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BELGIAN NATIONAL BURDEN OF DISEASE STUDY

Guidelines for the calculation of DALYs in Belgium

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CONTENTS

ACKNOWLEDGMENTS

The Belgian National Burden of Disease Study (BeBOD) is an initiative of the Lifestyle and Chronic Disease Service, Department of Epidemiology and Public Health, Sciensano.

BeBOD is conducted as part of the Health Status Report project, and receives financial support of the National Institute for Health and Disability Insurance.

1. General outline

1.1 INTRODUCTION

The main goal of public health policy is to protect and promote the population's health. This requires information on the health status of the population, often referred to as the "burden of disease". More than just the presence/absence of specific diseases and conditions, disease burden encompasses a comprehensive and comparable quantification of the physical and psychosocial health impact of diseases, injuries and risk factors (Devleesschauwer et al., 2014).

Evidence on the disease burden is important for decision-making processes within the health sector. In order to make relevant decisions and set appropriate priorities, policy makers need to be informed about the size of health problems in the population, the groups that are particularly at risk, and the health trends over time. In addition, an accurate estimate of the population's health status can be used for determining expected health care use and is vital for prioritizing effective interventions and evaluating their impact and cost-effectiveness (Tan-Torres Edejer et al., 2003).

The disease burden of a population can be described by a variety of indicators. Indeed, population health is a multifactorial phenomenon with many facets and different ways to measure it. Typical indicators of population health are life expectancy, cause-specific mortality rates, numbers of new and existing cases of specific diseases (i.e., incidence and prevalence), and self-perceived health. However, these indicators highlight only one facet of public health, i.e., either mortality or morbidity.

Summarizing population health in terms of mortality-based indicators, such as life expectancy, dates from the time when only reliable data for mortality existed. In many countries, however, one has been confronted with a demographic and epidemiological transition, replacing the importance of early mortality due to plagues and famine by that of chronic, non-communicable diseases (Marshall, 2004). Cardiovascular diseases and cancers have replaced infectious diseases as the main causes of death. However, these diseases are also associated with an important morbidity component, due to the life prolonging effect of continuously improving medical practice (Jelenc et al., 2012). Moreover, not only an extended life expectancy per se is desired, living these extra years in good health has become just as important (Cleemput et al., 2014). As a result, current health policy requires a global overview of population health, one that combines morbidity and mortality and takes into account health-related quality of life (Robine et al., 2013).

Given the importance of combining morbidity and mortality, the last few decades have seen important methodological advances in so-called summary measures of population health (SMPH) (Murray et al., 2000). By and large, SMPHs may be divided into two broad families, namely health expectancies and health gaps. Metrics of each family combine morbidity and mortality into a single figure. Health expectancy-based metrics, such as Disability-Free Life Expectancy, Healthy Life Years, and Disability-Adjusted Life Expectancy, translate these indicators into a health-adjusted life expectancy (Robine et al., 2013). Health gap metrics, such as the Disability-Adjusted Life Year (DALY), translate these indicators into a number of life years lost due to ill health and mortality.

Driven by the Global Burden of Disease (GBD) projects initiated in the early 1990s (Murray and Lopez, 1996), the DALY has become the key SMPH for quantifying burden of disease. DALYs measure the health gap from a life lived in perfect health, and quantify this health gap as the number of potentially healthy life years lost due to morbidity, disability and mortality. A disease burden of 100 DALYs per 1000 people-year would thus imply a loss of 100 healthy life years per 1000 people per year. Diseases or risk factors accounting for more DALYs thus have a higher population health impact. By quantifying the total disease burden and the contribution of different diseases and risk factors, DALYs are a highly valuable measure to set priorities for public health research and policy. Furthermore, DALYs may be calculated for different (sub)populations (e.g. gender, geographical areas, socioeconomic groups), allowing for a more detailed perspective on population health. By regularly updating the DALY estimates based on the best available data, trends in population health can be monitored over time, and the impact of macro-level policies can be evaluated. As a result, DALYs are an important tool to support policies that aim to improve population health and reduce health inequalities (Ikram et al., 2014).

Estimates on the burden of disease in Belgium, expressed as DALYs, are available from both international and national efforts. To date, the most comprehensive sources of disease burden estimates for Belgium are the GBD studies conducted by the World Health Organization [https://www.who.int/healthinfo/global_burden_disease/estimates/en/index1.html] and by the Institute for Health Metrics and Evaluation (IHME) [http://www.healthdata.org/Belgium]. These studies showed that non-communicable diseases dominate the overall disease burden, while tobacco smoking, dietary risks, and alcohol use are the major behavioral risk factors for ill health. So far, only few national efforts have been undertaken to study the disease burden in Belgium. The use of DALYs as a policy-relevant instrument in Belgium was first described in the Flemish Health Indicator Report 1998 (Baert et al., 2000). To demonstrate the use of DALYs, the authors initiated a pilot study, in collaboration with

Sciensano, in which they quantified the Flemish disease burden for reference year 1997 (Baert et al., 2002). The Flemish Institute for Technological Research (VITO) assessed the burden of environmental risk factors in Flanders, commissioned by the Flemish Environment Agency (Buekers et al., 2012). In addition to these larger studies, several researchers estimated the burden of specific health conditions in Belgium, i.e., transportation noise in Flanders (Stassen et al., 2008), road traffic accidents in Flanders and Brussels (Dhondt et al., 2013), haemophilia in Belgium (Henrard et al., 2014), melanoma in Belgium (Pil et al., 2016; Tromme et al., 2016), and legal and illegal drugs in Belgium (Lievens et al., 2016).

Despite these efforts, several constraints can be identified that hamper the policy relevance of the currently available estimates. While global estimates provide a broad overview of the health status in Belgium, it remains a question to what extent these estimates are grounded in the best available local data. These global exercises are currently also not able to respond to country-specific needs, such as the need for regional burden disaggregation. They also present hurdles in terms of timeliness and ownership. While national research groups did more efforts to apply local data sources, there appears to be little consistency in the applied DALY calculation methodology. As a result, the nationally generated estimates are not comparable, hampering the main use of DALYs as a tool for comparison and prioritization. Most DALY estimations also remained academic exercises, with little or no direct knowledge transfer to the concerned policy instances. Therefore, if disease burden were to support health policy, a more systematic approach is required, generating comparable estimates rooted in recent, local data.

1.2 OBJECTIVES

Given the need for disease burden estimates to guide decision-making processes within the health sector and the limitations of the currently available burden estimates, Sciensano has taken the lead in launching a Belgian National Burden of Disease Study, BeBOD, which builds on a coherent framework for routinely quantifying the burden of disease in Belgium using the DALY metric. The project is conducted as part of the Health Status Report project, and receives financial support of the National Institute for Health and Disability Insurance.

Implementing a national burden of disease study addresses several of the limitations of the currently available burden estimates:

- **Ownership and sustainability** are guaranteed.
- The study can be maximally embedded within the **local context**. Indeed, Sciensano and its partners have established expertise in the use and valorization of the various Belgian health information systems. As a result, they have access to more, better, and more up-to-date data than international groups. Furthermore, they have the necessary contextual

knowledge to properly interpret and appraise the available data and the resulting burden estimates. Finally, they have established modes of interaction with federal and regional policy-makers and stakeholders, supporting credibility and maximizing knowledge transfer.

- **Methodological flexibility and transparency** is ensured. Instead of relying on external analyses or global interpolations, BeBOD allows making own assumptions and setting own priorities. By adopting a harmonized methodology across health causes, transparency of the resulting burden estimates is ensured.
- The process as such benefits **capacity building**. In addition to the results of the project, the process of implementing a national burden of disease study also has important indirect outcomes. Indeed, the project is an impetus to appraise the quality of the local data and to address data gaps. Furthermore, the project also leads to substantial scientific capacity building, thereby increasing awareness and strengthening critical mass in Belgium, and furthering the scientific process.

Despite these benefits, it is also important to acknowledge the limitations of the BeBOD project. First, it should be clear that BeBOD will not be able to answer all possible policy-relevant questions. Indeed, the project allows measuring problems, but not their solutions. Burden estimates identify potential for health gain and unmet needs, but do not replace cost-effectiveness studies. Furthermore, when prioritizing diseases, it should be clear that health impact is just one of the many aspects that can be considered. Other factors include economic impact, general awareness, stakeholder interests, epidemic potential, and possible "shock" effects of rare but severe conditions.

1.3 IMPLEMENTATION

In 2001, the World Health Organization published guidelines for countries wishing to undertake a national burden of disease study (Mathers et al., 2001). They described the different steps in a national burden of disease study as follows:

1. Make the necessary methodological choices
    - levels of analysis: year, age groups, sexes, causes, sub-populations
    - social values
2. Establish a demographic baseline
3. Perform a cause of death analysis
4. Perform an epidemiological description non-fatal outcomes
5. Evaluate internal consistency of epidemiological estimates
6. Calculate YLLs, YLDs, DALYs, and HALE

7. Perform a comparative risk assessment
8. Perform a sensitivity analysis
9. Disseminate results

The overall philosophy of BeBOD consists of a stepwise implementation of these steps and a gradual scaling-up of activities and capacity. As far as possible, routine data sources are used (**Figure 1**), allowing the implementation of a framework for routinely quantifying the burden of disease in Belgium. BeBOD estimates the true disease burden in a transparent way, and includes actions to expand ownership of data and results. For each of the specific steps in the project, the subsequent chapters and annexes document the methodological choices.

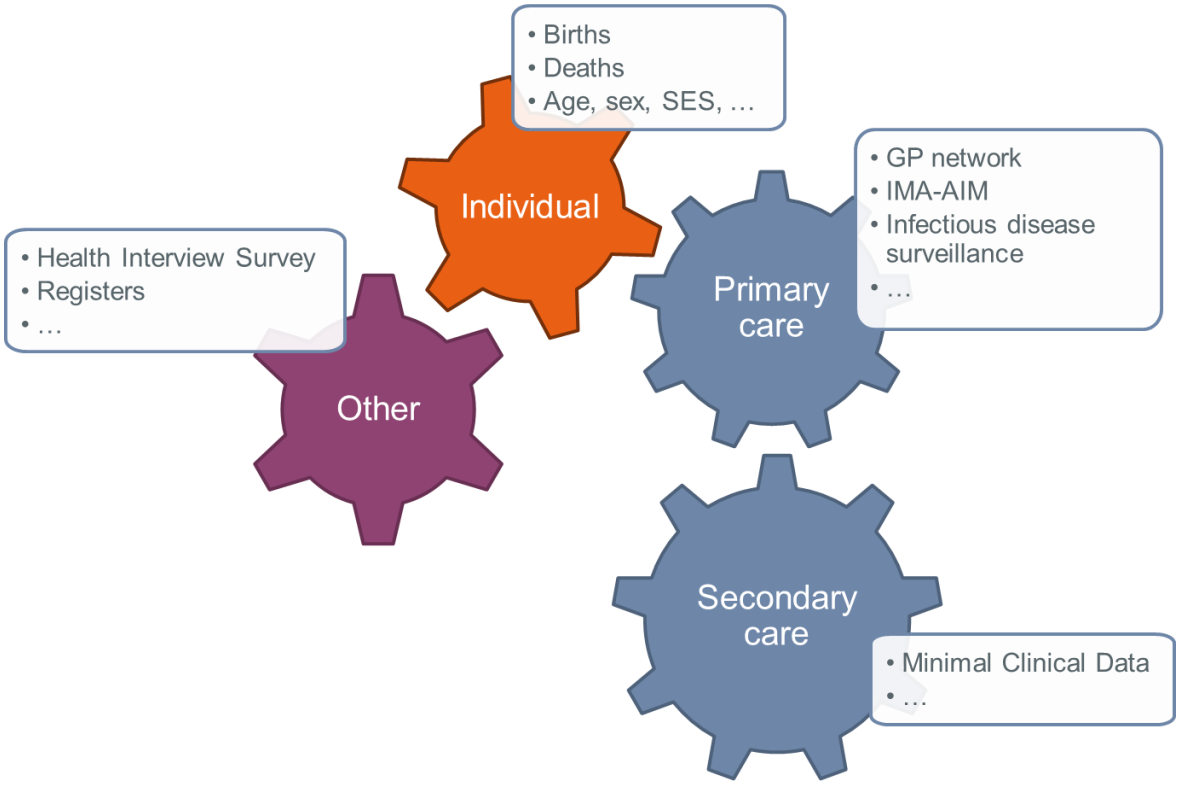

Figure 1. Data needs for the Belgian National Burden of Disease project

1.4 MANAGEMENT

BeBOD is managed by Sciensano and followed up by a steering committee comprised of external experts.

General coordinator

- Develop support tools (e.g., DALY calculation guidelines, DALY calculation workshop, and DALY calculation tools)

- Initiate, support and harmonize DALY initiatives
- Interact with stakeholders
- Act as link with national burden of disease studies in other countries and with related international activities (such as the WHO/EURO European Burden of Disease Network and the COST Action CA18218 www.burden-eu.net)

Scientific collaborators across Sciensano units

- Act as link between BeBOD coordinator and unit
- Identify ongoing DALY activities within the unit
- Explore opportunities for new DALY activities within the unit
- Follow-up on progress of ongoing and new DALY activities within the unit
- Interact with unit-specific stakeholders: put burden of disease on the agenda

Steering committee

- Follow-up on project progress through annual meetings
- Provide technical feedback through reviewing technical reports
- Identify opportunities for further developing resources and capacities (e.g., new collaborations, projects, human resources …)

The steering committee is composed of representatives from the following partner organizations:

- FPS Public Health, Environment and Food Safety
- RIZIV-INAMI
- Vlaams Agentschap Zorg en Gezondheid (VAZG)
- Agence pour une Vie de Qualité (AViQ)
- Brussels-Capital Health and Social Observatory
- Statbel
- InterMutualistic Agency (IMA-AIM)
- Academia

1.5 METHODOLOGICAL CHOICES

1.5.1 Levels of analyses

BeBOD adopts the list of disease and injury categories used for the Global Burden of Disease study (Murray et al., 2012). This classification system corresponds to a tree structure of causes of death, with four levels of disaggregation and more than 100 specific diseases and injuries. The first level defines three broad groups of causes: Group I, consisting of communicable diseases, maternal causes, conditions arising in the perinatal

period and nutritional deficiencies, Group II encompassing the non-communicable diseases; and Group III, comprising intentional and unintentional injuries. Each group has been divided into several sub-categories of disease and injury that are mutually exclusive and exhaustive. A third level of disaggregation is used to identify more specific causes within each of the subcategories. Finally, for some level 3 causes, a fourth level of disaggregation is provided, specifying further subtypes of the cause.

Given the currently limited resources for the BeBOD project, initial priority is given to conditions that are estimated by IHME and WHO to cause the greatest health burden in Belgium (e.g., the DALY top 30) (**Annex 1**).

The reference population for BeBOD is the Belgian population as defined by the national registry. Subnational estimates are generated for the Flemish, Walloon and Brussels-Capital region.

The reference year for BeBOD is the most recent year for which validated cause-of-death data are available. At the moment of writing, the reference year is 2016.

Estimates are generated by sex and age, with age group breaks compatible to (0, 1, 5, 10, 15, …, 85+). Results are presented by sex and broad age groups, i.e., 0-4, 5-14, 15-44, 45-64, and 65+.

1.5.2 DALY calculation methods

The calculation of Years of Life Lost (YLLs) is based on the standard life expectancy table used in the most recent Global Burden of Disease study. At the moment of writing, this would correspond to the standard life expectancy table developed for the GBD 2017 study (Murray et al., 2012; **Annex 2**).

Years Lived with Disability (YLDs) are calculated from a prevalence perspective for non-communicable and chronic diseases. This choice reflects the common use of prevalence to monitor chronic diseases (although exceptions exist), and is in line with the GBD study.

Disability weights for the calculation of YLDs are the set used in the most recent Global Burden of Disease study. At the moment of writing, this corresponds to the set developed for the GBD 2013 study (Salomon et al., 2015).

In the initial phase of the project, no external comorbidity adjustments are performed. This implies that disability weights are added when causes occur simultaneously.

Age weighting and time discounting functions are not applied, in line with current GBD methods.

1.5.3 Data adjustments

BeBOD aims to estimate the true disease burden, implying that biases in these data sources are evaluated and corrected, and best estimates are generated for the intermediary epidemiological parameters. In the initial phase of the project, no models are implemented to enforce internal consistency between epidemiological parameters.

1.5.4 Uncertainties

Throughout all steps, uncertainties are documented, quantified, and propagated. In the initial phase of the project, no formal sensitivity analyses are performed. Scenario analyses are performed on an ad hoc basis, if warranted by model uncertainties.

1.6 OUTLINE OF THE GUIDELINES

The following sections of the guidelines describe in more detail the methods used for key elements of the BeBOD study:

- Years of Life Lost
- Years Lived with Disability
- Cancer

2. Years of Life Lost

2.1 INTRODUCTION

Disability-Adjusted Life Years (DALYs) are composed of years of life lost due to premature mortality (YLLs) and years lived with disability, adjusted for severity (YLDs):

$$DALY = YLL + YLD$$

The YLL component reflects the impact of fatal health outcomes. For each considered cause, YLLs are obtained by multiplying the age specific number of deaths with the standard expected residual life expectancy at age of death:

$$YLL = \sum_{i=1}^{a} M_i * RLE_i$$

where $i = 1, \ldots, a$ is one of a considered age groups, M_i the age specific number of deaths due to the outcome, and RLE_i the age-specific residual life expectancy.

For the BeBOD study, a decision has been made to use the most recent GBD life expectancy table. At the moment of writing, this corresponds to the life expectancy table used in the GBD 2017 study. The corresponding age specific residual life expectancy values are provided in **Annex 2**.

According to the WHO national burden of disease manual (Mathers et al., 2001), countries with good vital registration systems such as Belgium can directly estimate YLLs from these data, considering adjustments for incompleteness and miscertification. In what follows, we described the different steps leading to the estimation of YLLs.

2.2 SOURCE OF MORTALITY DATA

Cause of death and population data for Belgium are provided by Statistics Belgium (Statbel), the directorate in charge of the production of vital statistics at the national level. The causes of death are specified in death certificates by a medical doctor; they are subsequently coded according to the ICD-10 rules by trained staff within two regional Health Agencies (one for Flanders and Brussels, one for Wallonia), before being pooled at the national level by Statistics Belgium. Regular coordination meetings between the regional and federal levels are organized in order to guarantee consistency in the coding/registration rules.

