, age, ethnicity, occupation, education, religion, and in general on whatever social and cultural values and condition.
- *Multidimensional*. The evaluation of an individual's state of health should be made relying on a wide range of indicators, in order to grasp as much of the possible nuances to which the concept is subjected. Basing on a single indicator, whatever it may be, could lead to focus on a very specific and limited connotation of health, bringing access to a partial knowledge of the phenomenon studied.

From this depiction clearly emerges what has been defined as the "essentially contested" (Senior and Viveash 1998, 5) nature of health, meaning that a single agreed definition of this concept cannot exist, since there is no consensus about what health and illness are, neither across disciplines nor within each field. However, what matters here is not so much to provide a universal definition of health, applicable to any strand of research. Rather, the intent is to highlight the peculiarity of the sociological definition of the concept, as counter-posed to the biomedical one, which is not rejected by social scientists, but included even if not considered exhaustive to define the concept.

1.2 Health Differences, Health Inequalities

Once outlined what health is, the better way to understand what health inequalities are is starting to describe what they are not. They are not health differences. People across and within different contexts are subjected to unquestionable and clear heterogeneities in health conditions: some people are healthier than others are. Nonetheless, this is not enough to properly talk about inequalities in health. Sociological theories accounting for the heterogeneity of health status can be traced back to two opposite perspectives: the *differences* and the *inequalities* paradigm (Lucchini and Sarti, 2009). On the one hand, theories referring to the differences paradigm are based on an individualized conception of health, which considers the single person, his genetic heritage and his behaviours and choices as the main factors contributing to his health status. From this biological and social Darwinist perspective, the most genetically endowed and health conscious individuals are more likely to reach the top of social stratification (Kitcher 2004; Sommers and Rosenberg 2003). On the other hand, approaches moving from the inequalities paradigm state that social characteristics are able to affect directly the distribution of health status across the population (Link and Phelan, 1995; Phelan *et al.,* 2010), focusing therefore on the social context and its capacity of shaping human behaviour. The controversy can be seen

also in the terms of the dichotomy *selection*/*causation* (Blane *et al.*, 1993; Cockerham, 2005; Mulatu and Schooler, 2002; Ross and Mirowsky, 1999) where the first paradigm considers health as the outcome of selective processes, while for the second health heterogeneities are directly or indirectly determined by the different distribution of socioeconomic resources across the population. Hence, when the observed heterogeneities in health conditions are proven to be the outcome of a socially structured disadvantage, deriving from social inequalities in the educational, occupational, and cultural sphere, it is possible to speak about inequalities instead of differences (Sarti *et al.,* 2011). More specifically, heterogeneities in health status can be defined health inequalities only when they are the product of existing social inequalities, which in the definition provided by Schizzerotto (1990) are objective and systematic disparities regarding the possession of social, economic, and cultural resources, with the related capacity to take advantage of these resources in order to maximize the propensity toward a full psycho-physical body efficiency. Basing on this definition, Sarti and colleagues (Sarti *et al.,* 2011) presented four elements useful to discern when differences in health conditions between individuals are properly definable as health inequalities, and not merely as health differences. First, the *socio-environmental context*, which is a set of properties of ecological dimension shared by individuals living in the same group (e.g. air pollution, the presence of good health services), and which affects groups independently of the individual characteristics of their members. Second, the *social conditions*, namely the material and symbolic resources proper of each individual, identifiable in the forms of capital outlined by Bourdieu (1986): social, economic, and cultural. Third, and obviously, there are *individual characteristics* determined by the biological capital of each person, namely his generic heritage. Finally, there are *health conditions*, declined in both negative (e.g. disease, illness) and positive (e.g. well-being) terms. According to these scholars, it is possible to speak about health inequalities only when differences in health conditions are associated with social conditions, at the same conditions of individual and socio-environmental characteristics[1]. In this perspective, while health differences are a matter of individual variability, being therefore someway unavoidable and

[1] At first glance, this definition seems to deny the role of the socio-environmental context as a contributor to the explanation of health inequalities. However, this theoretical model – which is aimed at describing health inequalities in an individual perspective – assumes that the context is *shared by* all the individuals of a group, a subpopulation. It is clear that, when differentials in health conditions are assessed between individuals exposed to different socio-environmental contexts (e.g. different subpopulations), that is not sharing the same exposure to some contextual risk factor, this higher-level dimension has a clear influence on health outcomes. Accordingly, the statement could be better rephrased as follows: *it is possible to speak about health inequalities only when differences in health conditions are associated with social conditions and socio-environmental characteristics, at the same individual conditions.*

acceptable, health inequalities are socially structured, and for this reason avoidable, unequal and unjust (Whitehead, 1991). Embracing this perspective, Terraneo speaks about a "health denied" (Terraneo, 2018) to the more disadvantaged, those in worse socioeconomic conditions, underlining both the moral dimension and the space for intervention to avoid inequalities. From this conceptualization, it is clear that health and diseases are associated with socioeconomic conditions through the resources available to each individual in relation to his social status, configuring differences in health outcomes as a matter of social inequalities. Pragmatically speaking, social inequalities in health are structured in different levels between societies, as well as within them. At a higher level, differences in health levels are visible between more and less affluent countries, strictly depending on the degree of social and economic development proper of each national situation, as well as their welfare and healthcare system, together with cultural predispositions and political leanings. This means that due to different structural socioeconomic characteristics, people across countries present different rates of mortality and morbidity, risk exposure, as well as limitations in ordinary life activities. However, the same differences – usually, but not necessarily, to a lesser extent – are observable within single countries, namely between different regions or areas – such as the typical Italian north/south divide – and, to a lower level, within the same city, relatively to the different distribution of health conditions across neighbourhoods, districts, blocks, or other local areas. The lowest level in this scale is reached by individuals: inequalities in health are undoubtedly rooted in their behaviours, but these are in turn affected by social and contextual conditions, so that analysing health inequalities in a micro perspective would not imply to deny their social origin and structuring.

1.3 Explanations for Health Inequalities

Resuming the discussion concerning the selection/causation dichotomy, the way in which we defined health inequalities implicitly assumes that we embrace a causation perspective. However, this does not intend to completely deny the possibility of selective pathways in the relationship between social conditions and health, but rather to relegate them as a minor contributor. Moreover, these are not the only possible explanations accounting for health inequalities. As empirical evidence linking socioeconomic conditions and health outcomes begun to become noticeable, several scholars attempted to provide a theoretical framework explaining the origin of this relationship. Here, we drew on one of the first contributions in this direction, presenting four possible explanations as articulated in *The Black Report* (Black *et al.*,

1980): a) artefact explanations; b) theories of natural or social selection; c) materialist or structuralist explanations; d) cultural/behavioural explanations.

The Artefact Explanation

This explanation states that both health and social class are artificial variables, and that the relationship between them may be an artefact of little causal significance. More specifically, this approach suggests that the way social class and health are measured may influence the apparent magnitude of, and trends in, observed inequalities in health (Macintyre, 1997). This explanation arose mostly as a consequence of limitations in data collection and data availability, in correspondence with the first attempts to measure health inequalities empirically. However, decades of research on the topic allowed us to safely state that among the four explanations presented, this is the only one not supported by empirical evidence, although some scholars have tried to endorse it (Bloor *et al.*, 1987).

Natural and Social Selection

As briefly introduced previously, this explanation relegates socioeconomic circumstances to the state of dependent variable, with health acquiring the greater degree of causal significance. This approach implies the presence of a real relationship between social class and health, with health determining socioeconomic conditions, and not the contrary. Thus, the unhealthy may be downwardly socially mobile, leading to a concentration of people with a higher risk of morbidity and mortality among groups of low socioeconomic status (Smith *et al.*, 1990). In this view, the term 'natural' has two connotations (Macintyre, 1997). First, it means biologically based, in the sense that health differences are a product of innate characteristics of the human being, such as his strength, vigour, disease resistance, etc.). Second – because of the first connotation – it means morally neutral, that is something about which there is no inequity or unfairness, and consequently nothing to be done to intervene and tackle differences in health conditions.

Materialist or Structural Explanations

The third explanation, which is the one that mostly explains differential in health conditions among individuals and groups, emphasizes the role of socioeconomic factors in the distribution of health and well-being. Therefore, this approach highlights hazards inherent in society, to which some people have no choice but to be exposed given the present distribution of income and opportunity status (Smith *et al.*, 1990). Macintyre pointed out the necessity to avoid confusion between the terms 'materialist' and 'material' (Macintyre, 1997). A *materialist*

explanation highlights the role of deprivation and resources distribution differentials as prominent causal factor for health conditions and inequalities. This is likely to happen through different pathways, which will be deepened later in this chapter. *Material* pathways include the direct influence of socioeconomic factors on health through the possibility of buying goods, accessing to services, and living in conditions that are valuable for health (e.g. buying healthy food and medicine, accessing healthcare, having a job with low risk exposure). However, a materialistic (or structural) explanation involves also the possibility of an effect of social conditions on health mediated by psychosocial pathways (e.g. negative life events, job control and autonomy, lack of social support, discrimination, etc.). Thus, it is the availability of a wide range of resources – which are not attributable just to the economic sphere – that structures people's opportunities to achieve desirable health outcomes. Given that these resources are differentially distributed among the population according to socioeconomic characteristics, the distribution of health conditions follows this class pattern, showing significant inequalities.

Cultural/Behavioural Explanations

This last approach is recognizable by the independent and autonomous causal role assigned to lifestyles and behaviours with respect to morbidity and mortality. The focus is on the individual as a unit of analysis, emphasizing unthinking, reckless or irresponsible behaviours or incautious life-styles as the moving determinants of poor health conditions. In this view, health-compromising behaviours such as poor diet, smoking, excessive alcohol consumption, lack of exercise, under-utilization of preventive healthcare, vaccination, and the like, are more prevalent among people of lower socioeconomic status, and this explains the distribution of health conditions across different groups of population. The fact that such behaviours are more common in the more disadvantaged individuals is undeniable; however, this explanation considers individual choices as if they were undertaken in a social vacuum, neglecting to contextualize human action in the social, cultural and economic setting in which they are embedded. The cultural/behavioural explanation implicitly embraces a rational action framework, according to which individuals act on the basis of their preferences, assuming the possession of all the relevant information necessary to guide their choices, with the aim of maximising their utility (Coleman and Fararo, 1992; Goldthorpe, 1998). However, it is widely accepted that such a theory fails to describe reality, where human action is driven by a more complex set of mechanisms (Green and Shapiro, 1996; Hodgson, 2012; Sen, 1977). Complete information about possible options and full knowledge about consequences of actions are often lacking; moreover, people's choices are not just rationally oriented, being affected by emotions

and strictly contingent to the range of opportunities determining the space of action. Thus, in relation to health-related behaviours, a cultural/behavioural explanation neglets to consider that health-threatening and health-damaging behaviour are mostly a product of social stratification, and not vice versa.

As stated, the four kind of explanations presented are not necessarily mutually exclusive. Stressing the structural foundations of health inequalities, Black and colleagues do not deny the possibility that, at least to some extent, differentials in health conditions may derive from alternative pathways. Deepening the issue, Macintyre (1997) highlighted how each explanation can be conceived in two versions, one 'hard' and the other 'soft', as listed in Table 1.1. Hard versions are intended to explain health inequalities excluding alternative explanations, whereas soft versions are more flexible, leaving space for other positions. Accordingly, the working group of the *Black Report* anticipate possible rejections of the significance of observed inequalities in health by raising, and then rejecting, the hard versions – but not the soft ones – of the artefact, selection, and behavioural explanation; however, when coming to the structuralist explanation, they embrace both the hard and the soft version.

Table 1.1: The two versions of explanations. Source: Macintyre, 1997.

Explanation	'Hard version'	'Soft version'
Artefact	No relation between class and mortality; purely an artefact of measurement.	Magnitude of observed class gradients will depend on the measurement of both class and health.
Natural/social selection	Health determines class position, therefore class gradients are morally neutral and explained "away".	Health can contribute to achieved class position and help to explain observed gradients.
Materialist/structural	Material, physical conditions of life associated with the class structure are the complete explanation for class gradients in health.	Physical and psychosocial features associated with the class structure influence health and contribute to observed gradients.
Cultural/behavioural	Health damaging behaviours freely chosen by individuals in different social classes explain away social class gradients.	Health damaging behaviours are differentially distributed across social classes and contribute to observed gradients.

1.4 A Theoretical Framework for Health Inequalities

1.4.1 The Fundamental Causes Theory

The idea of an effect of socioeconomic conditions on health is not a completely new one, since the relation between the two has raised interest already in the nineteenth-century, conducting

the physician Virchow (1848b) to define medicine as a social science, due to the strong association between indicators of poverty and health, noticed even then. Following Cipriani (2008), we can find pioneering studies of the relation between social conditions and health even before sociology emerged as an academic discipline and as a legitimate science. These groundbreaking studies are observable in Villermé (1840), Buret (1840), Engels (1845), and Le Play (1877), up to the famed contributes by Booth (1889) and Rowntree (1901). In general, the main purpose of these works was not specifically to assess the influence of social conditions on health, but rather to show – through empirical foundations – the disadvantage experienced by the working class during the period of the first industrial revolution. Nevertheless, the relevance of these contributions lies in being the first systematic attempts to bring evidence about the relation between social status and health conditions, as mediated by the living and working environment. Since then, many studies attempted and were able to uncover the social patterning of specific diseases, but it is just with Link and Phelan (Link and Phelan 1995; Phelan *et al.*, 2010) that is possible to find a strong theorization of the causal relationship between the variables in exam. The argument of the scholars is that epidemiological studies have been enormously successful in identifying risk factors for many diseases, heightening public awareness. However, most of this research have focused on risk factors such as diet, cholesterol level, hypertension, sedentary behaviour, exercise, smoking, and so on, that are relatively proximate causes of disease. Conversely, social conditions like education, occupation and income, but also sex, race and ethnicity, have received less attention, having been considered more distal factors in the causal chain leading to disease, and thus not deeply investigated. This is mostly the reflection of an implicit adoption of the differences paradigm, that is a flippant assumption that individuals have the full ability to make informed decision about their health, having complete control over their life, without being influenced by their personal and social background and by the overall context surrounding them. In such a perspective, would be reasonable to focus exclusively on individual risk factors, given that once the mechanisms linking them to disease are unveiled, everyone would equally benefit from the new knowledge generated, having the ability and the opportunity to intervene on his behaviours and choices to improve his health. Unfortunately, reality is different and Link and Phelan claim for the need to understand how people come to be exposed to individually-based risk factors. Therefore, without neglecting the importance of classical and pure epidemiologic studies in identifying risk factors, they emphasize the need to put attention on what they call the *risk of risk*. Once that we know that diet, exercise, smoking, and the like, are associated with a higher probability

of developing disease, we need to draw attention on why people come to be exposed to or protected from these risk factors, that is to what extent their lifestyles and behaviours are driven by social conditions. Relying on a massive flow of research in the previous forty years of social epidemiology, sociology of medicine and medical sociology, Link and Phelan provide numerous examples of this social patterning of disease, showing that a lower socioeconomic status is associated with lower life expectancy, higher overall mortality rates, higher rates of infant and perinatal mortality (Adler *et al.*, 1994; Buck, 1981; Dutton, 1986; Pappas *et al.*, 1993), and also with each of the fourteen major cause of death categories in the International Classification of Diseases (Illsley and Mullen, 1985), as well as with major mental disorders and many other health issues (Dohrenwend *et al.*, 1980; Kessler *et al.*, 1994). Starting from this evidence, the scholars elaborate two theoretical concepts that illustrate the critical importance of social factors in disease causation, which are the ideas of *contextualizing risk factors* and *fundamental causes*. The first concept refers to the need to contextualize individually-based risk factors in order to grasp why people come to be exposed to or protected from risk factors, and so to determine the social conditions under which individual risk factors are related to disease. In this view, researchers should ask themselves and inquire "what it is about people's life circumstances that shapes their exposure to such risk factors as unprotected sexual intercourse, poor diet, a sedentary lifestyle, or a stressful home life" (Link and Phelan 1995, 85) and so on, that is what expose people to a major *risk of risks*. Thus, researchers should explore the social origin of risks and find out if individually-based risk factors are context dependent, influencing health only in correspondence with a specific set of social conditions. Focusing on these factors is important, since efforts to reduce risk by changing individual behaviours may be ineffective without understanding the processes leading to exposure. For example, since there are powerful social, economic, and cultural factors shaping eating behaviours within a population, providing information about healthy diet to poor people and exhorting them to follow nutritional guidelines without an understanding of the context that leads to risk, would leave the responsibility for reducing the risk to the individual, with nothing done to alter the more fundamental factors that put people at risk of risk. Concerning the second concept, the persistent association between socioeconomic status and health, notwithstanding the dramatic changes in mechanisms linking the two, is the reason why Link and Phelan indicate social conditions as 'fundamental' causes of disease. According to the scholars, a fundamental cause of disease has four essential features. First, *it involves access to resources* "that can be used to avoid risk or to minimize the consequences of disease when it occurs" (Link and Phelan 1995, 87). These

resources range from economic factors to relational ones, including knowledge, money, power, prestige, social support, social network and the like, and they determine the extent to which individuals belonging to different social groups are exposed to different risk of morbidity and mortality. The effect of resources on individual health and well-being finds evidence in the fact that as new risk factors become apparent, people of higher socioeconomic status are more likely to know about and protect themselves from them, engaging in behaviours that allow avoiding jeopardization. Second, *it affects disease outcomes through multiple risk factors* and – third – as a consequence of this, *it influences multiple disease outcomes*. Fourth, *its association with health is reproduced over time through the replacement of intervening mechanism*, meaning that even when the profile of risk factors for a disease changes radically, the association with social conditions will endure because the resources entailed are transportable to new situations. Some classic examples about how social conditions operate determining disease outcomes will clarify the concepts. Up to the 1950s, there was no systematic evidence about the association between smoking and lung cancer. However, in the UK and the USA an increase in the rates of lung cancer, formerly defined as one "among the rarest forms of disease" (Adler, 1912) – was noted already by 1930s, with little knowledge about its causes. The credibility of these increases was also questioned as potentially caused by increased reporting and improved methods of diagnosis. At the same time, before the 1960s there was no evidence that smoking rates were higher among more disadvantaged individuals, those in with lower socioeconomic conditions, simply because there was no mechanism linking socioeconomic status to smoking (Link, 2008). However, in 1950 two seminal papers brought evidence about the link between smoking and lung cancer (Doll and Hill, 1950; Wynder and Graham, 1950), initiating a growing and incessant flow of research that culminated in 1954 with two prospective studies that unequivocally established a casual relation between smoking and lung cancer (Doll and Hill, 1954; Hammond and Horn, 1954). As a consequence of this, from 1954 onward research assessed the presence of a social gradient in smoking, with worse socioeconomic conditions associated with a higher probability of smoking. Conversely, people of higher socioeconomic status were less likely to start smoking and more likely to quit if they had started (Ernster, 1988; Hiscock *et al.*, 2012; Link, 2008; Novotny *et al.*, 1988;). The reason why after the publishing and dissemination of information concerning the link between smoking and lung cancer people of lower socioeconomic status showed higher rates of smoking – while before there was almost no difference between social groups – lies in access to resources. People of lower socioeconomic status had less opportunity to run across information warning about smoking

effects, being less likely to read newspapers or to discuss about health-related topics within the family or with colleagues, friends or peers. Moreover, even if they came across this information, they would have been less prone to change their behaviours in relation to it. However, it is not with smoking and lung cancer that was possible to first observe an association between social conditions, risk factors and disease outcomes. Formerly, the link between socioeconomic status and mortality was driven by infectious rather than non-communicable disease. Then, overall improvements in public health and medicine, together with a widespread access to care for poor people in modern welfare states, led to unprecedented decreases in rates of diseases like diphtheria, measles, typhoid fever, tuberculosis, and syphilis, followed by a decrease in social inequalities related to them. The fact that by the 1960s the majority of factors linking socioeconomic conditions to disease had been addressed, led someone to expect this association to wane, or even disappear (Kadushin, 1964). However, these predictions did not take into account the replacement of mechanisms involved in the relation between socioeconomic status and disease, with the emerging of previously weak or absent mechanisms, as illustrated in the case of smoking. Thus, the association between social conditions and disease persists despite the change in risk factors and disease, given that individual and groups of higher socioeconomic status are better equipped to take advantage of the new knowledge. This the case, for instance, of coronary heart disease, which decline has been greatest among people of higher socioeconomic status, given that they have been better informed about and more able to implement changes in health behaviours like smoking, exercise, and diet (Beaglehole, 1990). All these examples support the theoretical model proposed by Link and Phelan. Social conditions are related to multiple disease outcomes (in our examples lung cancer; infectious diseases; coronary heart disease) through multiple risk factors (respectively smoking; poor sanitation and access to care; poor diet, sedentary behaviours, and smoking). The link between the two is driven by different access to resources experienced by individuals or groups with different socioeconomic characteristics. Given this, those who are best positioned with regard to relevant social, economic, and cultural resources will be always less afflicted by disease and more likely to experience good health, regardless of the current profile of disease and known risk factors. This theoretical approach has clear research and policy implications: if one wants to alter the effect social conditions – the fundamental cause – on health and disease, one must address the fundamental cause itself. In a dynamic system in which risk factors, knowledge of risk factors, treatments, and patterns of disease are changing continuously, the association between social conditions and disease will endure because the resources involved are

transportable to new situations. Thus, focusing exclusively on individual risk factors would generate knowledge and interventions strictly contingent to the disease to which the risk applies, without altering the underlying mechanisms in the long run. On the contrary, contextualizing risk factors, focusing on what put people at risk of risks, would have an impact on many diseases at time, avoiding to rely on interventions aimed at changing behaviours that are socially structured and influenced by factors left untouched by individual-level interventions.

Link and Phelan have probably the merit of having first put order, clarified and systematized the relation between social conditions, resources, risk factors and disease outcomes, engendering a specific theoretical framework through which inquiring social inequalities in health. Nevertheless, despite lacking for a long time a theoretical conceptualization, a relevant tradition of research on the topic already existed long before the Fundamental Causes Theory, beginning in the early 1960s in the US with the birth of *Social Epidemiology* and in the late 1970s in the UK with *The Social Determinants of Health* paradigm.

1.4.2 Social Epidemiology

According to Susser (1973), epidemiology can be defined as the study of the distribution and determinants of states of health in populations. Since the pioneering studies that contributed to define this science, the focus has nearly always been put on the individuals, their diseases, and their proximate risk factors. The work of John Snow – known as the 'father' of epidemiology – on cholera epidemic in London (Snow, 1855) fits perfectly in this direction. Mapping out the spread of the disease, Snow realized that a common factor among the victims was the use of a communal water pump, which he removed, subsiding the outbreak. Since then, epidemiology has been successful in identifying and heightening public awareness of risk factors for several diseases, contributing to consistent improvements in infectious disease prevention and increases in life expectancy, mostly attributable to improvements in diet, housing, public sanitation, and personal hygiene, rather than to medical innovations (McKeown; 1979; Porter; 1997). Fostered by the increasing knowledge coming from epidemiological research, from the second half of the 19th century onward this process laid the foundations for what was subsequently defined as the *epidemiological transition* (Omran, 2005), namely the replacement of infectious diseases by chronic diseases as the leading cause of death, due to consistent improvements in public health and sanitation. Macintyre (1997) has framed the issue also in terms of a shift from *diseases of poverty* to *diseases of wealth*, referring to the fact that while infectious diseases (such as diphtheria, typhoid fever, tuberculosis, and syphilis) were traditionally predominant in the lower status individuals, chronic diseases (such as cardiovascular and respiratory diseases,

cancers, and diabetes) emerge in a situation of wider prosperity, when the average life expectancy is higher. Despite these great results, for more than a century epidemiology has focused nearly exclusively on individual risk factors, almost neglecting the potential influence of social conditions in shaping health and disease outcomes. It is just from the 1960s that, coming in touch with other disciplines, some epidemiologists started to claim for the need of attributing a prominent role to socioeconomic factors as determinants of health and disease. Contributions to the inclusion of social factors in the field of epidemiology came from a variety of disciplines, including physiology and psychosomatic, social, and preventive medicine, as well as medical sociology and health psychology, but also from within epidemiology itself (Berkman and Kawachi, 2014). The first mention of the term 'social epidemiology' appeared in a 1950 paper in the American Sociological Review (Yankauer, 1950), but the birth of the field is indicated to be a decade later, with several epidemiologists – among those we mention here John Cassel, Saxon Graham, Mervyn Susser, and Leonard Syme – who started to develop a distinct area of investigation in epidemiology centred on the health impact of social conditions, particularly cultural change, social status and status inconsistency, and life transitions. Even without referring to and giving a definition of social epidemiology, in a seminal article Graham (1963) suggested a union of sociology with the medical sciences in order to produce a new and more successful epidemiology, aiming at the understanding of the large-scale social patterning of disease, coherent with his theory of disease causation requiring social and biological data that are consistent with each other with regard to a specific disease. This idea of specific social circumstances leading to a chain of events in which specific behaviours are linked to specific diseases has been tackled more explicitly in the 1970s by the epidemiologists Susser and Cassel, who explored the "methodology controversies and paradigm shifts inherent in incorporating a deeper understanding of the social influences of disease into epidemiologic thinking" (Berkman and Kawachi 2014, 4). Arguing that epidemiology should broaden its base and move beyond its focus on individual-level risk factors, Susser (Susser and Susser 1996a; 1996b) suggested the shift from a *blackbox epidemiology* to a new *multilevel eco-epidemiology*, a *chinese boxes* model which takes into account both bio-chemical characteristics of human beings and broader contextual effects. Supporting the statement that epidemiology shares the study of population with other population sciences, such as sociology, human biology, and population genetics, he claimed for common methodology and conceptual ground with other sciences involved in the study of society. Susser pointed out that "states of health do not exist in a vacuum apart from people"

and, being people embedded in the societies where they live, "any study of the attributes of people is also a study of the manifestations of the form, the structure and the processes of social forces" (Susser, 1973, 6). Similarly, Cassel (1976), speaking about factors that are able to alter – both positively and negatively – human resistance to disease susceptibility, highlighted the role of "certain aspects of the social environment" (Cassel, 1976, 108). Among social and contextual factors, in Cassel stands out the role of relational ones, both in a situation of powerlessness – brought on by social disorganization, migration, discrimination, poverty, and low support at work – and in a protective way, with social support as the primary source of buffer for the individuals from the deleterious consequences of stressful and adverse situations. More recently, in the UK Rose (1992) has pointed out the need of pursuing a *population-based strategy*, instead of a *high-risk strategy*, since individuals are embedded in societies and populations. In this perspective, individuals' risks of illness cannot be considered in isolation from the disease risk of the population to which they belong. Here, there is an immediate connection with classical social theories, since this is exactly the same logic followed by Durkheim (1897) in discovering that the rate of suicide in a society is linked to collective social forces: yet the possible reasons for which individuals commit suicide are potentially infinites, the social rate of suicide remains predictable despite the change of people in societies. These are just some of the relevant contributions which led the way to a new paradigm – not an alternative, but rather an integrative one – in the field of epidemiology; however, here we are not as much interested in accurately reconstructing the origin of social epidemiology, as we are in pointing out a growing attention, among scholars of different disciplines, towards social conditions as determinants of states of health and disease in different populations and groups. Thus, adopting these theoretical and methodological developments, researchers are now suggested to incorporate the social context into explanations about individuals' health outcomes, in line with the definition of the new discipline outlined by Berkman and Kawachi:

> We define social epidemiology as the branch of epidemiology that studies the *social distribution* and *social determinants of states of health*. Defining the field in this way implies that we aim to identify *socio-environmental exposures* that may be related to a broad range of physical and mental outcomes. […] We focus on specific social phenomena such as socio-economic stratification, social networks and support, discrimination, work demands, and control rather than on specific disease outcomes. […] We suspect that the vast majority of diseases and other health outcomes such as functional status, disability, and well-being *are affected by the social world surrounding us all* (Berkman and Kawachi, 2014, 5-6; emphasis added).

Thus, in order to provide answers to the fundamental question of the discipline, that is how social conditions shape states of health and disease in individuals and populations, social epidemiologists have to deal with a variety of concepts, tools, and methods shared with other fields, such as sociology, psychology, economics, geography, demography, and biology, giving rise to a multidisciplinary approach widely adopted by scholars of different backgrounds.

1.4.3 The Social Determinants of Health

In the 1970s, about a decade later with respect to the USA and probably influenced by the pioneering works of the American colleagues, researchers in the UK started to inquire the social patterning of disease, contributing to the field not only with empirical evidence, but also with a broader theoretical framework providing possible explanations of health inequalities. Many years later, this led to conceptualization of *the social determinants of health* paradigm (Marmot and Wilkinson, 2006), a perspective adopted by the WHO as a standpoint through which studying and tackling health inequalities globally and locally (Wilkinson and Marmot, 2003; Solar and Irwin, 2010). This field of research started with the results coming from the so-called *Whitehall Study* (Marmot *et al.,* 1978), through which Marmot and colleagues provided strong evidence of social patterning of disease not only between different social classes, but also within social classes themselves. Analysing data about British male civil government employees, the scholars surprisingly discovered consistent differences in death rates in the population studied, made all of white-collar workers with stable, secure, and hazard-free jobs, all with free access to national healthcare. Despite the good positioning in the social ladder of everyone in the sample, the study shown that mortality was higher in the lower grade civil servants, especially for coronary heart disease. As Marmot states "in the higher grades of the civil service there is no poverty, yet those who are near the bottom have worse health than those at the top and the gradient continues all the way down" (Marmot 1996, 48). The Whitehall Study provided unassailable systematic evidence of the existence of a *social gradient* in health, meaning that shorter life expectancy and higher disease rates are more common further down the social ladder in each society. Nevertheless, this report was part of a long British tradition of studies assessing the existence of class variations in disease and early mortality, moving its step back in the middle of the 19th century, with Chadwick's (1842) analysis of mortality rates related to occupational status in Liverpool, resumed later by Humpreys (1887), who proposed social class classification as a tool to examine mortality differences, Stevenson (Registrar General, 1913), who pointed out the preventable and avoidable nature of a consistent percentage of infant mortality, and Titmuss, (1938) with his analysis of regional differences in mortality in different

parts of the UK. The element of novelty is that, through their results, Marmot and colleagues were able to demonstrate that social differences in health conditions are not limited to absolute poverty, that is to lack of resources ensuring the basic needs of human life; even when these fundamental necessities are fulfilled, the relative standing of individuals in society matters for health, characterizing health inequalities as a relative and relational phenomenon:

> Poor social and economic circumstances affect health throughout life. People further down the social ladder usually run at least twice the risk of serious illness and premature death as those near the top. Nor are the effects confined to the poor: the social gradient in health runs right across society, so that even among middle-class office workers, lower ranking staff suffer much more disease and earlier death than higher ranking staff (Wilkinson and Marmot 2003, 10).

These groundbreaking findings, together with the push from Wilkinson – who addressed an open letter to the Secretary of State for Social Services asking for efforts to inquire health inequalities and promote strategies to tackle them with policy interventions (Wilkinson, 1976) – led the Department of Health and Social Security to set up a working group on health inequalities in 1977. Three years later, *The Black Report* was published (Black *et al.*, 1980), a cornerstone for the inquire of social inequalities in health and disease for years to come. Driven by a growing body of research on the topic, Marmot and Wilkinson (2006) – similarly to what proposed by Link and Phelan, but more focused on stressing the mechanisms involved in the processes rather than providing a theoretical conceptualization – highlighted that the causes of the social gradient in health are to seek in the circumstances in which people live and work, and not just in individual risk factors for disease, as much of the modern epidemiology do (Pearce, 1996). Thus, they draw attention on the *causes of the causes*, a concept very close to the one of *contextualizing risk factors* mentioned above, as outlined by Link and Phelan. Following Marmot and Wilkinson:

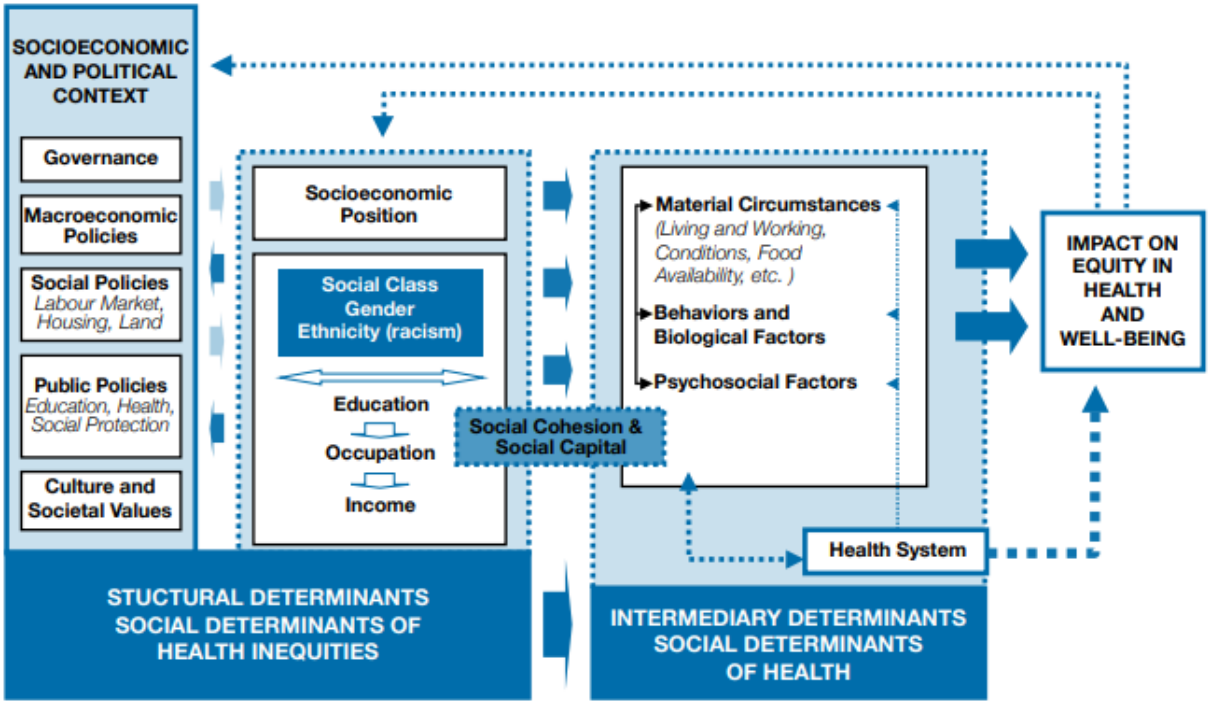
> It is not an accident that people consume diets high in saturated fat and salt. It represents the nature of the food supply, culture, affordability, and availability, among other influences. These are the *causes of the causes*. For example, given that smoking is such an important cause of premature disease and death, we need to understand the *social determinants* of smoking. In particular, in many rich countries now, there is a *social gradient* in smoking: the lower the socio-economic position, the higher the rate of smoking (Marmot and Wilkinson 2006, 3; emphasis added).

Again, the scholars do not pretend to deny the influence of genetic and behavioural factors on health, rather they claim for a prominent role of social and contextual characteristics in preventing diseases and premature death:

> […] the common causes of the ill health that affects populations are *environmental*: they come and go far more quickly than the slow pace of genetic change because they reflect the changes in the way we live. This is why life expectancy has improved so dramatically over recent generations; it is also why some European countries have improved their health while others have not, and it is *why health differences between different social groups* have widened or narrowed as *social and economic conditions have changed* (Wilkinson and Marmot 2003, 7-8; emphasis added).

Although Marmot and Wilkinson have been very effective in stressing the relevance of studying health inequalities and in highlighting the mechanisms underlying this phenomenon, they never attempted to provide an exhaustive conceptual framework aiming at describing the factors involved. This task has been well performed by Solar and Irwin (2010) in their conceptual framework developed within the Commission on Social Determinants of Health (CSDH), set up by the WHO and indeed chaired by Marmot. The final form of this framework is portrayed in Figure 1.1. The general model is consistent with Link and Phelan's fundamental causes theory, but it goes deeper in explaining the role of the factors intervening at each level.

Figure 1.1: Conceptual framework of health inequalities. Source: Solar and Irwin (2010).



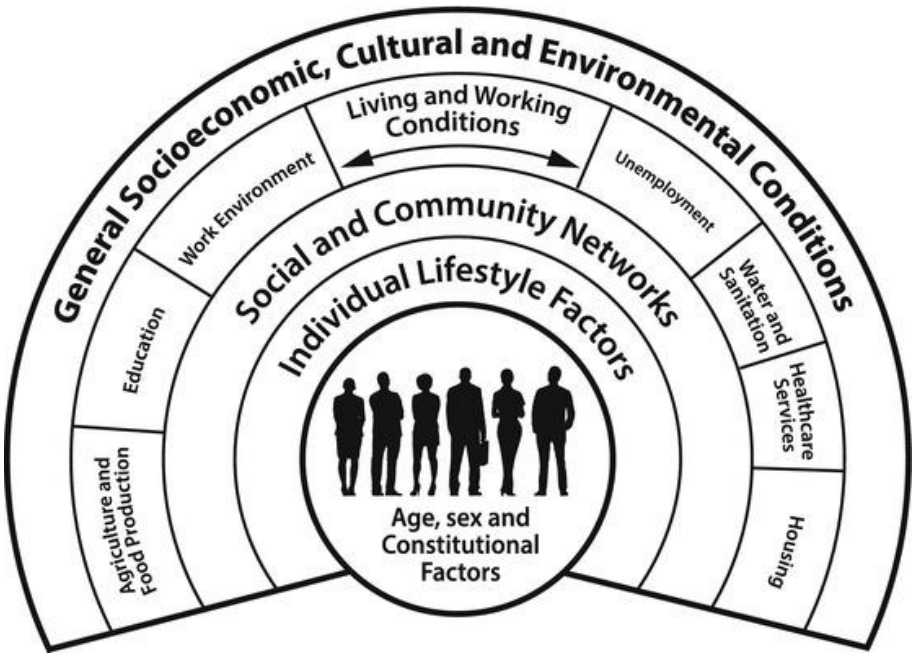
The conceptual framework shows how social, economic, political and cultural mechanisms give rise to a set of socioeconomic positions, whereby individuals are stratified according to their education, occupation, income, gender, race, ethnicity, as well as other factors. These socioeconomic factors in turn shape specific determinants of health status, which in the model are indicated as 'intermediary determinants', among which there are the proximate or

individually-based risk factors as outlined in the fundamental causes theory. These are reflective of individuals' place within social hierarchies and stratifications, in the sense that based on their respective social status, people experience differences in exposure and vulnerability to risk factors, diseases, and other health-compromising conditions. In this causation model, the authors leave space also for some selective pathways (the arrows going back from the health impact box to the structural determinants). Even if certainly a minor contributor, illness can feedback on a given individual's social position (e.g. by compromising employment opportunities and reducing income) or – though it is an extreme case – an epidemic could feedback to affect the functioning of social, economic, and political institutions. As structural determinants, the authors identify and describe two main set of factors influencing health conditions and shaping inequalities: the socioeconomic and political context, and the individual socioeconomic position (the first two rectangles in the figure). The first is broadly defined to include all social and political mechanisms that generate, configure, and maintain social hierarchies, such as the labour market, the educational system, political institutions, social and cultural values. Among all contextual factors, the authors indicate the welfare state as the most powerful factor affecting health, operating through its redistributive policies – or their lack. These structural mechanisms at the higher level are the ones contributing to generate stratifications and social class divisions in societies, defining individual socioeconomic position within hierarchies (different distributions) of money, knowledge, power, prestige and access to resources in general. In the CSDH framework, these two factors (the wider socioeconomic and political context and the socioeconomic position) are conceived as 'structural determinants', that is the real social determinants of health inequalities. These operate through a set of intermediary determinants (the third rectangle in the figure), which finally shape health outcomes. As Solar and Irwin highlight "the vocabulary of structural determinants and intermediary determinants underscores the casual priority of structural factors" (Solar and Irwin, 2010, 6) in generating social inequalities in health, a statement completely in line with the socio-epidemiological framework reviewed previously. In the model, three categories of intermediary determinants are listed: *material circumstances* (e.g. housing, neighbourhood quality, consumption potential, food availability, physical work environment, etc.); *psychosocial factors* (e.g. psychosocial stressors, stressful living circumstances, social support, coping styles, etc.); *behavioural and lifestyle factors* (nutrition, physical activity, tobacco and alcohol consumption). In addition to these, the CSDH framework – differently from many previous models – conceptualizes the healthcare system not as structural determinant, but rather

as a consequence of contextual and social characteristics, mainly through the issue of access. In this view, the health system plays an important role in mediating the differential consequences of disease and illness in individuals' lives. In-between structural and intermediary determinants, the authors place the concepts of social capital and social cohesion, which entail health-enhancing (or threatening) resources connecting the individual and the collective spheres.

The CSDH framework owes its conceptualization to many researches carried out in the previous decades, but specifically to two theoretical models developed earlier by Dahlgren and Whitehead (1991) and Diderichsen (Diderichsen and Hallqvist, 1998; Diderichsen *et al.*, 2001). Dahlgrend and Whitehead model (Fig. 1.2) shows the relation between the individual, the context, and his health conditions. In this view, health is affected by a range of factors, portrayed in concentric circles. The external layer refers to the major structural environment. Then, there are material and social conditions in which people live and work, as influenced by the educational, employment, and income opportunities, as well as by other structural conditions.

Figure 1.2: The main determinants of health. Source: Dahlgren and Whitehead (1991).

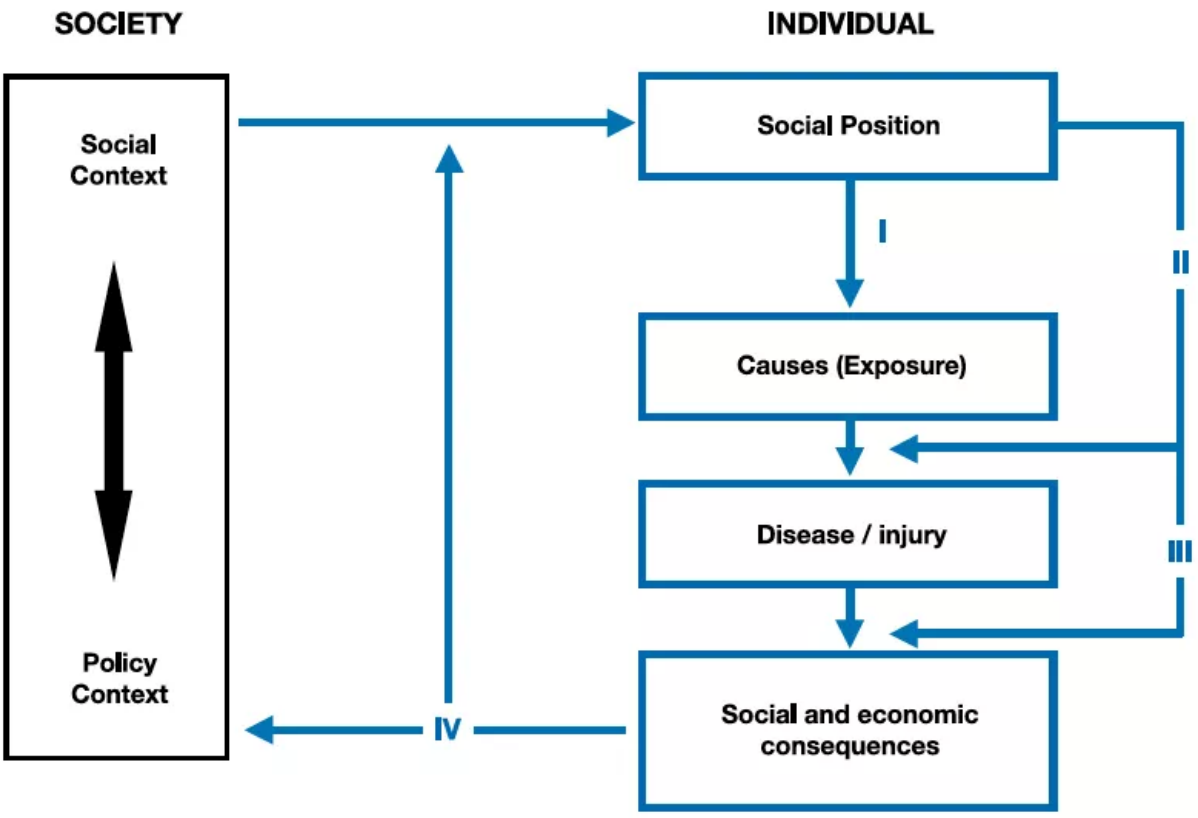


The third layer refers to the impact of social and community networks, which can be beneficial or damaging for the individual. Following, the layer closest to the individuals encompass lifestyle factors and behaviours, such as their diet, pattern of physical activities, smoking and drinking habits. The inner circle refers to individual biological conditions. The idea of this scheme, followed by Solar and Irwin, is that individual's health conditions are influenced by a

wide range of structural conditions, whereas "the age, sex, and the genetic make-up of each individual also play a part, of course, but these are fixed factors over which we have little control" (Dahlgren and Whitehead 1991, 11).

Diderichsen's model – which is explicitly recalled in the CSDH framework – focuses not so much on the factors influencing health conditions, but rather on the mechanisms that play a role in stratifying health outcomes. The model aims at emphasizing how social contexts create social stratification, assigning individuals to different social positions. Social stratification in turn engenders differential exposure to health risk and vulnerability, determining differential consequences of ill health for more and less advantaged groups. The model, portrayed in Figure 1.3, shows how both *differential exposure* (pathway I in the diagram) and *differential vulnerability* (II) may contribute to the relation between social position and health outcomes. Additionally, social position may affect not only the extent to which distinct groups are likely to experience different health conditions, but also the *differential consequences* (III) of this health conditions. The social and economic consequences of illness may feed back into the etiological pathways and contribute to the further development of disease in the individual (IV).

Fig 1.3: A framework for elucidating the pathways from the social context to health outcomes. Source: Solar and Irwin (2010) adaptation from Diderichsen et al. (2001).



The two models are far more complex and sophisticated than the way we presented them here; however, a deeper understanding of both factors/determinants and mechanisms/pathways leading to health conditions – and consequently to health inequalities – is left to the comprehensive specification of the CSDH framework, which we present in the subsequent paragraphs.

1.4.3.1 Socioeconomic and Political Context

The context "encompasses a broad set of structural, cultural and functional aspects of a social system, whose impact on individuals tends to elude quantification but which exert a powerful formative influence on pattern of social stratification and, thus, on people's health opportunities" (Solar and Irwin, 2010, 25). These factors cannot be measured at the individual level and involve those social and political mechanisms that generate social hierarchies, such as the labour market, the educational system, the welfare state or other political institutions. With this higher level, the CSDH framework aims at emphasizing the role of the political dimension in determining health outcomes. Despite a growing attention towards the social determinants of health, the way in which these are in turn shaped by policies that guide how societies distribute and redistribute material resources among individuals and groups has been substantially neglected by many researchers. As health depends on behaviours, lifestyles and group characteristics determined by access to resources, it is also the outcome of political forces and policy decisions made by governments. In the following, we report the main contextual factors exerting an indirect effect on health outcomes.

Governance

Governance "refers to all processes of governing, whether undertaken by a government, market, or network; whether over a family, tribe, corporation, or territory; and whether by laws, norms, power, or language. Governance is a broader term than government because it focuses not only on the state and its institutions but also on the creation of rule and order in social practices." (Bevir, 2013, 1). Relate to health, it embraces all the formal and informal systems and actors that contribute to define societal processes, needs, objectives, and opportunities that through their action impact on individuals and groups' well-being. It can be conceived as the overall set of characteristics affecting health conditions through the intertwining of macro, meso and micro factors and processes.

Macroeconomic, Social and Public Policies

Macroeconomic policies include – among all – fiscal, monetary, and trading policies, which are developed to stabilize national economy, reaching desirable levels of GDP and economic growth. The set of these characteristics underlies labour market structures, which are one of the factors most influencing health conditions in a population. Indeed, the most immediate way through which policies influence health is the resulting employment rate, defining the percentage of active population which is cut out from the occupational sphere, with consequent disadvantages in term of access to resources of various kind, such as economic, social, and relational ones. More specifically, labour market policies mediate between supply and demand, and the way in which such policies are implemented plays a fundamental role in fostering or reducing access to the labour market for disadvantaged individuals and groups (Benach *et al.*, 2007). Policies can contribute to directly match demand and supply, enhance workers' skills, reducing labour supply or increasing labour demand, and changing the structure of the labour market favouring the entry of the most disadvantaged. Such policies can be passive (e.g. unemployment insurance and assistance, early retirement) or active (labour market training, job creation, community work programmes, hiring subsides, programmes to promote enterprise creations). Obviously, the issue is not just one of quantity, but also of quality of the labour market. Labour market policies have a direct impact not only on the number of people employed, but also on working conditions, contributing to shape resource inequalities also among those inside the labour market. There are consistent differences, for instance, between those with full-time permanent employment and those with precarious employment, or between jobs with diverse hazard profiles and risk exposure. However, social and public policies affect a wide range of other factors, nearly all influencing health conditions and their distribution across the population. Examples are poverty reduction, social security, pensions, living conditions, pensions, healthcare, social housing, social exclusion, education policy, crime and criminal justice, urban development. Through such interventions, the welfare state attempts to redistribute resources, granting to everyone the same range opportunities to live in good health conditions, reached by economic and social well-being. Social policies may anticipate the problem of social inequalities or try to remedy this. In the first case, for instance, educational policies aiming at increasing educational attainment among the less advantaged could narrow the knowledge gap with the better off, as well as providing better working opportunities, resulting in better incomes and in a more equal distribution of key resources. Concerning the latter case, social housing is an example of policy aiming not at tackling the issue of

socioeconomic inequalities at its origin, but rather to fix it once it has already occurred. Thus, politics is a strong structural determinant of health, in the way in which it affects the distribution of resources across the population. This is clearly noticeable by the fact that countries exhibit distinctive levels of population health according to their regimes type, independently of their economic development. More specifically, comparative studies reported that Social Democratic countries showed significantly better health status compared to Christian Democratic, Liberal and Wage Earner countries, that those exhibited better population health status before neo-liberal reforms (Chung and Muntaner, 2006; 2007; Sakellariou and Rotarou, 2017), and that this achievement continued during the era of welfare state retrenchment (Huber and Stephens, 2010). A review of the literature indicated an association between politics expressed in terms of democracy, globalisation, political traditions, or welfare states and population health and health inequalities after adjustment for a common range of confounders (Muntaner *et al.*, 2011).

Culture and Societal Values

Albeit not so tangible as political and economic factors, culture and societal values are important yet often neglected contextual aspects able to affect health conditions and distribution. Countries differ in the social value attributed to health – the extent to which governments consider health a priority in their agenda, as reflected by the level of national resources allocated to healthcare – as well as in schemes of responsibility for health – the degree to which societies assume responsibility for financing, organizing and distributing the provision of health services (Kleczkowski *et al.*, 1984). Similarly, cultural beliefs, attitudes, practices, and behaviours affect social and health inequalities in several ways. For instance, gender and family roles, as well as racism, easily lead to discrimination in access to resources, while caste systems lead to legitimate inequalities in light of religious beliefs or sociocultural hierarchies.

1.4.3.2 Structural Determinants and Socioeconomic Position

The second range of structural determinants deals with the system of social stratification present in each society as a consequence of the inequal distribution of key resources, such as material, social, cultural and relational ones. Following Solar and Irwin, people "attain different positions in the social hierarchy according, mainly, to their social class, occupational status, educational achievement and income level. Their position in the social stratification system can be summarized as their socioeconomic position" (Solar and Irwin, 2010, 28). Social class, socioeconomic position, socioeconomic status and other similar concepts have different

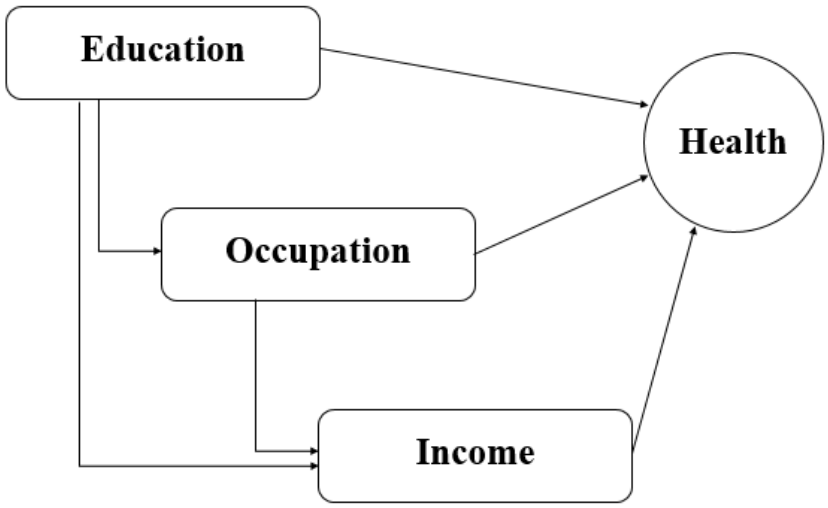
meanings in the sociological literature, referring to different aspects of stratification, hierarchy and inequality within a society. However, in health studies, where the interest in using these concepts is more empirical rather than theoretical, these terms have been commonly used interchangeably (Berkman and Macintyre, 1997; Liberatos *et al.*, 1988; Lipset, 1968). The two seminal figures in the study of social class and social position are Karl Marx and Max Weber. According to the first, social class is defined on the basis of a group's relation to the means of productions – a perspective focused on social relationships created by societies emphasizing social inequality – and, consequently, socioeconomic position is entirely determined by social class (Dahrendorf, 1959). This strict schematization is a product of the industrial society analysed by Marx and started to wane due to the emerging of new, multifaceted and flexibles productive relationships and social stratifications' forms (Clark and Lipset, 1991). The Neo-Marxist theorist Erik Olin Wright proposed an explicit adaption of Marxist social class theory to take into account contemporary employment and social circumstances. In his social class scheme, people are classified according to the interplay of three forms of exploitation: ownership of capital assets, control of organizational assets, and possession of skills or credential assets (Wright, 1979; 1995; Wright *et al.*, 1982). Weber (1946; 2015) developed a different idea of social class, based on three domains: class (ownership and economic resources), status (prestige or honour in the community), and power (in its political meaning). This tripartite definition – which surely inspired Wright's development of Marx's theory – has led many sociologists to identify stratifications relying on multiple indicators. The most common indicators used nowadays are educational attainment, occupational category, and income, representing Weber's class, status, and power domains and covering several aspects of social stratification (Kunst and Mackenbach, 2000). According to Lahelma and colleagues, each indicator is likely to reflect both common impacts of a general hierarchical ranking in society and particular impacts specific to the indicator (Lahelma *et al.*, 2004), so that the use of each of them, singly or combined with the others, is not just a question of data availability, being related to specific hypotheses concerning the pathways and mechanisms through which socioeconomic conditions affect health. As they state:

> (1) Educational attainment is usually acquired by early adulthood. The specific nature of education is knowledge and other non-material resources that are likely to promote healthy lifestyles. Additionally, education provides formal qualifications that contribute to the socioeconomic status of destination through occupation and income.
> (2) Occupation based social class relates people to social structure. Occupational

> social class positions indicate status and power, and reflect material conditions related to paid work.
> (3) Individual and household income derive primarily from paid employment. Income provides individuals and families necessary material resources and determines their purchasing power. Thus income contributes to resources needed in maintaining good health (Lahelma *et al.*, 2004, 327).

In this view, great emphasis is put also on the temporal ordering of each indicator in the relation to health outcomes. Education is seen to structure occupation and income, thus influencing health both directly – mainly through knowledge – but also indirectly, through its effect on the other two indicators. The same point is touched by Singh-Manoux and colleagues, who point out that the relationship between socioeconomic position and health is related to the time distance of the specific measure of social position being adopted from health outcomes (Singh-Manoux *et al.*, 2002). A schematic representation of the pathways leading education, occupation, and income to influence health and disease conditions is presented in Figure 1.4.

Figure 1.4: Direct and indirect effects of education, occupation, and income on health.



Different measures implicate distinct causal pathways and temporal ordering, but they are also sensitive to the outcome inquired, given that not all health outcomes develop in the same life period (Singh-Manoux *et al.*, 2002). Starting from these considerations, we summarily review the three indicators commonly used to operationalize socioeconomic position. Next, we discuss other three structural determinants identified in the CSDH model: gender, race, and ethnicity.

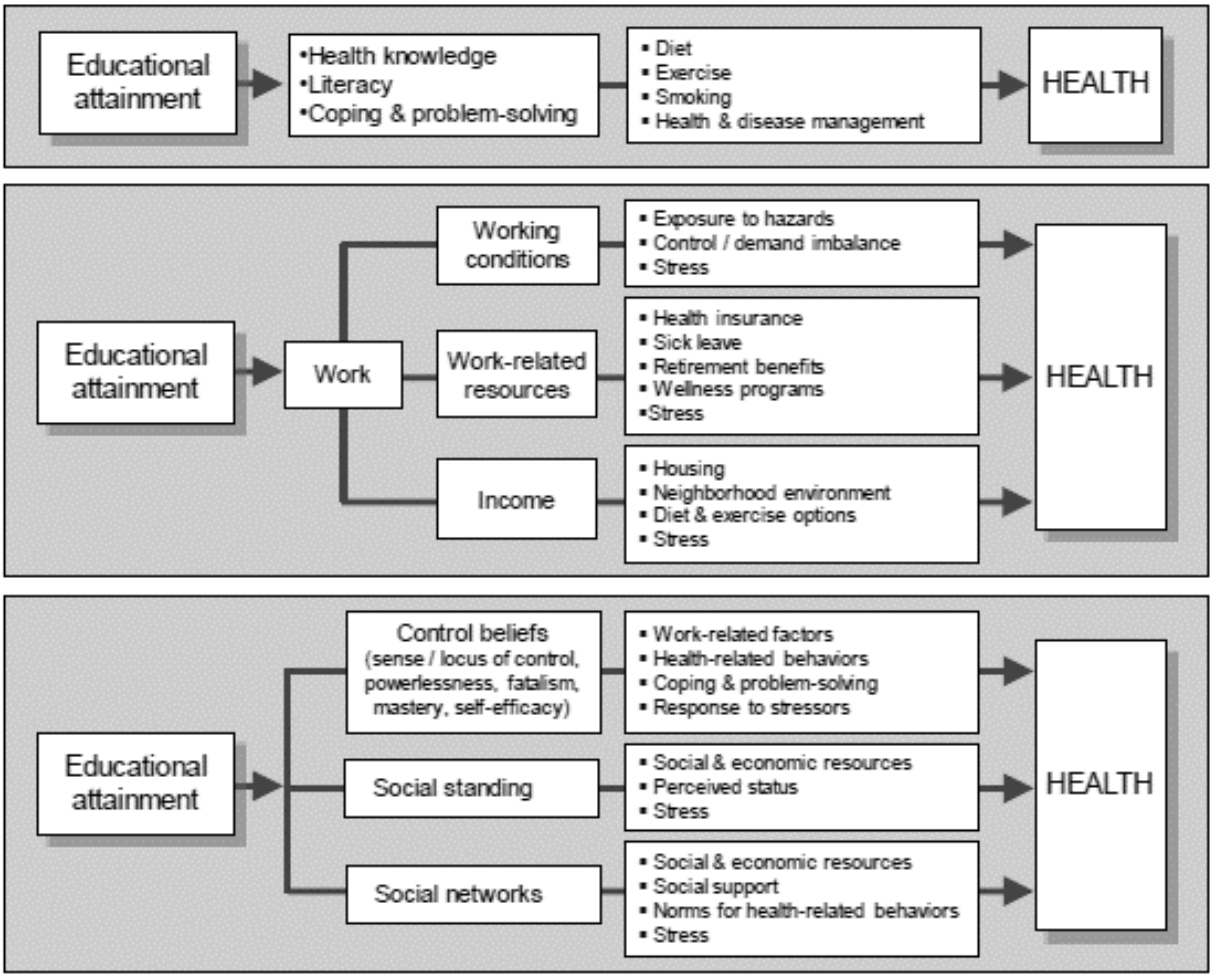
Education

According to Liberatos and colleagues, education is frequently more strongly associated with health and disease than any other indicator is, mostly due to its high correlation with health practices, lifestyle characteristics (e.g. diet, physical activity, smoking habits, weight, etc.), and

adoption of new medications or procedures (Liberatos *et al.*, 1988). The key resource involved by education in determining health conditions is knowledge. The direct mechanism through which education influence health is the development of cognitive functionings making the higher educated more receptive to health education messages and information, as well as better enabling them to communicate with and access to appropriate health services. However, education effect on health is not limited to non-material resources; given its importance in shaping occupation and income later in life, education affects health conditions also indirectly, through the disposition of material assets. The power of this indicator lies also in covering nearly ever life period. As formal education is usually completed in young adulthood and is strongly associated with parental characteristics and educational achievement, in a life-course perspective it can partially measure early life socioeconomic conditions (Galobardes *et al.*, 2006). Additionally, being a strong determinant of future employment and income, it captures the transition from parents' (received) to adulthood (own) socioeconomic status. Therefore, it captures the long-term influences of both early life circumstances and adult resources on health. Moreover, once reached, educational attainment is generally stable over life, differently from occupation and income which may be subjected to fluctuant variations. Egerter and colleaugues (Egerter *et al.*, 2011) exemplified three different pathways through which education could influence health (Fig. 1.5). First, education can lead to better health conditions fostering health-related knowledge and healthy behaviours. Education provides knowledge, problem solving capability, and coping strategies which enable the higher educated to take informed decisions when different options potentially affecting their well-being are available. Second, higher educational attainments lead to better occupational opportunities and higher incomes, which are in turn linked to better health. In this case, the effect of education is mediated by what happens in the labour market. A higher education provides skills that increase the chance to find a job, and to find more prestigious jobs, with less exposure to a wide range of risk factors, as well as to find better paid jobs. This implies positive consequences in terms of financial security, possibility to accumulate wealth, chances of access to valuable resources (e.g. buying healthy food, living in a comfortable house and in a safe neighbourhood, access to services and amenities, access to better healthcare, etc.), as well as insurance schemes protecting against risk of several potential situations (e.g. illness, injuries, disabilities, retirement, etc.). Third, education is associated with psychosocial factors affecting health. Education provides dispositions allowing to reduce stress, increasing the sense of control that individuals have over their lives, as well as increasing their support networks. Rather than being mutually exclusive,

these pathways operate jointly, making hard to understand which one is the most relevant in specific situations.

Figure 1.5: Pathways through which education can affect health. Source: Egerter et al. (2011)



Occupation

Despite having some limitations, occupation is a widely used indicator of socioeconomic position. This measure is relevant not just because it indicates exposure to specific occupational risks (toxic environment, dangerous jobs, ergonomic hazards, etc.), but also because it determines people's place in the societal hierarchy (Kunst and Mackenbach, 2000). Lying in an intermediate position between education and income, it captures several aspects of social stratification, such as social standing, intellect, and income. Moreover, it can identify working relations of domination and subordination between employers and employees (Galobardes *et al.*, 2006). Reflecting social standing, occupation may be related to health outcomes due to certain privileges, such as easier access to better healthcare. Reflecting income, the association with health may be one of a direct access with material resources, such as money, living

standards, salubrious residential facilities and the like. Additionally, occupation may reflect social networks, work-based stress, control and autonomy, affecting health through psychosocial processes. Despite its usefulness, this indicator is subjected to two important limitations. First, it cannot be assigned to people who – for any reason – are not currently employed. Thus, it implies the exclusion of retired people, people whose work is inside the home, disabled people, the unemployed, students, and people working in unpaid, informal or irregular jobs. Second, differently from levels of education and income, which can be naturally ordered from lower to higher levels, occupational categories may be problematic to rank, making difficult to assess the presence of a gradient in health outcomes.

Income

Income is the indicator of socioeconomic position that most directly measures the material resources component. Money and other material assets affect health through their conversion into health enhancing commodities and services. Even in presence of inclusive healthcare systems, in which every individual is entitled to medical assistance regardless of his characteristics and resources, a higher income allows to access to private care, avoiding long waiting to receive the service from the public sector. Similarly, higher family income allows higher educational achievements, or access to more prestigious schools, thus indirectly granting the already outlined beneficial effects of education, and consequently occupation. Nevertheless, income may have also an indirect effect on health, for instance fostering self-esteem and social standing by providing outward material characteristics relevant to participation in society. Thus, income may primarily influence health through a direct effect on material resources, which are in turn mediated by proximal factors in the causal chain, such as lifestyle and behaviours (Galobardes *et al.*, 2006). As any other indicator, it is also subjected to some intrinsic limitations. First, it is strongly associated with age – typically people reach their highest income level before retirement – with possible underestimations of health inequalities due to income differences. Second, questions about income are generally perceived as sensitive, resulting in large numbers of non-respondents. Third, income level may not reflect one individual's real purchasing power, since it does not take into account itself of the overall economic situation. Two persons with identical income may dispose of very different economic power depending, for instance, on housing tenure, debt situation, household size, and partner's income. The use of household income instead of individual income is generally used to overcome at least some of these problems, but it assumes that economic resources are evenly spread among family members, and this may not be always the case.

