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BELGIAN NATIONAL BURDEN OF DISEASE STUDY

Guidelines for the calculation of DALYs in Belgium

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Sponsors

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Updates to the protocol

Version 2020	• Initial version (disease-specific methods for 8 conditions)
Version 2021	• List of disease-specific methods expanded to 13 conditions
Version 2022	• Updated IDD redistribution algorithm • Added section on availability of results • List of disease-specific methods expanded to 28 conditions
Version 2023	• Updated IDD redistribution algorithm • Added section on interpolation and projection of the HIS-derived prevalence estimates for the inter-wave periods

CONTENTS

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. 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, but 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 the 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 the 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 a 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 the 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 of 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 from 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** are ensured. Instead of relying on external analyses or global interpolations, BeBOD allows one 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 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 of non-fatal outcomes
5. Evaluate the 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 transparently estimates the true disease burden 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.

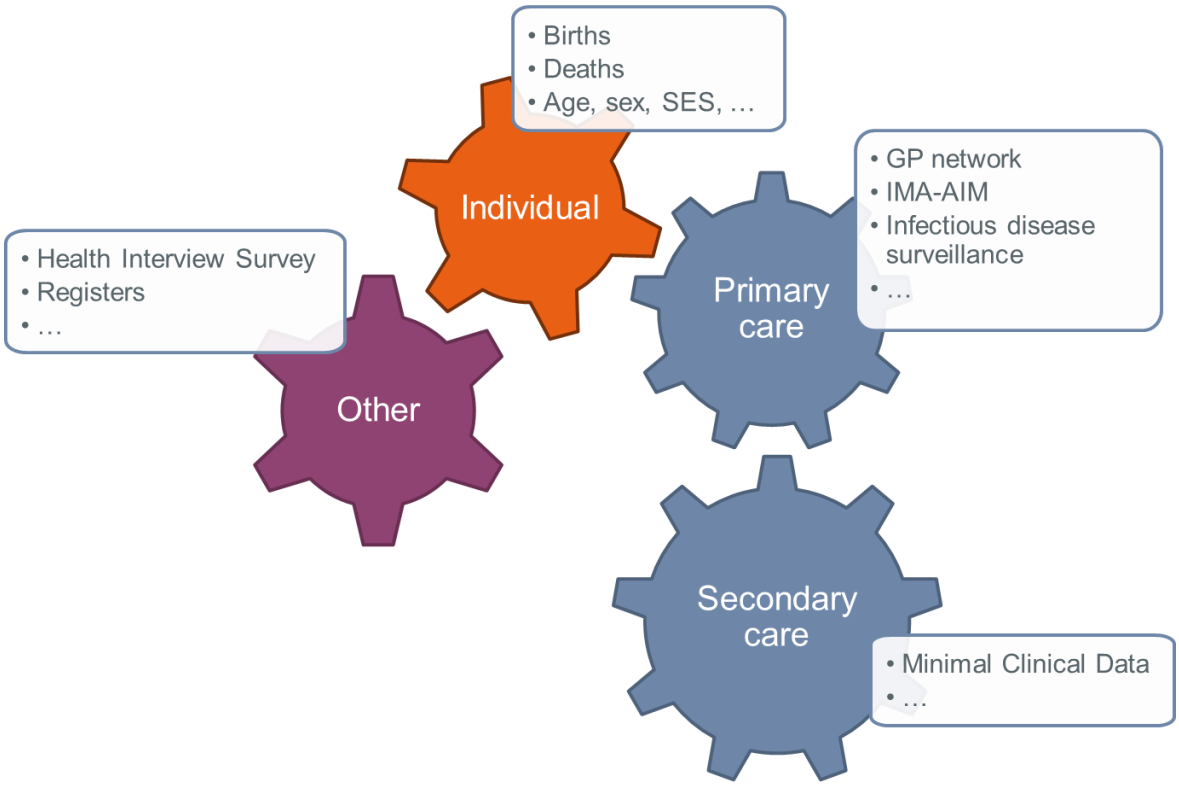

Figure 1. Data needs for the Belgian National Burden of Disease project

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 the link with the 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 a 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 the progress of ongoing and new DALY activities within the unit
- Interact with unit-specific stakeholders: put the burden of disease on the agenda

Steering committee

- Follow-up on project progress through annual meetings
- Provide technical feedback by 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 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. The third level of disaggregation is used to identify more specific causes within each of the subcategories. Finally, for some level 3 causes, the fourth level of disaggregation is provided, specifying further subtypes of the cause.

Given the currently limited resources for the BeBOD project, the 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 regions.

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 2018.

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
- Years Lived with Disability due to cancer

2. Years of Life Lost

2.1 INTRODUCTION

Disability-Adjusted Life Years (DALYs) are composed of standard expected years of life lost due to premature mortality (YLLs) and years lived with disability (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 $i = 1, \dots, a$ 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 2019 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 CAUSE OF DEATH DATA

Death certificates in Belgium are based on the World Health Organization (WHO) International Form of Medical Certificate of Cause of Death. The certifying physician specifies the underlying or external cause of death, possibly complemented with immediate, intermediate, and associated causes of death. The completed death certificates are collected by the municipal offices, and sent to the regional health authorities, i.e., the Flemish Agency for Care and Health (for deaths occurring in the Flemish or Brussels Capital Region), and the Walloon Agency for a Quality Life (for deaths occurring in the Walloon Region). These agencies use the IRIS software to encode the information listed on the death certificates into ICD-10 codes. The resulting datasets from both agencies are compiled by Statistics Belgium (Statbel), the national institute of statistics, which is thus responsible for managing the national cause of death database. Sciensano receives the national dataset for further analyses.