Deaths of non-residents are not excluded, as these account for only a minor proportion of all deaths registered in Belgium.

2.3 ALLOCATING DEATHS TO CAUSES

In a first step, the ICD-10 coded definition of the underlying cause of death is mapped to the GBD cause list (GBD 2017 Mortality and Causes of Death Collaborators, 2018). The GBD cause list arranges the 350 causes of health loss studied within the GBD in hierarchical nested categories – referred to as "levels". At the highest level, causes are split into very large categories: communicable, maternal, neonatal, and nutritional causes; non-communicable diseases; and injuries. Within each of those categories, causes of health loss are broken down with increasing specificity at each level. For example, consider acute myocardial infarct, which is a level 4 cause in the GBD cause list:

- Level 1: Non-communicable diseases
- Level 2: Cardiovascular diseases
- Level 3: Ischemic heart disease
- Level 4: Acute myocardial infarct

The cause list is mutually exclusive and collectively exhaustive at every level of aggregation; causes not individually specified are captured in residual categories, such as "other intestinal infectious diseases."

2.4 REDISTRIBUTION OF ILL-DEFINED DEATHS

When assigning each individual death on the basis of the ICD-10 code, the majority of ICD-10 codes are directly assigned to a specific cause of death. In some cases, the ICD-10 code is assigned to what are termed ill-defined causes of death (IDD) in burden of disease studies. These IDDs are causes of death that have been coded with ICD-10 codes in vital registers but for the purposes of burden of disease studies, are not regarded as sufficiently specific causes of death. These IDDs therefore need to be redistributed amongst specific causes of death across the burden of disease cause list. Specific examples of IDDs include the following:

- Causes that should not be considered as the underlying cause or that are implausible as a cause of death, such as hypertension and paraplegia;
- Intermediate causes: causes such as septicemia and pneumonitis that likely had some other precipitating cause;
- Immediate causes: causes that are generally observed as modes of dying, such as cardiac arrest, heart failure and respiratory failure; and
- Causes that are ill-defined or unspecified within a larger ICD cause group; for example, C26.0 "Malignant neoplasm of intestinal tract, part unspecified", or R99 "Ill-defined and unknown cause of mortality".

The BeBOD study reclassifies IDDs to cause-specific deaths respecting the methods which have been utilized in the GBD studies (Murray et al., 2012; Zhou et al., 2016; GBD 2015 Mortality and Causes of Death Collaborators, 2016), and adapted by the Scottish Public Health Office (ScotPHO) for their national burden of disease study.

The redistribution algorithm defines a set of IDD groupings and each IDD has a number of target causes upon which the IDD death should be allocated to. In the GBD study, this is done either using fixed coefficients or based on a regression model (Ahern et al., 2011). The latter method is not implemented as part of the BeBOD study because it requires data from multiple countries. Instead the IDD are redistributed to the target cause-specific diseases respecting their relative proportions by sex and age group (<1, 1-4, 5-14, 15-49, 50-59, 60+). The relative proportions are calculated based on all deaths in Belgium during the 5-year-period prior to the reference year. For each IDD, a specific cause is simulated based on the age and sex specific relative proportions. When no target specific causes are observed for a given age and sex group, each target cause receives an equal weight. The simulation process is repeated 100 times, thus resulting in 100 datasets containing only specific causes. The random draws are summarized by their mean and a 95% uncertainty interval.

The IDDs can be classified in two different ways:

According to the level of redistribution

- Level 0 includes all garbage codes for which a Level 1 GBD cause cannot be directly assigned. For example, the underlying causes of sepsis or peritonitis, if not specified in the data, could be an injury, a non-communicable disease, or a type of communicable disease. In these cases, deaths are redistributed across all three of these Level 1 causes. In addition, deaths coded to impossible or ill-defined causes of death, including senility and unspecified causes, fall into this category, as they are redistributed onto all causes.
- Level 1 includes all garbage codes that can be assigned to one specific Level 1 cause in the GBD cause list. This would include deaths coded to unspecified injuries (X59), which are redistributed onto all injuries.
- Level 2 includes all garbage codes for which we know the Level 2 cause of death, and can redistribute onto Level 3 causes. This includes deaths coded to causes such as unspecified cardiovascular disease, which falls within the Level 2 cause cardiovascular diseases, as well as those coded to unspecified cancer site, which falls within the Level 2 neoplasms cause.

- Level 3 includes all garbage codes for underlying causes of death that can be redistributed within a Level 3 cause. This includes garbage codes such as “unspecified stroke” or “unspecified road injuries.”

According to the redistribution target

- Target distributions defined in terms of ICD codes. This covers the largest proportion of IDDs.
- Target distributions defined in terms of GBD causes. This only covers a minor proportion of IDDs.
- Target distribution corresponding to all causes. For the sake of computational simplicity, these IDDs are redistributed to all GBD causes, because the number of GBD causes is much smaller than the number of ICD codes.

The three types of redistribution targets are implemented in a sequential way. First, all ICD-based redistributions are performed. Then, the GBD cause-based redistributions are performed, using the dataset resulting from the previous step to define the target distribution. Finally, the remaining IDDs are redistributed to all causes, using the dataset resulting from the previous two steps to defined the target distribution.

2.5 EXPERT EVALUATION OF METHODS AND RESULTS

Expert evaluations are set up to assess and evaluate the proposed methods and the ensuing results, in particular those of the redistribution of IDDs. The expert group comprises representatives of Statbel and the Belgian Mortality and Cause of Death evaluation group.

3. Years Lived with Disability

3.1 INTRODUCTION

Disability-Adjusted Life Years (DALYs) are composed of years of life lost due to premature mortality (YLLs) and years lived with disability, adjusted for severity (YLDs):

$$DALY = YLL + YLD$$

The YLD component reflects the impact of non-fatal health outcomes. In BeBOD, a prevalence approach is applied for estimating YLDs for non-communicable diseases:

$$YLD = p * DW$$

where p is the prevalence of the outcome and DW the associated disability weight.

This definition thus implies a need to derive age and sex specific prevalence estimates for all relevant non-fatal outcomes, as well as corresponding disability weights.

The World Health Organization provides a general step-by-step description of how to proceed with estimating YLDs (WHO, 2001). Based on this description, we define the following stepwise approach to estimate Belgian YLDs:

1. Prioritization of outcomes
2. Establishment of case definition for outcomes
3. Identification of data sources
4. Evaluation of data sources
5. Quantification of prevalence “best estimate”
6. Review of disease models
7. Calculation of YLDs
8. Expert evaluation of methods and results

For each individual outcome, the selected methods are documented in a dedicated technical appendix.

An exception to this general approach for calculating YLDs is cancer, for which the starting point is an incidence-based disease model. The specific methods for this group of conditions are explained in more detail in **Chapter 4**.

3.2 PRIORITIZATION OF OUTCOMES

Since there is no single comprehensive data source on prevalence of non-fatal health outcomes in Belgium, each outcome (or outcome cluster) needs to be addressed in an ad hoc way. This calls for a prioritization procedure, which would ensure that 1) available

knowledge and resources are optimally used, and 2) the top causes of disease burden are addressed. The following prioritization process is therefore applied:

- Top causes of disease burden in Belgium based on the WHO Global Health Estimates (but excluding ill-defined outcomes)
- Outcomes for which Sciensano has specific expertise and resources

Annex 1 shows the top 30 outcomes per the WHO Global Health Estimates 2016. Among these outcomes, Sciensano has specific knowledge and resources related to malignant neoplasms (Cancer Center), diabetes (Initiative for Quality promotion and Epidemiology in Diabetes care), and drug use disorders (Drugs Team).

To exploit synergies, the priority outcomes may be addressed in a clustered approach. **Figure 2** shows the relative contribution of different outcomes and outcome clusters to the disease burden in the Netherlands. According to the WHO Global Health Estimates 2016, malignant neoplasms and cardiovascular diseases are the two most important outcome clusters in Belgium, contributing 19% and 16% to the total disease burden, respectively.

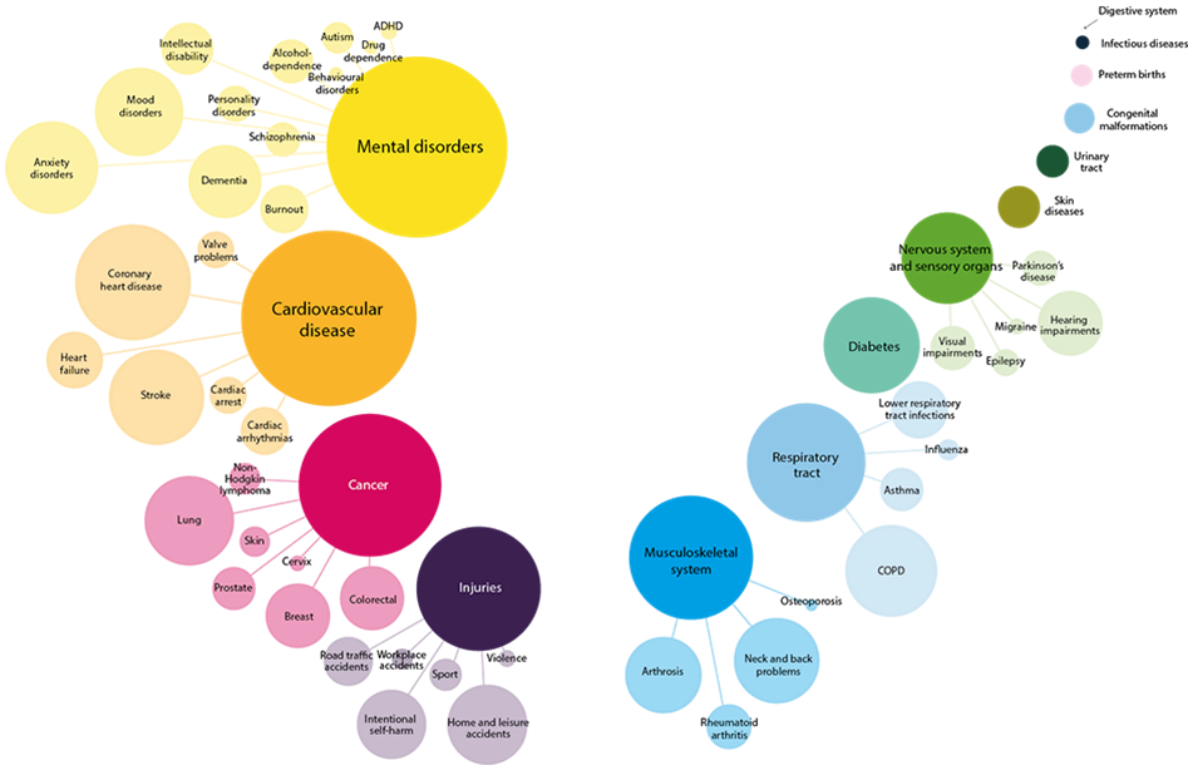

Figure 2. Relative contribution of outcomes and outcome clusters to the disease burden in the Netherlands.

3.3 ESTABLISHMENT OF CASE DEFINITION FOR OUTCOMES

Case definitions help to understand the value and validity of different data sources, and are consequently an important tool to compare the data obtained in different data sources. Case definitions furthermore allow making an explicit link between the prevalence data and the disease model, since the definition of what constitutes a case should be the same for both.

In addition to case definitions based on clinical signs and symptoms, standardized classification system can be used to define cases and improve interoperability. The main classification systems used in the Belgian health information system are described below.

3.3.1 International Classification of Diseases (ICD)

The ICD is a classification system created by the World Health Organization to use as an international standard for reporting diseases and conditions. It is the diagnostic classification standard for all clinical and research purposes. The current version is the ICD-10, but in the near future the ICD-11 will be launched. In Belgium, the ICD classification is used in the hospital discharge datasets. Before 2015, the ICD-9 classification in use, while from 2016 onwards, the ICD-10 classification is in use.

3.3.2 International Classification of Primary Care (ICPC-2)

The ICPC classification system is used to code both symptoms/complaints and diagnoses in primary care. In Belgium, the ICPC classification is used in the framework of registration based on general practitioner's health records.

3.3.3 Anatomical Therapeutic Chemical (ATC) classification system

The ATC classification system is a drug classification system of the active ingredients of drugs according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties. In Belgium, the ATC classification is used in the health insurance datasets.

3.3.4 Nomenclatures codes

Nomenclature codes are used to classify healthcare provisions partially or totally reimbursed by the healthcare insurance. In Belgium, nomenclature codes are used in the health insurance datasets.

3.3.5 Diagnostic and Statistical Manual of Mental Disorders (DSM)

The DSM is a classification of the mental disorders and diseases published by the American Psychiatric Association. This classification can be used for the case definition of mental diseases or substance use disorders. In Belgium, the DSM is used to guide the definition of questions on mental and substance use disorders in the Health Interview Survey.

The choice was made to use the DSM-IV instead of the more recent DSM-V (published in 2013) for several reasons. First, for comparability reasons since DSM-IV classification is widely used in research for more than twenty years. Second, the DSM-IV is the classification used in the GBD studies. Finally, evidence has shown that changes made in the DSM-V have a minimal impact on the prevalence of the substance use disorders diagnoses despite some undeniable advantages, e.g., the capacity to capture “diagnostic orphans” (individuals meeting one or two criteria for dependence and none for abuse, and thus not receiving a DSM-IV substance use disorders diagnosis) or the addition of a “craving” criterion. It has to be noticed that a major change from DSM-IV to DSM-V is the combination of substance abuse disorder and substance dependence into a single substance use disorder.

3.4 IDENTIFICATION OF DATA SOURCES

In the past, several initiatives have generated an overview of available health information sources in Belgium:

- The MORBIDAT project, an electronic overview of databases about morbidity and health-related behaviors and the corresponding regulations in Belgium (http://www.wiv-isp.be/epidemio/morbidat/);
- An inventory of health care databases in Belgium performed in 2006 by the Health Care Knowledge Centre (KCE);
- An inventory and analysis of existing data sources and indicators to meet as a Member State of the European Union the scientific requirements of the European system of health indicators performed by the Scientific Institute of Public Health in 2009-2010;
- An inventory made in the framework of the Eurostat pilot project on diagnosis-specific morbidity statistics (2011);
- The inventory of health information systems currently covered by healthdata.be (https://healthdata.Sciensano.be/nl/inventarisatie-van-registraties).

In the Belgian health information system, five (types of) data sources allow monitoring disease prevalence. These sources are presented below, along with an overview of general strengths and weaknesses.

3.4.1 Disease-specific registries

Disease-specific registers exist only for a very limited number of diseases. Nationally representative registries include the Belgian Cancer Registry and the registries for rare diseases (cystic fibrosis, neuromuscular disorders). Other registries are of regional or local scale.

The methods of data collection for disease-specific registers vary. In some cases, there may be a direct reporting from the diagnosing doctor or another health professional or institution (as is the case for the rare diseases registries). In other cases, the register is a secondary data source which collects together records from hospitals and other services (as is the case for the Belgian Cancer Registry).

Strengths

- Diagnoses are typically made by medical professionals, often following standardized protocols
- Routinely collected data, allowing for a longitudinal approach

Weaknesses

- Registries may not include all patients
- Regional and local registries offer incomplete geographical coverage
- Registries managed by academic research groups may have limited sustainability

3.4.2 Hospital discharge data

Belgium collects records for all hospital stays (general hospitals) in the Minimum Clinical Data (MCD). MCD registration for hospitalized patients was developed in the 1980s and recording this data for all patients became compulsory in 1990. The information in the MCD includes relevant clinical data (e.g. primary and secondary diagnosis) and demographic characteristics of patients. Records are pseudonymized, thus patients cannot be directly identified in the data set. The MCD are used to group hospitalized patients in Diagnosis Related Groups (DRGs). In 1995, All Patient DRGs (AP-DRGs) were chosen as the grouping method to establish hospital comparisons for financial purposes. In 2002, AP-DRGs were replaced by APR-DRGs (All Patient Refined DRGs, 3M HIS version 15.0) in order to pay more attention to the severity of illness. An integrated system for data collection, the Minimum Hospital Data Set (MHD-MZG-RHM) was launched in 2009, integrating the MCD, Minimum Nursing Data (MND) and Medical Urgencies Data (MUG). In addition to the MHD, Belgium collects records for all hospital stays in psychiatric hospitals, psychiatric departments of acute care hospitals, psychiatric nursing homes and initiatives for sheltered living in the Minimum Psychiatric Data (MPD). The MPD contains socioeconomic characteristics of the patient, diagnosis and pre-admission problems, treatment data, and diagnosis and residual problems at discharge.

The Hospital Discharge Data are mainly collected as tools for the measurement of hospital needs for public financing, and evaluation of the effectiveness and quality of hospital care.

Other objectives include the possibility of using the data for internal management and to determine population needs through epidemiological studies.

Strengths

- Official database, organized and managed by public health authorities
- National database
- Exhaustive information on all hospitalized cases
- Diagnoses by medical doctor

Weaknesses

- No information on patients who were not admitted to hospital during the reference year; this may represent a rather large proportion of all cases
- Hospital discharge data are primarily used for administrative purposes, which could result in some problems when data have to be used for epidemiological purposes
- No data are available for 2015, when the database switched from ICD-9 to ICD-10

3.4.3 Health insurance databases

In Belgium the compulsory health insurance is covering 98% of the population. This insurance either covers partially or in some cases completely the costs of a wide range of medical and paramedical services and medicines. There are several specific health insurance databases:

3.4.3.1 Pharmanet

Pharmanet is a database of the National Institute for Health and Disability Insurance (RIZIV-INAMI) that monitors since 1996 prescribing practices of general practitioners and specialist physicians. In the framework of Pharmanet, data are collected – by prescriber – on the pharmaceutical supplies (masterly preparations, diabetic sterile syringes, etc.) delivered by public dispensaries. As an information network, Pharmanet focuses exclusively on reimbursed prescription drugs (in ambulatory medicine) delivered by public dispensaries (pharmacies). Information on the unique beneficiary identification number is kept for a period of only 3 years.

The Pharmanet data has been used by RIZIV-INAMI to identify specific pathologies. These “pseudo-diagnosis”, or “pseudo-pathologies” have been determined by experts, based on the delivery of drugs in the public pharmacies, using the Anatomical Therapeutic Chemical Classification System (ATC codes), a system of alphanumeric codes developed by the World Health Organization for the classification of drugs and other medical products. A case of “pseudo-pathology” is attributed to a person when the total of the Defined Daily Dose

(DDD) is higher or equals 90 during the reference year. According to WHO, a DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults.