Gender

Differently from 'sex', which implies characteristics that are biologically determined, 'gender' refers to those characteristics of women and men which are socially constructed (WHO, 2002). Thus, gender involves culturally and socially embedded role, conventions, and behaviours that contribute to shape relations between males and females, especially in terms of power and discrimination. In many societies, females suffer systematic discrimination in access to power, prestige and resources, as a consequence of socially constructed models of masculinity, which result in women and girls bearing the major burden of negative health effects from gender-based social hierarchies. Health effects of gender discrimination can be direct and cruel (e.g. female infanticide, genital mutilation, rape, domestic violence) or subtle – but not less relevant – undermining women's possibilities to obtain the same educational, occupational and income opportunities of men. These patterns contribute to shape women's socioeconomic disadvantage, which in turn affects their risk profile. Gender norms and customs define differential employment conditions and earnings for women compared to men, as well as differential exposures and work-related health risks. Gender disadvantage is expressed also in women's often fragmented and economically uncertain work trajectories, with domestic responsibilities disrupting career paths, reducing lifetime earning capacity and increasing the risk of poverty (Walby, 2003).

Race and Ethnicity

The difference between race and ethnicity is like the one between sex and gender: 'race' is a biological concept, while 'ethnicity' is a social and cultural one. Races are genetically distinct populations of the human species, while ethnicities refer to people living in a given geographic area and sharing the same language, heritage, customs, or religion. Both race and ethnicities may be a source of health inequalities. In societies marked by racial discrimination and exclusion, people belonging to marginalized racial or ethnic groups are affected by disadvantaged conditions, opportunities, and trajectories throughout the life-course (Williams *et al.*, 2010). As a consequence of this, in many countries some of these populations – typically the non-Caucasians – report life expectancy and health indicators inferior to those of the rest of the population. As for the case of gender, these forms of discrimination are closely intertwined with the impact of other determinants associated with disadvantaged social position, such as poor education, employment conditions, income, and the like (Williams, 1999; Krieger, 2000).

1.4.3.3 Intermediary Determinants

The third and last range of determinants in the CSDH framework are the intermediary ones, to which the socioeconomic and political context and the structural determinants are antecedent in the causal chain leading to health conditions and inequalities. These intermediary factors flow from the configuration of underlying social stratification, determining in turn differences in exposure and vulnerability to health-compromising condition through a set of individual-level influences, including health-related behaviours and physiological factors. The main categories of these determinants are: material circumstances, psychosocial circumstances, behavioural and lifestyle factors, and the health system itself as a social determinant.

Material Circumstances

These includes determinants linked to the physical environment where people live and work (e.g. housing conditions, physical working environment and neighbourhood physical characteristics, etc.) as well as to people's consumption potential (the possibility to buy healthy food, exercise, buy medicines and access to care, etc.). Housing characteristics reflect aspects of socioeconomic circumstances. The physical structure of dwellings, building materials, indoor conditions such as damp and mould, possession of appliances, air temperature, overcrowding, and noise pollution are just some examples of housing characteristics able to affect health conditions. (Howden-Chapman, 2004). Similarly, neighbourhood characteristics such as air quality, lack of walkable paths and green spaces, crime rates, proximity to services and amenities are strictly dependent on someone's financial means and exert a direct influence on health and disease risk. Concerning the workplace, it can determine the health of the workers not in a physical way, for instance trough physical and ergonomic strain, risk of injuries, air and noise pollution, and the like.

Psychosocial Circumstances

These includes psychosocial stressors (e.g. negative life events, job strain, discrimination, etc.), stressful living circumstances (e.g. high debt, chronic poverty, etc.) and social isolation (e.g. lack of social support, copying styles, etc.). Both disruptive life events and chronic stress may play a fundamental role in the causal chain leading to disease outcomes. When people face emotional distressing situations, the body react stimulating biological stressful response, including an increased release of cortisol, the 'stress-hormone' (Lundberg, 2005), which can lead to increased inflammation, elevated heart rates, blood pressure and other consequences, thus directly fostering the insurgence of many diseases (Arcaya *et al.*, 2015). Concerning the

psychosocial effects of the working environment, two models are widely used to account for the pathways linking working conditions and health outcomes. According to Karasek, who developed the *demand/control model*, skill development and autonomy at work produce favourable effects on mental health (Karasek, 1979). High levels of physical demands combined with low levels of decision authority and skill utilization are predicted to increase the risk of stressful experiences and subsequent physical and mental illness. Conversely, job tasks profiles defined by high psychological demands together with high levels of job task control are likely to evoke feelings of mastery and self-efficacy, definable as the belief a person has in his or her ability to accomplish tasks (Bandura, 1997). This makes it likely that 'active' jobs may stimulate healthy functioning and buffer the adverse effects of stress at work (Karesek and Theorell, 1990). With his *effort/reward imbalance model*, Siegrist assumes that effort at work is spent as a part of a contract based on the norm of social reciprocity where rewards are provided in terms of money, esteem, and career opportunities including job security (Siegrist, 1996). Situations of lack of reciprocity between costs and gains (e.g. high cost/low gain conditions) elicit a sense of being treated unfairly and suffering injustice which afflicts the workers' self-esteem, defining states of emotional distress. On the other hand, adequate approval and esteem, whether experienced in terms of money or recognition, job promotion or job stability, enhances self-esteem and satisfaction, resulting beneficial for health conditions. In the view of the two models, that are complementary to each other, exposure to an adverse psychosocial environment elicits sustained stress reactions with negative long-term consequences for health. These exposures may be implicated in the association between socioeconomic status and health in two ways. First, they are likely to be experienced more frequently among those with lower socioeconomic resources. Second, the size of the effects on health produced by adverse working conditions are likely to be higher in the more disadvantaged, due to their increased vulnerability (Siegrist and Marmot, 2004).

Behavioural and Lifestyle Factors

Behavioural and lifestyle factors include health protecting and enhancing factors (e.g. healthy diet, physical activity, etc.) or, conversely, health damaging factors (e.g. poor diet, sedentary behaviour, lack of physical activity, smoking, excessive alcohol consumption, etc.). These intermediary determinants are somehow conceived to be the most important intervening factors in the link between socioeconomic conditions and health, given that health-related lifestyles and behaviours are closely tied to both socioeconomic status and health outcomes. However, despite the close relationship, the association of socioeconomic position and health is reduced,

but not eliminated, when these behaviours are statistically controlled in empirical research, indicating that the link between socioeconomic conditions and health outcomes is not driven exclusively by lifestyles and behaviours (Marmot *et al.*, 1984). Accordingly, the prominent role attributed to behaviours and lifestyles as the most important determinant of social inequalities in health is questionable. Each of the intermediary factors can influence health through specific physiological pathways, and sometimes differences in lifestyles can only explain a small proportion of health inequalities. Thus, material factors may act as source of psychosocial stress, which in turn may influence health-related behaviours. The adoption of health-threatening behaviours, for instance, is often a response to material deprivation and stress (Solar and Irwin, 2010). Tobacco smoking, excessive alcohol use, diets dense in carbohydrates, fats, and sugars, may be a means of coping with difficult and stressful circumstances, such as job loss, income insecurity or demanding working conditions (Mackenbach *et al.*, 2002). In such a situation, lifestyles and behaviours – usually conceived as the most proximal risk factor in the causal chain – may act as an amplifier of disease risk, whereby people are already exposed to health-threating conditions due to their material resources and psychosocial circumstances.

The Health System as a Determinant

Differently from many models who conceptualized the health system as a structural determinant, in the CSDH framework this is considered an intermediary determinant. This shift is due to the fact that differences in access to healthcare alone do not account for the social patterning of health outcomes (Adler *et al.*, 1994). In this view, the health system can directly address differences in exposure and vulnerability not only through equitable access, but also promoting intersectoral actions at different levels and in different ways, such as addressing the causal factors that mediate the effect of poverty on health (e.g. nutrition, sanitation, housing, working conditions, etc.) and reinforcing factors which reduce susceptibility to disease (e.g. vaccination, empowerment, social support, etc.) (Diderichsen *et al.*, 2001). However, as it is possible to notice from the kind of interventions suggested, the health system acts as a cross-cutting factor, sometimes operating at a higher and structural level and sometimes being very proximate to health conditions in the causal chain, so that the identification of this dimension as a purely intermediary determinant is at least questionable.

1.4.3.4 Social Cohesion and Social Capital

Another cross-cutting determinant is represented by the concepts of social cohesion and social capital. Sometimes used as synonymous, the two refer to clearly distinct concepts, whereby

social cohesion can be conceived as a part of social capital. The concept of social capital has been subjected to a variety of definitions focusing on distinct characteristics, resources and dimensions involved (Kawachi and Berkman, 2014). In a 'network perspective', social capital is "the aggregate of actual or potential resources linked to possession of a durable network" (Bourdieu, 1986, 248), therefore an individual relational resource enhancing people's possibilities to access to other types of valuable resources (Granovetter, 1977), taking advantage of them in order to maximize their health, or more in general their agency. Conversely, in a 'social cohesion' perspective, social capital is considered a measure of interdependence among individuals belonging to a community and indicates the level of reciprocity and solidarity that exists between people. Thus, it can be understood not as an individual property, but rather as a collective characteristic, an attribute of the social environment in which people are rooted (Coleman, 1990), which can have significant consequences on a broad set of outcomes, including health and well-being. Example of this collective resource are expectations and obligations of trust and reciprocity and establishing norms and values in relationships. All of these consist of some aspect of social structure, which facilitate certain actions of individuals who are within the structure (Coleman, 1988; Putnam 1993; 2000). This second conceptualization has been dominant within the field of population health, but both are relevant in influencing health conditions. While declined in a network perspective social capital acts as an amplifier of resources available to the individual, in a social cohesion perspective it affects individual health through different pathways (Kawachi, 2010). First, more cohesive groups are better equipped to undertake collective action (e.g. ability of a community to organize to protest the closure of local hospital, the passage of local ordinances to restrict smoking in public places, or the use of zoning restrictions to prevent the incursion of fast-food outlets). Second, social cohesion is expressed through the ability of the group to enforce and maintain social norms, mostly through informal social control (e.g. when adults within a community feel empowered to step in to intervene when they observe instances of deviant behaviour by adolescents, including underage smoking and drinking). Third, social cohesion influences health via reciprocity exchanges between members of a network. Fourth, social capital and cohesion are linked to health through the diffusion of innovations via information channels that exist within network structures. Although the examples reported have focused on the positive aspects of social capital, each mechanism described is equally applicable to the so-called 'downside of social capital' (Portes, 1998), that is the use of the relational characteristics and resources highlighted with social- and health-threatening

consequences (e.g. cohesive networks leading to outside exclusion and discrimination, reproduction of health-damaging behaviours, diffusion of non-beneficial information, etc.). In addition to the distinction outlined between the network and the cohesion approaches, Szreter and Woolcock have identified different forms of social capital looking at the way they connect individuals and groups, distinguishing between bonding, bridging and linking social capital:

> *Bonding social capital* refers to trusting and co-operative relations between members of a network who see themselves as being similar. *Bridging social capital*, by contrast, comprises relations of respect and mutuality between people who know that they are not alike in some socio-demographic (or social identity) sense (differing by age, ethnic group, class, etc). […] We would define *linking social capital* as norms of respect and networks of trusting relationships between people who are interacting across explicit, formal or institutionalized power or authority gradients in society. (Szreter and Woolcock, 2004, 654-655).

This explains why in the CSDH framework social capital and social cohesion are conceived as cross-cutting determinants. Depending on their forms, these concepts may act within networks (bonding) or between them (bridging). Linking social capital is a particular form of the bridging one, which instead of acting horizontally putting into contact two different networks with similar characteristics, operates vertically, connecting individuals and groups across explicit power and status differentials. Thus, the competing definitions and approaches suggest that social capital, in its broad meaning, cannot be regarded as a uniform concept. There is no agreement whether it should be seen as a property of individuals, groups, networks, or communities, and thus where it should be located in a conceptual framework defining health-determining conditions, given both its structural and intermediary types of action.

1.5. Spatial Inequalities: Neighbourhood Effects on Health

So far, we presented a framework for the study of health inequalities which takes into account mostly two levels of action: the individual and the broader context in which he or she is embedded. This latter is conceived as the social, cultural, economic and political framework which, directly or indirectly, affects people's opportunities, choices, and actions, characterizing itself as an important contributor of various individual's outcomes, including health conditions. However, in most of the theoretical descriptions of the factors and the mechanisms leading to health conditions and inequalities, this contextual dimension is not properly described, nor it is clear what its territorial definition should be. Conceiving the context as an institutional entity, which influence on health conditions is mostly the results of policies, it could be perceived as the country or the region where people live. However, when it comes to the social and cultural

influence of the context on health outcomes, the national and regional levels may not be the proper geographical scales through which understanding these processes, which can be highly heterogeneous within such large areas. The reality is that social inequalities in health conditions occur at various levels in societies (e.g. national, regional, municipal, neighbourhood, and individual level), but for long time researchers in the field of population health have focused almost exclusively on the two extremities. When the territorial dimension has been considered, it mostly concerned differences between countries, sometimes regions, while rarely cities or other lower level units. Besides, most frequently health differentials have been considered solely at the individual level, for instance comparing health conditions of different social groups within a nation without taking into account where people lived or worked. Thus, despite the great results reached by social scientists and epidemiologists in highlighting the social shaping of disease – shifting the attention from individually-based risk factors to social conditions as more important causes of disease – until the 1990s the issue of area effects on health has been underexplored. This does not imply that researchers have never "suspected that where one lives makes a difference to health in addition to who one is" (Kawachi and Berkman, 2003, V), but the strand of research on this issue has been limited for two main reasons, one conceptual, the other methodological. About the first one, contextual variables have been for long excluded from medical sociology and social epidemiology mainly because of the already discussed *epidemiological transition* (Omran, 2005). The point is made clear by Diez-Roux, according to whom in correspondence with the prevalence of infectious diseases as the main cause of mortality, public health was forced to be ecological, but with the advent of chronic diseases as the leading cause of death, contextual factors began to be put aside:

> In its origins, public health was essentially ecological, relating environmental and community characteristics to disease. With the advent of the germ theory and the associated unicausal theory of disease causation, infectious organisms became the "environmental" factors. [...] In this century, the growing importance of chronic diseases led to the search of new causal factors. Emphasis shifted from the environmental factors to individual-level factors, and research focused on behavioural and biological characteristics as risk factors for chronic diseases (Diez-Roux, 1998, 1).

We already stressed the fundamental role played by environmental improvements (e.g. public sanitation, housing, water and food supply, etc.) in determining the decline in mortality by infectious disease in the late 19th century, more than medical innovations (McKeown, 1979; Porter, 1997). From the 20th century onward instead, the growing importance of chronic diseases led to the search of causal factors proximate to the individual level. Consequently,

research for public health shifted from an environmental perspective to a more individual one, focusing mainly on biological and behavioural characteristics as risk factors for diseases. The paradigm shift in epidemiology is well described by Pearce (1996), who counterposes the first contributions of the 'traditional' epidemiology – such as John Snow's study of cholera mentioned previously – to the later development of the 'modern epidemiology'. Table 1.2 shows how, according to Pearce, in its origin epidemiology was highly contextual, aimed at studying populations rather than diseases, with a marked inclination to produce public health interventions rather than cumulative scientific knowledge. These 'lost' characteristics became retrievable again with the development of social epidemiology, as we described it earlier. Obviously, our purpose is not to lessen the importance of modern epidemiology, but just to highlight how in concomitance with important changes in the pattern of morbidity and mortality, the wider study of population health – which is not limited to epidemiology – began to disregard the environment, that is the context to which people are mostly exposed to during their living and working activities.

Table 1.2: Epidemiological paradigms. Source: Pearce (1996).

	Traditional Epidemiology	**Modern Epidemiology**
Motivation	Public health	Science
Level of study	Population	Individual/organ/tissue/cell/molecule
Context of study	Historical/cultural	Context free
Paradigms	Demography/social science	Clinical trial
Epistemological approach	Realist	Positivist
Epidemiological strategy	Top down (structural)	Bottom up (reductionist)
Level of intervention	Population (upstream)	Individual (downstream)

However – coming to the second reason – even when the over-estimation of individual risk factors has been downsized by a strand of research relying on the idea of a social determination of risk and health outcomes, an ecological perspective in health inequalities studies has still found difficult to emerge, due to a methodological scepticism deriving from the so-called *ecological fallacy* (Selvin, 1958). This bias involves inferring individual-level relationships from relationships observed at the aggregate level, producing inappropriate causal inference from group data to individual outcomes (Macintyre and Ellaway, 2000). From the 1950s onward, several studies have been carried out in order to demonstrate the lack of correspondence between individual and group level associations of the same variables (Blalock,

1961; Hauser, 1974; Robinson, 1950), leading a relevant number of scholars to avoid ecological approaches, given their misleading nature. On the other hand, other scholars have put in evidence the opposite mistake, namely the one "of using individuals as unit of analysis when they want to make inference about settings" (Richards, 1996, 223), an inappropriateness defined the *atomistic* (Alker, 1969; Riley, 1963) or *individualistic* (Scheuch, 1969; Valkonen, 1969) fallacy. Indeed, according to Schwarz (1994), the emphasis on the ecological fallacy encouraged the belief that individual level-models are better specified than ecological-level ones, that ecological correlations are substitutes of individual correlations, and that group-level variables do not cause diseases. These deceptive beliefs have led researchers to undervalue models and theories which take social or physical environment into account, inducing to rely almost exclusively on the individual in the study of health inequalities. However, in recent times, this ostracism toward the adoption of an ecological perspective within health studies has been partially overcome. A renewed interest in spatial analyses appeared in correspondence with the development from the 1990s of multilevel analysis techniques (Goldstein, 1986; 1987; Von Korff *et al.*, 1992), which allowed researchers to disentangle the ambiguity typically associated with individual and aggregated measurement (Stafford and McCarthy, 2006). Accordingly, health has been shown to be associated with neighbourhood economic factors, physical environment, social environment, amenities, and housing quality, with consistent effects demonstrated, among all, for health at early age (Buka *et al.*, 2003; Roberts, 1997), health-related behaviours (Duncan *et al.*, 1993; 1995; 1999; Weitzman and Kawachi, 2000), perceived general and mental health (Cummins *et al.*, 2005; Slogget and Joshi, 1998; Stafford *et al.*, 2004), crimes and violence (Sampson *et al.*, 1997; Shaw *et al.*, 2005), and mortality in general (Lochner *et al.*, 2003; Martikainen *et al.*, 2003). In the wake of such findings, many scholars began to claim for a return to the earlier emphasis on the spatial dimension in health studies (Kearns, 1993; Macintyre *et al.*, 1993). Therefore, despite never reaching the popularity of studies focusing on the individual, the interest in inquiring the ecological dimension in the field of population health grew, giving rise to a specific and relevant flow of research. Specifically, interest has risen toward the study of small area effects on health outcomes, focusing on the local environment where people live at a small scale, such as neighbourhoods, district, blocks, postcode areas, census tracts, or other geographical levels. Thus, following the relevant tradition of *neighbourhood effects* in the field of urban studies, social scientists and epidemiologists have increasingly paid attention to health outcomes in this strand of literature. Neighbourhood effects reflect the idea that living in deprived neighbourhood has a negative

effect on residents' life chances over and above the effect of their individual characteristics (Van Ham *et al.*, 2012). The literature on the issue can be traced back to the work of Gans in the 1960s (Gans, 1962; 1968), but the popularity of the concept is largely due to the publication of *The Truly Disadvantaged* by Wilson (1987), proposing a theory for why crime and poverty clustered, and persisted, in certain neighbourhoods, inspiring research concerning the connection between neighbourhoods and life outcomes (Galster, 2012; 2014). Indeed, subsequent research assessed the independent effect of neighbourhood conditions on many outcomes, such as educational achievement, school dropout rates, deviant behaviour (e.g. crime rates and drug use) social exclusion, employment and income opportunities, social and occupational mobility, and, more recently, health and disease (Dietz, 2002; Durlauf, 2004; Ellen and Turner, 1997; Galster, 2002). In the next paragraphs, we review the application of this concept to the study of health inequalities, focusing on the tensions emerged in the field, and on the mechanisms leading the context to influence health outcomes.

1.5.1 Contextual and Compositional Effects

The most important tension concerning the territorial structuring of health inequalities is relative to the extent to which differentials in health conditions between neighbourhoods – or other urban areas – within a city are actually the product of area features, rather than being merely the consequence of the clustering in the same areas of people sharing similar characteristics (Stafford and McCarthy, 2006). Despite the association between health and the place of living has been assessed by many studies, this is not enough to affirm a causal relationship between the two. The issue is known in the literature as the dichotomy between *compositional* and *contextual* explanations for geographical variations in health conditions. Once ascertained that there is a spatial variation in morbidity and mortality, the question is about its origin. A compositional explanation for these differences would be that since areas include different types of individuals, each with different personal and socioeconomic characteristics, the observed differences between places will be accounted for the individual ones. As Macintyre and Ellaway point out:

> It may be argued that poor people die earlier than rich people, so it is not surprising that areas with lots of poor people have low average life expectancy: poor people would die early wherever they live and rich people live longer wherever they live, so any observed *spatial patterning* in life expectancy is purely due to the *spatial concentration* of poor or rich people in different sorts of areas, and life expectancy is therefore a *property of the individual, not of areas* (Macintyre and Ellaway, 2000, 338; emphasis added).

Conversely, a contextual explanation would imply that there are features of the social or physical environment able to influence the health of the individuals and groups exposed to it, either in addition to or in interaction with individual characteristics. Again, following Macintyre and Ellaway:

> People of whatever levels of personal poverty or affluence might live longer if they lived in non-polluted areas with a pleasant climate and an excellent range of services and amenities; or, rich people might live just as long wherever they live because they have personal resources to cope with a range of environments, but poor people might die particularly early in under-resourced neighbourhoods (Macintyre and Ellaway 2000, 338).

Thus, a compositional explanation implies that poor people will have the same death and disease rates wherever they live, whereas a contextual explanation implies that mortality and morbidity of poor or affluent individuals will vary depending on what sort of area they live in (Macintyre and Ellaway, 2003). Hence, it is only in presence of contextual effects that is possible to speak about neighbourhood effects, that is the independent causal effect of a neighbourhood on any number of health or social outcomes (Jenks and Mayer, 1990; Mayer and Jenks, 1999). In two reviews of studies assessing the relation between neighbourhood socioeconomic context and health outcomes (Kawachi and Berkman, 2003; Picket and Pearl, 2001), the vast majority of them reported a statistically significant association between measures of social environment and health, even if after controlling for individual factors the impact of the context resulted smaller and less important than the one of individual socioeconomic conditions. Nevertheless, in real situations it is impossible to completely discern the two explanations, given that who a person is and where he lives are closely interrelated, influencing each other with many possibilities of interaction. As Macintyre and Ellaway argued, the distinction is somewhat artificial, given that "people create places, and places create people" (Macintyre and Ellaway, 2003, 26). Thus, when controlling for individual factors it is important to keep in mind that these may be determined as much by the person or by the place of living. For instance, occupation, and consequently income, may be determined by the local labour market; education by the available educational system and local provision; housing tenure and characteristics by the local housing market, and so on. Hence, rather than seeing these factors merely as properties of individuals, one should consider the extent to which they reflect features of the local environment, that is place characteristics creating people characteristics, and vice versa (Macintyre and Ellaway, 2003). What it is possible to do, instead, is to assess the magnitude of each explanations, in order to understand if – in each specific situation – context

matters for health, or health inequalities are exclusively a matter of individual variability. Hence, the distinction between the two kinds of explanations is not just a theoretical one, given that a predominant compositional explanation might tend to direct policy interventions toward individuals, while recognizing that the context also affects health conditions might direct attention toward health-damaging and health-promoting features of neighbourhoods (Macintyre and Ellaway, 2003).

1.5.2 Theoretical and Methodological Issues

Describing the most relevant tensions concerning the study of neighbourhood effects on health, Kawachi and Berkman (2003) identify a set of theoretical and methodological dichotomies, one of which is the contextual/compositional explanation treated above. First, as for the case of health inequalities studied at the individual level, a diatribe is present between those who conceive small-area differences in health conditions as the output of *social selection* processes, and those who conversely conceive them in a *social causation* framework. According to the firsts, residential preferences are the driving force of territorial differences; poor people, for instance, may choose to move in low-income neighbourhood because of the affordable cost of housing, or ethnic minorities may prefer to move in area where many people of the same group live. Hence, this issue is partially overlapping with the compositional/contextual effect one, except that it focuses on the mechanisms that lead people to choose their residential location. This explanation suffers some weaknesses already discussed here, assuming that people have complete choice over their decisions and behaviours. However, are mostly available resources and context which determine individuals' choices, and not vice versa, so that a social causation perspective is far more plausible than a selection one in explaining area variations in health. Second, there is a clear distinction between a subjective and an objective assessment of what neighbourhood is. Typically, research has been carried out relying on administrative definition of areas (e.g. neighbourhoods, census tracts, postcode areas, etc.); however, these spatial units may not correspond to the territorial space to which individuals are actually exposed, as well as they may not adequately identify what people perceive as the neighbourhood where they live. Concerning this latter issue, individuals often do not identify their life context with administrative boundaries; moreover, the perceptions of the area boundaries may vary among individuals. In this perspective, the context seems to possess blurred boundaries that can expand or shrink according to personal experience (Sastry *et al.*, 2002). This means that the effect of the context sometimes could be better understood adopting a relational perspective in which boundaries are not built ex ante, but as a consequence of the mutual influence between people

and places (Cummins *et al.*, 2007). Both the approaches are valid, and the adoption of one rather than the other should depend on research questions and hypothesis, although in real situations is mostly driven by data availability and research limitations. A third relevant issue concerns the distinction between neighbourhoods and other forms of community. In the age of globalization, people are less and less dependent on local areas for necessities of life, and local patterns of social affiliation are declining (Putnam, 2000), so that, differently from the past, the neighbourhood of residence may fail in capturing the social and physical environment to which individuals are mostly exposed to during their daily life. The most promising way to dealt with the issue is collecting data and analysing the influence of multiple contexts on health, such as residential location, workplace, schools, and other communities (Subramian *et al.*, 2003), but obviously this is not always a feasible strategy in empirical research. Event though, "it is crucial to recall that neighbourhood characteristics do not occur in a vacuum, that their physical and social environments are shaped by macroeconomic forces, political decisions, and patterns of migration, history, and culture" (Kawachi and Berkman, 2003, 16), as well as that residential, occupational, and educational patterns are closely interrelated, so that "some type of exposures may exhibit scant variations at smaller units of aggregation" (*ibidem*, 16). Thus, despite varying weight of geographical affiliations, the living context remains a relevant dimension through which inquire health inequalities. Fourth, the distinction between *material* and *psychosocial explanations* for health inequalities is valid also at the ecological level. Again, both the explanations are plausible, since neighbourhoods affects health conditions through several pathways, sometimes interacting and reinforcing (or weakening) each other, and the preponderance of one over the other may be strictly dependent on each specific situation.

1.5.3 Neighbourhoods and Health: Mechanisms and Pathways

As for the case of social inequalities in health studied at the individual level, researchers have not only provided evidence about the associations between neighbourhoods and health conditions, attempting also to uncover the causal mechanisms leading these relationships. However, less attention has been paid with regards to the possible explanations for neighbourhood effects on health, compared to literature aimed at quantifying the phenomenon. In one of the first attempts to identify aspects of the physical and social environment that may be health promoting or health damaging, Macintyre and colleagues (Macintyre *et al.*, 1993) described five types of features of local areas which might influence health, which are:

1) Physical features of the environment shared by all residents in a locality (e.g. quality of air and water, latitude, climate, etc.)

2) Availability of healthy environment at home, work, and play (e.g. housing conditions, hazard in workplace, safe play areas for children, etc.)

3) Services provided, publicly or privately, to support people in daily lives (e.g. education, transport, street cleaning and lighting, policing, health, and welfare services, etc.)

4) Socio-cultural features of a neighbourhood (e.g. political, economic, ethnic, and religious history of a community, norms and values, the degree of community integration, levels of crime, incivilities, threats to personal safety, networks of community support, etc.)

4) The reputation of an area (e.g. how areas are perceived by their residents, by service or amenity planners and providers, by banks and investors).

Although we reported here just the main categories, the work by Macintyre and colleagues provides for each group several examples of specific factors affecting health. More recently, Galster (2012) went beyond, offering not only a list of environmental factors influencing health conditions, but also a comprehensive list of causal mechanisms, reviewing a decade of literature prior to his contribution. Synthetizing previous contributions within the literature (Ellen and Turner, 1997; 2003; Ellen *et al.*, 2001; Friedrichs, 1998; Gephart, 1997; Jenks and Mayer, 1990; Leventhal and Brooks-Gunn, 2000; Sampson, 2001; Sampson *et al.*, 2002; Small and Newman, 2001), Galster groups fifteen mechanisms under four categories, which are *social interactive, environmental, geographical, and institutional mechanisms.* Some of them, such as social capital, social cohesion, and social networks, have been already discussed in previous paragraphs, given their cross-cutting nature, which places them in-between the individual and the contextual influence.

Social-Interactive Mechanisms

This set of mechanisms includes psychosocial processes which are endogenous to the neighbourhood, specifically:

1) Social Contagion: Behaviours, aspirations, and attitudes may be changed by contact with peers who are neighbours. The idea of social contagion suggests that "many behavioural phenomena have been found to spread interpersonally through social networks, in a manner similar to infectious diseases" (Hill *et al.*, 2010, 1).

2) Collective Socialization: Individuals may be encouraged to conform to local social norms conveyed by neighbourhood role models and other social pressures.

3) Social Networks: Individuals may be influenced by the interpersonal communication of information and resources of various kinds transmitted through neighbours.

4) Social cohesion and control: The degree of neighbourhood social disorder and its converse, collective efficacy (Sampson *et al.*, 1999), may influence a variety of behaviours and psychological reactions of residents.

5) Competition: Under the premise that certain local resources are limited and not pure public goods, this mechanism posits that groups within the neighbourhood will compete for these resources amongst themselves. Because the outcome is a zero-sum game, residents' access to these resources (and their resulting opportunities) may be influenced by the ultimate success of their group in winning this competition.

6) Relative Deprivation: This mechanism suggests that residents who have achieved some socioeconomic success will be a source of disamenities for their less well-off neighbours. The latter, it is argued, will view the successful with envy and/or will make them perceive their own relative inferiority as a source of dissatisfaction. Wilkinson and Picket suggest that income inequality has a detrimental effect on health, which is independent of poverty, access to resources, and material pathways, acting almost exclusively as a psychosocial mechanism (Picket and Wilkinson, 2015; Wilkinson and Pickett, 2010).

7) Parental Mediation: The neighbourhood may affect (through any of the mechanisms listed under all the categories described here) parents' physical and mental health, stress, coping skills, self-efficacy, behaviours, and material resources. All of these, in turn, may affect the home environment in which children are raised.

Environmental Mechanisms

Environmental mechanisms refer to natural and human-made attributes of the local space that may affect directly the mental and physical health of residents without affecting their behaviours, acting mostly on their opportunities.

8) Exposure to Violence: If people sense that their property or person is in danger they may suffer psychological and physical responses that may impair their functioning or perceived

well-being. These consequences are likely to be even more pronounced if the person has been victimized.

9) Physical Surroundings: Decayed physical conditions of the built environment (e.g., deteriorated structures and public infrastructure, litter, etc.) may impart psychological effects on residents, such as a sense of powerlessness. Noise may create stress and inhibit decision-making through a process of 'environmental overload' (Bell *et al.*, 1996).

10) *Toxic Exposure*: People may be exposed to unhealthy levels of air-, soil-, and water-borne pollutants because of the current and historical land uses and other ecological conditions in the neighbourhood.

Geographical Mechanisms

Geographical mechanisms refer to aspects of spaces that may affect residents' health conditions. These do not properly arise within the neighbourhood, but rather as a consequence of its location relative to larger-scale political and economic forces.

11) *Spatial Mismatch*: Certain neighbourhoods may have little accessibility (in either spatial proximity or as mediated by transportation networks) to job opportunities appropriate to the skills of their residents, thereby restricting their employment opportunities.

12) *Public Services*: Some neighbourhoods may be located within local political jurisdictions that offer inferior public services and facilities because of their limited tax based resources, incompetence, corruption, or other operational challenges. These, in turn, may adversely affect the personal development and educational opportunities of residents.

Institutional Mechanisms

This last category of mechanisms involves actions by those typically not residing in the given neighbourhood who control important institutional resources located there and points of interface between neighbourhood residents and vital markets.

13) Stigmatization: Neighbourhoods may be stigmatized on the basis of public stereotypes held by powerful institutional or private actors about its current residents. In other cases, this may occur regardless of the neighbourhood's current population because of its history, environmental or topographical disamenities, style, scale and type of dwellings, or condition of their commercial districts and public spaces. Such stigma may reduce the opportunities and

perceptions of residents of stigmatized areas in a variety of ways, such as job opportunities and self-esteem.

14) Local Institutional Resources: Some neighbourhoods may have access to few and/or high-quality private, non-profit, or public institutions and organizations, such as benevolent charities, day care facilities, schools, and medical clinics. The lack of same may adversely affect the personal development opportunities of residents.

15) Local Market Actors: There may be substantial spatial variations in the prevalence of certain private market actors that may encourage or discourage certain behaviours by neighbourhood residents, such as liquor stores, fresh food markets, fast food restaurants, and illegal drug markets.

Galster's contribution is far more detailed than the way we presented it here, not providing just a list of mechanisms, but also reviewing each of them on the basis of the current literature, quantifying their magnitude and evaluating their plausibility as relevant factors influencing health conditions. The relationship between area characteristics and individual outcomes may not be linear, involving multiple and complex factors, making difficult to discern the mechanisms operating in relation to specific outcomes and situations. Neighbourhood residents can be exposed to a certain composition of mechanisms, over a certain time, with a specific frequency and intensity; the effect may be temporary or long-lasting, take time to have an effect or acting immediately, have effect alone or only in combination with other factors. According to Galster, notwithstanding the growing literature on neighbourhood effects, existing studies have not been able to uncover the dominant neighbourhood effects mechanisms at work. Thus, despite a broad consensus that context matters for health, current knowledge about how and how much this spatial dimension is relevant in determining health inequalities is still limited.

Conclusion

In this chapter, we outlined a framework to understand what health inequalities are. Basing on the literature, we defined them as differentials in health conditions across a population, which are the result of structural characteristics determining different access to resources that are valuable for health. Thus, we shifted the focus from individual risk factors (e.g. biological characteristics, behaviours and lifestyles, etc.) to broader social conditions as major determinant of health. We need to stress again that this does not intend to deny the fundamental role played by such individual characteristics, but rather to frame them in a scheme that take into account

how these individual risk factors come to be unevenly distributed between social groups. Subsequently, we focused on an element that have been receiving increasing attention in the field, that is the territorial shaping of health inequalities. This implies two things. First, health inequalities are not exclusively a matter of individual features, being also the outcome of dynamics and processes happening in the local context in which people live. Second, the effect of small-area characteristics on health results into a spatial patterning of health inequalities, where people with unfavourable socioeconomic conditions are concentrated in specific urban areas, experiencing a "double jeopardy" (Macintyre and Ellaway, 2003, 34), whereby not only they are personally disadvantaged, but they are also likely to live in the sorts of neighbourhoods that lack the social and physical infrastructure to lead a health life. This leads us to spend some words about the policy implications of the overall framework presented. As we moved away from a perspective in which health conditions are a matter of individual choices, we are necessarily induced to abandon a view of people's responsibility for their health. We completely agree with Solar and Irwin when they state that "the state possesses a fundamental role in social protection, ensuring that public services are provided with equity and effectiveness" (Solar and Irwin, 2010, 42). Spreading information about risk factors and investing in medicalization is fundamental, but these kinds of individually-oriented policies are likely not to reach their potential until other fundamental causes of disease are addressed, intervening on the structural factors that generate different access to resources. Following Conrad and Baker:

> For sociologists, one of the most troubling results of medicalization is that it encourages medical solutions while ignoring or downplaying the social context of complicated problems. […] It seems that we have a social predilection toward treating human problems as individual or clinical – whether it be obesity, substance abuse, learning difficulties, aging, or alcoholism – rather than addressing the underlying causes for complex social problems and human suffering. We are quick to see individualized medical interventions as logically consistent responses to our troubles (Conrad and Barker, 2010, 75).

Blaming individuals for their choices and focusing on medicalization could bring to deflect attention away from the well-established link among diseases and social factors, also neglecting the role played by industries such as the alcohol, smoking, and food ones in promoting products that directly affect health outcomes. As Brown states, "sociologists have been in the forefront of those who show that health and illness are often more affected by political, economic, and cultural factors than by biomedical ones" (Brown, 1995, 49). However, instead of lessening the role of medicalization, we believe that the most important contribution coming from the joint efforts of social sciences and epidemiology is the one of having highlighted and emphasized

the role of resources as main source of health inequalities, and since then, in agreement with Link and Phelan, we argue that policy should be oriented toward their redistribution across the population in order to break the socioeconomic gradient, indirectly bringing to a decrease of such inequalities. Indeed, the scholars identify interventions in minimum wage, housing, taxation, parenting leave, social security, education, and lending as health-relevant policies, suggesting also that interventions that automatically benefit individuals irrespective of their own resources should be preferred (Link and Phelan 1995; Phelan *et al.*, 2010). Policies fail when they seek to address causes that are proximate to the individual level, being at most able to intervene in specific situations, without facing the structural mechanisms that bring systematically individuals to certain health outcomes. Similarly, policies may fail also if they focus on improving social conditions at the individual level, without paying attention to the local environment in which people are somehow embedded. In this sense, the claim for more attention to the ecological perspective in the study of health inequalities is not intended just to produce better causal models of determinants of health, but also to provide information on possible interventions to improve health conditions and reduce inequalities. Following Macintyre and Ellaway:

> An emphasis on compositional explanations for patterns of population health tends to imply that policies should be directed toward people (for example, by individually focused health education messages). A recognition that context may influence health may help to balance this individual focus by redirecting attention to interventions at the environmental level (for example, by improving housing stock and public transport, providing green spaces for healthy recreation, or regulating workplace hazards) (Macintyre and Ellaway, 2000, 345).

Thus, social sciences can bring great critical awareness to the policy-making processes, but much depends on how the issue studied is defined and framed. We saw that the study of the social determinants of health has been multidisciplinary from its very beginning, resulting then in what has been called social epidemiology, that is a medical science equipped with concepts, paradigms, theories, and models borrowed from social sciences. As Link suggests, it may be useful to conceive it as "epidemiological sociology, making sociology the subject and epidemiology the modifier" (Link, 2008, 369). This renaming is somehow provocative, and surely it does not intend to undermine the great findings reached by the research on the field so far, but rather to emphasize the role of sociology in understanding the social determinants of health. When social conditions appear to be the fundamental causes of disease, they shape the consequences of epidemiological and biomedical accomplishments, and thereby extant patterns

of disease and death. Even though, the ascendancy of social factors has largely been missed in the research and policy agenda. Despite the growing body of literature, this has not appeared enough to convince decision makers to draw up policies effective in tackling health inequalities, as the widening health gap between social groups demonstrate. Some argue that the increasing distance between the most and the least affluent is balanced by the overall improvement of life and health conditions in the modern age, but this idea does not find evidence in the literature of income inequality, which shows that a wide range of health and social problems are significantly worse in more unequal countries, whether rich or poor (Wilkinson and Pickett, 2010). Thus, we see no reason not to foster both the improvement of population health and the reduction of health inequalities.

Chapter 2

Type 2 Diabetes Mellitus

Introduction

Type 2 Diabetes Mellitus (T2DM) has a relevant tradition of studies concerning its uneven distribution across groups characterized by different socioeconomic characteristics (Agardh *et al.*, 2011). Despite a non-negligible biological and genetic predisposition to the disease, the onset is largely due to individual behaviours and lifestyles, especially unhealthy eating habits, sedentary behaviours and physical inactivity, which in developed countries are more common in less advantaged individuals, namely those with less cultural, economic and social resources. Thus, the prevalence of the disease shows large inequalities, disproportionally affecting deprived populations, making T2DM an emblematic case study to deepen the knowledge about social inequalities in health, both quantifying the extent to which socioeconomic circumstances are able to generate disparities in a specific population and unveiling the mechanisms through which these inequalities are generated are perpetuated, with the aim to understand how to intervene to break the gradient. We believe that a full comprehension of how socioeconomic conditions and T2DM mellitus are closely interrelated could be reached only with at least some basic knowledge of the pathophysiology and etiology of the disease, therefore this chapter begins describing the processes underlying the onset of the pathology. Thus, the first section makes use of medical terminology and concepts – which have been simplified and kept to a minimum – in order to understand what T2DM is and how it differs from other types of diabetes, which factors are involved in its pathogenesis, what its typical complications and consequences are, as well as how it is possible to cope with the disease. After having introduced T2DM, we provide a synthetic picture of the epidemiology of the disease, first worldwide, then in Italy. This second sections is aimed at quantifying the distribution of T2DM providing evidence for the so-called 'diabetic pandemic' (Ginter and Simko, 2013; van Dieren *et al.*, 2010), given the rapid and incessant increase of the disease from the second half of the 20th century onward, in high-, middle- and low-income countries, with clear consequences for people health and well-being, but also in terms of challenge and cost for public care expenditure (Riddle and Herman, 2018). In the third section, we directly inquire the association between socioeconomic conditions and T2DM, focusing our attention on the Italian situation, relying on data from the Italian National Institute of Statistics (Istat). Finally, in the fourth section we explore the

mechanisms and the pathways linking socioeconomic conditions and the disease, focusing both on individual and environmental factors.

2.1 Type 2 Diabetes Mellitus: an Overview

2.1.1 Diabetes Mellitus

According to the WHO's definition, diabetes mellitus is "a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both" (WHO, 1999, 2). Insulin is a hormone which main function is to regulate blood sugar, reducing glycaemia, the concentration on sugar in blood. When insulin – either due to insufficient production or inhibited action – is not able to fulfil its primary function, a situation of hyperglycaemia (raised blood sugar) may occur, causing short-term symptoms of increased thirst, urination, hunger, and weight loss, along with long-term serious consequences in terms of retinopathy (eye damage potentially leading to blindness), nephropathy (renal failure), neuropathy (nerves damage leading to impotence and foot disorders, with possibly amputation), cardiovascular disease and stroke.

2.1.2 Types of Diabetes Mellitus

Diabetes mellitus is typically classified in four categories, according to their different etiology: type 1, type 2, gestational, and a residual "other" category including rarer form of the pathology. Most of cases fall into the type 2 category, estimated to account for 90% of all diabetes mellitus cases worldwide, followed by the type 1, estimated to account for 10% (Melmed *et al.*, 2016). Gestational and other types of diabetes mellitus cover a minor proportion compared to the first two types mentioned and are related to a heterogeneity of causes, whose description goes beyond the interests of this work. Therefore, we will focus on T2DM, describing its commonalities and especially it differences from type 1, that lie in their etiology (how they originate), pathophysiology (how they develop) and – most important in the context of this project – in the role of prevention.

2.1.2.1 Type 1 Diabetes Mellitus

Type 1 Diabetes Mellitus (T1DM) is characterized by hyperglycaemia due to an absolute deficiency of the insulin hormone produced by the pancreas. Formerly known as 'juvenile diabetes', due to its typical development in childhood or adolescence, it is classified as an autoimmune disease: the immune system attacks and destroy the insulin-producing beta cells of the pancreas (Chiang *et al.*, 2014). Like for every autoimmune disease, the cause of T1DM

is still unknown, so that with current knowledge is not possible to prevent this disease. A combination of genetic (Pociot and Lernmark, 2016; Steck and Rewers, 2011) – e.g. family history, gene mutation – and external factors[2] (Knip and Simell, 2012; Rewers and Ludvigsson, 2016) – e.g. exposure to viruses and bacteria – is supposed to play a fundamental role in the onset. A diagnosis is made by the classic symptoms of hyperglycaemia – increased urinary frequency (polyuria), thirst (polydipsia), hunger (polyphagia), unexplained weight loss, numbness in extremities, pain in feet (dysesthesias), fatigue, blurred vision, ketoacidosis – and by an abnormal blood test following WHO diagnostic criteria (WHO, 2006), indicating specific thresholds for fasting blood glucose level (≥7.0 mmol/l) and blood glucose level two hours after a 75g glucose drink (≥11.1 mmol/l). Due to the inability of their pancreas to produce enough insulin to control blood sugar, patients with T1DM require lifelong daily insulin injections for survival, hence the name 'Insulin-Dependent Diabetes Mellitus'.

2.1.2.2 Type 2 Diabetes Mellitus

Differently from T1DM, T2DM usually develops in adulthood and is characterized by hyperglycaemia resulting from insulin resistance, which is the inability of cells to respond adequately to normal levels of insulin, causing the increase of glucose concentration in blood. Usually insulin resistance is accompanied by a relative (rather than absolute, as in the case of T1DM) insulin deficiency, deriving from beta cells dysfunction (but not autoimmune destruction, as it happens in T1DM). The proportion of insulin resistance and insulin defection differs among individuals with T2DM, ranging from predominantly insulin resistance with relative insulin deficiency to predominantly insulin secretory defect with insulin resistance (ADA, 2014a). Diagnostic criteria are the same for T1DM[3], while symptoms despite being analogous to the ones listed for T1DM, may be absent or minimal for years before being diagnosed. The onset, indeed, is gradual and it is estimated that a relevant number of people does not know to suffer of T2DM (NIH, 2006; PAHO, 2013) or discover it just by chance and several years after the onset, once complications have already arisen (WHO, 2018). Differently from T1DM, T2DM does not necessarily requires insulin injections as treatment – hence the name 'Non-Insulin-Dependent Diabetes Mellitus' – and the management of the disease focuses more on lifestyle interventions (especially diet and physical activity), to maintain blood glucose

[2] In the medical literature, these are referred to as 'environmental' factors. Here, we preferred to use the term 'external' to avoid confusion with the concept of environment as it is used in the work, that is the set of physical, social, economic, cultural and relational characteristics of the context where people live.

[3] Given that the diagnosis for T1DM and T2DM rely on the same tests, antibodies tests are used in case of doubt about whether the condition is T1DM or T2DM.

levels in the normal range and avoid complications.

Besides medical distinctions in the etiology and pathophysiology of the two types of diabetes described, in the frame of this project, the key distinction between T1DM and T2DM lies in the role of risk factors and, consequently, prevention. We have stated that there is no prevention possible for T1DM, since knowledge concerning the reason why the immune system attacks its own body's cells is scant. Similarly, in terms of etiology there is limited knowledge about insulin resistance, but T2DM onset is largely associated with obesity, scarce physical activity and bad dietary patterns as risk factors, making possible to prevent it with a healthy lifestyle.

2.1.3 Risk Factors for T2DM

The development of T2DM is caused by a combination of factors, some of which are under personal control (at least potentially), while others are not. Starting from the latter, T2DM risk increases with age, but obviously there is no way to intervene to modify this risk factor. Similarly, genetic has been demonstrated to play a fundamental role in the development of T2DM. To current knowledge, only about 10% of the heritability of T2DM can be explained (Herder and Roden, 2011), with the contribution of the identification of at least 36 genes directly involved in the development of the disease, but again these are not modifiable risk factors for disease prevention. Although estimates vary between different studies, research focusing on the concordance of T2DM for monozygotic twins – sharing the same genetic endowment – indicated that if one twin has T2DM, the other has great chances of developing diabetes within his lifetime, while the rate considerably decreases for nonidentical siblings (Matsuda and Kuzuya, 1994; Newman *et al.*, 1987). The fact that concordance for T2DM never reaches 100%, indicates not only that non-genetic factors may also influence diabetes development, but also that these non-genetic factors may able to outline different outcomes for individuals with identical or very similar genes.

This leads us to figure out the importance of those elements that are instead under personal control, generally referred to as lifestyle or modifiable risk factors.

2.1.3.1 Obesity

Being obese, technically having a Body-Mass-Index (BMI)[4] equal or greater than 30, is associated with higher risk of T2DM, due to the increased risk of developing insulin resistance,

[4] BMI is defined as the body mass divided by the square of the body height, thus expressed in units of kg/m^2. The WHO (Nuttall, 2015) provides specific thresholds indicating different situations of underweight (BMI<18.5), healthy weight (18.5≤BMI<25), and overweight (BMI≥25). Obesity is rated in six different classes, ranging from moderate obesity (30≤BMI<35) to hyper obesity (BMI>60).

deriving from adipose tissue secretion of chemical signals like metabolites, hormones, and cytokines (Al-Goblan *et al.*, 2014; Kahn *et al.*, 2006). Specially, it is visceral fat – the one located in the abdomen around internal organs – which matters more for insulin resistance releasing chemical signals straight into blood directed to the liver, the organ where glucose is absorbed and processed (Powell, 2007). Subcutaneous fat, accumulating under the skin, appears to be less metabolic active, resulting less determinant in the production of chemical signals involved in the process of development of insulin resistance and consequently T2DM. Since visceral fat is located in the abdomen and in the waist region, other measures may be more specific indicators of obesity (Qiao and Nyamdorj, 2010; Schmidt, 1992), such as a large waist circumference and a high waist-to-hip ratio.

2.1.3.2 Unhealthy Diet

It is not only a matter of quantity, but also of quality of food intake. An excessive consumption of sugar-sweetened drinks is associated with higher risk of developing T2DM (Malik *et al.*, 2010) through a double pathway. Directly, increasing level of glucose in blood, but also indirectly, fostering obesity. Also fat intake is linked to T2DM risk. Fatty acids influence glucose metabolism, and there is evidence that replacing them and saturated fats (the ones increasing "bad" cholesterol, LDL) with unsaturated fats (the ones maintaining "good" cholesterol, HDL) has beneficial effects on insulin sensitivity and is likely to reduce risk of T2DM (Risérus *et al.*, 2009). Metabolic studies show that a high-fat diet *per se* is not detrimental for insulin sensitivity: the quality of fat is more important than the total intake, with plant-based fats preferable over animal fats (Ley *et al.*, 2014). High white rice consumption has proven to be associated with a significantly increased risk of T2DM too (Hu *et al.*, 2012), indicating that a low cereal fiber diet with a high glycaemic load should be avoided, replacing refined grains products with wholegrain ones (Salmerón *et al*., 1997a; 1997b). For what concerns alcohol, research has shown that it is protective at a moderate consumption (about 23 grams per day), but becomes harmful at a higher consumption level (about 55 grams per day), mostly because of causing pancreas inflammation – limiting its ability to produce insulin – and increased sugar and caloric intake (Baliunas, 2009). Research has focused not only on food items in isolation, but also on food patterns. Diets rich in refined grains, red or processed meats, and sugar-sweetened beverages, while lower in wholegrains, fruits, vegetable, legumes, and nuts have been shown to increase the risk of T2DM (Ley *et al.*, 2014).

2.1.3.3 Sedentary Behaviour and Physical Inactivity

Physical activity and sedentary behaviour are not specular concepts, as well as physical inactivity and sedentary behaviour are not synonymous. The term sedentary behaviour refers to any waking behaviour characterised by a Metabolic Equivalent of Task (MET)[5] lower than 1.5, typically sitting, watching TV, or desk working (SBRN, 2014). The definition of physical inactivity is fundamentally different, referring to not achieving the minimum recommendation of 150 minutes of moderate-to-vigorous physical activity (MVPA) – as defined by a MET equal or greater than 3 – per week (WHO, 2010). Consequently, someone could not take part in any formal MVPA and yet being involved in very little sedentary behaviour because of occupational demands, while conversely it is possible for a person to comply health recommendations with 150 minutes per week of MVPA and being highly sedentary because of spending much of the time working sitting. Longitudinal studies have found that people engaged in physical activity had a lower risk of T2DM, independently of their sex, age, BMI and familiarity with the disease (Manson *et al., 1991)*. Moreover, the protective benefit of physical activity seems to be pronounced in persons at the highest risk for the disease (Helmrich *et al.*, 1994). Research has shown that time spent in sedentary behaviour is a risk factor for T2DM, and this association remains significant even after accounting for time spent in MVPA; therefore, it is not just that physical activity is protective against T2DM, but also that sedentary behaviour is detrimental for T2DM risk *per se* (Henson, 2016). Indeed, research suggested that public health campaign for T2DM prevention should promote not only increasing exercise levels but also decreasing sedentary behaviours (Hu, 2003). For instance, breaking prolonged sitting time with light walking, and simply substituting sitting for standing have been proven to be two efficient strategies to improve glucose regulation in sedentary people (Husemann, 2009; Thorp *et al.*, 2014). For what concerns the mechanisms involved, sedentary behaviour and physical inactivity increase T2DM both indirectly, being positively associated with obesity, and directly, lowering insulin sensitivity and glycaemic control (Bassuk and Manson, 2005).

[5] In epidemiology and public health research, MET is a widely used objective measure for expressing the energy cost of physical activities (Jette *et al.*, 1990). One MET is defined as the amount of the oxygen consumed by an individual while performing some specific physical activity compared to a reference set at an approximate equivalent of the oxygen consumed when sitting quietly (3.5 ml of oxygen per kilogram per minute), that is the ratio of the work metabolic rate to the resting metabolic rate. Activities with a MET value lower than 3 are conceived as light intensity ones (e.g. sleeping, watching TV, desk working, walking slowly); activities with a MET between 3 and 6 are conceived as moderate intensity ones (e.g. bicycling, walking fast, home exercise, sexual activity); Activities with a MET greater than 6 are conceived as vigorous intensity ones (e.g. jogging, cycling fast, doing calisthenics, rope jumping) (Ainsworth *et al.*, 2000).

2.1.3.4 Smoking

Cigarette smoking has been demonstrated to be a risk factor for T2DM (Maddatu *et al.*, 2017). The risk is greater for heavy smokers (more than 20 cigarettes a day) than for lighter ones, and lower for former smokers compared to active ones, indicating the presence of a dose-response relationship (Willi *et al.*, 2007). Among former smokers, the risk is increased in new quitters, but decreases substantially as the time since quitting increases. Not only active, but also passive smoking is associated with and increased risk (Pan *et al.*, 2015). Studies investigating the mechanisms involved in this association have shown that despite being linked to reduced body weight, smoking is associated with deleterious changes in body composition, especially in terms of hip-to-waist body ratio and visceral adipose tissue, supporting the evidence that smoking is linked to adverse fat distribution (Canoy *et al.*, 2005; Fujiyoshi *et al.*, 2016; Yun *et al.*, 2012). Moreover, even if a complete understanding of the molecular mechanisms through which nicotine and smoking exposure impacts on glucose homeostasis is lacking, there is evidence for a direct effect of nicotine on insulin action (Epifano *et al.*, 1992) and pancreatic beta cells functioning (Morimoto *et al.*, 2013).

2.1.3.5 Psychological Stress

Psychological stress is a broad term encompassing a range of phenomena including exposure to external challenges (e.g. stress condition in earlier life and work stress in adulthood), psychological distress (e.g. depression and anxiety), as well as negative personality traits (e.g. anger and hostility). In the literature, there is growing evidence suggesting a role for stress in the etiology of T2DM (Hackett and Steptoe, 2017). When facing stressful situations, the nervous system reacts releasing cortisol – the so-called 'stress hormone' – activating a series of detrimental consequences, including the release of glucose and lipids into the circulation and the decrease of insulin secretion due to lowered insulin sensitivity. Moreover, stress appeared to be connected with health-related behaviours, decreasing motivation for a healthy lifestyle, resulting in poor diet, lack of physical activity, and smoking, thus affecting T2DM also through indirect pathways (McEwen and Stellar, 1993).

2.1.3.6 Sleep

Short sleep duration and poor sleep quality have been demonstrated to be associated with an increased risk of T2DM (Touma and Pannain, 2011). Studies linked short-term sleep deprivation with measurable changes in glucose metabolism, hormone levels, and autonomic

nervous system activity (Broussard and Knutson, 2010), which are plausible mechanisms by which loss of sleep could contribute to T2DM.

2.1.4 T2DM Management

So far, we examined risk factors for T2DM, especially the preventable ones, attributable to lifestyle. These factors are important not only for a proper prevention of the disease, but continue to be crucial once T2DM has occurred, in order to properly manage it, avoiding progression and complications.

Lifestyle interventions meet the primary goal of T2DM management, which is to maintain blood glucose in the normal range. Thus, T2DM is usually treated in the first instance by increasing physical activity, which improves glycaemic control and reduces visceral adipose tissue, and with dietary interventions to promote weight loss, especially eliminating saturated fats and reducing sugar and carbohydrate intake. These can restore insulin sensitivity and decrease insulin resistance even when weight loss is null or modest (Thomas *et al.*, 2006). In association with lifestyle interventions, patients are typically treated with oral hypoglycaemics medications. The first-line medication for T2DM treatment is typically Metformin (Maruthur *et al.*, 2016), with an increasing tendency to prescribe it at initial diagnosis in conjunction with exercise and weight loss, as opposed to in the past, where it was prescribed if lifestyle interventions alone were not able to normalize glucose level, or when T2DM was diagnosed at a stage when glucose level was too high and was necessary to lower it quickly. Injections of insulin (Ripsin *et al.*, 2009) can be used acutely in patients newly diagnosed with T2DM to normalize blood glucose or can be added to a regimen of oral medication to improve glycaemic control. Whilst it is strictly necessary for patients with T1DM to survive (which indeed is called 'insulin-dependent'), most people with T2DM do not need insulin, especially at the initial stage of the disease (hence why it is referred to as 'non-insulin-dependent').

As T2DM is a risk factor for a wide range of diseases, its management cannot be limited to its direct effects, but needs to encompass the prevention of diabetes-related complications. Thus, lowering cardiovascular risk factors – focusing in particular on hypertension and cholesterol level – is often one of the primary goals of a proper treatment. In patients with T2DM, decreasing systolic blood pressure has been demonstrated to be associated with a lower mortality and a slower progression of the disease, protecting not only against cardiovascular complications, but also against renal, neural, and retinal ones (Emdin *et al.*, 2015). Moreover, regular follow-ups by health specialists are encouraged to prevent the development of diabetic

foot and diabetic retinopathy.

Finally, T2DM management is not a standard issue. First, there is no treatment that fits for every patient: lifestyle interventions, medications, and eventually insulin, need to be determined according to personal characteristics. Second, the treatment is not stable over time, and need to be fixed continuously according to individual response and change in conditions. Consequently, glucose management goals need to be individualized according to personal characteristics, especially age, duration of the disease, presence of comorbidities, risk of hypoglycaemia, and effectiveness of the therapy (ADA, 2014b).

Despite these general indications, T2DM management is anything but a simple thing, and requires a strong partnership between patients and healthcare providers, as well as what is called 'diabetes self-management education', the process of teaching individuals to manage their disease (Mensing *et al.*, 2007), providing a specific knowledge concerning their nutrition, exercise, monitoring, and medication, with the goal of optimizing metabolic control, preventing acute and chronic complications, and improving quality of life (Norris *et al.*, 2002).

2.1.5 T2DM Consequences

2.1.5.1 Complications

If not properly managed, T2DM can lead to complications in many parts of the body, resulting in increased hospitalizations and early death. As stated, persistently high blood glucose levels may cause vascular damage affecting the heart, eyes, kidney, and nerves, making T2DM one of the leading causes of cardiovascular disease, blindness, kidney failure, and lower-limb amputation. More specifically, T2DM complications can be divided into acute and chronic complications. Acute complications include hypoglycaemia, diabetic ketoacidosis, hyperglycaemic hyperosmolar state, hyperglycaemic diabetic coma, seizures or loss of consciousness and infections. Chronic complications are nephropathy, neuropathy, retinopathy, coronary artery disease leading to angina or myocardial infarction, peripheral artery disease contributing to stroke, diabetic encephalopathy, and diabetic foot (Cho *et al.*, 2018).

2.1.5.2 Mortality

Various studies have quantified the risk of death among patients with T2DM compared with people without it, overall confirming that T2DM is associated with an increased risk of all-cause mortality (Yu and Suissa, 2016). Though the magnitude of this excess is highly variable – depending upon characteristics of the population studied – there is common evidence that mortality is mainly attributable to cardiovascular causes (ERFC, 2011; Roper *et al.*, 2002).

Despite advances in treatment of the disease, relying on intensive intervention with multiple drug combinations and behaviour modification that has been shown to decrease cardiovascular and all-cause mortality (Gæde *et al.*, 2008), there is still an excess risk of mortality among patients with T2DM, for whom life expectancy is reduced by approximately ten years compared to people without it (Melmed *et al.*, 2016).

2.1.5.3 Psychosocial Consequences and Quality of Life

The impact of T2DM is not limited to the physical symptoms and complications of the disease. Even in absence of comorbidities, the burden of managing the disease is often detrimental for patients, leading to what has been defined 'diabetes distress'. The tasks associated with T2DM management can be very demanding and complex, generating emotional distress that have been demonstrated to be linked with poor glycaemic control, poor self-care, low diabetes self-efficacy, and poor quality-of-life (Fisher *et al.*, 2012; Young-Hyman *et al.*, 2016), thus triggering a vicious circle between psychological and physical consequences of the disease. Obviously, when at least one diabetic complication is present, the situation is even worse, and patients may find themselves to cope with functional limitations precluding the fulfilment of their possibilities both in their private and in their relational sphere. It is not difficult to imagine how having sight limitations or having been subjected to a lower limb amputation may have serious consequences in terms of daily activities as well as social interactions, leading rapidly to social exclusion. As a consequence of neuropathy, in male patients T2DM is sometimes source of erectile dysfunction, with clear difficulties in the sexual sphere. Moreover, for people with T2DM there is evidence for increased rates of physical (Wong *et al.*, 2013) and cognitive (Kodl and Seaquist, 2008) disability, depression (Goldney *et al.*, 2004), disordered eating behaviours and psychiatric disorders in general (Young-Hyman *et al.*, 2016), all leading to increased psychological distress, a worsening in overall quality of life, and potential reduction in social contacts (Feng and Astell-Burt, 2017). Differently from T1DM, research focusing on educational attainment and performance of people with T2DM is scant, consequence of the fact that the disease tends to develop more in adulthood, when education is already achieved. However, T2DM has been shown to have a detrimental impact on employment and labour market productivity (Lavigne *et al.*, 2003), not only by reducing employment but also by contributing to work loss and health-related work limitations for those who remain employed (Tunceli *et al.*, 2005).

2.2 Trends in Diabetes Prevalence

2.2.1 Worldwide

Referring to data coming from the most recent WHO report on diabetes (WHO, 2016b), an estimated 422 million adults were living with diabetes in 2014 worldwide, compared to 108 million in 1980, indicating ad incessant growth of the disease over time[6]. Since then, the global age-standardized prevalence has nearly doubled, rising from 4.7% to 8.5% in the adult population. Thus, the overall rise of the disease cannot be attributable just to population growth and increase in the average age of the population, but also to the rise of the prevalence at each age stage. More specifically, it is estimated that 39.7% of the rise in the number of people with diabetes was due to population growth and ageing, 28.5% due to the rise in age-specific prevalences, and the remaining 31.8%, due to the interaction between the two, that is an older and larger population with higher age-specific prevalences (NCD Risk Factor Collaboration, 2016). Looking at numbers in Table 2.1, in 2014 South-East Asia and Western Pacific Regions accounted for nearly half of diabetes cases in the world, but when looking at prevalence the picture appears quite difference, with the Eastern Mediterranean Region showing the highest percentage (13.7%), which are the results of the greatest rise in the period considered.

Table 2.1: Estimated prevalence and number of people with diabetes (adults 18+ years). Source: Global Report on Diabetes (WHO 2016).