The process of compiling the national cause of death data currently takes around 2 to 3 years, mainly because of delays in data transfer from the municipalities to the regions. Non-natural deaths are furthermore investigated by the prosecutor offices, which may add to the delay. Completeness of demographic data in the national cause of death database is very high.

Deaths with missing information on age or sex are excluded from further analyses. 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

As a first step in the analysis process, we map the ICD-10 codes 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.”

Since a detailed map from the GBD is not available, we adopted the map used by the Scottish Public Health Observatory, with some modifications. For drug-related deaths, we follow the definitions from the European Monitoring Centre for Drugs and Drug Addiction for combinations of ICD-10 X41, X44, X61, X64 or Y11 with T43.6, and X42, X62, or Y12 with T40 (mapped to ICD-10 F19). In line with WHO and GBD, stillbirths (ICD-10 P95) are excluded from the analyses.

In the mapping process, several ICD-10 codes are not matched with a specific GBD cause. These codes are also referred to as garbage codes, or ill-defined deaths (IDDs). The next section describes our approach for redistributing these IDDs to specific GBD causes.

2.4 REDISTRIBUTION OF ILL-DEFINED DEATHS

To redistribute the IDDs to specific GBD causes, we developed a probabilistic approach making optimal use of the multiple cause of death data available in Belgium. Our approach consists of four different steps, with at each step an update of the target distribution. These updated target distributions were used at each step and for each group within a given step. This to respect the sequence of redistributions, and the build-up of evidence along the redistribution process.

In the first step, selected IDDs are proportionally redistributed in function of predefined ICD-10 target codes ("ICD-based redistribution"). For example, malignant neoplasm of lower respiratory tract, part unspecified (ICD-10 C39.9) is redistributed to two groups of target codes – trachea, bronchus, and lung cancers (ICD-10 C30-C38) and malignant mesothelioma (C45) – pro rata to the occurrence of both diseases as underlying causes of death. The occurrence of these diseases is related to tobacco and asbestos exposure, which have been found to have a particularly strong impact on Belgian mortality compared with other countries. This example underlines the importance of accounting for country-specific trends in the redistribution of IDD. To incorporate recent trends and reduce random variation, the target distributions are defined based on the deaths that occurred in the past five years (i.e., the target for IDDs in year y are based on specific deaths occurring in year y-4 to y). This also implies that the first estimates are available for the year 2004, i.e., the first year for which a five-year period of cause of death data are available. To add to precision, the target distributions are stratified by age group (0–4, 5–14, 15–44, 45–64, 65–84, 85+) and sex. If there are not sufficient deaths in a given combination, a target based on sex only is used. If there are no observed deaths in the target, then the IDDs are redistributed to all causes. We also exclude sex-specific deaths from the target distributions of the opposite sex, e.g., we ensure that deaths in women could not be redistributed to prostate cancer.

The first step in the redistribution process is only applicable to IDDs that provide information on the possible underlying cause of death, and thus allow defining target codes a priori. In the second step, we rely on the Belgian multiple cause of death data to define targets and redistribute selected remaining IDDs that are intrinsically uninformative ("package redistribution"). For example, a death certificate states that the underlying cause of death is "Other specified pulmonary heart diseases" (ICD-10 I27.8). There is no specific GBD cause assigned for this code (it is an IDD) and there are no predefined targets code available (step 1). For these cases, we defined packages, i.e., sets of IDDs that are considered to have a similar redistribution target. In this example, the package created is called "Right heart failure and pulmonary heart disease" and is made up of the following ill-defined ICD-10 codes: I27.0, I27.2, I27.8, I27.9, and I28.9. For each package, the target distribution is defined as the

deaths, occurring in the past five years, that have one of the package IDDs as immediate, intermediate, or associated cause of death, and that have a specific or redistributed cause as underlying cause of death. As before, the redistribution is performed proportionally to the observed target codes, stratified by age group and sex. Because the target is defined in function of the multiple cause of death data of the preceding 5-year period, the targets are not fixed and may differ for the different years of the time series.

The remaining IDDs are those that are uninformative and that typically do not occur as immediate, intermediate, or associated cause of death. These include the codes of ICD-chapter R, “Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified”. To maximize the use of the available multiple cause of death data, we apply a the third step where we we perform an internal redistribution of IDDs (“internal redistribution”). In this approach, remaining IDDs are randomly assigned to a specific GBD cause that is recorded as immediate, intermediate, or associated cause of death for the deceased individual.

In the fourth and final step, all remaining IDDs are proportionally redistributed over all specific causes having occurred in the preceding five years, stratified by age group and sex as described above (“all-cause redistribution”).

GBD causes (level 3) with less than five occurrences in the five-year reference period (i.e., less than one per year in average), are excluded as possible targets. These rare causes (e.g., rabies (A82)) are typically very specific diseases, with a specific diagnosis, and would therefore be rarely missed as an underlying cause of death.

To capture the uncertainty that results from the probabilistic redistributions, the redistribution process was performed in a probabilistic way, using 100 iterations. Each iteration is a complete run of the four-step process, and results in a completely imputed cause of death dataset. For each of the summary statistics (as described below), 100 random estimates are thus generated. We present means and 95% uncertainty intervals of these 100 random estimates, the latter defined as the 2.5th and 97.5th percentile of the random estimates.

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 (Unit Illicit Drugs).

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.