3.4.3.2 Gezondheidszorg – Soins de Santé

Since January 2014, the IMA database also contains a permanent healthcare dataset called Gezondheidszorg – Soins de Santé (GZSS). For all insured persons within the mandatory health insurance, this dataset contains details of their reimbursed healthcare provisions using nomenclature codes, which is a coded list of the healthcare provisions partially or totally reimbursed by the healthcare insurance. Information on reimbursed prescription drugs in hospitals pharmacies is also available.

3.4.3.3 Echantillon permanent – Permanente steekproef

The administrative management of the health insurance is done by 7 health insurance organizations, the so-called “mutualiteiten” or “mutualités”. In 2002 an agency was found with as objective to collect and analyze the data from all 7 health insurance organizations: the InterMutualistic Agency (IMA). The IMA database contains the Pharmanet and GZSS datasets, as well as socio-demographic data for all Belgian citizens with (compulsory) health insurance. For research purposes, the IMA created the permanent sample (EPS), i.e., a sample of 1/40 of the IMA data, with an oversampling of 1/20 of the population older than 65 years. A legal framework regulates the modalities for using the EPS to study and monitor health care consumption and expenditure in Belgium. Data are available from 2002 onwards. In contrast to the Pharmanet dataset, the EPS data is a longitudinal dataset with a patient identifier that does not get deleted.

Strengths

- Routinely collected data, allowing for a longitudinal approach
- Validated “pseudo-diagnoses”, based on medication and care, for a certain number of conditions
- Health insurance data cover nearly 100% of the population
- The EPS is a sufficiently large and representative sample of the complete dataset

Weaknesses

- Health insurance data focus exclusively on reimbursed prescription drugs and medical acts; they thus exclude non-reimbursed drugs.
- The databases do not contain information on diagnoses; however, for a certain number of conditions “pseudo-diagnoses” are constructed based on medication and care

- The database will not capture patients that do not consume reimbursed medication or care, leading to a potentially high number of false negatives when estimating disease prevalence

3.4.4 Sentinel networks of general practitioners

In Belgium, there are two sentinel network of general practitioners: the Intego sentinel network of general practitioners and Sciensano network of general practitioners (SGPs).

3.4.4.1 Intego sentinel network of general practitioners

The Intego network, operational since 1994, is an electronic patient record (EPR)-based network of 54 voluntarily participating GP practices in Flanders, the northern region of the country, which all use the same EPR software. The network is coordinated by the Academic Centre for General Practice at the KU Leuven and covers approximately 2% of the Flemish population. The Intego database contains information on diagnoses (primarily based on the International Classification of Primary Care (ICPC) coding system) and prescribed drugs. Aggregated results for the most common disorders can be explored online via https://intego.gbiomed.kuleuven.be/intego-apps/inc_prev_v0/.

Strengths

- Diagnoses are made by medical professionals
- Routinely collected data, allowing for a longitudinal approach

Weaknesses

- Does not capture patients that bypass the GP (emergency department, hospitalization) unless the information is transmitted to the GP
- Results are limited to Flanders
- At the level of Flanders, the representativeness cannot be 100% guaranteed (the network only includes a sample of GPs using a specific software and interested in registration)
- While GPs are representative of the global group of GPs in Flanders according to age and sex, they might not be representative for their management of health problems
- Since there are no patient lists per GP in Belgium, it is difficult to estimate the denominator correctly

3.4.4.2 Sciensano network of general practitioners (SGPs)

The network of sentinel GPs exists since 1979. The network comprises about 120 general practices all over Belgium who weekly report data about 8 different health problems (infectious and non-infectious diseases). Other are monitored recurrently to gather data at

regular intervals . The coverage of the network is estimated at 1.1% – 1.5% of the Belgian population. The registration is done on the website of the network of sentinel general practitioners.

Strengths

- Diagnoses are made by medical professionals
- Routinely collected data, allowing for a longitudinal approach
- Representativeness of GPs in Belgium

Weaknesses

- Does not capture patients that bypass the GP (emergency department, hospitalization) unless the information is transmitted to the GP
- Some diseases are not yearly registered
- Since there are no patient lists per GP in Belgium, it is difficult to estimate the denominator correctly

3.4.5 Health interview survey

The Belgian Health Interview Survey (HIS) collects information on the health status, life style and medical consumption of a representative sample of the general Belgian population, including elderly staying in a home. Information is also collected on a wide range of sociodemographic background characteristics. Interviews are carried out through a face-to-face interview and a self-complete questionnaire. The basic sample consists of 10,000 persons but oversampling of specific population groups is possible. By using weighting factors representative results can be calculated at the level of the total population. To date, a HIS has been organized in Belgium in 1997, 2001, 2004, 2008, 2013, and 2018.

Strengths

- Based on information from a representative sample of the Belgian population
- Provides representative results at national and regional levels

Weaknesses

- Self-reported information may lead to false positive and false negatives
- Not yearly available (+/- every 5 years)
- Comparing estimates between subgroups of the sample might lack statistical precision

3.5 EVALUATION OF DATA SOURCES

For each of the included outcomes, an overview is made of the available databases, including an assessment of the operational case definition, strengths, weaknesses, and

sensitivity/specificity of the database. The latter is assessed in a qualitative way (i.e., high, medium, low), unless quantifications are available from scientific literature.

Several criteria are used to consider sources for best estimates:

- Is the database exhaustive or is it a sample?
- Is the case definition based on a medical diagnosis or a proxy?
- Will the source capture all the cases?
- Is it a regional or a national level?
- Are there yearly or periodic updates?

Figure 3 describes the steps followed in the choice of the best estimate.

Step 1: Is there in Belgium an exhaustive and reliable registry of the disease?

- If yes, registry is selected as best estimate.
- If no, go to step 2.

Step 2: Are most of the cases treated in the hospital?

- If yes, HDD is selected as best estimate.
- If no, go to step 3.

Step 3: Are there nomenclature codes or reimbursed drugs specific to the disease? Is the prescription rate for those drugs high?

- If yes, health insurance data is selected as best estimate.
- If no, go to step 4.

Step 4: Are people suffering from the disease frequently in contact with GPs? Is the disease known to be well recognized in primary care?

- If yes, sentinel GP network is selected as best estimate.
- If no, go to step 5.

Step 5: Is there a question related to the disease in the HIS? Is it a risk that question on the disease leads to a social desirability bias?

- If yes, HIS is selected as best estimate.
- If no, no best estimate can be selected. Then choose the best source available depending on the sensitivity/specificity assessment.

Depending on the disease and the type of the data source, and in absence of quantifications from the scientific literature, sensitivity is assessed using several indicators:

- **Hospital discharge data (HDD):** the hospitalization rate, i.e. the proportion of people usually hospitalized with this disease/condition as primary diagnosis in a year.
- **Health insurance data:** the prescription rate of a reimbursed drug specific to the disease in patients with the disease.
- **Health interview survey:** the importance of a potential social desirability bias, i.e. the fact that some people report an illness incorrectly because the disease is perceived as not socially acceptable.
- **Sentinel GPs Network:** the frequency of contacts with the GP when people are suffering from the disease and/or the recognition rate of the disease by the primary care practitioner.

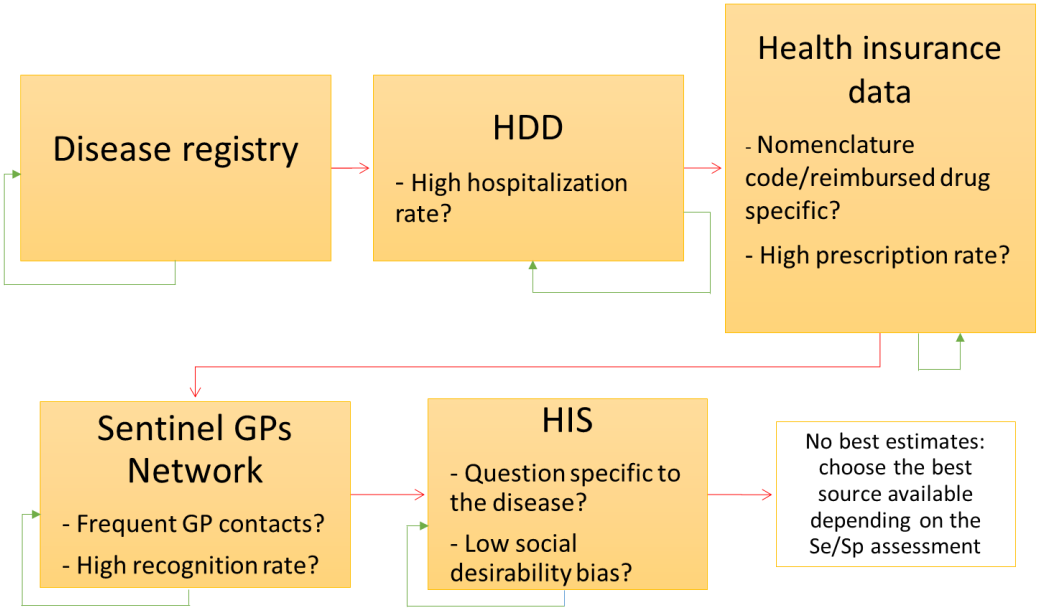

Figure 3. Evaluation process of the data sources

Regarding the validity of the health insurance data source using a defined set of ATC codes, an evaluation of the validity of the "pseudo-diagnoses" or "pseudo-pathologies" has been made in the HISLINK 2013 project (Berete et al., 2019) through a linkage between the Health Insurance data (IMA) and the data from the Health Interview Survey (HIS).

The agreement between the two databases has been assessed by calculating the following validity measures: the sensitivity, the specificity, the positive and negative predictive values and the Cohen's kappa coefficient, using the HIS 2008 data as gold standard. The same analysis is under way with data from the HIS 2013 and could be extended to the HIS 2018 edition.

In this case, the validity measures were defined as following:

- Sensitivity is the percentage of people with chronic disease in the HIS (true patients) who have been correctly identified as having this disease in the IMA database.
- Specificity is the percentage of people who do not suffer from chronic disease in the HIS and who are identified as not having this chronic disease in the IMA database.
- The positive predictive value (PPV) is the percentage of people who are identified as having a chronic disease in the IMA database and who actually suffer from this disease according to the HIS.
- The negative predictive value (NPV) is the percentage of people who are identified as not suffering from a pseudo-pathology according to the IMA database and who are effectively not suffering from this disease according to the HIS.
- The Cohen's Kappa Coefficient is used here to measure the agreement between the two databases, by computing the percentage of chance that the results are matching accidentally. Kappa = 0 means that the agreement between the two databases is random, and a kappa = 1 means that there is a perfect match between the two databases. The kappa agreement levels are: mediocre (k <0.20), weak (k = 0.20 to 0.39), moderate (k = 0.40 to 0.59), good (k = 0.60 to 0.79), and very good (k = 0.80 to 1.00).

The same analysis has been done in function of different cut-off points of DDD, allowing to increase the sensitivity, i.e. to identify more cases of the cases identified in the HIS, when using the IMA database.

3.6 QUANTIFICATION OF "BEST" ESTIMATES

For each outcome, one "best" national prevalence estimate needs to be generated. There are different ways of obtaining such a best estimate:

- Select one data source and correct for possible misclassification (cf **Section 3.4**)
- Develop triangulation based on multiple data sources
- Develop pooled estimate based on multiple data sources

For each outcome, the selection of the most appropriate method is based on an appraisal of the available data sources and based on practical considerations. **Annex 3** documents these evaluations for the considered diseases. Prevalence estimates by age group, sex, and region are registered in a standardized Excel spreadsheet.

3.7 REVIEW OF DISEASE MODELS

The relationship between the different health states associated with a given outcome may be visualized in a disease model or outcome tree. Health states include the different acute and chronic stages of the outcome (including complications), which may be stratified in different

severity levels (e.g., mild, moderate, severe). Disease models used in burden of disease studies primarily aim to document the considered health states, and do not aim at a representation of the complete clinical picture of the condition. The disease instead models help in understanding how the number of cases for each health state is calculated. Models typically start with one “parent node”, which contains all cases. This parent node then gives rise to multiple “child nodes”, with the terminal child nodes representing the individual health states. The number of cases for a given health state is then obtained by multiplying the number of cases in the parent node, with the proportions corresponding to each split.

Figure 4 shows a theoretical disease model.

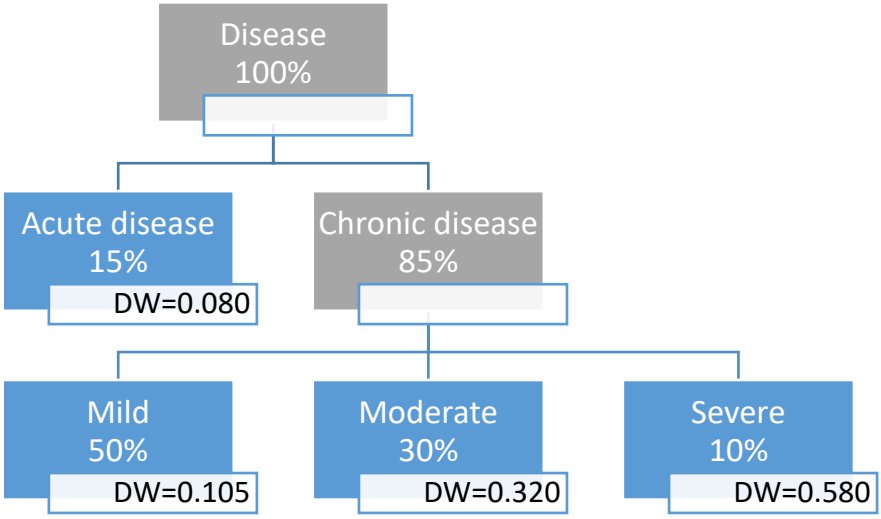

Figure 4. Theoretical disease model, severity distribution and disability weights.

This model presents a theoretical disease and the different associated health states. In the example, 15% of the cases are acute cases and 85% are chronic cases, which are split in 3 severity levels (i.e., mild, moderate and severe). The disability weights reflect the severity of each stage of the disease. Years of life Lost due to Disability (YLD) are calculated by multiplying the proportion of prevalent cases and disability weights for each health state of the condition. The model can also be represented in a table, which also facilitates the calculations (**Table 1**).

Based on the disease model, the average disability weight per case can be calculated, which is the weighted sum of the health state specific disability weights. The “weights” for this sum correspond to the proportion of patients in each of the health states that are associated with a disability weight (the blue boxes in **Figure 4**). In our example, the disability weight per case corresponds to 0.012+0.045+0.082+0.099=0.238. This disability weight per case is also referred to in this document as the “severity-weighted” disability weight.

Table 1. Proportion of patients in the different health states considered in the example disease model

Health state	Parent	Proportion	Disability Weight	Disability weight, proportional
Disease (parent)	N/A	100%	N/A	N/A
Acute disease	Disease (parent)	15%	0.080	15%*0.080=0.012
Chronic disease	Disease (parent)	85%	N/A	N/A
Chronic disease, mild	Chronic disease	50%	0.105	85%*50%*0.105 =0.045
Chronic disease, moderate	Chronic disease	30%	0.320	85%*30%*0.320 =0.082
Chronic disease, severe	Chronic disease	20%	0.580	85%*20%*0.580 =0.099

Disease models and severity distributions for the concerned outcomes are adapted from existing literature and national burden of disease studies conducted in other countries (e.g., the Netherlands, Scotland). The disease models and severity distributions used in the Global Burden of Disease study are used as a starting point (Burstein et al., 2015; GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). Where possible, severity distributions are adapted to the Belgian context. When no information on severity distribution is available, a default severity distribution is used that assumes milder health states to be more common than more severe outcomes. For instance, when there are 3 severity levels, it will be assumed that out of 6 patients, 3 have mild symptoms, 2 have moderate symptoms, and 1 has severe symptoms.

Disability weights are adapted from the Global Burden of Disease study (Salomon et al., 2015), as these provide an exhaustive set of internally consistent disability weights. Where relevant, internal comorbidity is addressed using a multiplicative model: $DW_{comb} = 1 - \prod_i (1 - DW_i)$.

Appendix 3 documents the disease models for the different diseases. Severity-weighted disability weights by age group, sex, and region are registered in a standardized Excel spreadsheet.

3.8 CALCULATION OF YLDS

Calculation of YLDs is conducted by integrating the “best” prevalence estimates with the disease model and severity-weighted disability weights. YLDs are calculated by age, sex and region. Results are registered in disease-specific, standardized csv files.

3.9 EXPERT EVALUATION OF METHODS AND RESULTS

For each outcome or outcome cluster, an expert evaluation is set up to assess and evaluate the proposed methods and the ensuing results. The expert evaluation addresses the following steps:

- Identification of data sources
- Selection of “best estimate”
- Selection of disease model

Experts are defined as individuals with relevant epidemiological and/or clinical knowledge with regards to the concerned outcome (cluster).

4. Cancer

4.1 INTRODUCTION

Cancer is a broad family of diseases that involve abnormal cell growth with the potential to invade or spread to other parts of the body. It is one of the most important disease groups in terms of premature mortality, ill health, and healthcare expenditure. According to the WHO Global Health Estimates 2016, cancer is the most important cluster of health outcomes in Belgium, contributing 19% of the total disease burden (**Annex 1**).

The approach for calculating DALYs for the different cancers does not follow the default calculation methods as described before and is therefore treated separately. The two main distinguishing features are 1) the availability of quasi complete data on cancer incidence from the Belgian Cancer Registry Foundation and 2) the application of a generic incidence-based disease model.

4.2 DATA SOURCE

Data on new cancer cases in Belgium are collected by the Belgian Cancer Registry Foundation. The Belgian Cancer Registry is nationally representative and exhaustive. It collects and records both clinical and pathological data from the anatomic pathology service. The recording of data (topography and morphology) is done using the International Classification of Diseases for Oncology.

Cancer incidence data for Belgium are obtained through the website of the Belgian Cancer Registry. They are extracted by cancer type, 5-year age group, sex, and region, for the period from 2004 to 2016. Cancer prevalence data for Belgium are not routinely available from the Belgian Cancer Registry.