WHO Region	Prevalence (%)		Number (millions)	
	1980	2014	1980	2014
African Region	3.1	7.10	4	25
Region of the Americas	5.0	8.30	18	62
Eastern Mediterranean Region	5.9	13.7	6	43
European Region	5.3	7.3	33	64
South-East Asia Region	4.1	8.6	17	96
Western Pacific Region	4.4	8.4	29	131
Total*	4.7	8.5	108	422

**Totals include non-Member States.*

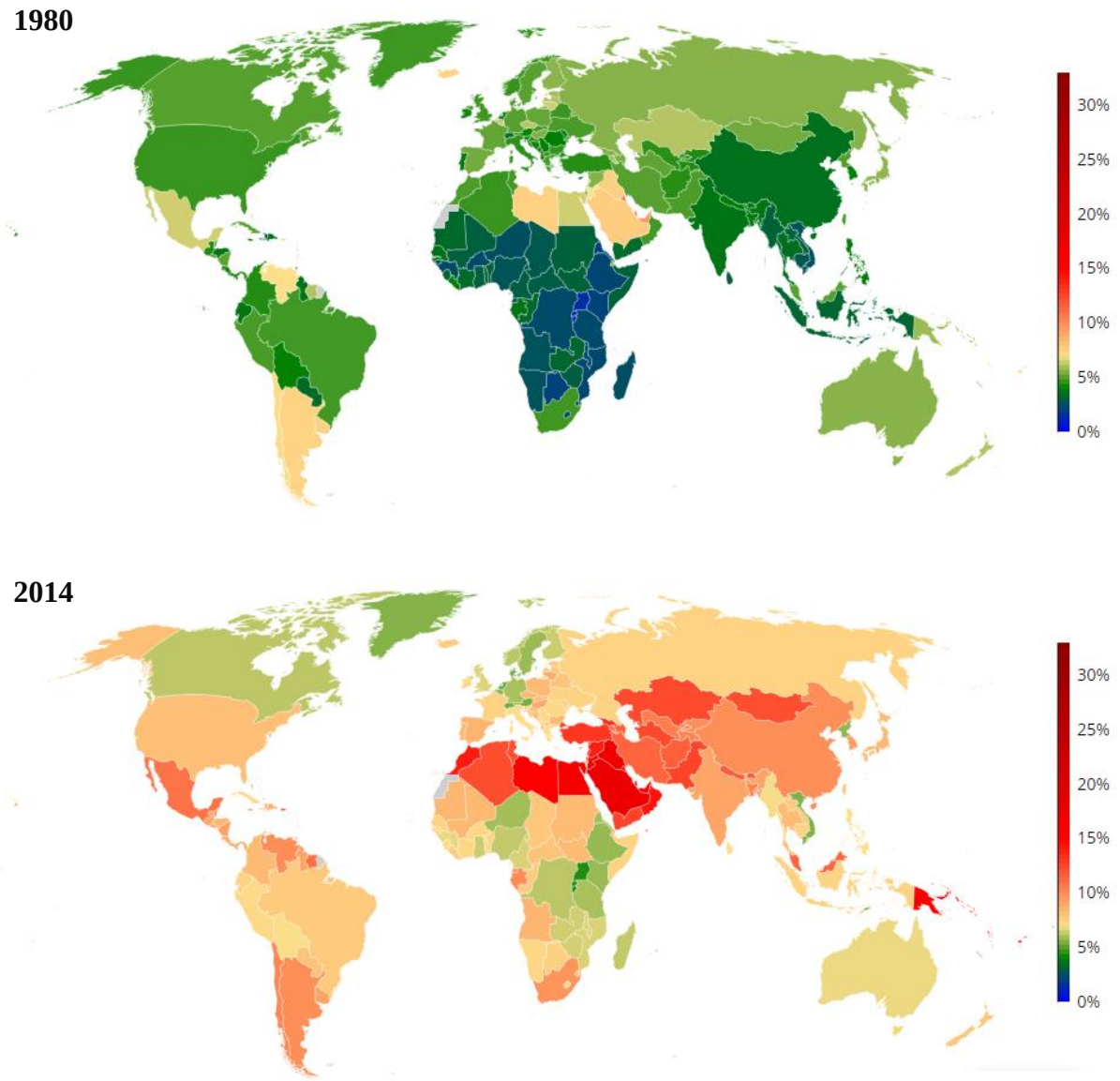
The same numbers are displayed graphically for men (Fig. 2.1) and women (Fig. 2.2) and disaggregated for single countries. The two pictures are quite similar and show clearly the change in diabetes prevalence from 1980 to 2014. The whole block of Central African countries moved from a situation of very low rates of diabetes, to one where the prevalence is in line with the rest of the world. Northern African countries have seen their situation worsening as well,

[6] This data does not distinguish between T1DM and T2DM, since – as stated in the report – separate global estimates of diabetes prevalence for type 1 and type 2 do not exist, but the majority of people (around 90%) with diabetes are affected by T2DM, which occurs more in adults – even if occurrence of the disease in children is increasing. Therefore, the figures reported can be generally conceived as a good representation of the prevalence of T2DM, without great bias.

from a situation where they were in line with the world average, to one where they are leading countries, together with Eastern Mediterranean and Southern Asian ones, for diabetes prevalence. This is what happened to nearly all countries in the past three decades, when the prevalence diabetes has risen substantially everywhere, regardless of countries' income levels, mirroring the global increase in overweightness and obesity. This is confirmed again by the maps, showing an increase of diabetes prevalence also for North America and Europe, both for men and women. However, despite the common trend, the greater increase of prevalence has occurred – and is still occurring – in low- and middle-income countries rather than in high-income ones. According to the WHO, in 2010 70% of people with diabetes in the world were living in developing countries, and by 2030 they will represent more than 80% (Blas and Kurup, 2010). Moreover, the distribution of diabetes prevalence varies not only between countries, but also within them, differing according to their income level. This is particularly the case of T2DM, which – as we will see in detail later in this chapter – is strongly socially patterned, whilst T1DM is not. In high-income countries, T2DM is usually inversely associated with socioeconomic position, with the highest prevalence in those of lower status (Robbins *et al*., 2005*)*. Conversely, studies focusing on low- and middle-income countries have reported a different picture, with a higher prevalence associated with a higher socioeconomic status (Sayeed *et al.*, 1997; Xu *et al.*, 2006)[7]. This process appears to be leaded by a combination of urbanization and globalization processes. According to the United Nations, urbanization – the process of movement of people from rural to urban areas – is expected to increase further in the forthcoming year, with a projection of 68% of the world population living in urban areas, from the current 55% (UN, 2018). The most dramatic increases are expected in low- and middle-income countries, especially in Africa and Asia. The link with T2DM lies in the fact that urban living is often associated with lower levels of physical activity, mostly due to encouragement of motorized transports, use of energy-sparing devices, and increasingly sedentary employments, which in turn increase the risk of overweight and obesity, metabolic syndrome, and consequently diabetes and cardiovascular disease. These risk factors are jointly promoted by the effects of globalization, which rapidly fostered the consumption of energy-dense foods, high in saturated fats, sugar, and salt, as well as of low cost highly refined oils and carbohydrates.

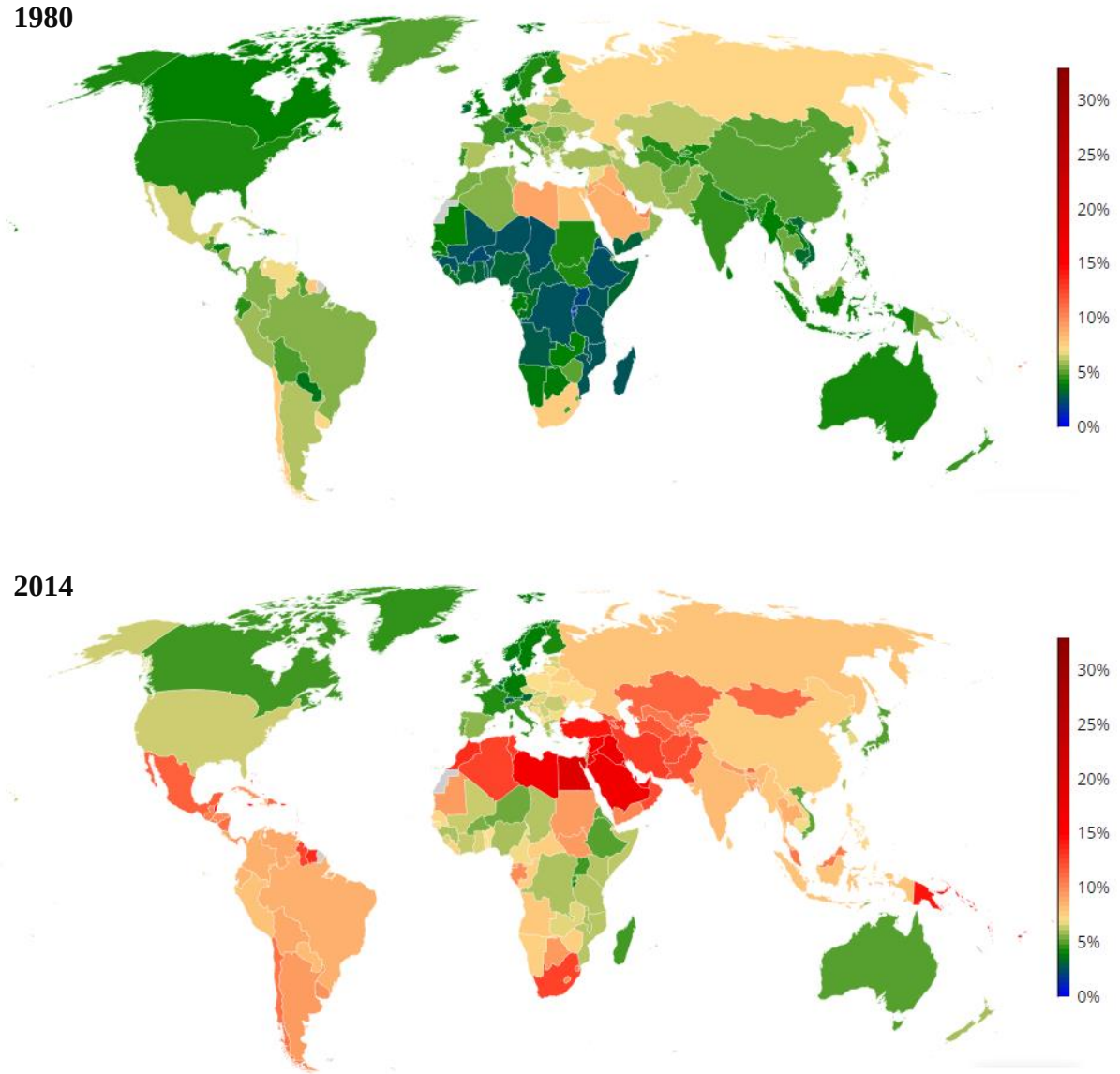
[7] Here, we are referring to the prevalence of T2DM. However, despite the different pattern of risk for people of low and high socioeconomic position in poor, developing, and affluent countries, the impact of diabetes – of whatever type – is greatest in the less advantaged groups.

Figure 2.1: Age-standardised prevalence of diabetes in adult men by country in 1980 and 2014. Source: NCD Risk Factor Collaboration (2016)



This trend towards the increased consumption of highly processed unhealthy foods, associated with urbanization in the developing world, has been referred to as the 'nutrition transition' (Popkin, 1999) and played a major role in spreading what has been defined the 'obesity pandemic' (Swinburn *et al.*, 2011), which is ecologically driven (Egger and Swinburn, 1997), given the importance of environmental factors in shaping individual behaviours. Under the pressure of global and local economic development, urban settings are becoming increasingly 'obesogenic' (Lake and Townshend, 2006) and people of different socioeconomic position in countries of different income levels react to them in different ways.

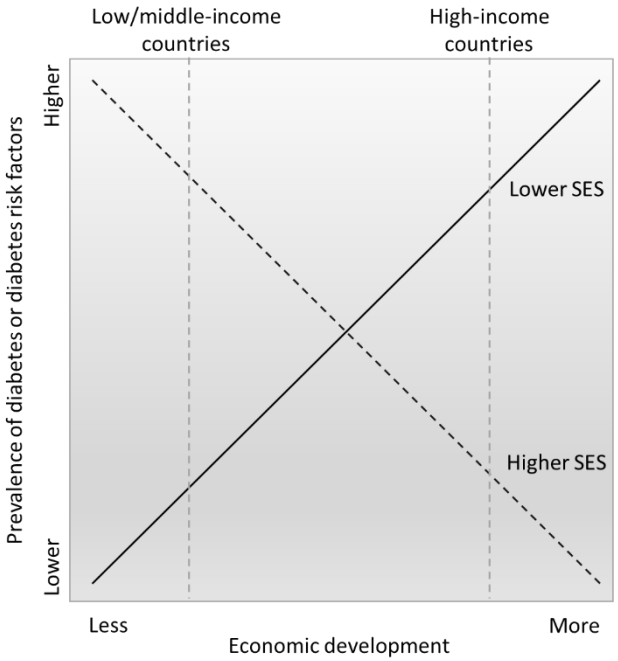
Figure 2.2: Age-standardised prevalence of diabetes in adult women by country in 1980 and 2014. Source: NCD Risk Factor Collaboration (2016)



Where income constraints among the poor are not too severe, the exposure to the risks of an obesogenic environment is likely to be greater among the poor than among the rich, and vice-versa (Popkin, 1999). That is, in affluent countries, educational background and access to information are more important than income in food choice and physical activity behaviours, since everyone could afford unhealthy food and lifestyle, but the less educated are more prone to do that. On the contrary, in low- and middle- income countries, those at the bottom of the socioeconomic ladder, due to their lack of economic resources may not be able to follow a westernized lifestyle, resulting 'protected' from its risks (but exposed to a wide range of other ones). The first to be affected by the influence of globalization processes in the poorest countries

are the wealthiest members of urban areas, but this is followed by a reversal of the socioeconomic gradient as risk factors in the long run becomes more common in the poor (Prentice, 2005). This is exactly what happened in affluent countries for T2DM, previously frequently labelled as a 'disease of affluence' and now increasingly common among the poor (Hu, 2011). This specific patterning is well portrayed in Figure 2.3, which shows the general trend of T2DM and its related risk factors between and within countries at different income levels, for people of low and high socioeconomic position.

Figure 2.3: Changing associations between economic development, socioeconomic status (SES) and prevalence of diabetes or diabetes risk factors. Source: adapted from Whiting et al. (2010).



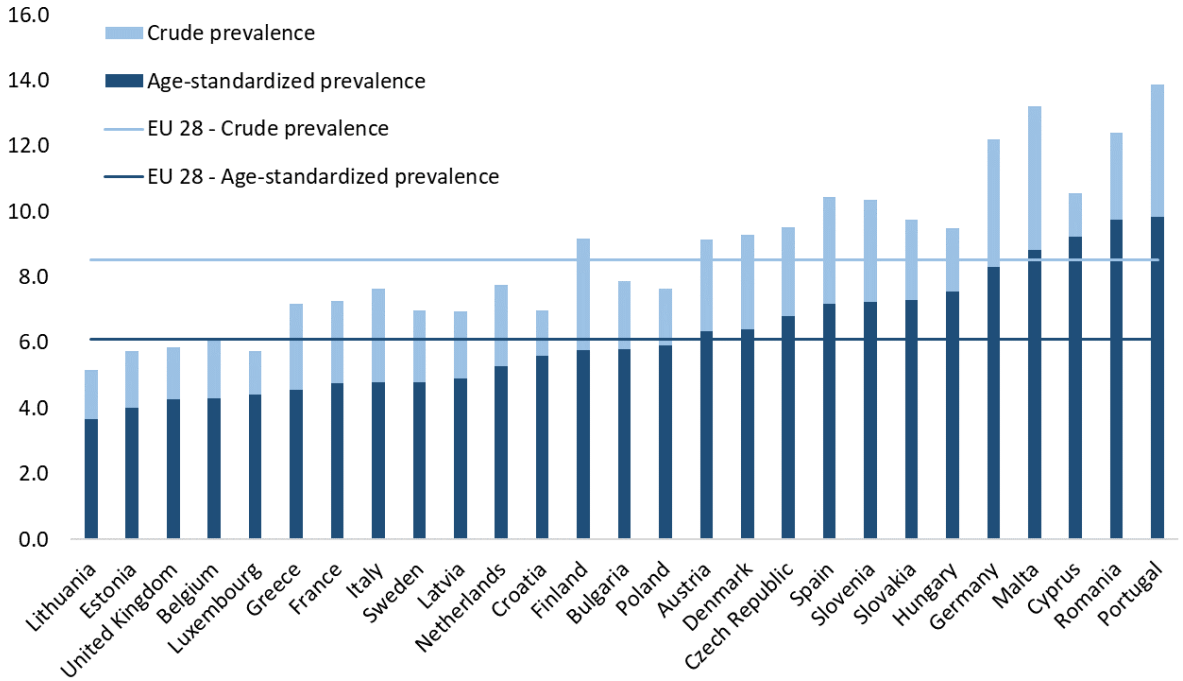
2.2.2 The Italian Case

According to Istat, in Italy more than 3.2 million reported to be affected by diabetes in 2016, corresponding to 5.3% of the total population (Istat, 2017)[8]. In line with the global trend, diabetes prevalence almost doubled from 1980, when it was 2.9%. Changes are due to population ageing, anticipation and improvement of the diagnosis, and decreasing mortality for diabetes patients (reduced by 20% in the last decade). Figure 2.4 shows data from the International Diabetes Federation (IDF), reporting crude and age-standardized prevalence for the 28 EU member states – estimates are slightly different from the one coming from Istat, due to the inclusion of an estimation of undiagnosed cases and the selection of cases aged between

[8] The data does not distinguish between T1DM and T2DM, since in EHIS questionnaire there is no distinction for types of diabetes.

20 and 79. Compared to the other countries, Italy performs quite good, being the ninth country with lower age-standardized prevalence, far below EU average.

Figure 2.4: Percentage of people (20-79 years) with chronic diabetes in the EU Member States, 2017. Sorted by age-standardized prevalence. Source: our elaboration of IDF Diabetes Atlas (http://www.diabetesatlas.org/across-the-globe.html).

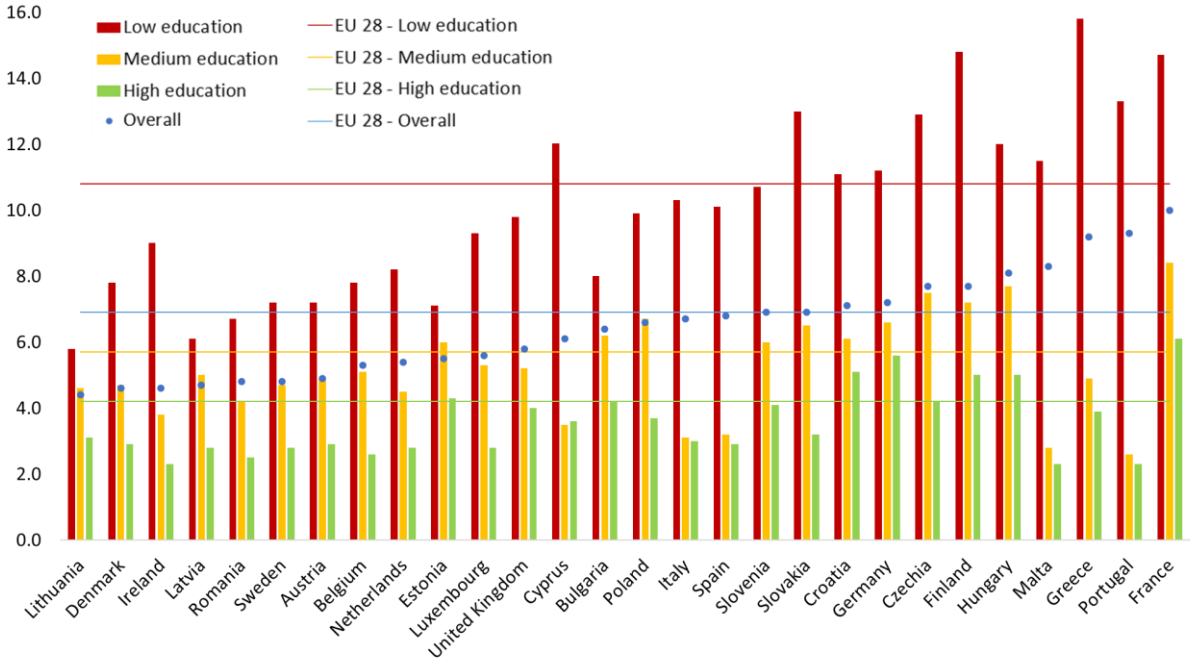


Through the European Health Interview Survey (EHIS), Eurostat provides estimates for the same countries, unfortunately not age-standardized, thus affected by the age composition of the populations. However, what is of interest is that diabetes estimates for single countries are given by educational level, in three categories (low, medium, high). As Figure 2.5 shows, a gradient is present in each country, and Italy is not an exception: the highest rates of diabetes are detectable in people with low education (ISCED 0-2)[9], followed by medium education (ISCED 3-4), and finally high education (ISCED 5-8). However, for most of the countries diabetes the rates are clearly different between people with medium and high education, whilst for Italy and other Mediterranean countries (Cyprus, Spain, Malta, and Portugal) this difference is less marked – or even reversed, as in the case of Cyprus – and the prevalence of diabetes for medium-educated people is even below the average EU prevalence of the higher educated. This

[9] The International Standard Classification of Education (ISCED) is a standard system provided by UNESCO to classify and compare educational levels in different countries. The last version ISCED 2011 is composed by eight categories: early childhood education (0), primary education (1), lower secondary education (2), upper secondary education (3), post-secondary non-tertiary education (4), short-cycle tertiary education (5), bachelor or equivalent (6), master or equivalent (7), doctoral or equivalent (8).

pattern appears to be independent from the overall rates of the countries involved, since Cyprus, Italy and Spain are slightly below EU average, whereas Malta and Portugal are the fourth- and the second-last worst performing countries in terms of diabetes rates among EU member states.

Figure 2.5: Percentage of people (15+ years) reporting chronic diabetes in the EU Member States, 2014. Sorted by overall percentage. Source: our elaboration of European Health Interview Survey (EHIS 2) data.

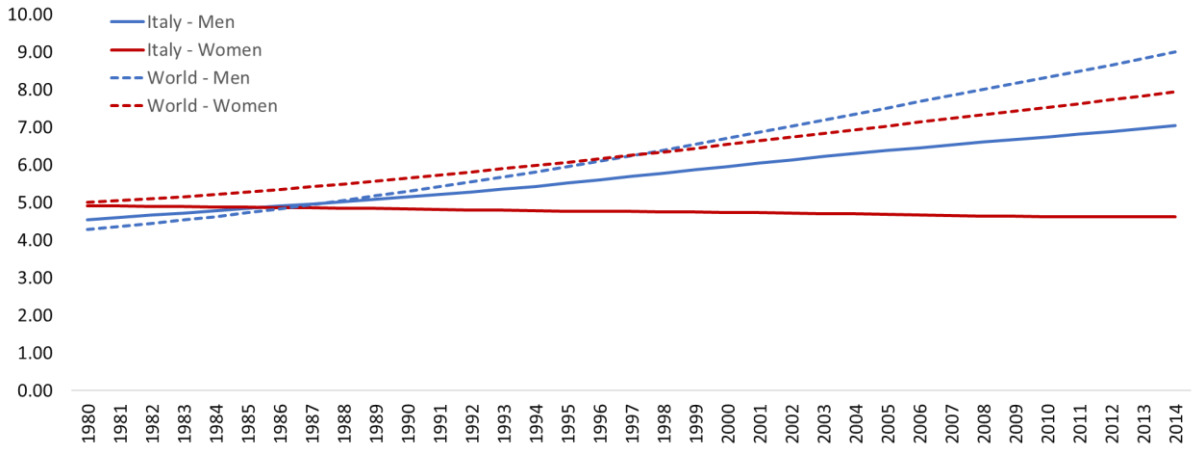


For these countries, the degree of inequality in diabetes prevalence is the highest in the whole EU, considering the striking difference reported between the less educated on one hand, and those with medium or high education on the other. Reminding that these data are not adjusted by age, the source of this inequality may be attributable – at least partially – to the low level of education of the elder people in the mentioned countries. Data from Eurostat confirms this suggestion. In 2014, 62.3% of Italian population aged between 55 and 74 had low education, far above EU average (38.6%). Portugal (81.9%), Malta (77.3%), and Spain (68.2%) were the only three countries doing worse than Italy in the EU, and Cyprus (48.9%) was far above EU average too (Eurostat, 2017). A plausible explanation could be that Italy, generally performing well for what concerns diabetes prevalence – thanks mostly to the contribution of the Mediterranean diet and an inclusive and well performing health system – presents a strong asymmetrical internal distribution of the disease due to the interaction between age and educational level in an important part of the population.

Relying on the same data adopted in the previous paragraph to show the global trend in diabetes, Figure 2.6 focuses on the Italian case, comparing it with the overall situation worldwide. What

emerges clearly is that, as already stated, there has been an increase in diabetes prevalence worldwide from 1980 to 2014, and this happened in Italy as well. However, the crossing lines for men and women show that the prevalence, initially higher for women, became subsequently higher for men, and this happened in Italy about ten years before the general trend in the rest of the world. Moreover, while the trend worldwide is homogeneous for men and women – both prevalences have increased steadily – in Italy the overall increase is driven by men (who moved from 4.6% in 1980 to 7.0% in 2014), whereas for women there has been a slow and moderate decrease (from 4.9% to 4.6%).

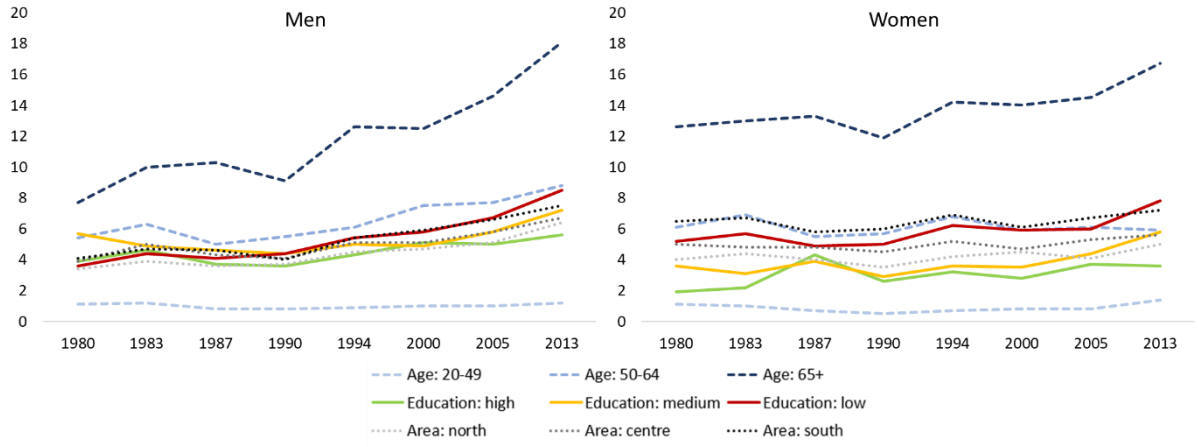
Figure 2.6: Age-standardized diabetes prevalence by sex in Italy (18+ years) and worldwide, 1980-2014. Source: Our elaboration of NCD Risk Factor Collaboration data (http://ncdrisc.org/country-profile.html).



Relying on eight health interview surveys conducted by Istat over a 34-year period (from 1980 to 2013), an Italian study (Gnavi *et al.*, 2018) examined the trend in diabetes prevalence by sex, age, educational level, area of residence and BMI for the Italian population aged 20 years and over. The study confirms the different patterns for men and women. In the period considered, the age-standardized prevalence increased from 3.8% to 6.8% for the first ones and from 5.0% to 5.8% for the latter. Diabetes prevalence increased across all ages, with the highest increase among those aged 65 years and over, especially men, the main contributors to the increase in the absolute number of people with diabetes. Concerning educational level, the prevalence increased across all levels, again with different patterns by sex. For men, the highest increase was among those with a lower educational level, while for women among those with a higher level of education. Differences by area of residence were constant across all surveys, with higher rates in the Southern regions. As it is possible to see in Figure 2.7, the prevalence remained almost stable during the 1980s, starting to rise from the beginning of the 1990s. The

largest distance between the lines referring to educational level of women indicate the presence of greater social inequalities in diabetes rates as compared to men. Overweight and obesity (data not displayed in the graph, see Tables A2.1 and A2.2 in the appendix) increased both in men and women, but to a lesser extent than diabetes. These increased more among those aged 65 and over, especially men, but accounted for the increase in diabetes mostly among the youngest age group, while for the oldest one a higher predisposition to central fat deposition is a stronger determinant of diabetes, as reported also by studies in the US (Cheng *et al.*, 2013; Mokdad *et al.*, 2000).

Figure 2.7: Trend of diabetes prevalence by age, educational level (age-standardized) and area of residence (age- standardized) in Italian men and women (20+ years). Source: our elaboration of Gnavi et al. (2018).



According to the authors, the constant increase in diabetes prevalence from the eighties onward in Italy and worldwide is attributable to several processes. First of all, the improvement of survival rate of patients with established diabetes, as a consequence of improvements in the quality of diabetes care, alongside with increased awareness of the disease, driven by the publications from the early nineties of the results of major trials demonstrating the strong relationship between hyperglycaemia and occurrence of complications. Specifically, the UK Prospective Diabetes Study (Turner and Holman, 1995; 1996) showed conclusively that the complications of T2DM, previously often regarded as inevitable, could be reduced by improving blood glucose and blood pressure control. Increased awareness caused also the identification of cases previously undiagnosed, whose prevalence has reduced in recent years. In Italy, in 1987 a specific diabetes law defined the pathology as a 'high-interest social disease', putting emphasis on its social patterning and promoting the establishment of diabetes centres all over the country, with a clear impact of diagnosis, managing of complications and survival rates. Moreover, even if the prevalence was already rising from the beginning of the nineties,

the change in diagnostic criteria introduced in 1998 by the WHO (Wareham and O'Rahilly, 1998), which lowered the fasting plasma glucose threshold for diabetes from 7.8 to 7.0 mmol/L, could have played an important role. Finally, according to the authors these driving forces of increased awareness and improvements in the care of patients are likely to have had a greater impact on those more prone to disregard their health and make less use of healthcare services, such as men, the elderly and those of low socioeconomic status, explaining the steeper increase in prevalence among these groups, as showed. In light of these considerations, the picture emerging is one of a country where diabetes prevalence increased not so much due to a parallel increase in overweight and obesity or to changes in the incidence, but rather due to population ageing and improved survival. Thus, considered the importance of ageing in the prevalence of diabetes, and considering that the number of people in the oldest age groups is expected to grow incessantly, the number of people with diabetes is destined to rise dramatically year by year, representing a severe challenge for the national health system.

2.3 Diabetes and Social Inequalities in Italy

After having showed the general trends in diabetes prevalence worldwide and in Italy from the 1980s onward, in this section we provide a detailed picture of the Italian situation nowadays, focusing not as much on diabetes prevalence, but rather on its relationship with specific characteristics of the population, paying attention to how T2DM and educational level are strictly connected. To do that, we relied on individual data from the Italian survey 'Health Conditions and Use of Health Services' (Istat, 2013), collected by Istat and referred to the year 2013[10]. The survey is based on a sample of almost 120,000 individuals (belonging to almost 50,000 family units) and it is representative of the Italian population at the regional level[11]. The survey is based on a structured questionnaire with standardized questions and items on health conditions and health-related outcomes, as perceived by the respondents themselves. In the questionnaire, diabetes status was assessed by asking respondents if they have, or if they had in the past, diabetes, and if the diagnosis was provided by a physician. All the respondents reporting diabetes stated that it was diagnosed by a physician. As for most of studies inquiring

[10] To date, these are not the most recent data concerning diabetes prevalence in Italy, representative of the whole population. European Health Interview Survey (EHIS) data for 2015 and Istat 'Aspects of Daily Life' data for 2016 are the latest available. However, we opted to rely on 2013 Health Conditions and Use of Health Service data because they encompass a higher number of health-related indicators, as well as a far larger sample size, leading to more accurate estimates.

[11] The survey is based on a multistage stratified sampling design with a specific system of weighting factors, which allows calculating estimates for the whole Italian population. More information concerning the study design is available on the Istat website (https://www.istat.it/it/archivio/5471).

diabetes, unfortunately in this survey there is no distinction between the different types of the disease. However, as T2DM is estimated to account for approximately 90% of diabetes cases, estimates are largely related to this type, especially if referred to an adult population, leaving out cases that given their age are most likely to be attributable to T1DM. Therefore, the distortion deriving from the missing distinction between different types of diabetes should be minimal, with little possibility of biasing the results, also in light of the weak (or null) association between socioeconomic conditions and T1DM. Here, we focus on the population aged between 30 and 83 years, where 30 years represent a reasonable threshold to cut out younger cases with diabetes, being most likely to be attributable to T1DM (indeed called 'juvenile'), whilst 83 years is life expectancy at birth for the Italian population in 2013 (UN, 2017). We opted not to consider people in the oldest age group, given the decreasing contribution of socioeconomic conditions in shaping health conditions and health inequalities at older ages (Herd, 20016; McMunn *et al.*, 2008; Mishra *et al.*, 2004). There is no common agreement about the reasons of the loosening of the relationship between educational attainment and health in the elder populations, but it seems that this is not attributable only to selective mortality (Beckett, 2000), a survival effect leading the most disadvantaged to die earlier, diluting the association between socioeconomic indicators and health in later life, giving the appearance of a narrowing of health inequalities with age. A possible additional explanation could be that, once a certain age threshold has been reached, biological factors may gain an increasing influence in shaping health outcomes, reducing the relative contribution of other factors, such as the socioeconomic ones. Thus, focusing on the 30-83 year-old population allows us to better grasp the social patterning of T2DM in Italy, reducing the chance both to include in the analysis T1DM cases and to describe patterns and dynamics that little have to do with the social structuring of the disease.

2.3.1 Age and Regional Distribution

Among the population selected, diabetes prevalence is 7.3% (7.7% for men and 6.9% for women), with clear differences across age groups and between sexes. As Figure 2.8 shows, apart from the youngest age group, rates are higher in men compared to women, with the greatest difference in those aged between 55 and 65 years. Prevalence increases steeply moving from the younger to the older population, for both sexes.

Figure 2.8: Diabetes prevalence for different age groups in men and women (30-83 years) in Italy, 2013. Source: Our elaboration of Istat Health Conditions and Use of Health Services survey data.

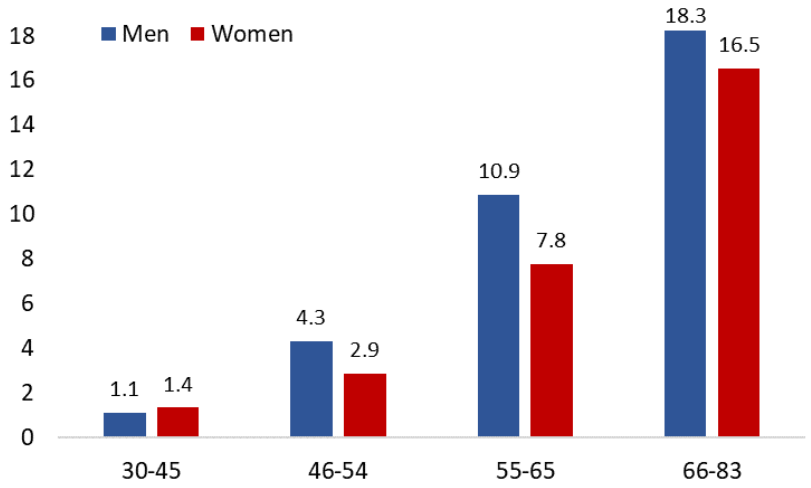
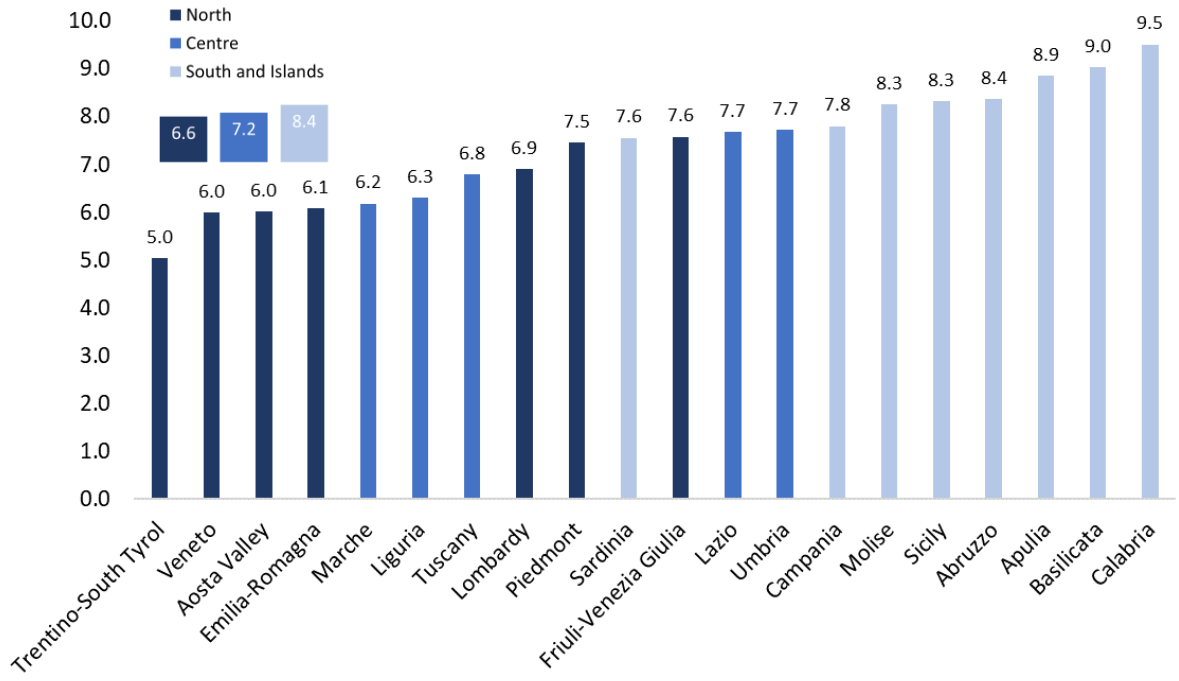


Figure 2.9 shows diabetes prevalence across Italian regions. A clear pattern emerges, that is higher rates in the southern regions, all above the national average of 7.3%.

Figure 2.9: Diabetes prevalence for different Regions and areas in Italian population (30-83 years), 2013. Source: Our elaboration of Istat Health Conditions and Use of Health Services survey data.



The difference between the best and the worst performing regions is noticeable, with Calabria (9.5%) showing a prevalence almost double compared to Trentino-South Tyrol (5.0%). Looking at sex differences (see table A2.3 in the appendix), is possible to notice that women face a disadvantage in the Southern regions: whilst in the North their prevalence is clearly lower

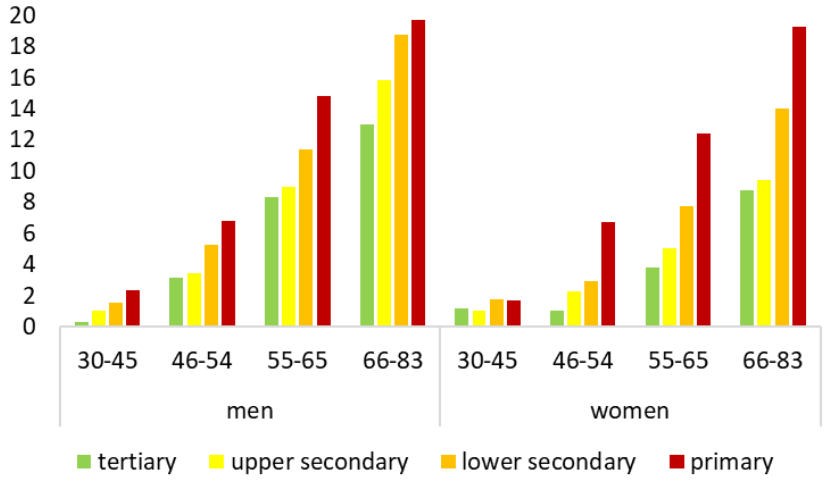
than the one of men, in the South this difference is reduced and sometimes reversed, with some regions showing a higher prevalence for women rather than men. Examining in detail the geographical variation of every lifestyle aspect that may contribute to define the regional gradient in diabetes goes beyond the interest of this chapter, however, these differences are probably due – among all – to different eating habits and patterns of physical activity between regions. Although the issue concerning food is controversial, with studies reporting a better adherence to the Mediterranean diet – characterized by low total fat, low saturated fat, high complex carbohydrates, and high dietary fibre – in the Southern Regions (Ferro-Luzzi and Branca, 1995; Vitale *et al.*, 2013), the BMI clearly increases moving from the North to the South, both for men and women (see table A2.4 in the appendix), and levels of self-reported physical activity follow the same pattern, in a more remarkable way (see table A2.5 in the appendix).

2.3.2 T2DM and Education

As already stated, diabetes prevalence disproportionally affects individuals with less educational attainment. Previously in this chapter we showed the presence of a clear social gradient in Italy and in the other EU member states in 2014 (see figure 2.5), as well as the trend of social inequalities in diabetes prevalence in Italy for men and women in a time span of 34 years, from 1980 onward (see Figure 2.7). Here, we are interested in going deeper in this relationship. Given that the majority of people with at most primary education belongs to the oldest age group, one could object that the negative association between T2DM and educational attainment – the lower the level of education, the higher the prevalence – is an artefact of age composition, with less educated individuals reporting higher rates of diabetes simply because they are older, knowing that age is a risk factor for the disease. To prove that education is associated with T2DM over and above age, Figure 2.10 shows diabetes prevalence by educational attainment, accounting for different age groups. The graphs show both the effects of age and education on diabetes. Concerning the first, it is evident how the prevalence increases in correspondence with higher age categories, both for men and women. However, inside each age group a clear social gradient is noticeable. Except for women aged between 30 and 45 years, in every set of columns those with primary education report higher diabetes rates compared to everyone else in the same age group. In addition, those with lower secondary education reports higher rates compared to those with upper secondary and tertiary education, and so on up to those with higher education, whose rates are lower than everyone else. Moreover, the graphs confirm – in a more detailed way – what already emerged while exploring diabetes trend in

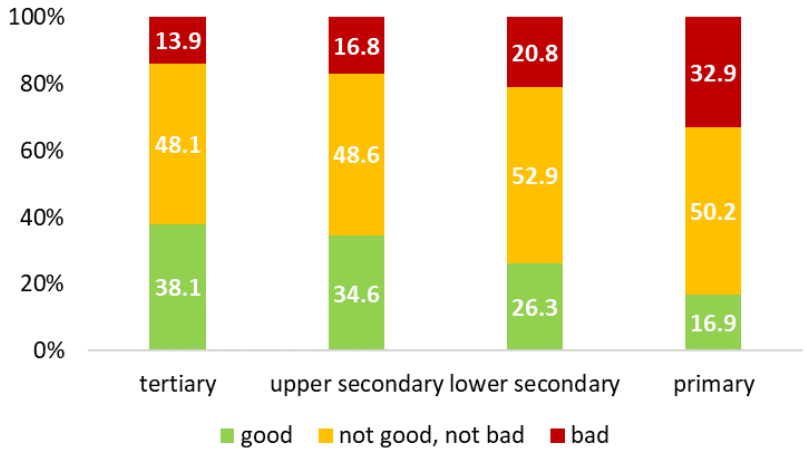
Italy, that is a larger degree of social inequalities in the diseases for women rather than for men, as noticeable from the greater distance between columns in almost each age group.

Figure 2.10: Diabetes prevalence by educational attainment for different age groups in men and women (30-83 years) in Italy, 2013. Source: Our elaboration of Istat Health Conditions and Use of Health Services survey data.



The effect of educational attainment on diabetes is not limited to the prevalence of the disease. As Figure 2.11 shows, diabetes patients with tertiary education are more likely to report a good health status (38.1%) instead of a bad one (13.9%).

Figure 2.11: Self-perceived health by educational attainment in people with diabetes (30-83 years) in Italy, 2013. Source: Our elaboration of Istat Health Conditions and Use of Health Services survey data.

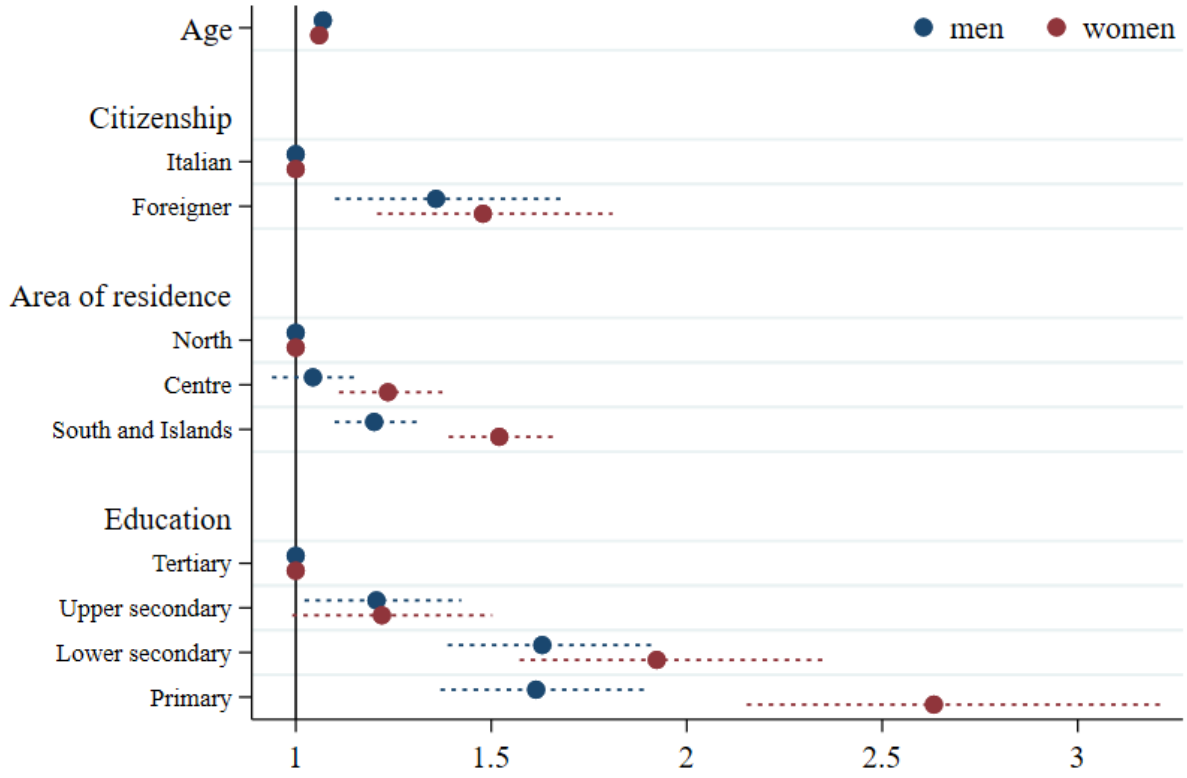


Moving from higher to lower levels of education, the percentage of those reporting good health condition decreases, up to diabetes patients with at most primary education, for which the pattern is inverted. Thus, educational background seems to predict a better quality of life for people with diabetes, again with the presence of a visible gradient in favour of those with higher attainment. However, this is just a quick overview of the topic, the relationship between

education and quality of life in diabetic people will be deepened in the next section. After examining the association between age, region and area of residence, education and diabetes separately, we ran a multivariate analysis to assess the joint effect of all the indicators on the probability of having the disease, introducing also citizenship. Figure 2.11 reports the odds ratio for men and women in our sample (for estimates see Table A2.6 in the Appendix). Concerning age, the graph shows that every additional year is associated with a significant increase in the probability of reporting the disease, which is 7% for men and 6% for women. Focusing on citizenship, both non-Italian men and women living in Italy show a higher prevalence compared to those with Italian citizenship, with women having a higher probability of reporting the disease (+48%) compared to men (+36%). Compared to those living in the Northern regions, people living in the South have a greater probability of reporting the disease. We already observed this pattern in Figure 2.9, but here it is enriched by the fact that effects of age, citizenship and educations are taken into account, permitting to exclude that the relation is biased by the different composition of the population between regions. The geographical dimension appears to be more relevant for women than men: for the latter, living in the Centre rather than in the North does not really affect diabetes (as visible by the error bars crossing the value 1), and living in the Southern Regions or Islands increases the probability by 20%. For women, instead, the probability of reporting diabetes increases by 24% for those living in the Centre, and by 52% for those living in the South or Islands rather than in the North. Looking at education, women show a higher degree of inequality. For those having at most primary education, the probability of reporting diabetes (+163%) is much higher than the one of men with the same educational attainment (+61%). The same pattern is visible for those with lower secondary education, for which diabetes risk increases by 63% in men and 92% in women. Having an upper secondary education instead of a tertiary one increases T2DM risk by 21% in men and by 22% in women, though for these latter the odds ratio is not statistically significant. Moreover, differently from the bivariate figure, when the other variables are taken into account, men with at most primary education are slightly less exposed to diabetes risk compared to those with lower secondary education. Overall, the graph provides a picture of the situation of diabetes in Italy clearly highlighting its social structuring. Although age is highly associated with the disease – possibly leading to argue that the link between education and diabetes is mostly a result of the less educated being older – even adjusting for this variable education is highly associated with the disease. As already reported by other studies in Italy (Gnavi *et al.* 2008) and abroad (Robbins *et al*., 2005), social inequalities in diabetes are more pronounced in

women, even if their risk of having the disease is lower compared to men. This may reflect different pathways through which socioeconomic characteristics affect diabetes risk in men and women. Moreover, socioeconomic risk factors for diabetes do not affect all the population equally: some groups are exposed to a cumulative disadvantage (Ferraro and Kelley-Moore, 2003) that makes them more vulnerable. For instance, despite the fact that educational attainment is strongly associated with diabetes, having at most primary instead of a higher level of education matters more for a woman living in the South compared to a man living in the North.

Figure 2.11: Probabilities (odds ratio with 95% confidence interval) of reporting diabetes by education, age, citizenship and area of residence in men and women (30-83 years) in Italy, 2013. Men N = 38.687; Women N = 42.563. Source: Our elaboration of Istat Health Conditions and Use of Health Services survey data.



2.3.3 Diabetes, Education, Quality of Life

Above we quickly introduced the issue of quality of life and its association with education, highlighting the differing percentages of self-perceived health between educational levels, with a clear pattern emerging in favour of those with higher attainment. Self-perceived health is only one of the items available in the 'Health Conditions and Use of Health Services' survey among those referred to the Short Form 12 Health Survey (SF-12), an instrument designed to measure

Health-Related Quality of Life (HRQoL) in a variety of population groups (Jenkinson *et al.*, 1997; Ware *et al.*, 1996). The SF-12 is a short version of the extended SF-36 survey (Ware *et al.*, 1994). This latter allows the calculation of eight scaled scores referring to different dimensions of HRQoL, specifically: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, mental health. The SF-12 allows the calculation of only two synthetic indices[12], the Physical Component Summary (PCS) and the Mental Component Summary (MCS), but with the addition of other eight items from the SF-36 Istat made possible to calculate two supplementary indices of Mental Health (MH) and Vitality (VT). PCS is composed of four scales assessing physical function, role limitations caused by physical problems, bodily pain, and general health; MCS is composed of four scales assessing role limitations caused by emotional problems, vitality, social functioning, and mental health. As perceivable by the choice of the scales adopted to represent the concepts, both the indices are not developed to measure physical and mental health *per se*, but rather to directly frame them in the concept of quality of life, with a specific focus on the extent to which individuals are limited in functionings due to their health conditions, both physical and mental. Thus, the connection with Sen's (1992; 1993) capability approach is immediate, conceiving the items and the scales composing the indices as the necessary capabilities to reach the desirable functionings of good physical and mental health conditions, well-being and quality of life, in its broader meaning. Thus, very low PCS and MCS scores reflect substantial functional limitations, severe social and role disability, distress and very unfavourable evaluations of health status and outlook; conversely, very high scores are earned only in absence of limitations and disability in social or usual role activities, as well as with high levels of well-being and very favourable personal health evaluations (Ware *et al.*, 1994). MH and VT are two measures partially overlapping with MCS, being some of their items used also in the calculation of this last, but denoting some specific aspects of mental well-being, rather than representing this concept broadly. More specifically, MH encompasses indicators of mental well-being that are strictly related to emotions (feeling nervous, down in dumps, peaceful, blue or sad, happy) whereas VT is more related to life force, encompassing indicators partially representing also the physical sphere (feeling lively, energetic, worn out, tired). Here, we use these four indices first to assess the different levels of HRQoL reported by the diabetic

[12] For a list of items and scales included in SF-36 and SF-12, see Table A2.7 in the appendix. Different empirical studies have shown that the synthetic indices of the questionnaire SF-12 correlate with the corresponding indices of the SF-36 questionnaire with a range of values between 0.93 and 0.97 (Gandek *et al.*, 1998).

population in Italy as compared to the non-diabetic population, and second – most importantly – to assess the association between education and HRQoL in people with diabetes. Table 2.2 shows the average score for each index – all the indices have been normalized to vary between 0 and 100, with higher values indicating better outcomes – providing a useful initial picture of the difference between diabetic and non-diabetic individuals in terms of quality of life. As expected, diabetes has a negative impact on each HRQoL domain, both in men and women, with significant decrease in all the indices. At first glance, men experience a better quality of life compared to women, and diabetes seems to affect more the latter than the first. Moreover, comparing the different indices, the larger decrease due to diabetes is observable in the physical dimension, especially in women.

Table 2.2: Average scores of Physical Component Summary (PCS), Mental Component Summary (MCS), Mental Health (MH) and Vitality (VT) in men and women (30-83 years) with and without diabetes in Italy, 2013. All the indices vary between 0 and 100, higher levels indicate better physical and mental conditions. Source: Our elaboration of Istat Health Conditions and Use of Health Services survey data.

	Men				Women			
	Overall	Non-Diabetic	Diabetic	δ	Overall	Non-Diabetic	Diabetic	δ
PCS	68.0	69.0	56.3	12.8	64.7	65.9	48.5	17.4
MCS	65.8	66.2	61.4	4.8	62.5	63.0	56.1	6.9
MH	71.5	72.2	63.9	8.2	67.1	67.9	56.3	11.6
VT	63.1	64.0	53.9	10.1	57.3	58.3	44.5	13.8
N	*38,687*	*35,524*	*3,163*		*42,563*	*39,485*	*3,078*	

However, these numbers do not take into account age composition of the groups. So that the lower scores in women, both with and without diabetes, may be a consequence of the fact that women tend to live longer, and ageing is associated with a decrease in HRQoL, especially in presence of a chronic disease involving functional limitations. The effect of age is taken into account in Table 2.3, which provides estimates of the regression models for each HRQoL index by education, also adjusting by citizenship and area of residence, in the diabetic population. In each model, age is centred on 30 years, thus the value of the intercept represents the average score for a diabetic man or woman aged 30 years, of Italian citizenship, living in a Northern Region and with tertiary education. The coefficients for age represent the variation in the score for every additional year, while the coefficients for the other predictors represent the variation when belonging to another category instead of to the reference category. For instance, the average PCS of an Italian diabetic man, aged 30 years, with tertiary education, living in the North is 83.23, while for a 60 years-old diabetic man, without Italian citizenship, living in the South, with at most primary education is 49.20. A difference of more than 34 points in an index

ranging from 0 to 100 is considerable, moving from a situation of a very good quality of life – also keeping in mind the chronic disease of the individual – to a less favourable one, indicating a noticeable effect of all the independent variables on our outcome. However, focusing on our predictor, education, we can notice that contrary to what emerged from the raw mean scores in Table 2.2, the effect on the indices is greater in men rather than women. This apparent controversial finding is explained by the greater effect of age for women: both men and women experience a significant decrease of HRQoL when they have diabetes, but the nature of this change is different between them, being mostly due to education in men and to age in women. Indeed, the PCS of a diabetic woman in advantaged conditions (30 years-old, Italian, living in the North, with tertiary education) is 76.57, while it falls to 43.04 for an average woman in more disadvantaged conditions (60 years-old, non-Italian, living in the South, with at most primary education). Thus, in the case selected, the decrease in PCS is approximately by 41% in men and by 40% in women, but nevertheless these very similar percentages are mostly driven by different processes, specifically ageing in women and social inequalities in men.

Table 2.3: Linear regression models of Physical Component Summary (PCS), Mental Component Summary (MCS), Mental Health (MH) and Vitality (VT) in men and women with diabetes (30-83 years) in Italy, by age (centred on 30 years), citizenship, area of residence and education, 2013. N men = 2,976; N women = 2,895. Source: Our elaboration of Istat Health Conditions and Use of Health Services survey data.

	Men				Women			
	PCS	MCS	MH	VT	PCS	MCS	MH	VT
Age	-0.44***	0.03	-0.09*	-0.22***	-0.59***	-0.09**	-0.24***	-0.36***
Citizenship								
Italian	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Foreigner	-4.64*	-1.34	-4.72*	-5.90**	-6.06***	2.13	1.11	1.00
Area of residence								
North	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Centre	-2.15*	-2.87***	-4.77***	-5.20***	-1.52	-3.64***	-4.62***	-1.18
South and islands	-5.31***	-4.45***	-7.83***	-6.64***	-5.53***	-5.60***	-7.51***	-5.10***
Education								
Tertiary	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Upp. secondary	-6.19***	-0.94	-3.14	-2.58	-1.30	1.24	-0.22	1.62
Low. secondary	-8.26***	-3.18*	-6.70***	-5.29**	-2.50	-1.27	-4.20	-0.65
Primary	-10.88***	-4.80***	-8.37***	-8.94***	-4.24*	-1.64	-5.86**	-2.51
Intercept (all***)	83.23	65.59	77.56	71.74	76.57	63.48	73.80	61.69
R^2	0.12	0.02	0.05	0.06	0.16	0.03	0.06	0.07

* P-value ≤0.050; ** P-value ≤0.010; *** P-value ≤0.001

Comparing different indices, we can notice the greater importance of educational level for the physical dimension (PCS) rather than for the mental dimension (MCS, MH, VT) in men, for whom all the models are statistically significant at least for primary and lower secondary education, while in women just the PCS and MH are statistically significant and only for primary education, without the presence of any social gradient for any index. In men, differently, every index presents a social gradient. Having upper secondary instead of tertiary education does not really make a difference in terms of quality of life – execpt for the PCS – but then a lower level of education, all other things being equal, have a detrimental effect on every HRQoL measure. These findings add another piece of knowledge to the relationship between educational attainment and diabetes. Overall, we saw that lower levels of education are associated with higher diabetes prevalence, but also that even if diabetes prevalence is higher in men compared to women, social inequalities in the onset of the disease are larger for the latter. Moreover, we saw that education is associated also with quality of life, again with lower attainment being related to less physical and mental functionings. Nevertheless, despite the fact that social inequalities in diabetes are greater in woman rather than men, their impact on quality of life is considerable in men, whereas only limited in women, for whom other factors – above all age – seem to play a more important role. Though statistically significant, all the regression models fitted reported small R^2 values. This is a consequence of the fact that the indicators selected are not the major determinants of HRQoL, despite being associated with it. Some other factors not included in the models are problably more relevant in shaping the association, such as, for instance, early-life conditions, stress level, job conditions, social support, and the like.

2.4 Diabetes and Social Inequalities: Mechanisms in Action

Previously in this chapter we reviewed the most important risk factors for T2DM, namely obesity, dietary pattern, sedentary behaviour and physical inactivity, smoking, stress, and sleep. Framing them in the CSDH model of social determinants of health presented in the first chapter, these can be conceived as intermediary determinants, namely the factors that are closest to the onset of the disease in the causal chain, influenced by antecedent structural determinants, such as the socioeconomic and political context and socioeconomic status. Adopting a behavioural explanation, we would be led to consider inequalities in T2DM as a matter of individual choice, given their marked association with individual lifestyles. However, we already explained in the previous chapter how conceiving individuals' choices and actions as undertaken in a social vacuum may be misleading, given that behaviours and lifestyles are strongly socially structured.

Hence, this section is aimed at unveiling the mechanisms through which structural factors shape T2DM outcomes, passing through the intermediary determinants (or individually-based risk factors). Doing that, we focus both on individual and neighbourhood factors able to affect T2DM inequalities, keeping in mind that these are often intertwined, and it is not possible to consider them as entirely separated entities. Educational attainment, for instance, influences the degree of knowledge that an individual may have in order to prevent the onset of the disease, while the neighbourhood of living may exert an effect through the availability of green spaces and walkable pathways, which are protective against the risk of developing T2DM. However, people with higher education are generally more likely to live in neighbourhood with a higher disposition of health-protective and health-enhancing resources, and conversely, the place of living may affect employment opportunities. Thus, what we define as individual triggers of health inequalities have necessarily consequences on the spatial structuring of the disease, and vice-versa. Moreover, it is important to underline that the mechanisms described are sometimes oversimplifications of reality, but nevertheless they are effective in showing how access to resources is influenced by individuals' socioeconomic background, as well as how different types of explanations (material, psychosocial, cultural, behavioural, relational) converge in explaining how socioeconomic conditions operate in determining differentials in T2DM risk through macro, meso and micro processes.

2.4.1 Socioeconomic and Political Context

Examples of T2DM determinants at the level of socioeconomic and political context have been already discussed previously, showing the worldwide trend in diabetes comparing low-, medium-, and high-income countries. We already stressed the role of globalization and urbanization in defining lifestyles and behaviours, a remarkable example of how macroeconomic, individual, and environmental factors are intertwined in shaping population health. Globalization may radically alter food provision, hindering access to healthy food, given its decreasing availability in favour of low-cost, highly processed, ready to serve products. These are typically high in sugar, salt, calories, and fats, and their ordinary consumption is a well-assessed risk factors for obesity, cardiovascular disease, high blood pressure, and of course T2DM. However, the fact that international trade contributed to the westernization of lifestyles, does not affect everyone equally within the same context. The most educated may be more aware of the risks of following a certain food regime, making efforts to avoid it, a strategy that it is possible to pursue in presence of adequate economic resources. Moreover, even if economically affordable, the possibility of adopting a healthy food regime may be discouraged

by the distance from supermarkets and food outlets. Hence, it is clear first how behaviours may be structured by constraints that are outside the control of individual choice, and second that these constraints do not affect everyone equally: those with lower education and income are generally disadvantaged, and the type of job may play a role, too. People working on long or night shifts may be forced to skip meals (another health-threatening habit), or to rely on a restricted range of options to have a meal. Although we initially presented these processes to account for differences in T2DM rates between developed and less developed countries, it is important to highlight that these are not restricted to less affluent nations. Considering the case of Italy, for instance, the growing incidence in T2DM showed may be attributable – in addition to the factors exposed (change in diagnostic criteria, improvements in diagnosis, and population aging) – to changes in nutrition and also pattern of physical activity. In correspondence with the economic boom after the Second World War, also referred to as the 'Italian economic miracle', the country went through a rapid transformation from a relatively poor and mostly rural nation into a global industrial power (Forgacs & Gundle, 2007). It is arguable that this led to changes in food provision similar to the ones just described, with a transition from a strong reliance on internal market (autarchy was pursued during the fascist period), to an open economy, in parallel with a growing influence of American lifestyles and culture. Thus, in absence of knowledge concerning the risks connected to the emerging pattern of nutrition (and lifestyles in general), it is likely that these changes initially affected the population more or less equally, whereas subsequently, as information highlighting their dangerous potential became available, a gradient in favour of the more equipped with social, cultural, and economic resources began to emerge, as we saw for the case of tobacco smoking. Although it may seem exaggerated to consider globalization as a cause of disease, especially for a country like Italy, considering the chain of factors involved in the pathways leading to T2DM, it is reasonable to attribute to such a phenomenon a role, surely mediated by more proximal factors (Navarro, 2007). Urbanization plays a similar role, being at the same time strictly connected with the characteristics of the local environment. Indeed, despite being dependent on macrolevel processes (e.g. industrialization, commercialization, public and private investments, etc.), it exerts its effects at a very local level, in the way it influences the urban setting in its material and social characteristics, with influence again on dietary patterns, physically activity, working conditions, stress, and the like. The political context may also affect citizens' chances of being exposed to T2DM both directly, for instance through the amount of resources that are earmarked for spreading information to prevent the disease, encouraging preventive screening,

and assuming overall responsibilities for people's care, and indirectly, in the way it affects patterns of working activities, educational attainment, food provision, and the like. Specifically, in the previous chapter we already highlighted how neoliberal reforms have been empirically linked to a worsening of health outcomes, with reduced social expenditures, austerity, privatization, and growing inequality affecting people's health and well-being not only through a reduction of resources available for individuals (Coburn, 2004) but also through psychosocial mechanisms related to the perception of inequality (De Vogli, 2011), highlighting the need to integrate the understanding of neoliberalism and political economy into the study and the theorization of health inequalities (Peacock *et al.*, 2014). Thus, while healthcare cuts, privatization, and restriction in access to services are usually conceived as the most immediate pathways through which the political sphere may affect health, there are also several subtle and indirect mechanisms in place. The increased flexibilization of the labour market, for instance, is one them, shifting the risks connected to the enterprise from employers to employees, leading to increase in unstable jobs, which in turn influences health both through the diminishing of material resources (e.g. lack of continuous income and forms of social insurance), and the stress deriving from the insecurity engendered by such precarious working conditions. Again, the connection of this higher-level structural dimension with individual behaviours is immediate, given that people are often likely to start smoking, drinking alcohol, to adopt an imbalanced diet, or to avoid physical activity as coping strategies to face stressful situations (Krueger & Chang, 2008; Ng & Jeffery, 2003). Finally, also social and cultural values may play an important role in defining T2DM outcomes. Belief about what is a desirable body size and shape, for instance, are not the same for every population, and these are like to interact positively or negatively with obesogenic features of the living environment. To give an example, a study aimed at assessing knowledge, attitudes, risk factors, and behaviours related to T2DM in Cameroon found that it was generally considered desirable for local men and women to be overweight and even obese, this being a distinctive sign of wealth and health (Kiawi *et al.*, 2006). These beliefs and attitudes are common in several sub-Saharan countries (Renzaho, 2004), and with migration processes they are likely to be observable also in wealthy countries, contributing to explain ethnicity differences in T2DM rates. Moreover, due to a lack of knowledge about diabetes and the role of insulin therapy, some Hispanic, Asian, and African Americans groups believe that the use insulin causes complication in the long term, or they also may see the initiation of insulin as indicative of a failure of the patient to care for himself, rather than as a result of the natural progression of diabetes (Rebolledo & Arellano, 2016). Again, this

cultural dimension is strictly connected to individual socioeconomic characteristics, given that within the same groups, the more advantaged are more likely to get proper information and diabetes education (awareness, understanding of causality, and clinical knowledge about the disease and its treatment), avoiding to follow deceptive beliefs. Concerning religion, some precepts may influence dietary patterns limiting some types of food or imposing fasting periods.