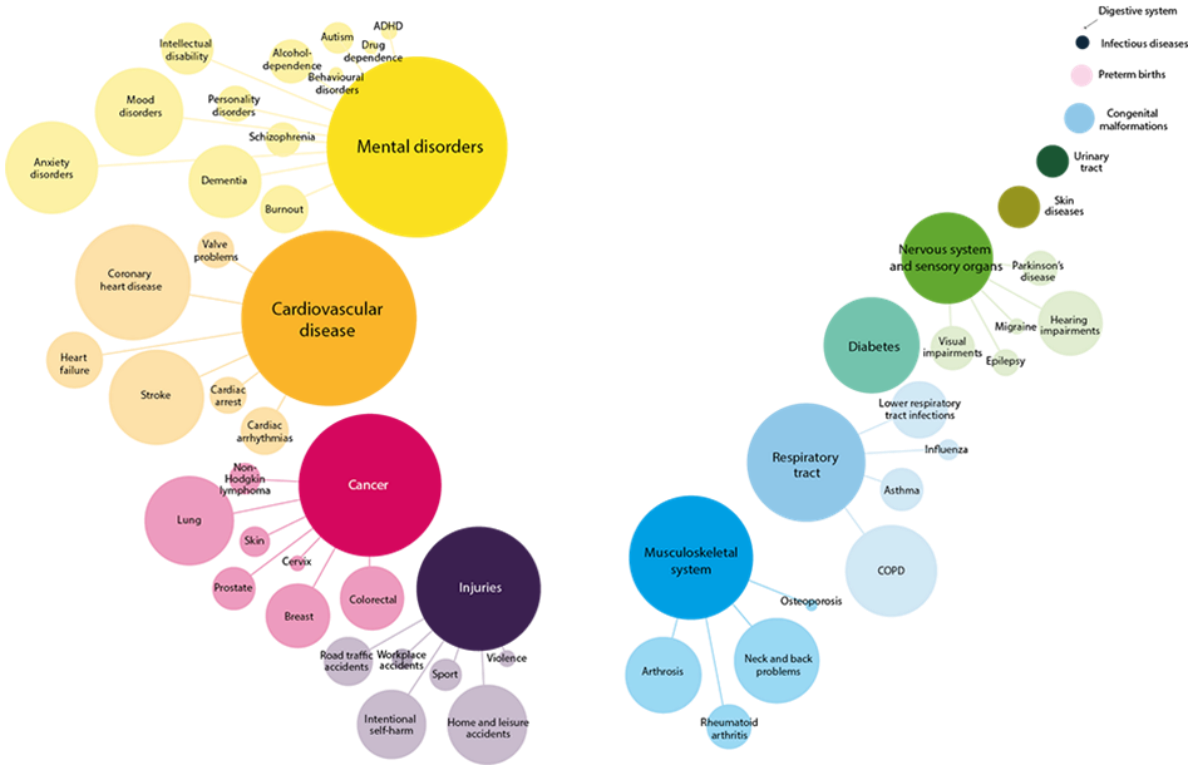

Figure 2. Relative contribution of outcomes and outcome clusters to the disease burden in the Netherlands.

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 was 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. It is also

used in the Hospital discharge dataset (Minimum Hospital Data and Minimum Psychiatric Data sets, see 3.4.2.)

The choice has been 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 99% 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 there a low risk that the question on the disease will lead 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.

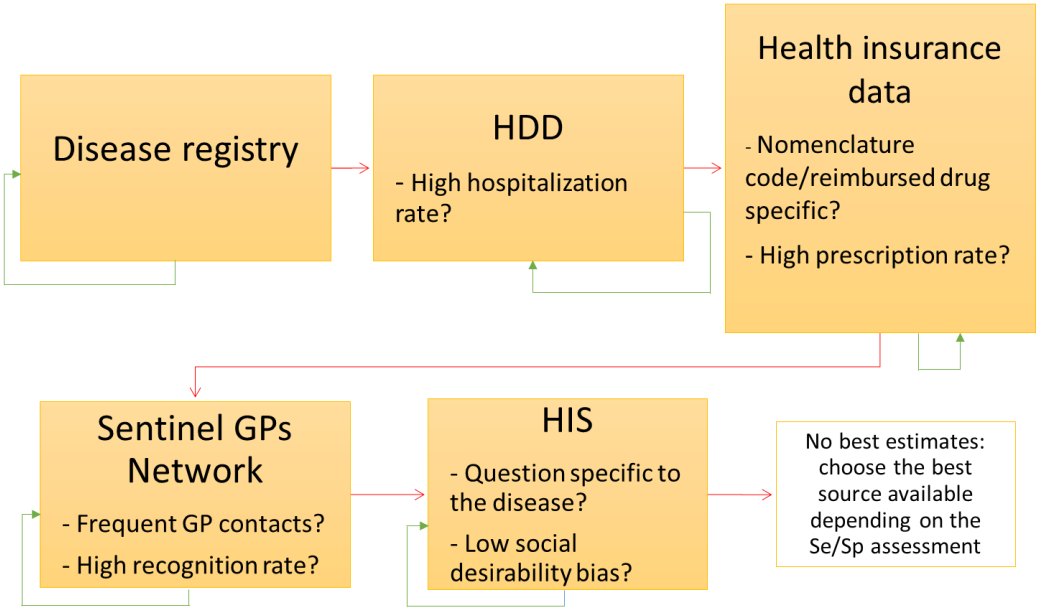

Figure 3. Evaluation process of the data sources

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 IMPUTATION OF PREVALENCE ESTIMATES

For each outcome, information is required on the entire period that is part of the BeBOD project – i.e., from 2013 to the most recent reference year. For prevalence estimates that are derived from the HIS, which is collected every 5 years, an imputation of the prevalence estimates for

the years in-between the subsequent waves is required. The method for the imputation of these prevalence estimates during the years that are missing in the HIS depends on the number of available data points:

- When data are only available during one year, the prevalence estimate for the missing years is imputed as the known prevalence estimate in the year for which data is available.
- When data are available for at least two years, the prevalence estimate for the missing years is imputed by applying a Bayesian generalised linear regression model with binomial link function including year, age, sex, and region as independent factors, and an indicator for the presence of a specific disease as the dependent factor.