Data on the relative survival, by cancer type, age, sex, year, and region, are obtained from the Belgian Cancer Registry Foundation through a personal communication.

4.3 DISEASE MODEL

We adopted the generic incidence-based disease model used in the Global Burden of Disease study and the Scottish Burden of Disease Study. The model illustrates different cancer stages from diagnosis to death or to remission (**Figure 5**). Incident cases are divided as follows: for a defined period of 10 years, each new case of cancer will evolve either to remission or to death. In either case, the first stage of the disease is the period during which a diagnosis is made and treatment initiated. Then comes the "control" stage, in which the survivors will stay for a certain time (10 years after the diagnosis stage), and through which will pass the deceased patients. The latter will then go through the last two stages, namely that of a cancer with metastases and the terminal stage before dying.

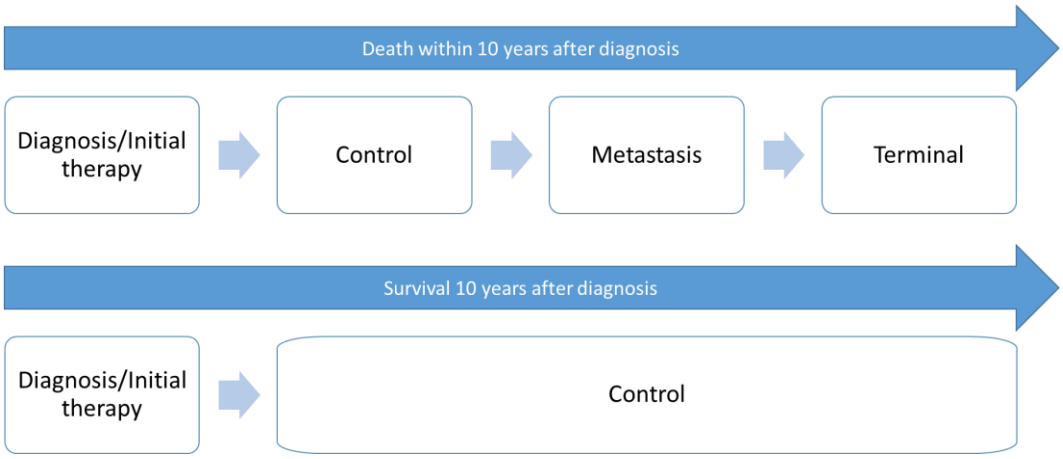

Figure 5. Generic incidence-based cancer disease model

The disability weights for the cancer health states are derived from Salomon et al. (2015) and shown in **Table 2**. The (cancer type-dependent) durations for the different cancer health states are derived from the GBD 2017 study (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018) and are shown in **Table 3**.

Table 2. Health states and disability weights for the generic incidence-based cancer disease model.

Health state	Lay description	Disability Weight
Cancer, diagnosis and primary therapy	This person has pain, nausea, fatigue, weight loss and high anxiety	0.288
Cancer, controlled phase	This person has a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities.	0.049
Cancer, metastatic	This person has severe pain, extreme fatigue, weight loss and high anxiety.	0.451
Terminal phase, with medication	This person has lost a lot of weight and regularly uses strong medication to avoid constant pain. The person has no appetite, feels nauseous, and needs to spend most of the day in bed.	0.540

Table 3. Health states and durations (in months) for the generic incidence-based cancer disease model.

Cancer	Diagnosis/Treatment	Controlled	Metastatic	Terminal
Esophagus	5.0	Calculated based on remainder of time after attributing other cancer stages.	4.60	1 month
Stomach	5.2		3.88	
Liver	4.0		2.51	
Larynx	5.3		8.84	
Lung	3.3		4.51	
Breast	3.0		17.7	
Cervical	4.8		9.21	
Uterus	4.6		11.60	
Prostate	4.0		30.35	
Colorectal	4.0		9.69	
Oral	5.3		9.33	
Nasopharynx	5.3		13.19	
Other part of pharynx	5.3		7.91	
Gallbladder	4.0		3.47	
Pancreas	4.1		2.54	
Melanoma	2.9		7.18	
Ovary	3.2		25.60	
Testicle	3.7		19.47	
Kidney	5.3		5.38	
Bladder	5.1		5.80	
Brain	5.0		6.93	
Thyroid	3.0		19.39	
Mesothelioma	4.0		7.75	
Hodgkin lymphoma	3.7		26.00	
Non-Hodgkin lymphoma	3.7		7.70	
Multiple myeloma	7.0		36.82	
Leukemia	5.0		43.67	
Acute lymphocytic leukemia	12		7.02	
Acute myeloid leukemia	6.0		4.60	
Chronic lymphocytic leukemia	6.0		48.00	
Chronic myeloid leukemia	6.0		4.60	
Leukemia, other	6.0		48.00	
Other	4.4 (mean of other cancer durations)		15.81	

4.4 DALY CALCULATION

The calculation of YLDs and YLLs follows a step-wise approach based on the generic disease model (**Figure 5**). Calculations are performed per cancer type, sex, age, region, and year, and consequently aggregated to obtain (sub)totals.

For each number of incident cases, relative survival rates at year y={1,2,…,10} after diagnosis are applied to obtain the number of survivors and deaths at year y.

For the individuals that die within 10 years after diagnosis, YLDs are calculated by assigning the 4 different cancer health states in the following order:

1. Terminal phase: duration = 1 month
2. Diagnosis/treatment: duration = min(health state duration, remaining time till death)
3. Metastasis = min(health state duration, remaining time till death)
4. Control = remaining time till death

For the individuals that survive 10 years after diagnosis, YLDs are calculated by assigning the 2 different cancer health states in the following order:

1. Diagnosis/treatment: duration = health state duration
2. Control = remaining time till death

Finally, for the individuals that die within 10 years after diagnosis, YLLs are calculated as the product of the number of deaths with the residual life expectancy at the average age of death (**Annex 1**). The latter is obtained as the sum of the age at diagnosis and the time till death.

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ANNEXES

Annex 1. Top 30 specific causes of DALYs according to WHO Global Health Estimates 2016

Rank	Cause	DALYs ('000)	DALYs (% of total)
1	Ischemic heart disease	234	7.2%
2	Trachea, bronchus, lung cancers	155	4.8%
3	Back and neck pain	136	4.2%
4	Alzheimer disease and other dementias	129	4.0%
5	Stroke	128	3.9%
6	Chronic obstructive pulmonary disease	124	3.8%
7	Falls	97	3.0%
8	Self-harm	90	2.8%
9	Depressive disorders	87	2.7%
10	Lower respiratory infections	73	2.3%
11	Diabetes mellitus	67	2.1%
12	Colon and rectum cancers	62	1.9%
13	Breast cancer	60	1.9%
14	Migraine	59	1.8%
15	Road injury	55	1.7%
16	Anxiety disorders	55	1.7%
17	Cirrhosis of the liver	46	1.4%
18	Kidney diseases	40	1.2%
19	Pancreas cancer	36	1.1%
20	Edentulism	35	1.1%
21	Uncorrected refractive errors	35	1.1%
22	Skin diseases	34	1.0%
23	Alcohol use disorders	32	1.0%
24	Osteoarthritis	30	0.9%
25	Lymphomas, multiple myeloma	29	0.9%
26	Prostate cancer	28	0.9%
27	Drug use disorders	27	0.8%
28	Asthma	27	0.8%
29	Bipolar disorder	26	0.8%
30	Brain and nervous system cancers	23	0.7%

Source: Global Health Estimates 2016: Disease burden by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018. https://www.who.int/healthinfo/global_burden_disease/estimates/en/index1.html

Annex 2. GBD2017 theoretical minimum risk reference life table

0	Life expectancy
0	87.89
1	87.01
5	83.04
10	78.05
15	73.07
20	68.11
25	63.16
30	58.21
35	53.27
40	48.37
45	43.50
50	38.70
55	33.98
60	29.32
65	24.73
70	20.32
75	16.09
80	12.18
85	8.78
90	6.06
95	3.90
100	2.23
105	1.61
110	1.36

Source: GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1736-1788. https://doi.org/10.1016/S0140-6736(18)32203-7

Annex 3. Disease-specific methods

1 ACUTE MYOCARDIAL INFARCTION (AMI)

1.1 Case definition

Acute myocardial infarction (AMI), commonly known as a heart attack, is the interruption of blood supply to a part of the heart, causing heart cells to die. This is most commonly due to occlusion (blockage) of a coronary artery following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids (fatty acids) and white blood cells (especially macrophages) in the wall of an artery. The resulting ischemia (restriction in blood supply) and oxygen shortage, if left untreated for a sufficient period of time, can cause damage or death (infarction) of heart muscle tissue (myocardium).

The definitions of definite and possible myocardial infarction (AMI) according to the third universal definition of myocardial infarction are as follows:

1. When there is clinical evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia or
2. Detection of a rise and/or fall of cardiac biomarker values and with at least one of the following: i) symptoms of ischemia, ii) new or presumed new ST-segment-T wave changes or new left bundle branch block, iii) development of pathological Q waves in the ECG, iv) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality, or v) identification of an intracoronary thrombus by angiography or autopsy.
3. Sudden (abrupt) unexplained cardiac death, involving cardiac arrest or no evidence of a non-coronary cause of death. These cases however do not contribute Years Lived with Disability.

Prevalent AMI is considered to last from the onset of the event to 28 days after the event and is divided into an acute phase (0-2 days) and subacute (3-28 days).

1.1.1 Corresponding disease classification codes

ICD-10 codes

- I21 Acute myocardial infarction
- I22 Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
- I23 Certain current complications following acute myocardial infarction
- I24 Other acute ischemic heart diseases

ICD-9 codes

- 410 Acute myocardial infarction
- 411 Other acute and subacute forms of ischemic heart disease

ICPC-2 codes

- K75 Acute myocardial infarction
- K76 Ischemic heart disease w/o angina

ATC codes

- Not applicable: there are no drugs sufficiently specific for treatment of AMI.

Nomenclature codes

- Not applicable: there are no nomenclature codes sufficiently specific to match the case definition of AMI.

1.2 Disease model

1.2.1 Health states

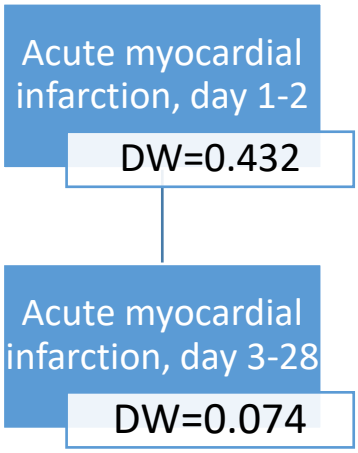

Figure 1. Acute myocardial infarction disease model

1.2.2 Disability weights

Table 1. Disability weights (DW) by health state for acute myocardial infarction according to the Global Burden of Disease study (Salomon et al., 2015)

Health state	Lay description	DW
Acute myocardial infarction, days 1-2	Has severe chest pain that becomes worse with any physical activity. The person feels nauseated, short of breath, and very anxious.	0.432
Acute myocardial infarction, days 3-28	Gets short of breath after heavy physical activity, and tires easily, but has no problems when at rest. The person has to take medication every day and has some anxiety.	0.074

1.2.3 Proportion of patients in the considered health states

Table 2. Proportion of patients in the different health states considered in the acute myocardial infarction disease model, Belgium.

Health state	Parent	Proportion	Source
Acute myocardial infarction, days 1-2	N/A	100%	Per definition
Acute myocardial infarction, days 3-28	Acute myocardial infarction, days 1-2	100%	Per definition

1.2.4 Discussion

Disability weights for the Belgian national burden of disease study are adapted from the Global Burden of Disease study (1), as these provide an exhaustive set of internally consistent disability weights.

The definition of the disease model for AMI closely follows the case definition of AMI. It is assumed that each (non-fatal) case of AMI has a duration of 28 days, including an acute phase of 2 days with severe symptoms, followed by a subacute phase of 26 days with mild symptoms.

1.3 Prevalence

1.3.1 Data sources

Different data sources exist for AMI, each with a specific case definition:

1. **MONICA Registries of Acute Coronary Attacks (RACA):** person with AMI recorded in the registries of Ischemic heart diseases of Charleroi, Ghent/Bruges and Luxembourg during the reference year.
2. **Hospital discharge data:** patient with AMI admitted to the hospital during the reference year (before 2015: ICD-9 codes 410 and 411; after 2015 ICD-10 codes: I21, I22, I23, and I24).
3. **Health insurance data:** not applicable; there are no (reimbursed) medications or health care usages that would allow a sufficiently specific diagnosis of AMI
4. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you had myocardial infarction?”.
5. **Sentinel GP network data (Intego):** number of individuals with myocardial infarction diagnosis ever recorded by GP (ICPC code K75 and K76) who had a GP contact during the reference year.
6. **Sentinel GP network data (Sciensano):** number of individuals with AMI diagnosis recorded by a sentinel GP (ICPC-2 code K75 and K76) during the reference year.

Table 3. Potential sources and methods for the computation of acute myocardial infarction prevalence in Belgium.

Source	Strengths	Weaknesses	Evaluation
MONICA Registries of Acute Coronary Attacks (RACA)	• Use of an international standard protocol and case definition • Long and solid history	• Limited geographical area • Only population 25-74 included (25-69 in Charleroi) • Retrospective data collection • No longer operational since 2009	• Sensitivity: low • Specificity: high
Hospital discharge data	• Exhaustive information on all cases hospitalized for AMI • Diagnoses by medical doctor • Official database, organized and managed by public health authorities • National database	• No information on AMI patients who were not admitted to hospital during the reference year; this is only assumed to be a small proportion of all (non-fatal) AMI patients • HDD is primarily used for administrative purposes, which could result in some problems when data have to be used for epidemiological purposes	• Sensitivity: high • Specificity: high
Health insurance data (IMA/EPS)	N/A: there are no (reimbursed) medications or health care usages that would allow a sufficiently specific diagnosis of AMI		
Health Interview Survey	• Based on information from a representative sample • Provides representative results at national and regional levels	• Self-reported information; it is assumed that there may be many false positive and false negatives • Not yearly available (+/- every 5 years) • Comparing estimates between subgroups of the sample might lack statistical precision	• Sensitivity: medium • Specificity: medium
Sentinel GP network data (Intego)	• Diagnosis by medical professional • Longitudinal approach	• Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP • Results are limited to Flanders • At the level of Flanders, the representativeness	• Sensitivity: low • Specificity: high

		cannot be 100% guaranteed (the network only includes a sample of GPs using a specific software and interested in registration) • For the PP: not possible to identify the reason for consultation, so might not be related to AMI.	
Sentinel GP network data (Sciensano)	• Diagnosis by medical professionals • 120 GP distributed evenly all over the country • Representativeness of GPs in Belgium (for age and sex)	• Will not capture patients that bypass the GP (ED, hospitalization) unless the information is transmitted to the GP • Only periodic registration • Last registration: 1985-1987	• Sensitivity: medium • Specificity: high

1.3.2 National best estimate

Although the MONICA registries provide the most reliable data, they are limited in coverage. It is therefore proposed to use the hospital discharge data as the best national estimate for AMI incidence. To obtain prevalence estimates, incidence estimates can be multiplied with the duration of the condition in years, i.e., 28/365.

1.4 References

GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018 Nov 10;392(10159):1736-88.

Salomon JA, Haagsma JA, Davis A, de Noordhout CM, Polinder S, Havelaar AH, et al. Disability weights for the Global Burden of Disease 2013 study. Lancet Glob Health 2015 Nov;3(11):e712-e723.

2 ANGINA PECTORIS

2.1 Case definition

Angina pectoris is the chronic manifestation of ischemic heart disease. It can be defined as clinically diagnosed stable exertional angina pectoris or definite angina pectoris according to the Rose Angina Questionnaire, physician diagnosis, or taking nitrate medication for the relief of chest pain.

2.1.1 Corresponding disease classification codes

ICD-10 codes

- I20 Angina pectoris
- I25 Chronic ischemic heart disease

ICD-9 codes

- 413 Angina pectoris
- 414 Other forms of chronic ischemic heart disease

ICPC-2 codes

- K74 Ischemic heart disease w/ angina

ATC codes

- C01DA Organic nitrates
- C01DX12 Molsidomine
- C01DX16 Nicorandil

Nomenclature codes

- Not applicable: there are no nomenclature codes sufficiently specific to match the case definition of angina pectoris.

2.2 Disease model

2.2.1 Health states

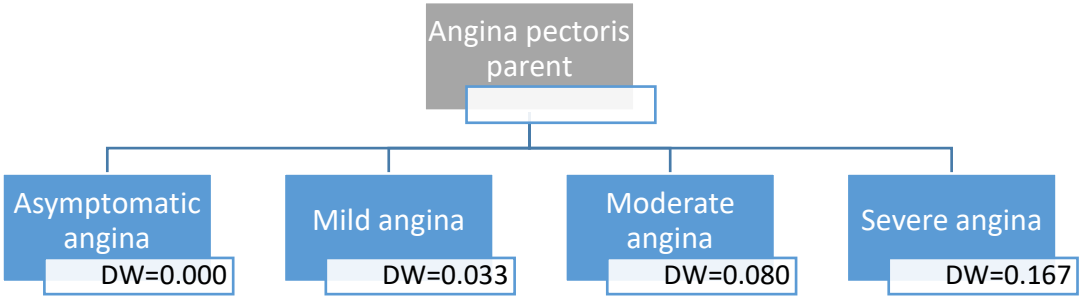

Figure 2. Angina pectoris disease model

2.2.2 Disability weights

Table 1. Disability weights (DW) by health state for angina pectoris according to the Global Burden of Disease study (Salomon et al., 2015)

Health state	Lay description	DW
Asymptomatic angina	N/A	0.000
Mild angina	Has chest pain that occurs with strenuous physical activity, such as running or lifting heavy objects. After a brief rest, the pain goes away.	0.033
Moderate angina	Has chest pain that occurs with moderate physical activity, such as walking uphill or more than half a kilometer (around a quarter-mile) on level ground. After a brief rest, the pain goes away.	0.080
Severe angina	Has chest pain that occurs with minimal physical activity, such as walking only a short distance. After a brief rest, the pain goes away. The person avoids most physical activities because of the pain.	0.167

2.2.3 Proportion of patients in the considered health states

Table 2. Proportion of patients in the different health states considered in the angina pectoris disease model, Belgium.