2.4.2 Structural Determinants and Socioeconomic Position

The effects of socioeconomic conditions on T2DM risk may start at early age, and even before birth. Prenatal conditions such as malnutrition, low protein diet, overnutrition, hormone administration, tobacco and alcohol consumption during pregnancy, artificial feeding and maternal stress may cause strong and permanent effects on the foetus, increasing the risk of developing T2DM later in life (Jiang *et al.*, 2013; Young *et al.*, 2002). Accordingly, given that the onset of the disease, which typically occurs in adulthood, is strongly determined by conditions and exposure to risk factors throughout the whole life-course, family socioeconomic conditions may be even more important in determining the disease than the socioeconomic status acquired later in life. According to Barker (1994; 1995; 2002), adverse nutrition in early life and before birth increases susceptibility to the metabolic syndrome, which includes obesity, diabetes, insulin insensitivity, hypertension, and hyperlipidemia, 'programming' the development of several risk factors manifesting their effects later in life, such as it would be reductive to focus on inappropriate behaviours and lifestyle as the only determinants of diseases. Moreover, besides the biological pathways described, early life and family socioeconomic conditions exert their effect in shaping lifestyle behaviours. Children of smoking parents, for instance, are more likely to start smoking and may also be subjected to passive smoking at home, while eating habits in the family influence eating habits for the whole life-course, impacting on diet-related T2DM risk factors (overweight, obesity, high sugar and salt, and low fiber diets, and the like). Furthermore, parents' socioeconomic status is strongly predictive of their offspring educational achievement and earnings, (Causa and Johansson, 2009; Checchi *et al.*, 1999), so that family background may have an impact on the chance of having T2DM in adulthood not only directly, through the exposure to risk factors in early life or the transmission of behaviours and habits which may be adopted during the whole life-course, but also indirectly, in the way in which it influences the probability of getting access to health-protective and health-enhancing resources of various kind later in life. One of the key elements through which socioeconomic status influences T2DM is *health literacy*, a concept referring to individuals' capability to effectively function in the healthcare environment

(Berkman *et al.*, 2010). More specifically, it denotes "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions" (Ratzan and Parker, 2006, 713). Health literacy involves a set of skills of various kind, such as functional (the ability to read and understand written text, locate and interpret information in documents, and write or complete forms), interactive (the ability to speak and listen effectively and communicate about health-related information), critical (the ability to navigate the healthcare system and make appropriate health decisions), and numeracy (the ability to use numeric information for tasks, such as interpreting medication dosages and food labels). These are associated with a wide range of adverse effects on care processes and health outcomes, including T2DM, both in preventing and coping with the disease (Al Sayah *et al.*, 2013; Powell *et al.*, 2007; Schillinger *et al.*, 2002). Health literacy is strictly dependent on individuals' cognitive and coping resources, and consequently on socioeconomic conditions; thus, it can be conceived as one of the leading mechanisms through which education, occupation, and income may influence health and T2DM outcomes. In a context where information and knowledge about risk factors for T2DM are present and spread across the population, the possibility to take advantage of them to prevent the onset of the disease is not the same for everyone. Those with more resources are more likely not only to have more diabetes-related knowledge in advance, but also to process new information when it comes. Moreover, they are more likely to encounter useful information, for different reasons. A white-collar employee may have more chance to read newspapers and magazine where health-related information is reported compared to a blue-collar worker, due both to the type of job and the availability of time. Moreover, people with highly qualified jobs may have more opportunity to discuss with more informed persons in the workplace. Additionally, disposable income may be determinant in shaping different possibilities for people to access to information relevant for preventing diseases and running a healthier lifestyle. Even if eager to do that, some may be forced to allocate their economic resources for basic needs, being limited in the possibility to spend money for recreational purposes and reading. Despite the strong correlation between the two, health literacy is not entirely assimilable to education, given that it encompasses aspects related also to the occupational and economic spheres (Van der Heide *et al.*, 2013). Concerning working activity, it may influence T2DM in several ways. In relation to diet, manual workers subjected to physically demanding tasks may be more likely to feel the need for higher calories intake, which may easily lead to follow an imbalanced diet. Similarly, those working in an office may be less likely to smoke compared to manual workers who carry

out their activities outside, or they may be induced to smoke less. In the previous chapter we presented Karasek's *demand/control model* (Karasek, 1979) and Siegreist's *effort/reward model* (Siegrist, 1996), according to which individuals exposed to imbalanced conditions between costs and benefits in the work environment are more prone to be subjected to detrimental psychological conditions, leading to worse mental and physical health outcomes. These psychosocial mechanisms are effective in the pathway leading to T2DM, given that stress response increases secretion of cortisol, which stimulates glucose production in the liver and limits the action of insulin. Thus, socioeconomic conditions may increase T2DM risk not only through the mediation of material and behavioural factors, but also through psychosocial pathways, which directly affect the pathophysiology of the disease (Leynen *et al.*, 2003; Nyberg *et al.*, 2014). This highlights again the independent role of each socioeconomic indicator in the causal pathway leading to the disease. Psychological stress due to an imbalanced perception between efforts and rewards in the workplace may be experienced also by well-educated and high-income people, putting an individual without material difficulties to a higher risk of the disease, compared to an individual in the same conditions who experiences a better job satisfaction. Psychosocial, material, and behavioural explanations converge when considering *time perspective* as a mediator of the relationship between socioeconomic status and health (Zimbardo and Boyd, 2015). Time perspective is a psychological construct that describes how one's perception or weighing of the past, present, and future influences decision making. It is thought to represent a subconscious cognitive structure that one accesses when making decisions about short-term and long-term actions and goals. In some circumstances, the foremost influence comes from the events of the past; in others, it is based in the immediate cues of the present environment. In other cases, an individual's motivations may be primarily based on consideration of future consequences (Guthrie *et al.*, 2009b). Time perspective has been related to differences in health behaviours, being associated with socioeconomic conditions (D'Alessio *et al.*, 2003; Fuchs, 1982; Lamm *et al.*, 1976). People of lower status seem to be more likely to overlook their future, attributing more importance to present gratifications, given the uncertainty of their time to come. Smoking, excessive alcohol consumption, a diet rich in sugar, fats, and carbohydrates, as well as physical inactivity, are all behaviours that may be more satisfactory in the present, but potentially leading to health problems in the long run. Thus, people with less disposition of resources of various kind, who are subjected to less expectations for the future, may perceive no way to improve their conditions, preferring to enjoy what they can afford immediately, disregarding their health,

although they are aware of the risk potential of their lifestyles. A study of women on low income, for instance, revealed that almost all the money they had was spent for the household and the children, and the only personal expenditure they allowed themselves was cigarettes, the only immediate form of pleasure they could afford (Graham, 1993). Conversely, those who are more equipped with social, economic, and cultural resources may find it easier to get pleasure from less risky behaviours, and to value future as well as present. Moreover, we already anticipated how these health-threatening behaviours are conceived as coping strategies: people facing stressful conditions at home or in the workplace may benefit from taking time for themselves smoking a cigarette, enjoying the only moments in the day they concede to themselves, stopping worrying and being exposed to straining situations for a while. Physical inactivity and sedentarism are not exempted to be put in relationship with socioeconomic circumstances. Again, those facing physically demanding jobs may be too worn out after a day at work to exercise, while people working in the office may compensate their sedentary lifestyle by feeling more willing to practice a sport after work, being likely to be subjected to mental stress, but not physical strain. Finally, in a relational perspective, people of higher socioeconomic status may benefit from their acquaintances' behaviours and resources. As discussed highlighting the role of family in influencing behaviours, people may tend to reproduce their peers' behaviours. In a school or working environment where most people smoke, other people may be more likely to start smoking, or less likely to quit, even if they had intention to do it. Research has shown that behaviours may spread in social networks (Christakis and Fowler, 2007; 2008; Rosenquist *et al.*, 2010). Obesity in alters, for instance, might influence obesity in egos by diverse psychosocial mechanisms, not only affecting behaviours, but also changing the perception about the acceptability of being overweight: if a lot of friends or peers are overweight, someone may feel more comfortable to be the same, without worrying about losing weight or limiting food intake. The same logic is not restricted to smoking and obesity, being applicable to other risky behaviours, such as alcohol consumption, physical activity, and the like. Like behaviours, also resources are transmittable from person to person. People of higher socioeconomic status are generally more likely to know other people of high status, who may help in extending the possibility to pursue a healthy lifestyle, or in expanding one's access to resources of various kind. Having a doctor, a pharmacist, or another healthcare professional between the intimate acquaintances may expand health literacy or facilitate access to proper care when needed. Similarly, knowing and being in contact with someone with specific expertise may be helpful in a variety of specific situations. Recommendations and intercessions

may favour career, permitting to access to a prestigious education or to a profitable job. Those who attended at least upper secondary education may be likely to keep in touch with former schoolmates who subsequently specialized in different fields in university, being able to rely on people with different knowledge and resources when needed. Conversely, those who stopped education earlier may be limited in this, knowing mostly people of similar educational and working profiles.

2.4.3 Ecological Determinants

As we stated, T2DM is hypothesized to be the outcome of the interaction between biological, material, psychosocial, behavioural, and environmental risk factors. Environmental characteristics may increase or decrease exposure to T2DM risk factors by enhancing, constraining, or limiting behavioural, psychosocial and physical stressors (Dendup et al., 2018). The physical and social characteristics of the living context can influence choices and behaviours in several ways. Availability ofand proximity to recreational resources, green spaces, open spaces, walkable paths, sidewalks, well-connected public spaces, can encourage physical activity and social interaction (Gordon-Larsen *et al.*, 2006; Renalds *et al.*, 2010; Richardson *et al.*, 2013). A highly walkable environment may induce people to limit the use of car or public transport, walking more and reducing the risk of overweight and obesity. Similarly, living close to supermarkets may expand food choice and encourage a healthy diet, whereas limited access to supermarkets may motivate visits to convenience stores and fast-food outlets, which may increase the probability of unhealthy food intake, given the restricted range of products available and their quality (Gordon-Larsen, 2014). Proximity and accessibility to healthcare services may also shape the possibility for a proper T2DM prevention. Among the psychosocial stressors, crime, social disorder, and unsafe neighbourhoods may incite social isolation and fear, inducing people not to go outside if not strictly necessary and to rely heavily on cars, inhibiting physical activity (Bennet *et al.*, 2007). However, the effects of an adverse neighbourhood environment are not limited to physical and material resources. Prolonged exposure to multiple environmental stressors can lead to allostatic load, that is the biological wear and tear of the body physiological system. Thus, perceived unsafety in the living context may generate chronic stress, stimulating the release of substances like cortisol and cytokines than can damage the immune and body systems, affecting insulin resistance and accelerating the progression of chronic disease, including T2DM (McEwen and Wingfield, 2003; Stockdale *et al.*, 2007). We already highlighted how stress can in turn motivate unhealthy eating, smoking, drinking, and affect sleep. Another source of stress in the residential context may be noise

pollution, whether it is caused by traffic, people, or other sources (Dzhambov, 2015). Thus, behavioural and psychosocial pathways at the individual and the neighbourhood level may trigger each other, creating a vicious circle in which it would be difficult to discern the causes from the effects. Air pollution is another environmental factor that can have a both a direct influence in physiological processes leading to T2DM, triggering vascular dysfunction and insulin resistance (Krämer *et al.*, 2010; Rajagopalan and Brook, 2012), and an indirect one, in the way in which it may discourage walking and exercise. If all the environmental risk factors discussed were equally spread across the territory, these would affect people of different socioeconomic status without relevant distinctions, and thus without being source of inequalities. However, without the need to mention how living in a city of a low-income country rather than of a highly developed one may lead to different levels of exposure, the area of residence may lead to consistent differentials in risk exposure also between countries and between cities. Living in an urban rather than a rural setting, for instance, is known to be associated with higher T2DM risk and prevalence (den Braver et al., 2018; Pasala *et al.*, 2010), mostly for a higher exposure to unhealthy food environments, limitations in physical activity due to use of car and public transport, as well as worse air quality and higher presence of environmental stressor such as noise, crime and unsafety. However, even within the urban environment, clear differences persist between neighbourhoods, which are both the cause and the consequence of different residential patterns according to individual and family socioeconomic conditions. Phenomena such as social segregation, that is the spatial separation of population according to their socioeconomic position (Musterd, 2005), occur because people tend to choose their residence according to their preferences and economic accessibility. Thus, residential patterns typically follow the distribution of resources among the population, with people with similar characteristics tending to cluster in similar areas. Hence, further down the social ladder individuals are more likely to live in areas with less services and amenities, less green spaces and walkable pathways, higher rates of crimes, and the like. However, despite being concentrated in areas where less affluent people live, these risk factors are often a problem also for the better off. The point is that those with less resources experience the double jeopardy of being disadvantaged and living in unfavourable neighbourhoods (Macintyre and Ellaway, 2003), while the more equipped may find alternative ways to cope with such environmental deprivation. Nonetheless, the contribution of social and built environmental characteristics as risk factors for T2DM is independent from individual characteristics. Local food provision, for instance, can characterize an environment as obesogenic, and it is up to each inhabitant's

resources to be exposed to such risk or not, but the risk is there. Thus, despite it may seems that environmental risk factors hit everyone in the same urban context indistinctly, individual socioeconomic conditions still play an important role in defining exposure, but nevertheless they do not account entirely for spatial inequalities in T2DM. More affluent people, for instance, may be able to move to other areas if the ones where they live are perceived as unsafe or do not provide enough services and amenities, but nevertheless they may need to live close to their workplace in a polluted area in the city, being exposed to other detrimental conditions. Moreover, neighbourhood conditions may also deteriorate or failing to improve due to the characteristics of its resident, in the way in which the reputation of an area may discourage private investors (Macintyre *et al.*, 1993), or the lack of power, cohesion, and organization of its inhabitants may lead decision-makers to locate landfills, high traffic roads, industrial areas or other undesirable structures there instead of somewhere else (Kawachi, 2010).

Conclusion

In this chapter we first introduced what T2DM is, presenting the most common factors that are known to be associated with an increased risk of having the disease, focusing also on the typical consequences associated with the pathology and on how patients can manage it. Subsequently, we examined the global trend of the disease worldwide, stressing the prominent role of global changes in lifestyles and nutrition patterns as a consequence of macro-scale processes such as globalization and urbanization that have been rapidly altering the local contexts in which people live. According to this explanation, the increasing incidence of overweight and obesity, sedentary behaviours, physical inactivity, stress, as well as other individually-based risk factors for T2DM has not been happening in a social vacuum, but rather as the consequence, among all, of global dynamics like the nutrition transition (Popkin, 1999) and the westernization of lifestyles, pushed by the pursuit of economic growth guided by the principles of laissez-faire, ignoring both the limited control that many people have over their exposure to the mentioned risk factors, and the contribution of macro processes like trade liberalization and the marketing activities of transnational corporations to the global burden of non-communicable diseases (Glasgow and Schrecker, 2016). The concept of *coca-colonization* is the one that probably better summarizes the main macro determinants involved in the spread of one of the biggest epidemics of human history (Koestler, 1976; Zimmet, 2000; 2017). Moreover, these processes not only have been increasing the incidence of the T2DM in nearly every country on the globe, but they have been doing it unevenly, disproportionally affecting low- and middle-income countries, the ones inhabited by people more vulnerable to the disease and its risk

factors, given the less amount of their socioeconomic resources. However, as our focus on Europe and the Italian case showed, social inequalities in T2DM are consistent in high-income countries as well. These inequalities concern both the prevention and the consequences of the disease, with clear social gradients in T2DM prevalence among the whole Italian population and in quality of life among those with T2DM. Finally, we discussed the possible pathways and mechanisms through which socioeconomic conditions may affect inequalities in T2DM prevalence. We opted to divide them in three classes, but nonetheless we stressed the importance of not considering them as independent processes, given the influence that each one may exert on each other, in various direction. The wider socioeconomic context, for instance, is of clear importance both for the availability of resources at the individual level and for the configuration of the local environment where people live. The same is true for this latter, which is the frame in which people of different socioeconomic status act, but it may be one of the factors influencing individual availability of resources as well. Thus, given the intertwinement of different mechanisms at different levels, it may be difficult to identify the most relevant factors contributing to T2DM inequalities in each specific real situation. What is clear, instead, is that individual choices are not the only factor explaining T2DM inequalities, and that the disease is strongly socially patterned. T2DM risk is socially structured, and this structuring involved different levels (we identified three of them, but in reality the hierarchy is probably far more complex), each of them need to be addressed with proper policy interventions if decision makers really want to contain the epidemic and narrow the gap.

Chapter 3

Social and Spatial Inequalities in Type 2 Diabetes Mellitus in Milan: a Multilevel Study

Introduction

Health in certain areas is worse than in other areas and T2DM – one of the most socially patterned diseases – is not an exception. When thinking about social inequalities in health, the most immediate connection is the one between high- and low-income countries: a child born in 2015 Sierra Leone (one of the poorest countries in the world) can expect to live around 50 years, while a child born in Italy in the same year has a life expectancy at birth about 33 years higher (WHO, 2016a). Such inequalities in health outcomes, however, are not present only between countries, but also within them. Someone may find surprising that in Turin, one of the most developed cities in north-western Italy, there are more than four years of difference in life expectancy between the most affluent and the most deprived neighbourhoods (Costa *et al.*, 2017). As anticipated, the question is whether these and all the other fine-grained differences in health outcomes occurring within the urban environment are merely attributable to the clustering of people sharing similar socioeconomic profile in the same areas, or if the area of living is able to influence such outcomes independently of (or in interaction with) individual characteristics. That is, if the spatial patterning of health outcomes is just a matter of a compositional effect, or if the place of living exerts an additional contextual effect (Macintyre *et al.*, 2002). In this chapter, we seek to answer this question for the specific case of T2DM in the city of Milan, with the unprecedented use of administrative healthcare data and the adoption of a multilevel framework to properly disentangle the impact of compositional and contextual explanations on the origin of inequalities in T2DM outcomes. Rather than being a methodological exercise with an end in itself, the findings deriving from this study could be of relevance to conceive and design policies aimed at tackling T2DM inequalities addressing mechanisms at each specific level of action.

3.1 Background

The association between low SES and T2DM is well established in the literature. However, to our knowledge, there are no studies focusing specifically on the city of Milan. Every year, through the use of national sample surveys such as ‘Aspects of Daily Life’ (Istat, 2016) or

'Health Conditions and Use of Health Services' (Istat, 2013), Istat provides figures of the prevalence of the disease at the national and regional level, permitting also to verify the extent to which educational level is associated with the disease. Nevertheless, a quantification of this relationship in the Milanese population seems to be missing. Similarly, there is general knowledge and consensus about the fact that T2DM prevalence is also related to the geographical context where people live, which can shape individuals' health outcomes through different pathways, resulting in a clear patterning of the disease at various geographical levels (e.g. national, regional, urban). However, as for the case of the relationship between individual SES and T2DM, the association between neighbourhood SES and T2DM has never been studied systematically in the city of Milan. The importance of assessing the extent to which neighbourhood characteristics may influence T2DM risk independently of individual SES in Milan is not limited to gaining unprecedented information relating to the specific case, being of interest also from a wider perspective. The study of the association between individual SES and T2DM, and the one between neighbourhood SES and T2DM, come often as two parallel issues, flowing into different strands of research. A review and meta-analysis of the existing literature reported that low levels of education, occupation and income – used as proxies for individual SES – were associated with an increased risk of T2DM in high-, middle- and low-income countries, even after controlling for risk factors such as dietary patterns, physical activity, and smoking (Agardh *et al*., 2011). However, the studies reviewed rarely considered the spatial characterization of the phenomenon, focusing exclusively on the individual level. Another strand of research has focused on the role played by the environment in which people live in contributing to determine T2DM outcomes. Studies in a review and meta-analysis of the literature focused on the characteristics of the built environment (green spaces, walkability, food environment, air and noise pollution), providing useful insights as regards the structural characterizations of the place of living in relation to T2DM risk (den Braver *et al.*, 2018). However, these studies tend to neglect the role of individual socioeconomic conditions, which are often not taken into account nor adjusted for as confounders. Thus, despite knowing that individual and contextual characteristics may influence the possibility of developing T2DM – both providing an independent contribution or interacting with each other – research that simultaneously considers the effects of both individual and contextual SES on T2DM risk and prevalence is lacking. Moreover, the study could be of interest not merely in relation to the outcome examined, contributing to enrich the wider literature concerning neighbourhood effects on health inequalities, which – as already highlighted in the first chapter – so far has

brought to contrasting results (Kawachi and Berkman, 2003; Picket and Pearl, 2001). Knowing that processes influencing T2DM outcomes take place at different levels in individuals' lives, each of these levels should be included in analyses aimed at estimating the effects of personal social circumstances and the surrounding environment. Thus, in this study, making use of administrative healthcare data for the identification of persons with T2DM, we relied on educational attainment as an indicator of individual SES, and on a census block-level deprivation index as an indicator of neighbourhood SES.

3.1.1 Individual SES

As already described in the first chapter, individual SES is typically measured by educational level, occupational class, income, or a combination of the three. Each indicator has its own strengths and limitations, covering different aspects of SES, so that different measures cannot be assumed to be interchangeable (Braveman *et al.*, 2005). While in the administrative databases we used to build the dataset for our analysis – which will be described more accurately later in this chapter – there is no information available regarding income, we opted for relying exclusively on education, and not on occupation, for methodological reasons. First, the occupational categories available in the databases are not prone to be ranked from lower to higher levels, with some categories simply reflecting age class (e.g. students, retired worked), not providing any relevant information about the amount and the type of health-protecting resources that an individual may have available. Second, due to the origin of the data used, both education and occupation in our dataset present a high number of missing values. Having opted for a complete case analysis, choosing to include occupation in the models would have implied to include in the study only those cases for which both measures are present, reducing sample size without a counterbalancing gain in data quality. However, the fact of relying exclusively on education as an indicator for individual SES should not conceived as a limitation in the study. We already highlighted how this measure is considered to be the most strongly associated with health outcomes among the three (Liberatos *et al.*, 1988). Moreover, compared to the other two indicators, education may be a more reliable indicator of SES given its stability. Indeed, once acquired in early adulthood, it does not change during the life-course, and it is not modified by chronic disease, as instead it may happen to occupation and income, susceptible to change as a consequence of adverse health conditions, involving selective pathways in the explanation of social inequalities in health. Rather than being conceivable simply as a proxy for individual SES, education may be able to capture the mechanisms linking social conditions to T2DM risk, such as knowledge, cognitive abilities, health literacy, problem solving capability, and coping

strategies. Additionally, even if the relationship is not univocal, on average the higher educated are also those who get more prestigious, better paid, and less health-threatening jobs, so that, even if not included in the representation of SES, occupation and income may be at least partly embodied by educational attainment.

3.1.2 Neighbourhood SES

According to Townsend, "deprivation may be defined as a state of observable and demonstrable disadvantage relative to the local community or the wider society or nation to which an individual, family or group belongs" (Townsend, 1987, 5). Deprivation can be regarded as a property of the individual, of a group, or of a geographical area. In this latter case, deprivation could be measured by the absence of services and amenities, by crime rate, air pollution, or any other indicator regarding the availability of material and social resources directly or indirectly influencing the quality of life of its inhabitants. Unfortunately, data of this kind are rarely available at a small-area level, and within the social and health research literature, rather than focusing on the characteristics and the structure of the territory itself, area deprivation is typically conceived as the clustering of socioeconomically disadvantaged people in the same area. Thus, the same indicators generally employed to measure individual SES can be used to evaluate the extent of deprivation in local areas. Anderson and colleagues claim that area deprivation "may summarise an area's potential for health risk from ecological concentration of poverty, unemployment, economic disinvestment, and social disorganisation" (Anderson *et al.*, 1997, 42). According to Massey (1996), indeed, when disadvantaged individuals are concentrated in geographically defined areas, disadvantage becomes a characteristic of the areas too. The clustering of individuals with socioeconomic disadvantage in specific neighbourhoods does not happen by chance, being the consequence of the unattractiveness of the local housing market. Property value reflects not only the characteristics of the house itself (e.g. number of rooms, energy efficiency, building maintenance, etc.), but also the quality of the surrounding environment in which it is located. Thus, the cheapest areas are usually those less equipped with schools, supermarkets, grocery stores, health facilities, parks, shops, places for recreational activities, and any other kind of services and amenities; contrariwise, these are more likely to be in proximity of undesirable facilities such as landfills and highly trafficked roads, and to be characterised by physical and social disorder (e.g. abandoned buildings, vandalism, crime, filth, conflicts, noise, etc.) (Ross and Mirowsky, 2001). With the most disadvantaged concentrating in the less valuable areas, aggregate measures of individual SES act as reliable indicators of neighbourhood SES. The use of composite indices in the study of

area-based deprivation has a long tradition both in Italy (Biggeri *et al.*, 2006; Cadum *et al.*, 1999; Cesaroni *et al.*, 2003; Grisotto *et al.*, 2007; Michelozzi *et al.*, 1999; Milani *et al.*, 1983; 2006; Tello *et al.*, 2006; Testi and Ivaldi, 2005; Valerio and Vitullo, 2000) and abroad (Benach and Yasui, 1999; Carstairs and Morris, 1990; Challier and Viel, 200; Forrest and Gordon, 1993; Fukuda *et al.*, 2007; Garcıa-Gil *et al.*, 2004; Gordon, 1995; Jarman, 1984; Jordan *et al.*, 2004 ; Morris and Carstairs, 1991; Noble *et al.*, 2006; Pampalon and Raymond, 2000; Townsend, 1987). All the indices developed are based on aggregate indicators of socioeconomic disadvantage, related to the educational, occupational, and housing sphere. The most commonly used indicators are the percentage in each area of people with at most primary education, of unemployed, of manual or unqualified workers, of immigrants (especially from ethnic minorities or poor countries), of families living on rent, of single-parent families, of overcrowded households, of families living in bad conditions (e.g. damp, mould, leakings, noise or darkness in the dwelling), or of households lacking access to fundamental resources (e.g. a car, a fridge, an indoor toilet, running water, etc.). Basing on the current literature, Caranci and colleagues proposed a census block-level deprivation index for the whole Italian territory, composed of five indicators: the percentage of low-educated, of unemployed, of households living on rent, of single-parents family, and of overcrowded households (Caranci *et al.*, 2010). The index proved to be efficient in describing the general pattern of area deprivation in the country, highlighting a marked gradient between northern and southern regions, as well as showing a high correlation with mortality data. However, we believe that measures of deprivation should be built taking into account the specificities of the territory in which they have to be applied. Housing tenure, for instance, is conceived as an indicator of the concentration in a specific area of families in economic disadvantage, with the implicit assumption that those who are better-off can afford home ownership. While generically valid, this assumption may not be correct when applied to specific contexts. In Milan, a city with a high residential turnover due to student and temporary high-skilled migrations, living on rent may not necessary be a sign of economic constrains. If so, in what is one of the richest areas of the country, we would expect less households to live on rent, while Istat census data show the opposite: in 2011, about 18% of households were living on rent in the whole country, nearly 21% in Lombardy, and slightly more than 29% in Milan[13]. Thus, if adopted to detect deprived areas in this city, this indicator could contribute to depict as disadvantaged some areas

[13] These data are accessible from Istat data warehouse site: http://dati-censimentopopolazione.istat.it/Index.aspx.

characterized instead by a clustering of affluent people, who may choose to live on rent to grant themselves an easier residential mobility. Conversely, the percentage of immigrants may work very well in metropolitan and urban contexts, with newcomers from low- and middle-income countries concentrating in cheaper areas, while it could be less relevant in peripheral areas with low migration rates. Similarly, not having a car may be a serious problem for those living in the peripheries or in rural areas, but not for those living in urban settings highly served by public transport. Besides, the choice of the indicators composing a deprivation index is strictly contingent on the data available. The only source of information about socioeconomic characteristics of the territory of Milan at the census block level is census data. Istat provides access to census data with several restrictions, making available a limited number of variables among those existing, precluding the possibility to calculate most of the indicators generally used in the literature cited. Thus, from 2011 census – which is the most recent to date – among those available, we selected the indicators best able to depict the state of deprivation of different areas within the city. These are the percentage of low-educated, the percentage of unemployed, and the percentage of foreign persons in each census block. Each of them may contribute to capture some aspects of territorial deprivation. The concentration of low-educated individuals may reflect a high presence of low qualified workers with limited economic resources, and consequently able to afford to live only in underprivileged areas. Similarly, a massive presence of unemployed people may indirectly detect areas dedicated to public or social housing, which typically lack the benefits of richer neighbourhoods. Concerning the last indicator, the concentration of foreigners in an area is linked with deprivation in the way in which, when moving in, immigrants tend to choose their residence mostly according to their economic resources and relying on migration networks, locating themselves in areas where other people from the same country of origin have already established (Garip and Asad, 2015; Ligh *et al.*, 1993). This, combined with the difficulties in escaping from unfavourable conditions, makes the high density of foreigners stable in some areas, and also a reliable indicator of disadvantaged areas. Some neighbourhoods, due to their characteristics, may be attractive for all the three categories, and many individuals may fall under more than one of them (e.g. a low-educated unemployed foreigner). Thus, the three indicators may surely overlap, contributing to detect areas with a strong or a moderate proportion of each of them, but also stand alone, identifying areas with a marked percentage of just one of them. Therefore, an area does not need to show high values for all the indicators to be identified as deprived by the composite index computed.

3.1.3 Defining Neighbourhood

Before proceeding, it is necessary to discuss two issues involved in the definition of the contextual dimension adopted for the analysis. First, in this study, we opted for using administrative divisions to delimit the context in which people live. Although this practice is widely used in the literature, we are aware of some limitations related to this choice. Individuals often do not identify their life context with administrative boundaries, which are defined to meet statistical, bureaucratic, and administrative needs. Moreover, the perceptions of area boundaries may vary among individuals living in the same context: the context seems to possess blurred boundaries that can expand or shrink according to personal experience (Sastry *et al.*, 2002). Thus, some scholars argued that the effect of the context could be better understood adopting a relational perspective in which boundaries are not built ex ante, but as a consequence of the mutual influence between people and places (Coulton *et al.*, 2001; Cummins *et al.*, 2007). Although including in the analysis each individuals' subjective definition of what is the environment to which he is exposed to during his daily life would lead to interesting findings, this may be unfeasible. Working with the large numbers of administrative data, gathering specific information of this kind for each individual would be an impractical task, and relying on what is offered by administrative sources remains the only option. Second, even when the use of administrative boundaries is justified, the problem of which territorial division should be applied is still present. In the literature, research has been carried out employing different units, such as census tracts or blocks, electoral wards, postcodes, districts, or others, depending both on analytical aims and data availability. However, these units cannot be used interchangeably, and the results may vary considerably when different territorial definitions are applied. This potential bias is known in the literature as the *Modifiable Area Unit Problem* (MAUP) (Waller and Gotway, 2004), suggesting that the measurement of spatial effects for any outcome may be significantly affected by the choices in terms of geographic scales and data aggregation. Clearly, the decision concerning which unit to use should be made according to the territorial division best able to represent the environment to which people are actually exposed. In our study, we are not exempt from such a sensitive choice, given the presence of several administrative division concerning the city of Milan, as following (see Figure A3.1 in the appendix):

- Electoral wards (*Collegi elettorali*) - number or units: 6; average size: 30 km^2; average population in 2018: 232,546 inhabitants.

- Boroughs (*Zone di Decentramento*) - number or units: 9; average size: 20 km^2; average population in 2018: 155,030 inhabitants.
- Census tracts (*Aree di Censimento*, ACE) - number or units: 86; average size: 2.1 km^2; average population in 2018: 16,224 inhabitants
- Units of Local Identity (*Nuclei di Identità Locale*, NIL) - number or units: 88; average size: 2.1 km^2; average population in 2018: 15,855 inhabitants
- Functional areas (*Aree funzionali*) - number or units: 180; average size: 1 km^2; average population in 2018: 7,752 inhabitants.
- Census blocks (*Sezioni di censimento*) - number or units: 6,085; average size: 0.03 km^2; average population in 2018: 229 inhabitants.

We opted for using the smallest unit available, the census block. This choice is in line with suggestions from several scholars who argued that smaller areas should result in a more valid and stable measure of area deprivation (Crayford *et al.*, 1995; Hobbs and Cole, 1996; Jarman, 1997; Majeed *et al.*, 1996; Reijneveld *et al.*, 2000; Talbot, 1991), tending to provide a more accurate estimation of neighbourhood effects and representing the concept of neighbourhood in a more sociologically meaningful way (Boyle and Willms, 1999; Diez-Roux *et al.*, 1997; Guest and Lee, 1984; Macintyre *et al.*, 1993; Tienda, 1991; Wells and Horm, 1998). According to Boyle and Willms, there is an inverse association between "the size of a geographic area and potential to explain variability in health outcomes" (Boyle and Willms, 1999, 583). The smaller the size of the spatial unit, the more likely one is to be able to identify contextual-level factors that influence health outcomes. This happens as a consequence of both a statistical and a theoretical consideration. Regarding the first, the inverse relationship is related to homogeneity/heterogeneity, with smaller units composed by individuals and households sharing similar characteristics, while bigger aggregation can expect to include more diversity, lowering the potential to identify and explain place effects (Boyle and Willms, 1999). Concerning the latter, smaller areas are closer to what people usually identify as their neighbourhood and to a sociological definition of the concept. Research by Guest and Lee (1984) indicated that individuals tend to define their neighbourhoods mostly as 'nearby people', whereas a minority of respondents offered a definition that was solely geographical. Thus, individuals tended to identify their neighbourhoods in more social than spatial terms, offering insights to what may constitute a sociologically meaningful neighbourhood, that is social contact within a relatively small geographic area (Huie, 2001). In line with this, Hallman (1984)

and Tienda (1991) provided definitions of the concept emphasizing the role of social interactions, in the same way as Chaskin (1997) described neighbourhood both as social and a spatial unit. Thus, although the NIL division is intended to identify 88 city areas properly definable as neighbourhoods, characterised by an internal social, cultural, and physical homogeneity, we chose to identify neighbourhood boundaries with the smallest division available, the census block, given that NIL areas represent broad aggregates, with too much heterogeneity within them. The same problem is present for census tracts, slightly differing in boundaries from NIL areas, but with a similar dimension. Electoral wards and boroughs are definitely too broad, while functional areas – composed by aggregating contiguous census blocks – with dimensions in between the NILs and the census blocks, were defined for administrative and operational purposes, and do not represent areas characterised by internal homogeneity.

3.1.4 Research Questions

In light of the above, we aimed at answering at the following questions:

1. Is there a spatial heterogeneity in T2DM rates within the city of Milan? Or rather, does the disease show an uneven distribution across different neighbourhoods in the city?
2. Is there an association between neighbourhood SES and T2DM rates, independently of individual SES? Or rather, does the context of residence influence the chance of having T2DM over and above individual characteristics?
3. Is the neighbourhood effect the same for individuals with different profiles? Or rather, has neighbourhood SES a different impact on T2DM risk for individuals differing in terms of age, sex, nationality, and individual SES?

3.2 Methods

As a consequence of the research questions, we conducted a multilevel population-based case-control study. The case-control study is an observational study in which subjects who have the outcome of interest (the ‘cases’) are compared with subjects without it, but with other similar characteristics (the ‘controls’) (Porta, 2014). This study design allows to determine retrospectively the relative importance of a predictor variable in relation to the presence or absence of the disease (Mann, 2003). Given the hierarchical structure of the data and the will to estimate the effect of neighbourhood SES on the probability of having T2DM net of individual SES, we relied on multilevel techniques, which specifically fit this purpose, permitting to estimate the proportion of variance due to each level of analysis (Goldstein, 2011).

3.2.1 Study Population

The study was conducted querying the Administrative Healthcare Databases (AHD) of the Health Protection Agency (*Agenzia di Tutela della Salute*, ATS) of the Metropolitan City of Milan, which gathers data for people living in the provinces of Milan and Lodi (195 municipalities), with a population of almost 3.5 million people in 2018. In Italy, since 1978, the population is fully covered by a universal and tax funded healthcare system, and in the Lombardy Region, since 1997 its management has been associated with an automated system of databases, which collect a variety of information concerning services provided to beneficiaries of the healthcare system. AHD-ATS allows to build specific datasets of interest from eight different databases: 1) outpatients, 2) hospital discharges, 3) co-payment Exemptions Register, 4) emergency department (ED) access, 5) rehabilitation interventions database, 6) territorial-based psychiatry interventions database, 7) pharmaceutical prescriptions database, 8) community and social services (CSS). These databases can be linked by a unique identifier code (fiscal code), through which it is possible also to link demographic information present in the civil registry (*Nuova Anagrafe Regionale*, NAR). Eligible for the study were all people aged between 30 and 83 living in the municipality of Milan as of 31st December 2018, with T2DM (cases) or without it (controls). People with T1DM were excluded from the analysis.

3.2.2 Measures

Type 2 Diabetes Mellitus

People with T2DM in 2018 were identified according to the criteria established by the 2017 Lombardy Region's deliberation n° X/6164 (Regione Lombardia, 2017), which aimed at developing an innovative system to improve the assistance to patients with chronic diseases or in vulnerable conditions. The Region provided codes to detect from the databases individuals affected by chronic conditions. For T2DM, four out of the eight AHD-ATS databases were used; the ATS developed an algorithm to identify as T2DM patients individuals with at least one of the criteria listed in Table 3.1. More specifically, individuals were classified as T2DM patients if they had a diabetes-related exemption (free supply of medical devices for blood glucose self-monitoring and insulin therapy) in the last ten years; if they were discharged from hospital with T2DM as main diagnosis at least once in the last five years; if they have been prescribed a certain dose of T2DM specific drugs in the last year; or if they made use of outpatient diabetes-related services at least once in the last year.

Table 3.1: Lombardy region codes of the identification of patients with T2DM.

Source Database	Inclusion Criteria (at least one)	Time range
Co-payment Exemptions Register	013.250 (exemption starting after 35 y.o.)	0 - 10 years
Hospital Discharges - Diagnosis Related Group (DRG)	294 Diabetes Mellitus after 35 y.o. 285 Lower limb amputation for endocrinological disorders	0 - 5 years
Hospital Discharges - 1° and 2° Medical Diagnosis	250.00 T2DM without complications 250.02 T2DM without complications, DC† 250.10 T2DM with ketoacidosis 250.12 T2DM with ketoacidosis, DC† 250.20 T2DM with hyperosmolarity 250.22 T2DM with hyperosmolarity, DC† 250.30 T2DM with other chronic complications 250.32 T2DM with other chronic complications, DC† 250.40 T2DM with renal complications 250.42 T2DM with renal complications, DC† 250.50 T2DM with ocular complications 250.52 T2DM with ocular complications, DC† 250.60 T2DM with neuropathic complications 250.62 T2DM with neuropathic complications, DC† 250.70 T2DM with peripheral circulatory complications 250.72 T2DM with peripheral circulatory complications, DC† 250.80 T2DM with other specified complications 250.82 T2DM with other specified complications, DC† 250.90 T2DM with unspecified complications 250.92 T2DM with unspecified complications, DC† 362.01 - 363.07 diabetic-related retinopathy 357.2 diabetic polyneuropathy	0 - 5 years
Pharmaceutical Prescriptions Database	A10B* (DDD‡>50%) Hypoglycaemics, excluded insulins N03AX16 or N03AX12 (DDD‡>30%) Peripheral neuropathic pain treatment drugs	0 – 1 years
Outpatients	14.33 Retinal laceration repair by photocoagulation 14.34 Retinal laceration repair with argon (laser) 14.75 Intravitreal injection of therapeutic substances 96.59.1 - 96.59.6 Advanced wound dressings	0 - 1 years

† DC = *Decompensated T2DM*
‡ *DDD = Defined Daily Dose*

However, some codes do not permit to distinguish between different types of diabetes. For instance, the exemption code 013.250 is the same for every diabetes mellitus type, and it is suggested to identify T2DM if the patient is older than 35 years old, and T1DM if younger. However, one could develop T2DM before age 35, so the exemption code may misleadingly

lead to identify as T1DM patients those who developed T2DM at a younger age. Similarly, lower limb amputations (DRG code 285) may be necessary for both types of diabetes, so the code does not allow to distinguish between T12DM and T2DM. To overcome these ambiguities, if more than one code was available for a patient, and one allowed to identify the disease unequivocally, the algorithm privileged this last. However, the algorithm is subjected to an unavoidable margin of error. For instance, a 30 years old T2DM patient with a diabetes exemption who has never been hospitalized in the last five year, nor took any drug or made use of any outpatient service in the last year, would be improperly classified as T1DM, given the combination of the only code available for him and of his age. Nevertheless, situations like the one described are residual and should not affect the reliability of the cases' identification process.

Educational Level

Individual educational attainment was obtained querying the AHD-ATS databases. Health personnel is required to fill out a form reporting a wide range of information for patients making use of health services (e.g. hospitalization, community and social services, territorial-based psychiatric interventions, rehabilitation interventions), such as educational level, occupational class, and marital status. The ATS developed an algorithm to extract information (if present) concerning the educational level of each case and control from the databases available, linking it to the study dataset by the fiscal code. The variable was reported through four ordinal categories, 1) no education, primary education not completed, primary education; 2) lower secondary education; 3) upper secondary education; 4) tertiary education.

Deprivation Index

The census block-level deprivation index was built using data from the most recent Italian census, dated 2011 (Istat, 2011). Among those available in the census, three indicators were chosen to represent different aspects of socioeconomic deprivation at the contextual level: the percentage of low-educated (maximum primary education), the percentage of unemployed, and the percentage of foreigners in each census block. The single indicators were computed as follows:

Percentage of low-educated

$$x_1 = \frac{y_1 + y_2 + y_3}{y_4} * 100$$

Where y_1 is the number of people (15+ y.o.) with primary education, y_2 is the number of literate people (15+ y.o.) without any formal education achievement, y_3 is the number of illiterate people (15+ y.o.), and y_4 is the number of people in school-living age (15+ y.o.)

Percentage of unemployed

$$x_2 = \frac{y_5 + y_6}{y_7} * 100$$

Where y_5 is the number of people (15+ y.o.) seeking for a new occupation, y_6 is the number of people (15+ y.o.) seeking for the first occupation, and y_7 is the number of people (15+ y.o.) available for work (labor force).

Percentage of foreigners

$$x_3 = \frac{y_8}{y_9} * 100$$

Where y_8 is the number of foreigners living in Milan, and y_9 is the total population of the City.

The overall deprivation index was computed as the sum of the z-scores of each indicator. Z-scores are standardized values obtained by subtracting the mean from the score, dividing then by the standard deviation of the distribution (Abdi, 2007). This procedure generates distributions with a mean of 0 and a standard deviation equal to 1, allowing to compare scores measured with different units or on different populations. A z-score represents the number of standard deviations from the mean of a certain data point. In our case, in relation to each indicator, the z-score of a census block identified how much that specific territorial unit was below or above the average of the city of Milan. In formulas:

$$Deprivation\ Index = \sum_{i=1}^{3} z_i \qquad z_i = \frac{x_i - \mu_{x_i}}{\sigma_{x_i}}$$

Where x_1 is the percentage of low-educated, x_2 is the percentage of unemployed, x_3 is the percentage of foreigners, μ is the mean of the distribution, and σ is the standard deviation of the distribution.

The continuous index obtained was subsequently categorized in quintiles, becoming an ordinal variable in five categories, each identifying the 20% of the census blocks falling in very low, low, medium, high, and very high deprivation areas. This criterion allowed to obtain a variable that is little influenced by the census blocks with few residents, resulting in a weighting that

attributes more importance to those census blocks with more inhabitants. Moreover, using quintiles simplifies the issue of non-linearity. The index computed had 361 out of 6,058 census blocks with missing data, corresponding to those areas inhabited when census data were collected. However, in years subsequent to 2011, some empty lots have been developed and inhabited, thus, to avoid excluding from the study individuals living in previously uninhabited areas, we used areal interpolation methods (Mugglin *et al.*, 1999) to impute a deprivation score for those census tracts with missing data. The procedure was carried out with the Geographic Information System (GIS) software ArcMap 10.6.

Confounders
Sex, age, and citizenships were used as covariates.

3.2.3 Statistical Analysis

Given the hierarchical structure of the data, with individuals nested in neighbourhoods, multilevel regression models (Goldstein, 2011) were used to assess simultaneously the effect of individual and contextual characteristics, enabling the estimation of the effect of the neighbourhood of residence on the probability of having T2DM, independently of individual SES. Assuming that health outcomes are simultaneously affected by individual characteristics and by the environment in which they live, multilevel models are widely used in the literature to analyse data with such hierarchical structure, permitting to disentangle the contributions of compositional and contextual effects in explaining different health conditions across different neighbourhoods (or other spatial units) within the same urban setting. In multilevel techniques, rather than being fixed for each contextual unit, the regression coefficients are allowed to vary from one unit to another. In an ordinary single-level regression model, the intercept and the slope are fixed, meaning that even if a hierarchical structure is present (e.g. individuals nested in neighbourhoods; pupils nested in schools), it will be ignored[14]. Conversely, in multilevel models both the intercept and the slope are allowed to be 'random'. A *random intercept model* is a model with as many intercepts as the number of higher-level units, each allowed to vary randomly. In such a model, while the intercept may vary from one group to another, the slope is assumed to be the same for each group. Conversely, a *random slope model* (which is rarely used) implies a fixed intercept for every group, allowing the slope to be different across them.

[14] Fitting a single-level model when hierarchies are present is not only incorrect from the study design perspective, but involves also a methodological error. Ignoring data structure generates smaller standard errors, leading to incorrect inferences with a higher risk of type I error, concluding that effects that might be ascribed to chance are 'real' (Merlo, 2003; Steele, 2008).

In a *random intercept and slope model*, both the coefficients are allowed to vary across groups. A detailed explanation of how multilevel models work can be found elsewhere, both generally (Goldstein, 2011; Raudenbush and Bryk, 2002; Snijders and Bosker, 1999) and focusing specifically on health research (Duncan *et al*., 1998; Leyland and Goldstein, 2001; Subramanian *et al*., 2003). Multilevel models building strategies can be either top-down or bottom-up. Here, we adopted a bottom-up approach in which the different models are developed incrementally (Hox, 2010), following a procedure well established in the literature (Jones and Subramanian, 2019; Merlo *et al*., 2005a; 2005b; 2005c; 2006; Sommet and Morselli, 2017; Steele, 2009). Given that our outcome is dichotomous (having or not having T2DM), multilevel binary logistic regression was used. A first model, called 'empty', 'null', or 'intercept-only' model permitted to assess the spatial heterogeneity in T2DM in Milan. The empty model is called like that because it does not contain any independent variable, but just the outcome (Model 1). Its usefulness lies in the fact that it makes it possible to split the variability of the outcome among the different levels of analysis, enabling to measure the extent to which the probability of having the disease varies from one area to another. The variance partition coefficient (VPC) revealed the proportion of variability in the outcome at each level of analysis, providing a first description of the spatial distribution of the disease within the city, and evidencing the existence of a possible contextual dimension for the prevalence of T2DM in Milan. To the first basic empty model were subsequently added covariates at different levels, to evaluate the specific contribution of individual and neighbourhood SES on the probability of having T2DM. Thus, the model was first integrated with predictors at level-1 (educational level as a proxy for individual SES) to investigate the extent to which area level differences were explained by the individual composition of the areas (Model 2). Next, the level-2 predictor (deprivation index of the census block of residence) was added to check if neighbourhood SES was associated with T2DM independently of individual SES, that is to assess the existence of a contextual effect for T2DM in the population studied (Model 3). Model 2 and 3 were adjusted for age, sex and citizenship as confounders. We additionally tested models with random slope for individual-level variables, to examine whether the effect of individual characteristics and individual SES differed across neighbourhoods; and models with cross-level interactions between individual-level variables and neighbourhood SES, to examine whether the effect of neighbourhood deprivation was the same for all individuals, regardless of their own age, sex, citizenship, and educational level. To deal with the MAUP, we ran the same models with different area units

(functional areas and NILs). We also tested Model 3 divided by sex, with deprivation index as a continuous variable, and with disaggregated measures of deprivation index.

The main models are defined by the following equations:

1) $Y_{ij} \sim Binomial(\mathrm{N}_{ij}, \pi_{ij})$
2) $logit(\pi_{ij}) = \beta_{0ij} + \beta_1 X_{1ij} + \beta_2 X_{2ij} + \beta_3 X_{3ij} + \beta_4 X_{4ij} + \beta_5 X_{5j}$
3) $\beta_{0ij} = \beta_0 + u_{0j} + e_{0ij}$
4) $[u_{0j}] \sim \mathrm{N}(0, \Omega_u) : \Omega_u = [\sigma^2_{u0}]$
5) $\sigma^2_{u0} (Y_{ij} | \pi_{ij}) = \pi_{ij}(1 - \pi_{ij})$

Where *Y* is the dependent variable 'T2DM' with a binomial distribution; X_1 is the individual-level predictor 'age'; X_2 is the individual-level predictor 'sex'; X_3 is the individual-level predictor 'citizenship'; X_4 is the individual-level predictor 'educational level'; X_5 is the contextual-level predictor 'deprivation index'; the suffix *i* represents individuals; the suffix *j* represents census blocks; the letters *u* and *e* denote, respectively, the residuals at the second and first level; β are the regression coefficients to estimate. The random effects are assumed to follow a normal distribution with covariance matrix Ω_u, which in random intercept models contains just one element, the between-community variance σ^2_{u0}. The models were estimated with Maximum Likelihood Estimation method using STATA 15 software.

3.2.4 Missing Data

Before showing the results of the analysis, some considerations about missing data in the study are necessary. The variables 'T2DM', 'age', 'sex', 'citizenship', and 'deprivation index' had no information missing (Tab. 3.2), whilst 'educational level' had a high percentage of missing data (72.20%), as a direct consequence of how this variable has been extracted from the AHD-ATS databases.

Tab 3.2: Pattern of missing data in the study variables (population 30-83 y.o; n=936,304).

	Missing Data	**Total**	**% Missing**
T2DM	0	*936,304*	0
Age	0	*936,304*	0
Sex	0	*936,304*	0
Citizenship	0	*936,304*	0
Educational Level	677,041	*936,304*	72.20
Deprivation Index	0	*936,304*	0

This issue is strictly related to the missing data mechanism. Data could be *Missing Completely At Random* (MCAR), when there is no relationship between the missingness of the data and any values, observed or missing; *Missing At Random* (MAR), when there is a systematic relationship between the propensity of missing values and the observed data, but not the missing data; or *Missing Not At Random* (MNAR), when there is a relationship between the propensity of a value to be missing and its values (Little, 1988). As confirmed by Little's test (P-value=0.000) – which allows to examine whether the data are MCAR or MAR – we can exclude that our data are MCAR, and consequently that our dataset is a random subset of the real population. However, once ascertained that the data are not MCAR, there is not statistical way allowing to examine whether they are MAR or MNAR (Little and Rubin, 2002), and the missingness mechanism can only be supposed exploring patterns in the data and speculating about its origin. Table 3.3 shows the distribution of the study variables by missing data on educational level. All the study variables are significantly different between the two populations (missing/not missing). The percentage of T2DM patients is more than double in the population for which data on educational level are present as compared to the missing population. Moreover, the first is on average almost 4.5 years older than the one without information on education, more representative of women and Italians rather than men and foreigners, whilst regarding neighbourhood deprivation there are only minor differences.

Tab 3.3: Distribution of variables by missing data in educational level (population 30-83 y.o; n= 936,304).

	Missing Education	**Not Missing Education**	**P-value**
T2DM (%)			0.000
Yes	4.66	9.56	
No	95.34	90.44	
Age (mean)	53.12	57.60	0.000
Sex (%)			0.000
Female	49.28	60.68	
Male	50.72	39.32	
Citizenship (%)			0.000
Italian	79.01	87.57	
Foreign	20.99	12.43	
Deprivation Index (%)			0.000
Very low	15.26	16.82	
Low	20.15	21.45	
Medium	21.74	21.76	
High	21.79	20.45	
Very High	21.05	19.50	

Given the differences in the distribution of the other variables, the population with missing data could substantially differ in the distribution of educational level from the one with complete information, in which case the missingness could not be ignored, potentially leading to substantial bias in the results. Thus, we compared the distribution of the variable with missing data in our dataset with one from another source. Table 3.4 shows the distribution of educational level in the AHD-ATS dataset and in the Istat 2018 *Labour Force Survey* (Istat, 2018) for people older than 30 years[15]. Despite the large amount of missing data, the distribution of educational level in our dataset approximates the one in the Istat one, with a slight underrepresentation of the more educated, and conversely a slight overrepresentation of the less educated. This suggests the possibility to rely on a complete case analysis (listwise deletion) without incurring in a considerable risk of bias. To evaluate more stringently the impact of the choice of running complete case analyses – excluding cases for which educational level is missing – we also estimated models relying on the full dataset, withouth including educational level as covariate.

Tab 3.4: Percentage distribution of educational level in the AHD-ATS dataset and the Istat 2018 Labour Force Survey (population older than 30 years).

	AHD-ATS (n= 296,604)	**Istat Labour Force Survey** (n= 991,410)	**Δ***
Educational Level			
Tertiary	26.95	31.80	-4.85
Higher-secondary	36.30	36.84	-0.54
Lower secondary	23.69	21.08	+2.61
Primary	13.06	10.28	+2.78

Δ = Percentage-point difference between the two distributions.

3.3 Data Presentation

T2DM prevalence in Milan in 2018 was 4.94%, affecting 67,457 persons. Figure 3.1 shows the prevalence by age in men (5.52%) and women (4.42%). As noticeable, the rates of the disease increase steadily with age in both sexes, rapidly decreasing after the age of 85. The prevalence is generally higher for men at every age, except for the age-class 20-45, for which the rates are markedly higher for women, in all probability as a consequence of gestational diabetes, a

[15] As stated, in our analysis we considered all individuals aged between 30 and 83. However, in the Istat dataset used for the comparison – which among all those available is the only one allowing to examine the distribution of educational level specifically for the city of Milan – individuals older than 75 years are aggregated in a unique category. Thus, to make a reasonable comparison we showed the distribution of the variable in the two datasets within the same age range.

condition in which a woman without diabetes mellitus develops hyperglycaemia during pregnancy[16].

Figure 3.1: T2DM prevalence by age in males (n=36,002) and females (n=31,455). Milan, 2018.

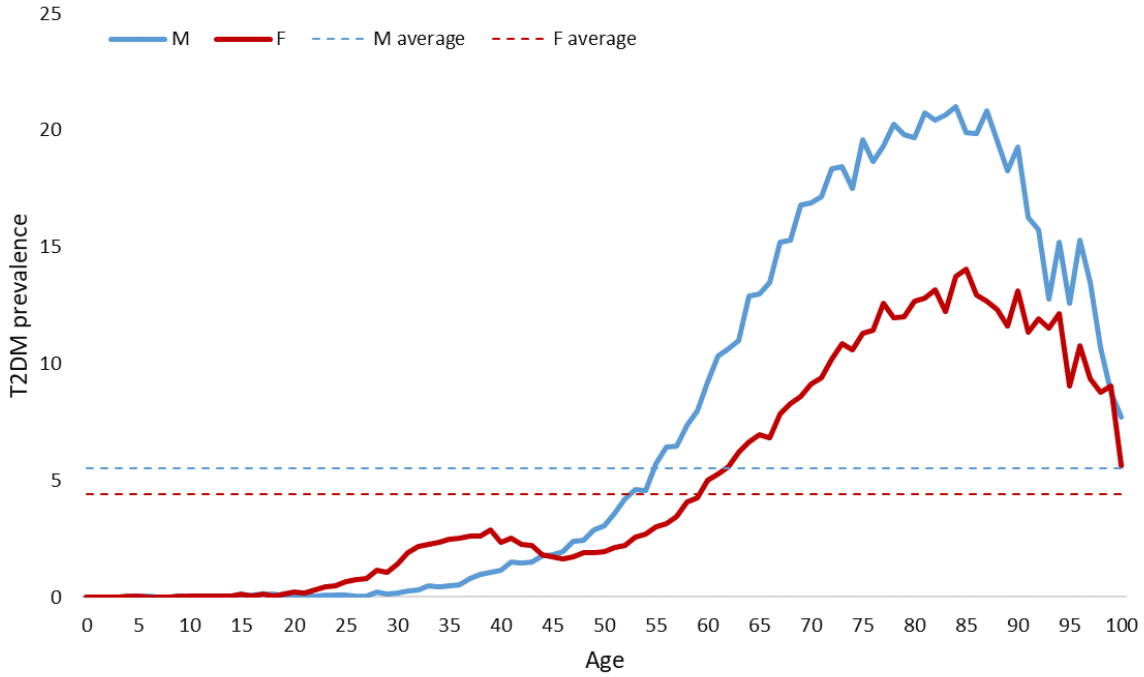


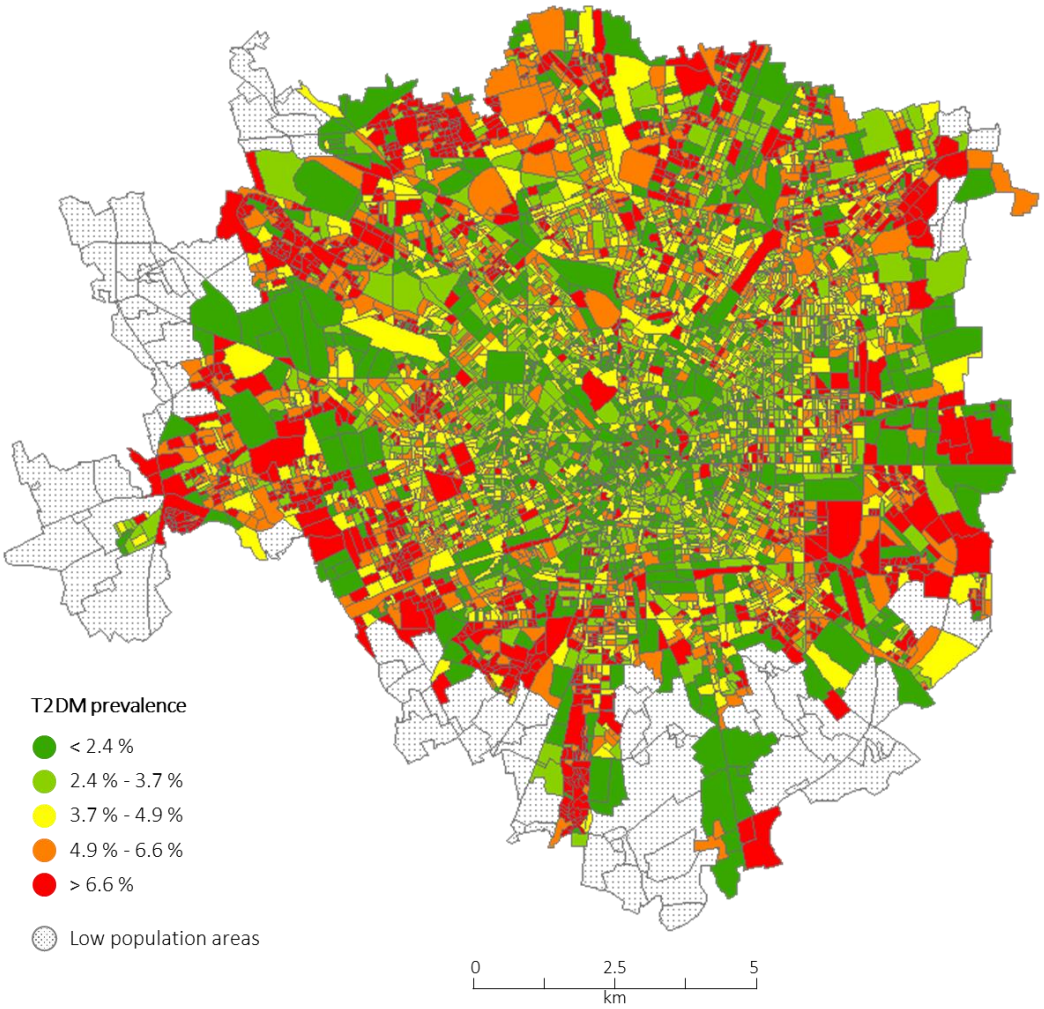
Figure 3.2 depicts the distribution of T2DM within the city, across different census blocks. The map shows a clear spatial heterogeneity, with the typical centre-periphery pattern. Green-coloured areas – with a lower average percentage of T2DM – are highly concentrated in the core of the city, whilst orange- and red-coloured areas – with a higher average percentage of T2DM – are more distributed all around the suburbs. The dotted areas on the map represent low-density census blocks (less than 1,000 pop./km^2)[17]. Although being useful to catch a first impression of the spatial patterning of the disease in Milan, this map suffers from several limitations. First, the prevalence plotted is not age-adjusted, so that some areas may report a high prevalence merely as a consequence of a higher concentration of older people (a compositional effect), and not because of specific characteristics of the territory. Second, the

[16] Unfortunately, the information available to develop the algorithm allows only to discern between T1DM and T2DM, precluding the possibility to identify other rarer forms of diabetes mellitus. In the majority of cases, gestational diabetes will resolve after childbirth, but those affected are at higher risk of developing T2DM later in life (Bellamy *et al.*, 2009). Moreover, individual SES – and more specifically educational level – has been proved to be associated with a higher risk of gestational diabetes (Song *et al.*, 2017).

[17] Here and in the subsequent maps, we opted not to display data relative to low-density areas. Indeed, given that they report rates and distributions based on small denominators, but nonetheless concerning relatively large areas (if compared to other census blocks), they could contribute to alter the perception of the real territorial distribution of the indicators showed.

map does not account for population density of the area units. Generally, the smaller the census block, the higher the population density. Thus larger census blocks are usually fields, parks, industrial or rural areas, or other empty lots. This implies that large areas may report an average T2DM prevalence based on very small populations, altering the overall image of the distribution of the city (e.g. the north-western group of large green blocks, or the south-eastern group of large red blocks). As we will see below, both these limitations can be easily overcome in the models presented, first controlling for age (as well as for other covariates) as confounders, and second applying a shrinkage factor to the estimates of each census block basing on its population numerosity.

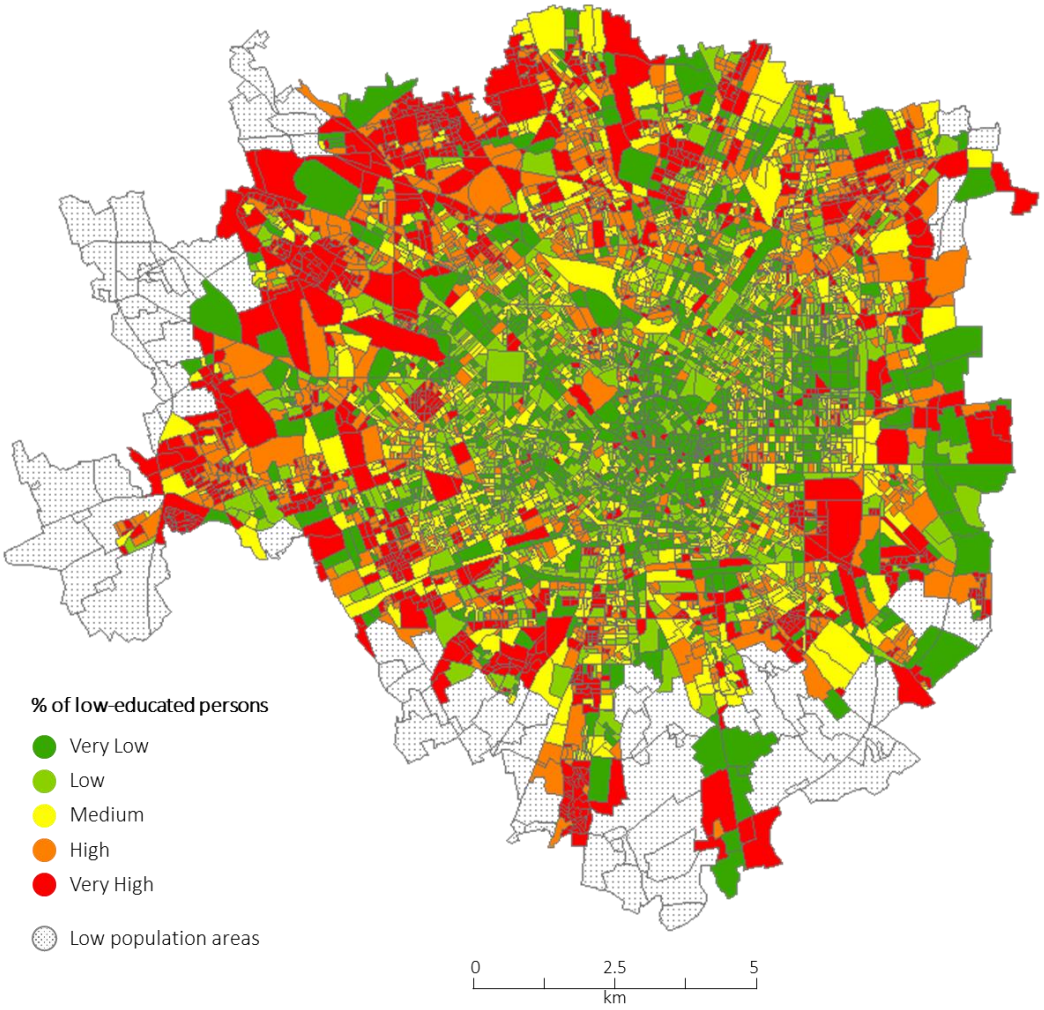
Figure 3.2: T2DM prevalence in Milan, 2018. (T2DM cases = 67,457; overall population = 1,364,377).