For prevalence estimates that are derived from the HDD, imputation is necessary for the year, in which a change takes place between versions of the ICD-coding tool. In Belgium, the switch from ICD-10 to ICD-11 took place in 2015. Imputation of prevalence rates for each disease in 2015, whereby data from the HDD is used, is achieved by linear interpolation (i.e. averaging the prevalence rate from 2014 and 2016).

3.7.1 Imputation in the HIS when data are available for one year

For some of the diseases for which the HIS is selected as the most appropriate data source, only one year of data is available. To this end, the imputation of the prevalence estimate in the missing years is obtained by calculating the weighted prevalence by age, sex, and region based on the data in the available year and using this estimated prevalence to impute the prevalence estimates for the years at which no data in the HIS is available. Hence the prevalence estimate is considered constant over time. If for example the prevalence estimate in men with an age between 15 and 45 years in the Flemish Region equaled 15% for low back pain in 2018, the same prevalence estimate is considered for the years 2013 to 2017.

3.7.2 Imputation in the HIS when data are available for at least two years

For the largest share of diseases, for which the HIS is selected as the most appropriate data source, there are at least two years in which information on disease prevalence estimates is available. In this scenario, imputation of the missing years is obtained by building a Bayesian generalised linear regression model including year, age, sex, and region as independent factors, and the presence of a specific disease (dummy variable with “0” for no disease present and “1” for disease present) as a dependent factor. The Bayesian model using a *binomial link function* is fitted using the INLA package for R (Rue et al., 2009). INLA stands for Integrated Nested Laplace Approximation, a novel approach that makes Bayesian inference faster compared to the computer-intensive Bayesian Markov chain Monte Carlo methods. Multiple Bayesian INLA models are fitted to the data with different specification and combinations of the independent factors:

- **Fixed factors model** with year, age, sex, and region included as fixed factors without considering any interactions.
- **Fixed factors model with interactions**, whereby year, age, sex, and region are included as fixed factors and all two-way interactions among the included factors are considered.
- **Mixed factors model with random intercepts**, whereby year is included as a fixed factor, and sex, age, and year as random factors which are distributed according to a Gaussian model.
- **Mixed factors model with random slopes**, whereby sex-, age- and region-level random slopes on year are included which are distributed according to a Gaussian model.

The most suitable model is selected based on the Watanabe–Akaike information criterion (WAIC), whereby a lower WAIC is associated with a better fit of the model to the data. Therefore, the model with the lowest WAIC is selected for the imputation. After model selection, the estimated prevalence estimates and their surrounding 95% uncertainty intervals for the years with no information on the prevalence are extracted from the posterior distribution of the Bayesian model fitted with INLA by age, sex, and region. In addition, we also use the estimated and smoothed prevalence rate derived from the most suitable model for the years in which data are available, to allow for a coherent time series.

3.7.3 Demographic data

Demographic data for the different years that are included in the BeBOD project are mid-year population estimates derived from the Statbel demographic data, and available via the Standardized Procedures for Mortality Analysis (SPMA) tool (https://spma.sciensano.be/). These data on population size by age, sex and region are combined with the estimated prevalence ratios to calculate the number of cases for each of the diseases included in the BeBOD project.

3.8 PROJECTION OF PREVALENCE ESTIMATES

Projection of prevalence estimates is necessary for years that are included in the BeBOD project, but fall later than the latest available time of information available in the most suitable data source. This is in particular the case for the HIS, for which the latest information coincides with the final wave, which was conducted in 2018. For all time-points after 2018, the prevalence ratios will be projected using the same methodological approach as described under **Section 3.7**.

3.9 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.

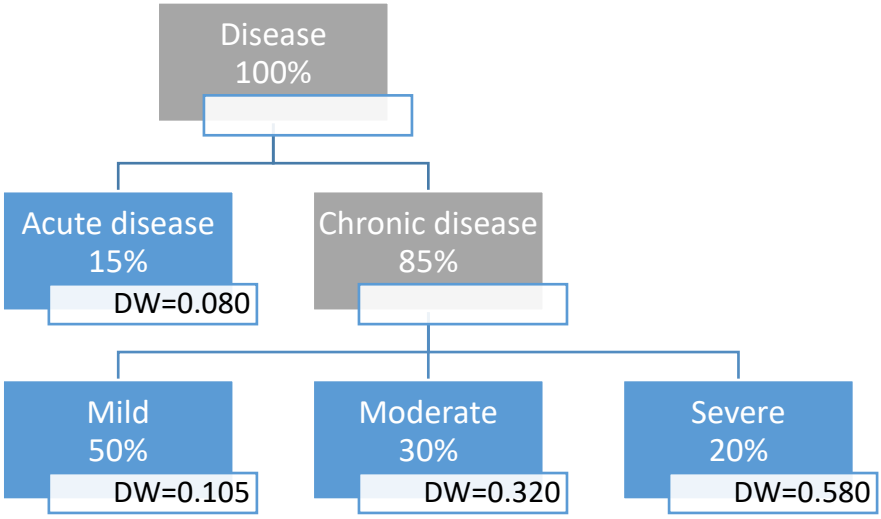

Figure 4. Theoretical disease model, severity distribution and disability weights.

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.

3.10 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.

3.11 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. Experts are defined as individuals with

relevant epidemiological and/or clinical knowledge with regards to the concerned outcome (cluster). The expert evaluation addresses the following steps:

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

4. Years Lived with Disability due to 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. The methodology is described in detail by Gorasso et al. (2022).