Health state	Parent	Proportion	Source
Angina pectoris, parent	N/A	100%	Per definition
Asymptomatic angina	Angina pectoris, parent	30.5%	Burstein et al. (2015)
Mild angina	Angina pectoris, parent	24.0%	Burstein et al. (2015)
Moderate angina	Angina pectoris, parent	12.6%	Burstein et al. (2015)
Severe angina	Angina pectoris, parent	33.0%	Burstein et al. (2015)

2.2.4 Discussion

Disability weights for the Belgian national burden of disease study are adapted from the Global Burden of Disease study (1), as these provide an exhaustive set of internally consistent disability weights.

The severity distribution in the GBD model is based exclusively on data from the USA, raising questions on applicability for the Belgian context. The severity distribution was derived from an analysis of the Medical Expenditure Panel Surveys (MEPS) in the USA (https://meps.ahrq.gov/mepsweb/). MEPS is an overlapping continuous panel survey of the United States non-institutionalized population whose primary purpose is to collect

information on the use and cost of health care. Panels are two years long and are conducted in five rounds, which are conducted every five to six months. Each panel typically contains about 30,000 to 35,000 individual respondents. Respondents self-administer the SF-12 twice per panel, at rounds 2 and 4, typically about a year apart. Only adults 18 years and older completed the SF-12. MEPS also usually collects information on diagnoses based on self-report of reasons for encounters with health services. In addition, diagnoses are derived through additional questions on “problems that bother you” or conditions that led to “disability days”, i.e., days out of role due to illness. Professional coders translate the verbatim text into three-digit ICD-9 codes. The main reason for angina pectoris being measured in MEPS relates to health care contact. For GBD 2017, data were used from 2000-2014.

Since the health states are not defined in terms of clinical grading scales, comparability with available epidemiological and clinical evidence is hampered.

2.3 Prevalence

2.3.1 Data sources

Different data sources exist for angina pectoris, each with a specific case definition:

1. **Hospital discharge data:** patient with angina pectoris admitted to the hospital during the reference year (before 2015: ICD-9 codes 413 and 414; after 2015 ICD-10 codes: I20 and I25).
2. **Health insurance data:** person with a prescription for ATC codes C01DA, C01DX12 AND/OR with C01DX16 referring nomenclature during the reference year.
3. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you had coronary heart disease (angina pectoris)?”.
4. **Sentinel GP network data (Intego):** number of individuals with angina pectoris diagnosis ever recorded by GP (ICPC-2 code K74) who had a GP contact during the reference year.
5. **Sentinel GP network data (Sciensano):** not applicable; angina pectoris has not been registered by the Sciensano SGPs network.

Table 3. Potential sources and methods for the computation of angina pectoris prevalence in Belgium.

Source	Strengths	Weaknesses	Evaluation
Hospital discharge data	• Exhaustive information on all cases hospitalized for angina pectoris	• No information on angina pectoris patients who were not admitted to hospital during the reference year; this may represent a rather	• Sensitivity: low • Specificity: high

	• Diagnoses by medical doctor • Official database, organized and managed by public health authorities • National database	large proportion of all cases • HDD is primarily used for administrative purposes, which could result in some problems when data have to be used for epidemiological purposes	
Health insurance data (IMA/EPS)	• Case definition based on medication and care • Large, representative sample • Longitudinal approach	• Case definitions based on prescription of medicines and not on a medical diagnosis, may generate false positives and false negatives → False positives: patients without angina, treated with the concerned drugs for other reasons → False negatives: angina patients without medical treatment • People who are not insured (e.g. homeless and illegal people, foreigners with their official residence abroad) are not included; this however comprises a small part of the total population (~2%)	• Sensitivity: medium • Specificity: medium
Health Interview Survey	• Based on information from a representative sample • Provides representative results at national and regional levels	• Self-reported information may lead to false positive and false negatives • Not yearly available (+/- every 5 years) • Comparing estimates between subgroups of the sample might lack statistical precision	• Sensitivity: medium • Specificity: medium
Sentinel GP network data (Intego)	• Diagnosis by medical professional • Longitudinal approach	• Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP • Results are limited to Flanders • At the level of Flanders, the representativeness cannot be 100% guaranteed (the network only includes a sample of GPs using a specific software and interested in registration) • For the PP: not possible to identify the reason for consultation, so might not	• Sensitivity: low • Specificity: high

		be related to the condition in question.
Sentinel GP network data (Sciensano)	Not available. Angina pectoris has not been registered by the Sciensano SGPs network.	

2.3.2 National best estimate

All available data sources are to a lesser or more extent limited in providing nationally representative and accurate information on the prevalence of angina pectoris. Given the lack of a validated “pseudodiagnosis” in the health insurance dataset, the use of the Health Interview Survey data is preferred over the health insurance data.

2.3.3 Discussion

The validity of the selected data source remains unclear. Additional research, using linked datasets, is needed to assess the sensitivity and specificity of the HIS data. The question on coronary heart disease (angina pectoris) was introduced in the HIS2013. Therefore, limited information is available on historical trends.

2.4 References

Burstein R, Fleming T, Haagsma J, Salomon JA, Vos T, Murray CJ. Estimating distributions of health state severity for the global burden of disease study. Popul Health Metr 2015;13:31.

GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018 Nov 10;392(10159):1736-88.

Salomon JA, Haagsma JA, Davis A, de Noordhout CM, Polinder S, Havelaar AH, et al. Disability weights for the Global Burden of Disease 2013 study. Lancet Glob Health 2015 Nov;3(11):e712-e723.

3 CEREBROVASCULAR DISEASE

3.1 Case definition

Cerebrovascular diseases (CVD) refer to a group of diseases, conditions or troubles that affect the circulation of blood in the brain, either because of a vascular occlusion or because of a vascular bleeding, leading to a lack of the oxygen supply to the brain cells, resulting in a brain infarction or hemorrhage (Ferrer and Vidal, 2018). Cerebrovascular diseases include stroke, aneurysm, transient ischemic attack (TIA) and vascular malformation. However, we excluded the TIA from the case definition as it does not contribute to the Years Lived with Disability because of its very short duration.

Since most of cerebrovascular diseases manifest themselves as ischemic or hemorrhagic strokes (Ferrer and Vidal, 2018), and for reasons of consistency, the burden of CVDs is calculated based on the stroke model, as in the GBD methodology (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). We therefore refer to the stroke disease model and the stroke severity distribution when estimating the burden of CVDs, making the assumption that CVDs follow the same disease model as stroke.

According to the World Health Organization (WHO), strokes are caused by disruption of the blood supply to the brain. This is the consequence either of a blockage (**ischemic stroke**) or of a rupture of a blood vessel (**hemorrhagic stroke**).

A distinction is furthermore made between:

- **Acute stroke:** Stroke cases are considered acute from the day of incidence of a first-ever stroke through day 28 following the event.
- **Chronic stroke:** Stroke cases are considered chronic beginning 28 days following the occurrence of an event. Chronic stroke includes the sequelae of an acute stroke AND all recurrent stroke events.

3.1.1 Corresponding disease classification codes

The ICD-10 classification contains several codes for cerebrovascular diseases (I60-I69). Here, the choice was made to exclude transient ischemic attack (TIA; ICD-10 code G45; ICD-9 code 435) from the case definition for the calculation of the Years Lived with Disability (YLDs) since, by definition, the duration of TIA is very short (<24h) and causes no permanent disability. We have also excluded ICD-10 code I69 (sequelae of cerebrovascular disease) from the acute stroke prevalence calculation, since, by definition, it refers to chronic stroke.

ICD-10 codes

- I60 Subarachnoid hemorrhage
- I61 Intracerebral hemorrhage
- I62 Other, non-traumatic intracranial hemorrhage
- I63 Cerebral infarction
- I64 Stroke, not specified as hemorrhage or infarction
- I65 Occlusion/stenosis of pre-cerebral arteries without infarction
- I66 Occlusion/stenosis of cerebral arteries without infarction
- I67 Other cerebrovascular diseases
- I68 Cerebrovascular diseases in disorders classified elsewhere
- ~~I69 Sequelae of cerebrovascular disease (excluded)~~
- ~~G45 Transient ischemic attack (TIA) (excluded)~~
- G46 Vascular syndromes of brain in cerebrovascular disease

ICD-9 codes

- 430 Subarachnoid hemorrhage
- 431 Intracerebral hemorrhage
- 432 Other and unspecified intracranial hemorrhage
- 433 Occlusion and stenosis of precerebral arteries
- 434 Occlusion of cerebral arteries
- ~~435 Transient cerebral ischemia (excluded)~~
- 436 Acute, but ill-defined, cerebrovascular disease
- 437 Other and ill-defined cerebrovascular disease

ICPC-2 codes

- K90 Stroke/cerebrovascular accident
- K91 Cerebrovascular disease

ATC codes

- Not applicable: there are no drugs sufficiently specific for treatment of CVD.

Nomenclature codes

- 477724 Fees for the neurology specialist for the coordination of a diagnostic and the establishment of a treatment plan by a multidisciplinary team in stroke care when taking charge of the treatment of a patient hospitalized due to a recent stroke (date of creation 01/09/2012)
- 477746 Fees for the accredited neurology specialist for the coordination of a diagnostic and the establishment of a treatment plan by a multidisciplinary team in stroke care when

taking charge of the treatment of a patient hospitalized due to a recent stroke (date of creation 01/09/2012)

- 477761 Fees for the neurology specialist to coordinate a multi-disciplinary stroke care team to establish a care plan for a patient hospitalized due to a stroke (date of creation 01/09/2012)
- 477783 Fees for the accredited neurology specialist to coordinate a multi-disciplinary stroke care team to establish a care plan for a patient hospitalized due to a stroke (date of creation 01/09/2012)

3.2 Disease model

In the case of cerebrovascular diseases, the choice has been made to follow the stroke disease model, since strokes represent most of the CVDs cases (Ferrer and Vidal, 2018). The same choice has been made in the GBD study (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). A distinction is furthermore made between acute stroke (≤28 days) and chronic stroke (>28 days). Both models have the same health states with the same disability weights, but different severity distributions; the chronic stroke disease model furthermore has an asymptomatic health state (with DW=0).

3.2.1 Health states

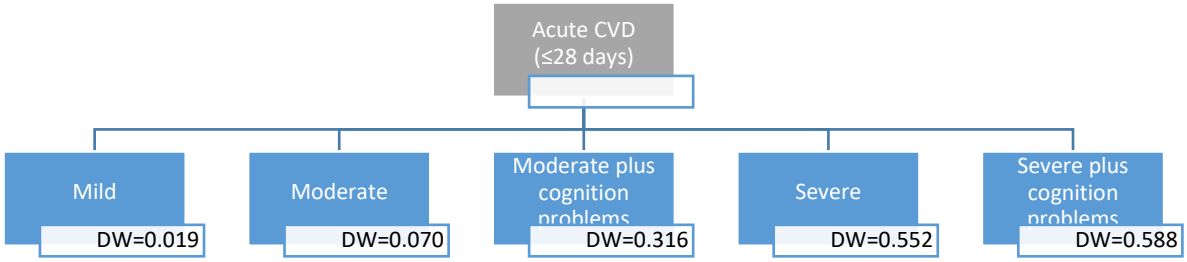

Figure 1. Acute cerebrovascular disease (stroke) disease model

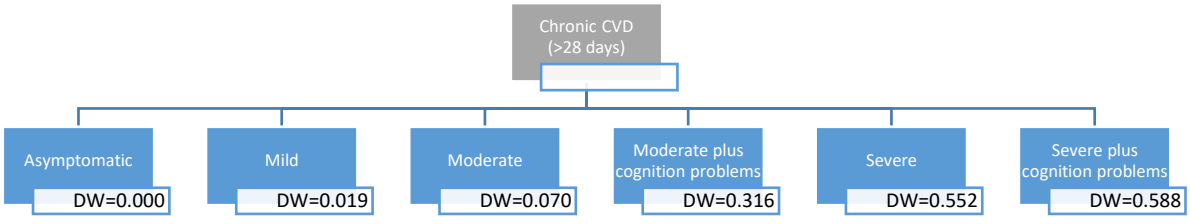

Figure 2. Chronic cerebrovascular disease (stroke) disease model

3.2.2 Disability weights

Table 1. Disability weights (DW) by health state for cerebrovascular disease (stroke) according to the Global Burden of Disease study (Salomon et al., 2015)

Health state	Lay description	DW
Chronic, asymptomatic	Has suffered a stroke but experiences no symptoms by virtue of, for instance being on treatment or because of the natural course of the condition	0.000
Mild	Has some difficulty in moving around and some weakness in one hand, but is able to walk without help.	0.019
Moderate	Has some difficulty in moving around, and in using the hands for lifting and holding things, dressing, and grooming.	0.070
Moderate plus cognition problems	Has some difficulty in moving around, in using the hands for lifting and holding things, dressing and grooming, and in speaking. The person is often forgetful and confused.	0.316
Severe	Is confined to a bed or a wheelchair, has difficulty speaking, and depends on others for feeding, toileting, and dressing.	0.552
Severe plus cognition problems	Is confined to a bed or a wheelchair, depends on others for feeding, toileting, and dressing, and has difficulty speaking, thinking clearly, and remembering things.	0.588

3.2.3 Proportion of patients in the considered health states

Table 2. Proportion of patients in the different health states considered in the acute cerebrovascular disease (stroke) disease model, Belgium.

Health state	Parent	Proportion	Source
Acute CVD	N/A	100%	Per definition
Mild	Acute CVD	34%	GBD 2017
Moderate	Acute CVD	15%	GBD 2017
Moderate plus cognition problems	Acute CVD	18%	GBD 2017
Severe	Acute CVD	17%	GBD 2017
Severe plus cognition problems	Acute CVD	16%	GBD 2017

Table 3. Proportion of patients in the different health states considered in the chronic cerebrovascular disease (stroke) disease model, Belgium.

Health state	Parent	Proportion	Source
Chronic CVD	N/A	100%	Per definition
Asymptomatic	Chronic CVD	19%	GBD 2017
Mild	Chronic CVD	25%	GBD 2017

Moderate	Chronic CVD	15%	GBD 2017
Moderate plus cognition problems	Chronic CVD	20%	GBD 2017
Severe	Chronic CVD	10%	GBD 2017
Severe plus cognition problems	Chronic CVD	12%	GBD 2017

3.2.4 Discussion

No national data were found on the prevalence of the cases in the different health states. Therefore, we have used the severity distribution based on the GBD model. The severity distribution in the GBD model is based exclusively on data from the USA, raising questions on applicability for the Belgian context. The severity distribution was derived from an analysis of the Medical Expenditure Panel Surveys (MEPS) in the USA (https://meps.ahrq.gov/mepsweb/). MEPS is an overlapping continuous panel survey of the United States non-institutionalized population whose primary purpose is to collect information on the use and cost of health care. Panels are two years long and are conducted in five rounds, which are conducted every five to six months. Each panel typically contains about 30,000 to 35,000 individual respondents. Respondents self-administer the SF-12 twice per panel, at rounds 2 and 4, typically about a year apart. Only adults 18 years and older completed the SF-12. MEPS also usually collects information on diagnoses based on self-report of reasons for encounters with health services. In addition, diagnoses are derived through additional questions on “problems that bother you” or conditions that led to “disability days”, i.e., days out of role due to illness. Professional coders translate the verbatim text into three-digit ICD-9 codes. The main reason for stroke being measured in MEPS relates to health care contact. For GBD 2017, data were used from 2000-2014.

Since the health states are not defined in terms of clinical grading scales, comparability with available epidemiological and clinical evidence is hampered.

3.3 Prevalence

3.3.1 Data sources

Different data sources exist for cerebrovascular disease (stroke), each with a specific case definition:

- **Hospital discharge data:** patient with CVD admitted to the hospital during the reference year (before 2015: ICD-9 codes 430-434, 436-437; after 2015 ICD-10 codes: I60-I68).
- **Health insurance data:** person with a health-care provided certificate for nomenclature codes 477724, 477746, 477761 or 477783 during the reference year. Patient with stroke

admitted to the hospital during the reference year, for which a diagnosis and a care plan was established by a neurologist and a multidisciplinary team specialized in stroke care management.

- **Health Interview Survey:** number of respondents with positive answer to the question "in the past 12 months, have you had stroke?".
- **Sentinel GP network data (Intego):** number of individuals with CVD diagnosis ever recorded by GP (ICPC code K90 or K91) who had a GP contact during the reference year.
- **Sentinel GP network data (Sciensano):** number of individuals with stroke diagnosis recorded by a sentinel GP (ICPC-2 code K90 or K91) + GP patients who were hospitalized for stroke without a preceding contact with GP during the reference year.

Table 4. Potential sources and methods for the computation of cerebrovascular disease (stroke) prevalence in Belgium.

Source	Strengths	Weaknesses	Evaluation
Hospital discharge data	• Exhaustive information on all cases hospitalized for CVD • Diagnoses by medical doctor • Official database, organized and managed by public health authorities • National database	• No information on CVD patients who were not admitted to hospital during the reference year; this may represent between 5% and 23% of all cases (Devroey et al., 2003) • Although this number is probably low, some mild CVD cases among older people may be treated directly by the GP and are thus not sent to hospital; hospital based data could thus lead to underestimation • HDD is primarily used for administrative purposes, which could result in some problems when data have to be used for epidemiological purposes	• Sensitivity: high • Specificity: high
Health insurance data (IMA/EPS)	• Case definition based on medication and care • Large, representative sample	• Nomenclature codes are only for hospitalized cases of stroke	• Sensitivity: low • Specificity: medium
Health Interview Survey	• Based on information from a representative sample	• Self-reported information; it is assumed that there may	• Sensitivity: medium

	• Provides representative results at national and regional levels	be many false positive and false negatives • Not yearly available (+/- every 5 years) • Comparing estimates between subgroups of the sample might lack statistical precision	• Specificity: medium
Sentinel GP network data (Intego)	• Diagnosis by medical professional • Longitudinal approach	• Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP; 27% of patients are estimated to bypass the GP (Devroey et al., 2005) • Results are limited to Flanders • At the level of Flanders, the representativeness cannot be 100% guaranteed (the network only includes a sample of GPs using a specific software and interested in registration) • For the PP: not possible to identify the reason for consultation, so might not be related to CVD	• Sensitivity: low • Specificity: high
Sentinel GP network data (Sciensano)	• Diagnosis by medical professionals • 120 GP distributed evenly all over the country • Representativeness of GPs in Belgium (for age and sex) • A distinction is made between ischemic and hemorrhagic stroke	• Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP; 27% of patients are estimated to bypass the GP (Devroey et al., 2005) • Data available for stroke only, and not for CVD as a whole • Only periodic registration	• Sensitivity: medium • Specificity: high

3.3.2 National best estimate

We have selected a combination of two data sources as national best estimate.

