Cancer by migrant background in Belgium

Van Hemelrijck, Wanda

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Chapter 1

General introduction

1.1 Focus and relevance of the dissertation

Cancer is a growing health issue that caused about one in every six deaths worldwide and was the second leading cause of death in highly-industrialised countries in 2018 (after cardiovascular diseases) [1]. Although substantial improvements in cancer survival have been made globally in the last decades, the burden of cancer is expected to increase in the future due to population ageing and a growing prevalence of a number of lifestyle-related risk factors for this disease [2]. Of the expanding group of people diagnosed throughout their lifetime, there will be an increasing share of people with migrant background in Europe: migration to and within Europe since the second World War (WW) implies that migrants and their offspring are now reaching ages with a higher risk of health problems including cancer. Yet, research has demonstrated lower all-cause and cancer mortality despite poorer self-rated and physical health at adult ages for many migrant groups in Europe [3,4]. The knowledge on differences in mortality, risk, and survival for a wide range of cancers between migrants and non-migrants in Europe is growing [5–10], but our understanding of how these differences come about and our knowledge of how they change with time is limited to date. Partially due to data limitations, studies on differential patterns in cancer mortality, incidence and survival have, for example, not fully understood the importance of duration of stay of migrants or changes over migrant generations [11,12]. Moreover, studies accounting for socioeconomic position (SEP) usually do so with aggregated rather than individual measures [8,13–15], and analyses of risk and survival are rarely combined [5,6,9].

To help fill these gaps in knowledge, this dissertation focuses on cancer mortality, incidence, and survival by migrant background and its determinants during the early 2000s. It is based on nationwide data for Belgium, a country that is subject to population ageing and has about 20% of individuals with migrant background in its population, thus constituting a diverse and high-risk setting for cancer. The main study

objectives of this dissertation are *(1) to analyse site-specific cancer mortality, incidence, and survival for native Belgian adults as well as those from the largest migrant background groups residing in Belgium; and (2) to examine determinants for the outcomes observed by breaking down findings into generational status and duration of stay in Belgium, and by adjusting for SEP, demographic traits, and tumour stage at diagnosis*.

The following two research questions are at the core of this work:

RQ1. *Are there differences in site-specific cancer mortality, incidence, and survival between migrant background groups and native Belgians, and, if so in what way and to what extent?*

RQ2. *How can potential differences in outcomes between migrant and non-migrant origin groups, as well as within migrant origin groups, be explained?*

Knowing how cancer outcomes differ by migrant background and how they change over time and generations can be used to infer the importance of external influences (e.g. lifestyle, environmental exposure) versus inherited susceptibility in cancer aetiology and prognosis [12,16,17]. For starters, migrants' cancer mortality, incidence, and survival on arrival in the country of destination can reflect differences in underlying risk and prognostic factors in the origin country. When outcomes furthermore change with time or for migrant offspring in the country of destination, this is suggestive of the role of external factors in the risk and prognosis of a particular cancer, whereas stable patterns across migrant generations point to genetic mechanisms [12,16,17]. Examining how SEP, demographic, and tumour traits such as stage at diagnosis, contribute to these differences adds to our understanding of how cancer discrepancies come about and what can be done to prevent them.

Insight in site-specific cancer mortality, incidence, and survival differences between Belgian native and migrant background groups is also necessary to point to areas for

policy intervention aimed at promoting equal health opportunities: when incidence varies between groups, this suggests relevance of preventive policy measures, whereas unequal survival outcomes indicate that equal access to early detection and treatment are priorities [18–20]. Identifying similarities in mortality, incidence, and survival across groups can be useful for public health as well: equally detrimental levels point to important priorities for policy in order to improve the overall health of the population, whereas similarly beneficial results can point out prior policy achievements [21–23].

In the remainder of this introduction, I will first delineate what is meant by 'migrant background' (Section 1.2) and describe the Belgian context for this thesis (Section 1.3). Next, the focus shifts to cancer in Section 1.4 to define what kind of condition it is and provide important information on its risk factors and outcome measures, as these concepts will repeatedly be mentioned throughout the dissertation. This section ends with a short overview of worldwide variation in cancer burden. In Section 1.5 I will provide a more detailed account of the scientific and theoretical background of this dissertation. A description of the research approach and data used to answer the main research questions is given in Section 1.6. In a final paragraph I will outline the separate empirical studies that have been conducted as part of the thesis (Section 1.7).

1.2 Defining 'migrant background'

In this dissertation I study cancer outcomes of individuals with migrant background and compare them to those of non-migrant Belgians (referred to as 'host country natives', 'native Belgians'). The term '*migrant background*' aims to encompass all those with roots in a country other than Belgium either by birth and/or nationality. These foreign roots imply that at some point in the individual's ancestry, migration took place between the country of birth (also 'country of origin' in thesis) and the country of destination (or 'host country'). In the empirical work for this thesis, we use the terms

'migrant background' and 'migrant origin' interchangeably and consider *first- and second-generation* migrants. First-generation migrants encompass those migrating to Belgium from a different country themselves, whereas second-generation migrants (or 'migrant offspring') are born in Belgium but have at least one parent who migrated.

Importantly, the concept of 'migrant background' needs to be distinguished from other commonly used constructs in the research on migrant and ethnic minority health. Especially US-based work traditionally subdivides the population by 'race' or 'ethnicity'. *Race* is then defined as the group you (are perceived to) belong to, based on a limited range of physical factors (usually skin colour). Describing a population by racial group is thought to help clarify the genetic and external basis of disease but is also known to reflect social divisions that may affect health. *Ethnicity* is multifaceted and refers to the group you (are perceived to) belong to, based on shared characteristics such as geographic, ancestral origin. It emphasises a shared cultural tradition and language, and how these might affect lifestyle and, consequently, health. Different strategies are used to identify racial and ethnic groups, such as self-reported belonging by individuals, name algorithms, or more formal categories such as country of birth [22]. In continental Europe however, defining population subgroups based on ethnicity or race is less common and such data are often not collected. Instead, country of birth (of the person and parents) and nationality are generally used. Especially country of birth allows comparisons over time and between studies, and can be used to identify second-generation migrants [24,25]. The empirical data used in this thesis include information on country of birth and nationality but not on ethnicity. I therefore use 'migrant background' or 'migrant origin' as an indicator for a migratory past and show caution in interpretations that go beyond this including race or ethnicity. Subdivisions will be made in the empirical chapters of this thesis according to the specific country or origin, generational status, and duration of stay in Belgium to capture the variety within the group of migrant background and changes in cancer outcomes through time and migrant generations.

1.3 Research Setting

Belgium is a highly industrialised and urbanised country with an ageing population and is a high-risk setting for cancer [26–28]. This dissertation's study population consists of Belgian natives and individuals of migrant background that were registered as residents in Belgium at the time of the 2001 Census (administered on October 1st). Although the migrant population in Belgium is on average younger than natives (11% versus 17% aged 65 and over in 2005, 11% versus 18% in 2020) [28,29], both groups are increasingly subject to ageing and cancer risk.