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 2019. 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**). The models make a distinction between surviving cases, and cases that die within 10 years after diagnosis. For surviving cases, the disease models define two health states 1) diagnosis and primary therapy; and 2) control phase when the cancer becomes a chronic diseases and requires daily medication that do not interfere with daily activity. The duration of the diagnosis stage is cancer specific and the duration of the control stage is given by the remainder of the 10-year period. For fatal cases, the disease models define four health states – i.e., diagnosis, control, metastasis, and

terminal. The duration of each stage depends on both the cancer type and the survival time. The durations are assigned in the following sequence:

1. Terminal: 1 month
2. Diagnosis: cancer specific duration (or remainder of total survival time)
3. Metastasis: 18 months (or remainder of total survival time)
4. Control: remainder of total survival time

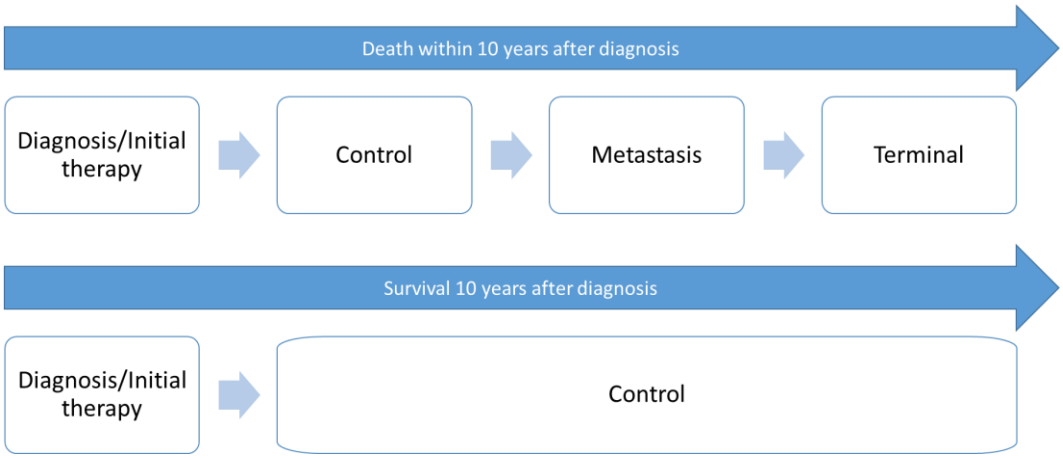

Figure 5. Generic incidence-based cancer disease model

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	

For some cancers, the disease models also included specific treatment or surgery-induced complications for the entire duration of illness. These complications comprised mastectomy (breast cancer; DW = 0.036), stoma (colorectal cancer; DW = 0.095), laryngectomy (larynx cancer; DW = 0.051), incontinence (prostate and bladder cancer; DW = 0.139), and impotence (prostate cancer; DW = 0.017).

To assess the proportion of cases for which these complications occur, we performed an expert elicitation exercise among experts in contact with our institution. Belgian oncologists, gynecologists and urologists from different hospitals and clinics in Belgium were contacted through email. Each expert was asked to provide a minimal and maximal plausible value for the proportion of complications among the specific cancers for which they had most expertise. The elicitation was done through an online questionnaire.

4.4 ESTIMATION OF PREVALENCE FROM INCIDENCE

Based on the disease models, we projected the time spent in the different health states for each incident cohort (2004–2019). This implies that from the year 2013 onwards, we were able to define the prevalence in a given year as the sum of person-months spent in the different health states. We used the observed survival probabilities to model the fraction of surviving vs non-surviving cases, as well as the moment of death (in terms of time since diagnosis) for the non-surviving cases. Specifically, we used a microsimulation approach to simulate future health states for each year-, age-, sex-, region- and cancer-specific cohort of incident cases. For each incident case in the specific cohort, age at diagnosis was randomly assigned using a uniform random number generator taking the minimum and maximum of the concerned age group as limits. Then, we used sampling with replacement to assign, for each incident case in the specific cohort, one of 11 possible outcomes according to the survival probabilities, i.e., death within year 1, 2, …, 10 after diagnosis, or survival. For the fatal cases, simulated to die within year y after diagnosis, we randomly assigned the moment of death using a uniform random number generator taking $y - 1$ and y as limits. The age at death was thus a function of the randomly assigned age at diagnosis, and the randomly assigned time between diagnosis and death. In a final step, we assigned the health states of the cancer disease model to each incident case, in function of their simulated outcome, and, for the fatal cases, their simulated time till death. The durations of each health states, and the sequence in which the health states are defined, were explained before.

4.5 YLD CALCULATION

Prevalence-based YLD were estimated for the period 2013–2019. For each reference year, the YLDs were calculated as the sum of the disability-weighted time spent in each health state, for all the cases that were alive during the reference year.