It is proposed to use the Hospital Discharge Data as the best national estimate for the acute CVD incidence. To obtain prevalence estimates, incidence estimates can be multiplied with the duration of the condition in years, i.e., 28/365. Depending on the availability of the data,

we could use an alternative way to obtain the acute stroke incidence using the referring nomenclature codes from the health insurance data.

Chronic CVD prevalence is estimated by subtracting the HDD cases (i.e., the acute cases) from the stroke cases reported in the Health Interview Survey.

3.3.3 Discussion

Using the Hospital Discharge Data as national best estimate induces several limitations. First, patients suffering from CVD who have not been hospitalized will be missed and there are no recent data on the proportion of those patient treated in the community. However, data on stroke collected in 2009-2010 by the Sciensano Sentinel GP have shown a high hospitalization rate of 94.8% (N Boffin, personal communication).

Secondly, data quality depends on both the quality of the medical documentation and of the expertise of the coder (Aboa-Eboulé et al., 2012). The quality of the documentation in the medical chart depends on the qualification of the medical practitioner (e.g. neurologist or intern). Similarly, the coders are not specialists which may lead to coding errors. Miscoding may induce false positives (e.g. a stroke diagnosis is coded instead of another diagnosis) and false negatives (e.g. encoding stroke on the second diagnosis instead of the main diagnosis).

However, the hospital discharge data contain clinical data on CVDs at a national level which is a strength in estimating the prevalence of these diseases in the whole population.

The Belgian Health interview survey (HIS) has been selected to estimate the prevalence of chronic stroke. A limitation here is that the case definition is not the same as the one used to estimate the incidence of acute CVDs, based on the hospital discharge data. In the HIS, a question is asked about the presence of stroke and not about cerebrovascular diseases as a whole, leading to a potential underestimation of CVD cases.

The health insurance data are not the best source available since there is no drug sufficiently specific to the treatment of CVDs. Nomenclature codes exist but they only refer to acute stroke, which could lead to miss some other CVDs cases.

The Sentinel GP networks are not assumed to be the best source since stroke is usually managed at the hospital and information of hospitalization may not be transmitted to the GP. Furthermore, representativeness of the country is not guaranteed in the Intego sentinel GP network, although a correction factor could be applied using the HIS data. Finally, the Sciensano GP Network has registered the stroke prevalence but the last data available are for 2009-2010.

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4 DIABETES

4.1 Case definition

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

Diabetes is an important cause of morbidity. It is an important risk factor for cardio- and cerebrovascular disease and peripheral arterial disease. It contributes substantially to mortality, although mainly as a secondary cause, as a result of which the impact of diabetes on mortality is often underestimated.

4.1.1 Corresponding disease classification codes

ICD-10 codes

- E08 Diabetes mellitus due to underlying condition
- E09 Drug or chemical induced diabetes mellitus
- E10 Insulin-dependent diabetes mellitus (including brittle, juvenile-onset, ketosis-prone, type I)
- E11 Non-insulin-dependent diabetes mellitus (including diabetes with adult-onset, maturity-onset, non-ketotic, stable, type II, non-insulin-dependent diabetes of the young)
- E12 Malnutrition-related diabetes mellitus (both insulin-dependent and non-insulin-dependent
- E13 Other specified diabetes mellitus
- E14 Unspecified diabetes mellitus (including diabetes NOS)

E08 (“Diabetes mellitus due to underlying condition”) is considered a garbage code in the GBD framework, because it refers to an unknown underlying condition. Diabetes due to an underlying condition (E08) is never used as a primary diagnosis and is reserved for individuals who develop diabetes as the result of an underlying condition such as pancreatitis, malnutrition, or malignancy.

E09 (“Drug or chemical induced diabetes mellitus”) codes for diabetes mellitus secondary to medical treatment, and is therefore attributed to “Adverse effects of medical treatment” instead of to “diabetes mellitus”. The main ICD-10 codes attributed to diabetes mellitus are therefore E10-E14.

ICD-9 codes

- 249 Secondary diabetes mellitus
- 250 Diabetes mellitus

As for the ICD-10 classification, 249 (“Secondary diabetes mellitus”) is considered a garbage code because it refers to an unknown underlying condition. The main ICD-9 code attributed to diabetes mellitus is therefore 250.

ICPC-2 codes

- T89 Diabetes insulin dependent
- T90 Diabetes non-insulin dependent
- W85 Gestational diabetes

ATC codes

- A10A Insulins and analogues
- A10B Blood glucose lowering drugs, excl. insulins

Nomenclature codes

- Not applicable: there are no nomenclature codes sufficiently specific for epilepsy.

4.2 Disease model

4.2.1 Health states

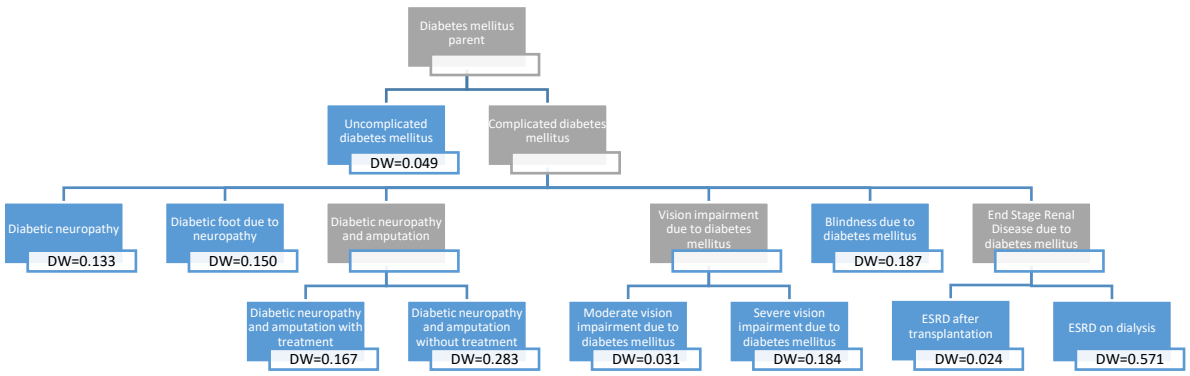

Figure 1. Diabetes disease model

4.2.2 Disability weights

Table 1. Disability weights (DW) by health state for diabetes according to the Global Burden of Disease study (Salomon et al., 2015)

Health state	Lay description	DW
Uncomplicated diabetes mellitus	Has a chronic disease that requires medication every day and causes some worry, but minimal interference with daily activities	0.049
Diabetic neuropathy	Has pain, tingling, and numbness in the arms, legs, hands, and feet. The person sometimes gets cramps and muscle weakness.	0.133
Diabetic neuropathy with diabetic foot	Has a sore on the foot that is swollen and causes some difficulty in walking.	0.150†
Diabetic neuropathy with treated amputation	Has lost part of one leg, leaving pain and tingling in the stump. The person has an artificial leg that helps in moving around.	0.167‡
Diabetic neuropathy with untreated amputation	Has lost part of one leg, leaving pain and tingling in the stump. The person does not have an artificial leg, has frequent sores, and uses crutches.	0.283§
Moderate vision loss due to diabetes mellitus	Has vision problems that make it difficult to recognize faces or objects across a room.	0.031
Severe vision loss due to diabetes mellitus	Has severe vision loss, which causes difficulty in daily activities, some emotional impact (for example worry), and some difficulty going outside the home without assistance	0.184
Blindness due to diabetes mellitus	Is completely blind, which causes great difficulty in some daily activities, worry and anxiety, and great difficulty going outside the home without assistance.	0.187
End-stage renal disease after transplant due to diabetes mellitus	Sometimes feels tired and down, and has some difficulty with daily activities	0.024
End-stage renal disease on dialysis due to diabetes mellitus	Is tired and has itching, cramps, headache, joint pains and shortness of breath. The person needs intensive medical care every other day lasting about half a day.	0.571

†*Combined DW of neuropathy (0.133) and diabetic foot (0.020)*

‡*Combined DW of neuropathy (0.133) and amputation of one leg, long-term, with treatment (0.039)*

§*Combined DW of neuropathy (0.133) and amputation of one leg, long-term, without treatment (0.173)*

4.2.3 Proportion of patients in the considered health states

For most health states, Belgian data from the GUIDANCE study (Stone et al., 2013) were used to derive the proportion of patients in the respective health states. This study included patients from both primary and specialist care. A total of 1044 Belgian patients participated, with a mean age at recruitment of 68.7. The vast majority (96.1%) was recruited from primary care, and was reported to take any diabetes medication (96.4%), in line with the definition of the disease model, which only considers individuals taking diabetes medication.

For some of the health states Belgian data could not be found:

- For end stage renal disease a European study was used instead (Kramer et al., 2018).
- For other health states no estimates were available. The assumption was then made that patients would be equally distributed over the concerned health states (for instance among the patients with vision impairment, 50% would have moderate impairment and 50% would have severe impairment).

Table 2. Proportion of patients in the different health states considered in the diabetes disease model, Belgium.

Health state	Parent	Proportion	Source
Diabetes mellitus parent	N/A	100%	Per definition
Uncomplicated diabetes mellitus	Diabetes mellitus parent	Varying from 72 to 99% in function of age and sex	GUIDANCE study (Stone et al., 2013)
Diabetic neuropathy	Diabetes mellitus parent	Varying from 0 to 10% in function of age and sex	GUIDANCE study (Stone et al., 2013)
Diabetic neuropathy with diabetic foot	Diabetes mellitus parent	Varying from 0 to 4% in function of age and sex	GUIDANCE study (Stone et al., 2013)
Diabetic neuropathy with amputation	Diabetes mellitus parent	Varying from 0 to 2% in function of age and sex	GUIDANCE study (Stone et al., 2013)
Diabetic neuropathy with treated amputation	Diabetic neuropathy with amputation	50%	Assumption, in absence of data
Diabetic neuropathy with untreated amputation	Diabetic neuropathy with amputation	50%	Assumption, in absence of data
Vision loss due to diabetes mellitus	Diabetes mellitus parent	Varying from 1 to 12% in function of age and sex	GUIDANCE study (Stone et al., 2013)
Moderate vision loss due to diabetes mellitus	Vision loss due to diabetes mellitus	50%	Assumption, in absence of data
Severe vision loss due to diabetes mellitus	Vision loss due to diabetes mellitus	50%	Assumption, in absence of data
Blindness due to diabetes mellitus	Diabetes mellitus parent	Varying from 0 to 1% in function of age and sex	GUIDANCE study (Stone et al., 2013)
End-stage renal disease due to diabetes mellitus	Diabetes mellitus parent	Varying from 0 to 1% in function of age and sex	GUIDANCE study (Stone et al., 2013)

End-stage renal disease after transplant due to diabetes mellitus	End-stage renal disease due to diabetes mellitus	28%	Kramer et al. (2018)
End-stage renal disease on dialysis due to diabetes mellitus	End-stage renal disease due to diabetes mellitus	72%	Kramer et al. (2018)

4.2.4 Discussion

The diabetes disease model does not consider acute complications such as hypo- or hyperglycemia. Although the impact of these conditions may be severe, the duration is typically very short, leading to few YLDs. This of course does not exclude death from hyperglycemia, which would be captured by the YLL component of the DALY metric, but not by the YLD component.

Diabetes patients are usually not suffering / dying from the disease itself, but rather from its complications. These complications are included in the model but only for those related to neurologic and microvascular problems. In line with the GBD study, however, macrovascular complications such as coronary artery disease, peripheral arterial disease, and stroke, are not considered here. The main reason for doing so is to avoid that those vascular diseases are counted twice in the DALY calculation: once with diabetes and a second time with cardiovascular diseases, since these macrovascular conditions are included in the cardiovascular disease categories. In an additional step a proportion of these cases may be attributed to hyperglycemia as risk factor. For instance, Huxley et al. (2006) found that the relative risk for fatal coronary heart disease in patients with diabetes compared with no diabetes, was 3.5 in men and 2.1 in women. Given a diabetes prevalence of 6.6% in men and 6.1% in women, this would result in (p(RR-1))/(p(RR-1)+1)=14% of coronary heart disease deaths being attributed to diabetes in men, and 6.3% in women.

The disease model may also not fully capture the reduced quality of life patients may experience due to interference of the disease with daily activities.

Disability weights for the Belgian national burden of disease study are adapted from the Global Burden of Disease study (Salomon et al., 2015), as these provide an exhaustive set of internally consistent disability weights.

The severity distribution (proportion of the cases in the different health states) for the diabetes disease model are largely based on Belgian data (GUIDANCE study). For end stage renal diseases, a European study was used (Kramer et al., 2018). For the proportion of treated vs untreated amputation, as well as for the proportion of moderate vs severe

vision, no data were available, hence a 50:50 split was assumed. In future iterations of the Belgian national burden of disease study, new and updated Belgian data should be incorporated.

The prevalence applied severity distribution of health states represent the national average, and may therefore hide regional differences. Sufficiently powered studies are needed to provide valid regional estimates.

4.3 Prevalence

4.3.1 Data sources

Different data sources exist for diabetes, each with a specific case definition:

1. **Diabetes registry:** diabetic patients diagnosed under the age of 40 who are registered by their treating diabetologist for the diabetes registry
2. **Hospital discharge data:** patients admitted to hospital during the reference year with diabetes (before 2015: ICD-9 code 250; after 2015: ICD-10 code E10-E14) as primary or secondary diagnosis for the hospital discharge.
3. **Health insurance data:** person with a prescription for ATC codes A10A or A10B AND/OR with diabetes referring nomenclature (diabetes convention, diabetes pass, diabetes care trajectory) during the reference year for health insurance. Women who gave birth during the year under review are excluded to exclude gestational diabetes.
4. **Health Interview Survey:** Number of respondents with positive answer to the question “in the past 12 months, have you had diabetes?”.
5. **Sentinel GP network data (Intego):** number of individuals with a diabetes diagnosis ever recorded by the GP (ICPC code T89-T90) who had a GP contact during the reference year.
6. **Sentinel GP network data (Sciensano):** number of individuals with diabetes diagnosis recorded by a sentinel GP during the reference year.

Table 3. Potential sources and methods for the computation of epilepsy prevalence in Belgium.

Source	Strengths	Weaknesses	Evaluation
Diabetes registry	• Based on a diagnosis by a diabetologist • National coverage	• As the registry only includes patients with diabetes diagnosed under the age of 40, it cannot be used to produce prevalence estimates for diabetic patients at all ages in Belgium	• Sensitivity: low • Specificity: high

		• Based on voluntary reporting • No recent data available • Managed by clinicians; no government funding; the future of this database is uncertain • Important geographical differences in the completeness of the results (although studies have been done to correct for this and obtain representative results at the level of the total Belgian population)	
Hospital discharge data	• Exhaustive information on all cases hospitalized for epilepsy • Diagnoses by medical doctor • Official database, organized and managed by public health authorities • National database	• No information on diabetic patients who were not admitted to hospital during the reference year. This is assumed to represent a substantial proportion of all cases. • HDD is primarily used for administrative purposes, which could result in some problems when data have to be used for epidemiological purposes	• Sensitivity: low • Specificity: high
Health insurance data (IMA/EPS)	• Case definition based on medication and care • Large, representative sample • Longitudinal approach	• Case definitions are based on the prescription of medicines, not on a medical diagnosis, which generates false positives and false negatives: →False positives: patients without diabetes, treated with antidiabetics for other reasons, for instance slimming → False negatives: diabetic patients treated with diet only and without any nomenclature codes • People who are not insured (e.g. homeless and illegal people, foreigners with their official residence abroad) are not included	• Sensitivity: high • Specificity: high
Health Interview Survey	• Based on information from a representative sample • Provides representative results	• Self-reported information, which may lead to false positive and false negative results	• Sensitivity: high (90%; Vaes et al. (2018)) • Specificity: high

	at national and regional levels.	• Not yearly available (+/- every 5 years) • Comparing estimates between subgroups of the sample might lack statistical precision	
Sentinel GP network data (Intego)	• Diagnosis by medical professional • Longitudinal approach	• Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP • Results are limited to Flanders • At the level of Flanders, the representativeness cannot be 100% guaranteed (the network only includes a sample of GPs using a specific software and interested in registration) • For the PP: not possible to identify the reason for consultation, so might not be related to diabetes; However, the condition is expected to require continuous treatment. Patients are thus expected to seek regular GP contact.	• Sensitivity: low (57%; Vaes et al. (2018)) • Specificity: high
Sentinel GP network data (Sciensano)	• Diagnosis by medical professionals • 120 GP distributed evenly all over the country • Representativeness of GPs in Belgium (for age and sex)	• Will not capture patients that bypass the GP (ED, hospitalization) unless the information is transmitted to the GP • Only periodic registration • Last registration: 2010	• Sensitivity: low • Specificity: high

4.3.2 National best estimate

Vaes et al. (2018) performed cross-tabulations of different data sources on the prevalence of diabetes in Belgium–i.e., health insurance data, health interview survey data, and sentinel GP network data. They concluded that disease prevalence estimates based on dispensed medications (health insurance data) were higher than disease estimates based on prescribed medications and self-reported medication use. Furthermore, the sensitivity and specificity of dispensed medication for self-reported diagnoses was shown to be high.

Based on the results Vaes et al. (2018), and in line with the conclusions of the Morbistat project (Van der Heyden, 2011), the estimate of the Intermutualistic Agency (IMA), available

through the IMA ATLAS (http://atlas.ima-aim.be/databanken), is proposed as “best estimate” of the prevalence of known (treated) diabetes mellitus in Belgium.

4.3.3 Discussion

Despite showing high sensitivity and specificity, health insurance data remain administrative data that have to be used with caution for epidemiological purpose (Vaes et al., 2018). In addition, these data probably underestimate the true total number of diabetes cases as they do not take into account diabetes patients who do not take medical treatment, but only follow initial control based on lifestyle changes (in line with the diabetes treatment guidelines). This definition is however consistent with the disease model, which assigns a disability weight to diabetes as a “chronic disease that requires medication every day”.