Figures 3.3, 3.4, and 3.5 show the territorial distribution of the three indicators of deprivation, while figure 3.6 shows the overall deprivation index computed as the sum of the z-scores of the single indicators (see Tab. A3.1 in the appendix for summary statistics). Although not in a

homogeneous way, all of them report the same centre-periphery pattern, reporting higher deprivation in the suburbs. The indicators and the overall index were computed at the smallest unit available, the census block, to preserve the spatial variability of the measures. However, for a more immediate and intuitive overview – especially for those who have knowledge of the territory of Milan – it could be useful to look at this variability at the NIL level. Table A3.2 in the appendix reports the distribution of each measure across the different NILs (Figure A3.2 in the appendix shows NILs' location), together with the population and the population density of each unit[18].

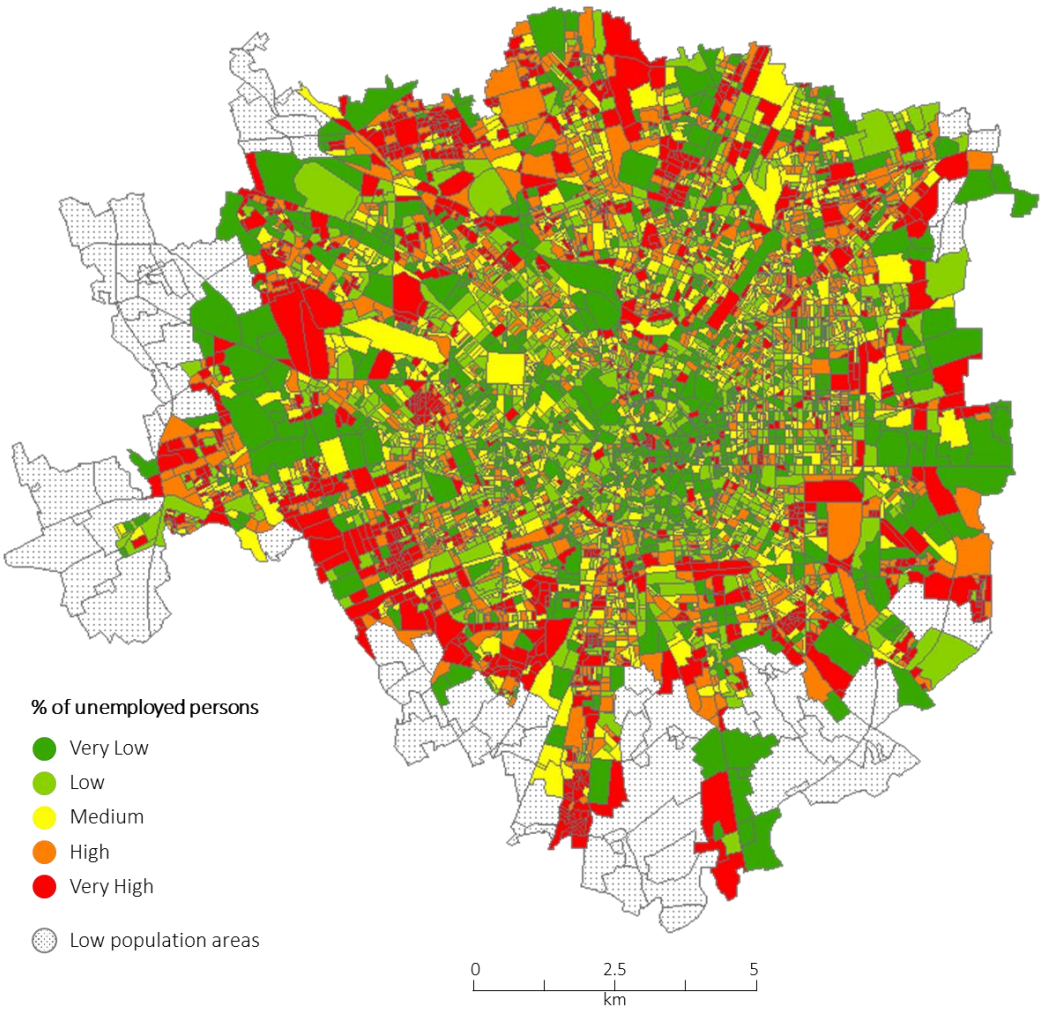
Figure 3.3: Average percentage of low-educated persons in each census block. Milan, 2011. Source: our elaboration of Istat 2011 census data (Istat, 2011).



[18] Reporting population numbers for each NIL is crucial, given that some units show measures based on a few residents. For instance, Parco Sempione has the highest percentage of low-educated persons (50%), but this value is based on the only 3 inhabitants of the NIL, which is a public park in the very core of the city. Thus, stating that this is a deprived area would be clearly misleading.

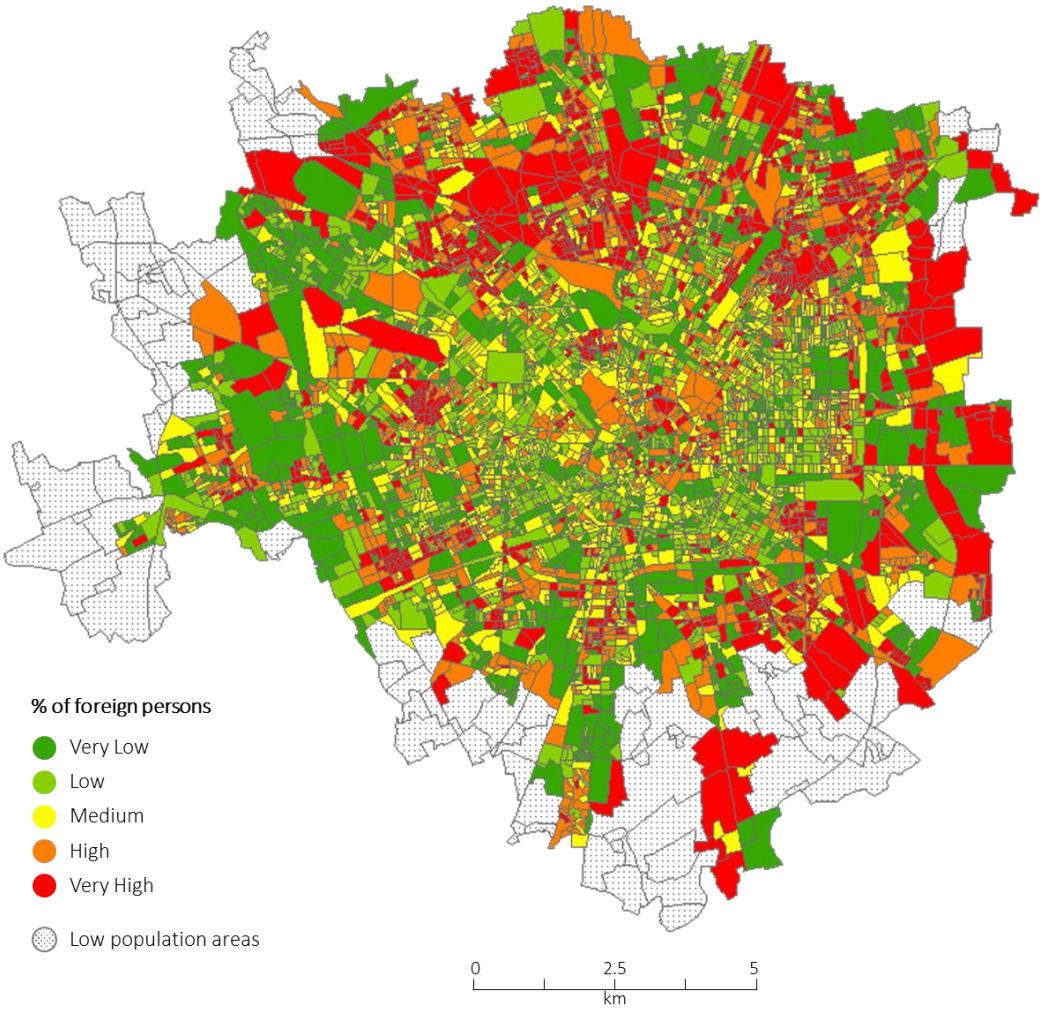
Concerning the first indicator (Fig. 3.3), areas with a high percentage of low-educated persons are concentrated in the northern peripheries, including the NILs Gallaratese, Villapizzone, Quarto Oggiaro, Bovisasca, Affori, Comasina, Dergano, Bovisa, Niguarda-Ca' Granda, Adriano, Padova, and Parco Lambro-Cimiano, as well as in other outlying areas located elsewhere, such as Selinunte, Baggio, Forze Armate, Lorenteggio, Giambellino, Barona, Gratosoglio-Ticinello, Lodi-Corvetto, and Mecenate. Areas with a high percentage of unemployed persons show a similar pattern (Fig. 3.4), though not identical. The northern neighbourhoods are not as homogenous as in the previous case, whilst some areas – among all Isola, Garibaldi-Repubblica, and Ticinese, but also Buenos Aires-Venezia and Città Studi – stand out for above than average rates of unemployment despite being just before the centre.

Figure 3.4: Average percentage of unemployed persons in each census block. Milan, 2011. Source: our elaboration of Istat 2011 census data (Istat, 2011).



The distribution of foreigners in the city (Fig. 3.5) overlaps with one or both the previous indicators in some areas, whilst being radically different in some others. Most of the northern areas characterized by a high concentration of low-educated people stand out for a massive concentration of foreigners. People without Italian citizenship are especially clustered in Villapizzone, Bovisa, Dergano, Maciachini, Affori, and Comasina (the red contiguous cluster on the top of the map), as well as in Padova, Loreto, Viale Monza (the north-eastern cluster). Selinunte shows a high concentration for all the three indicators, while Gallaratese – a higher than average unemployment and an extremely low-educated area – shows a very low percentage of foreigners.

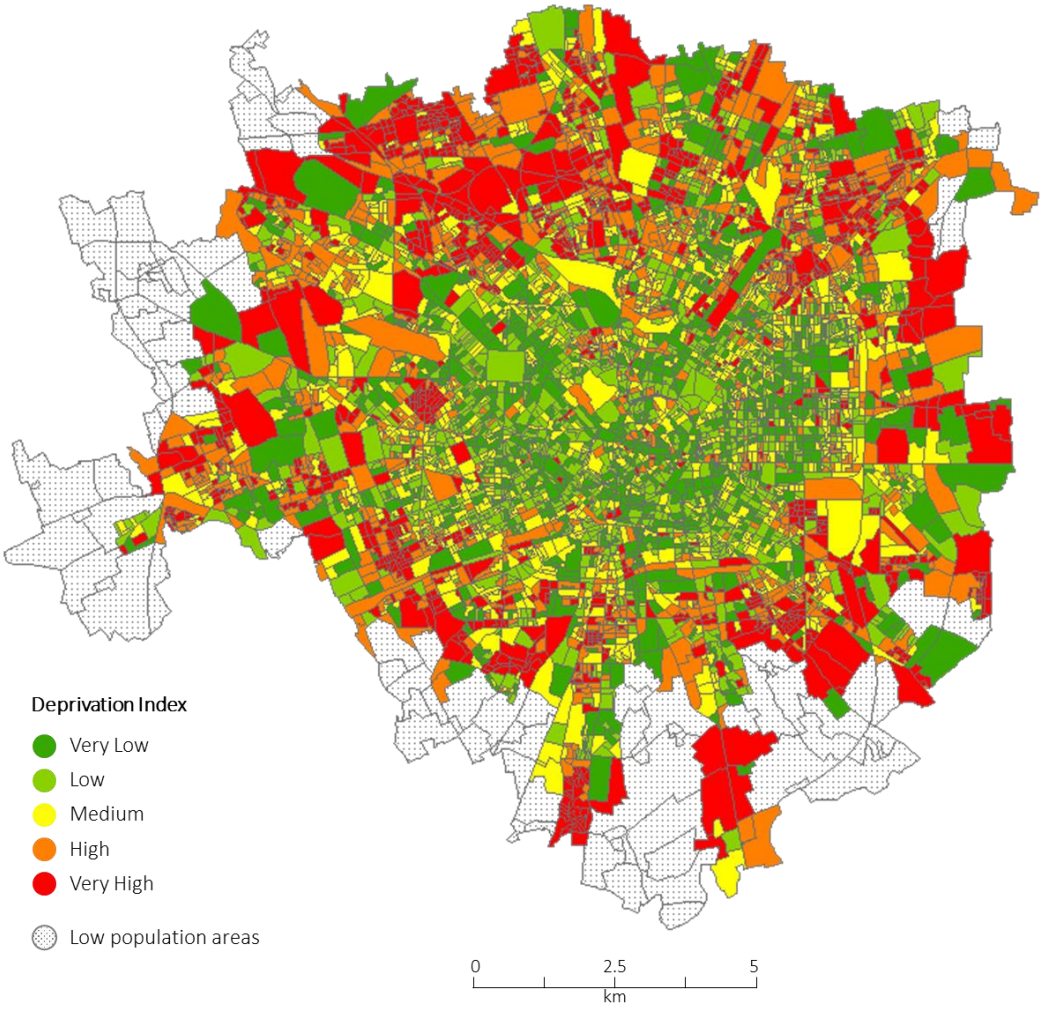
Figure 3.5: Average percentage of foreign persons in each census block. Milan, 2011. Source: our elaboration of Istat 2011 census data (Istat, 2011).



Other areas with a relevant presence of low-educated and/or unemployed persons, which are instead characterized by less noticeable presence of foreigners are Lorenteggio, Barona, and

partly Quarto Oggiaro, Forze Armate, and Stadera. Differently from the other two indicators, in this case a high concentration is present also in the city centre, in an area across Duomo, Guastalla, Brera, and Giardini Porta Venezia, as well as – within easy reach – Sarpi. This last is the Milanese Chinatown, while foreigners living in the centre may be of higher SES compared to those living in the periphery, as the distribution of employed foreigners showed in Figure A3.7 in the appendix seems to suggest. The overall index (Fig. 3.6) summarises the information provided by the single indicators. As stated above, the general picture provides evidence of a peripheral belt of deprivation relatively to the inner parts of the city. This picture is confirmed by the distribution of other indicators, made available by Istat only at the census tract level, and thus not usable for the census block-level index computer here.

Figure 3.6: Deprivation index. Milan, 2011. Source: our elaboration of Istat 2011 census data (Istat, 2011).



Nevertheless, these may be useful to triangulate the results, testing the social status of different areas of the city relying on other measures. Figures A3.3-A3.7 in the appendix show

respectively the percentage of high-skilled workers, low-skilled workers, NEET, unemployed young people, and employed foreigners in each census tract. All the five indicators report the same pattern, with a concentration of residents in more favourable social conditions in the inner areas (approximately within the internal bypass road), with few exceptions, providing a description consistent with the existing literature (Petsimeris and Rimoldi, 2015; Kazepov, 1995). Table 3.5 reports the distribution of the variables included in the analysis.

Table 3.5: Absolute and percentage distribution of the variables T2DM, sex, age, citizenship, educational level, and deprivation index (N = 260,088).

	n	**%**
T2DM		
No	235,216	90.44
Yes	24,872	9.56
Sex		
Male	102,277	39.32
Female	157,811	60.68
Age		
30-39	41,282	15.87
40-49	53,596	20.61
50-59	44,609	17.15
60-69	42,185	16.22
70-83	78,416	30.15
Citizenship		
Italian	227,770	87.57
Foreign	32,318	12.43
Educational Level		
Tertiary	75,894	29.18
Higher-secondary	98,775	37.98
Lower-secondary	59,390	22.83
Primary	26,029	10.01
Deprivation Index		
Very low	43,776	16.83
Low	55,799	21.45
Medium	56,608	21.76
High	53,177	20.45
Very High	50,728	19.5
N	260,088	

The data shown are relative to the population aged between 30 and 83 for which data about educational attainment are available, and not to the whole Milanese population. Thus from the 1,364,377 subjects extracted from the databases, the final population size was reduced to 260,088 (19% of the total population) due to the exclusion of individuals younger than 30 (n=352,880), older than 83 (n=73,724), and/or with T1DM (n=2,031), and/or missing data for

educational attainment (n=953,829). The analysis included 24,872 individuals with T2DM (cases) and 235,216 without the disease (controls). Table 3.6 shows the composition of the study population by T2DM. In the sample there are slightly more men (54.94%) than women (45.06%) with T2DM, the presence of T2DM patients increases with age, and the vast majority of T2DM cases are of Italian citizenships (88.06%). Concerning SES, most of T2DM patients in the sample have lower- (33.19%) and upper-secondary (34.05%) education, and are gradually more present in more deprived areas.

Table 3.6: Composition of the variables sex, age, citizenship, educational level, and deprivation index by T2DM (N = 24,872).

	n T2DM	**% T2DM**
Sex		
Male	13,664	54.94
Female	11,208	45.06
Age		
30-39	1,397	5.62
40-49	1,580	6.35
50-59	2,521	10.14
60-69	5,377	21.62
70-83	13,997	56.28
Citizenship		
Italian	21,902	88.06
Foreign	2,970	11.94
Educational Level		
Tertiary	3,505	14.09
Upper-secondary	8,469	34.05
Lower-secondary	8,256	33.19
Primary	4,642	18.66
Deprivation Index		
Very low	3,071	12.35
Low	4,244	17.06
Medium	4,833	19.43
High	5,684	22.85
Very High	7,040	28.30
N	24,872	

3.4 Results

It is firstly useful to look at the bivariate relationships between the predictors and the outcome selected. As Table 3.7 shows, T2DM is more common in men (13.36%) than women (7.10%), and it is positively associated with age (Table 3.8), while differences between Italian people (9.62%) and foreigners (9.19%) are negligible (Table 3.9). Concerning SES, there is evidence for a marked social gradient in T2DM both at the individual and the contextual level. T2DM

rates grow incrementally moving from the higher to the lower educated (Table 3.10), with those with at most primary education (17.83%) having a nearly four times higher T2DM percentage than those with tertiary education (4.62%).

Table 3.7: Percentage of T2DM by Sex (N = 260,088). P-value = 0.00.

	Sex	
	Male	*Female*
T2DM	13.36	7.10
No T2DM	86.64	92.90
Tot	100	100

Table 3.8: Percentage of T2DM by Age (N = 260,088). P-value = 0.00.

	Age				
	30-39	*40-49*	*50-59*	*60-69*	*70-83*
T2DM	3.38	2.95	5.65	12.75	17.85
no T2DM	96.62	97.05	94.35	87.25	82.15
Tot	100	100	100	100	100

Table 3.9: Percentage of T2DM by Citizenship (N = 260,088). P-value = 0.02.

	Citizenship	
	Italian	*Foreign*
T2DM	9.62	9.19
no T2DM	90.38	90.81
Tot	100	100

Table 3.10: Percentage of T2DM by Educational Level (N = 260,088). P-value = 0.00.

	Educational Level			
	Tertiary	*Upper-secondary*	*Lower-secondary*	*Primary*
T2DM	4.62	8.57	13.9	17.83
no T2DM	95.38	91.43	86.10	82.17
Tot	100	100	100	100

Table 3.11: Percentage of T2DM by Deprivation Index (N = 260,088). P-value = 0.00.

	Deprivation Index				
	Very low	*Low*	*Medium*	*High*	*Very High*
T2DM	7.02	7.61	8.54	10.69	13.88
no T2DM	92.98	92.39	91.46	89.31	86.12
Tot	100	100	100	100	100

Similarly, T2DM rates increase gradually moving from those living in more affluent to those living in more deprived areas (Table 3.11), with those living in very high deprivation areas (13.88%) having a nearly double T2DM percentage than those living in very low deprivation areas (7.02%). Table 3.12 shows the result of the main analysis, the multilevel logistic regression models of T2DM. Summing up, the analysis is based on a sample of 260,088 individuals (of which 24,872 with T2DM) living in 5,674 census blocks. Each census block contained minimum 1 and maximum 387 individuals, with an average value of 45.8 individuals per area.

Table 3.12: Multilevel logistic regression of T2DM (0=no, 1=yes; N = 260,088).

	Model 1		**Model 2**		**Model 3**	
	Odds Ratio	**[95% CI]**	**Odds Ratio**	**[95% CI]**	**Odds Ratio**	**[95% CI]**
Age			1.05	[1.05 - 1.05]	1.05	[1.05 - 1.05]
Sex						
Female			1.00	-	1.00	-
Male			1.75	[1.70 - 1.80]	1.74	[1.69 - 1.79]
Citizenship						
Italian			1.00	-	1.00	-
Foreign			2.08	[1.98 - 2.18]	1.95	[1.86 - 2.04]
Educational Level						
Tertiary			1.00	-	1.00	-
Upper-secondary			1.51	[1.45 - 1.57]	1.42	[1.36 - 1.48]
Lower-secondary			1.96	[1.88 - 2.05]	1.74	[1.66 - 1.82]
Primary			2.16	[2.05 - 2.27]	1.85	[1.76 - 1.95]
Deprivation Index						
Very Low					1.00	-
Low					1.07	[1.01 - 1.13]
Medium					1.18	[1.12 - 1.25]
High					1.46	[1.38 - 1.54]
Very High					1.85	[1.75 - 1.94]
LR ($P>chi^2$)*	0.000		0.000		0.000	
AIC†	163043.5		147678.7		146936.0	
BIC‡	163064.5		147762.5		147061.6	
VPC§	0.046		0.023		0.010	
MOR**	1.46		1.30		1.19	

* LR ($P>chi^2$)* = Likelihood Ratio test
† AIC = Akaike Information Criterion
‡ BIC = Bayesian Information Criterion
§ VPC = Variance Partition Coefficient
** MOR = Median Odds Ratio

As anticipated, Model 1 contains no predictors, and its usefulness lies in the estimation of the VPC[19], which provides information about the proportion of variance in each level of analysis. In our case, the VPC of 0.046 informed us that approximately 4.6% of the total variance in T2DM lies at the neighbourhood level. Thus, even if most of the variance was found at the individual level, there was a significant contextual variation in T2DM outcome, as confirmed by the Likelihood Ratio (LR) test[20], indicating that the two-level model is preferable over the single-level one, and that there is a spatial heterogeneity in T2DM distribution within the city. In Model 2, we considered all individual predictors to account for differences in T2DM outcomes, without including any contextual variable. All the variables are significantly associated with T2DM. Concerning age (OR=1.05), each additional year increases the odds of T2DM by 5%, whilst men (OR=1.75), have a considerably higher probability than women. Regarding citizenship, foreigners (OR=2.08) report a more than double probability of having the disease[21] compared to Italians. The social gradient in T2DM was confirmed also in this multivariate analysis. Even controlling for age, sex, and nationality, having upper-secondary instead of tertiary education is associated with a 50% (OR=1.51) higher T2DM probability, and the odds is higher for those with lower-secondary (OR=1.96) and primary (OR=2.16) education, for which the odds is double. The values of both the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC)[22] informed us that the model with individual-level predictors is preferable over the empty model, namely that the variables introduced are able to explain part of the spatial heterogeneity in T2DM. Finally, in Model 3 we included all individual-level predictors already present in Model 2, introducing the contextual variable

[19] The VPC is the ratio between level 2 residual variance and the total variance (level 1 + level 2 residual variance), given by the formula $VPC = \frac{\sigma_{\mu}^2}{\sigma_{\mu}^2 + \sigma_{e*}^2}$ in which σ_{μ}^2 is the level 2 residual variance, and σ_{e*}^2 is the level 1 residual variance, which in multilevel logistic regression is not estimated directly from the data, but is constrained to the value of 3.29 (Steele, 2009). This coefficient measures the proportion of the total residual variance that is due to between-group variation, in our case the proportion of the total residual variance in the propensity to have T2DM that is due to differences between neighbourhoods.

[20] In multilevel models, the LR is used to test nested models. Comparing the likelihood values of the single-level and multilevel models, the test statistic LR is compared with a chi-squared distribution with degrees of freedom equal to the number of extra parameters in the more complex model. Rejection of the null hypothesis implies that there are 'real' group differences, in which case the multilevel model is preferable over the single-level model (Steele, 2008). Thus, in our case, a P-value equal to 0.000 implies that the nested model is preferable over the single-level one, indicating the presence of a spatial heterogeneity in T2DM rates.

[21] At first glance, this may appear to be contradictory, given that table 3.6 reported no differences in T2DM percentages between the two categories. However, the bivariate relationship did not take into account the different age composition of the two groups, with the Italian population in the sample almost 14 years older on average than the foreigner one. Thus, when controlling for age and sex, a substantially different picture emerges.

[22] AIC and BIC are two criterion useful to select among a set of models the one with the best goodness of fit, allowing to compare models with a different number of parameters, and avoiding the problem of overfitting. The model with the lowest AIC/BIC is preferable.

'deprivation index of the census block of residence' as level-2 predictor. The results showed that, even after controlling for individual characteristics and SES, socioeconomic characteristics of the neighbourhood of residence are associated with T2DM, with an incremental probability moving from less to more deprived areas. Thus, living in a low instead of a very low deprivation neighbourhood increases the probability of having T2DM by 7% (OR=1.07), and the probability is higher for those living in areas with medium (OR=1.08), high (OR=1.46), and very high (OR=1.85) deprivation. Significance and direction of level-1 predictors remained substantially the same on moving from Model 2 to Model 3, with odds ratios – especially for educational level – slightly reduced due to the introduction of the level-2 predictor. The decreasing AIC and BIC indicated a better fit of the final model with all level-1 and level-2 predictors, as compared with the previous models, while the decreasing VPC suggested that the predictors included in each step were able to explain most of the contextual variance in T2DM rates. The Median Odds Ratio[23] (MOR) – an alternative measure to the VPC – provides similar insights. In the empty model, the MOR equal to 1.46 indicates a considerable between neighbourhoods variation in the probability of having T2DM (confirming the spatial heterogeneity of the disease already suggested by the VPC). Subsequent models show a reduction of the MOR, indicating, as for the VPC, an efficient explanation of the contextual variance by the variables introduced in the models. Given that the MOR is directly comparable with the odds ratios of individual or area variable, it is interesting to look at the model including individual-level predictors, but not the contextual level one (Model 2). The MOR equal to 1.30 suggests that in the median case the residual heterogeneity between areas increased by 30% the individual odds of having T2DM when randomly picking out two individuals in different areas – that is, if a person moves to another area with a higher T2DM risk, his or her probability of having T2DM will (in median) increase 1.30 times. Thus, the residual heterogeneity between

[23] The MOR is defined as the median value of the odds ratio between the area at highest risk and the area at lowest risk when randomly picking out two areas, and it can be conceptualized as the increased risk that (in median) an individual would have if moving to another area with higher risk. As Larsen and Merlo states "the MOR quantifies the variation between clusters (the second-level variation) by comparing two persons from two randomly chosen, different clusters. Consider two persons with the same covariates, chosen randomly from two different clusters. The MOR is the median odds ratio between the person of higher propensity and the person of lower propensity." (Larsen and Merlo, 2005, 82). Its aim is to translate the area level variance in the odds ratio scale, which has a consistent and intuitive interpretation (Merlo *et al.*, 2006). It is given by the formula:

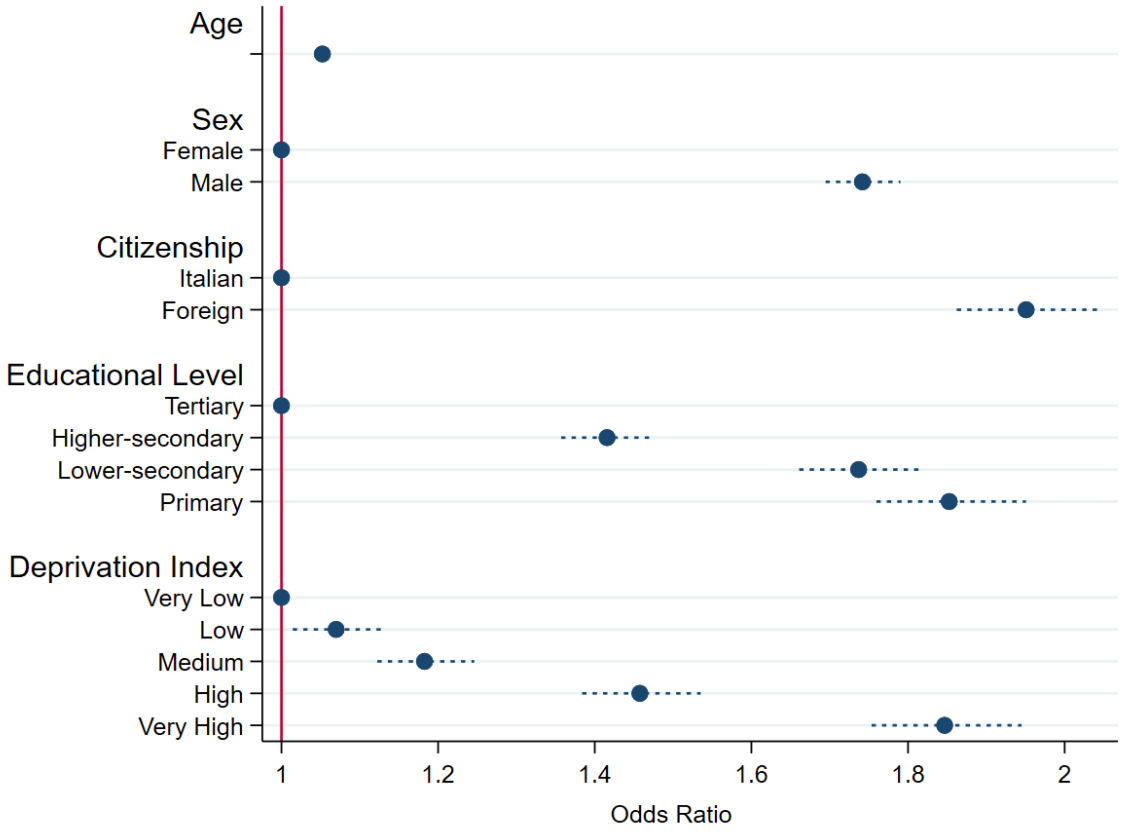
$$MOR = \exp\sqrt{\left(2 * \sigma_{\mu}^{2}\right)} * 0.6745$$

where σ_{μ}^{2} is the area level variance, and 0.6745 is the 75th percentile of the cumulative distribution function of the normal distribution with mean 0 and variance 1 (Larsen and Merlo, 2005; Larsen *et al.*, 2000). In our case, a MOR equal to 1 would have implied that there were no differences between areas in the probability of having T2DM, while a MOR greater than 1 suggest the relevance of the area of residence in understanding the individual probability of having T2DM.

areas (MOR=1.30) is smaller than the impact of the individual educational level (OR=1.51; 1.96; 2.16) for understanding variations in the odds of having T2DM, but still statistically significant and relevant, revealing the presence of a good amount of between-clusters variability that is not accounted for by individual-level predictors, and thus suggesting that the spatial heterogeneity in T2DM is not just a matter of compositional characteristics of individuals. The further decrease of the value in Model 3 (MOR=1.19), indicates that the area-level predictor introduced accounted for part of the residual heterogeneity between areas, suggesting a role of the socioeconomic characteristics of the neighbourhood of residence in determining T2DM outcomes, independently of personal characteristics and individual SES.

Figure 3.7 displays the results of Model 3 in the so-called forest plot. Despite reporting the same odds ratios showed in Table 3.9, the graph visualization is helpful in conveying information that is not immediately visible with numbers.

Figure 3.7: T2DM odds ratios, multilevel logistic regression Model 3.



Looking at educational level, it is possible to see that inequalities in T2DM decrease moving from higher to lower attainment. Despite the presence of a marked social gradient in the disease risk – the lower the education, the higher the probability of having T2DM – the distance

between the odds ratio gets shorter as educational level decreases. The opposite is true for area deprivation, for which together with the social gradient is noticeable an increase of inequalities moving from less to more deprived areas. Thus, despite the odds ratio of the 'worst' versus the 'best' categories are similar, the underlying patterns are quite different. Regarding education, having an upper-secondary instead of a tertiary education appears to be very detrimental for T2DM risk (increasing the probability of having the disease by 42%), whereas for area deprivation, living in a lowly instead of a very lowly deprived neighbourhood makes a much less sizable difference (increasing the probability of having the disease by only 7%. Conversely, the difference between those having primary and lower-secondary education is limited (1.85 - 1.74 = 0.11), whereas the difference between those living in very high and high deprivation areas is considerable (1.85 - 1.46 = 0.39). Table 3.13 shows the results of Model 3 disaggregated by sex.

Table 3.13: Multilevel logistic regression of T2DM by sex, Model 3 only (N Females = 157,811; N Males = 102,277).

	Model 3			
	Females		**Males**	
	Odds Ratio	**[95% CI]**	**Odds Ratio**	**[95% CI]**
Age	1.04	[1.04 - 1.04]	1.07	[1.06 - 1.07]
Citizenship				
Italian	1.00	-	1.00	-
Foreign	1.86	[1.75 - 1.98]	1.84	[1.71 - 1.98]
Educational Level				
Tertiary	1.00	-	1.00	-
Higher-secondary	1.40	[1.31 - 1.50]	1.53	[1.45 - 1.62]
Lower-secondary	1.92	[1.80 - 2.06]	1.80	[1.70 - 1.91]
Primary	2.27	[2.10 - 2.45]	1.74	[1.63 - 1.87]
Deprivation Index				
Very Low	1.00	-	1.00	-
Low	1.06	[0.98 - 1.15]	1.07	[0.99 - 1.15]
Medium	1.22	[1.13 - 1.32]	1.14	[1.07 - 1.23]
High	1.54	[1.43 - 1.65]	1.39	[1.29 - 1.48]
Very High	1.96	[1.83 - 2.11]	1.75	[1.63 - 1.87]
LR ($P>chi^2$)*	0.002		0.000	
AIC†	74226.0		72204.0	
BIC‡	74335.7		72308.9	
VPC§	0.01		0.01	
MOR**	1.16		1.19	

Women reported higher odds ratio concerning both individual and neighbourhood SES, suggesting that they are more susceptible to T2DM inequalities than men. Having primary

instead of tertiary education is associated with an increased T2DM odds of 121% in women (OR=2.21) and 74% in men (OR=1.74). Concerning neighbourhood deprivation, the differences between sexes are much more limited. Living in very high instead of very low deprivation areas is associated with an increased T2DM odds of 96% in women (OR=1.96) and of 75% (OR=1.75) in men. A gradient is visible in both sexes for both SES measures, with women reporting higher odds ratios for nearly each category.

The maps below show the distribution of residuals for each model. Multilevel regression generates a value (usually called μ_0) for each group in the analysis (in our case for each census block) relative to the deviation of the intercept of a group from the overall intercept[24]. Plotted on a map of the city, these μ_0 residuals show how each census block scores in T2DM probability in relation to the city as a whole. To obtain more reliable estimations, residuals are multiplied by a shrinkage factor tending to leave unaltered groups with a high number of observations, while shrinking towards the overall mean estimates relative to groups with fewer observations[25]. Figure 3.8 shows the quintiles distribution of (shrunken) residuals deriving from Model 1, which is the empty-model, containing no predictors. This simply shows the distribution of T2DM across different census block for the individuals included in the analysis (not to be confused with Figure 3.2, showing the raw prevalence of the disease for the whole population). The map displays the usual centre-periphery pattern already seen for T2DM prevalence and for the deprivation index (and single indicators), but rather than focusing again on the description of areas with a higher concentration of T2DM, it is useful to look at it in comparison with the maps derived from subsequent models.

[24] In a multilevel model, there are as many intercepts as the number of groups included in the analysis. The overall intercept represents the average intercept, the one that would have resulted fitting a single-level model, without introducing group-level distinctions. The intercept of each group is expressed as a deviation from the overall intercept, which value is zero. Thus, groups with an intercept lower than the overall one (in our case census blocks with T2DM odds lower than the Milanese average) show negative μ_0 values, whilst groups with an intercept higher than the overall one (census blocks with T2DM oddds higher than average) show positive μ_0 values.

[25] The estimates obtained are called *shrunken residuals* (or *empirical Bayes estimates* or *posterior estimates* or *precision-weighted estimates*) and are given by the formula: $\hat{u}_{0j} = \frac{\sigma^2_{u0}}{\sigma^2_{u0} + \sigma^2_{e0}/\eta_j} * r_j$ where σ^2_{u0} is the between-group variation; σ^2_{e0} is the within-group (between-individual) variation; η_j is the number of individual in that group; r_j is the raw residual for that group. Thus, reliable estimates with large numerosity will be kept close to their raw residual values, while conversely unreliable estimates with small numerosity (e.g. a group with just one or few observations) will be shrunk towards the mean. However, the shrinkage factor is also a function of level-1 (within-group) and level-2 (between-group) variance. In brief, there is a lot of shrinkage when there are not many level one units in the group, or when the level one variance is big, or when the level two variance is small; and there is not much shrinkage when there are a lot of level one units in the group, or when the level one variance is small, or when the level two variance is big.

Figure 3.8: Quintile distribution of Model 1 residuals.

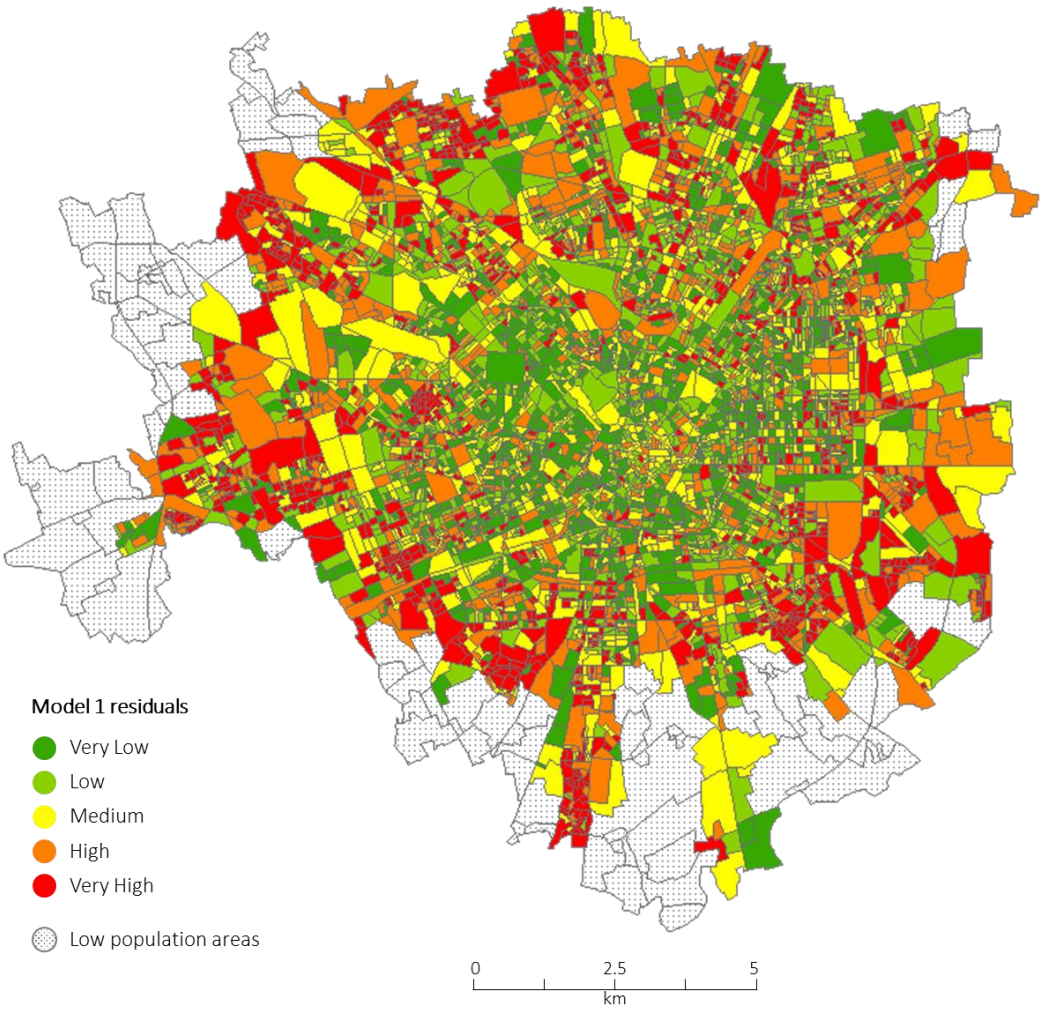
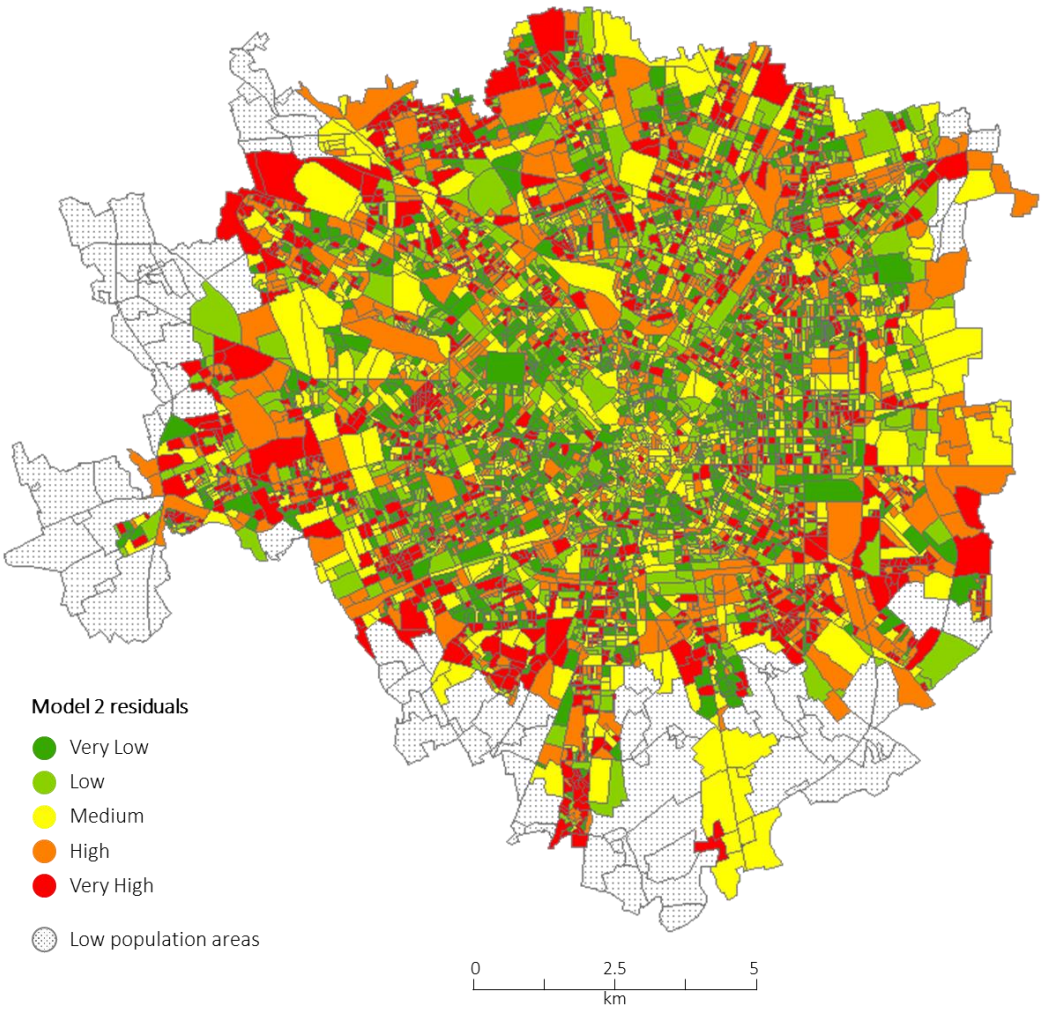


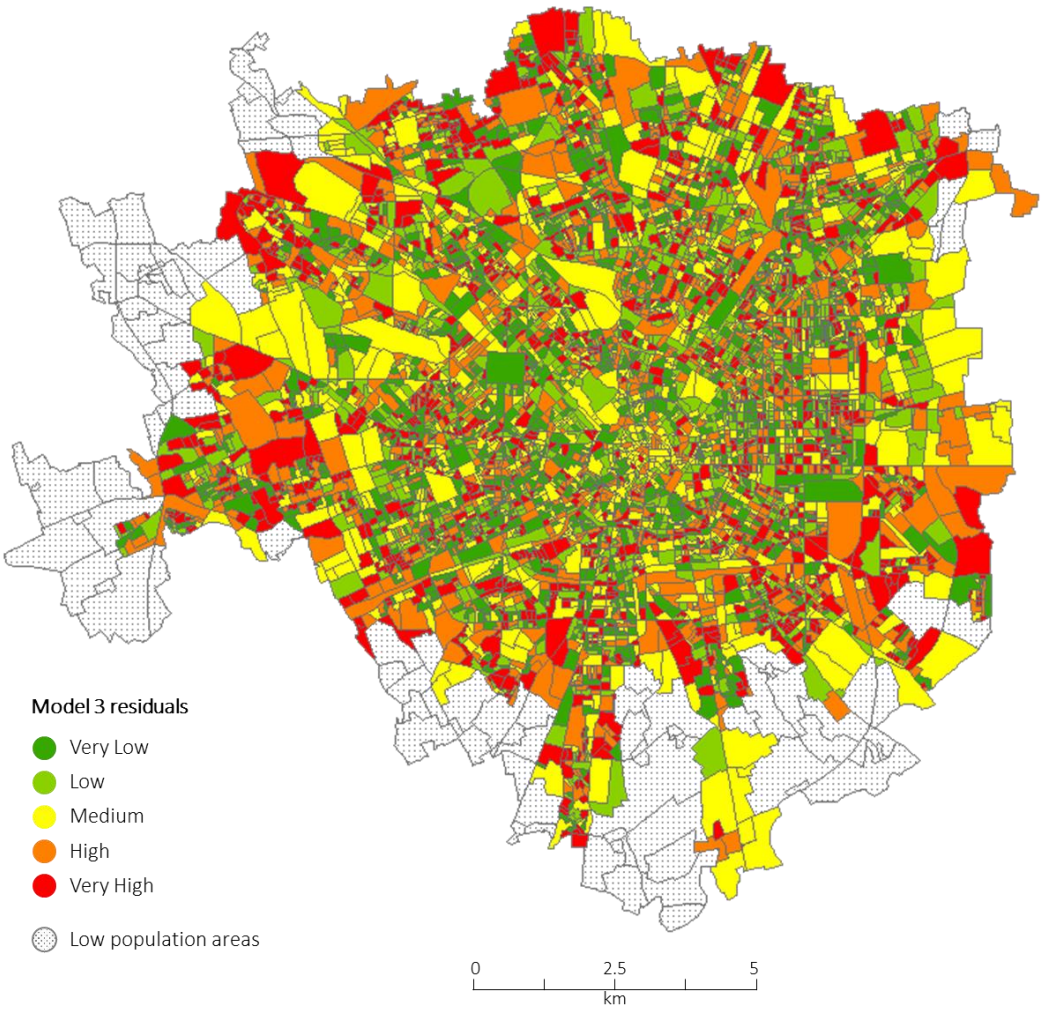
Figure 3.9 shows the same distribution but related to Model 2, including individual predictors. This provides an efficient visual tool to evaluate the presence of a compositional effect: if the spatial heterogeneity in T2DM found in Model 1 was attributable exclusively to the individual predictors included in the model, the residuals obtained after the introduction of these variables would make the pattern in Figure 3.8 disappear, given that all the variability in the outcome would be explained by the covariates selected. Instead, despite a mitigation of the pattern, this heterogeneity seems to endure, suggesting that the territorial differences in T2DM within the city are not attributable merely to individuals sharing similar characteristics clustering in the same areas.

Figure 3.9: Quintile distribution of Model 2 residuals.



Finally, Figure 3.10 shows the residuals' distribution after the introduction of the neighbourhood deprivation index (Model 3). In this case, the spatial heterogeneity gets almost entirely lost, suggesting than when accounting for both individual and contextual socioeconomic characteristics, the territorial variability in T2DM outcome is explained to a great extent – though not completely as, referring to table 3.12, the VPC and the MOR have not decreased to zero, indicating that T2DM spatial heterogeneity might be affected by other factors not included in the model, both at the individual (e.g. occupation, income, social networks, etc.) and the contextual level (e.g. other dimensions of deprivation not grasped by the index adopted here, such as social cohesion, crime, etc.).

Figure 3.10: Quintile distribution of Model 3 residuals.



Concerning models with random slopes and cross-level interactions, none of these was statistically significant (tables not reported). This implied that the effect of age, sex, citizenship, and educational level on T2DM was the same in each neighbourhood (no significant random slope models), and that the effect of neighbourhood deprivation on T2DM was the same for all individuals, regardless of their own age, sex, citizenship, and educational level (no significant cross-level interactions). Finally, the same models with different area units (Tables A3.3 and A3.4 in the appendix) led to similar results. Adopting the 177 functional areas or the 88 NILs, the models were still statistically significant, with a lower second-level variance compared to the model with census blocks as area units, consequently showing smaller VPC and MOR values (Table 3.14).

Table 3.14: Second-level variance, Variance Partition Coefficient (VPC) and Median Odds Ratio (MOR) in Model 1 with three different area units.

	Census blocks (n=5,674)	**Functional Areas** (n=177)	**NILs** (n=88)
Level-2 variance	0.16	0.09	0.09
VPC	0.046	0.027	0.026
MOR	1.46	1.34	1.32

Thus, as expected, relying on larger area units led to detect a smaller neighbourhood effect on T2DM, as Table 3.15 – comparing the estimates only for Model 3 with each area unit – shows.

Table 3.15: Estimates for Model 3 with different area units (N=260,088).
Census blocks: num. of areas=5,674; individuals per area: min=1; max=387; average=45.8).
Functional Areas: num. of areas =177; individuals per area: min=798; max=2,852; average= 1469.4).
NILs: num. of areas =88; individuals per area: min=11; max=11,805; average= 2,955.5).

	Census blocks (n=5,674)	**Functional Areas** (n=177)	**NILs** (n=88)
	Odds Ratio [95% CI]	**Odds Ratio [95% CI]**	**Odds Ratio [95% CI]**
Age	1.05 [1.05 - 1.05]	1.05 [1.05 - 1.05]	1.05 [1.05 - 1.05]
Sex			
Female	1.00 -	1.00 -	1.00 -
Male	1.74 [1.69 - 1.79]	1.74 [1.69 - 1.79]	1.74 [1.69 - 1.79]
Citizenship			
Italian	1.00 -	1.00 -	1.00 -
Foreign	1.95 [1.86 - 2.04]	2.07 [1.97 - 2.17]	2.09 [1.99 - 2.19]
Educational Level			
Tertiary	1.00 -	1.00 -	1.00 -
Upper-secondary	1.42 [1.36 - 1.48]	1.40 [1.35 - 1.47]	1.41 [1.35 - 1.47]
Lower-secondary	1.74 [1.66 - 1.82]	1.77 [1.70 - 1.85]	1.80 [1.72 - 1.88]
Primary	1.85 [1.76 - 1.95]	1.93 [1.84 - 2.04]	1.98 [1.88 - 2.08]
Deprivation Index			
Very Low	1.00 -	1.00 -	1.00 -
Low	1.07 [1.01 - 1.13]	1.19 [1.11 - 1.28]	1.20 [1.08 - 1.32]
Medium	1.18 [1.12 - 1.25]	1.30 [1.21 - 1.40]	1.41 [1.29 - 1.54]
High	1.46 [1.38 - 1.54]	1.52 [1.42 - 1.64]	1.51 [1.38 - 1.66]
Very High	1.85 [1.75 - 1.94]	1.70 [1.58 - 1.82]	1.63 [1.48 - 1.80]
LR ($P>chi^2$)*	0.000	0.000	0.000
AIC†	146936	147243.7	147388.5
BIC‡	147061.6	147369.3	147514.1
VPC§	0.010	0.003	0.003
MOR**	1.19	1.11	1.10

* LR ($P>chi^2$)* = Likelihood Ratio test
† AIC = Akaike Information Criterion
‡ BIC = Bayesian Information Criterion
§ VPC = Variance Partition Coefficient
** MOR = Median Odds Ratio

The odds of having T2DM living in a very high deprivation instead of a very low deprivation area decrease as the number of area units adopted increases, while conversely in models with functional areas and NILs the effect of educational level is even stronger, highlighting the higher relevance of individual SES for T2DM probability when larger definitions of neighbourhood are adopted. We also tested Model 3 with deprivation index as a continuous variable and with the deprivation index disaggregated into the three distinct indicators composing it. Regarding the first (Table 3.16), despite not being very informative in terms of effect, the statistically significance of the continuous variable confirms the presence of a linear association between neighbourhood SES and T2DM (OR=1.12) that is not simply due to the categorization of the deprivation in quintiles.

Table 3.16: Multilevel logistic regression of T2DM, continuous deprivation index, Model 3 (N = 260,088).

	Model 3	
	Odds Ratio	**95% CI**
Age	1.05	[1.05 - 1.05]
Sex		
Female	1.00	-
Male	1.74	[1.69 - 1.79]
Citizenship		
Italian	1.00	-
Foreign	1.94	[1.85 - 2.03]
Educational Level		
Tertiary	1.00	-
Upper-secondary	1.43	[1.37 – 1.49]
Lower-secondary	1.75	[1.67 – 1.83]
Primary	1.86	[1.77 - 1.96]
Deprivation Index	1.12	[1.11 – 1.13]
LR ($P>chi^2$)*	0.000	
AIC†	146934.7	
BIC‡	147029.0	
VPC§	0.010	
MOR**	1.19	

Concerning the latter (Table 3.17), the single indicators provide useful information about the contribution of each specific dimension to the association between neighbourhood SES and T2DM (the indicators have been standardized, enabling the comparison between them). The most important dimension of deprivation appears to be the percentage of low-educated persons in each census-block, for which a unit of change in standard deviation is associated with a 21% increase (OR=1.21) in T2DM probability. The association of the other two indicators with T2DM is smaller compared to the one of area education (percentage of unemployed: OR=1.10;

percentage of foreigners: OR=1.06), but nonetheless statistically significant, supporting the choice of including them as indicators of the latent concept of neighbourhood deprivation.

Table 3.17: Multilevel logistic regression of T2DM, disaggregated measures of deprivation index (z-scores), Model 3 (N = 260,088).

	Model 3	
	Odds Ratio	**95% CI**
Age	1.05	[1.05 - 1.05]
Sex		
Female	1.00	-
Male	1.74	[1.69 - 1.79]
Citizenship		
Italian	1.00	-
Foreign	1.99	[1.90- 2.09]
Educational Level		
Tertiary	1.00	-
Upper-secondary	1.42	[1.36 – 1.48]
Lower-secondary	1.72	[1.65 – 1.80]
Primary	1.83	[1.73 - 1.92]
Deprivation Index		
% Low-educated	1.21	[1.18 – 1.23]
% Unemployed	1.10	[1.08 – 1.13]
% Foreigners	1.06	[1.04 – 1.07]
LR ($P>chi^2$)*	0.000	
AIC†	145820.8	
BIC‡	145935.9	
VPC§	0.010	
MOR**	1.17	

Finally, Table 3.18 reports the results of the full data analysis referred to all the individuals in the dataset, without including educational level as individual SES predictor. The results appeared to be in line with those from the main models (Table 3.12), suggesting that despite the large amount of missing data inherent to this indicator, including educational level as covariate – reducing the numerosity of the sample – did not alter the overall findings reached. Indeed, as noticeable, the VPCs and MORs in Model 1 are almost identical between the two analyses (complete case: VPC=0.046, MOR=1.46; full data: VPC=0.047, MOR=1.47). This implies that the exclusion of cases for which information on educational achievement was missing did not biased the results in relation to the amount of spatial heterogeneity in the distribution of the disease. Moreover, though Model 2 and Model 3 are not directly comparable between the two kinds of analyses, given that they differ in sample numerosity and in the presence of one indicator, we can notice that the magnitude and the direction of the other covariates are consistent between them. The coefficients are only slightly higher for all the

variables in the full data models compared to the complete case ones, indicating that the introduction of educational level – with the consequent loss of cases – attenuates the association between all the other variables and T2DM without changing the overall patterns identified through the models with full data.

Table 3.18: Multilevel logistic regression of T2DM (0=no, 1=yes); full data analysis (educational level not included; N = 936,304). Num. of areas=5,828; individuals per area: min=1; max=1,359; average= 160.7).

	Model 1		**Model 2**		**Model 3**	
	Odds Ratio	**[95% CI]**	**Odds Ratio**	**[95% CI]**	**Odds Ratio**	**[95% CI]**
Age			1.07	[1.07 - 1.07]	1.07	[1.07 - 1.07]
Sex						
Female			1.00	-	1.00	-
Male			1.67	[1.64 - 1.70]	1.67	[1.64 - 1.70]
Citizenship						
Italian			1.00	-	1.00	-
Foreign			2.06	[2.01 - 2.11]	1.93	[1.88 – 1.98]
Deprivation Index						
Very Low					1.00	-
Low					1.09	[1.05 - 1.14]
Medium					1.27	[1.22 - 1.32]
High					1.61	[1.55 - 1.67]
Very High					2.12	[2.04 - 2.21]
LR ($P>chi^2$)*	0.000		0.000		0.000	
AIC†	422270.6		377479.9		375746.1	
BIC‡	422294.1		377538.7		375851.8	
VPC§	0.047		0.039		0.017	
MOR**	1.47		1.42		1.26	

* LR ($P>chi^2$)* = Likelihood Ratio test
† AIC = Akaike Information Criterion
‡ BIC = Bayesian Information Criterion
§ VPC = Variance Partition Coefficient
** MOR = Median Odds Ratio

3.5 Discussion

Our results showed a statistically significant area variation in T2DM rates within the city of Milan. The heterogeneous distribution of the disease found across neighbourhoods is at least partially attributable to socioeconomic characteristics of the context of residence, since we detected a statistically significant association between neighbourhood deprivation and T2DM outcomes, over and above individual educational level, while controlling for age, sex, and citizenship. The magnitude of this association resulted to be stable across different neighbourhoods, and the impact of neighbourhood SES on T2DM appeared not to be different for people differing in terms of individual characteristics and SES. This means that living in

relatively disadvantaged neighbourhood does not matter only for those with low individual socioeconomic profile, but also for the better-off. However, while these latter may mitigate the adverse effect of living in low SES areas with their personal resources, people with low individual SES suffer the cumulative disadvantage of being exposed to the risks deriving from their personal conditions as well as to those deriving from the context in which they live (Macintyre and Ellaway, 2003). Focusing on the individual level, our findings are consistent with the existing literature. A review and meta-analyses of the association between T2DM and individual SES found that in high-income countries T2DM is more prevalent in lower socioeconomic groups, measured by educational level, occupation, or income. Educational level was the most commonly used measure of SES, and also most consistently associated with increased risk of the disease (Agardh *et al.*, 2011). As in our case, and consistently with the literature (Espelt *et al.*, 2008) the studies included in the review found also more pronounced socioeconomic inequalities in T2DM in women rather than men. Possible explanations suggested are that lower SES women are overweight/obese, physical inactive, and experience psychosocial stress to a higher extent than men with the same socioeconomic profile (Loucks *et al.*, 2007; Robbins *et al.* 2005; Smith *et al.*, 2011; Tang *et al.*, 2003). As the study is cross-sectional, we are aware of potential reverse causality, but it should be less of a problem in studies that define SES by measures determined early in life, before the onset of the disease, and not susceptible to change when the disease occurs. Moreover, studies in different contexts have reached similar findings with the adoption of a longitudinal design (Everson *et al.*, 2002; Stringhini *et al.*, 2013; 2016), revealing that at least part of the strong association between SES and T2DM can be attributed to the causal effect of SES. In section 2.4.2 we already discussed the possible mechanisms operating in the association between individual SES and T2DM (while section 1.4.3 provided a broader description of the mechanisms driving the relationship between individual SES and health in general). Educational level, for instance, is known to be associated with lower cognitive skills, health literacy, social support, economic resources, and with higher psychosocial stressors, all of which in turn lead to a higher prevalence of health-damaging behaviours (Egerter *et al.*, 2011), such as unhealthy eating, physical inactivity, sedentary life-style, smoking, excessive alcohol-drinking, putting individuals at higher T2DM risk. Concerning the neighbourhood level, studies investigating the association of neighbourhood characteristics or SES with T2DM risk have obtained similar findings also in other high-income countries. A multilevel study of small-area SES in south-eastern France, reported a significantly higher prevalence of diabetes in the more deprived areas independently of individual SES

(Bocquier *et al.*, 2011). Similar results have been reached at the municipality level in Germany (Grundmann *et al.*, 2014) and at the neighbourhood level in the Netherlands (Consolazio *et al.*, forthcoming). In Australia, a study reported a lower risk of T2DM in greener neighbourhoods, even after controlling for demographic and cultural factors (Astell-Burt *et al.*, 2014), and another found that residents of disadvantaged neighbourhoods are more likely to report T2DM independently of individual SES (Rachele *et al.*, 2016). A Swedish study found that characteristics of the food environment were significantly associated with T2DM risk (Mezuk *et al.*, 2016). A study in Canada reported that neighbourhood walkability was inversely associated with the development of diabetes (Booth *et al.*, 2013), while a series of studies in the United States reported an association of neighbourhood resources supporting physical activity and healthy foods with lower incidence of insulin resistance (Auchincloss *et al.*, 2008) and T2DM (Auchincloss *et al.*, 2009); of neighbourhood physical and social environments with T2DM incidence (Christine *et al.*, 2015); of neighbourhood healthy food price accessibility with T2DM and insulin resistance (Kern *et al.*, 2018); of neighbourhood SES with metabolic syndrome (Chichlowska *et al.*, 2008), and of neighbourhood SES with T2DM (Cunningham *et al.*, 2018; Liu and Núñez, 2014). Several studies recently reviewed by den Braver and colleagues (den Braver *et al.*, 2018) also reported an association between area characteristics and T2DM, but most of them were ecological, without a multilevel design, and thus unable to properly disentangle the compositional/contextual effect issue. Differently from studies that used multiple measures for specific environmental features, here we used neighbourhood SES as contextual-level predictor. This may be a proxy for many interrelated neighbourhood features (Diez-Roux, 2004), while specific measures can be used to evaluate which features of the local environment may be most critical for T2DM risk. However, neighbourhood SES may grasp the variety of mechanisms involved in the relationships between the neighbourhood environment and T2DM, which have been discussed in section 2.4.3 (1.5.3 for health in general). Areas characterized by a concentration of individual deprivation are likely to be those with less physical activity resources, green spaces, walkability, healthy food environment, amenities, health services, public transport, safety, social cohesion, and the like, and conversely more exposed to air and noise pollution, traffic, crime and unsafety, social isolation, and the like (Dendup *et al.*, 2017; Giles-Corti *et al.*, 2016; Northridge *et al.*, 2003; Poortinga, 2006). All these (and other) features of the living environment may influence the exposure to more proximate (individual) risk factors, such as physical inactivity, sedentary lifestyle, unhealthy diet, smoking, drinking, stress, and disturbed sleep, which in turn lead to higher T2DM risk.

Thus, the contextual effect on T2DM may be driven by both characteristics of the built environment (Connoly *et al.*, 2000; Lovasi *et al.*, 2009; Meadows, 1995) and psychosocial mechanisms. Regarding these latter, some scholars have highlighted how socioeconomic inequalities may be detrimental to health outcomes due to higher levels of chronic stress resulting from the psychosocial impact of the perceived relative social position (Cox *et al.*, 2007; Pickett *et al., 2005).* In the case of T2DM, this may be related to physiological and metabolic alterations due to stress response, including overstimulation of the neuroendocrine system, which could influence the development of the disease (Cox *et al.*, 2007). People living in unfavourable neighbourhoods may compare themselves with those living in more affluent areas, feeling inadequate and fostering processes of exclusion and stigmatization. In this sense, neighbourhood SES could be also more than just a proxy for unmeasured neighbourhood characteristics and accessibility to resources through availability from the built environment, making an intrinsic contribution itself to the social and spatial patterning of T2DM.