5. Availability of results

The BeBOD study generates a large number of disease burden estimates by cause, age, sex, region, and year. To explore these detailed estimates, a series of interactive visualisation tools have been developed. These tools allow creating graphs of the relative contribution of different causes, trends over time, comparisons across regions, patterns by age, and much more. The following tools are available:

- Estimates of mortality and years of life lost for all causes of death: https://burden.sciensano.be/shiny/mortality
- Estimates of the non-fatal burden for all cancer types: https://burden.sciensano.be/shiny/cancer
- Estimates of the disease burden for 37 conditions: https://burden.sciensano.be/shiny/daly

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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. GBD2019 theoretical minimum risk reference life table

Age	Life expectancy
0	88.87
1	88.00
5	84.03
10	79.05
15	74.07
20	69.11
25	64.15
30	59.20
35	54.25
40	49.32
45	44.43
50	39.63
55	34.91
60	30.25
65	25.68
70	21.29
75	17.10
80	13.24
85	9.99
90	7.62
95	5.92

Source: Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019) Reference Life Table. Seattle, United States of America: Institute for Health Metrics and Evaluation (IHME), 2021. http://ghdx.healthdata.org/record/ihme-data/global-burden-disease-study-2019-gbd-2019-reference-life-table

Annex 3. Disease-specific methods

1 ACUTE MYOCARDIAL INFARCTION

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

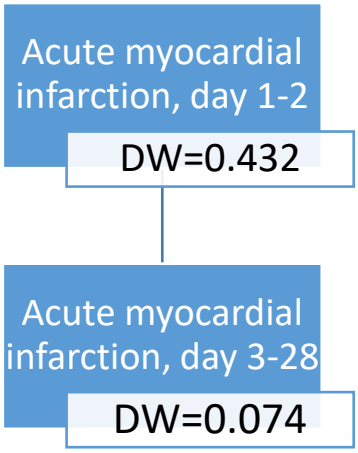

Figure 1. Acute myocardial infarction disease model

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 (Salomon et al., 2015), 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 cannot be 100% guaranteed (the network	Sensitivity: low Specificity: high

		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

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2 ALCOHOL DEPENDENCE

2.1 Case definition

Alcohol use disorders (AUD) are a group of substance-related conditions affecting the use of alcohol. Different classifications can be used in relation to these conditions.

The first one is the Diagnostic and Statistical Manual of Mental Disorders, version IV, text revised (DSM-IV-TR) (APA, 2000), in which the distinction is made between alcohol abuse (AA) and alcohol dependence (AD), which is the most severe form of AUD. AUD are divided into three stages: alcohol consumption without any dependence or abuse (stage I), alcohol abuse without dependence (stage II) and alcohol dependence with or without alcohol abuse (stage III).

The case definition used here is also used in the GBD 2017 study (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018), and corresponds to the definition of alcohol dependence in the DSM IV (stage III), and is defined as “A maladaptive pattern of drinking, leading to clinically significant impairment or distress, as manifested by three or more of the following occurring at any time in the same 12-month period” (APA, 2000).

Three of the following criteria must occur in the past 12 months in order to consider a case of AD:

- Having increased tolerance for alcohol (i.e. a person must drink more to feel its effects)
- Experiencing withdrawal symptoms when not drinking
- Consuming alcohol in greater amounts than intended, or over a longer time
- Making unsuccessful attempts to cut down or control alcohol use
- Spending a great deal of time obtaining alcohol, drinking it, or recovering from its use
- Giving up or reducing former social, occupational, or recreational activities
- Continuing to drink despite knowledge of alcohol’s physical and psychological damages.

The choice has been made to use the fourth version of the DSM instead of the most recent version being the fifth (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-5 have a minimal impact on the prevalence of the substance use disorders diagnoses, despite some undeniable advantages e.g., the capacity to capture low alcohol dependent cases (“diagnostic orphans”) or the addition of a “craving” criterion (Peer et al., 2013). 12-months prevalence of alcohol use disorders is slightly to modestly higher

when using the DSM-5 instead of the fourth version (Grant et al., 2015; Bartoli et al., 2015). It has to be noticed that a major change from DSM-IV to DSM-5 is the combination of substance abuse disorder and substance dependence into a single substance use disorder, which requires 2 out of 11 criteria in a 12-month period for diagnosis.

2.1.1 Corresponding disease classification codes

DSM-IV-TR code

- 303.90 Alcohol dependence

ICD-10 code

- F10.2 Mental and behavioral disorders due to use of alcohol: dependence syndrome

ICD-9 code

- 303 Alcohol dependence syndrome

ICPC-2 code

- P15 Chronic alcohol abuse

ATC codes

- N07BB Drugs used in alcohol dependence
- N07BB01 disulfiram
- N07BB02 calcium carbimide
- N07BB03 acamprosate
- N07BB04 naltrexone
- N07BB05 nalmefene

Nomenclature codes referring to alcohol dependence

- Not applicable: there are no nomenclature codes sufficiently specific to match the case definition for alcohol dependence.

2.2 Disease model

2.2.1 Health states

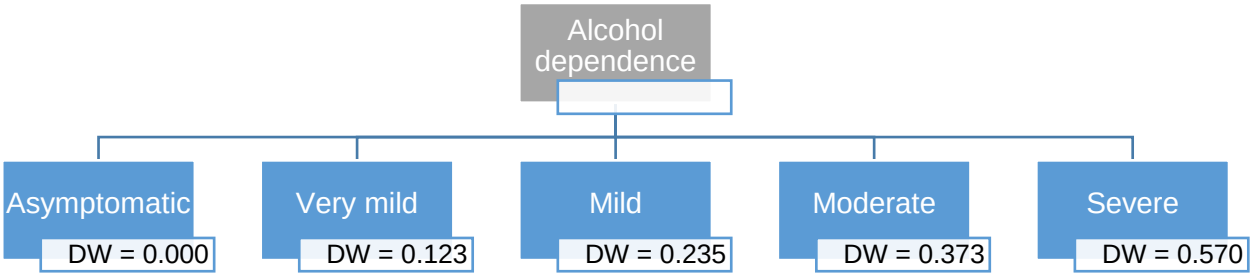

Figure 1. Alcohol dependence disease model

2.2.2 Disability weights

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

Health state	Lay description	DW
Asymptomatic	Not applicable	0.000
Very mild	Drinks alcohol daily and has difficulty controlling the urge to drink. When sober, the person functions normally.	0.123
Mild	Drinks a lot of alcohol and sometimes has difficulty controlling the urge to drink. While intoxicated, the person has difficulty performing daily activities.	0.235
Moderate	Drinks a lot, gets drunk almost every week and has great difficulty controlling the urge to drink. Drinking and recovery cause great difficulty in daily activities, sleep loss, and fatigue.	0.373
Severe	Gets drunk almost every day and is unable to control the urge to drink. Drinking and recovery replace most daily activities. The person has difficulty thinking, remembering and communicating, and feels constant pain and fatigue.	0.570