Three migration flows since WW II until the end of the 1990s shaped the study population of this thesis: *a constant proximal flow* from neighbouring countries throughout the 20th century; *a flow of historical 'preference'* through organised labour recruitment from southern and eastern Europe, Morocco, and Turkey on the one hand, and post-colonial migration from the Democratic Republic of Congo (DRC) on the other; and *a more recent flow from an increasing variety of countries*. Immigration from neighbouring countries has been a steady 20-30% of immigration to Belgium throughout, but the two other immigration streams have been more driven by historical circumstances [30–32].

First, after WWII until 1974 Belgium organised labour recruitment to meet the country's increasing need for workers [31]. Initially Italian and Polish workers were recruited, but during the 1950s the industry and rapidly growing service sector required new labour, leading Belgian policymakers to attract workers from southern Europe (i.e., Italian, Greek, Spanish, and Portuguese migrants). Economic prosperity during the 'golden' 1960s resulted in a persistently high demand for heavy and low-paid labour, resulting in additional bilateral migration agreements between Belgium on the one hand, and Morocco and Turkey on the other hand in 1964 [30,31]. Tides turned as Belgian borders were closed to labour migration in response to the 1973 oil crisis and consequent economic recession. Recruited labour forces were initially

intended to return to their countries of origin, but many were discouraged from doing so due to the dire economic situations in these settings. Demographic and political pressures moreover persuaded Belgian government to allow family reunification for this largely male population group, hence ending the conjunctural nature of immigration to Belgium by the end of the 1970s [30,31].

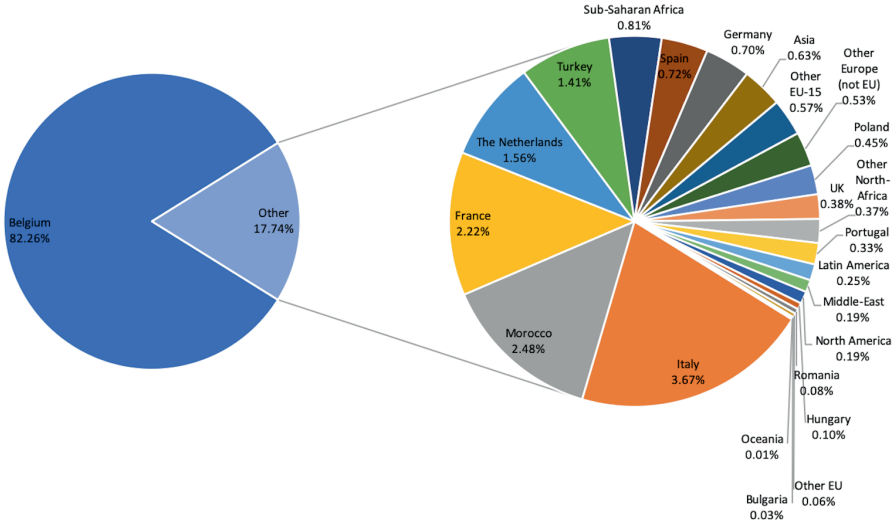
Second, migration from the DRC started after Congolese independence from Belgium was declared in 1960 [32,33]. Student immigration, diplomacy and migration of businessmen were important from the outset, and economic migration grew in importance as of the 1980s. The first refugees from the DRC also migrated to Belgium around that time [32]. This trend continued through the 1990s and was complemented by refugees from other Sub-Saharan African countries, mainly Burundi and Rwanda [30].

Third, diversification of migration to Belgium occurred during the 1980s and 1990s for several reasons. Refugees from a range of countries migrated to Belgium for economic and humanitarian reasons from the global South (including Sub-Saharan Africa as mentioned above) and former Yugoslavia. Also, the fall of the Iron Curtain in 1989 increased immigration from eastern Europe [31]. Finally, Belgium has attracted diverse migrants from the European Union (EU) during the 1990s given the EU's expansion and Brussels' central role in EU politics [31,34,35].

As a result of these dynamics, the largest share of the population of migrant origin in 2001 was of EU origin, but people of Moroccan, Turkish, and Sub-Saharan origin (especially the DRC) also shaped the population to an important extent (see Figure 1.1). This thesis focuses on the six largest groups of migrant background at the time of the 2001 census, i.e., French, Dutch, Italian, Turkish, Moroccan, and Sub-Saharan African migrants.

For labour migrants from Italy, Turkey, and Morocco, the industrial parts of Limburg, Hainaut and Liège were popular settlement zones after WWII. As the need for workers in the service industry increased, the Brussels Capital Region and Antwerp also attracted migrants from these origin countries [31]. These migrants' SEP was generally lower compared to that of Belgian natives. Overall, their offspring was socioeconomically better off than they were, but not compared to their Belgian native counterparts [36–38]. Importantly, migration from Italy during the 1980s and 90s was less characterised by male manual work and family reunification but can be seen in the context of EU enlargement and the increasing role of Brussels as a worksite for high-skilled migrants [34]. Furthermore, for each of these three traditional groups of labour migrants and family reunification, recent migration has seen a wider range of socioeconomic profiles (SEPs) and age groups [35].

Figure 1.1 Composition of the resident population by migrant background in Belgium, October 1st, 2001



Source: Statistics Belgium (2001), own graph

Migrant background is defined by the first of the following pieces of information that is available and identifies one as 'non-Belgian': (i) nationality at birth/census of the father, (ii) nationality at birth/census of the mother, (iii) own nationality at birth, (iv) own nationality at census

Migrants from Sub-Saharan Africa have settled mostly in cities in Wallonia and the Brussels Capital region due to the French-speaking facilities for higher education and employment opportunities [32]. The populations of French and Dutch origin more commonly reside in bordering regions between Belgium on the one hand, and France and the Netherlands on the other [31]. The SEPs of these groups are more comparable to those of Belgians, although the data used in this thesis suggest slightly lower financial resources among Sub-Saharan African and French migrants because home ownership is less common in these groups (see infra).

Research on the health of the traditional labour migrant groups has generally demonstrated lower mortality as compared to Belgians [39–42]. Fewer suicides and lower cardiovascular disease mortality offset the higher mortality from infectious and parasitic diseases [39–41,43]. Although no Belgian study has focused only on cancer so far, studies on cause-specific mortality have included a variety of cancer sites and have also reported that compared to Belgian natives most origin groups are less prone to different types of cancer [39,41,42,44]. Adjusting for socioeconomic differences further increased the migrant-to-native gap [41,44]. For many lifestyle-related diseases the mortality benefits were considered attributable to a healthier diet and lower alcohol and tobacco consumption, but also to reproductive behaviour lowering the risk of breast cancer for migrant women [39,45]. Nonetheless the health advantages observed in these studies tended to decrease with migrant generations and longer duration of stay in Belgium [41,43]. Moreover, some health outcomes were actually worse from the onset for a number of migrant origin groups, namely overall mortality among Turkish migrants over the age of 50, healthy life expectancy for older non-western migrants, and self-rated health and diabetes morbidity and mortality among adult individuals of Turkish and Moroccan descent in Belgium [40,41,46–48].

Prior to the start of the empirical work for this dissertation, research looking at discrepancies in cancer outcomes in Belgium had not covered mortality from a wide range of cancer sites and, to date, work on cancer incidence and survival is lacking.

This study contributes to the knowledge on social discrepancies in cancer in Belgium by examining mortality, incidence, and survival by migrant background. Prior to turning to the empirical and theoretical literature on this subject, the next section provides a background on cancer as a disease to support the reader throughout this dissertation.