The disability weight for diabetes patients who do not take medical treatment is probably smaller than that for those taking medication, and is implicitly assumed to be zero.

In addition, according to the Belgian Health Interview Survey 2018, 91.5% of the individuals aged 15 and over that reported having diabetes, also indicated that they used anti-diabetic medication (Van der Heyden and Charafeddine, 2019). As a consequence, potentially only 7% of the diabetic patients are missing in the current estimate (and those patients probably have low disability weights related to diabetes). Furthermore, the Belgian Health Examination Survey 2018 showed that 10% of the Belgian adults has diabetes, but that one out of three of them are not aware of their condition (Van der Heyden et al., 2019).

Health insurance data may also yield false positives if patients who have no diabetes take antidiabetic treatment. For instance, metformin is sometimes used for other indications than diabetes. The proportion of false positives is however likely to be relatively small.

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5 EPILEPSY

5.1 Case definition

The case definition for epilepsy encompasses:

1. Epilepsy, a condition characterized by recurrent (two or more) epileptic seizures, unprovoked by any immediate identified cause. An epileptic seizure is defined as “a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain” (Fisher et al. 2005).
2. Active epilepsy: a prevalent case of active epilepsy is defined as a person with epilepsy who has had at least one epileptic seizure in the previous five years, regardless of antiepileptic drug (AED) treatment.

5.1.1 Corresponding disease classification codes

ICD-10 codes

- G40 Epilepsy
- G41 Status epilepticus

ICD-9 codes

- 345 Epilepsy and recurrent seizures

ICPC-2 codes

- N88 Epilepsy

ATC codes

- N03A Antiepileptics

Nomenclature codes

- Not applicable: there are no nomenclature codes sufficiently specific for epilepsy.

5.2 Disease model

5.2.1 Health states

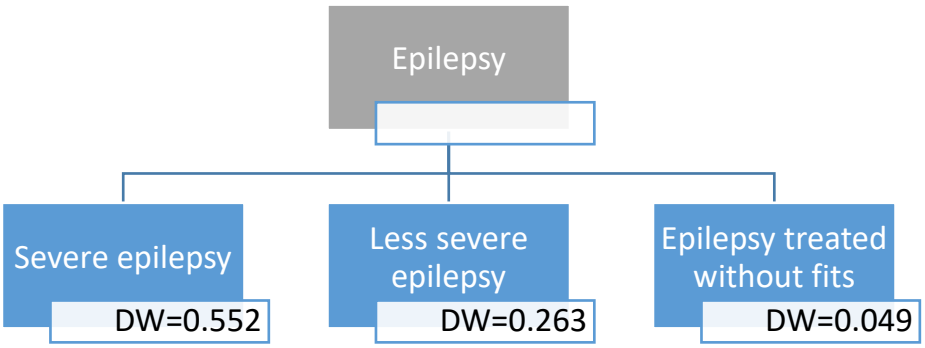

Figure 1. Epilepsy disease model

5.2.2 Disability weights

Table 1. Disability weights (DW) by health state for epilepsy according to the Global Burden of Disease study (Salomon et al., 2015)

Health state	Lay description	DW
Severe epilepsy (seizures at least once per month)	This person has sudden seizures one or more times each month, with violent muscle contractions and stiffness, loss of consciousness, and loss of urine or bowel control. Between seizures the person has memory loss and difficulty concentrating.	0.552
Less severe epilepsy (seizures less than once per month)	This person has sudden seizures two to five times a year, with violent muscle contractions and stiffness, loss of consciousness, and loss of urine or bowel control.	0.263
Epilepsy treated without fits	This person has a chronic disease that requires medication every day and causes some worry but minimal interference with daily activities.	0.049

5.2.3 Proportion of patients in the considered health states

Table 2. Proportion of patients in the different health states considered in the epilepsy disease model, Belgium.

Health state	Parent	Proportion	Source
Epilepsy	N/A	100%	Per definition
Severe epilepsy	Epilepsy	31.1%	GBD 2017
Less severe epilepsy	Epilepsy	21.5%	GBD 2017
Epilepsy treated without fits	Epilepsy	47.3%	GBD 2017

5.2.4 Discussion

The severity distribution in the GBD model is based on the calculation of epilepsy impairment. Impairments in GBD are conditions or specific domains of functional health loss which are spread across many GBD causes as sequelae and for which there are better data to estimate the occurrence of the overall impairment than for each sequela based on the underlying cause.

In the GBD, the severity distribution of epilepsy impairment was calculated as followed: the proportions with idiopathic and secondary epilepsy as well as for the proportions with severe and less severe epilepsy were determined using mixed effects regressions. The sparse data for the proportion of treated epilepsy were pooled in a random effects meta-analysis. Since data are not specific to Belgium, the question of applicability to the Belgian context is raised.

5.3 Prevalence

5.3.1 Data sources

Different data sources exist for epilepsy, each with a specific case definition:

1. **Hospital Discharge data:** patient with epilepsy admitted to the hospital during the reference year (before 2015: ICD-9 codes 345; after 2015 ICD-10 codes: G40, G41).
2. **Health insurance data:** person with a prescription for ATC codes N03 during the reference year.
3. **Health Interview Survey:** number of respondents with positive answer to the question "in the past 12 months, have you had epilepsy?".
4. **Sentinel GP network data (Intego):** Number of individuals with epilepsy diagnosis ever recorded by GP (ICPC-2 code N88) who had a GP contact during the reference year.

Table 3. Potential sources and methods for the computation of epilepsy prevalence in Belgium.

Source	Strengths	Weaknesses	Evaluation
Hospital discharge data	• Exhaustive information on all cases hospitalized for epilepsy • Diagnoses by medical doctor • Official database, organized and managed by public health authorities • National database	• No information on epileptic patients who were not admitted to hospital during the reference year. This may represent a rather large proportion of all cases since hospitalization in patients with epilepsy is uncommon (Franchi et al., 2013; Jetté et al., 2010; Mitchell et al., 2018) • HDD is primarily used for administrative purposes, which could result in some problems when data have to be used for epidemiological purposes • Evidence has shown a poor detection of the epilepsy cases using HDD (Tu et al., 2014)	• Sensitivity: low • Specificity: high
Health insurance data (IMA/EPS)	• Large, representative sample • Longitudinal approach	• Case definitions are based on the prescription of medicines, not on a medical diagnosis, which generates false positives and false negatives: →False positives: includes patients having received this treatment for another indication (30%-64% of anti-epileptic drugs are	• Sensitivity: high • Specificity: low

		prescribed for another indication) (Hamer et al., 2012; Johannessen et al., 2009; Ettinger et al., 2007) → False negatives: patients with the condition who do not take this treatment (assumption of few false negatives since not taking this treatment is very disabling) • People who are not insured (e.g. homeless and illegal people, foreigners with their official residence abroad) are not included	
Health Interview Survey	• Based on information from a representative sample • Provides representative results at national and regional levels.	• Self-reported information, which may lead to false positive and false negative results • Not yearly available (+/- every 5 years) • Comparing estimates between subgroups of the sample might lack statistical precision	• Sensitivity: medium • Specificity: medium
Sentinel GP network data (Intego)	• Diagnosis by medical professional • Longitudinal approach	• Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP • Results are limited to Flanders • At the level of Flanders, the representativeness cannot be 100% guaranteed (the network only includes a sample of GPs using a specific software and interested in registration) • For the PP: not possible to identify the reason for consultation, so might not be related to NP.	• Sensitivity: medium • Specificity: high
Sentinel GP network data (Sciensano)	• Not applicable. Epilepsy has not been registered by the Sciensano SGPs.		

5.3.2 National best estimate

The sentinel GP network Intego is assumed to yield the best estimate of epilepsy prevalence. Patients suffering from this affection are supposed to have close contacts with the GP as their condition requires regular drug prescriptions. Representativeness for Belgium could be obtained by applying a correction factor based on the ratio of the prevalence of epilepsy in Belgium and the prevalence of the disease in Flanders (from the HIS or the EPS data).

5.3.3 Discussion

Given the potentially high burden of epilepsy, further studies are needed to quantify the validity (sensitivity/specificity) of the proposed approach for defining the prevalence of epilepsy.

Hospital discharge data are not recommended to monitor the epilepsy prevalence in the general population since the hospitalization rate is low in people with epilepsy (Franchi et al., 2013; Jetté et al., 2010; Mitchell et al., 2018). Furthermore, evidence has shown a poor detection of the population epilepsy cases using the hospital discharge data (Tu et al., 2014).

The Health insurance data (pharmaceutical dataset) are not recommended since anti-epileptic drugs are often prescribed in other conditions, e.g. psychiatry disorders (bipolar disorder, anxiety disorder), migraine and neuropathic pain (Hamer et al., 2012; Johannessen et al., 2009; Ettinger et al., 2007), which would generate a lot of false positives.

The HIS data are self-reported, which may lead to false positives since cases are not diagnosed by a medical practitioner. Furthermore, data are not yearly available.

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6 PARKINSON'S DISEASE

6.1 Case definition

According to the World Health Organization (WHO 2007), Parkinson's disease (PD) is a chronic neurodegenerative disease defined by the progressive loss of dopamine-containing neurons in a specific zone of the brain called the substantia nigra, and characterized by motors symptoms (i.e., tremors, muscular rigidity, and bradykinesia) and non-motor symptomatology (e.g. speech and swallowing difficulties), with late-onset motor symptoms (e.g., postural instability and falls).

Parkinsonism is a term used to refer to a group of neurological symptoms that are "Parkinson-like" such as bradykinesia or postural instability, regardless of the cause. Also called atypical parkinsonism syndrome, its evolution is more aggressive than PD and it has a poorer response to the treatment. The differential diagnosis can be difficult between those pathologies, especially in the early stages of the disease (Tsuda et al., 2019).

The case definition of Parkinson's disease is the presence of at least two of the four primary symptoms: (1) tremors/trembling, (2) bradykinesia, (3) stiffness of limbs and torso, and (4) posture instability.

It has to be noticed that the choice was made to include parkinsonism in the case definition, for several reasons:

- Parkinsonism syndrome is responsible for "Parkinson-like" neurological symptoms that cause alteration of the quality of life that has to be quantified in YLD. Otherwise, disability linked to parkinsonism would be ignored.
- Since the differential diagnosis is difficult to establish between PD and parkinsonism, not including parkinsonism would exclude a lot of PD cases of the analysis.
- The same methodology was used in the GBD studies, allowing international comparisons.

6.1.1 Corresponding disease classification codes

ICD-10 codes

- G20 Parkinson disease (included: hemiparkinsonism, paralysis agitans, parkinsonism or Parkinson disease: NOS, idiopathic, primary)
- G21 Secondary parkinsonism
- G22 Parkinsonism in diseases classified elsewhere (included: syphilitic parkinsonism)

ICD-9 codes

- 332 Parkinson's disease

ICPC-2 codes

- N87 Parkinsonism

ATC codes

- N04 Anti-Parkinson drugs
- N04AB Ethers chemically close to antihistamines
- N04AC Ethers of tropine or tropine derivatives
- N04B Dopaminergic agents

Nomenclature codes

- Not applicable: there are no nomenclature codes sufficiently specific for Parkinson's disease.

6.2 Disease model

6.2.1 Health states

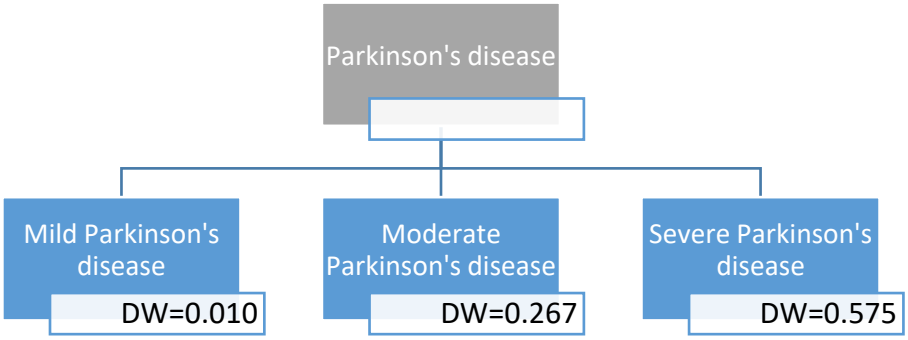

Figure 1. Parkinson's disease disease model

6.2.2 Disability weights

Table 1. Disability weights (DW) by health state for Parkinson's disease according to the Global Burden of Disease study (Salomon et al., 2015)

Health state	Lay description	DW
Mild Parkinson's disease	Has mild tremors and moves a little slowly, but is able to walk and do daily activities without assistance.	0.010
Moderate Parkinson's disease	Has moderate tremors and moves slowly, which causes some difficulty in walking and daily activities. The person has some trouble swallowing, talking, sleeping, and remembering things	0.267
Severe Parkinson's disease	Has severe tremors and moves very slowly, which causes great difficulty in walking and daily activities. The person falls easily and has a lot of difficulty talking, swallowing, sleeping, and remembering things.	0.575

6.2.3 Proportion of patients in the considered health states

Table 2. Proportion of patients in the different health states considered in the Parkinson's disease disease model, Belgium.

Health state	Parent	Proportion	Source	Hoehn and Yahr stage
Parkinson's disease	N/A	100%	Per definition	N/A
Parkinson's disease, mild	Parkinson's disease, parent	52%	GBD 2017	≤2.0
Parkinson's disease, moderate	Parkinson's disease, parent	32%	GBD 2017	2.5–3.0
Parkinson's disease, severe	Parkinson's disease, parent	13%	GBD 2017	≥4

6.2.4 Discussion

The severity distribution in the GBD model is based on data from a systematic review that covered 1/1/2008 to 11/10/2016 and captured studies reporting the prevalence of PD by Hoehn and Yahr stage (GBD 2016 Parkinson's Disease Collaborators, 2018). Thirty unique sources were used, covering 21 world regions. A score of 2.0 or less on the Hoehn and Yahr scale equated to mild PD, a score of 2.5–3.0 to moderate PD, and a score of 4.0–5.0 to severe PD. A meta-analysis was performed on these data to obtain the proportion of PD that is mild, moderate and severe. Belgian data were not included in the systematic review, raising questions on the applicability of the severity distributions for the Belgian context. However, the studies covered several Western European countries (e.g. Netherlands, Scotland, England, Germany, …), with a high Socio-Demographic Index, allowing extrapolations to Belgium.

Since health states are defined in terms of clinical grading scale, comparability with available epidemiological and clinical evidence is allowed.

6.3 Prevalence

6.3.1 Data sources

Different data sources exist for Parkinson's diseases, each with a specific case definition:

1. **Hospital Discharge data:** patient with PD admitted to the hospital during the reference year (before 2015: ICD-9 codes 332; after 2015 ICD-10 codes: G20).
2. **Health insurance data:** person with a prescription for one of the following ATC codes: N04B, N04AB, N04AC, during the reference year.

3. **Health Interview Survey:** number of respondents with a positive answer to the question "in the past 12 months, have you suffered from Parkinson disease?".
4. **Sentinel GP network data (Intego):** Number of individuals with PD diagnosis ever recorded by GP (ICPC-2 code N87) who had a GP contact during the reference year.

Table 3. Potential sources and methods for the computation of Parkinson's disease prevalence in Belgium.

Source	Strengths	Weaknesses	Evaluation
Hospital discharge data	• Exhaustive information on all cases hospitalized for PD • Diagnoses by medical doctor • Official database, organized and managed by public health authorities • National database	• No information on PD patients who were not admitted to hospital during the reference year. This may represent a rather large proportion of all cases since only 7 to 30% of all PD patients are hospitalized each year (Hassan et al., 2013; Shahgoli et al., 2017; Gerlach et al., 2011) • HDD is primarily used for administrative purposes, which could result in some problems when data have to be used for epidemiological purposes • Evidence has shown a poor detection of the epilepsy cases using HDD (Tu et al., 2014)	• Sensitivity: medium • Specificity: high
Health insurance data (IMA/EPS)	• Large, representative sample • Longitudinal approach	• Case definitions are based on the prescription of medicines, not on a medical diagnosis, which generates false positives and false negatives: →False positives: includes patients with no PD having received this treatment for another indication → False negatives: patients with the condition who do not take this treatment (assumption of few false negatives since not taking this treatment is very disabling) • People who are not insured (e.g. homeless and illegal people, foreigners with their official residence abroad) are not included	• Sensitivity: medium • Specificity: high

Health Interview Survey	• Based on information from a representative sample • Provides representative results at national and regional levels.	• Self-reported information, which may lead to false positive and false negative results • Not yearly available (+/- every 5 years) • Comparing estimates between subgroups of the sample might lack statistical precision	• Sensitivity: medium • Specificity: medium
Sentinel GP network data (Intego)	• Diagnosis by medical professional • Longitudinal approach	• Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP • Results are limited to Flanders • At the level of Flanders, the representativeness cannot be 100% guaranteed (the network only includes a sample of GPs using a specific software and interested in registration) • For the PP: not possible to identify the reason for consultation, so might not be related to NP. • ICPC code N87 includes both PD and parkinsonism	• Sensitivity: low • Specificity: high
Sentinel GP network data (Sciensano)	• Not applicable. PD has not been registered by the Sciensano SGPs.		

6.3.2 National best estimate

The health insurance dataset is assumed to be the best estimate since a validated “pseudo-diagnosis” exists. Data on the delivery of anti-Parkinson drugs in the public pharmacies and in the hospitals pharmacies are available in the Inter Mutualistic Agency (IMA) database (Pharmanet and GZSS).

Furthermore, evidence has shown that using a pharmaceutical dataset can provide reliable estimates of the Parkinson’s disease prevalence in the population (Slobbe et al., 2019; Chini et al., 2011). However, since the pharmaceutical dataset of the health insurance only contains reimbursed drugs, prevalence estimates may be underestimated.

6.3.3 Discussion

The validity of the ATC codes selected to define PD has been explored in the Project HISLINK 2013 (Berete et al., 2019), through a linkage between the Health Insurance data (IMA) and the data from the Health Interview Survey (HIS).

The agreement between the two databases has been assessed by calculating the following validity measures: the sensitivity, the specificity, the positive and negative predicting values and the Cohen's kappa coefficient, using the HIS 2008 data as gold standard (see **Section 3.4** for more information on the HISLINK project).

When comparing the PD prevalence from IMA with HIS 2008 (gold standard), the agreement is good (Kappa coefficient: 0.64), the sensitivity is 56.6%, the specificity is 99.95%, the PPV is 82.74%, and the NPV is 99.8% (with a cut-off point of ≥90 DDD).