2.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Alcohol dependence	N/A	100%	Per definition
Alcohol dependence, asymptomatic	Alcohol dependence	40.9%	GBD 2017
Alcohol dependence, very mild	Alcohol dependence	46.9%	GBD 2017
Alcohol dependence, mild	Alcohol dependence	4.0%	GBD 2017
Alcohol dependence, moderate	Alcohol dependence	3.4%	GBD 2017
Alcohol dependence, severe	Alcohol dependence	4.8%	GBD 2017

2.2.4 Discussion

The distribution of the alcohol dependence cases into the different health states was adapted from the severity splits used in the GBD 2017 study. In the GBD 2017 study, 3 population surveys were used to estimate the proportion of alcohol dependence cases in the asymptomatic; very mild; mild; moderate and severe diseases categories.:

- 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 12-item Short Form Health Survey (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 (US) National Epidemiological Survey on Alcohol and Related Conditions (NESARC) (Grant & Dawson, 2006). Wave 1 was conducted in 2000-2001 and Wave 2 was conducted in 2004-2005. NESARC is a representative sample of the non-institutionalized US population aged 18 and older. Information on the occurrence of more than one psychological disorder or substance use disorder in the same person are collected, using definitions from the DSM-IV. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV) was used to derive the AUD prevalence. AUDADIS-IV is a validated instrument used in diagnostic interviews in population studies, with high reliability for alcohol consumption (Grant et al., 2003; Üstün et al., 1997). Information on 12-month prevalence of alcohol dependence is available.
- The Australian National Survey of Mental Health and Wellbeing of Adults (NSMHWB) 1997 (Andrews et al., 1999). NSMHWB is a representative sample of non-institutionalized adults in Australia. They were screened for mental and substance use disorders via the Composite International Diagnostic Interview (CIDI), a standard questionnaire based on criteria from ICD-10 and DSM-IV. Both 1-month and 12-month prevalence are available.

It has to be noticed that the proportion of the alcohol dependence cases in the different health states may not be fully representative of the Belgian population because of cross-cultural

differences in alcohol consumption (Bloomfield et al., 1995). However, the diagnostic instruments used in these 3 population surveys have been validated to derive the alcohol dependence prevalence in the general population and have shown good reliability (Grant et al., 2003; Üstün et al., 1997).

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 alcohol dependence (AD), each with a specific case definition:

1. **Belgian Treatment Demand Indicator registry (TDI)**: patient in contact with an inpatient or outpatient treatment centre that have started a new treatment for alcohol dependence during the reference year. Treatment centres are defined as facilities or practitioners providing treatment for drug or alcohol addiction. A treatment episode is defined as a treatment process separated by at least 6 months from a previous one in outpatient settings. In residential settings, an episode occurs each time a patient is admitted and ends when the patient leaves the centre and no further admission is foreseen.
2. **Hospital Discharge data**: patient with alcohol dependence admitted to the hospital during the reference year (before 2015: ICD-9 code 303; after 2015 ICD-10 code F10.2).
3. **Health insurance data**: person with a prescription for ATC codes N07BB during the reference year.
4. **Health Interview Survey**: number of individuals who reported drinking more than 6 glasses (men) or more than 4 glasses (women) of alcohol a day during the last 12 months.
5. **Sentinel GP network data (Intego)**: number of individuals with alcohol dependence diagnosis ever recorded by GP (ICPC-2 code P15) who had a GP contact during the reference year.
6. **Sentinel GP Network data (Sciensano)**: patient with an alcohol problem in contact for the first time with the GP and that begins a new treatment for this problem. The treatment is defined as any activity that can be lead in order to enhance the physical, psychological or mental health state of a person with an alcohol problem. A treatment episode is defined as a treatment process separated by at least 6 months from a previous one.

Table 3. Potential sources and methods for the computation of alcohol dependence (AD) prevalence in Belgium

Source	Strengths	Weaknesses	Evaluation
Belgian Treatment Demand Indicator Registry (TDI)	Reliable data on drug users in treatment at a national level; Longitudinal approach; Mandatory registration in hospitals and specialized centres; Registration by professionals; National database; Possibility to identify 80% of the patients uniquely via the SSIN; Possibility to link these data with other databases through the SSIN (TDIR-IMA databases) (Van Baelen et al., 2018)	TDI concerns only new treatment demand: incidence indicator instead of prevalence indicator → False positives: the registration using the SSIN is not mandatory: about 20% of the patients are anonymous and can be registered several times leading to a potential overestimation of the number of AD cases (Antoine, 2018). → False negatives: the treatment rate of alcohol dependence is low in Europe: 22% of people with AD seek and receive a professional help (counselling, pharmacotherapy, individual or group therapy from health professionals i.e. GPs, psychotherapists, psychiatrists and other specialists for alcohol problems) (Rehm et al., 2015). Lack of registration in the non-specialized sector (GPs, medical house, private practice,…).	Sensitivity: low Specificity: high
Hospital discharge data	Exhaustive information on all cases hospitalized for alcohol dependence; Diagnoses by medical doctor; Official database, organised and managed by public health authorities; National database	No information on alcohol dependent patients who were not admitted to the hospital during the reference year. This number is supposed to be important since evidence has shown an inverse relation (Armstrong et al., 1998; Baumeister et al., 2006; Rodriguez Artalejo et al., 2000) or a U-shaped curve (Anzai et al., 2005; Longnecker & MacMahon, 1988) between the level of alcohol consumption and inpatient healthcare	Sensitivity: low Specificity: high