1.4 Cancer: definitions and context

This thesis is situated at the crossroads of social epidemiology, demography, and public health and as such does not claim to give an exhaustive medical account of cancer by migrant background. Nevertheless, I provide a short description of cancer as a disease and how it is measured in research because that helps to understand how differences between migrant background groups and Belgian natives come about.

1.4.1 Cancer as a (group of) disease(s)

Cancer or '*Malignant neoplasia*' is a family of diseases [49,50], encompassing *"continuing, purposeless, unwanted, uncontrolled and damaging growth of cells that differ structurally and functionally from the normal cells from which they developed"* [50]. What makes a cancer patient 'sick' is the surplus of cells that causes damage to other cells and tissues in the body, which can occur in various organs and bodily tissues [50]. Cancers can be subdivided in solid *tumours* in organs and more dense tissues, and nonsolid *leukaemia* in the circulatory system [49].

Broadly speaking, cancers are caused by damage to DNA (deoxyribonucleic acid). Because DNA controls cell growth, damage to it can disturb cell division and growth processes in one or more cells, causing those cells to divide continuously and increase in number when they should not [50]. This problem can occur with older age or due to external exposures but can also be inherited (ca. 5% to 10% of cancers). *Age* is a

first important risk factor due to the accumulation of cell division and growth processes over the course of a lifetime, which increases the odds of errors in these cell mechanisms [50]. Second, *external risk factors* with 'carcinogenic' effects can play a role in disturbing DNA cell growth mechanisms [50,51]. Individuals can be subject to a number of these risks due to environmental circumstances that are not always subject to choice, such as large-scale radiation, pollution, chemical exposure, ultraviolet radiation (UV), and even viral and bacterial infections; others are a consequence of individual lifestyle in the form of alcohol consumption, physical activity, diet, reproductive behaviour, and most notoriously, smoking [49–51]. Third, a smaller proportion of cancers is caused by *hereditary genetic mutations* that put those carrying them at high risk of being diagnosed with specific cancers. BRCA1 and BRCA2 are the best known examples, and confer strongly elevated breast and ovarian cancer risks to carriers [51,52]. Nowadays, a growing field of research on gene-environment interactions called 'epigenetics' attempts to add to the existing knowledge on cancer causation by showing how genetic make-up might alter cancer risks due to environmental exposures, and/or the other way around [52].

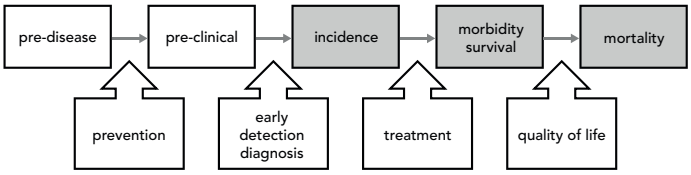
1.4.2 Cancer mortality, incidence, and survival

Aside from its multiple causes that make it a disease of multifactorial aetiology, cancer is described as a 'progressive' disease. This means that a prospective cancer cell accumulates genetic flaws due to the inferred DNA damage, which can increase the level of harm to the body [49]. This evolving nature of cancer is captured by *the cancer (care) continuum* developed by the United States (US) National Cancer Institute (NCI) (Figure 1.2). The continuum encompasses the phases in which an individual is disease-free, to where they have asymptomatic cancer, to when they are diagnosed with cancer, and either survive it or not. Each of these phases affects the indicators that measure cancer burden at the population level (incidence, survival, mortality), and are a focus for different health policy interventions [53,54]. In a variety of countries

worldwide, cancer plans for policy generally address key components of the continuum [53], and the Belgian Oncological College formulated good clinical practice guidelines for breast cancer detection and treatment using the phased nature of the continuum [55].

Cancer mortality, incidence, and survival are the most used *cancer outcomes* in research to measure its burden. Cancer *incidence* represents the occurrence of cancer as the number of new cancer diagnoses over a certain time period and population (usually expressed per 100,000 person years), and says something about the risk in a population [19,56,57]. Prevention measures for cancer are targeted at this early stage of the continuum as they aim to lower the prevalence of risk factors in the population [56].

Figure 1.2 The cancer (control) continuum



Source: National Cancer Institute (2010) [54], Hiatt & Breen (2008) [56]

Cancer *survival* gives information about the proportion of patients that are still alive at a specified time after cancer diagnosis (usually five years). It teaches us about cancer prognosis among those diagnosed and is strongly affected by how early a cancer was detected and the subsequent stage at diagnosis. The *tumour stage at diagnosis*, often declared as 'TNM-stage', reflects how far developed a tumour is when diagnosed. It is the combined result of the observed tumour size (T), invasion in surrounding normal tissue, lymph node involvement (N), and spread to distant organs ('metastases') (M) [50]. Generally, a higher stage implies a worse prognosis. Advanced tumour stage is used in research as a marker for lower access to timely screening or care [58], but can

also be indicative of a particularly aggressive tumour type. In that sense, survival can be affected by the biological characteristics of a tumour (e.g. where in the organ it is located, specificities of the cancer cells) [19,56,57], patient help-seeking behaviour that determines how early the diagnosis occurs, the timing of and preferences regarding treatment, and the timeliness of care and treatment decisions at the level of the care system. Policy initiatives for early detection such as population screening and improvements in (accessibility of) care are intended to improve survival. Early detection procedures are particularly meant to expedite a diagnosis by finding a cancer at the earliest possible stage.

The most historically used indicator of the cancer burden is cancer *mortality*. It represents the occurrence of death from cancer in a population (also expressed per 100,000 person years). Cancer mortality has been used for longer than the other two indicators as it has been 'easier' to measure it in the past: mortality records and death certificates at the population level were available earlier than population wide high-quality cancer registration that monitors diagnoses (incidence) and their progression (survival). Strictly speaking, cancer mortality is determined by combined incidence and survival, as dying from cancer depends on the chance of getting it in the first place, and subsequently of surviving it [19]. Because each of these three measures of cancer burden represents a different aspect, a more accurate picture can thus be drawn by jointly examining incidence, survival, and mortality [19].

1.4.3 Cancer epidemiology

Between-country differences in cancer outcomes give us some idea of the variability in cancer burden

in Belgium and the countries of origin of the study population (France, the Netherlands, Italy, Turkey, Morocco, and Sub-Saharan Africa), to which this thesis will

add by focussing on within-country discrepancies in cancer between migrant background groups from these countries and Belgian natives.