3.5.1 Methodological Caveats

The results reached need to be discussed in light of some specificities of the methods adopted and the phenomenon studied. From a methodological perspective, a consideration about the magnitude of the effect identified is necessary. The models developed reported large odds ratios for the contextual variable, together with a relatively small second-level variance. This may seem counterintuitive, but it is consistent with the fact that the two measures provide different and complementary information. The second-level variance is fundamental to understand the extent to which T2DM varies between different neighbourhoods and not simply between individuals, while the odds ratio of the contextual variable quantifies how much neighbourhood deprivation explains the differences in T2DM found among the various areas. However, as suggested by the existing literature, if the amount of variation between areas is small, a large odds ratio would simply predict a great deal of very little (Aitkin and Longford, 1986; Merlo *et al.*, 2001; 2005c; Singer, 1998). Thus, it is crucial to interpret the magnitude of the odds ratios in relation to the area-level variance. In our analysis, both the VPC and the likelihood ratio test confirmed a statistically significant neighbourhood variation in T2DM. Nonetheless, the amount of area-level variation is scant if compared to individual-level variance. With the VPC we found only less than 5% of the variance lying at the second level, and this may suggest that, despite the statistically significance, the results reached are not so relevant. However, there are

some potential pitfalls in relying exclusively on the VPC in multilevel logistic models[26], whilst resorting to the MOR is identified as a better option (Larsen *et al.*, 2000; Larsen and Merlo, 2005; Merlo *et al.*, 2006). In our case, the MOR of the empty model (Model 1) indicates a non-negligible – though not huge – area variation in T2DM outcome. However, as the magnitude of the MOR compared to the educational level odds ratios in Model 2 highlights, individual SES is a more important predictor of T2DM than neighbourhood SES, so that in the Milanese case, 'who you are' is clearly predominant over 'where you live' in determining T2DM risk. Nonetheless, it is well-established that individual SES affects residential location, with those more equipped with socioeconomic resources living in better-off neighbourhoods. Thus, it is conceivable to think that a portion of the contextual effect could be intrinsically already expressed by the individual SES variable, leading to a possible underestimation of the real neighbourhood and T2DM association. Another methodological issue concerns the choice of the area unit of analysis. Being aware that administrative boundaries may fail to identify the proper context of residence experienced by each individual in his or her daily life, we dealt with the MAUP by running the same models with different area units (functional areas and NILs). The results were in line with those shown in the main models with census blocks as area units, but with smaller odds ratios. These findings are consistent with the literature indicating an inverse relationship between the size of the area unit and the area-level variance (Boyle and Willms, 1999; Gulliford *et al.*, 1999), and suggest the validity of the results reached beyond the arbitrary choice of the area unit.

[26] In multilevel linear models both the individual and the contextual level variances are expressed in the same scale (the unit of measurement of the outcome), so that it is easy to perform a partition of variance between different levels and obtaining relevant information about the relevance of area-level variance. Contrarywise, in multilevel logistic models the individual- and the contextual-level variance are not directly comparable, given that the first is expressed in the probability scale, while the latter in the logistic scale. To overcome these difficulties, some methods have been developed to compute the VPC in the logistic case in more effective ways, like the *simulation method* or the *linear threshold model method* (Goldstein *et al.*, 2002). This last is the one adopted here, which assumes that the area-level variance is always equal to $\pi^2/3$ (that is 3.29). According to Merlo and colleagues, the simulation method leads to VPCs that are statistically dependent on the prevalence of the outcome and can therefore not be used to compare the magnitude of clustering between phenomena with a different prevalence; while the threshold method necessitates conversion of binary outcomes into continuous linear latent variables, which may not be adequate for all phenomena. Additionally, both these methods have interpretative drawbacks when it comes to measuring clustering of phenomena, because of inherent difficulty of distinguishing the individual- and the area-level variance in the logistic case (Merlo *et al.*, 2006). According to the scholars "computing the MOR is […] a more suitable option for obtaining measures of variance in logistic regression. It is not statistically dependent on the prevalence of the outcome and furthermore permits expression of the area level variance on the well-known OR scale. Therefore, it permits comparison of the magnitude of area level variations with the impact of specific factors" (Merlo *et al.*, 2006, 297).

3.5.2 Limitations

As any study, this one is not exempt from some possible limitations, which we need to highlight. First, given that we relied on cross-sectional data, we are unable to assess the direction of causation in our findings, and we can only present them in terms of association. Nonetheless, it is arguable that having T2DM mellitus could affect residential choices and mobility, rather than the opposite. Selective pathways at the origins of social and territorial inequalities in T2DM are surely conceivable, but – as the wider literature about the social determinants of health agrees – their contribution in the social patterning of the disease should be only minor (see section 1.3). Second, our study is characterized by a considerable amount of missing data, which may have altered the real distribution of variables and consequently the results reached. We saw that the population included in the analysis significantly differs from the one excluded in each predictor, being on average four years older and with a T2DM rate higher of almost five percentage points. However, notwithstanding the missing data, the distribution of educational level in the final population resembles the one provided by Istat for the same period, with a slight overrepresentation of the less educated, and conversely a slight underrepresentation of the more educated. This may indicate that the possibility in incurring in selection bias is limited, despite the pattern of missing data, as confirmed by the analysis performed relying on the whole dataset, but without including educational level as individual SES predictor. The fact that the magnitude and the direction of all the other covariates remained stable suggested that opting for a listwise deletion did not alter the results, and that educational level operated adjusting the association between neighbourhood SES and T2DM without changing its pattern. Third, T2DM is the outcome of life-course processes encompassing social and contextual exposures to multiple risk factors long before the moment in which people were involved in the study. Thus, in case of residential mobility, the neighbourhood of residence in earlier life may have had a bigger effect than the current one in shaping T2DM risk. Unfortunately, we had no data to keep track of this possible residential mobility. Finally, there is a mismatch between the reference period of the individual and contextual SES variables, with all the individual-level predictors referring to the 2018 Milanese population, and the deprivation index computed basing on the 2011 national census. Phenomena such as population growth, migration, urban requalification, and gentrification, can alter neighbourhood composition, implying that area-based indicators developed in previous years may fail to depict the current neighbourhood socioeconomic profile (Krieger, 1992). However, like in most of other countries census in Italy are carried out every ten years, and there is no other source of information concerning socioeconomic characteristics

of the place of living at a such detailed level. In relation to this, the practice of relying on different periods for individual and contextual data is widespread within the literature and should not be a source of great concern if the distance between the data periods is not large. Finally, we are aware that there are some other factors playing a fundamental role in shaping social and spatial inequalities in T2DM, which have not been included in our analysis. This leads our analysis to be potentially subjected to omitted variable bias (Clarke, 2005), given that other components of individual SES (e.g. occupation, income, parental background, etc.) or of neighbourhood characteristics (e.g. property value, availability of services and amenities, etc.), as well as other indicators (e.g. social support, social cohesion, social networks, household composion, marital status, etc.) may shape or mediate the association between SES and T2DM. Nonetheless, our models were specificied relying on the most pertinent indicators among those available from the healthcare databases.

3.5.3 Strengths

Nonetheless, this study has also several strengths. The structure of the data used allowed us to measure each indicator at the proper level of analysis, without incurring the typical fallacies encountered when variables at one level are derived from data collected for units at a different level. Moreover, the sample numerosity permitted to have robust estimations, and the use of high-quality administrative healthcare data has no precedent for the phenomenon and context studied. Concerning the results, we found a large odds ratio predicting higher T2DM rates for individuals living in the most deprived neighbourhoods compared to those living in the better-off areas. Since we controlled for individual SES, we may have faced over-adjustment (Jager *et al.*, 2008), given that we cannot exclude a causal pathway between individual SES and neighbourhood SES, in either direction. Thus, the real association between neighbourhood SES and T2DM could be even stronger than the one reported, due to a possible underestimation. We also conducted several sensitivity analyses, and they all confirmed our findings: the results from the model with different area units provide stronger evidence for the hypotheses tested, suggesting that the findings are not due to chance. Another strength is the use of educational level as individual SES predictor. Several studies with similar design relied on occupational level, personal or household income, or other indicators that are not as powerful and comprehensive as educational achievement in grasping the meaning of individual SES. Education has the merit of encompassing in a single indicator multiple dimensions and mechanisms involved in the process of generation of health inequalities, being influenced by family background, stable over the life course, and influencing subsequent career and income

opportunities, as well as the disposition of social, cultural, economic, cognitive and relational resources (Liberatos *et al.*, 1988). Regarding the neighbourhood SES variable adopted, being composed of multiple indicators (percentage of low educated, unemployed, and foreign people), it is able to account for a multidimensional definition of neighbourhood deprivation, which contributed to unequivocally identify disadvantaged areas within the city.

Conclusion

Our analyses suggested that regarding the specific case of Milan, a significant spatial heterogeneity in T2DM risk is present. Different neighbourhoods showed different T2DM rates, with the context playing a significant role in determining this uneven territorial distribution of the disease. However, most of the variability in the outcome was found to be attributable to individual SES rather than neighbourhood SES, revealing that geographical differences in T2DM in Milan were mostly explained by individual-level factors. Nonetheless, a non-negligible area effect was found, making necessary some considerations about the policy implications of our findings. In light of the traditional emphasis put by decision makers on individual interventions to tackle health inequalities, advocates of neighbourhood effects often claim for greater attention to be paid on area-level interventions. The rationale behind this claim is that an exclusive (or excessive) focus on the individual dimension may implicitly foster a victim-blaming view of the processes leading to social inequalities in health outcomes, neglecting the relevance of structural and institutional forces shaping such health outcomes beyond personal choices and behaviours. Thus, in a situation where health outcomes are significantly affected by material and psychosocial characteristics of the context in which people live, interventions exclusively addressed to the individual dimension are likely to fail to produce desirable results. Area-level interventions, however, should not be considered the cure-all for social and spatial inequalities in health, even when a contextual effect has been proved to exist. Allocating resources to prevent T2DM exclusively to the more underprivileged areas would leave disadvantaged people who reside in non-deprived areas unattended. Effective interventions should encompass the understanding of both individual and neighbourhood pathways linking SES to T2DM (and health outcomes in general). Accordingly, our study should be conceived as a first stage in the examination of the relationship between SES and T2DM in the city of Milan. A necessary next step would be the replication of the study adopting measures of specific neighbourhood characteristics instead of the SES indicator. To date, detailed data of this kind at the census-block (or other neighbourhood definitions) level are not available, and an important work on data collection would be needed. However, having

knowledge of which specific features of the place of living influence T2DM risk would be of great help, allowing to discern if the residence context acts mainly through material or psychosocial pathways and, more deeply, if for instance walkability and green environment play a greater role than healthy food accessibility, or if crime and safety have a stronger influence than social cohesion. As Istat from 2011 census owns individual data about educational level and occupational class, it would be also interesting to replicate the study matching such individual-level SES information with our dataset, limiting the amount of missing data to reach more robust, reliable, and representative estimations. Unfortunately, getting access to Istat's individual census data is not an easy task, and this is the reason why we had to extract individual SES information from healthcare administrative sources. Given the richness of information available from the AHD-ATS databases, it would be interesting to test the models developed here with other disease outcomes, to verify if the association found is limited to the case of T2DM or if instead there is a common outline of spatial inequalities for a wider range of socially-patterned diseases.

Chapter 4

Quality of Care in Type 2 Diabetes Mellitus Patients

Introduction

So far, in this study we have focused on what lies before T2DM, namely on the individual and contextual factors associated with the onset of the disease. Nonetheless, it is interesting to observe what happens after the diagnosis, examining the extent to which different factors, among which personal and neighbourhood socioeconomic characteristics, shape the process of care.

4.1 Background

Good T2DM care is crucial to prevent or delay diabetes-related complications and mortality, and the process of care involves several actors and levels. Thus, through different mechanisms and pathways, some population groups are unequally affected by T2DM, with an increased occurrence of cardiovascular diseases, retinopathy, diabetic foot, as well as any other diabetes-related acute or chronic complication. Differences in T2DM care are present in relation to sex, age, ethnicity/race, and SES. All these aspects may influence diabetes-related knowledge, communication with providers, treatment choices, and the ability to adhere to recommended medication, exercise, and dietary regimes (Brown *et al.*, 2004; Grintsova *et al.*, 2014). Accordingly, social inequalities in T2DM are not limited to the onset of the disease – with a higher prevalence in people of lower socioeconomic profile – being of concern also for what comes next: healthcare and health are worse for T2DM patients of lower socioeconomic conditions compared to the better-off (Espelt *et al.*, 2011). A first review of the existing literature (Ricci-Cabello *et al.*, 2010) in Organization for Economic Co-operation and Development (OECD) countries – all with universal healthcare systems – pointed out the existence of socioeconomic inequalities in the diagnosis and control (measured by clinical variables) of the disease, as well as consistent ethnic inequalities in treatment, metabolic control, and use of healthcare services. A more recent literature review (Grintsova *et al.*, 2014) focused on inequalities in diabetes care in terms of individual SES and residential area deprivation, confirming the existence of both across different healthcare systems. To operationalize and quantify the concept of *quality of care*, most of the existing literature relies on process and outcome indicators (Donabedian, 1988; Mant, 2001). In relation to each health condition, healthcare systems set out specific programs of interventions aiming at monitoring the disease, in order to control its development and prevent further complications. In this sense, *process indicators* measure the implementation of the program (the delivery of assessment), while *outcome indicators* assess if the program goals have been achieved. In the case

of T2DM, the aim of improving medical care producing better health outcomes is pursued by a periodic monitoring of some specific key parameters, such as glycated hemoglobin, BMI, blood pressure, lipid profile, micro-albuminuria, and others. In light of this, process indicators assess the proportion of T2DM patients who actually underwent the measurement of such parameters, while outcome indicators are represented by their quantitative measurement. Both process and outcome indicators are directly related to healthcare provision, though they are also influenced by other factors outside the domain of healthcare, such as individual choices, behaviours, dispositions, and resources of various kind. Consequently, they are not to be intended as indicators exhaustively and exclusively reflecting the level of quality of care, but rather as measures providing information about the intertwinement of individual and institutional factors in shaping T2DM management and compliance to treatment. Moreover, process and outcome indicators provide distinct and complementary information about the overall process of care. The first are a direct measure of the quality of a program, allowing to monitor the activities conducted (e.g. the number of T2DM patients undergoing eye examination over the total of T2DM patients in a year). The latter, instead, refer more specifically to the objective of an intervention and its results, allowing to know if the desired outcome has been achieved (e.g. a reduction in the numbers of diabetic retinopathy diagnosed in the same year).

4.1.2 T2DM Quality of Care Indicators: Glycated Hemoglobin (HbA1c)

The OECD has determined nine diabetes care quality indicators to compare health systems in its member countries (Nicolucci *et al.*, 2006) and the literature clearly suggests that their use improves disease management and reduces related complications and treatment costs (Borgermans *et al.*, 2008; Calsbeek *et al.*, 2013; Glasgow *et al.*, 2008; Gray *et al.*, 2013; Schneiders *et al.*, 2019). Accordingly, within the literature such indicators have been regularly used to evaluate both the performance of the health system in following diabetic patients and the adherence to therapy of the patients themselves. The indicators are split into three areas:

- *Process indicators*: annual HbA1c testing; annual LDL cholesterol testing; annual screening for nephropathy; annual eye examination.
- *Proximal outcomes*: HbA1c values; LDL cholesterol values.
- *Distal outcomes*: lower-extremity amputation rates; kidney disease in persons with diabetes; cardiovascular mortality in patients with diabetes.

However, research is not limited to the indicators suggested by the OECD, and – depending much on what medical records makes available to researchers – diabetes quality of care can be analysed with process and outcome measures considerably differing from the ones proposed by the OECD

framework. Some of the contributes reviewed by Grintsova (2014), for instance, focus additionally on the assessment of blood pressure, BMI, smoking status, and albuminuria as process indicators, and on the quantitative measurement of blood pressure as intermediate outcome indicators. Among such a variety of indicators, one of the most reliable and widely used is the concentration of Glycated Hemoglobin (HbA1c) in blood. HbA1c is a form of hemoglobin linked to sugar through a process of glycation, useful to detect the presence of excessive sugar in bloodstream. Differently from glucose tolerance test, which is sensible to short-term variations mostly deriving from food intake, HbA1c is stable over the course of approximately three months, consequently being a more reliable indicator of glycaemic control and compliance in diabetic patients. A constant HbA1c measurement allows to detect situations of bad diabetes management, where therapeutic goals are being missed. HbA1c is increasingly used as a diagnostic test for T1DM and T2DM, with values equal or above 6.5% (or equivalently 48 mmol/mol) indicating the presence of the disease, whilst higher values (e.g. 7.0%, 7.4%, 7.5%, 8.5%, 9.0%, 10.0%) are commonly used to detect situations of poor control in diabetic patients. HbA1c has been used since the 1980s as a gold standard for monitoring glycaemic control and predicting diabetic complications (Abbas, 2011), with epidemiological analyses showing, for instance, that a 1% decrease in HbA1c value is associated with consistent reductions in risk for any complications and death related to diabetes (Stratton *et al.*, 2000). In line with international standards, Italian diabetes care guidelines suggest to take a HbA1c test at least twice a year (AMD-SID, 2018). Therefore, in diabetes quality of care analysis, HbA1c is useful not only as an outcome indicator – assessing the proportion of patients who achieved target values – but also as a process indicator, assessing the proportion of patients who followed the recommendation of undergoing regular HbA1c controls. Concerning the relation between SES and HbA1c, a review of the literature provided strong evidence that T2DM patients of low SES have higher HbA1c levels than people of high SES, measured by education, income, area-based deprivation, employment status, or other variables, regardless of countries' income levels (Bijlsma-Rutte *et al.*, 2018).

4.1.3 Research Questions

In this section, we aimed at assessing the presence of an association between SES (individual and neighbourhood) and process and outcome indicators of diabetes quality of care in the Milanese T2DM population, answering at the following questions:

1. Are T2DM patients with lower education less likely to follow recommended guidelines and assess their glycaemic status regularly compared to T2DM patients with higher education? Additionally, does the probability of being uncontrolled vary by neighbourhood deprivation, independently of individual SES?

2. Are T2DM patients with lower education less likely to meet blood sugar targets compared to T2DM patients with higher education? Additionally, does the risk of not meeting the targets vary by neighbourhood deprivation, independently of individual SES?

4.2 Methods

As in previous chapter (see section 3.2), we conducted a multilevel population-based case-control study, where the study population is composed by the T2DM population, with patients not fulfilling the recommended guidelines of glycaemic control and glycaemic targets included as 'cases', and those controlling their glycaemic status and reaching Hb1Ac targets included as 'controls'. Multilevel techniques were used to estimate the separate effects of individual and neighbourhood SES on the probability of having good quality of diabetes care.

4.2.1 Study Population

The study was conducted on a subsection of the dataset built querying AHD-ATS databases, presented in the previous chapter (see section 3.2.1). In this section we focused exclusively on individuals identified as T2DM patients (n=67,457). The final models were run including only the population for which data on educational level are present and – consistently with previous analysis – aged between 30 and 83. The final population consisted of 24.872 cases for the process indicator and of 14,893 cases for the outcome indicator analysis.

4.2.2 Measures

Glycaemic Control

As a process measure, T2DM patients were considered 'controlled' if they underwent Hb1Ac test at least twice in the previous 12 months, and considered 'uncontrolled' otherwise.

HbA1c Targets

As an outcome measure, patients were considered in target with HbA1c level if their most recent values were below specific thresholds. Given that within the literature several thresholds are suggested as possible indicators of poor disease management (Bijlsma-Rutte *et al.*, 2018; Grintsova *et al.*, 2014), we opted for considering the achievement of HbA1c targets at different levels: 6.5%; 7.5%; 8.5% (or, equivalently: 48 mmol/mol; 58 mmol/mol; 69 mmol/mol). Patients above the thresholds were considered out of target.

Educational Level, Deprivation Index

Individual and neighbourhood SES measures were identified as described in the previous chapter (see section 3.2.2). Educational level was reported through four ordinal categories, 1) no education, primary education not completed, primary education; 2) lower secondary education; 3) higher

secondary education; 4) tertiary education. The neighbourhood deprivation index was computed summing the standardized scores of the percentage of low-educated, percentage of unemployed, and percentage of foreigners in each census block, subsequently categorizing the continuous variable obtained in quintiles.

Confounders

Sex, age, and citizenships were used as covariates. Additionally, we adjusted the models for three variables, which may play a role in influencing the relationship between SES and quality of care. These are the type of treatment (diet only; oral hypoglycaemic drugs; insulin), the type of diabetes care supplier (general practitioner; diabetes specialist) and the number of diabetes-related comorbidities (zero; one; two; three or more).

4.2.3 Statistical Analysis

The analysis procedure in analogous to the one described in the previous chapter (see section 3.2.3). Given the dichotomous nature of the outcomes selected, we performed several multilevel binary logistic regression random-intercept models. For each outcome, a first empty-model containing no predictors was performed, aimed at evaluating if the probability of being uncontrolled and not meeting HbA1c targets varies from one area to another (Model 1). Subsequently, second models were fitted adding all individual-level covariates (age, sex, citizenship, type of treatment, care supplier, comorbidities, education), to investigate whether these explained area level differences (Model 2). Finally, we added the second-level predictor (deprivation index of the census block of residence), to examine if neighbourhood SES was associated with the process and outcome measures included in the models independently of individual SES (Model 3). The models were estimated with Maximum Likelihood Estimation method using STATA 15 software.

4.3 Results

Table 4.1 shows the composition of the study population according to the process indicator, namely the proportion of T2DM patients who underwent the HbA1c assessment at least twice in the last 12 months. Among the study population (N=24,872), nearly 66% of patients followed the recommended guidelines regarding HbA1c monitoring. However, for 1,518 of them data on Hb1Ac values were missing[27]. Thus, for the outcome indicator (Hb1Ac targets) analyses were carried out on the 14,892 patients for which data were available.

[27] From the AHD-ATS databases was possible to retrieve the number of patients who underwent the Hb1Ac assessment at least twice in the previous 12 months, for whom the ATS requested to the healthcare unit that performed the measurement to communicate the values. Therefore, despite reaching full knowledge about the total number of

Table 4.1: Values and percentages of glycaemic control in the T2DM population aged 30-83 with data on educational level available. Milan, 2018.

		HbA1c Controlled		
		Yes (%)	*No (%)*	*Tot. (%)*
HbA1c Value Present	*Yes (%)*	14,892 (59.87)	-	14,892 (59.87)
	No (%)	1,518 (6.10)	8,462 (34.02)	9,980 (40.13)
	Tot. (%)	16,410 (65.98)	8,462 (34.02)	24,872 (100.00)

Table 4.2 shows the bivariate relationships between the different outcomes and the other variables included in the models. Percentages of uncontrolled patients decrease with age, while HbA1c levels increase moving from the youngest age class (30-39) to the middle one (50-59) – which is the one showing the highest proportion of patients above the thresholds – subsequently decreasing in older age classes. Control was lower in women compared to men, but there were no statistically significant sex differences in HbA1c levels at any threshold. Compared to Italians, foreigners had worse control and higher HbA1c values, except for the 6.5% threshold, for which there was no difference. Consistent differences in glycaemic control were found between patients followed for their T2DM only by their general practitioner (GP) and those who attended at least one specialist consultant, with these last much more likely to follow the guidelines. When considering differences in terms of HbA1c targets, however, the relationship is reversed, with the GP group showing better achievements for the 6.5% and 7.5% thresholds, whilst no significant differences were found for the highest threshold. Not having diabetes-related complications was associated with higher percentages of uncontrolled glycaemic status compared to having one or more of them, with lower percentages in correspondence with more comorbidities. A different picture emerged when looking at HbA1c levels, which are lower in those without comorbidities compared to those with at least one complication only for the 6.5% threshold. Glycaemic control appeared to be worse in patients under diet only treatment, whilst the difference between those treated with insulin and those treated with oral hypoglycaemics was less evident. Again, the relationship was reversed when looking at HbA1c targets, in relation to which lower levels were found among patients in diet only treatment, followed by those in oral hypoglycaemics, and finally by those in insulin therapy, who reported higher probabilities of being out of threshold.

controlled patients, HbA1c values resulted missing for 9.25% of them, due to lack of data communication from some healthcare units.

Table 4.2: Percentages of uncontrolled and not-in-target T2DM patients by sex, age, citizenship, treatment, supplier, comorbidities, educational level, and deprivation index (row percentages).

	Uncontrolled HbA1c	**HbA1c Targets ≥ 6.5%**	**≥ 7.5%**	**≥ 8.5%**
%	34.02	54.28	19.00	6.68
N	8,462	8,084	2,829	995
Denominator	24,872	14,892	14,892	14,892
Age				
30-39	71.51	13.39	7.65	5.74
40-49	59.11	45.49	23.44	13.89
50-59	34.79	58.48	28.64	13.42
60-69	30.09	57.01	20.94	7.47
70-83	28.82	54.78	16.85	4.85
(P-value)	(0.000)	(0.000)	(0.000)	(0.000)
Sex				
Male	30.62	54.33	18.80	6.48
Female	38.17	54.23	19.27	6.96
(P-value)	(0.000)	(0.906)	(0.465)	(0.253)
Citizenship				
Italian	31.55	54.29	18.16	5.90
Foreigner	52.29	54.24	27.58	14.70
(P-value)	(0.000)	(0.975)	(0.000)	(0.000)
Treatment Type				
Diet only	57.55	23.68	6.01	2.50
Oral drugs	24.81	48.54	9.67	2.79
Insulin	26.77	70.21	31.83	11.60
(P-value)	(0.000)	(0.000)	(0.000)	(0.000)
T2DM Care Supplier				
Specialist	18.03	56.72	19.69	6.69
GP	59.83	45.66	16.55	6.64
(P-value)	(0.000)	(0.000)	(0.000)	(0.923)
Comorbidities				
0	51.42	47.52	20.77	9.69
1	32.80	55.51	19.11	6.73
2	27.77	55.92	18.78	5.78
3 or more	23.18	54.66	17.33	5.48
(P-value)	(0.000)	(0.000)	(0.032)	(0.000)
Educational Level				
Tertiary	41.91	46.74	16.24	5.66
Upper-secondary	33.82	51.93	18.19	6.40
Lower-secondary	32.17	56.58	19.50	6.80
Primary	31.73	59.33	21.34	7.63
(P-value)	(0.000)	(0.000)	(0.000)	(0.047)
Deprivation Index				
Very Low	32.40	51.42	17.21	4.83
Low	31.48	51.92	15.77	5.21
Medium	33.87	53.28	17.82	5.27
High	35.15	54.60	19.17	7.12
Very High	35.45	57.61	22.61	9.14
(P-value)	(0.000)	(0.000)	(0.000)	(0.000)

Concerning individual SES, higher percentages of uncontrolled patients were found in correspondence with higher educational level for glycaemic control. Large differences were present between those with tertiary education and those with at most secondary education, while lower down educational levels the values were more similar. When looking at the outcome measure, however, the relationship appeared to be reversed, with out-of-threshold values increasing as educational level decreases in all the indicators. Finally, concerning neighbourhood SES higher percentages of uncontrolled patients in the two most deprived quintiles, as well as slightly increasing Hb1Ac values moving from patients living in less to patients living in more deprived areas were found. Concerning the multilevel analysis, according to the models' diagnostic (Table 4.3), a clear spatial patterning emerges and remains present after the introduction of the deprivation index only for HbA1c control. For all the other indicators, the fact that likelihood ratio tests are never statistically significant in Models 2 and 3 implies a scant spatial heterogeneity of the phenomena inquired, which is not even accounted for by the neighbourhood SES variable[28]. Accordingly, the deprivation index ORs are statistically significant only for the HbA1c control indicator, whereas for the others outcomes the diagnostics suggest that single-level models were preferable to multilevel ones. Hence, in relation to HbA1c targets indicators we performed and presented single-level logistic regression models.

Table 4.3: Multilevel logistic regression models' diagnostics.

		LR (P>chi2)*	**AIC†**	**BIC‡**	**VPC§**	**MOR****
Uncontrolled HbA1c	***Model 1***	0.000	31849.3	31865.5	0.035	1.39
	Model 2	0.000	26152.1	26265.8	0.053	1.50
	Model 3	0.000	26132.1	26278.3	0.051	1.50
HbA1c ≥ 6.5%	***Model 1***	0.022	20535.1	20550.4	0.014	1.23
	Model 2	0.261	18790.9	18897.5	0.005	1.13
	Model 3	0.280	18794.9	18931.8	0.004	1.12
HbA1c ≥ 7.5%	***Model 1***	0.030	14480.7	14495.9	0.020	1.28
	Model 2	0.309	12990.4	13096.9	0.006	1.14
	Model 3	0.366	12978.7	13115.6	0.004	1.12
HbA1c ≥ 8.5%	***Model 1***	0.012	7305.51	7320.73	0.054	1.51
	Model 2	0.137	6580.9	6687.5	0.027	1.38
	Model 3	0.207	6564.8	6701.8	0.020	1.28

* LR (P>chi^2)* = Likelihood Ratio test
† AIC = Akaike Information Criterion
‡ BIC = Bayesian Information Criterion
§ VPC = Variance Partition Coefficient
** MOR = Median Odds Ratio

[28] Additionally, this statement is confirmed by the increasing BIC values from model 2 to model 3, indicating that the addition of the second-level variable does not provide any useful improvement to the model, and that model 2 is preferable.

Table 4.4 shows the results of the final multilevel model for HbA1c control, after the inclusion of all the study variables (Model 3) and of logistic regressions for HbA1c targets.

Table 4.4: Multilevel logistic regression of uncontrolled T2DM patients, Model 3; Logistic regression of not-in-target T2DM patients.

	Uncontrolled HbA1c		**HbA1c Targets**					
			≥ 6.5%		**≥ 7.5%**		**≥ 8.5%**	
	OR	**P***	**OR**	**P***	**OR**	**P***	**OR**	**P***
Age	0.98	0.000	1.00	0.066	0.98	0.000	0.97	0.000
Sex								
Female	1	-	1	-	1	-	1	-
Male	0.92	0.014	0.93	0.063	0.94	0.188	0.96	0.600
Citizenship								
Italian	1	-	1	-	1	-	1	-
Foreigner	1.19	0.001	1.13	0.069	1.34	0.000	1.62	0.000
Treatment Type								
Diet Only	1	-	1	-	1	-	1	-
Oral drugs	0.41	0.000	2.88	0.000	1.99	0.000	1.72	0.001
Insulin	0.54	0.000	7.14	0.000	9.02	0.000	8.36	0.000
T2DM Care Supplier								
Specialist	1	-	1	-	1	-	1	-
GP	5.88	0.000	0.85	0.000	1.09	0.108	1.36	0.000
Comorbidities								
0	1	-	1	-	1	-	1	-
1	0.91	0.049	1.08	0.183	0.88	0.063	0.81	0.040
2	0.86	0.002	1.04	0.507	0.85	0.028	0.73	0.002
3	0.78	0.000	0.91	0.185	0.71	0.000	0.67	0.002
Educational Level								
Tertiary	1	-	1	-	1	-	1	-
Upper-secondary	0.96	0.389	1.09	0.119	1.11	0.189	1.17	0.191
Lower-secondary	1.03	0.531	1.25	0.000	1.18	0.031	1.27	0.045
Primary	1.07	0.253	1.31	0.000	1.31	0.001	1.53	0.001
Deprivation Index								
Very Low	1	-						
Low	1.00	0.962						
Medium	1.19	0.005						
High	1.25	0.000						
Very High	1.24	0.000						

* P = P-value

Age resulted to be inversely associated with all but one indicator (HbA1c ≥ 6.5%), with each additional year of age predicting a slight decrease in the probability of being uncontrolled and not achieving glucose targets. Regarding sex, it appeared to be relevant only for the control indicator, with men showing a lower probability of being uncontrolled for HbA1c than women (OR=0.92). Citizenship was significant in all but one indicator (HbA1c ≥ 6.5%), with higher probability of being uncontrolled and not being in target for foreigners rather than Italians. Opposite yet always

significant results between the control and the target indicators were found in relation to treatment type. Patients in therapy with oral hypoglycaemics or insulin showed a lower probability of being uncontrolled but a higher probability not achieving HbA1c targets as compared to patients in diet-only treatment. Differences were found also in relation to T2DM care supplier, with patients followed only by their GP at noticeable higher probability of being uncontrolled compared to those who attended at least one specialist consultant (OR=5.88), whereas in relation to HbA1c targets results were mixed and not always statistically significant. Similarly, an increasing number of diabetes-related complications was found to be associated with a decreasing probability of being uncontrolled and out-of-target for all but the 6.5% threshold. Coming to individual SES, an educational gradient was present in all the indicators, but the results were not always statistically significant, suggesting a diminished role for educational level in determining T2DM quality of care output when all other variables were accounted for. The contribution of educational level was null in relation to the control indicator, while in relation to HbA1c targets no differences were found between patients with at most upper-secondary and tertiary education in any indicator. However, having at most primary or secondary instead of tertiary education was associated with an increased probability of not achieving the targets. Finally, concerning neighbourhood SES, patients living in areas of the three highest deprivation quintiles had a significantly higher probability of being uncontrolled compared to those living in very low deprivation areas.

4.4 Discussion

Our analysis found mixed evidence for a social and spatial patterning of quality of care in the Milanese T2DM population. Educational level appeared to influence achievement of glucose target levels, but not compliance to blood glucose control. Conversely, neighbourhood deprivation appeared to be relevant only for the latter. Findings in the existing literature are mixed, with the relationship between individual or neighbourhood SES and quality of care indicators depending also on the context studied. Characteristics of the national health system and welfare state arrangements may clearly mediate the relationship between SES and T2DM control and management, whereby countries or regions with a universal healthcare coverage and with more redistributive welfare may mitigate social inequalities in the disease management. On the opposite, differing healthcare and welfare dispositions may leave the relationship unaltered or even reinforce pre-existing inequalities in the care process. In Italy, a study in Turin (Gnavi *et al.*, 2009) reported that elderly individuals and patients with less severe forms of the disease are those less likely properly cared for, and that patients followed by diabetes specialist are more likely to adhere to guidelines than those followed exclusively by their GP. On the other hand, the study found no differences in quality of care by SES and only a very slight advantage among men. Thus, such

findings generally differ from ours, which in relation to the role of sex and age recall conclusions from studies reporting marked sex difference in the process but not in the outcome measures and quality of care improving as age increases (Goyder *et al.*, 2000; Gray *et al.*, 2006; Guthrie *et al.*, 2009a). Concerning SES, quality of care have been demonstrated to vary according to individual deprivation, with stronger association for process rather than for outcome indicators (Goudswaard *et al.*, 2004; McLean *et al.*, 2006), even if much depends on the choice of the indicators and the cut-offs adopted. The literature suggests also an important role of area deprivation in shaping T2DM quality of care (Grintsova *et al.*, 2014; Hippisley-Cox *et al.*, 2004), but such findings are generally influenced by a misuse of area deprivation variables, often fitted in single-level models and/or not accounting for individual SES.

The results reached here led to remarkable considerations about the role of individual characteristics and the healthcare system in the process of care for T2DM patients. Starting from compliance to blood glucose control, the results from the bivariate relationships are somehow counterintuitive. Patients with higher educational achievements showed a higher probability of being uncontrolled as compared to those with lower education, while we would have expected the higher educated having a better control of their disease, in light of a better equipment of health-related resources, among which health literacy. However, when accounting for all the variables together in the same model, a far different picture emerges. The fact that educational level is not statistically significant in multivariate analysis suggests that the association between education and T2DM control is spurious. It is reasonable to assume that the lower educated, having on average worse disease management and worse health, are necessarily more followed by the healthcare system, which exhorts them to have more frequent glucose assessments. Gnavi and colleagues refer to this as a possible 'severity-of-disease effect' (Gnavi *et al.*, 2009). This statement appeared to be supported by the relationship between glucose control and comorbidities, care supplier, and treatment type, respectively. Patients with a higher number of diabetes-related complications are presumably in worse overall health conditions and have worse disease management; however, they are less likely to be uncontrolled, having probably been taken strongly in charge by the healthcare system, due to their more precarious conditions. Similarly, patients who attended at least one specialist consultant are probably in an advanced state of their disease progression compared to those who have been followed by their GP only, but nonetheless they shower higher control. Again, the same pattern is observable in relation to type of treatment, with patients cured without medications being much more uncontrolled than those using oral hypoglycaemics therapy, which are in turn less controlled than those in insulin therapy are. Thus, it seems that in bivariate models educational level embodies information about the progression of the disease, with the most

educated having higher probability of being uncontrolled mainly because they are in better health conditions, and vice-versa. Being on average less likely to be in medication treatment, to have been visited by a specialist, or to have one or more comorbidities as compared to the least educated (see Tables A4.1, A4.2, and A4.3 in the appendix), the higher educated are consequently also less likely to be have been taken intensively in charge by the healthcare system, and so to be 'forced' to have their blood glucose monitored more frequently. Indeed, the multivariate analyses suggest two things. First, when the effect of treatment type, type of care supplier and diabetes-related complications is accounted for, educational level restores its typical gradient in favour of the most educated. Second, the fact that this gradient is not statistically significant implies that systemic features appear to be more important than individual characteristics in shaping the probability of being uncontrolled. Accordingly, this aspect of T2DM quality of care appears to be strictly dependent on the efficacy of the healthcare system rather than on personal characteristics. An effective healthcare system should be able to 'push' its patients to undergo the recommended assessment beyond their socioeconomic profile, and this is what it seems to happen in the case of Milan. The social gradient in blood glucose control vanish when systemic variables are accounted for, meaning that, in our specific case, we face a system that is able to let social inequalities disappear when considering this process indicator. Differently from the onset of the disease – for which educational level is strongly associated with a higher probability of developing T2DM (see Chapter 3) – among individuals already diagnosed with T2DM, socioeconomic profile does not seem to be relevant in shaping the probability of being uncontrolled and consequently having higher chances of bad management. However, despite the apparent absence of social obstacles, the healthcare system seems to face some ethnic and geographical barriers. Concerning the first, it is clear that the individual factor most strongly associated with less control is citizenship, with healthcare system probably not able to communicate, spread information, and 'push' foreigners to glucose control as it effectively does with Italians. This may be due to language barriers, as well as to lack of knowledge about how the healthcare system works and what services it offers (Henderson and Kendall, 2011). About the second, a gradient was found for neighbourhood SES in HbA1c control, implying that despite effectively carrying disadvantaged patients to fulfil control guidelines, the healthcare system still finds problematic to reach patients living in medium, high, and very high deprivation areas, compared to those living in better-off neighbourhoods. However, reasons for this evidence remain unclear. If this was an additional burden of socially disadvantaged people living in deprived areas (the previously mentioned 'double jeopardy'), we should have found a significant effect for educational level too. The presence of a spatial but not of a social effect in HbA1c control suggests that the mechanisms involved could be related to the

geographical location itself rather than to social characteristics of the place of living. For instance, knowing that more deprived areas are generally less strategically located in proximity of health services (Dussault and Franceschini, 2006; Jordan *et al.*, 2004; Rosenthal *et al.*, 2005), we may speculate that individuals living in such areas could be less prone to check HbA1c because of the distance from clinics or facilities where the assessment takes place, independently of their socioeconomic profile. However, in absence of data confirming this, it remains a conjecture. So far, we have focused on the control indicator. Concerning the outcome indicators, that is the achievement of different HbA1c targets, the overall picture is quite different. Differently from the case of control indicators, for which in multivariate models educational level was never statistically significant, here education matters to some extent. Having primary or lower-secondary education instead of tertiary education is associated with higher risk of being out of target at any threshold, with the three indicators referring to the progression of the disease not accounting for all the variability in the outcome. Regarding these, contrary to what we saw for glucose control, those in medication therapy show worse outcomes compared to patients in diet only therapy. The difference between patients followed by their GP only and those who attended at least one specialist consultant is not considerable as before, for the 7.5% threshold is not significant and for the 6.5% one, the relationship is reversed. The presence and number of diabetes-related complications follows the same pattern, though not being statistically significant in relation to the lower threshold. Finally, differently from the case of HbA1c control, the achievement of glucose targets did not seemed to be subjected to geographical variability. On an overall comparison, it emerges that compliance to HbA1c control and target levels are two phenomena with different structure and influenced by distinct elements and processes. HbA1c assessment appeared to have a strong systemic component, with the healthcare system presumably able to intervene and persuade patients to keep their glucose level controlled. On the contrary, for those who underwent the measurement, the achievement of the recommended targets is less influenced by external factor, and more dependent by individual ones. This double dynamic highlights strengths and limits of the process of care for T2DM patients. On the one hand, we find an effective system, capable to limit social inequalities in adherence to periodic monitoring, which is crucial to ensure a better disease management. Moreover, the system seems to be more effective with those having troubles with their disease progression, following them more intensively and ensuring that the recommended control guidelines are met. On the other hand, the fact that, in relation to the outcome indicators educational level 'recovers' its role in shaping treatment compliance, is a signal that the healthcare system alone is not able to tackle social inequalities in T2DM management. Processes and mechanisms involved in adherence to T2DM therapy are deeply rooted in individual

socioeconomic background. This means that the availability of social, economic, cultural, and relational resources is a key factor in determining good disease management and compliance, even among a population that is effectively supported by the healthcare system. This implies that investing on the process of care without addressing the fundamentals factors shaping individuals' capability to adhere to recommended guidelines would act merely as a palliative, failing in breaking the perpetuation of social inequalities in T2DM care.

This study is subjected to some limitations. First, the cross-sectional nature of the data used prevents us from talking about causation. While some indicators are logically consequent to others (HbA1c, which may be fluctuant, cannot predict educational level, which is acquired in early adulthood), others are not. Specifically, treatment type, type of T2DM care supplier, and the number of diabetes-related complications may be both influence and be influenced by blood sugar levels, in the way in which an increase in HbA1c levels may induce a change of therapy, the recourse to diabetes specialists, and also trigger one or more comorbidities. To properly assess the direction of association between the variables, longitudinal data would be necessary. Second, as already discussed in section 3.5.2, missing data for educational level variable may have altered the results. However, we saw that the distribution of the variable in the final population resembles the one provided by Istat for the same period, suggesting the possibility to perform complete case analysis without worrying bias. Some data were missing also in relation to HbA1c levels, but we have no means to check for the existence a selection bias.

The study has nonetheless several strengths. First, we were able to perform analyses with both process and outcome indicators, which refers to different aspects of quality of care, as the contrasting resulted confirmed. Moreover, these data were from high-quality administrative sources. Second, we adjusted our models for three indicators than may reasonably be influenced by individual SES. Thus, including in the analyses treatment type, the type of T2DM care supplier, and the number of comorbidities may have led to over-adjustment, with the consequence that the real association between educational level and HbA1c targets could be even stronger than the one reported.

Conclusion

In this section, we examined the association between individual and neighbourhood SES and quality of care in T2DM patients. Following the existing literature, we relied both on process and on outcome indicators, representing the implementation of a program and the achievement of the program goals, respectively. Our process measure was the fulfilment of recommended guidelines, suggesting T2DM patients to undergo HbA1c measurement at least twice a year. Our outcome measure was the achievement of specific HbA1c levels commonly identified as thresholds

indicating the overall degree of disease management and adherence to therapy. Our analyses found that glucose control (process measure) was significantly associated with neighbourhood but not individuals SES, while contrarily the achievement of HbA1c targets (outcome measure) was significantly associated with individual but now neighbourhood SES. The two phenomena appeared to be driven by different factors, with the first having to deal largely with the healthcare system, which in our case seemed to be able to overcome the effect of individual factors, inducing patients to undergo HbA1c measurement independently of their educational level. Conversely, the achievement of blood glucose targets resulted less dependent on systemic features, but instead socially patterned. This suggested that on one side, the Italian universal healthcare system, with his 'aggressive' approach on patients with severe disease, is effective in making people adhere to care programs without distinctions due to social class belonging, but one the other side that the overcoming of socioeconomic inequalities in the process of care is only apparent. While HbA1c monitoring is a one-time event that patients can comply easily, the maintenance of long-term blood glucose under a certain threshold is a demanding task that may require considerable efforts to patients, specifically to those with less health literacy and support. Accordingly, the structure of social inequalities contributing to the onset of the disease, once partially hidden, re-emerges in relation to disease management and development, with people of different socioeconomic profile being differently able to comply with therapy and adhere to recommendations. The results reached have relevant policy implications, suggesting that healthcare interventions and programs alone could rarely be able to solve the issue of differential and unequal disease management among patients with different degree of social disadvantage. Without addressing the roots of inequalities, every intervention would be only temporary and partially effective, with uneven outcomes resurfacing again, or emerging in different ways. In UK, and later in other countries, pay-for-performance programs have been implemented, rewarding health-care providers by paying them more if they succeed in meeting performance targets. These have been quite extensively applied to T2DM (and T1DM) patients, reporting mixed results, ranging from an increased achievement of targets (Vaghela *et al.*, 2009) to an irrelevant contribution to the improvement of blood sugar control (Coleman *et al.*, 2007). Moreover, such programs have also been reported to work on several ethnic groups, but without addressing ethnic disparities, thus potentially widening existing inequalities in care (Millet *et al.*, 2007; 2009). Despite the effectiveness of such programs, we believe that these fail in identifying the mechanisms on which is necessary to work to reduce the gap in T2DM care. Identifying practitioners as those primarily in charge of patients' compliance and disease management – and paying them progressively according to patients' achievements – shifts away the responsibility from the overall system (both the healthcare and the more

comprehensive intuitional asset) to individuals, also neglecting to actively involve the patient in the process of care. Our beliefs is that improving health literacy and empowering patients, together with actions aimed at tackling the root causes of health inequalities, would be a more effective (and efficient in the long run) strategy to break the gradient in T2DM management and compliance.

Conclusion

In this PhD thesis, we adopted a multidisciplinary approach to study health inequalities, focusing on the specific case of Type 2 Diabetes Mellitus in the city of Milan. Though the boundaries are not so well defined, we made large use of sociological concepts and theories together with methods and techniques mostly deriving from epidemiology and geography. Our research has moved from the will (and the need) to study the social and spatial distribution of a disease within the Milanese territory. A fine-grained mapping of health conditions among the neighbourhoods composing the city was missing, and Type 2 Diabetes Mellitus represented an extremely interesting case study, considering its typical association with both individual socioeconomic conditions (Agardh *et al.*, 2011) and environmental characteristics (den Braver *et al.*, 2018). Indeed, the disease proved to be heterogeneously distributed within the city, with the socioeconomic profile of its inhabitants not accounting for all the variability detected. A significant share of the uneven presence of diabetic patients among neighbourhoods was found to be attributable to area socioeconomic status, independently of the composition of such areas. This highlighted the double disadvantage experienced by people living in deprived conditions, whose risk profile is not shaped only by their individual attributes (age, sex, citizenship, educational achievement or socioeconomic status in general), but also by the exposure to environmental features of the context in which they live (Macintyre and Ellaway, 2003). Relying on the existing literature, we postulated that the residence context might influence individual risk exposure both through material and psychosocial pathways. Regarding the first, we described how the physical structure of the living place (e.g., lack of transportations, green and recreational spaces, supermarkets, walkable pathways, etc.) could mediate, for instance, the access to health services, the provision of healthy food, and the possibility to practice physical activity. These may in turn expose people to higher risk of being overweight/obese, to follow an unbalanced diet or an unhealthy lifestyle, increasing the possibility of developing Type 2 Diabetes Mellitus. Concerning the latter, the area of residence may intervene through less tangible, but nonetheless important pathways. Deprived areas (e.g. with crime, pollution, noise, etc.) may foster sense of unsafety, inducing people not to go out of home if avoidable, again mediating the relation between lifestyles and the risk of developing the disease. Nevertheless, area deprivation may shape risk exposure not only through indirect mechanisms, influencing lifestyles, as well as constraining choices and behaviours, but also through direct pathways, given the capacity of psychosocial stressor of altering biological functions of the body, influencing for instance the production of insulin (McEwen and Wingfield, 2003; Stockdale *et al.*, 2007). Thus, our findings highlight the importance of social and spatial structure in determining

health conditions, providing additional empirical evidence in support of the predominance of a social causation perspective in the explanation of health inequalities. A clear role for social structure emerged, even in relation to a disease that is strongly determined by individual behaviours. This supports the idea that an ontological perspective of methodological individualism, involving the preponderance of selective pathways in the genesis of social inequalities in health, should be overcome. Beyond the specific case study analysed, our research surely contributed to the debate about the presence of neighbourhood effects in health. Coherently with the literature, we found that compositional explanations play a major role in shaping the heterogeneous distribution of Type 2 Diabetes Mellitus in Milan, but also that the impact of the context is not negligible (Pickett and Pearl, 2001). Related to this issue, we have reasons to believe that the attempts to disentangle compositional and contextual effects should move beyond the solely quantitative assessment of variance at each level of analysis after accounting for individual and contextual socioeconomic measures. The circularity between personal and environmental characteristics makes it impossible to completely isolate the relative contribution of each one in purely statistical terms (Macintyre and Ellaway, 2003). We suggest that to obtain deeper knowledge about the extent to which area characteristics could influence health, other methods should be implemented in support of multilevel analysis. For instance, though not allowing a quantification of the phenomenon, qualitative interviews or focus groups with patients and health professionals may enable to let emerge the mechanisms bringing individuals, their socioeconomic conditions, and the place where they live to interact with each other and influence health outcomes. However, the issue is not just the one of mixing different methods of analysis. Sticking to quantitative methods, gathering precise data about the distribution of services, amenities, as well as about geographic characteristics of the area, and analysing them in relation to the distribution of disease outcomes within the area itself, may provide clues about what specific features of the local environment affect health status.

An additional value of our work is that we implemented a methodology involving the joint use of healthcare administrative geo-referenced data and census data, obtaining measures of disease presence and socioeconomic status at distinct levels. This has no precedent in the Milanese case and, despite the procedure is consolidated in the international literature, its application in the Italian context is limited. Once the method is established, nothing prevents us or other researchers from adopting it in relation to other outcomes or socioeconomic status measures, to obtain a mapping of health conditions in the territory not limited to one disease and testing the presence of social and spatial inequalities in relation to health in a systematic way.

Our research has focused also on the management of Type 2 Diabetes Mellitus, evaluating both

the adherence to recommended guidelines in relation to blood glucose assessment and the levels of glycated haemoglobin – a marker of compliance to therapy – in the Milanese diabetic population. The first appeared to be slightly influenced by patients' area of residence, but not by their own socioeconomic status, while conversely the latter showed no significant territorial variability but a slight individual socioeconomic status dependency. Despite some patterns emerged, these phenomena appeared to be in general less socially and spatially structured compared to the onset of the disease, with an emerging role of the healthcare system in mitigating social inequalities existing at the onset of the disease to some extent. However, there is also evidence that the healthcare system alone is not able to effectively tackle such inequalities. This leads us to the last point we want to discuss, relative to the policy implications of the work presented. If one thing is clear is that interventions to prevent Type 2 Diabetes Mellitus from increasing and to tackle social inequalities in its distribution should go beyond the excessive focus on individually-based risk factors, encompassing important structural changes in the society and the urban setting in which people are embedded. Our consideration here is referred to the disease we studied, but the argument may be extended for other diseases with similar risk profiles. It may seem utopistic, but without a critical rethinking of the relations between governments, market, individuals and societies, any intervention aimed at preventing the disease and the amount of inequity and injustice related to it would be only a palliative, destined to fail in addressing the key factors involved in the process. If policies are designed to foster people's possibilities of conducting a healthy lifestyle, but at the same time some heavy structural constraints exist and limit their choices, or worse, induce them to pursue detrimental behaviours, it is clear that interventions can work only partially, at best. More than once throughout this work we highlighted how the forces of globalization and urbanization have had a critical role in reshaping risk exposure for several non-communicable disease in the latest decades (Lake and Townshend, 2006; Popkin, 1999). If on one hand they both had sure a great impact in improving overall levels of life-expectancy and quality of life, on the other hand their 'dark sides' have increasingly put at higher disease risk some individuals and groups that would not have been so otherwise. Thus, if policy interventions to subvert globalization would be clearly unfeasible, intervening on the urban environment, instead, could be a walkable way. Moreover, we would like to highlight the need to support such local-level actions with national-level policies aimed at contrasting the development of social inequalities at their birth. We believe that a more equitable system is possible, granting everyone access to and achievement of higher education, supporting the more disadvantaged with redistributive policies, while tackling the neoliberal drift that is widening current inequalities putting the interests of corporations before the ones of citizens. While we write, in Italy politics

are approving the so-called ‘sugar tax’ (better known worldwide as ‘soda tax’), a surcharge conceived to reduce the consumption of drinks with added sugar, which are among the responsible of the steep increase in overweight and obesity rates, leading to Type 2 Diabetes Mellitus (Gostin, 2017). We have no means to judge if it could be a potentially working policy or if it will just represent a further tax on the most deprived, who may keep their sugar drinks consumption levels, but a higher cost. What is clear, however, is that interventions of this kind will hardly be effective if left alone. Our belief is that providing people the instruments to make informed choices, heightening their health literacy and empowering them, to enable individuals to gain control over decisions and actions affecting their health, could be the only long-standing viable strategy to tackle the growth of the disease and the social inequalities accompanying it. However, individual level policies aimed at increasing educational attainment and redistributing resources are likely not be effective if not accompanied by environmental interventions improving the food environment and the physical activity environment. Moreover, redistributive policies may be implemented also at this level, distributing the burden of harmful environmental conditions more proportionally on the territory, pursuing *environmental justice* (Taylor *et al.*, 2006). Nonetheless, the higher level should not be neglected. An effective action to tackle Type 2 Diabetes Mellitus (but also many other diseases sharing similar risk profiles) prevalence and inequalities is not possible without a critical rethinking of the engine of economic development. As long as corporations, market, and profit will be the only driving forces of growth, all the efforts would be made just to address the symptoms, and not the fundamental causes, of health inequalities.

Appendix

Appendix Chapter 2

Table A2.1: Secular trends of crude and standardised diabetes and of overweight/obesity prevalence in Italian men aged 20 years or over by age, area of residence and educational level. Source: Gnavi et al. (2018)

Men	1980	1983	1987	1990	1994	2000	2005	2013	Variation (1980-2013%)
Diabetes									
Number	626,651	783,767	677,508	667,389	883,300	1,030,934	1,209,863	1,647,353	+162
Crude prevalence	3.3	4.0	3.4	3.2	4.2	4.7	5.4	7.1	+115
STD Prevalence	3.8	4.4	4.1	3.9	4.9	5.2	5.7	6.8	+79
Age									
20-49	1.1	1.2	0.8	0.8	0.9	1.0	1.0	1.2	+9
50-64	5.4	6.3	5.0	5.5	6.1	7.5	7.7	8.8	+63
≥ 65	7.7	10	10.3	9.1	12.6	12.5	14.6	18.1	+135
Education									
High-std	3.9	4.6	3.7	3.6	4.3	5.1	5.0	5.6	+44
Medium-std	5.7	4.9	4.6	4.4	5.0	4.9	5.8	7.2	+26
Low-std	3.6	4.4	4.1	4.4	5.4	5.8	6.7	8.5	+136
Area									
North-std	3.4	3.9	3.6	3.7	4.5	4.7	5.1	6.4	+88
Centre-std	3.9	5.0	4.3	4.1	5.1	5.1	5.8	6.7	+72
South-std	4.1	4.7	4.6	4.0	5.4	5.9	6.6	7.5	+83
Overweight/obesity									
STD Prevalence	n.a.	43.6	n.a.	45	49	51.6	53.7	53.7	+23

Table A2.2: Secular trends of crude and standardised diabetes and of overweight/obesity prevalence in Italian women aged 20 years or over by age, area of residence and educational level. Source: Gnavi et al. (2018).

Women	1980	1983	1987	1990	1994	2000	2005	2013	Variation (1980-2013%)
Diabetes									
Number	974,412	1,066,661	967,382	938,755	1,191,386	1,254,714	1,375,729	1,746,686	+79
Crude prevalence	4.7	5.0	4.4	4.2	5.2	5.3	5.6	6.8	+45
STD Prevalence	5.0	5.2	4.7	4.5	5.3	5.1	5.2	5.8	+14
Age									
20-49	1.1	1.0	0.7	0.5	0.7	0.8	0.8	1.4	+27
50-64	6.1	6.9	5.5	5.7	6.8	5.9	6.1	5.9	-3
≥ 65	12.6	13.0	13.3	11.9	14.2	14.0	14.5	16.7	+33
Education									
High-std	1.9	2.2	4.3	2.6	3.2	2.8	3.7	3.6	+89
Medium-std	3.6	3.1	3.9	2.9	3.6	3.5	4.4	5.8	+61
Low-std	5.2	5.7	4.9	5.0	6.2	5.9	6.0	7.8	+50
Area									
North-std	4.0	4.4	4.0	3.5	4.2	4.5	4.1	5.0	+25
Centre-std	5.0	4.8	4.8	4.5	5.2	4.7	5.3	5.6	+12
South-std	6.5	6.7	5.8	6.0	6.9	6.1	6.7	7.2	+10
Overweight/obesity									
STD Prevalence	n.a.	30.5	n.a.	29.1	31.7	33.3	35.2	34.4	+13

Table A2.3: Diabetes prevalence for different Regions and areas in men and women (30-83 years) in Italy, 2013. Source: Our elaboration of Istat Health Conditions and Use of Health Services survey data.

Area	Region	Men	Women	Men & Women
North	Piedmont	8.4	6.6	7.5
	Aosta Valley	6.7	5.4	6.0
	Lombardy	7.6	6.3	6.9
	Trentino-South Tyrol	5.2	4.9	5.0
	Veneto	6.6	5.4	6.0
	Friuli-Venezia Giulia	9.0	6.3	7.6
	Liguria	7.2	5.5	6.3
	Emilia-Romagna	6.9	5.4	6.1
Centre	Tuscany	7.0	6.6	6.8
	Umbria	8.9	6.6	7.7
	Marche	7.1	5.4	6.2
	Lazio	7.8	7.6	7.7
South	Abruzzo	9.2	7.6	8.4
	Molise	7.6	8.9	8.3
	Campania	7.6	8.0	7.8
	Apulia	8.8	8.9	8.9
	Basilicata	9.5	8.6	9.0
	Calabria	9.4	9.6	9.5
Island	Sicily	8.7	8.0	8.3
	Sardinia	7.1	8.0	7.6

Table A2.4: BMI by area of residence in men and women (30-83 years) in Italy, 2013. Source: Our elaboration of Istat Health Conditions and Use of Health Services survey data.

	BMI	North	Centre	South and Islands	Total
Men	Normal/underweight	42.2	40.9	35.3	39.7
	Overweight	45.0	46.0	49.0	46.5
	Obesity	12.8	13.1	15.7	13.8
Women	Normal/underweight	61.9	60.5	54.0	59.0
	Overweight	27.5	28.2	32.7	29.4
	Obesity	10.6	11.3	13.3	11.6

Table A2.5: Light, moderate, and vigorous intensity physical activity (percentages of those reporting 'yes' to each item) by area of residence in men and women (30-83 years) in Italy, 2013. Note Source: Our elaboration of Istat Health Conditions and Use of Health Services survey data.

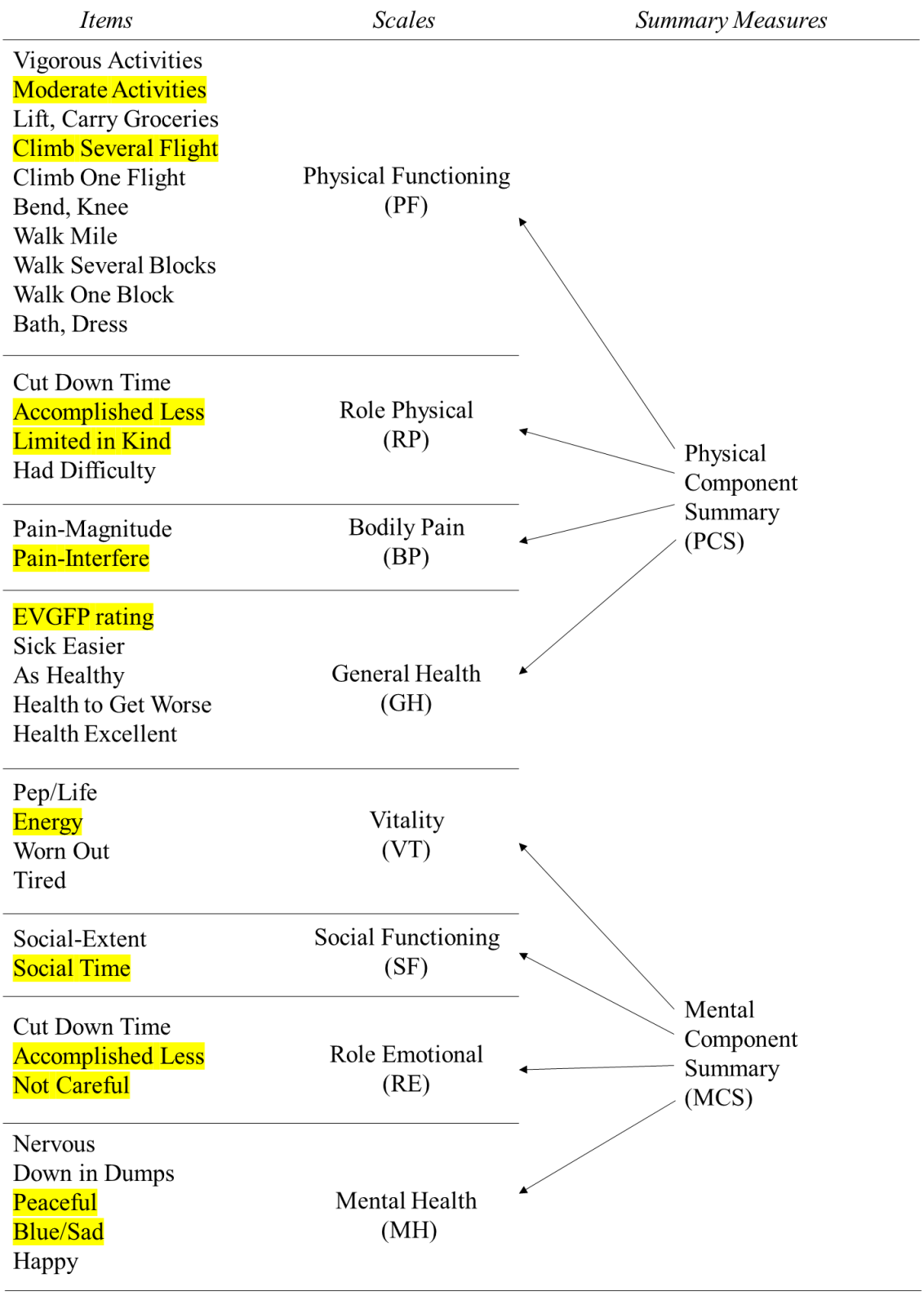
	Physical activity	North	Centre	South and Islands
Men	Light intensity	42.1	38.7	30.0
	Moderate intensity	26.3	21.1	14.7
	Vigorous intensity	14.7	12.8	8.4
Women	Light intensity	45.6	40.1	26.3
	Moderate intensity	20.2	16.0	8.7
	Vigorous intensity	6.0	5.3	2.9

Table A2.6: Models of logistic regression, probability of reporting diabetes by education, age citizenship and area of residence in men and women (30-83 years) in Italy, 2013. Men N = 38.687; Women N = 42.563. Source: Our elaboration of Istat Health Conditions and Use of Health Services survey data.

	Men		Women	
	Odds Ratio	95% C.I.	Odds Ratio	95% C.I.
Age	1.07***	1.07 - 1.07	1.06***	1.06 - 1.06
Citizenship				
Italian	1.00	- -	1.00	- -
Foreigner	1.36**	1.10 - 1.68	1.48***	1.21 - 1.81
Area of residence				
North	1.00	- -	1.00	- -
Centre	1.04	0.94 - 1.16	1.24***	1.11 - 1.38
South and islands	1.20***	1.10 - 1.31	1.52***	1.39 - 1.66
Education				
Tertiary	1.00	- -	1.00	- -
Upper secondary	1.21*	1.02 - 1.42	1.22	0.99 - 1.50
Lower secondary	1.63***	1.39 - 1.91	1.92***	1.57 - 2.35
Primary	1.61***	1.37 - 1.90	2.63***	2.15 - 3.22

* P-value ≤0.050; ** P-value ≤0.010; *** P-value ≤0.001

Table A2.7: SF-36 and SF-12 (highlighted) items, scales and summary measures. Source: Ware et al., 1996.



Appendix Chapter 3

Figure A3.1: Administrative divisions of the city of Milan.

Figure A3.2: NIL division with neighbourhoods' names.

Table A3.1: Summary statistics of deprivation measures. Source: our elaboration of Istat 2011 census data (Istat, 2011).