The same analysis has been made in function of different cut-off points of DDD, allowing to increase the sensitivity, i.e., to identify more cases of the PD cases identified in the HIS, when using the IMA database.

The results show that setting up a cut-off point of 0 DDD allow to increase the sensitivity from 57% to 69%, with no variation of the specificity and the NPV. The PPV decreases from 82% to 61%. However, it has to be noticed that the PPV is very sensitive to the prevalence of a disease. When the prevalence is high, the PPV remains good but when the number of cases is very low (as in PD), the PPV decreases strongly. Notwithstanding this, we recommend to use a cut-off point of 0 DDD.

Given the potentially high burden of PD, further studies are needed to quantify the validity (sensitivity/specificity) of the proposed approach for defining the prevalence of this disease.

The Intego sentinel GP network data is another source to estimate the PD prevalence, since PD patients are supposed to have close contacts with their GP as the disease prevalence strongly increases with age, requires regular drug prescriptions, and is often associated with multimorbidity. However, results are limited to Flanders which can induce a lack of representativeness of the Belgian population. This limitation could be avoided by applying a correction factor based on either the HIS or the EPS data.

The HDD may underestimate the PD prevalence by missing the cases that are not hospitalized, even though studies have shown a hospitalization rate of up to 30% of PD patients, which could be used to extrapolate the prevalence of the disease in the population. However, the hospitalization rate is not specific to Belgium, thus extrapolations should be interpreted with caution.

The HIS data are self-reported, which may lead to false positives since cases are not diagnosed by a medical practitioner.

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7 LOW BACK PAIN (LBP)

7.1 Case definition

Low back pain (LBP) is defined as low back pain (with or without pain referred into one or both lower limbs) that lasts for at least one day. The low back is defined as the area on the posterior aspect of the body from the lower margin of the twelfth ribs to the lower gluteal folds.

7.1.1 Corresponding disease classification codes

ICD-10 codes

- M54.3 Sciatica
- M54.4 Lumbago with sciatica
- M54.5 Low back pain

ICD-9 codes

- 724 Other and unspecified disorders of back

ICPC-2 codes

- L03 Low back symptom/complaint
- L84 Back syndrome w/o radiating pain
- L86 Back syndrome with radiating pain

ATC codes

- Not applicable: there are no drugs sufficiently specific for treatment of LBP.

Nomenclature codes

- Not applicable: there are no nomenclature codes sufficiently specific for LBP.

7.2 Disease model

7.2.1 Health states

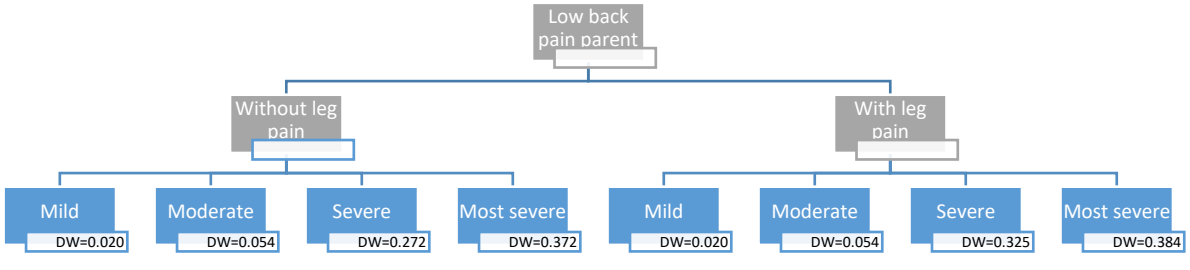

Figure 1. Low back pain disease model

7.2.2 Disability weights

Table 1. Disability weights (DW) by health state for low back pain according to the Global Burden of Disease study (Salomon et al., 2015)

Health state	Lay description	DW
Low back pain, mild	This person has mild back pain, which causes some difficulty dressing, standing, and lifting things.	0.020
Low back pain, moderate	This person has moderate back pain, which causes difficulty dressing, sitting, standing, walking, and lifting things.	0.054
Low back pain, severe without leg pain	This person has severe back pain, which causes difficulty dressing, sitting, standing, walking, and lifting things. The person sleeps poorly and feels worried.	0.272
Low back pain, severe with leg pain	This person has severe back and leg pain, which causes difficulty dressing, sitting, standing, walking, and lifting things. The person sleeps poorly and feels worried.	0.325
Low back pain, most severe without leg pain	This person has constant back pain, which causes difficulty dressing, sitting, standing, walking, and lifting things. The person sleeps poorly, is worried, and has lost some enjoyment in life.	0.372
Low back pain, most severe with leg pain	This person has constant back and leg pain, which causes difficulty dressing, sitting, standing, walking, and lifting things. The person sleeps poorly, is worried, and has lost some enjoyment in life.	0.384

7.2.3 Proportion of patients in the considered health states

Table 2. Proportion of patients in the different health states considered in the low back pain disease model, Belgium.

Health state	Parent	Proportion	Source
Low back pain parent	N/A	100%	Per definition
Low back pain with leg pain	Low back pain parent	~age (9.4–37.4%) (Table 3)	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Low back pain without leg pain, mild	Low back pain without leg pain	0.41	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Low back pain without leg pain, moderate	Low back pain without leg pain	0.35	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Low back pain without leg pain, severe	Low back pain without leg pain	0.10	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)

Low back pain without leg pain, most severe	Low back pain without leg pain	0.14	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Low back pain with leg pain, mild	Low back pain with leg pain	0.27	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Low back pain with leg pain, moderate	Low back pain with leg pain	0.36	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Low back pain with leg pain, severe	Low back pain with leg pain	0.14	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Low back pain with leg pain, most severe	Low back pain with leg pain	0.23	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)

Table 3. Proportion of individuals with low back pain that also suffer from leg pain (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018)

Age group	Proportion with leg pain	Age group	Proportion with leg pain
5-9	0.094	55-59	0.371
10-14	0.109	60-64	0.374
15-19	0.159	65-69	0.371
20-24	0.232	70-74	0.365
25-29	0.288	75-79	0.350
30-34	0.314	80-84	0.321
35-39	0.331	85-89	0.283
40-44	0.343	90-94	0.237
45-49	0.355	95-100	0.192
50-54	0.364		

7.2.4 Discussion

Disability weights for the Belgian national burden of disease study are adapted from the Global Burden of Disease study (4), as these provide an exhaustive set of internally consistent disability weights.

The severity distribution in the GBD model is based exclusively on data from the USA, raising questions on applicability for the Belgian context. The proportion of cases with low back pain who report leg pain (by age) was derived using USA 2012 claims data. The

severity distributions were derived from an analysis of the Medical Expenditure Panel Surveys (MEPS) in the USA (https://meps.ahrq.gov/mepsweb/). MEPS is an overlapping continuous panel survey of the United States non-institutionalized population whose primary purpose is to collect information on the use and cost of health care. Panels are two years long and are conducted in five rounds, which are conducted every five to six months. Each panel typically contains about 30,000 to 35,000 individual respondents. Respondents self-administer the SF-12 twice per panel, at rounds 2 and 4, typically about a year apart. Only adults 18 years and older completed the SF-12. MEPS also usually collects information on diagnoses based on self-report of reasons for encounters with health services. In addition, diagnoses are derived through additional questions on “problems that bother you” or conditions that led to “disability days”, ie, days out of role due to illness. Professional coders translate the verbatim text into three-digit ICD-9 codes. The main reason for LBP being measured in MEPS relates to health care contact. For GBD 2017, data were used from 2000-2014.

Since the health states are not defined in terms of clinical grading scales, comparability with available epidemiological and clinical evidence is hampered.

7.3 Prevalence

7.3.1 Data sources

Different data sources exist for LBP, each with a specific case definition:

1. **Hospital discharge data:** patient with low back pain admitted to the hospital during the reference year (before 2015: ICD-9 code 724; after 2015 ICD-10 codes: M54.3, M54.4 and M54.5).
2. **Health insurance data:** not applicable; there are no (reimbursed) medications or health care usages that would allow a sufficiently specific diagnosis of low back pain.
3. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you had a low back disorder or other chronic back defect?”.
4. **Sentinel GP network data (Intego):** number of individuals with low back pain diagnosis ever recorded by GP (ICPC-2 codes L03, L84 and/or L86) who had a GP contact during the reference year.
5. **Sentinel GP network data (Sciensano):** not applicable; low back pain has not been registered by the Sciensano SGPs.

Table 4. Potential sources and methods for the computation of low back pain prevalence in Belgium.

Source	Strengths	Weaknesses	Evaluation
Hospital discharge data	• Exhaustive information on all cases hospitalized for low back pain • Diagnoses by medical doctor • Official database, organized and managed by public health authorities • National database	• No information on low back pain patients who were not admitted to hospital during the reference year; this is a substantial proportion of the low back pain patients • HDD is primarily used for administrative purposes, which could result in some problems when data have to be used for epidemiological purposes	• Sensitivity: low • Specificity: high
Health insurance data (IMA/EPS)	N/A: there are no (reimbursed) medications or health care usages that would allow a sufficiently specific diagnosis of low back pain		
Health Interview Survey	• Based on information from a representative sample • Provides representative results at national and regional levels.	• Self-reported information, which may induce an overestimation of LBP prevalence; integration with information on disability or health-related quality of life may increase specificity • Not yearly available (+/- every 5 years) • Comparing estimates between subgroups of the sample might lack statistical precision	• Sensitivity: high • Specificity: high
Sentinel GP network data (Intego)	• Diagnosis by medical professional • Longitudinal approach	• Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP • Results are limited to Flanders • At the level of Flanders, the representativeness cannot be 100% guaranteed (the network only includes a sample of GPs using a specific software and interested in registration) • For the PP: not possible to identify the reason for	• Sensitivity: low • Specificity: high

		consultation, so might not be related to LBP.
Sentinel GP network data (Sciensano)	• Not applicable. Low back pain has not been registered by the Sciensano SGPs.	

7.3.2 National best estimate

The Health Interview Survey appears to be the most complete source of information on the prevalence of low back pain in Belgium. To correct the possible overestimation due to the self-report nature of the survey, cases of low back pain are defined as those individuals reporting both the presence of low back pain and disability, as measured by the Global Activity Limitation Indicator (GALI). This combination of indicators closely resembles the lay descriptions of the health states, which combine the presence of low back pain with the presence of, at least, problems in mobility.

7.3.3 Discussion

Given the potentially high burden of low back pain, further studies are needed to quantify the validity (sensitivity/specificity) of the proposed approach for defining the prevalence of low back pain.

The question on low back pain was introduced in the HIS2013. Therefore, limited information is available on historical trends.

7.4 References

GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1789-1858.

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8 NECK PAIN (NP)

8.1 Case definition

Neck pain (NP) is defined as neck pain (with or without pain referred into the upper limb(s)) that lasts for at least one day.

8.1.1 Corresponding disease classification codes

ICD-10 codes

- M54.2 Cervicalgia

ICD-9 codes

- 723.1 Cervicalgia

ICPC-2 codes

- L01 Neck symptom/complaint
- L83 Neck syndrome

ATC codes

- Not applicable: there are no drugs sufficiently specific for treatment of NP.

Nomenclature codes

- Not applicable: there are no nomenclature codes sufficiently specific for NP.

8.2 Disease model

8.2.1 Health states

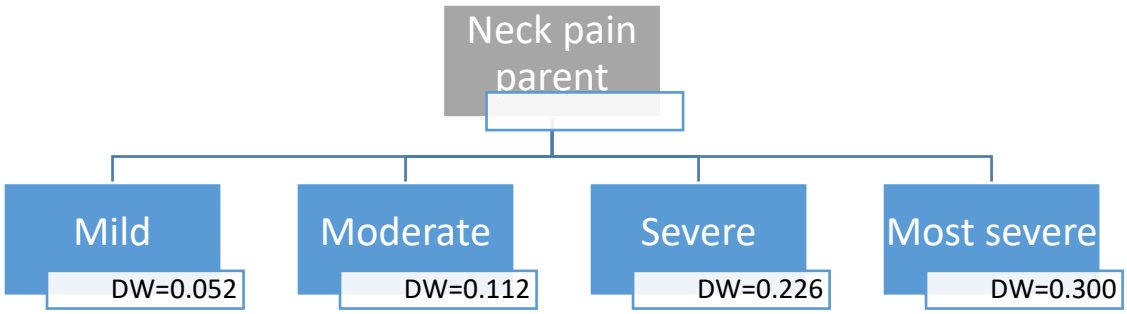

Figure 1. Neck pain disease model

8.2.2 Disability weights

Table 1. Disability weights (DW) by health state for neck pain according to the Global Burden of Disease study (Salomon et al., 2015)

Health state	Lay description	DW
Neck pain, mild	This person has neck pain, and has difficulty turning the head and lifting things	0.052
Neck pain, moderate	This person has constant neck pain, and has difficulty turning the head, holding arms up, and lifting things	0.112
Neck pain, severe	This person has severe neck pain, and difficulty turning the head and lifting things. The person gets headaches and arm pain, sleeps poorly, and feels tired and worried	0.226
Neck pain, most severe	This person has constant neck pain and arm pain, and difficulty turning the head, holding arms up, and lifting things. The person gets headaches, sleeps poorly, and feels tired and worried	0.300

8.2.3 Proportion of patients in the considered health states

Table 2. Proportion of patients in the different health states considered in the neck pain disease model, Belgium.

Health state	Parent	Proportion	Source
Neck pain parent	N/A	100%	Per definition
Neck pain, mild	Neck pain parent	0.67	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Neck pain, moderate	Neck pain parent	0.12	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Neck pain, severe	Neck pain parent	0.06	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Neck pain, most severe	Neck pain parent	0.15	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)

8.2.4 Discussion

Disability weights for the Belgian national burden of disease study are adapted from the Global Burden of Disease study (4), as these provide an exhaustive set of internally consistent disability weights.

The severity distribution in the GBD model is based exclusively on data from the USA, raising questions on applicability for the Belgian context. The proportion of cases with low back pain who report leg pain (by age) was derived using USA 2012 claims data. The severity distributions were derived from an analysis of the Medical Expenditure Panel Surveys (MEPS) in the USA (https://meps.ahrq.gov/mepsweb/). MEPS is an overlapping continuous panel survey of the United States non-institutionalized population whose primary purpose is to collect information on the use and cost of health care. Panels are two years long and are conducted in five rounds, which are conducted every five to six months. Each panel typically contains about 30,000 to 35,000 individual respondents. Respondents self-administer the SF-12 twice per panel, at rounds 2 and 4, typically about a year apart. Only adults 18 years and older completed the SF-12. MEPS also usually collects information on diagnoses based on self-report of reasons for encounters with health services. In addition, diagnoses are derived through additional questions on “problems that bother you” or conditions that led to “disability days”, ie, days out of role due to illness. Professional coders translate the verbatim text into three-digit ICD-9 codes. The main reason for LBP being measured in MEPS relates to health care contact. For GBD 2017, data were used from 2000-2014.

Since the health states are not defined in terms of clinical grading scales, comparability with available epidemiological and clinical evidence is hampered.

8.3 Prevalence

8.3.1 Data sources

Different data sources exist for NP, each with a specific case definition:

1. **Hospital discharge data:** patient with neck pain admitted to the hospital during the reference year (before 2015: ICD-9 code; after 2015 ICD-10 code M54.2).
2. **Health insurance data:** not applicable; there are no (reimbursed) medications or health care usages that would allow a sufficiently specific diagnosis of neck pain.
3. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you had a neck disorder or other chronic neck defect?”.
4. **Sentinel GP network data (Intego):** number of individuals with neck pain diagnosis ever recorded by GP (ICPC-2 codes L01 and/or L83) who had a GP contact during the reference year.
5. **Sentinel GP network data (Sciensano):** not applicable; neck pain has not been registered by the Sciensano SGPs network.

Table 3. Potential sources and methods for the computation of low back pain prevalence in Belgium.

Source	Strengths	Weaknesses	Evaluation
Hospital discharge data	• Exhaustive information on all cases hospitalized for neck pain • Diagnoses by medical doctor • Official database, organized and managed by public health authorities • National database	• No information on neck pain patients who were not admitted to hospital during the reference year; this is a substantial proportion of the neck pain patients • HDD is primarily used for administrative purposes, which could result in some problems when data have to be used for epidemiological purposes	• Sensitivity: low • Specificity: high
Health insurance data (IMA/EPS)	N/A: there are no (reimbursed) medications or health care usages that would allow a sufficiently specific diagnosis of neck pain		
Health Interview Survey	• Based on information from a representative sample • Provides representative results at national and regional levels.	• Self-reported information, which may induce an overestimation of NP prevalence; integration with information on disability or health-related quality of life may increase specificity • Not yearly available (+/- every 5 years) • Comparing estimates between subgroups of the sample might lack statistical precision	• Sensitivity: high • Specificity: high
Sentinel GP network data (Intego)	• Diagnosis by medical professional • Longitudinal approach	• Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP • Results are limited to Flanders • At the level of Flanders, the representativeness cannot be 100% guaranteed (the network only includes a sample of GPs using a specific software and interested in registration) • For the PP: not possible to identify the reason for	• Sensitivity: low • Specificity: high

		consultation, so might not be related to NP.
Sentinel GP network data (Sciensano)	• Not applicable. Neck pain has not been registered by the Sciensano SGPs.	

8.3.2 National best estimate

The Health Interview Survey appears to be the most complete source of information on the prevalence of neck pain in Belgium. To correct the possible overestimation due to the self-report nature of the survey, cases of neck pain are defined as those individuals reporting both the presence of neck pain and disability, as measured by the Global Activity Limitation Indicator (GALI). This combination of indicators closely resembles the lay descriptions of the health states, which combine the presence of neck pain with the presence of, at least, problems in mobility.

8.3.3 Discussion

Given the potentially high burden of neck pain, further studies are needed to quantify the validity (sensitivity/specificity) of the proposed approach for defining the prevalence of neck pain.

The question on neck pain was introduced in the HIS2013. Therefore, limited information is available on historical trends.

8.4 References

GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1789-1858.

Salomon JA, Haagsma JA, Davis A, de Noordhout CM, Polinder S, Havelaar AH, et al. Disability weights for the Global Burden of Disease 2013 study. Lancet Glob Health 2015 Nov;3(11):e712-e723.