Variability in the how *the epidemiologic transition* occurred up until now explains the varying prominence of infection- and lifestyle-related cancers between countries. The transition entails a mortality decrease and a displacement of infections by degenerative and man-made causes of morbidity and mortality [59]. The *'classic' or 'western' model of the transition* took place in most of western Europe (including Belgium, France, and the Netherlands) and Italy, with a complete switch from infectious to man-made leading causes of mortality by WWII [59,60]. Therefore, lifestyle-related cancers such as female breast, lung, colorectal, and prostate cancer have dominated the picture of cancer diagnoses and deaths in Belgium, France, the Netherlands, and Italy during the 2000s [26,61,62]. In 2018, all-cancer incidence was furthermore very high in western European and only slightly lower in southern European countries, with age-standardised rates of 363.5 diagnoses per 100,000 person years among men and 292.1 among women in the first [63,64]. Turkey, Morocco, and Sub-Saharan African countries experience *contemporary/delayed transition models* in which infectious disease has not entirely been displaced [59]. North African countries (incl. Morocco) and Turkey are far along in this process, with the most common cancers in these countries similar to those in western Europe. Incidence rates in Turkey and Morocco were far lower and some cancer sites that are rarer in Europe were more commonly observed in 2016 (e.g., cancer of the brain and nervous system in Turkey, cervical cancer in Morocco) [62]. Sub-Saharan African countries (here: Burundi, DRC, and Rwanda) are at earlier stages of the epidemiologic transition due to the impact of HIV and the occurrence of wars and other forms of political violence [65,66]. These events hamper increases in life expectancy and form an environment in which infectious diseases remain frequent and where curbing them is challenging. Infection-related cancers such as cervical, stomach, and liver cancer were diagnosed more frequently in these countries [62,63].

The different availability of medical technologies underlies international variation in cancer survival [59,67]. In Belgium, five-year cancer survival observed between 2013 and 2017 was good for prostate, female breast and colorectal cancer (over 80%) in contrast to a worse outlook for lung cancer (under 30%) [26]. Rates were estimated to be similar for the EU origin countries included in the study population [68], and prior research suggested a five-year survival rate of 65% for colon and almost 80% for breast cancer in Turkey [67]. However, painting a clear picture of cancer survival in most origin countries of our study population is difficult due to cancer registries that cover the entire population and monitor the vital status of patients not being available.

1.5 The intersection between cancer and migrant background: an overview of the scientific knowledge and literature

1.5.1 Cancer discrepancies between migrant groups and natives in European countries of destination: empirical observations

Substantial variation in cancer mortality and incidence has been shown between host country native and migrant background groups in highly industrialised countries, which seemed to correspond to underlying differences in rates between the country of origin and destination. All- and lifestyle-related cancer mortality and incidence, such as lung, colorectal, prostate, and female breast cancer, were generally lower for migrants from less-industrialised (e.g. Turkish, Moroccan, South-East Asian) and southern European (i.e. Italian, Spanish, Greek) countries than natives in their highly industrialised countries of destination [5,7,7,9,39,41,42,69–74]. In contrast, their infection-related cancer mortality and incidence levels were higher-than-native corresponding to the cancer profiles in their countries of origin [5,7,69,72,73].

Studies into survival inequalities are less common at the European level and have shown mixed results. A number of researchers detected no important differences or slight survival advantages among migrants such as for prostate cancer in Sweden, and colorectal and stomach cancer among non-European migrants in the Netherlands [5,9,75]. Other scholars found (usually small) disadvantages for migrant background groups, mostly for breast and cervical cancer. Surinamese women in the Netherlands, for example, have lower breast cancer survival and Indonesian women lower cervical cancer survival than Dutch natives [5,6]. Non-European migrants at a low risk of cervical cancer in Sweden also have lower chances of surviving it than Swedish women (e.g. Turkish, South-East Asian, Chilean women) [76].

European studies on cancer by migrant background generally focus on groups from outside of the EU or less-industrialised country settings, whereas it has been less common to include other European or western countries of origin. Although some of the authors that have involved such groups in their analyses on cancer mortality reported few differences from host country natives, for example all-cancer mortality among French and Dutch migrants in Belgium [41]; elevated mortality has been observed in a number of cases, such as all-cancer for the Finnish in Sweden and the Scottish and Irish in England and Wales [70,74,77], cervical cancer among Danish and Norwegian women in Sweden [9,70], and breast cancer mortality for Danish, Icelandic, Austrian and Dutch women in Sweden [70]. Lower breast cancer mortality rates were observed for Norwegian women in Sweden as compared to Swedish natives [70].

In general, explanations for discrepancies in cancer between groups range from the selectivity of migration to differences in the social determinants of cancer and the 'import' of epidemiologic circumstances from the country of origin to the country of destination. Below is an overview of these explanatory frameworks.

1.5.2 Explaining cancer discrepancies between migrant background groups and natives in the country of destination

1.5.2.1 The selectivity of migration

Health selection of migrants has been a widely discussed reason for lower migrant mortality in the US and somewhat in western and northern Europe, including their fewer deaths from cancer.

First, *selective immigration* of those in good health has been thought to result in better health outcomes among immigrants compared to those in the country of settlement and those remaining in the origin country (the '*healthy migrant effect*') [17,78,79]. This mechanism is especially relevant for first-generation (manual) labour migrants from the Mediterranean to western European countries (i.e. Italy, Greece, Spain, Portugal, Turkey, Tunisia, and Morocco) [7,39,41,73,80]. From this perspective, it seems highly unlikely that individuals diagnosed with cancer would decide to migrate to conduct manual work abroad, which in turn contributes to lower cancer mortality. After some time spent in the host country, this initially better health was expected to wear off [17,79].

Second, *selective return-migration* of first-generation migrants that are facing health issues results in an overall lower mortality of the migrant population staying at destination (the '*salmon bias*') [17,78,79]. For cancer, this would translate into migrants leaving the host country due to a cancer diagnosis, resulting in potential cancer deaths that are not detected in the host country.

Although there has been some proof for these two selection mechanisms, the magnitude of the (cancer) mortality benefits observed was too large to account for based on health selection hypotheses alone [41,74]. For example, the mortality among those returning to their country of origin due to ill health would have to be

remarkably high to offset the mortality advantage of those remaining in the country of destination [41]. Furthermore, research that compared the health status of return migrants to those remaining abroad did not necessarily find the former in worse health [81]. It could also be argued that leaving the country of destination with healthcare that is often viewed as high-quality and more affordable than in the country of origin would make little sense [39,82]. Finally, these selection hypotheses were initially framed as explanations for mortality advantages among migrants, but they do not explain the site-specific variety in mortality and incidence between migrants and natives in the country of destination such as higher infection-related cancer incidence and mortality.

1.5.2.2 Differences in the social determinants of cancer between migrants and natives in the country of destination

Other than selection hypotheses, the social determinants framework for health in general and cancer in particular describes how multiple layers in society interact with one another and affect outcomes from cancer risk to prognosis [56,83,84]. Influences on cancer then occur from the 'macro' level of broad social conditions and policies that shape an individual's position in society and the health system, behavioural factors, and finally the biological mechanisms of carcinogenesis. Figure 1.3 visualises the influences considered for this dissertation. Shaded boxes indicate aspects covered explicitly in the empirical chapters.