	Mean	Standard Deviation	Min.	Max.
Percentage of low-educated persons	21.03	11.47	0	100
Percentage of unemployed persons	6.93	6.61	0	100
Percentage of foreign persons	19.92	13.71	0	100
Deprivation Index	0.00	2.06	-3.90	18.52

Table A3.2: Indicators of deprivation and deprivation index by neighbourhood (NIL). Source: our elaboration of Istat 2011 census data (Istat, 2011).

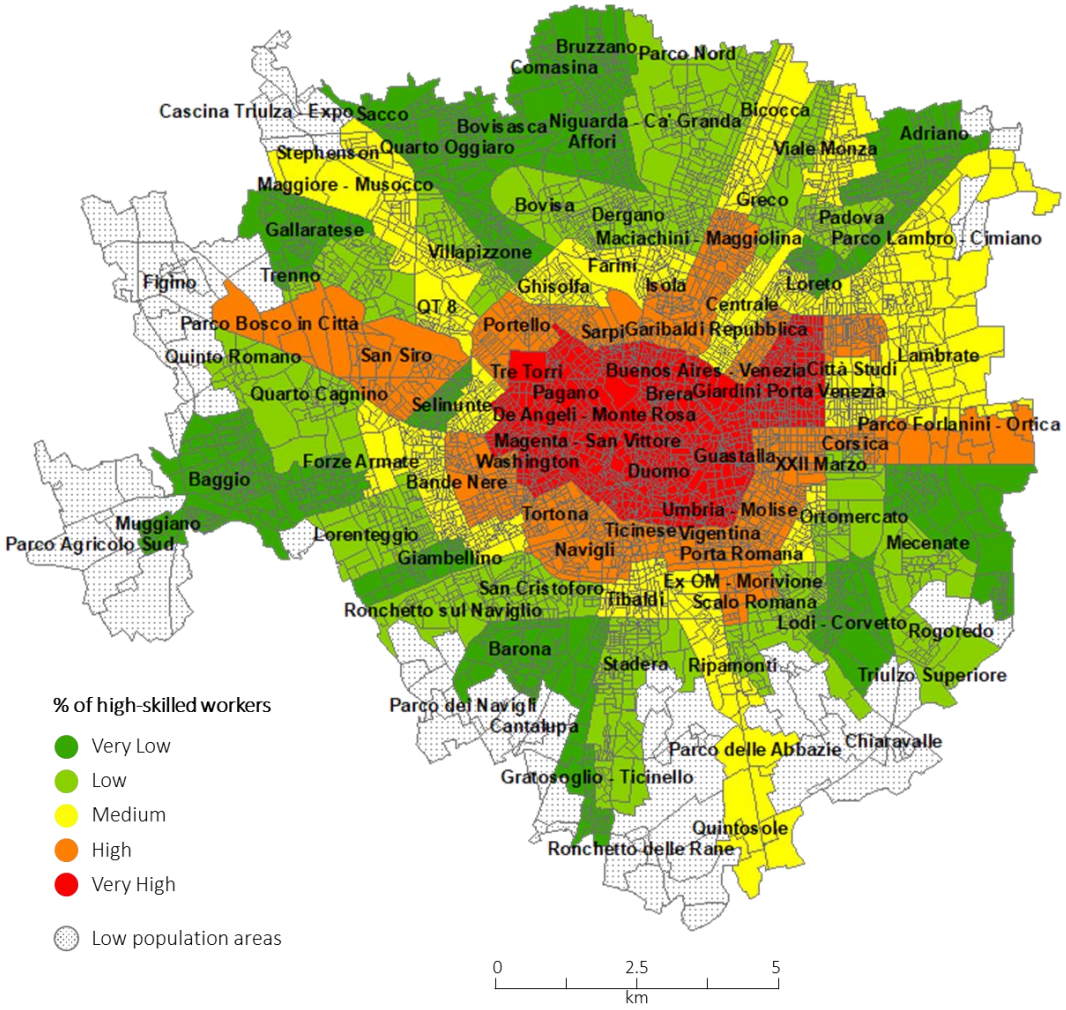
Neighbourhood (NIL)	A *	B †	C ‡	D §	Population	Pop./km^2
Adriano	24.9	6.9	14.8	0.4	13,170	5,353
Affori	24.4	7.0	22.2	0.9	21,224	10,249
Baggio	30.4	8.4	12.9	1.0	28,028	8,085
Bande Nere	18.6	5.5	10.5	-0.7	40,646	15,259
Barona	28.3	11.3	9.1	0.9	16,467	8,208
Bicocca	20.1	8.6	12.8	0.1	6,393	4,113
Bovisa	23.6	6.5	27.4	1.1	11,202	5,855
Bovisasca	26.4	9.1	11.1	0.6	7,039	4,465
Brera	12.7	5.2	12.1	-1.1	16,656	10,172
Bruzzano	25.8	8.1	13.3	0.6	11,440	6,861
Buenos Aires - Venezia	15.9	5.5	9.6	-1.0	57,087	19,839
Cantalupa	16.2	3.8	16.6	-0.7	425	459
Cascina Triulza - Expo	30.0	7.5	1.0	-0.1	249	144
Centrale	14.8	5.6	16.1	-0.6	15,711	10,097
Chiaravalle	23.5	11.1	13.1	0.8	1,031	3,289
Città Studi	17.5	6.0	10.7	-0.7	34,221	15,503
Comasina	29.8	8.3	22.7	1.6	8,749	9,440
Corsica	16.1	5.9	12.8	-0.7	17,815	16,475
De Angeli - Monte Rosa	15.2	4.3	8.9	-1.3	19,119	14,451
Dergano	23.2	7.1	26.6	1.1	19,159	14,102
Duomo	12.7	3.9	11.1	-1.4	15,556	6,643
Ex OM - Morivione	26.1	6.5	13.1	0.3	7,255	8,870
Farini	19.2	5.8	26.1	0.6	3,269	3,236
Figino	36.1	7.4	5.8	0.8	1,600	1,123
Forze Armate	27.5	8.3	13.2	0.7	22,159	6,902
Gallaratese	29.3	7.8	6.5	0.3	31,851	8,210
Garibaldi Repubblica	15.5	6.5	10.3	-0.8	4,911	6,251
Ghisolfa	18.8	5.4	13.0	-0.5	15,946	15,079
Giambellino	23.6	9.0	19.8	1.0	28,703	14,579
Giardini Porta Venezia	23.3	4.5	18.5	0.2	54	216
Gratosoglio - Ticinello	31.3	11.8	10.2	1.3	17,599	5,320
Greco	21.3	6.4	19.8	0.4	13,766	7,874
Guastalla	12.6	4.2	11.1	-1.4	14,028	9,062
Isola	19.6	6.5	13.5	-0.2	20,236	15,297
Lambrate	22.1	6.0	20.7	0.4	9,359	3,027
Lodi - Corvetto	24.2	8.4	20.3	1.0	32,482	8,926
Lorenteggio	22.8	11.2	9.0	0.4	12,559	4,733
Loreto	20.0	7.2	24.4	0.7	37,253	21,318
Maciachini - Maggiolina	17.0	5.7	12.8	-0.6	23,928	14,286

Magenta - San Vittore	14.9	4.4	10.8	-1.1	16,242	11,684
Maggiore - Musocco	22.6	4.4	12.8	-0.3	4,530	1,486
Mecenate	23.9	7.3	11.5	0.1	17,876	4,670
Muggiano	28.2	4.0	6.0	-0.4	2,803	6,310
Navigli	18.1	7.0	10.8	-0.5	15,631	10,534
Niguarda - Ca' Granda	25.7	9.1	10.7	0.5	34,545	8,126
Ortomercato	29.4	8.2	22.2	1.5	3,584	2,555
Padova	24.6	7.0	24.4	1.1	31,518	15,286
Pagano	14.6	4.2	8.2	-1.4	15,960	12,375
Parco Agricolo Sud	46.6	21.9	16.2	4.7	267	45
Parco Bosco in Città	30.8	9.8	34.1	2.7	534	68
Parco dei Navigli	22.6	13.1	13.3	1.0	274	76
Parco delle Abbazie	27.0	6.4	23.4	1.1	382	28
Parco Forlanini - Ortica	26.6	6.4	20.8	0.9	779	270
Parco Lambro - Cimiano	22.8	6.6	14.5	0.1	18,689	3,765
Parco Monlué - Ponte Lambro	30.2	11.8	25.3	2.3	4,075	1,537
Parco Nord	22.7	10.0	17.7	0.9	97	63
Parco Sempione	50.0	0.0	0.0	0.5	3	6
Porta Romana	17.0	4.8	8.6	-1.1	15,526	15,483
Portello	13.7	5.4	6.6	-1.4	7,328	8,056
QT 8	19.1	6.2	6.0	-0.9	3,879	3,787
Quarto Cagnino	21.0	6.9	7.8	-0.4	9,125	9,251
Quarto Oggiaro	34.7	12.7	17.1	2.3	29,401	10,583
Quinto Romano	32.6	7.8	6.7	0.6	4,722	2,869
Quintosole	25.4	8.3	30.2	1.8	1,284	1,203
Ripamonti	19.4	5.8	9.3	-0.6	12,612	6,806
Rogoredo	21.5	5.6	14.3	-0.1	8,321	6,973
Ronchetto delle Rane	31.7	9.6	16.0	1.5	740	3,918
Ronchetto sul Naviglio	24.8	10.3	11.2	0.6	13,917	5,779
Sacco	20.5	35.2	5.8	3.6	246	347
San Cristoforo	23.6	8.0	12.7	0.3	12,070	7,562
San Siro	17.5	5.6	14.2	-0.5	11,739	3,417
Sarpi	17.8	5.4	13.1	-0.6	27,090	15,001
Scalo Romana	25.5	11.2	25.0	1.8	9,354	5,386
Selinunte	24.5	8.5	22.6	1.2	22,871	23,222
Stadera	24.7	8.7	14.7	0.6	26,777	8,272
Stephenson	21.5	2.8	15.8	-0.4	52	93
Tibaldi	20.0	7.2	13.6	-0.1	10,701	13,611
Ticinese	16.7	6.9	8.3	-0.8	18,524	14,760
Tortona	16.7	5.4	7.4	-1.1	14,229	14,275
Tre Torri	11.8	4.5	10.8	-1.4	1,226	2,388
Trenno	22.1	8.9	4.3	-0.3	4,104	8,381
Triulzo Superiore	28.0	8.3	39.1	2.6	1,266	930
Umbria - Molise	20.9	7.4	14.9	0.1	20,674	17,339
Viale Monza	23.3	6.8	16.9	0.4	25,434	8,463
Vigentina	15.6	4.7	8.5	-1.2	12,563	11,067
Villapizzone	24.2	8.9	22.4	1.2	35,752	10,433
Washington	15.5	4.4	8.1	-1.3	25,120	19,228
XXII Marzo	17.0	5.4	7.5	-1.0	29,342	17,919
Tot.	**21.0**	**6.9**	**13.9**	**0.10**	**1,242,123**	**6,837**

[*] A = Percentage of low-educated persons [†] B = Percentage of unemployed persons

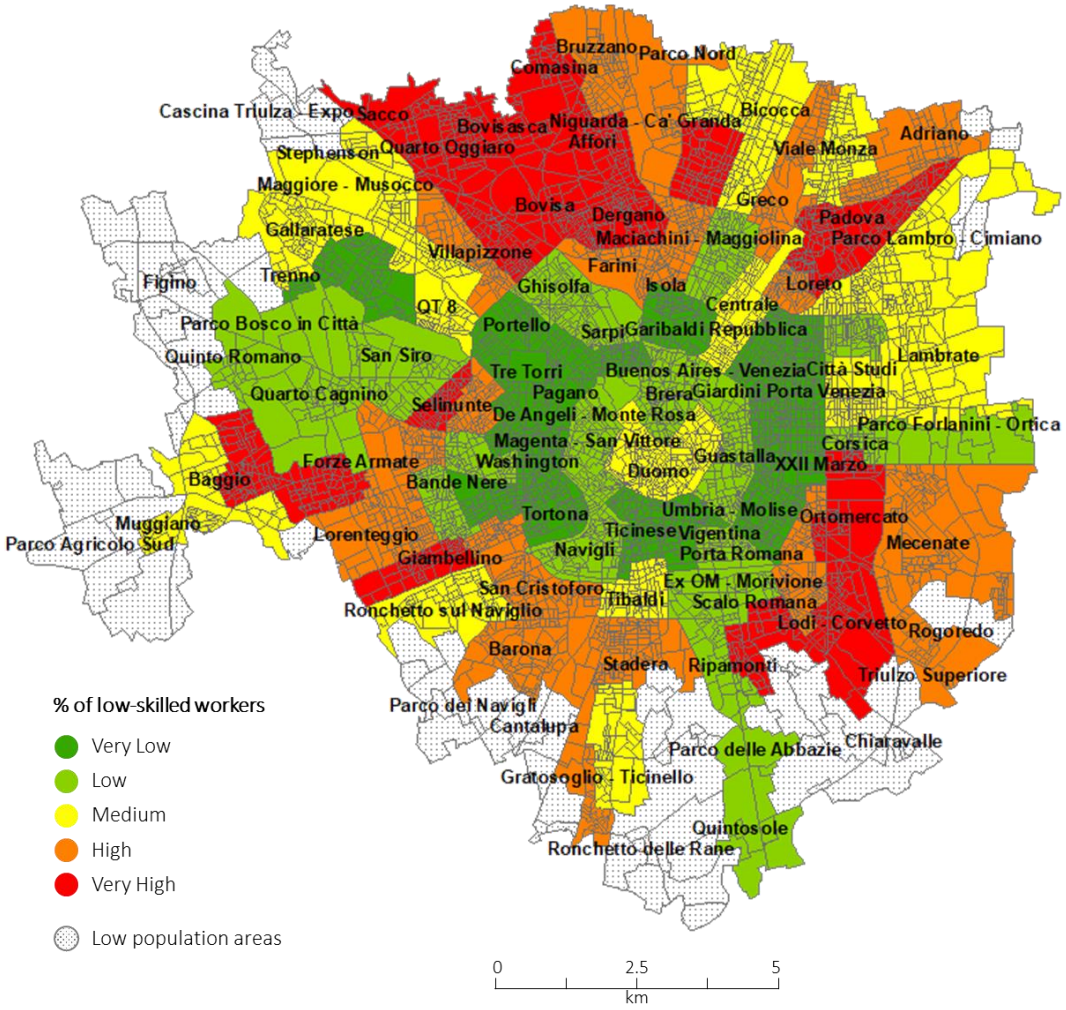
[‡] C = Percentage of foreign persons [§] D = Deprivation Index

Figure A3.3: Quintile distribution of percentage of employed persons with medium- and high-qualified jobs in each census tract, with NIL names. Milan, 2011. Source: our elaboration of Istat data: http://ottomilacensus.istat.it/



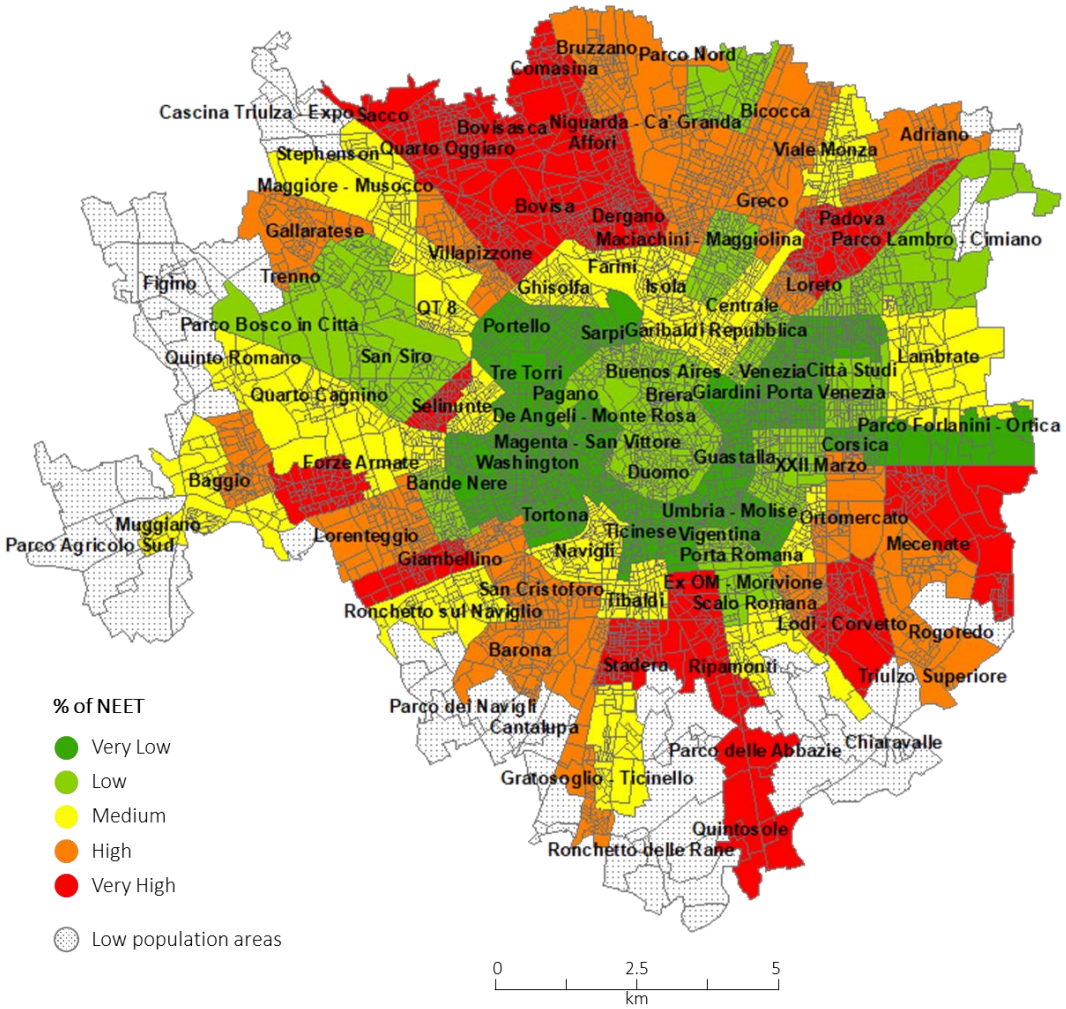
Ratio of employees in types 1, 2, 3 working activities (legislators, entrepreneurs, managers; highly-specialized intellectual and scientific professionals; technical professionals) out of total employment.

Figure A3.4: Quintile distribution of percentage of employed persons with low-qualified jobs in each census tract, with NIL names. Milan, 2011. Source: our elaboration of Istat data: http://ottomilacensus.istat.it/



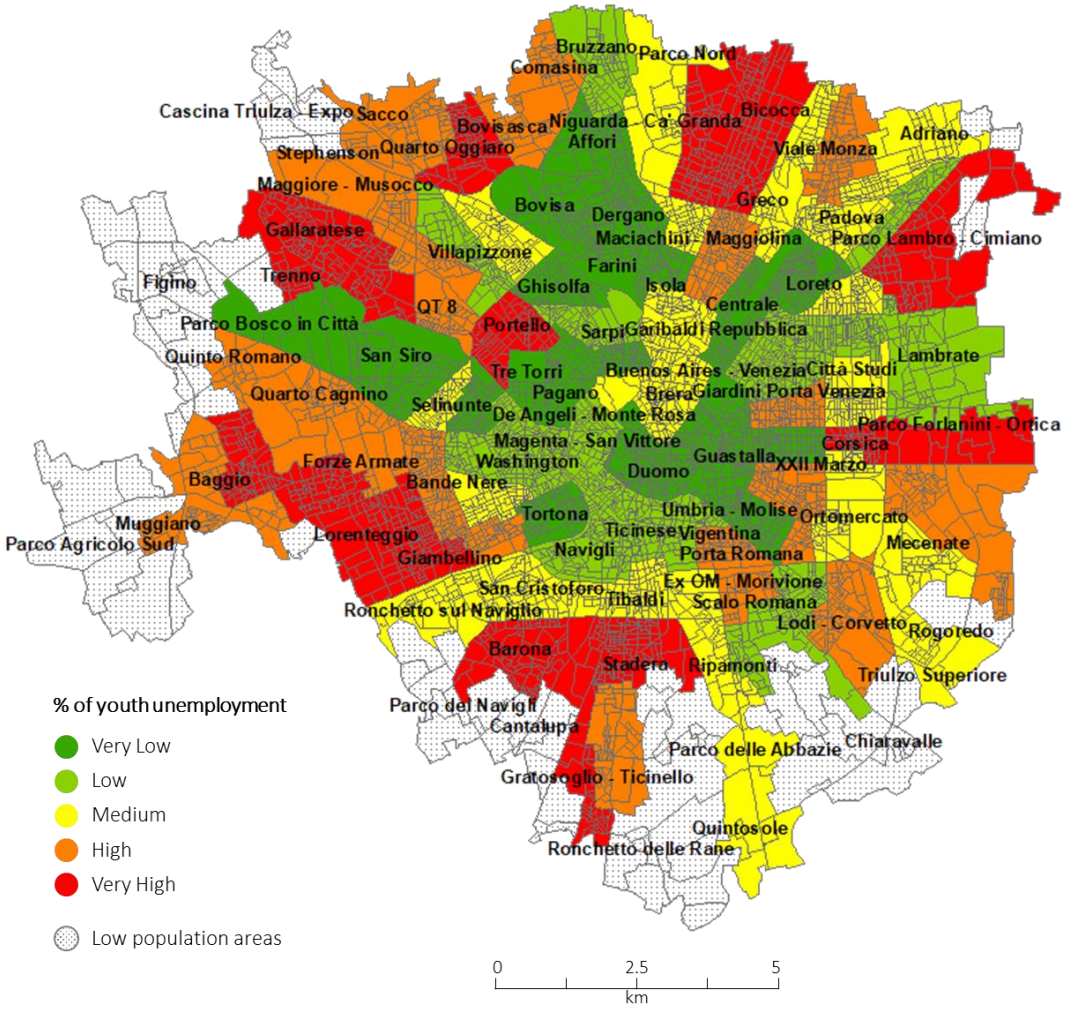
Ratio of employees in type 8 working activities (unqualified workers) out of total employment.

Figure A3.5: Quintile distribution of percentage of NEET in each census tract, with NIL names. Milan, 2011. Source: our elaboration of Istat data: http://ottomilacensus.istat.it/



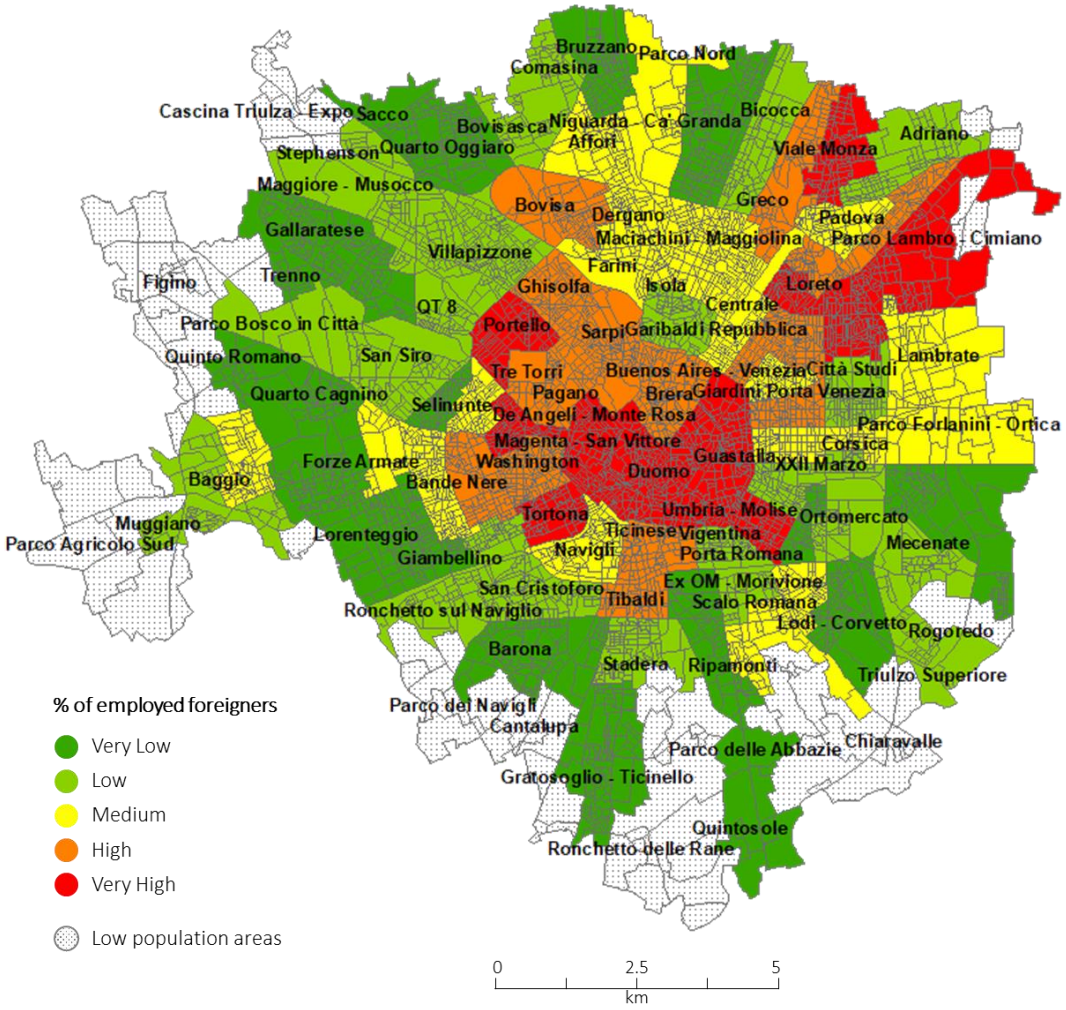
Ratio of 15-29 y.o. 'Not in Education, Employment, or Training' persons out of the 15-29 y.o. population.

Figure A3.6: Quintile distribution of percentage of youth unemployment in each census tract, with NIL names. Milan, 2011. Source: our elaboration of Istat data: http://ottomilacensus.istat.it/



Ratio of 15-24 y.o. persons looking for the first occupation out of the total 15-24 population.

Figure A3.7: Quintile distribution of percentage of employed foreigners in each census tract, with NIL names. Milan, 2011. Source: our elaboration of Istat data: http://ottomilacensus.istat.it/



Ratio of 15+ y.o. employeed foreigners out of the total of 15+ y.o. foreigners.

Table A3.3: Multilevel logistic regression of T2DM (0=no, 1=yes; N = 260,088). Functional Areas (n=177) as area units.

	Model 1		Model 2		Model 3	
	Odds Ratio	**95% CI**	**Odds Ratio**	**95% CI**	**Odds Ratio**	**95% CI**
Age			1.05	[1.05 - 1.05]	1.05	[1.05 - 1.05]
Sex						
Female			1.00	-		-
Male			1.74	[1.69 - 1.79]	1.74	[1.69 - 1.79]
Citizenship						
Italian			1.00	-		-
Foreign			2.08	[1.99 - 2.19]	2.07	[1.97 - 2.16]
Educational Level						
Tertiary			1.00	-		-
Upper-secondary			1.42	[1.36 - 1.48]	1.40	[1.35 - 1.47]
Lower-secondary			1.81	[1.73 - 1.89]	1.77	[1.69 - 1.85]
Primary			1.98	[1.88 - 2.08]	1.93	[1.84- 2.03]
Deprivation Index						
Very Low					1.00	-
Low					1.19	[1.11 - 1.28]
Medium					1.30	[1.21 - 1.40]
High					1.52	[1.42 - 1.64]
Very High					1.70	[1.58 - 1.82]
LR ($P>chi^2$)*	0.000		0.000		0.000	
AIC†	162484.6		147404.8		147243.7	
BIC‡	162505.5		147488.6		147369.3	
VPC§	0.027		0.013		0.003	
MOR**	1.34		1.22		1.11	

* LR ($P>chi^2$)* = Likelihood Ratio test

† AIC = Akaike Information Criterion

‡ BIC = Bayesian Information Criterion

§ VPC = Variance Partition Coefficient

** MOR = Median Odds Ratio

Table 3.4: Multilevel logistic regression of T2DM (0=no, 1=yes; N = 260,088). NILs (n=88) as area units.

	Model 1		Model 2		Model 3	
	Odds Ratio	**95% CI**	**Odds Ratio**	**95% CI**	**Odds Ratio**	**95% CI**
Age			1.05	[1.05 - 1.05]	1.05	[1.05 - 1.05]
Sex						
Female			1.00	-		-
Male			1.74	[1.69 - 1.79]	1.74	[1.69 - 1.79]
Citizenship						
Italian			1.00	-		-
Foreign			2.09	[2.00 - 2.19]	2.09	[1.99 - 2.19]
Educational Level						
Tertiary			1.00	-		-
Upper-secondary			1.42	[1.36 - 1.48]	1.41	[1.35 - 1.47]
Lower-secondary			1.81	[1.73 - 1.90]	1.80	[1.72 - 1.88]
Primary			1.99	[1.89 - 2.10]	1.98	[1.88- 2.08]
Deprivation Index						
Very Low					1.00	-
Low					1.20	[1.08 - 1.32]
Medium					1.41	[1.29 - 1.54]
High					1.51	[1.38 - 1.66]
Very High					1.63	[1.48 - 1.80]
LR ($P>chi^2$)*	0.000		0.000		0.000	
AIC†	162570.3		147458.6		147388.5	
BIC‡	162591.2		147542.3		147514.1	
VPC§	0.026		0.012		0.003	
MOR**	1.32		1.21		1.10	

* LR ($P>chi^2$)* = Likelihood Ratio test

† AIC = Akaike Information Criterion

‡ BIC = Bayesian Information Criterion

§ VPC = Variance Partition Coefficient

** MOR = Median Odds Ratio

Appendix Chapter 4

Tab A4.1: Treatment type by educational level (N=24,872).

	Educational Level				
Treatment Type	*Tertiary*	*Upper-secondary*	*Lower-secondary*	*Primary*	Tot.
Diet only	40.06	27.33	21.77	19.56	25.83
Oral drugs	29.19	36.05	37.56	36.17	35.61
Insulin	30.76	36.62	40.67	44.27	38.57
Tot.	100	100	100	100	100

Tab A4.2: T2DM Care Supplier by educational level (N=24,872).

	Educational Level				
T2DM Care Supplier	*Tertiary*	*Upper-secondary*	*Lower-secondary*	*Primary*	Tot.
Specialist	47.50	61.32	66.10	65.53	61.74
GP	52.50	38.68	33.90	34.47	38.26
Tot.	100	100	100	100	100

Tab A4.3: Comorbidities by educational level (N=24,872).

	Educational Level				
Comorbidities	*Tertiary*	*Upper-secondary*	*Lower-secondary*	*Primary*	Tot.
0	32.90	22.33	19.13	15.12	21.41
1	31.27	33.94	34.96	37.98	34.65
2	26.59	31.05	33.33	34.90	31.90
3 or more	9.24	12.68	12.58	12.00	12.04
Tot.	100	100	100	100	100

References

Abbas, Y. (2011). Glycosylated Hemoglobin: the importance in management of type 2 diabetes. *Journal of Stress Physiology & Biochemistry*, *7*(4).

Abdi, H. (2007). Z-scores. *Encyclopedia of measurement and statistics*, *3*, 1055-1058.

Adler, I. (1912). Primary malignant growths of the lungs and bronchi. Longmans, Green, and Company.

Adler, N. E., Boyce, T., Chesney, M. A., Cohen, S., Folkman, S., Kahn, R. L. & Syme, S. L. (1994). Socioeconomic status and health: the challenge of the gradient. *American psychologist*, 49(1), 15.

Agardh, E., Allebeck, P., Hallqvist, J., Moradi, T., & Sidorchuk, A. (2011). Type 2 diabetes incidence and socio-economic position: a systematic review and meta-analysis. *International journal of epidemiology*, *40*(3), 804-818.

Ainsworth, B. E., Haskell, W. L., Whitt, M. C., Irwin, M. L., Swartz, A. M., Strath, S. J., ... & Jacobs, D. R. (2000). Compendium of physical activities: an update of activity codes and MET intensities. *Medicine and science in sports and exercise*, *32*(9; SUPP/1), S498-S504.

Aitkin, M., & Longford, N. (1986). Statistical modelling issues in school effectiveness studies. *Journal of the Royal Statistical Society: Series A (General)*, *149*(1), 1-26.

Al Sayah, F., Majumdar, S. R., Williams, B., Robertson, S. & Johnson, J. A. (2013). Health literacy and health outcomes in diabetes: a systematic review. *Journal of general internal medicine*, *28*(3), 444-452.

Al-Goblan, A. S., Al-Alfi, M. A., & Khan, M. Z. (2014). Mechanism linking diabetes mellitus and obesity. *Diabetes, metabolic syndrome and obesity: targets and therapy*, *7*, 587.

Alker, H.R. (1969). A typology of ecological fallacies. In Dogan, M. & Rokkam, S. (eds.) *Quantitative ecological analyses in the social science*. Cambridge, MA: MIT Press.

American Diabetes Association. (2014a). Diagnosis and classification of diabetes mellitus. *Diabetes care*, *37*(Supplement 1), S81-S90.

American Diabetes Association. (2014b). Standards of medical care in diabetes—2014. *Diabetes care*, *37*(Supplement 1), S14-S80.

Anderson, R. T., Sorlie, P., Backlund, E., Johnson, N., & Kaplan, G. A. (1997). Mortality effects of community socioeconomic status. *Epidemiology*, 42-47.

Arcaya, M. C., Arcaya, A. L., & Subramanian, S. V. (2015). Inequalities in health: definitions, concepts, and theories. *Global health action*, *8*(1), 27106.

Associazione Medici Diabetologi (AMD) - Società Italiana di Diabetologia (SID) (2018). Standard Italiani per la cura del Diabete Mellito. 2018. https://aemmedi.it/wp-content/uploads/2009/06/AMD-Standard-unico1.pdf

Astell-Burt, T., Feng, X., & Kolt, G. S. (2014). Is neighborhood green space associated with a lower risk of type 2 diabetes? Evidence from 267,072 Australians. *Diabetes care*, *37*(1), 197-201.

Auchincloss, A. H., Roux, A. V. D., Brown, D. G., Erdmann, C. A., & Bertoni, A. G. (2008). Neighborhood resources for physical activity and healthy foods and their association with insulin resistance. *Epidemiology*, 146-157.

Auchincloss, A. H., Roux, A. V. D., Mujahid, M. S., Shen, M., Bertoni, A. G., & Carnethon, M. R. (2009). Neighborhood resources for physical activity and healthy foods and incidence of type 2 diabetes mellitus: the Multi-Ethnic study of Atherosclerosis. *Archives of internal medicine*, *169*(18), 1698-1704.

Auchincloss, A. H., Roux, A. V. D., Mujahid, M. S., Shen, M., Bertoni, A. G., & Carnethon, M. R. (2009). Neighborhood resources for physical activity and healthy foods and incidence of type 2 diabetes mellitus: the Multi-Ethnic study of Atherosclerosis. *Archives of internal medicine*, *169*(18), 1698-1704.

Baliunas, D. O., Taylor, B. J., Irving, H., Roerecke, M., Patra, J., Mohapatra, S., & Rehm, J. (2009). Alcohol as a risk factor for type 2 diabetes: a systematic review and meta-analysis. *Diabetes care*, *32*(11), 2123-2132.

Bandura, A. (1997). *Self-efficacy: The exercise of control* (pp. 3-604). New York: wH Freeman.

Barker, D. J. P. (1994). *Mothers, babies, and disease in later life*. London: BMJ Publishing Group.

Barker, D. J. P. (1995). The fetal and infant origins of disease. *European journal of clinical investigation*, *25*(7), 457-463.

Barker, D. J. P. (2002). Fetal programming of coronary heart disease. *Trends in Endocrinology & Metabolism*, *13*(9), 364-368.

Bassuk, S. S., & Manson, J. E. (2005). Epidemiological evidence for the role of physical activity in reducing risk of type 2 diabetes and cardiovascular disease. *Journal of applied physiology*, *99*(3), 1193-1204.

Beaglehole, R. (1990). International trends in coronary heart disease mortality morbidity and risk factors. *Epidemiologic reviews*, *12*, 1-15.

Beckett, M. (2000). Converging health inequalities in later life-an artifact of mortality selection? *Journal of health and social behavior*, 106-119.

Bell, P., Greene, T., Fisher, J. & Baum, A. (1996). *Environmental psychology* (4th ed.). New York: Harcourt, Brace College Publishers.

Bellamy, L., Casas, J. P., Hingorani, A. D., & Williams, D. (2009). Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *The Lancet*, *373*(9677), 1773-1779.

Benach, J., & Yasui, Y. (1999). Geographical patterns of excess mortality in Spain explained by two indices of deprivation. *Journal of Epidemiology & Community Health*, *53*(7), 423-431.

Benach, J., Muntaner, C., Santana, V. & The Employment Conditions Knowledge Network (EMCONET). (2007). Final report of the Employment Conditions Knowledge Network of the Commission on Social Determinants of Health. Geneve: World Health Organization.

Bennett, G. G., McNeill, L. H., Wolin, K. Y., Duncan, D. T., Puleo, E. & Emmons, K. M. (2007). Safe to walk? Neighborhood safety and physical activity among public housing residents. *PLoS medicine*, *4*(10), e306.

Berkman, L. F. & Kawachi, I. (2014). A Historical Framework for Social Epidemiology: Social Determinants of Population Health, in Berkman, L. F., Kawachi, I. & Glymour, M. M. (eds.). *Social epidemiology*. Oxford University Press.

Berkman, L.F. & Macintyre, S. (1997) The measurement of social class in health studies: old measures and new formulations. In Kogevinas, M., Pearce, N., Susser, M. & Boffetta, P. (eds.) *Social Inequalities and Cancer. IARC scientific publications*, *138*, 51. Lyon: International Agency for Research on Cancer.

Berkman, N. D., Davis, T. C. & McCormack, L. (2010). Health literacy: what is it? *Journal of health communication*, *15*(S2), 9-19.

Bevir, M. (2013). *A theory of governance*, Berkley and Los Angeles, CA: University of California Press.

Biggeri, A., Lagazio, C., Catelan, D., PIRASTU, R. A., Casson, F., & Terracini, B. (2006). Rapporto sullo stato di salute delle popolazioni residenti nelle aree interessate da poli industriali, minerari o militari della Sardegna. *Epidemiol Prev*, *30*(1 Suppl 1), 5-95.

Bijlsma-Rutte, A., Rutters, F., Elders, P. J., Bot, S. D., & Nijpels, G. (2018). Socio-economic status and HbA1c in type 2 diabetes: A systematic review and meta-analysis. *Diabetes/metabolism research and reviews*, *34*(6), e3008.

Black, D., Morris, J. N., Smith, C., & Townsend, P. (1980). *The black report: inequalities in health*. London: DHSS.

Blalock, H. M. (1961). *Causal inferences in non-experimental research*. Chapel Hill: University of North Carolina Press.

Blane, D., Smith, G. D. & Bartley, M. (1993). Social selection: what does it contribute to social class differences in health? *Sociology of Health & Illness*, *15*(1), 1-15.

Blas, E., & Kurup, A. S. (eds.). (2010). *Equity, social determinants and public health programmes*. Geneve: World Health Organization.

Blaxter, M. (1990). *Health and Lifestyles*. New York: Routledge.

Bloor, M., Samphier, M., & Prior, L. (1987). Artefact explanations of inequalities in health: an assessment of the evidence. *Sociology of health & illness*, *9*(3), 231-264.

Bocquier, A., Cortaredona, S., Nauleau, S., Jardin, M., & Verger, P. (2011). Prevalence of treated diabetes: Geographical variations at the small-area level and their association with area-level characteristics. A multilevel analysis in Southeastern France. *Diabetes & metabolism*, *37*(1), 39-46.

Booth, C. (1889): *Labour and Life of the People in London*. London: Macmillan

Booth, G. L., Creatore, M. I., Moineddin, R., Gozdyra, P., Weyman, J. T., Matheson, F. I., & Glazier, R. H. (2013). Unwalkable neighborhoods, poverty, and the risk of diabetes among recent immigrants to Canada compared with long-term residents. *Diabetes Care*, *36*(2), 302-308.

Borgermans, L. A., Goderis, G., Ouwens, M., Wens, J., Heyrman, J., & Grol, R. P. (2008). Diversity in diabetes care programmes and views on high quality diabetes care: are we in need of a standardized framework?. *International Journal of Integrated Care*, *8*.

Bourdieu, P. (1986). The Forms of Capital. In Richardson, J. (eds.) *Handbook of theory and research for the sociology of education*. New York: Greenwood Publishing Group.

Boyle, M. H., & Willms, J. D. (1999). Place effects for areas defined by administrative boundaries. *American Journal of Epidemiology*, *149*(6), 577-585.

Braveman, P. A., Cubbin, C., Egerter, S., Chideya, S., Marchi, K. S., Metzler, M., & Posner, S. (2005). Socioeconomic status in health research: one size does not fit all. *Jama*, *294*(22), 2879-2888.

Broussard, J., & Knutson, K. L. (2010). Sleep and metabolic disease. In: Cappuccio F.P., Miller M.A., Lockley S.W. (eds.) *Sleep, health and society: from aetiology to public health.* Oxford, UK: Oxford University Press, 111-140.

Brown, A. F., Ettner, S. L., Piette, J., Weinberger, M., Gregg, E., Shapiro, M. F., Karter, A.J., Safford, M., Waitzfelder, B., Prata, P.A., & Beckles, G. L. (2004). Socioeconomic position and health among persons with diabetes mellitus: a conceptual framework and review of the literature. *Epidemiologic reviews*, *26*(1), 63-77.

Brown, P. (1995). Naming and framing: the social construction of diagnosis and illness. *Journal of health and social behavior*, 34-52.

Buck, C. W. (1981). Prenatal and perinatal causes of early death and defect. *Preventive and Community Medicine*, 149-66.

Buka, S.L., Brennan, R.T., Rich-Edwards, J.W., Raudenbush, S.W. & Earls, D. (2003). Neighbourhood support and the birth weight of urban infants. *American Journal of Epidemiology*, 3, 157, 1-8.

Buret, E. (1840). *De la misère des classes laborieuses en Angleterre et en France* (Vol. 2). Paris: Paulin.

Cadum, E., Costa, G., Biggeri, A., & Martuzzi, M. (1999). Deprivazione e mortalità: un indice di deprivazione per l'analisi delle disuguaglianze su base geografica. *Epidemiol Prev*, *23*(3), 175-87.

Calsbeek, H., Ketelaar, N. A., Faber, M. J., Wensing, M., & Braspenning, J. (2013). Performance measurements in diabetes care: the complex task of selecting quality indicators. *International journal for quality in health care*, *25*(6), 704-709.

Canoy, D., Wareham, N., Luben, R., Welch, A., Bingham, S., Day, N., & Khaw, K. T. (2005). Cigarette Smoking and Fat Distribution in 21, 828 British Men and Women: A Population-based Study. *Obesity research*, *13*(8), 1466-1475.

Caranci, N., Biggeri, A., Grisotto, L., Pacelli, B., Spadea, T., & Costa, G. (2010). The Italian deprivation index at census block level: definition, description and association with general mortality. *Epidemiologia e prevenzione*, *34*(4), 167-176.

Carstairs, V., & Morris, R. (1990). Deprivation and health in Scotland. *Health bulletin*, *48*(4), 162-175.

Cassel, J. (1976). The contribution of the social environment to host resistance. *American Journal of Epidemiology*, 104(2), 107-23.

Causa, O. & Johansson, Å. (2009*). Intergenerational social mobility*. OECD Economics Department Working Papers, No. 707, Paris: OECD Publishing.

Cesaroni, G., Agabiti, N., Rosati, R., Forastiere, F., & Perucci, C. A. (2006). Un indicatore sintetico di posizione socioeconomica basato sui dati del censimento 2001 per la città di Roma. *Epidemiologia e Prevenzione*, *30*(6), 352-357.

Cesaroni, G., Farchi, S., Davoli, M., Forastiere, F., & Perucci, C. A. (2003). Individual and area-based indicators of socioeconomic status and childhood asthma. *European Respiratory Journal*, *22*(4), 619-624.

Chadwick, E. (1842). *Report on the sanitary condition of the labouring population of Great: Britain: supplementary report on the results of special inquiry into the practice of interment in towns* (Vol. 1). HM Stationery Office.

Challier, B., & Viel, J. F. (2001). Pertinence et validité d'un nouvel indice composite français mesurant la pauvreté au niveau géographique.

Chaskin, R. J. (1997). Perspectives on neighborhood and community: A review of the literature. *Social Service Review*, *71*(4), 521-547.

Checchi, D., Ichino, A. & Rustichini, A. (1999). More equal but less mobile?: Education financing and intergenerational mobility in Italy and in the US. *Journal of public economics*, *74*(3), 351-393.

Cheng, Y. J., Imperatore, G., Geiss, L. S., Wang, J., Saydah, S. H., Cowie, C. C., & Gregg, E. W. (2013). Secular changes in the age-specific prevalence of diabetes among US adults: 1988–2010. *Diabetes care*, DC_122074.

Chiang, J. L., Kirkman, M. S., Laffel, L. M., & Peters, A. L. (2014). Type 1 diabetes through the life span: a position statement of the American Diabetes Association. *Diabetes care*, *37*(7), 2034-2054.

Chichlowska, K. L., Rose, K. M., Diez-Roux, A. V., Golden, S. H., McNeill, A. M., & Heiss, G. (2008). Individual and Neighborhood Socioeconomic Status Characteristics and Prevalence of Metabolic Syndrome. The Atherosclerosis Risk in Communities (ARIC) Study. *Psychosomatic medicine*, *70*(9), 986.

Cho, N. H., Shaw, J. E., Karuranga, S., Huang, Y., da Rocha Fernandes, J. D., Ohlrogge, A. W., & Malanda, B. (2018). IDF Diabetes Atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes research and clinical practice*, *138*, 271-281.

Christakis, N. A. & Fowler, J. H. (2007). The spread of obesity in a large social network over 32 years. *New England journal of medicine*, *357*(4), 370-379.

Christakis, N. A. & Fowler, J. H. (2008). The collective dynamics of smoking in a large social network. *New England journal of medicine*, *358*(21), 2249-2258.

Christine, P. J., Auchincloss, A. H., Bertoni, A. G., Carnethon, M. R., Sánchez, B. N., Moore, K., Adar, S.D., Horwich T.B., Watson, K.E., & Roux, A. V. D. (2015). Longitudinal associations between neighborhood physical and social environments and incident type 2 diabetes mellitus: the Multi-Ethnic Study of Atherosclerosis (MESA). *JAMA internal medicine*, *175*(8), 1311-1320.

Chung, H., & Muntaner, C. (2006). Political and welfare state determinants of infant and child health indicators: an analysis of wealthy countries. *Social science & medicine*, *63*(3), 829-842.

Chung, H., & Muntaner, C. (2007). Welfare state matters: a typological multilevel analysis of wealthy countries. Health policy, 80(2), 328-339.

Cipriani, R. (2008). Alle origini della salute urbana, in Nuvolati G. & Tognetti Bordogna,l M. (eds), *Salute, ambiente e qualità della vita nel contesto urbano*. Milano: Franco Angeli.

Clarke, K. A. (2005). The phantom menace: Omitted variable bias in econometric research. *Conflict management and peace science*, *22*(4), 341-352.

Clark, T. N. & Lipset, S. M. (1991). Are social classes dying? International sociology, 6(4), 397-410.

Coburn, D. (2004). Beyond the income inequality hypothesis: class, neo-liberalism, and health inequalities. *Social science & medicine*, *58*(1), 41-56.

Cockerham, W. C. (2005). Health lifestyle theory and the convergence of agency and structure. *Journal of health and social behavior*, *46*(1), 51-67.

Cockerham, W.C. (2007). *Medical Sociology*. New Jersey: Prentice Hall.

Coleman, J. S. & Fararo, T. J. (eds.) (1992). *Rational choice theory. Advocacy and Critique*. *New York: Sage*.

Coleman, J. S. (1988) Social capital in the creation of human capital. *American journal of sociology*, 94, S95-S120.

Coleman, J. S. (1990). *Foundations of social theory*, Cambridge, MA: Belknap.

Coleman, K., Reiter, K. L., & Fulwiler, D. (2007). The impact of pay-for-performance on diabetes care in a large network of community health centers. *Journal of Health Care for the Poor and Underserved*, *18*(5), 966-983.

Connolly, V., Unwin, N., Sherriff, P., Bilous, R., & Kelly, W. (2000). Diabetes prevalence and socioeconomic status: a population based study showing increased prevalence of type 2 diabetes mellitus in deprived areas. *Journal of Epidemiology & Community Health*, *54*(3), 173-177.

Conrad, P. & Barker, K. K. (2010). The social construction of illness key insights and policy implications. *Journal of health and social behavior*, 51(1), 67-79.

Conrad, P. (2005). *The sociology of health and illness*. Macmillan.

Consolazio, D., Koster, A., Sarti, S., Schram, M.T., Stehouwer, C.D.A, Timmermans, E.J., Wesselius, A., & Bosma, H. (forthcoming). Neighbourhood Property Value and Type 2 Diabetes Mellitus in the Maastricht Study: a Multilevel Study.

Costa, G., Stroscia, M., Zengarini, N., Demaria, M. (eds.) (2017). 40 anni di salute a Torino, spunti per leggere i bisogni e i risultati delle politiche, Inferenze, Milano.

Coulton, C. J., Korbin, J., Chan, T. & Su, M. (2001). Mapping residents' perceptions of neighborhood boundaries: a methodological note. *American journal of community psychology*, *29*(2), 371-383.

Cox, M., Boyle, P. J., Davey, P. G., Feng, Z., & Morris, A. D. (2007). Locality deprivation and Type 2 diabetes incidence: a local test of relative inequalities. *Social science & medicine*, *65*(9), 1953-1964.

Crayford, T., Shanks, J., Bajekal, M., Langford, S., & Bajekal, M. (1995). Analysis from inner London of deprivation payments based on enumeration districts rather than wards. *BMJ*, *311*(7008), 787-788.

Cummins, S., Curtis, S., Diez-Roux, A. V. & Macintyre, S. (2007) Understanding and representing 'place'in health research: a relational approach. *Social science & medicine*, 65(9), 1825-1838.

Cummins, S., Stafford, M., Macintyre, S., Marmot, M. & Ellaway, A. (2005). Neighbourhood environment and its association with self-rated health: evidence from Scotland and England. *Journal of Epidemiology and Community Health*, 59, 207-213.

Cunningham, S. A., Patel, S. A., Beckles, G. L., Geiss, L. S., Mehta, N., Xie, H., & Imperatore, G. (2018). County-level contextual factors associated with diabetes incidence in the United States. *Annals of epidemiology*, *28*(1), 20-25.

D'Alessio, M., Guarino, A., De Pascalis, V. & Zimbardo, P. G. (2003). Testing Zimbardo's Stanford time perspective inventory (STPI)-short form. *Time & Society*, *12*(2-3), 333-347.

Dahlgren, G. & Whitehead, M. (1991). Policies and strategies to promote social equity in health. *Stockholm: Institute for future studies*.

Dahrendorf, R. (1959). *Class and class conflict in industrial society* (Vol. 15). Stanford, CA: Stanford University Press.

De Vogli, R. (2011). Neoliberal globalisation and health in a time of economic crisis. *Social Theory & Health*, *9*(4), 311-325.

den Braver, N. R., Lakerveld, J., Rutters, F., Schoonmade, L. J., Brug, J. & Beulens, J. W. J. (2018). Built environmental characteristics and diabetes: a systematic review and meta-analysis. *BMC medicine*, *16*(1), 12.

Dendup, T., Feng, X., Clingan, S. & Astell-Burt, T. (2018). Environmental risk factors for developing type 2 diabetes mellitus: a systematic review. *International journal of environmental research and public health*, *15*(1), 78.

Diderichsen, F. & Hallqvist, J. (1998). Social inequalities in health: some methodological considerations for the study of social position and social context. *Inequality in health—a Swedish perspective*. Stockholm: Swedish Council for Social Research.

Diderichsen, F., Evans, T., & Whitehead, M. (2001). The social basis of disparities in health. In Evans, T., Whitehead, M., Diderichsen, F., Bhuiya, A. & Wirth, M. (eds.) *Challenging inequities in health: From ethics to action*. New York: Oxford UP.

Dietz, R. D. (2002). The estimation of neighborhood effects in the social sciences: An interdisciplinary approach. *Social science research*, *31*(4), 539-575.

Diez-Roux, A. V. (1998). Bringing context back into epidemiology: variables and fallacies in multilevel analysis. *American journal of public health*, 88(2), 216-222.

Diez-Roux, A. V. (2004). Estimating the neighborhood health effects: The challenges of casual inference in a complex world.

Diez-Roux, A. V., Nieto, F. J., Muntaner, C., Tyroler, H. A., Comstock, G. W., Shahar, E., ... & Szklo, M. (1997). Neighborhood environments and coronary heart disease: a multilevel analysis. *American journal of epidemiology*, *146*(1), 48-63.

Dohrenwend, B. P. (1980). *Mental illness in the United States: Epidemiological estimates*. Praeger Publishers.

Doll, R. & Hill, A. B. (1950). Smoking and carcinoma of the lung. Preliminary report. *British Medical Journal*, 2(4682), 739-48.

Doll, R. & Hill, A. B. (1954). The mortality of doctors in relation to their smoking habits. *British medical journal*, *1*(4877), 1451.

Donabedian, A. (1988). The quality of care: how can it be assessed?. *Jama*, *260*(12), 1743-1748.

Dubos, R.J. (1959). *Mirage of health*. New York: Harper & Row.

Dubos, R.J. (1978). Health and creative adaptation. *Human Nature*, 1(1), 74-82.

Duncan, C., Jones, K. & Moon, G. (1993). Do places matter? A multi-level analysis of regional variations in health-related behaviour in Britain. *Social science & medicine*, 37(6), 725-733.

Duncan, C., Jones, K. & Moon, G. (1995). Psychiatric morbidity: a multilevel approach to regional variations in the UK. *Journal of Epidemiology and Community Health*, 49(3), 290-295.

Duncan, C., Jones, K. & Moon, G. (1999). Smoking and deprivation: are there neighbourhood effects? *Social science & medicine*, 48(4), 497-505.

Duncan, C., Jones, K. & Moon, G. (1998). Context, composition and heterogeneity: using multilevel models in health research. *Social science & medicine*, *46*(1), 97-117.

Durkheim, E. (1897). *Suicide*. New York: Free Press.

Durlauf, S. N. (2004). Neighborhood effects, in Henderson, J.V & Thisse, J.F. (eds) *Handbook of regional and urban economics. Vol. 4 Cities and* Geographies. Amsterdam: Elsevier.

Dussault, G., & Franceschini, M. C. (2006). Not enough there, too many here: understanding geographical imbalances in the distribution of the health workforce. *Human resources for health*, *4*(1), 12.

Dutton, D. B. (1986). Social class, health and illness. *Applications of social science to clinical medicine and health policy*, 31-62.

Egerter, S., Braveman, P., Sadegh-Nobari, T., Grossman-Kahn, R. & Dekker, M. (2011). *Education and health.* Exploring the social determinants of health: Issue Brief no. 5. Princeton, NJ: Robert Wood Johnson Foundation.

Egger, G., & Swinburn, B. (1997). An" ecological" approach to the obesity pandemic. *BMJ: British Medical Journal*, *315*(7106), 477.

Eisenberg, L. (1977). Disease and illness Distinctions between professional and popular ideas of sickness. *Culture, medicine and psychiatry*, *1*(1), 9-23.

Ellen, I. G. & Turner, M. A. (2003). Do neighborhoods matter and why? In Goering. J. & Feins, J. (eds.), *Choosing a better life? Evaluating the moving to opportunity experiment* (pp. 313–338). Washington, DC: Urban Institute Press.

Ellen, I. G., & Turner, M. A. (1997). Does neighborhood matter? Assessing recent evidence. *Housing Policy Debate*, *8* (4), 833–866.

Ellen, I. G., Mijanovich, T. & Dillman, K. (2001). Neighborhood effects on health: Exploring the links and assessing the evidence. *Journal of Urban Affairs, 23* (3), 391–408.

Emdin, C. A., Rahimi, K., Neal, B., Callender, T., Perkovic, V., & Patel, A. (2015). Blood pressure lowering in type 2 diabetes: a systematic review and meta-analysis. *Jama*, *313*(6), 603-615.

Emerging Risk Factors Collaboration. (2011). Diabetes mellitus, fasting glucose, and risk of cause-specific death. *New England Journal of Medicine*, *364*(9), 829-841.

Engels, F. (1845). *Die Lage der arbeitenden Klasse in England*. Leizpig.

Epifano, L., Di Vincenzo, A., Fanelli, C., Porcellati, E., Perriello, G., De Feo, P., Motolse, M., Brunetti, P. & Bolli, G. B. (1992). Effect of cigarette smoking and of a transdermal nicotine delivery system on glucoregulation in type 2 diabetes mellitus. *European journal of clinical pharmacology*, *43*(3), 257-263.

Ernster, V. L. (1988). Trends in smoking, cancer risk, and cigarette promotion current priorities for reducing tobacco exposure. *Cancer*, *62*(S1), 1702-1712.

Espelt, A., Arriola, L., Borrell, C., Larranaga, I., Sandin, M., & Escolar-Pujolar, A. (2011). Socioeconomic position and type 2 diabetes mellitus in Europe 1999-2009: a panorama of inequalities. *Current diabetes reviews*, *7*(3), 148-158.

Espelt, A., Borrell, C., Roskam, A. J., Rodriguez-Sanz, M., Stirbu, I., Dalmau-Bueno, A., ... & Artnik, B. (2008). Socioeconomic inequalities in diabetes mellitus across Europe at the beginning of the 21st century. *Diabetologia*, *51*(11), 1971.

Eurostat. (2017). Chronic diabetes affects millions of people in the EU. https://ec.europa.eu/eurostat/web/products-eurostat-news/-/EDN-20171113-1?inheritRedirect=true (last checked, 15/01/2019).

Everson, S. A., Maty, S. C., Lynch, J. W., & Kaplan, G. A. (2002). Epidemiologic evidence for the relation between socioeconomic status and depression, obesity, and diabetes. *Journal of psychosomatic research*, *53*(4), 891-895.

Feng, X., & Astell-Burt, T. (2017). Impact of a type 2 diabetes diagnosis on mental health, quality of life, and social contacts: a longitudinal study. *BMJ Open Diabetes Research and Care*, *5*(1), e000198.

Ferraro, K. F., & Kelley-Moore, J. A. (2003). Cumulative disadvantage and health: long-term consequences of obesity?. *American sociological review*, *68*(5), 707.

Ferro-Luzzi, A., & Branca, F. (1995). Mediterranean diet, Italian-style: prototype of a healthy diet. *The American journal of clinical nutrition*, *61*(6), 1338S-1345S.

Fisher, L., Hessler, D. M., Polonsky, W. H., & Mullan, J. (2012). When is diabetes distress clinically meaningful?: establishing cut points for the Diabetes Distress Scale. *Diabetes care*, DC_111572.

Forgacs, D. & Gundle, S. (2007). *Mass culture and Italian society from Fascism to the Cold War*. Bloomington, IN: Indiana University Press.

Forrest, R., & Gordon, D. (1993). *People and places: a 1991 census atlas of England*. Bristol England University of Bristol School for Advanced Urban Studies [SAUS].

Foucault, M. (1973). *The Birth of the Clinic*. London: Tavistock.

Friedrichs, J. (1998). Do poor neighborhoods make their residents poorer? Context effects of poverty neighborhoods on their residents. In H. Andress (eds.), *Empirical poverty research in a comparative perspective* (pp. 77–99). Aldershot: Ashgate.

Fuchs, V. R. (1982). Time Preference and Health: An Explanatory Study, in Fuchs V. R. (eds.), *Economic Aspects of Health*, Chigago: The University of Chicago Press.

Fujiyoshi, A., Miura, K., Kadowaki, S., Azuma, K., Tanaka, S., Hisamatsu, T., Arima H., Kadota A., Miyagawa N., Takashima N., Ohkubo T., Saitoh Y., Torii S., Miyazawa I., Maegawa H., Murata K., Ueshima H.& SESSA Research Group (2016). Lifetime cigarette smoking is associated with abdominal obesity in a community-based sample of Japanese men: The Shiga Epidemiological Study of Subclinical Atherosclerosis (SESSA). *Preventive medicine reports*, *4*, 225-232.

Fukuda, Y., Nakamura, K., & Takano, T. (2007). Higher mortality in areas of lower socioeconomic position measured by a single index of deprivation in Japan. *Public Health*, *121*(3), 163-173.

Gæde, P., Lund-Andersen, H., Parving, H. H., & Pedersen, O. (2008). Effect of a multifactorial intervention on mortality in type 2 diabetes. *New England Journal of Medicine*, *358*(6), 580-591.

Galobardes, B., Shaw, M., Lawlor, D. A., Lynch, J. W., & Smith, G. D. (2006). Indicators of socioeconomic position (part 1). *Journal of Epidemiology & Community Health*, *60*(1), 7-12.

Galster, G. C. (2002). An economic efficiency analysis of deconcentrating poverty populations. *Journal of housing economics*, *11*(4), 303-329.

Galster, G. C. (2012). The mechanism(s) of neighbourhood effects: Theory, evidence, and policy implications. In *Neighbourhood effects research: New perspectives* (pp. 23-56). Springer, Dordrecht.

Galster, G. C. (2014). How neighborhoods affect health, well-being, and young people's futures. *Chicago, IL: MacArthur Foundation*.

Gandek, B., Ware, J. E., Aaronson, N. K., Apolone, G., Bjorner, J. B., Brazier, J. E., Bullinger, M, Kaasa, S., Leplege, A., Prieto, L. & Sullivan, M. (1998). Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries: results from the IQOLA Project. *Journal of clinical epidemiology*, *51*(11), 1171-1178.

Gans, H. J. (1962). *The urban villagers: Group and Class in the Life of Italian-Americans***.** New York: Free Press.

Gans, H. J. (1968). Culture and class in the study of poverty: An approach to anti-poverty research, in Moynihan, D. P. (eds.) *On understanding poverty: Perspectives from the social sciences*. New York: Basic Books.

Garcıa-Gil, C., Cruz-Rojo, C., Álvarez-Girón, M., & Solano-Pares, A. (2004). Health inequalities in Seville, Spain: use of indicators of social deprivation and mortality in small areas. *Public health*, *118*(1), 11-20.

Garip, F., & Asad, A. L. (2015). Migrant networks. *Emerging Trends in the Social and Behavioral Sciences: An Interdisciplinary, Searchable, and Linkable Resource*, 1-13.

Gephart, M. (1997). Neighborhoods and communities as contexts for development. In J. Brooks-Gunn, G. J. Duncan & J. L. Aber (eds.), *Neighborhood poverty* (Context and consequences for Children, Vol. I, pp. 1–43). New York: Russell Sage.

Giles-Corti, B., Vernez-Moudon, A., Reis, R., Turrell, G., Dannenberg, A. L., Badland, H., Foster, S., Lowe, M., Sallis, J.F., Stevenson, M., & Owen, N. (2016). City planning and population health: a global challenge. *The lancet*, *388*(10062), 2912-2924.

Ginter, E., & Simko, V. (2013). Type 2 diabetes mellitus, pandemic in 21st century. In *Diabetes* (pp. 42-50). Springer, New York, NY.

Glasgow, R. E., Peeples, M., & Skovlund, S. E. (2008). Where Is the Patient in Diabetes Performance Measures?: The case for including patient-centered and self-management measures. *Diabetes Care*, *31*(5), 1046-1050.

Glasgow, S. & Schrecker, T. (2016). The double burden of neoliberalism? Noncommunicable disease policies and the global political economy of risk. *Health & place*, *39*, 204-211.

Gnavi, R., Karaghiosoff, L., Costa, G., Merletti, F., & Bruno, G. (2008). Socio-economic differences in the prevalence of diabetes in Italy: the population-based Turin study. *Nutrition, Metabolism and Cardiovascular Diseases*, *18*(10), 678-682.

Gnavi, R., Migliardi, A., Maggini, M., & Costa, G. (2018). Prevalence of and secular trends in diagnosed diabetes in Italy: 1980–2013. *Nutrition, Metabolism and Cardiovascular Diseases*, *28*(3), 219-225.

Goldney, R. D., Phillips, P. J., Fisher, L. J., & Wilson, D. H. (2004). Diabetes, depression, and quality of life: a population study. *Diabetes care*, *27*(5), 1066-1070.

Goldstein, H. (1986). Multilevel mixed linear model analysis using iterative generalized least squares. *Biometrika*, *73*(1), 43-56.

Goldstein, H. (1987). *Multilevel models in education and social research*. Oxford University Press.

Goldstein, H. (2011). *Multilevel statistical models* (Vol. 922). John Wiley & Sons.

Goldstein, H., Browne, W., & Rasbash, J. (2002). Partitioning variation in multilevel models. *Understanding Statistics: Statistical Issues in Psychology, Education, and the Social Sciences*, *1*(4), 223-231.