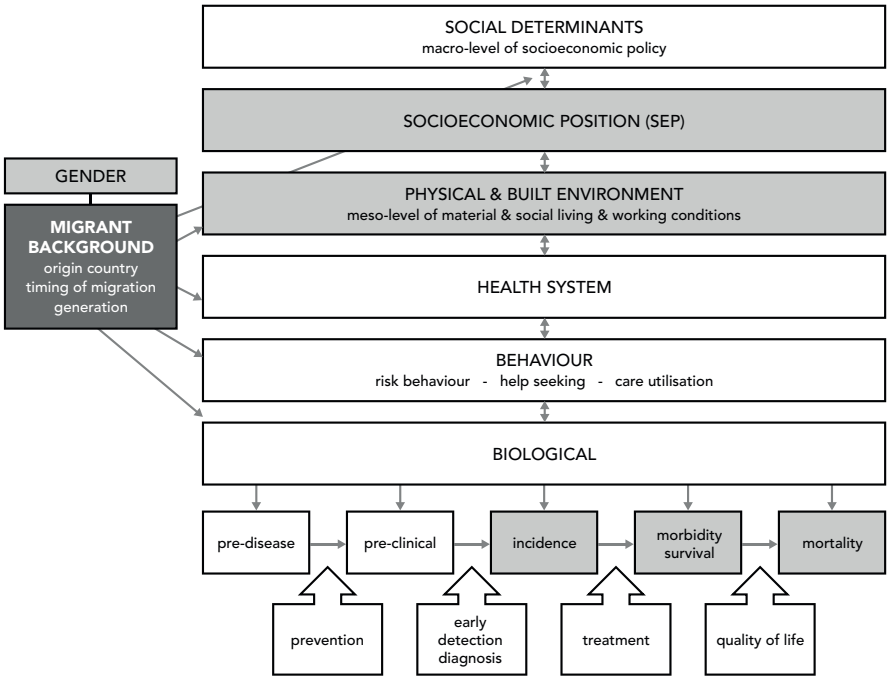
The social determinants at the *'macro-level' of socioeconomic policy*, shaped by the norms and values prevailing in a country, determine how power, prestige and socioeconomic resources are distributed in the population. This mechanism can occur along different lines, among which gender and migrant background [56,83,84]. For individuals of migrant background, this social stratification process can imply a different *SEP* than natives in the country of destination [83]. SEP which was in fact

generally lower for migrants from outside of the EU in Europe during the 2000s [33,85,86]. SEP is a multidimensional concept that locates individuals in a society's socioeconomic hierarchy in terms of their unequally distributed resources and prestige. These aspects are linked to childhood and adult social circumstances, the most acknowledged ones being occupational prestige, income, and educational level of the person themselves or of their parents earlier on [87]. SEP manifests itself in so-called economic, cultural and social capital. Economic capital is most 'tangible' and is reflected in possessed material goods (e.g., income, wealth, homes, cars). Cultural or human capital reflects symbolic and informational resources such as education, credentials, knowledge; but also fixed traits of the individual like personality, appearance, talents, and cognitive abilities. Social capital represents the actual or potential informational, material and emotional resources a person has access to via their relationships with others. These three forms of capital at least partly depend on one another, and can be accumulated, converted and have separate as well as combined effects on health [88–90]. Social epidemiological studies most commonly measure SEP with indicators of educational attainment, occupation, and income or wealth [91]. The macro level also impacts to which extent opportunities for a health-promoting lifestyle and access to the health system are dependent on a high SEP, for example by how unhealthy foods or alcohol are taxed and in the shape of more or less extensive welfare systems [83,92].

Policy furthermore influences how people's *physical and built working and living environments* at a meso-level are organised in terms of the environmental carcinogens individuals are exposed to and how their neighbourhoods and working places are organised. Individuals on the lower end of the social ladder are disproportionally affected by higher exposures to carcinogens in their living and working environments, as well as neighbourhoods with fewer services, green spaces and more vendors specialising in the sales of tobacco and alcohol spaces [56,92–94]. The latter further translate into risk factors for cancer due to lower socioeconomic opportunities, less

physical activity (e.g. green spaces), lower accessibility of healthy foods and potentially higher smoking and alcohol consumption [56,92–95]. Moreover, the availability and proximity of health care services (e.g. primary care centres, general practitioners, hospitals providing cancer care) may differ, which plays a role for the (timely) usage and accessibility of care when in need of medical help and might impact on cancer survival [96–98]. Because migrants do not settle randomly, they may also be differently affected by these aspects. Especially migrant groups from non-EU countries tend to be socioeconomically and ethnically segregated in more deprived urban areas in Belgium, but also migrants from the EU tend to cluster together albeit more likely due to residential preferences instead of socioeconomic mechanisms [99–102].

Figure 1.3 The social determinants of cancer in the country of destination



Source: adapted from Hiatt and Breen 2008 [56] & WHO 2010 [84]

Because individual behavioural choices and care access can furthermore not be considered outside of the social realm in which they take place [84,90,103], the clustering of migrants among peers from the same country of origin may also entail that their behaviour important to cancer risk and survival is strongly affected by those peers through *social capital effects*. This can occur through informational, practical and emotional support, but also through influences like role-modelling and peer pressure on risk and help-seeking behaviour [90]. This is one of the ways in which the '*ethnic density*' literature suggests that the built environment affects cancer incidence and survival by migrant background, although it also stresses the aforementioned (usually detrimental) effects of socioeconomic segregation [104,105].

The *health system or delivery-level* is an intermediary determinant of cancer outcomes [84], and its organisation and availability to individuals is partly dependent on the macro-level and built environment described above. The health system moreover influences (inequalities in) cancer outcomes through its affordability, how health insurance is organised, the quality of care and timely access [56,84]. In Belgium, the system of mandatory health insurance coverage decreases the health care system's role in creating disparities, in contrast to the larger role it is assigned by scholars in the US [56]. Nevertheless, SEP and migrant background may produce barriers to the system through limited proficiency in French and Dutch, a lack of knowledge about the health system, and practical issues in the shape of lack of sick leave, transportation and the need to supply child-care [56,106]. Importantly, the health system is more likely to affect cancer survival and somewhat mortality than incidence, with cancers for which early-detection procedures are available as notable exceptions (i.e. breast, cervix, colon, prostate) [11,56]. The health system itself may moreover be characterised by variations in cultural competence among practitioners and implicit and explicit discrimination among providers and inherent to the system's organisation [106,107].

The *behavioural* level is described in the literature as connecting SEP and migrant background on the one hand and cancer outcomes on the other hand [56,83,84,108]. Behaviour entails both lifestyle choices and how individuals access and utilise care.

A higher SEP for example provides a person with resources that can be used to avoid disease risk or minimise the consequences of a diagnosis [109]. As such, a high SEP generally discourages *risk behaviours* such as smoking, diet, alcohol consumption and high-risk sexual behaviour and facilitates health care access and utilisation for those diagnosed [56,92]. Interestingly, the connections between migrant background and a lower SEP do not necessarily mean that non-EU migrants' health-related behaviour is completely determined by their SEP. In fact, migrants behaviour is also shaped by norms and values specific to their upbringing, which may occur in the country of origin [11,110]. SEP and what are thought to be cultural aspects can therefore have unequal, enhancing and counteracting influences on behaviour that affect cancer risk which research has not fully grasped to date [111]. Overall, largely healthier behaviour compared to that of host country natives has been considered the main reason for lifestyle-related cancer mortality and risk advantages among migrants of South East Asian and Mediterranean descent in northern and western Europe [7,39,41,74]. Especially lower smoking rates (particularly among women), less heavy alcohol consumption, a diet consisting of little red meat and a high intake of grains, fruits and vegetables and physical activity are lifestyle-elements more commonly found within these groups (albeit with between-group variation) [108,112,113]. Also *reproductive behaviour* that underlies lower breast cancer risks is more common, namely earlier ages at childbearing, having more children on average and breastfeeding for longer durations of time [108,112,113].

In addition to behaviour important for cancer risk (and mortality by extension), *health care and preventive service utilisation* may differ between migrant and host country native populations [11]. A number of migrant groups have lower cancer screening participation rates and seek help from medical professionals later than natives when

they show symptoms that may be indicative of cancer [114–117]. This can lead to more advanced stages at diagnosis and lower survival. This health system use is impacted by health and cancer beliefs specific to migrant background groups, but less norm- and value-driven factors such as limited host country language proficiency, low cancer risk awareness, lack of knowledge and information about the healthcare system, financial barriers and competing priorities such as work and childcare are also thought to underlie this behaviour [106,115,116,118–120]. Some of these are specific to migrant background, but others are more socioeconomically driven.

The *biological level* is closest in proximity to cancer occurrence and prognosis and forms the final layer that connects the layers of social determinants described above to cancer outcomes [56].

I adopt this multi-layered view on how cancer outcomes result from risk, help-, and care-seeking behaviour and how this may occur differently for migrants and non-migrants in Belgium. Because being of migrant background can entail behavioural differences, but also different socioeconomic resources that affect behaviour, I take the differential distribution of socioeconomic resources between Belgian natives and various migrant background groups into account by analysing how SEP contributes to discrepancies in cancer outcomes. Because settlement patterns of migrants furthermore imply that they cluster in the same (urban) areas, their behaviour may additionally be impacted by interactions with peers of the same origin in Belgium. The level of urbanisation of the area of residence is therefore considered in an overview of cancer mortality by migrant background, to account for the mostly urbanised settlement areas of migrant groups in Belgium as one aspect of their 'built environment'. The current literature on neighbourhood ethnic density effects for migrant cancer outcomes being limited in Europe, this thesis furthermore wishes to explore how the clustering of migrant origin groups may have important effects. Such studies can highlight the importance of the local context and community measures as useful tools to alleviate health disadvantages. At the behavioural level, this thesis

directly studies how reproductive behaviour such as parity (i.e. the number of children) and age at first childbearing affect breast cancer mortality, incidence and survival discrepancies by migrant background. By furthermore taking the tumour stage at diagnosis into account in our survival analyses, we can indicate whether timely use and/or access of diagnostic services affects survival discrepancies between groups. The biological and specific health system layers will not be the focus of the empirical chapters because they seem best reserved for medical and health systems or services research. Section 1.5.4 discusses a number of remaining connections depicted in Figure 1.3 that were less covered in the social determinants of health and cancer literature (for migrants).

1.5.2.3 Migration as a change in epidemiologic context

Beyond the fact that the social determinants of health and cancer likely affect Belgian natives and those of migrant background differently, the general epidemiological contexts in the country of origin and destination also influence the nature of health risks migrants are exposed to. The theory of migration as a '*rapid epidemiologic transition*' by Razum and Twardella [121] explains migrant cause-specific mortality from this perspective: the authors describe migration from less- to more industrialised countries as a process that effectively implies a change in epidemiological context and renders these migrants epidemiological time travellers. They were born in a country that is in an earlier phase of the epidemiological transition where communicable diseases are still important and find themselves in a later stage characterised by 'man-made' diseases after migration [121,122].

For cancer mortality and incidence, the theory implies a change from a context where infection-related cancer risks (such as liver, cervical, stomach) are important, to one where they are less common but where lifestyle-related ones are high (such as colorectal, female breast, lung prostate). Upon arrival, this is reflected in their cancer profile as compared to that of natives in the country of destination: lower cancer risk

and mortality and a higher occurrence of infection-related types as compared to natives. But because the migration process from less- to more-industrialised settings usually implies better access and effectiveness of health care (the '*therapeutic component*') and a lower prevalence of infectious agents due to improved hygienic and environmental conditions, their infection-related risks decrease rapidly after migration and they have a cancer mortality and risk advantage in the country of destination for years [121]. However, chronic disease risks are expected to increase rather slowly with time spent in the host country (the '*risk factor component*'). Exposures to important risks during early life can moreover manifest at later ages (the '*unfinished agenda of the transition*') [11,121]. Migrants then go through a transition that is rapid in terms of the availability of treatment and slow in terms of exposure to behavioural risk factors. Importantly, the theory of migration as a rapid epidemiologic transition has yet to be tested explicitly for cancer. This thesis includes such a test.

1.5.3 Adopting a life course perspective on cancer discrepancies between migrant origin groups and natives

The theory of migration as a rapid epidemiologic transition suggests that aside from an actual change in epidemiologic context, the timing and duration of exposure to each context are important for cancer mortality and risk [121]. It implies that cancer outcomes differ with early-life exposures in the country of origin, but also with time and subsequent generations in the country of destination. How cancer is affected differently for individuals of migrant background than for natives in Belgium is therefore best studied from a *life course perspective*. This perspective acknowledges that risk factors and cancer outcomes can occur in different life phases of migrants and in different countries depending on the timing of migration [122].

A life course perspective on health acknowledges that exposure during *critical periods* in early life can predispose to cancer in later life and take place in the origin rather

than the host country [11,122,123]. The repeatedly observed stomach cancer mortality disadvantage among Moroccan and Sub-Sahara African origin groups in Europe that persists after migration is an empirical example: large portions of these individuals migrate at adult ages but may have experienced childhood deprivation in their origin countries. Those circumstances increase the risk of Helicobacter pylori (H. pylori) infection, an infectious agent known to predispose to (non-cardia) stomach cancer manifestation in older adulthood. Such a 'pre-programmed' risk for cancer was described as 'the unfinished agenda of the epidemiologic transition' above [121].

Second, a life course perspective considers the possible *accumulation* of cancer risks through time [122,123]. Longer stays in a country may imply an accumulation of influences from that setting. This not only involves increased direct material exposures to carcinogens (e.g. due to pollution in the neighbourhood), but can entail gradual changes in health-related behaviour and health care utilisation as well, indirectly affecting cancer risks and survival post-migration [122]. Those behavioural changes are at the core of the migrant health literature about acculturation.

Acculturation has been expected to translate into a lifestyle pattern among migrants that increasingly resembles that of natives with time in the country of destination [124–126]. This implies that migrant mortality and incidence rates change towards those of native non-migrants in the country of destination ('*convergence*'). Scholars have examined this by introducing duration of stay in their analyses of cancer mortality and risk. They have repeatedly demonstrated increasing risks of lifestyle-related cancers such as breast and colorectal cancer and decreasing risks of infection-related cancer risks through time in groups with initially lower and higher rates, respectively [42,127–131]. Importantly, a pattern of convergence with longer stay is not observed in all studies, nor all cancers and migrant groups [10,131–133]. Scholars focusing in depth on changing health-related behaviours in migrant populations have moreover argued that these behavioural alterations underlying cancer risk are more complex than a unilateral shift towards the behaviour of natives in the country of destination among

all origin groups [125,126]. This thesis examines cancer incidence according to duration of stay to verify whether and to which extent risk convergence occurs for migrant background groups in Belgium. Those findings will offer insights to the literature by studying multiple cancer sites in a variety of origin groups.