Goldthorpe, J. H. (1998). Rational action theory for sociology. *British Journal of Sociology*, 167-192.

Gordon, D. (1995). Census based deprivation indices: their weighting and validation. *Journal of Epidemiology & Community Health*, *49*(Suppl 2), S39-S44.

Gordon-Larsen, P. (2014). Food availability/convenience and obesity. *Advances in nutrition*, *5*(6), 809-817.

Gordon-Larsen, P., Nelson, M. C., Page, P. & Popkin, B. M. (2006). Inequality in the built environment underlies key health disparities in physical activity and obesity. *Pediatrics*, *117*(2), 417-424.

Gostin, L. O. (2017). 2016: The Year of the Soda Tax. *The Milbank Quarterly*, *95*(1), 19.

Goudswaard, A. N., Stolk, R. P., Zuithoff, P., & Rutten, G. E. (2004). Patient characteristics do not predict poor glycaemic control in type 2 diabetes patients treated in primary care. *European journal of epidemiology*, *19*(6), 541-545.

Goyder, E. C., Botha, J. L., & McNally, P. G. (2000). Inequalities in access to diabetes care: evidence from a historical cohort study. *BMJ Quality & Safety*, *9*(2), 85-89.

Graham, H. (1993). *Hardship & Health Womens Lives*. London: Harvester Wheatsheaf.

Graham, S. (1963). Social factors in relation to chronic illness. In Freeman, H., Levine, S., Reeder, L.G. (edited by) *Handbook of Medical Sociology*. New Jersey: Prentice Hall.

Granovetter, M. S. (1977). The strength of weak ties. In *Social networks* (pp. 347-367). Academic Press.

Gray, J., Millett, C., O'Sullivan, C., Omar, R. Z., & Majeed, A. (2006). Association of age, sex and deprivation with quality indicators for diabetes: population-based cross sectional survey in primary care. *Journal of the Royal Society of Medicine*, *99*(11), 576-581.

Gray, P. A., Drayton-Brooks, S., & Williamson, K. M. (2013). Diabetes: follow-up support for patients with uncontrolled diabetes. *The Nurse Practitioner*, *38*(4), 49-53.

Green, D. & Shapiro, I. (1996). *Pathologies of rational choice theory: A critique of applications in political science*. Yale University Press.

Grintsova, O., Maier, W., & Mielck, A. (2014). Inequalities in health care among patients with type 2 diabetes by individual socio-economic status (SES) and regional deprivation: a systematic literature review. *International journal for equity in health*, *13*(1), 43.

Grisotto, L., Catelan, D., Lagazio, C., & Biggeri, A. (2007). Uso dell'indice di deprivazione materiale in epidemiologia descrittiva. *RAPPORTI ISTISAN*, *50*, 123.

Grundmann, N., Mielck, A., Siegel, M., & Maier, W. (2014). Area deprivation and the prevalence of type 2 diabetes and obesity: analysis at the municipality level in Germany. *BMC Public Health, 14*(1), 1264.

Guest, A. M., & Lee, B. A. (1984). How urbanites define their neighborhoods. *Population and Environment, 7*(1), 32-56.

Gulliford, M. C., Ukoumunne, O. C., & Chinn, S. (1999). Components of variance and intraclass correlations for the design of community-based surveys and intervention studies: data from the Health Survey for England 1994. *American Journal of Epidemiology*, *149*(9), 876-883.

Guthrie, B., Emslie-Smith, A., & Morris, A. D. (2009a). Which people with Type 2 diabetes achieve good control of intermediate outcomes? Population database study in a UK region. *Diabetic Medicine*, *26*(12), 1269-1276.

Guthrie, L. C., Butler, S. C. & Ward, M. M. (2009b). Time perspective and socioeconomic status: A link to socioeconomic disparities in health?. *Social science & medicine*, *68*(12), 2145-2151.

Hackett, R. A., & Steptoe, A. (2017). Type 2 diabetes mellitus and psychological stress—a modifiable risk factor. *Nature Reviews Endocrinology*, *13*(9), 547.

Hallman, H. W. (1984). *Neighborhoods: Their place in urban life* (Vol. 154). Beverly Hills, CA: Sage

Hammond, E. C. & Horn, D. (1954). The relationship between human smoking habits and death rates: a follow-up study of 187,766 men. *Journal of the American Medical Association*, *155*(15), 1316-1328.

Hauser, R. M. (1974). Contextual analysis revisited. *Sociological methods & research*, 2(3), 365-375.

Helmrich, S. P., Ragland, D. R., & Paffenbarger, J. R. (1994). Prevention of non-insulin-dependent diabetes mellitus with physical activity. *Medicine and Science in Sports and Exercise*, *26*(7), 824-830.

Henderson, S., & Kendall, E. (2011). Culturally and linguistically diverse peoples' knowledge of accessibility and utilisation of health services: exploring the need for improvement in health service delivery. *Australian journal of primary health*, *17*(2), 195-201.

Henson, J., Dunstan, D. W., Davies, M. J., & Yates, T. (2016). Sedentary behaviour as a new behavioural target in the prevention and treatment of type 2 diabetes. *Diabetes/metabolism research and reviews*, *32*, 213-220.

Herd, P. (2006). Do functional health inequalities decrease in old age? Educational status and functional decline among the 1931-1941 birth cohort. *Research on Aging*, *28*(3), 375-392.

Herder, C., & Roden, M. (2011). Genetics of type 2 diabetes: pathophysiologic and clinical relevance. *European journal of clinical investigation*, *41*(6), 679-692.

Herzlich, C. (1973). *Health and illness: A social psychological analysis*. London, Academic Press.

Hill, A. L., Rand, D. G., Nowak, M. A. & Christakis, N. A. (2010). Infectious disease modeling of social contagion in networks. *PLOS Computational Biology*, 6(11): e1000968.

Hippisley-Cox, J., O'Hanlon, S., & Coupland, C. (2004). Association of deprivation, ethnicity, and sex with quality indicators for diabetes: population based survey of 53 000 patients in primary care. *Bmj*, *329*(7477), 1267-1269.

Hiscock, R., Bauld, L., Amos, A., Fidler, J. A. & Munafò, M. (2012). Socioeconomic status and smoking: a review. *Annals of the New York Academy of Sciences*, *1248*(1), 107-123.

Hobbs, R., & Cole, T. (1996). Deprivation payments revisited (again).

Hodgson, G. M. (2012). On the limits of rational choice theory. *Economic Thought*, *1*(1, 2012).

Howden-Chapman, P. (2004). Housing standards: a glossary of housing and health. *Journal of Epidemiology & Community Health*, *58*(3), 162-168.

Hox, J. J. (2010). *Multilevel analysis: Techniques and applications*, Taylor & Francis.

Hu, E. A., Pan, A., Malik, V., & Sun, Q. (2012). White rice consumption and risk of type 2 diabetes: meta-analysis and systematic review. *Bmj*, *344*, e1454.

Hu, F. B. (2003). Sedentary lifestyle and risk of obesity and type 2 diabetes. *Lipids*, *38*(2), 103-108.

Hu, F. B. (2011). Globalization of diabetes: the role of diet, lifestyle, and genes. *Diabetes care*, *34*(6), 1249-1257.

Huber, E., & Stephens, J. D. (2010). *Development and crisis of the welfare state: Parties and policies in global markets*. University of Chicago press.

Huber, M., Knottnerus, J. A., Green, L., van der Horst, H., Jadad, A. R., Kromhout, D., Leonard, B., Loureiro, M.I, van der Meer, J.W.M, Schanbel, P., Smith, R., van Weel, C. & Smid, H. (2011). How should we define health? *British Medical Journal*, 343, d4163.

Huie, S. A. B. (2001). The concept of neighborhood in health and mortality research. *Sociological Spectrum*, *21*(3), 341-358.

Humphreys, N. A. (1887). *Class Mortality Statistics*. Journal of the Royal statistical society, 50(2), 255-292.

Husemann, B., Von Mach, C. Y., Borsotto, D., Zepf, K. I., & Scharnbacher, J. (2009). Comparisons of musculoskeletal complaints and data entry between a sitting and a sit-stand workstation paradigm. *Human factors*, *51*(3), 310-320.

Illsley, R. & Mullen, K. (1985). The health needs of disadvantaged client groups. *Oxford textbook of public health*, 389-402.

Ingrosso, M. (eds.). (2006). *La promozione del benessere sociale: progetti e politiche nelle comunità locali* (Vol. 25). FrancoAngeli.

Istat. (2011). 15° Censimento della popolazione e delle abitazioni 2011. https://www.istat.it/it/censimenti-permanenti/censimenti-precedenti/popolazione-e-abitazioni/popolazione-2011

Istat. (2013) Multiscopo ISTAT – Condizioni di salute e ricorso ai servizi sanitari. UniData - Bicocca Data Archive, Milano. Codice indagine SN128. Versione del file di dati 2.0

Istat. (2016) *Aspetti della vita quotidiana*. UniData - Bicocca Data Archive, Milano. Codice indagine SN190. Versione del file di dati 1.0

Istat. (2017.) Il diabete in Italia. Anni 2000-2016. https://www.istat.it/it/files//2017/07/REPORT_DIABETE.pdf (last checked, 15/01/2019)

Istat. (2018) *Rilevazione Continua sulle Forze di Lavoro – Ottobre*. UniData - Bicocca Data Archive, Milano. Codice indagine SN202. Versione del file di dati 1.0

Jadad, A. R. & O'Grady, L. (2008). How should health be defined? *BMJ: British Medical Journal (Online), 337*.

Jager, K. J., Zoccali, C., Macleod, A., & Dekker, F. W. (2008). Confounding: what it is and how to deal with it. *Kidney international*, *73*(3), 256-260.

Jarman, B. (1984). Underprivileged areas: validation and distribution of scores. *Br Med J (Clin Res Ed), 289*(6458), 1587-1592.

Jarman, B. (1997). Deprivation payments to general practitioners. Scores should be based on enumeration districts, and payments should be phased in gradually. *BMJ: British Medical Journal*, *314*(7075), 228.

Jenkinson, C., Layte, R., Jenkinson, D., Lawrence, K., Petersen, S., Paice, C., & Stradling, J. (1997). A shorter form health survey: can the SF-12 replicate results from the SF-36 in longitudinal studies? *Journal of Public Health*, *19*(2), 179-186.

Jenks, C. & Mayer, S.E. (1990). The social consequences of growing up in a poor neighborhood. In McGeary, M. (eds.) *Inner-city poverty in the United States*, 111–186. Washington, DC: National Academy Press.

Jette, M., Sidney, K., & Blümchen, G. (1990). Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. *Clinical cardiology*, *13*(8), 555-565.

Jiang, X., Ma, H., Wang, Y. & Liu, Y. (2013). Early life factors and type 2 diabetes mellitus. *Journal of diabetes research*, *2013*.

Jones, K., & Subramanian, S. V. (2019). *Developing multilevel models for analysing contextuality, heterogeneity and change using MLwiN 3 Volume*. Centre for Multilevel Modelling, University of Bristol, UK. https://www.researchgate.net/publication/260771330

Jordan, H., Roderick, P., & Martin, D. (2004). The Index of Multiple Deprivation 2000 and accessibility effects on health. *Journal of Epidemiology & Community Health*, *58*(3), 250-257.

Kadushin, C. (1964). Social class and the experience of ill health. *Sociological Inquiry*, 34(1), 67-80.

Kahn, S. E., Hull, R. L., & Utzschneider, K. M. (2006). Mechanisms linking obesity to insulin resistance and type 2 diabetes. *Nature*, *444*(7121), 840.

Karasek Jr, R. A. (1979). Job demands, job decision latitude, and mental strain: Implications for job redesign. *Administrative science quarterly*, 285-308.

Karesek, R. & Theorell, T. (1990). Healthy work. Stress, productivity and the reconstruction of work life.

Kawachi, I. & Berkman, L. F. (eds.). (2003). *Neighborhoods and health*. Oxford University Press.

Kawachi, I. & Berkman, L.F. (2014). Social capital, social cohesion, and health, in Berkman, L. F., Kawachi, I. & Glymour, M. M. (eds.). *Social epidemiology*. Oxford University Press.

Kawachi, I. (2010). Social Capital and Health, in Bird, C. E., Conrad, P., Fremont, A. M. & Timmermans, S. (eds.) *Handbook of medical sociology*. Vanderbilt University Press.

Kazepov, Y. (1995). Urban poverty patterns in Italy: The case of Milan. *Espace Populations Sociétés*, *13*(3), 329-340.

Kearns, R.A. (1993). Place and health: towards a reformed medical geography. *Professional Geographer*, 45, 139-147.

Kern, D. M., Auchincloss, A. H., Stehr, M. F., Roux, A. V. D., Moore, K. A., Kanter, G. P., & Robinson, L. F. (2018). Neighborhood price of healthier food relative to unhealthy food and its association with type 2 diabetes and insulin resistance: The multi-ethnic study of atherosclerosis. *Preventive medicine*, *106*, 122-129.

Kessler, R. C., McGonagle, K. A., Zhao, S., Nelson, C. B., Hughes, M., Eshleman, S. & Kendler, K. S. (1994). Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. *Archives of general psychiatry*, 51(1), 8-19.

Kiawi, E., Edwards, R., Shu, J., Unwin, N., Kamadjeu, R. & Mbanya, J. C. (2006). Knowledge, attitudes, and behavior relating to diabetes and its main risk factors among urban residents in Cameroon: a qualitative survey. *Ethnicity & disease*, *16*(2), 503-509.

Kitcher, P. (2004). Evolutionary theory and the social uses of biology. *Biology and Philosophy*, 19(1), 1-15.

Kleczkowski, B. M., Roemer, M. I. & Werff, A. V. D. (1984). National health systems and their reorientation towards health for all: Guidelines for policy-making.

Knip, M., & Simell, O. (2012). Environmental triggers of type 1 diabetes. *Cold Spring Harbor perspectives in medicine*, a007690.

Kodl, C. T., & Seaquist, E. R. (2008). Cognitive dysfunction and diabetes mellitus. *Endocrine reviews*, *29*(4), 494-511.

Koestler, A. (1976) *The Call Girls.* London and Sydney: Pan Books.

Krämer, U., Herder, C., Sugiri, D., Strassburger, K., Schikowski, T., Ranft, U. & Rathmann, W. (2010). Traffic-related air pollution and incident type 2 diabetes: results from the SALIA cohort study. *Environmental health perspectives*, *118*(9), 1273-1279.

Krieger, N. (1992). Overcoming the absence of socioeconomic data in medical records: validation and application of a census-based methodology. *American journal of public health*, *82*(5), 703-710.

Krieger, N. (2000). Refiguring "race": epidemiology, racialized biology, and biological expressions of race relations. *International Journal of Health Services*, *30*(1), 211-216.

Krueger, P. M., & Chang, V. W. (2008). Being poor and coping with stress: health behaviors and the risk of death. *American journal of public health*, *98*(5), 889-896.

Kunst, A. & Mackenbach, J. (2000). *Measuring socioeconomic inequalities in health*. Copenaghen: WHO Regional Office Europe.

Lahelma, E., Martikainen, P., Laaksonen, M. & Aittomäki, A. (2004). Pathways between socioeconomic determinants of health. *Journal of Epidemiology & Community Health*, *58*(4), 327-332.

Lake, A., & Townshend, T. (2006). Obesogenic environments: exploring the built and food environments. *The Journal of the Royal society for the Promotion of Health*, *126*(6), 262-267.

Lam, D. W., & LeRoith, D. (2012). The worldwide diabetes epidemic. *Current Opinion in Endocrinology, Diabetes and Obesity*, *19*(2), 93-96.

Lamm, H., Schmidt, R. W. & Trommsdorff, G. (1976). Sex and social class as determinants of future orientation (time perspective) in adolescents. *Journal of Personality and Social Psychology*, *34*(3), 317-326.

Larsen, K., & Merlo, J. (2005). Appropriate assessment of neighborhood effects on individual health: integrating random and fixed effects in multilevel logistic regression. *American journal of epidemiology*, *161*(1), 81-88.

Larsen, K., Petersen, J. H., Budtz-Jørgensen, E., & Endahl, L. (2000). Interpreting parameters in the logistic regression model with random effects. *Biometrics*, *56*(3), 909-914.

Lavigne, J. E., Phelps, C. E., Mushlin, A., & Lednar, W. M. (2003). Reductions in individual work productivity associated with type 2 diabetes mellitus. *Pharmacoeconomics*, *21*(15), 1123-1134.

Le Play, F. (1877). *Les ouvriers européens*. Paris: Mame et fils.

Leventhal, T., & Brooks-Gunn, J. (2000). The neighborhoods they live. *Psychological Bulletin, 126* (2), 309–337.

Ley, S. H., Hamdy, O., Mohan, V., & Hu, F. B. (2014). Prevention and management of type 2 diabetes: dietary components and nutritional strategies. *The Lancet*, *383*(9933), 1999-2007.

Leyland, A. H., & Goldstein, H. (2001). *Multilevel modelling of health statistics*. Wiley.

Leynen, F., Moreau, M., Pelfrene, E., Clays, E., De Backer, G. & Kornitzer, M. (2003). Job stress and prevalence of diabetes: results from the Belstress study. *situations*, *2*, 4.

Liberatos, P., Link, B. G. & Kelsey, J. L. (1988). The measurement of social class in epidemiology. Epidemiologic reviews, 10(1), 87-121.

Light, I., Bhachu, P., & Karageorgis, S. (1993). Migration networks and immigrant entrepreneurship. *Immigration and entrepreneurship: Culture, capital, and ethnic networks*, 25-50.

Link, B. G. & Phelan, J. (1995). Social conditions as fundamental causes of disease. *Journal of health and social behavior*, 80-94.

Link, B. G. (2008). Epidemiological sociology and the social shaping of population health. Journal of health and social behavior, 49(4), 367-384.

Lipset, S.M. (1968) Social class. *International Encycolpedia of Social Science and Medicine*, 15, 298-316.

Little, R. J. (1988). A test of missing completely at random for multivariate data with missing values. *Journal of the American statistical Association*, *83*(404), 1198-1202.

Little, R. J., & Rubin, D. B. (2002). Statistical analysis with missing data. John Wiley & Sons. *New York*.

Liu, L., & Núñez, A. E. (2014). Multilevel and urban health modeling of risk factors for diabetes mellitus: a new insight into public health and preventive medicine. *Advances in preventive medicine*, *2014*.

Lochner, K. A., Kawachi, I., Brennan, R. T. & Buka, S. L. (2003). Social capital and neighborhood mortality rates in Chicago. *Social Science & Medicine*, 56(8), 1797-1805.

Loucks, E. B., Rehkopf, D. H., Thurston, R. C., & Kawachi, I. (2007). Socioeconomic disparities in metabolic syndrome differ by gender: evidence from NHANES III. *Annals of epidemiology*, *17*(1), 19-26.

Lovasi, G. S., Hutson, M. A., Guerra, M., & Neckerman, K. M. (2009). Built environments and obesity in disadvantaged populations. *Epidemiologic reviews*, *31*(1), 7-20.

Lucchini, M. & Sarti, S. (2009). Il peso dei fattori ascrittivi ed acquisitivi nelle disuguaglianze di salute: un modello di'Health Attainment'. *Polis*, *23*(1), 57-81.

Lundberg, U. (2005). Stress hormones in health and illness: the roles of work and gender. *Psychoneuroendocrinology*, *30*(10), 1017-1021.

Macintyre, S. & Ellaway, A. (2000). Ecological Approaches: Rediscovering the Role of the Pyshical and Social Environment, in Berkman, L.S. & Kawachi, I. (eds.) *Social Epidemiology*. Oxford University Press.

Macintyre, S. & Ellaway, A. (2003). Neighborhood and Health: An Overview, in Kawachi, I. & Berkman, L. F. (eds.) *Neighborhoods and health*. Oxford University Press.

Macintyre, S. (1997). The black report and beyond what are the issues? *Social science & medicine*, *44*(6), 723-745.

Macintyre, S., Ellaway, A., & Cummins, S. (2002). Place effects on health: how can we conceptualise, operationalise and measure them? *Social science & medicine*, *55*(1), 125-139.

Macintyre, S., Maciver, S., & Sooman, A. (1993). Area, class and health: should we be focusing on places or people? *Journal of social policy*, 22(2), 213-234.

Mackenbach, J. P., Bakker, M. J., Kunst, A. E. & Diderichsen, F. (2002). Socioeconomic inequalities in health in Europe. *Reducing inequalities in health: a European perspective*, 3-24.

Maddatu, J., Anderson-Baucum, E., & Evans-Molina, C. (2017). Smoking and the risk of type 2 diabetes. *Translational Research*, *184*, 101-107.

Majeed, F. A., Martin, D., & Crayford, T. (1996). Deprivation payments to general practitioners: limitations of census data. *BMJ*, *313*(7058), 669-670.

Malik, V. S., Popkin, B. M., Bray, G. A., Després, J. P., Willett, W. C., & Hu, F. B. (2010). Sugar sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. *Diabetes care*.

Mann, C. J. (2003). Observational research methods. Research design II: cohort, cross sectional, and case-control studies. *Emergency medicine journal*, *20*(1), 54-60.

Manson, J. E., Stampfer, M. J., Colditz, G. A., Willett, W. C., Rosner, B., Hennekens, C. H., Speizer, F.E., Rimm, E.B. & Krolewski, A. S. (1991). Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. *The Lancet*, *338*(8770), 774-778.

Mant, J. (2001). Process versus outcome indicators in the assessment of quality of health care. *International Journal for Quality in Health Care*, *13*(6), 475-480.

Marmot, M. & Wilkinson, R.G. (2006). *Social Determinants of Health*. Oxford, UK: Oxford University Press.

Marmot, M. (1996). The social pattern of health and disease. In Blane, D., Brunner, E., Wilkinson, R.G. (eds) Marmot, M. G., Rose, G., Shipley, M. & Hamilton, P. J. (1978). Employment grade and coronary heart disease in British civil servants. *Journal of epidemiology and community health*, 32(4), 244-249.

Marmot, M. G., Shipley, M. J. & Rose, G. (1984). Inequalities in death—specific explanations of a general pattern? *The Lancet*, *323*(8384), 1003-1006.

Marmot, M., G., Rose, G., Shipley, M. & Hamilton, P. J. (1978). Employment grade and coronary heart disease in British civil servants. *Journal of Epidemiology & Community Health*, *32*(4), 244-249.

Martikainen, P., Kauppinen, T. M. & Valkonen, T. (2003). Effects of the characteristics of neighbourhoods and the characteristics of people on cause specific mortality: a register based follow up study of 252 000 men. *Journal of Epidemiology and Community Health*, 57(3), 210-217.

Maruthur, N. M., Tseng, E., Hutfless, S., Wilson, L. M., Suarez-Cuervo, C., Berger, Z., Chu, Y., Iyoha, E., Segal, J.B. & Bolen, S. (2016). Diabetes medications as monotherapy or metformin-based combination therapy for type 2 diabetes: a systematic review and meta-analysis. *Annals of internal medicine*, *164*(11), 740-751.

Massey, D. S. (1996). The age of extremes: Concentrated affluence and poverty in the twenty-first century. *Demography*, *33*(4), 395-412.

Matsuda, A., & Kuzuya, T. (1994). Relationship between obesity and concordance rate for type 2 (non-insulin-dependent) diabetes mellitus among twins. *Diabetes research and clinical practice*, *26*(2), 137-143.

Mayer, S.E. & Jenks, C. (1999). Growing up in poor neighborhoods: How much does it matter? *Science*, 243, 1441–1445.

McEwen, B. S. & Wingfield, J. C. (2003). The concept of allostasis in biology and biomedicine. *Hormones and behavior*, *43*(1), 2-15.

McEwen, B. S., & Stellar, E. (1993). Stress and the individual: mechanisms leading to disease. *Archives of internal medicine*, *153*(18), 2093-2101.

McKeown, T. (1979). *The role of medicine*. Oxford, UK: Blackwell.

McLean, G., Sutton, M., & Guthrie, B. (2006). Deprivation and quality of primary care services: evidence for persistence of the inverse care law from the UK Quality and Outcomes Framework. *Journal of Epidemiology & Community Health*, *60*(11), 917-922.

McMunn, A., Nazroo, J., & Breeze, E. (2008). Inequalities in health at older ages: a longitudinal investigation of the onset of illness and survival effects in England. *Age and ageing*, *38*(2), 181-187.

Meadows, P. (1995). Variation of diabetes mellitus prevalence in general practice and its relation to deprivation. *Diabetic medicine*, *12*(8), 696-700.

Melmed, S., Polonsky, K.S., Larsen, P.R. & Kronenberg, H.M. (2016). *Williams textbook of endocrinology, 13th Edition*. Philadelphia, PA: Elsevier Health Sciences.

Mensing, C., Boucher, J., Cypress, M., Weinger, K., Mulcahy, K., Barta, P., Hosey, G., Kopher, W., Lasichak, A., Lamb, B., Mangan, M., Norman, J., Tanja, J., Yauk, L., Wisdom, K. & Mangan, M. (2007). National standards for diabetes self-management education. *Diabetes care*, *30*(suppl 1), S96-S103.

Merlo, J. (2003). Multilevel analytical approaches in social epidemiology: measures of health variation compared with traditional measures of association. *Journal of Epidemiology and Community Health*, 57, 550-552.

Merlo, J., Chaix, B., Ohlsson, H., Beckman, A., Johnell, K., Hjerpe, P., Råstam, L. & Larsen, K. (2006). A brief conceptual tutorial of multilevel analysis in social epidemiology: using measures of clustering in multilevel logistic regression to investigate contextual phenomena. *Journal of Epidemiology & Community Health*, *60*(4), 290-297.

Merlo, J., Chaix, B., Yang, M., Lynch, J., & Råstam, L. (2005a). A brief conceptual tutorial of multilevel analysis in social epidemiology: linking the statistical concept of clustering to the idea of contextual phenomenon. *Journal of Epidemiology & Community Health*, *59*(6), 443-449.

Merlo, J., Chaix, B., Yang, M., Lynch, J., & Råstam, L. (2005c). A brief conceptual tutorial on multilevel analysis in social epidemiology: interpreting neighbourhood differences and the effect of neighbourhood characteristics on individual health. *Journal of Epidemiology & Community Health*, *59*(12), 1022-1029.

Merlo, J., Östergren, P. O., Hagberg, O., Lindström, M., Lindgren, A., Melander, A., & Berglund, G. (2001). Diastolic blood pressure and area of residence: multilevel versus ecological analysis of social inequity. *Journal of Epidemiology & Community Health*, *55*(11), 791-798.

Merlo, J., Yang, M., Chaix, B., Lynch, J., & Råstam, L. (2005b). A brief conceptual tutorial on multilevel analysis in social epidemiology: investigating contextual phenomena in different groups of people. *Journal of Epidemiology & Community Health*, *59*(9), 729-736.

Mezuk, B., Li, X., Cederin, K., Rice, K., Sundquist, J., & Sundquist, K. (2016). Beyond access: characteristics of the food environment and risk of diabetes. *American journal of epidemiology*, *183*(12), 1129-1137.

Michelozzi, P., Perucci, C., Forastiere, F., Fusco, D., Ancona, A., & Dell'Orco, V. (1999). Differenze sociali nella mortalità a Roma negli anni 1990-1995. *Epidemiologia e Prevenzione*, *23*(1), 230-238.

Milani, S., Cortinovis, I., Rainisio, M., Fognini, G., & Marubini, E. (1983). Structural analysis of a set of socioeconomic indexes as an aid in defining the socioeconomic level of a family: results from an italian multicentric survey. *Social science & medicine*, *17*(12), 803-818.

Millett, C., Gray, J., Saxena, S., Netuveli, G., Khunti, K., & Majeed, A. (2007). Ethnic disparities in diabetes management and pay-for-performance in the UK: the Wandsworth Prospective Diabetes Study. *PLoS medicine*, *4*(6), e191.

Millett, C., Netuveli, G., Saxena, S., & Majeed, A. (2009). Impact of pay for performance on ethnic disparities in intermediate outcomes for diabetes: a longitudinal study. *Diabetes Care*, *32*(3), 404-409.

Mishra, G. D., Ball, K., Dobson, A. J., & Byles, J. E. (2004). Do socioeconomic gradients in women's health widen over time and with age?. *Social science & medicine*, *58*(9), 1585-1595.

Mokdad, A. H., Ford, E. S., Bowman, B. A., Nelson, D. E., Engelgau, M. M., Vinicor, F., & Marks, J. S. (2000). Diabetes trends in the US: 1990-1998. *Diabetes care*, *23*(9), 1278-1283.

Morimoto, A., Tatsumi, Y., Deura, K., Mizuno, S., Ohno, Y., & Watanabe, S. (2013). Impact of cigarette smoking on impaired insulin secretion and insulin resistance in J apanese men: The S aku S tudy. *Journal of diabetes investigation*, *4*(3), 274-280.

Morris, R., & Carstairs, V. (1991). Which deprivation? A comparison of selected deprivation indexes. *Journal of Public Health*, *13*(4), 318-326.

Mugglin, A. S., Carlin, B. P., Zhu, L., & Conlon, E. (1999). Bayesian areal interpolation, estimation, and smoothing: an inferential approach for geographic information systems. *Environment and Planning A*, *31*(8), 1337-1352.

Mulatu, M.S. & Schooler, C. (2002). Casual Connections between Socio-economic Status and Health: Reciprocal Effects and Mediating, *Journal of Health and Social Behavior*, 43(1), 22-41.

Muntaner, C., Borrell, C., Ng, E., Chung, H., Espelt, A., Rodriguez-Sanz, M., Benach, J. & O'Campo, P. (2011). Politics, welfare regimes, and population health: controversies and evidence. *Sociology of health & illness*, *33*(6), 946-964.

Musterd, S. (2005). Social and ethnic segregation in Europe: levels, causes, and effects. *Journal of urban affairs*, *27*(3), 331-348.

National Institute of Health. (2006). One-Third of Adults with Diabetes Still Don't Know They Have It https://www.nih.gov/news-events/news-releases/one-third-adults-diabetes-still-dont-know-they-have-it (last checked, 15/01/2019).

Navarro, V. (eds.). (2007). *Neoliberalism, globalization, and inequalities: Consequences for health and quality of life*. Amityville, NY: Baywood Publishing

NCD Risk Factor Collaboration. (2016). Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4· 4 million participants. *The Lancet*, *387*(10027), 1513-1530.

Newman, B., Selby, J. V., King, M. C., Slemenda, C., Fabsitz, R., & Friedman, G. D. (1987). Concordance for type 2 (non-insulin-dependent) diabetes mellitus in male twins. *Diabetologia*, *30*(10), 763-768.

Ng, D. M. & Jeffery, R. W. (2003). Relationships between perceived stress and health behaviors in a sample of working adults. *Health Psychology*, *22*(6), 638.

Nicolucci, A., Greenfield, S., & Mattke, S. (2006). Selecting indicators for the quality of diabetes care at the health systems level in OECD countries. *International Journal for Quality in Health Care*, *18*(suppl_1), 26-30.

Noble, M., Wright, G., Smith, G., & Dibben, C. (2006). Measuring multiple deprivation at the small-area level. *Environment and planning A*, *38*(1), 169-185.

Norris, S. L., Lau, J., Smith, S. J., Schmid, C. H., & Engelgau, M. M. (2002). Self-management education for adults with type 2 diabetes: a meta-analysis of the effect on glycemic control. *Diabetes care*, *25*(7), 1159-1171.

Northridge, M. E., Sclar, E. D., & Biswas, P. (2003). Sorting out the connections between the built environment and health: a conceptual framework for navigating pathways and planning healthy cities. *Journal of Urban Health*, *80*(4), 556-568.

Novotny, T. E., Warner, K. E., Kendrick, J. S. & Remington, P. L. (1988). Smoking by blacks and whites: socioeconomic and demographic differences. *American journal of public health*, *78*(9), 1187-1189.

Nussbaum, M. (2003). Capabilities as fundamental entitlements: Sen and social justice. *Feminist economics*, 9(2-3), 33-59.

Nuttall, F. Q. (2015). Body mass index: obesity, BMI, and health: a critical review. *Nutrition today*, *50*(3), 117.

Nyberg, S. T., Fransson, E. I., Heikkilä, K., Ahola, K., Alfredsson, L., Bjorner, J. B., ... & Hamer, M. (2014). Job strain as a risk factor for type 2 diabetes: a pooled analysis of 124,808 men and women. *Diabetes care*, *37*(8), 2268-2275.

Omran, A. R. (2005). The epidemiologic transition: a theory of the epidemiology of population change. *The Milbank Quarterly*, *83*(4), 731-757.

Pampalon, R., & Raymond, G. (2000). A deprivation index for health and welfare planning in Quebec. *Chronic Dis Can*, *21*(3), 104-113.

Pan American Health Organization. (2013). Half of people who have diabetes don't know it https://www.paho.org/hq/index.php?option=com_content&view=article&id=9157:2013-half-people-who-have-diabetes-dont-know-it&Itemid=1926&lang=en (last checked, 15/01/2019).

Pan, A., Wang, Y., Talaei, M., Hu, F. B., & Wu, T. (2015). Relation of active, passive, and quitting smoking with incident type 2 diabetes: a systematic review and meta-analysis. *The lancet Diabetes & endocrinology*, *3*(12), 958-967.

Pappas, G., Queen, S., Hadden, W. & Fisher, G. (1993). The increasing disparity in mortality between socioeconomic groups in the United States, 1960 and 1986. *New England journal of medicine*, 329(2), 103-109.

Pasala, S. K., Rao, A. A. & Sridhar, G. R. (2010). Built environment and diabetes. *International Journal of Diabetes in developing countries*, *30*(2), 63.

Peacock, M., Bissell, P. & Owen, J. (2014). Dependency denied: health inequalities in the neo-liberal era. *Social Science & Medicine*, 118, 173-180.

Pearce, N. (1996). Traditional epidemiology, modern epidemiology, and public health. *American journal of public health*, *86*(5), 678-683.

Petsimeris, P., & Rimoldi, S. (2015). Socio-economic divisions of space in Milan in the post-Fordist era. In *Socio-Economic Segregation in European Capital Cities* (pp. 210-237). Routledge. In Van Ham, M., Marcińczak, S., Tammaru, T., & Musterd, S. (2015). *Socio-Economic Segregation in European Capital Cities: East Meets West*. Taylor & Francis.

Phelan, J. C., Link, B. G. & Tehranifar, P. (2010). Social conditions as fundamental causes of health inequalities: theory, evidence, and policy implications. *Journal of health and social behavior*, *51*(1_suppl), S28-S40.

Pickett, K. E. & Pearl, M. (2001). Multilevel analyses of neighbourhood socioeconomic context and health outcomes: a critical review. *Journal of Epidemiology & Community Health*, *55*(2), 111-122.

Pickett, K. E. & Wilkinson, R. G. (2015). Income inequality and health: a causal review. *Social science & medicine*, *128*, 316-326.

Pickett, K. E., Kelly, S., Brunner, E., Lobstein, T., & Wilkinson, R. G. (2005). Wider income gaps, wider waistbands? An ecological study of obesity and income inequality. *Journal of Epidemiology & Community Health*, *59*(8), 670-674.

Pociot, F., & Lernmark, Å. (2016). Genetic risk factors for type 1 diabetes. *The Lancet*, *387*(10035), 2331-2339.

Poortinga, W. (2006). Perceptions of the environment, physical activity, and obesity. *Social science & medicine*, *63*(11), 2835-2846.

Popkin, B. M. (1999). Urbanization, lifestyle changes and the nutrition transition. *World development*, *27*(11), 1905-1916.

Porta, M. (eds.) (2014). *A dictionary of epidemiology (6th ed.)*. New York: Oxford University Press.

Porter, R. (1997). *The greatest benefit to mankind: A medical history of humanity*. New York: Norton.

Portes, A. (1998). Social capital: Its origins and applications in modern sociology. *Annual review of sociology*, *24*(1), 1-24.

Powell, C. K., Hill, E. G. & Clancy, D. E. (2007). The relationship between health literacy and diabetes knowledge and readiness to take health actions. *The diabetes educator*, *33*(1), 144-151.

Powell, K. (2007). The two faces of fat. *Nature*, 447, 525-527.

Prentice, A. M. (2005). The emerging epidemic of obesity in developing countries. *International journal of epidemiology*, *35*(1), 93-99.

Putnam, R.D. (1993), *Making democracy work: Civic traditions in modern Italy*. Princeton: Princeton University Press.

Putnam, R.D. (2000), *Bowling alone: The collapse and revival of American* community. New York: Simon & Schuster.

Qiao, Q., & Nyamdorj, R. (2010). Is the association of type II diabetes with waist circumference or waist-to-hip ratio stronger than that with body mass index?. *European journal of clinical nutrition*, *64*(1), 30.

Rachele, J. N., Giles-Corti, B., & Turrell, G. (2016). Neighbourhood disadvantage and self-reported type 2 diabetes, heart disease and comorbidity: a cross-sectional multilevel study. *Annals of epidemiology*, *26*(2), 146-150.

Rajagopalan, S. & Brook, R. D. (2012). Air pollution and type 2 diabetes: mechanistic insights. *Diabetes*, *61*(12), 3037-3045.

Dzhambov, A. M. (2015). Long-term noise exposure and the risk for type 2 diabetes: a meta-analysis. *Noise & health*, *17*(74), 23.

Ratzan, S. C. & Parker, R. M. (2006). Health literacy - identification and response. *Journal of Health Communication*, 11, 713-715.

Raudenbush, S. W., & Bryk, A. S. (2002). *Hierarchical linear models: Applications and data analysis methods*. 2nd ed. Newbury Park, CA: Sage.

Rebolledo, J. A. & Arellano, R. (2016). Cultural differences and considerations when initiating insulin. *Diabetes Spectrum*, 29(3), 185-190.

Regione Lombardia (2017). Governo della domanda: avvio della presa in carico di pazienti cronici e fragili. Determinazioni in attuazione dell'art. 9 della legge n. 23/2015. http://www.regione.lombardia.it/wps/portal/istituzionale/HP/DettaglioRedazionale/servizi-e-informazioni/Enti-e-Operatori/sistema-welfare/attuazione-della-riforma-sociosanitaria-lombarda/avvio-presa-carico-pazienti-cronici-fragili/dgr2017-6164-avvio-presa-carico-pazienti-cronici-fragili

Registrar General (1913). *Registrar General's 74th annual report, 1911*. London: Registrar General Office.

Reijneveld, S. A., Verheij, R. A., & de Bakker, D. H. (2000). The impact of area deprivation on differences in health: does the choice of the geographical classification matter?. *Journal of Epidemiology & Community Health*, *54*(4), 306-313.

Renalds, A., Smith, T. H. & Hale, P. J. (2010). A systematic review of built environment and health. *Family & community health*, *33*(1), 68-78.

Renzaho, A. M. (2004). Fat, rich and beautiful: changing socio-cultural paradigms associated with obesity risk, nutritional status and refugee children from sub-Saharan Africa. *Health & place*, *10*(1), 105-113.

Rewers, M., & Ludvigsson, J. (2016). Environmental risk factors for type 1 diabetes. *The Lancet*, *387*(10035), 2340-2348.

Ricci-Cabello, I., Ruiz-Perez, I., De Labry-Lima, A. O., & Marquez-Calderon, S. (2010). Do social inequalities exist in terms of the prevention, diagnosis, treatment, control and monitoring of diabetes? A systematic review. *Health & social care in the community*, *18*(6), 572-587.

Richards, J. M. (1996). Units of analysis, measurement theory, and environmental assessment: A response and clarification. *Environment and Behavior*, 28(2), 220-236.

Richardson, E. A., Pearce, J., Mitchell, R. & Kingham, S. (2013). Role of physical activity in the relationship between urban green space and health. *Public health*, *127*(4), 318-324.

Riddle, M. C., & Herman, W. H. (2018). The cost of diabetes care—an elephant in the room. *Diabetes care*, *41*(5), 929-932.

Riley, M. W. (1963). *Special problems of sociological analysis. Sociological research I: a case approach*. New York, NY: Harcourt, Brace & World Inc; 1963:700-725.

Ripsin, C. M., Kang, H., & Urban, R. J. (2009). Management of blood glucose in type 2 diabetes mellitus. *Am Fam Physician*, *79*(1), 29-36.

Risérus, U., Willett, W. C., & Hu, F. B. (2009). Dietary fats and prevention of type 2 diabetes. *Progress in lipid research*, *48*(1), 44-51.

Robbins, J. M., Vaccarino, V., Zhang, H., & Kasl, S. V. (2005). Socioeconomic status and diagnosed diabetes incidence. *Diabetes research and clinical practice*, *68*(3), 230-236.

Roberts, E.M. (1997). Neighbourhood social environments and the distribution of low birthweight in Chicago. *American Journal of Public Health*, 87, 597-603.

Robinson, W. S. (1950). Ecological correlations and the behavior of individuals. *American Sociological Review,* 15, 351-357.

Roper, N. A., Bilous, R. W., Kelly, W. F., Unwin, N. C., & Connolly, V. M. (2002). Cause-specific mortality in a population with diabetes: South Tees Diabetes Mortality Study. *Diabetes care*, *25*(1), 43-48.

Rose, G. (1992). *The strategy of preventive medicine*. Oxford, England: Oxford University.

Rosen, G. (1979). The Evolution of Social Medicine, in Freeman, H., Levine, S., Reeder, L. (eds.) *The Handbook of Medical Sociology*, 3rd ed. Englewood Cliffs, NJ: Prentice Hall.

Rosenquist, J. N., Murabito, J., Fowler, J. H. & Christakis, N. A. (2010). The spread of alcohol consumption behavior in a large social network. *Annals of internal medicine*, *152*(7), 426-433.

Rosenthal, M. B., Zaslavsky, A., & Newhouse, J. P. (2005). The geographic distribution of physicians revisited. *Health services research*, *40*(6p1), 1931-1952.

Ross, C. E. & Mirowsky, J. (1999). Refining the association between education and health: the effects of quantity, credential, and selectivity. *Demography*, *36*(4), 445-460.

Ross, C. E., & Mirowsky, J. (2001). Neighborhood disadvantage, disorder, and health. *Journal of health and social behavior*, 258-276.

Rowntree, S.B. (1901): *Poverty: a study of townlife*. London: Macmillan.

Sakellariou, D. & Rotarou, E. S. (2017). The effects of neoliberal policies on access to healthcare for people with disabilities. *International journal for equity in health*, *16*(1), 199.

Salmerón, J., Ascherio, A., Rimm, E. B., Colditz, G. A., Spiegelman, D., Jenkins, D. J., Stampfer, M.D., Wing, A.L. & Willett, W. C. (1997a). Dietary fiber, glycemic load, and risk of NIDDM in men. *Diabetes care*, *20*(4), 545-550.

Salmeron, J., Manson, J. E., Stampfer, M. J., Colditz, G. A., Wing, A. L., & Willett, W. C. (1997b). Dietary fiber, glycemic load, and risk of non—insulin-dependent diabetes mellitus in women. *Jama*, *277*(6), 472-477.

Sampson, R. J. (2001). How do Communities Undergrid or Undermine Human Development? Relevant Contexts and Social Mechanisms, in Booth, A., & Crouter, A. (eds.) *Does it take a village? Community effects on children, adolescents and families*. London/Mahwah: N. J. Lawrence Erlbaum Publishers.

Sampson, R. J., Morenoff, J. D. & Gannon-Rowley, T. (2002). Assessing "neighborhood effects": Social processes and new directions in research. *Annual review of sociology*, *28*(1), 443-478.

Sampson, R.J., Raudenbush, S.W. & Earls, F. (1997). Neighbourhoods and violent crime: a multilevel study of collective efficacy. *Science*, 277, 918-924.

Sarti, S., Della Bella, S., Lucchini, M. & Tognetti Bordogna, M. (2011). Le disuguaglianze sociali nella salute: una riflessione sulle basi dati e sugli indicatori attualmente impiegati in letteratura. *Rassegna Italiana di Sociologia*, *52*(4), 681-702.

Sastry, N., Pebley, A. R. & Zonta, M. (2002). Neighborhood Definitions and the Spatial Dimension of Daily Life in Los Angeles. California Center for Population Research On-Line Working Paper Series.

Sayeed, M. A., Ali, L., Hussain, M. Z., Rumi, M. A., Banu, A., & Khan, A. A. (1997). Effect of socioeconomic risk factors on the difference in prevalence of diabetes between rural and urban populations in Bangladesh. *Diabetes care*, *20*(4), 551-555.

Scheuch, E. (1969). Social context and individual behavior. In Dogan, M. & Rokkam, S. (eds.*) Quantitative ecological analyses in the social science*. Cambridge, MA: MIT Press.

Schillinger, D., Grumbach, K., Piette, J., Wang, F., Osmond, D., Daher, C., Palacios, J., Sullivan, G. D. & Bindman, A. B. (2002). Association of health literacy with diabetes outcomes. *Jama*, *288*(4), 475-482.

Schizzerotto, A. (1990). *Classi sociali e società contemporanea*. Milano: Franco Angeli.

Schmidt, M. I., Duncan, B. B., Canani, L. H., Karohl, C., & Chambless, L. (1992). Association of waist-hip ratio with diabetes mellitus: strength and possible modifiers. *Diabetes care*, *15*(7), 912-914.

Schneiders, J., Telo, G. H., Bottino, L. G., Pasinato, B., Neyeloff, J. L., & Schaan, B. D. (2019). Quality indicators in type 2 diabetes patient care: analysis per care-complexity level. *Diabetology & metabolic syndrome*, *11*(1), 34.

Schwartz, S. (1994). The fallacy of the ecological fallacy: the potential misuse of a concept and the consequences. *American journal of public health*, 84(5), 819-824.

Sedentary Behaviour Research Network (2012). Letter to the Editor: Standardized use of the terms" sedentary" and" sedentary behaviours". *Applied Physiology Nutrition and Metabolism-Physiologie Appliquee Nutrition Et Metabolisme*, *37*(3), 540-542.

Selvin, H. C. (1958). Durkheim's suicide and problems of empirical research. *American journal of sociology*, 63(6), 607-619.

Sen, A. K. (1983). Poor, relatively speaking. *Oxford economic papers*, *35*(2), 153-169.

Sen, A. K. (1985). *Commodities and Capabilities*. Amsterdam: North-Holland.

Sen, A. K. (1977). Rational fools: A critique of the behavioral foundations of economic theory. *Philosophy & Public Affairs*, 317-344.

Sen, A.K. (1992). Inequality, Re-Examined. Cambridge, MA: USA-Harvard University Press.

Sen, A.K. (1993) Capability and Well-being, in Nussbaum, M.C. & SEN, A.K. (eds.) *The Quality of Life*. Oxford: Clarendon Press.

Senior, M., & Viveash, B. (1998). *Health and illness*. London: Macmillan.

Shaw, M., Tunstall, H. & Dorling, D. (2005). Increasing inequalities in risk of murder in Britain: trends in the demographic and spatial distribution of murder, 1981-2000. *Health and Place*, 11, 45-54.

Siegrist, J. (1996). Adverse health effects of high-effort/low-reward conditions. *Journal of occupational health psychology*, *1*(1), 27.

Siegrist, J., & Marmot, M. (2004). Health inequalities and the psychosocial environment—two scientific challenges. *Social science & medicine*, *58*(8), 1463-1473.

Singer, J. D. (1998). Using SAS PROC MIXED to fit multilevel models, hierarchical models, and individual growth models. *Journal of educational and behavioral statistics*, *23*(4), 323-355.

Singh-Manoux, A., Clarke, P. & Marmot, M. (2002). Multiple measures of socio-economic position and psychosocial health: proximal and distal measures. *International Journal of Epidemiology*, *31*(6), 1192-1199.

Sloggett, A. & Joshi, H. (1998) Deprivation indicators as predictors of life events, 1981-1992, based on the UK ONS longitudinal study. *Journal of Epidemiology and Community Health*, 52, 228-233.

Small, M. L. & Newman, K. (2001). Urban poverty after the truly disadvantaged: The rediscovery of the family, the neighborhood, and culture. *Annual Review of sociology*, *27*(1), 23-45.

Smith, B. T., Lynch, J. W., Fox, C. S., Harper, S., Abrahamowicz, M., Almeida, N. D., & Loucks, E. B. (2011). Life-course socioeconomic position and type 2 diabetes mellitus: The Framingham Offspring Study. *American Journal of Epidemiology*, *173*(4), 438-447.

Smith, G. D., Bartley, M. & Blane, D. (1990). The Black report on socioeconomic inequalities in health 10 years on. *BMJ: British Medical Journal*, *301*(6748), 373.

Snijders, T. A. B., & Bosker, R. J. (1999). *Multilevel analysis: an introduction to basic and advanced multilevel modelling.* 1st ed. Thousand Oaks, CA: Sage.

Snow, J. (1855). *On the mode of communication of cholera.* London: John Churchill.

Solar, O. & Irwin, A. (2010) A conceptual framework for action on the social determinants of health. Social Determinants of Health Discussion Paper 2 (Policy and Practice). Geneve: World Health Organization.

Sommers, T. & Rosenberg, A. (2003). Darwin's nihilistic idea: evolution and the meaninglessness of life. *Biology and Philosophy*, 18(5), 653-668.

Sommet, N., & Morselli, D. (2017). Keep calm and learn multilevel logistic modeling: A simplified three-step procedure using Stata, R, Mplus, and SPSS. *International Review of Social Psychology*, *30*(1).

Song, L., Shen, L., Li, H., Liu, B., Zheng, X., Zhang, L., Xu, S. & Wang, Y. (2017). Socio-economic status and risk of gestational diabetes mellitus among Chinese women. *Diabetic Medicine*, *34*(10), 1421-1427.

Stafford, M. & McCarthy, M. (2006). Neighbourhoods, housing, and health, in Marmot, M. & Wilkinson, R.G. (eds.) *Social Determinants of Health*. Oxford, UK: Oxford University Press.

Stafford, M., Bartley, M., Boreham, R., Thomas, R., Wilkinson, R. & Marmot, M. (2004). Neighbourhood social cohesion and health: investigating associations and possible mechanisms. In Morgan, A. & Swann, C. (eds.) Social capital for health. Issues of definition, measurement and links to health. London: Health Development Agency.

Steck, A. K., & Rewers, M. J. (2011). Genetics of type 1 diabetes. *Clinical chemistry*, *57*(2), 176-185.

Steele, F. (2008). Module 5: Introduction to multilevel modelling concepts. *LEMMA (Learning Environment for Multilevel Methodology and Applications), Centre for Multilevel Modelling, University of Bristol*.

Steele, F. (2009). Module 7: Multilevel Models for Binary Responses: Concepts. *Multilevel models for binary responses. Bristol: Center for Multilevel Modelling*.

Stockdale, S. E., Wells, K. B., Tang, L., Belin, T. R., Zhang, L. & Sherbourne, C. D. (2007). The importance of social context: neighborhood stressors, stress-buffering mechanisms, and alcohol, drug, and mental health disorders. *Social science & medicine*, *65*(9), 1867-1881.

Stratton, I. M., Adler, A. I., Neil, H. A. W., Matthews, D. R., Manley, S. E., Cull, C. A., Hadden, D., Turner, R.C., & Holman, R. R. (2000). Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *Bmj*, *321*(7258), 405-412.

Stringhini, S., Batty, G. D., Bovet, P., Shipley, M. J., Marmot, M. G., Kumari, M., ... & Kivimäki, M. (2013). Association of lifecourse socioeconomic status with chronic inflammation and type 2 diabetes risk: the Whitehall II prospective cohort study. *PLoS medicine*, *10*(7), e1001479.

Stringhini, S., Zaninotto, P., Kumari, M., Kivimäki, M., & Batty, G. D. (2016). Lifecourse socioeconomic status and type 2 diabetes: the role of chronic inflammation in the English Longitudinal Study of Ageing. *Scientific reports*, *6*, 24780.

Subramanian, S. V., Jones, K., & Duncan, C. (2003). *Multilevel methods for public health research* (pp. 65-111), in Kawachi, I. & Berkman, L. F. (eds.) *Neighborhoods and health*. Oxford University Press.

Subramian, S. V., Jones, K. & Duncan, C. (2003). Multilevel methods for public health research, in Kawachi, I. & Berkman, L. F. (eds.) *Neighborhoods and health*. Oxford University Press.

Susser, M. & Susser, E. (1996a). Choosing a future for epidemiology: I. Eras and paradigms. *American Journal of Public Health*, 86(5), 668-673.

Susser, M. & Susser, E. (1996b). Choosing a future for epidemiology: II. From black box to Chinese boxes and eco-epidemiology. *American Journal of Public Health*, 86(5), 674-677.

Susser, M. (1973). *Causal thinking in the health sciences: concepts and strategies in epidemiology*. New York: Oxford Press.

Swinburn, B. A., Sacks, G., Hall, K. D., McPherson, K., Finegood, D. T., Moodie, M. L., & Gortmaker, S. L. (2011). The global obesity pandemic: shaped by global drivers and local environments. *The Lancet*, *378*(9793), 804-814.

Szreter, S. & Woolcock, M. (2004). Health by association? Social capital, social theory, and the political economy of public health. *International journal of epidemiology*, *33*(4), 650-667.

Talbot, R. J. (1991). Underprivileged areas and health care planning: implications of use of Jarman indicators of urban deprivation. *BMJ*, *302*(6773), 383-386.

Tang, M., Chen, Y., & Krewski, D. (2003). Gender-related differences in the association between socioeconomic status and self-reported diabetes. *International Journal of Epidemiology*, *32*(3), 381-385.x

Taylor, W. C., Poston, W. S. C., Jones, L. & Kraft, M. K. (2006). Environmental justice: obesity, physical activity, and healthy eating. *Journal of Physical Activity and Health*, *3*(s1), S30-S54.

Tello, J. E., Jones, J., Bonizzato, P., Mazzi, M., Amaddeo, F., & Tansella, M. (2005). A census-based socio-economic status (SES) index as a tool to examine the relationship between mental health services use and deprivation. *Social science & medicine*, *61*(10), 2096-2105.

Terraneo, M. (2018). *La salute negata: le sfide dell'equità in prospettiva sociologica*. Milano: FrancoAngeli.

Testi, A., & Ivaldi, E. (2005). Una proposta di indicatore di deprivazione. *Politiche sanitarie*, *6*(2), 67-77.

Thomas, D., Elliott, E. J., & Naughton, G. A. (2006). Exercise for type 2 diabetes mellitus. *Cochrane database of systematic reviews*, (3).

Thorp, A. A., Kingwell, B. A., Owen, N., & Dunstan, D. W. (2014). Breaking up workplace sitting time with intermittent standing bouts improves fatigue and musculoskeletal discomfort in overweight/obese office workers. *Occup Environ Med*, *71*(11), 765-771.

Tienda, M. (1991). Poor People and Poor places: Deciphering Neighborhood Effects on Poverty Outcomes. In Huber, J. (eds.) *Macro-Micro Linkages in Sociology*, 244-62. London: Sage.

Timmermans, S., & Haas, S. (2008). Towards a sociology of disease. *Sociology of health & illness*, *30*(5), 659-676.

Titmuss, R. (1938). *Poverty and population*. London: Macmillan.

Touma, C., & Pannain, S. (2011). Does lack of sleep cause diabetes. *Cleveland Clinical Journal of Medicine*, *78*(8), 549-58.

Townsend, P. (1987). Deprivation. *Journal of social policy*, *16*(2), 125-146.

Tunceli, K., Bradley, C. J., Nerenz, D., Williams, L. K., Pladevall, M., & Lafata, J. E. (2005). The impact of diabetes on employment and work productivity. *Diabetes care*, *28*(11), 2662-2667.

Turner, R. C., & Holman, R. R. (1995). Lessons from UK prospective diabetes study. *Diabetes research and clinical practice*, *28*, S151-S157.

Turner, R. C., & Holman, R. R. (1996). The UK prospective diabetes study. *Annals of medicine*, *28*(5), 439-444.

United Nations, Department of Economic and Social Affairs, Population Division (2017). World Population Prospects: The 2017 Revision. New York: United Nations.

United Nations, Department of Economic and Social Affairs, Population Division (2018). World Urbanization Prospects: The 2018 Revision. New York: United Nations.

Vaghela, P., Ashworth, M., Schofield, P., & Gulliford, M. C. (2009). Population intermediate outcomes of diabetes under pay-for-performance incentives in England from 2004 to 2008. *Diabetes care*, *32*(3), 427-429.

Valerio, M., & Vitullo, F. (2000). Sperimentazione di un indice di svantaggio sociale in Basilicata. *Epidemiologia e Prevenzione*, *24*, 315-26.

Valkonen T. (1969). Individual and structural effects in ecological research. In Dogan, M. & Rokkam, S. (eds.) *Quantitative ecological analyses in the social science*. Cambridge, MA: MIT Press.

Van der Heide, I., Wang, J., Droomers, M., Spreeuwenberg, P., Rademakers, J. & Uiters, E. (2013). The relationship between health, education, and health literacy: results from the Dutch Adult Literacy and Life Skills Survey. *Journal of health communication*, *18*(sup1), 172-184.

van Dieren, S., Beulens, J. W., Yvonne T. van der, S., Grobbee, D. E., & Nealb, B. (2010). The global burden of diabetes and its complications: an emerging pandemic. *European Journal of Cardiovascular Prevention & Rehabilitation*, *17*(1_suppl), s3-s8.

Van Ham, M., Manley, D., Bailey, N., Simpson, L. & Maclennan, D. (eds.) (2012). *Neighbourhood effects research: New perspectives*. Dordrecht, NL: Springer.

Villermé, L.R. (1830). De la mortalité dans divers quarters de la ville de Paris. *Annales d'hygiene publique*, 3, 294-341.

Villermé, L.R. (1840). *Tableau de l'état physique et moral des ouvriers employés dans les manufactures de coton, de laine et de soie*. Paris: Jules Renouard et Compagnie.

Virchow, R. (1848a). Report on the thypus epidemic in Upper Silesia. In Rather, L.J. (eds.), *Rudolph Virchow: collected essays on public health and epidemiology*. Canton, MA: Science History, 1, 205-20.

Virchow, R. (1848b). The public health service. *Medizinische Reform*, 5, 21-22.

Vitale, M., Masulli, M., Turco, A., Ciano, O., Riccardi, G., Rivellese, A. A. & Vaccaro, O. (2013). Abitudini alimentari dei pazienti con diabete di tipo 2: impatto delle tradizioni gastronomiche regionali. *G It Diabetol Metab*, *33*, 135-140.

Von Korff, M., Koepsell, T., Curry, S. & Diehr, P. (1992). Multi-level analysis in epidemiologic research on health behaviors and outcomes. *American Journal of Epidemiology*, *135*(10), 1077-1082.

Walby, S. (2003). *Gender transformations*. Routledge.

Waller, L. A., & Gotway, C. A. (2004). *Applied spatial statistics for public health data* (Vol. 368). John Wiley & Sons.

Ware, J.E., Kosinski, M. & Keller, S. D. (1994). *SF-36 physical and mental health summary scales: a User's Manual*. Boston, MA: Health Assessment Lab.

Ware, J.E., Kosinski, M., & Keller, S. D. (1996). A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Medical care*, *34*(3), 220-233.

Wareham, N. J., & O'Rahilly, S. (1998). The changing classification and diagnosis of diabetes: new classification is based on pathogenesis, not insulin dependence. *BMJ: British Medical Journal*, *317*(7155), 359.

Weber, M. (1946). Class, status and party. In Gerth, H. & Mills, C.W. (eds.) *From Max Weber: essays in sociology*. New York: Oxford University Press,

Weber, M. (2015). The Distribution of Power Within the Gemeinschaft: Classes, Stände, Parties. In Waters, T. & Waters, D (eds.) *Weber's Rationalism and Modern Society: New Translations on Politics, Bureaucracy and Social Stratification.* New Tork: Palgrave Macmillan.

Weitzman, E.R. & Kawachi, I. (2000). Giving means receiving: the protective effect of social capital on binge drinking on college campuses. *American Journal of Public Health*, 90, 1936-1939.

Wells, B. L., & Horm, J. W. (1998). Targeting the underserved for breast and cervical cancer screening: the utility of ecological analysis using the National Health Interview Survey. *American Journal of Public Health*, *88*(10), 1484-1489.

Whitehead, M. (1991). The concepts and principles of equity and health. *Health promotion international*, *6*(3), 217-228.

World Health Organization (1948). World Health Organization Constitution. Geneva: World Health Organization.

World Health Organization. (2002). Integrating gender perspectives in the work of WHO: WHO gender policy. Geneva: World Health Organization.

Wilkinson, R. & Pickett, K. (2010). *The spirit level*. *Why equality is better for everyone*. London: Penguin.

Wilkinson, R. G. (1976). Dear David Ennals, *New Society*, 38, 567-8.

Wilkinson, R. G., & Marmot, M. (eds.). (2003). *Social determinants of health: the solid facts*. Geneve: World Health Organization.

Willi, C., Bodenmann, P., Ghali, W. A., Faris, P. D., & Cornuz, J. (2007). Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. *Jama*, *298*(22), 2654-2664.

Williams, D. R. (1999). Race, socioeconomic status, and health the added effects of racism and discrimination. *Annals of the New York Academy of Sciences*, *896*(1), 173-188.

Williams, D. R., Mohammed, S. A., Leavell, J., & Collins, C. (2010). Race, socioeconomic status, and health: complexities, ongoing challenges, and research opportunities. *Annals of the New York Academy of Sciences*, *1186*(1), 69-101.

Wilson, W. J. (1987). *The truly disadvantaged: The inner city, the underclass, and public policy*. Chicago, IL: University of Chicago Press.

Wong, E., Backholer, K., Gearon, E., Harding, J., Freak-Poli, R., Stevenson, C., & Peeters, A. (2013). Diabetes and risk of physical disability in adults: a systematic review and meta-analysis. *The lancet Diabetes & endocrinology*, *1*(2), 106-114.

World Health Organization. (1999). *Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Part 1, Diagnosis and classification of diabetes mellitus* (No. WHO/NCD/NCS/99.2). Geneva: World health organization.

World Health Organization. (2006). Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation.

World Health Organization. (2010). *Global recommendations on physical activity for health*. Geneva: World health organization.

World Health Organization. (2016a). Life expectancy increased by 5 years since 2000, but health inequalities persist. *World Health Statistics*.

World Health Organization. (2016b). *Global report on diabetes*. Geneva: World Health Organization.

World Health Organization. (2018). Diabetes. Key facts. https://www.who.int/news-room/fact-sheets/detail/diabetes (last checked, 15/01/2019).

Wright, E. O. (1979). Class structure and income determination. New York: Academic Press.

Wright, E. O. (1995). The class analysis of poverty. *International Journal of Health Services*, *25*(1), 85-100.

Wright, E. O., Costello, C., Hachen, D. & Sprague, J. (1982). The American class structure. *American Sociological Review*, 709-726.

Wynder, E. L. & Graham, E. A. (1950). Tobacco smoking as a possible etiologic factor in bronchiogenic carcinoma: A study of six hundred and eighty-four proved cases. *Journal of the American Medical Association*, 143, 329-36.

Xu, F., Yin, X. M., Zhang, M., Leslie, E., Ware, R., & Owen, N. (2006). Family average income and diagnosed type 2 diabetes in urban and rural residents in regional mainland China. *Diabetic Medicine*, *23*(11), 1239-1246.

Yankauer, A. (1950). The relationship of fetal and infant mortality to residential segregation: an inquiry into social epidemiology. *American Sociological Review*, *15*(5), 644-648.

Young, T. K., Martens, P. J., Taback, S. P., Sellers, E. A., Dean, H. J., Cheang, M. & Flett, B. (2002). Type 2 diabetes mellitus in children: prenatal and early infancy risk factors among native Canadians. *Archives of pediatrics & adolescent medicine*, 156(7), 651-655.

Young-Hyman, D., De Groot, M., Hill-Briggs, F., Gonzalez, J. S., Hood, K., & Peyrot, M. (2016). Psychosocial care for people with diabetes: a position statement of the American Diabetes Association. *Diabetes care*, *39*(12), 2126-2140.

Yu, O. H. Y., & Suissa, S. (2016). Identifying causes for excess mortality in patients with diabetes: closer but not there yet. *Diabetes care*, *39*(11), 1851-1853.

Yun, J. E., Kimm, H., Choi, Y. J., Jee, S. H., & Huh, K. B. (2012). Smoking is associated with abdominal obesity, not overall obesity, in men with type 2 diabetes. *Journal of Preventive Medicine and Public Health*, *45*(5), 316.

Zimbardo, P. G. & Boyd, J. N. (2015). Putting time in perspective: A valid, reliable individual-differences metric. In *Time perspective theory; review, research and application* (pp. 17-55). Springer, Cham.

Zimmet, P. (2000). Globalization, coca-colonization and the chronic disease epidemic: can the Doomsday scenario be averted? *Journal of internal medicine*, *247*(3), 301-310.

Zimmet, P. Z. (2017). Diabetes and its drivers: the largest epidemic in human history?. *Clinical diabetes and endocrinology*, *3*(1), 1.

Zimmet, P., Alberti, K. G. M. M., & Shaw, J. (2001). Global and societal implications of the diabetes epidemic. *Nature*, *414*(6865), 782.