An 'accumulation' over the life course of specific host country effects on cancer might be considered even larger for second-generation migrants. This group inherits genetic endowments from their parents and their SEP and norms and values are strongly affected by those of their migrant parents as well, but they are born and raised in the country of destination [122]. This could explain why second-generation migrants often exhibit cancer risk and mortality levels in-between those of their first-generation and non-migrant native counterparts [7,41]. Some studies have even shown higher-than-native cancer mortality rates for some groups in Sweden and Belgium [41,134].

Variations in cancer survival are less covered by life course perspectives on migrant health. Scientific evidence on survival by duration of stay and generational status is scant, in large part due to the still young age structures of these groups with limited numbers of cancer diagnoses. Possibly, their 'in-between'-position in terms of risk translates to survival too. It could be hypothesised that second-generation migrants' access to useful resources for early cancer detection and high-quality care is improved compared to first-generation migrants due to a stronger familiarity with the host country language, health system, and improved SEP compared to their parents [135,136]. Nevertheless, the second generation of many migrant origin groups is known to still have lower SEP compared to natives in the country of destination [36]. They may moreover experience discriminatory practices in health care or lower-quality care that natives do not [107,122,137]. Although their survival rates may therefore differ less from natives than those observed among their first-generation counterparts, second-generation migrants could still be at a survival disadvantage.

Although there is currently no extensive body of evidence on cancer mortality, incidence and survival changes with time and generations, this information is crucial in unravelling genetic and external contributions to risk and survival of a range of cancer types [12]. To meet the need for more evidence, this thesis subdivides the migrant background groups where this is statistically reasonable considering decreasing group sizes when we do so. Cancer incidence rates are examined by duration of stay for various cancers. Moreover, site-specific cancer mortality and breast cancer incidence and survival rates are scrutinised for first- and second-generation migrants.

5.4 Do common explanations fit 'all'?

This thesis can capitalise on the literature covering social determinants of health and cancer, migration as an epidemiologic transition and the life course perspective on the health of migrants. These are strong foundations for helping us understand how differences in cancer mortality, incidence and survival come about. Nevertheless, caution is warranted in how they are applied to the study population of this thesis considering the variety or origin countries included, and how mechanisms may apply differently by migrant generation and gender.

First, the *range of migrant background groups* that has settled in Belgium has done so under diverse circumstances. Italian, Turkish, and Moroccan men have been recruited as labour migrants, for which positive health selection may have been important to enable their work in Belgian industry. Even so, it is worth noting that more recent migration from these three countries to Belgium (starting after 1974) is less characterised by industrial labour migration [35,138,139], and therefore common explanations for health differences may apply less to these newer cohorts. For French and Dutch migrants, the constant immigration from the neighbouring countries makes health selection or migration between epidemiologic contexts unlikely. Finally, Sub-Saharan African migrants immigrated under various circumstances (education,

business, seeking refuge) [32,33] and their overall mortality has been shown to actually be higher than that of Belgians [41]. Although the Sub-Saharan African countries best represented in our study population (Burundi, DRC, Rwanda) were described as 'at an earlier stage of the epidemiologic transition' earlier in this introduction, their mortality profile does not correspond to what is expected from 'migration as a rapid epidemiologic transition' (i.e., with mortality lower than that of Belgians) and health selection and differences in SEP seem less ubiquitous mechanisms for this group.

The situation of *the second generation* in terms of cancer outcomes is also rarely addressed in the literature, especially with respect to their survival outcomes in different settings. Nevertheless, the second generation of EU-origin in Belgium is ageing similarly to the Belgian native population and children of Turkish, Moroccan, and Sub-Saharan African migrants are now also reaching older ages at higher risks of cancer and should be included in the empirical and theoretical literature [29].

Finally, the context of migration and social determinants that affect cancer outcomes may be different for *women and men*. For example, labour migration recruitment schemes concerned Mediterranean migrant men whereas women from these countries generally migrated with the aim of family reunification [31]. As such, health selection is less relevant for women. Men and women are furthermore subject to different occupational exposures, social networks, discrimination, care utilisation and show different health behaviour in general [140,141].

To avoid one-fits-all interpretations of study findings, the study chapters involve analyses that were stratified by gender and will discuss important outcomes separately for each migrant background group and, where groups were subdivided, by generation or duration of stay.

1.6 Data sources

The study chapters are based on linkages between administrative data sources, namely the 2001 Census, the population registry, death certificates, the Belgian Cancer Registry and the Crossroads Bank for Social Security. Depending on the outcome studied, different data linkages are used.

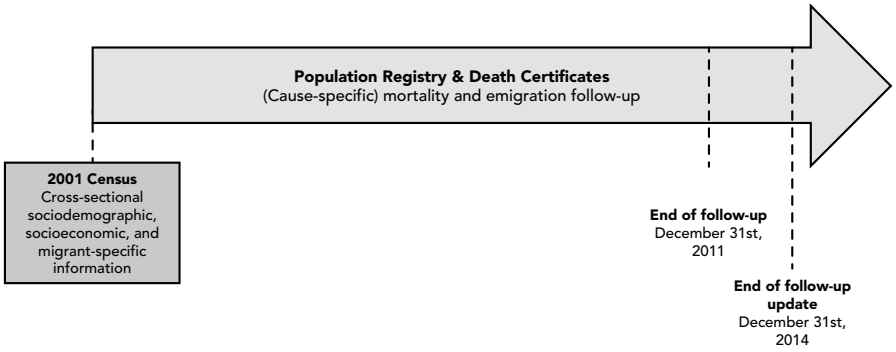
1.6.1 Mortality: The Census-linked Registry Data

Our cancer mortality analyses are based on a dataset with census and registry information covering the whole de jure population in Belgium. The data consist of a linkage between the *2001 census* ('Algemene socio-economische enquête' or 'General socioeconomic survey'), the *population registry* information on emigration and mortality and *death certificates* adding data on causes of death [142]. We use cross-sectional information about migrant background, SEP and demographic data from the census administered on October 1st, 2001 with a ten-year cause-specific mortality and emigration follow-up until December 31st, 2011 (updated to 2014 during the study period) (Figure 1.4). The linkage between the census and the registry was performed by Statistics Belgium (StatBel) using the security identification number (SSIN) as a unique identifier. In a second stage, information from death certificates was added using a probabilistic identification key based on information available in both datasets: the date of birth, date of death and gender. In total, almost 96% of death certificates from the follow-up period could be linked to the Census and Registry data.

The dataset is the most exhaustive resource of cross-sectional socioeconomic and migrant-specific information with longitudinal data on emigration and cause-specific mortality for the population residing in Belgium. This dataset was used for the empirical chapters on site-specific cancer mortality by migrant background (Chapters 2 and 3). The studies capitalised on the richness of the database by adjusting for

important socioeconomic and demographic confounders and explore the role of the neighbourhood using information about place of residence.

Figure 1.4 Structure of the Census-linked Registry Data used for the mortality analyses



1.6.2 Incidence and survival: The Census – Belgian Cancer Registry linkage

Although socioeconomic and migrant patterns in site-specific cancer mortality give clues about the importance of determinants affecting cancer outcomes, they do not reveal whether patterns reflect differences in risk, survival, or both. Therefore, an additional data linkage using 2001-2013 Census and (cause-specific) mortality data was established with diagnostic information from the Belgian Cancer Registry (BCR).

The BCR is a population-based cancer registry that collects nationwide information on cancer diagnoses since incidence year 2004 [143]. Cancer registration in Belgium is mandated by law through the 2003 Royal Decree for oncological care programs and laboratories of pathological anatomy, using the SSIN as a patient identifier. A linkage with the Crossroads Bank for Social Security (CBSS) enables the Registry to follow-up on vital status and date of death of diagnosed patients. The BCR covers more than 95% of the cancer diagnoses in Belgium. Incompleteness is most likely reserved for

elderly cancer patients with a very poor prognosis at diagnosis and outpatients with a clinical diagnosis only. The validity of the registered information is checked using manual validation procedures based on the International Agency for Research on Cancer guidelines to ensure quality of the data [143].

In this merged database we know which members of the population living in Belgium on October 1st, 2001 were diagnosed with cancer between January 1st, 2004 and December 31st, 2013. Moreover, we have information on everyone's vital status and emigration until July 1st, 2017 from the CBSS. For incidence analyses, we focus on the 2004 to 2013 diagnostic follow-up (Figure 1.5). For the survival analyses, we use the CBSS vital status information which allows a follow-up until July 2017 (Figure 1.6). Important clinical confounders such as date of diagnosis and combined TNM-stage at diagnosis were added from the BCR.

Figure 1.5 Structure of the Census-Belgian Cancer Registry Data used for the incidence analyses

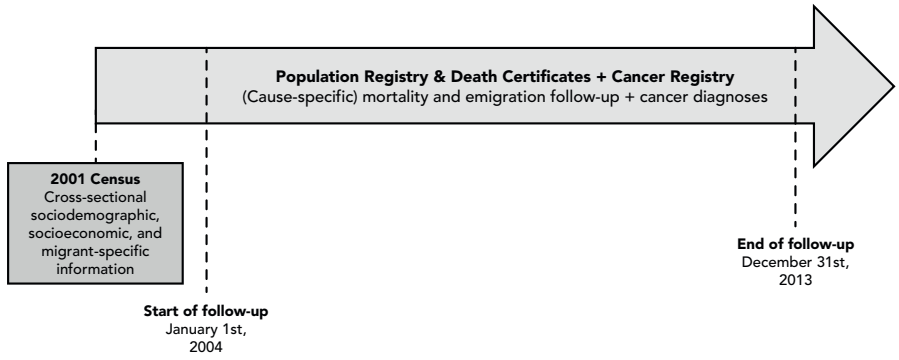
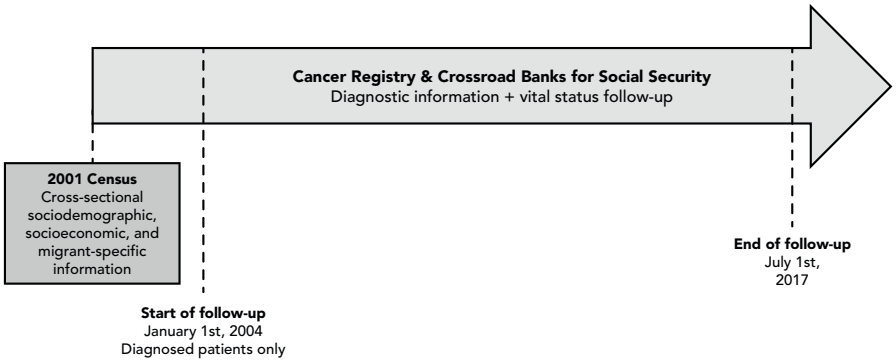


Figure 1.6 Structure of the Census-Belgian Cancer Registry Data used for the survival analyses



This database facilitates research on incidence and survival patterning in Belgium. It has the added advantage of including crucial clinical confounders. Such nation-wide data on cancer at the individual level is unique and has thus far only been in use in the Netherlands where country of birth is registered in the national cancer registry [5], and in the Nordic countries which have a long history of linking administrative data sources.

1.7 Outline of this thesis

The remainder of this dissertation consists of four empirical chapters and a concluding chapter in which the main findings are summarised and the scientific and societal implications of the results are discussed.

The empirical chapters were written as scientific journal articles and aim to provide a picture of the patterning in cancer mortality, incidence, and survival for the largest migrant background groups in Belgium, as well as its socioeconomic, demographic and clinical (stage at diagnosis) determinants.

Chapter 2 on site-specific cancer mortality by migrant background aims to answer the following research questions: what does the mortality pattern from 2001 to 2011 look like for native Belgians and the largest first-and second-generation migrant origin groups for the most common cancer sites in Belgium? How do SEP and urbanisation contribute to this pattern? Indirect standardisation and Poisson regression are used to obtain absolute and relative mortality rates for all cancers combined, cancer of the head and neck, stomach, colon and rectum, liver, lung, breast, and prostate. The patterns observed are adjusted for SEP and urbanicity of the living environment. The findings give us a general overview of the cancer mortality patterning in Belgium and of the extent to which the patterning corresponds to migrant mortality hypotheses (i.e., the healthy migrant effect, the salmon bias, epidemiologic transition).

In *Chapter 3*, I delve deeper into how cancer mortality for migrant origin groups may be affected by social determinants and mechanisms at different levels. More specifically, a multilevel analysis is performed of *tobacco-related cancer mortality and its associations with ethnic density or 'same-origin group presence' in the neighbourhood in the largest Belgian cities*. In addition, how such a same-origin effect may depend on individual educational level and migrant generation is analysed. Different measures for same-origin group presence are used with both linear and categorical specifications to verify whether these aspects were important for effects on cancer. This approach gives more insight into how the same-origin networks of migrant origin individuals in Belgium may affect their risk behaviour and consequently influence their cancer risk and mortality.

Whereas Chapters 2 and 3 focus on site-specific cancer mortality based on linked census and registry data, Chapters 4 and 5 capitalise on added diagnostic information from the Belgian Cancer Registry. These chapters are guided by the following research questions: what did the patterning of cancer incidence and survival look like by migrant background in Belgium in the 2000s? Can the observed differences between migrant origin groups and native Belgians be explained by determinants

suggested in the literature? *Chapter 4* scrutinises female breast cancer incidence and survival. This choice is based on Belgium's breast cancer risk being ranked first worldwide, combined with a generally good prognosis when diagnosed early. The analyses thus reveal the extent to which this high risk and survival are observed for native and migrant subgroups in Belgium, while taking account of differing educational levels, reproductive behaviour, and tumour stages at diagnosis.

The *fifth chapter* focuses on cancer incidence among first-generation migrants and how it changes with time spent in Belgium. It focuses on colorectal cancer as a lifestyle-related cancer site, grouped infection-related cancers, and non-cardia stomach cancer as an infection-related subtype with early-life risks. Incidence rates among migrant background groups from Turkey and Morocco with shorter and longer lengths of stay are studied to test the hypothesis of '*migration as a rapid epidemiologic transition*' for cancer. French, Dutch and Italian migrants are included to examine the uniqueness of the transition to migrants from non-EU countries. The findings give further insight into how cancer risks and their underlying causes change post-migration.