		utilisation. Moreover, the recognition rate of alcohol use disorders in secondary care is 52%, and the recording is correct in 37% of the cases (Mitchell et al., 2012). 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 are based on the prescription of medicines, not on a medical diagnosis, which generates false-positives and false-negatives → False positives: patients having received this treatment for another indication (e.g. Naltrexone is also used in opioid dependence) → False negatives: patients with the condition who do not take this treatment. Alcohol dependence is a condition with a low treatment rate in Europe (Rehm et al., 2015; KCE, 2015). 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: low Specificity: low
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 positives and false negatives → False negatives: Alcohol consumption is underreported in population surveys. Underestimates of alcohol consumption:	Sensitivity: medium Specificity: high

			40%–50% (Livingston et al., 2015). → False positives are assumed to be low. Not yearly available (+/- every 5 years) Comparing estimates between subgroups of the sample might lack statistical precision	
Sentinel network (Intego)	**GP data**	Diagnosis by medical professional Longitudinal approach	Will not capture patients that bypass the GP (ED, hospitalization, people living in a long-term care facility) 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 specific software and interested in registration) For the PP: not possible to identify the reason for consultation, so might not be related to the condition in question. Recognition rate of alcohol dependence in primary care is low (33%-50%) (Mitchell et al., 2012; Üstün & Sartorius, 1995; Hoeksema et al., 1991) In Belgium, only 17% of the people that have a problem with alcohol seek for a professional help (GP, psychiatrist or psychologist) (Bruffaerts et al., 2004)	Sensitivity: low Specificity: medium
Sentinel network (Sciensano)	**GP data**	Diagnosis by medical professionals 120 GP distributed evenly all over the country Representativeness of GPs in Belgium (for age and sex)	Only incidence data on AD cases that have started a new treatment during the reference year. Will not capture patients that bypass the GP (ED, hospitalization) unless the information is transmitted to the GP	Sensitivity: low Specificity: medium

Only periodic registration. The last registration was made in 2016.

Recognition rate of alcohol dependence in primary care is low (33%-50%) Mitchell et al., 2012; Üstün & Sartorius, 1995; Hoeksema et al., 1991

In Belgium, only 17% of the people that have a problem with alcohol seek for a professional help (GP, psychiatrist or psychologist) (Bruffaerts et al., 2004)

The case definition encompasses AD patients that begin a new treatment for this problem; but in Europe, the treatment rate for AD is low (Rehm et al., 2015; KCE, 2015).

2.3.2 National best estimate

The **Belgian Health Interview Survey** is assumed to yield the best estimate of alcohol dependence prevalence.

2.3.3 Discussion

It must be noticed that the number of alcohol dependence (AD) cases in the general population may be underestimated using the HIS as best estimate, for several reasons:

- Population surveys do not include homeless people, people in mental institutions and prisons, however there is supposed to be a lot of cases of alcohol dependence in these populations (Rehm et al., 2015; Rehm et al., 2014).
- Alcohol dependence is commonly underreported in population surveys (Stockwell et al., 2004) due to a memory bias (a poor recall of the past alcohol consumption); a denial or underestimation of the alcohol use; and more particularly due to a bias of selection: people with AD are less likely to participate to general population surveys.

Evidence has shown good reliability to assess alcohol dependence via the “heavy drinking” indicator, measured by thresholds set by the European Medicines Agency: 60 and more grams on average per day of pure alcohol for men, and 40+ grams for women (Rehm, 2016). On average, one glass of alcohol contains 10 grams of pure alcohol, heavy drinking corresponds

thus to the consumption of more than 6 glasses (men) or more than 4 glasses (women) of alcohol a day.

The HIS has been selected to be the best estimate to assess the prevalence of alcohol dependence, after having considered other possibilities:

The Belgian Treatment Demand Indicator Registry does not allow to compute the prevalence of the AD cases in the population, only the incidence of the new started treatments for an alcohol problem. Plus, in Europe, the treatment rate for alcohol dependence is low: 22% of people with AD seek and receive a professional help (counselling, pharmacotherapy, individual or group therapy from health professionals i.e. GPs, psychotherapists, psychiatrists and other specialists for alcohol problems) (Rehm et al., 2015).

The hospital discharge data may miss a lot of cases since evidence has shown an inverse relation (Armstrong et al., 1998; Baumeister et al., 2006; Rodriguez Artalejo et al., 2000) or a U-shaped curve (Anzai et al., 2005; Longnecker & MacMahon, 1988) between the level of alcohol consumption and inpatient healthcare utilization. Furthermore, the recognition rate of alcohol use disorders in secondary care is moderate (52%), and the recording is correct in only 37% of the cases (Mitchell et al., 2012).

Using the health insurance data is not enough sensitive since the treatment rate of alcohol dependence is low in Europe, and drugs used to treat this condition are not sufficiently specific to alcohol dependence as they are also used in other addictions (e.g. opioid addiction).

Finally, we have decided not to use the sentinel GP network as a source to compute the AD prevalence since the recognition rate of this disease in the primary care seems to be quite low (33%-50%) (Mitchell et al., 2012; Üstün & Sartorius, 1995; Hoeksema et al., 1991). Furthermore, it is established that the use of outpatient care decreases with the level of alcohol consumption (Armstrong et al., 1998; Baumeister et al., 2006; Rodriguez Artalejo et al., 2000). In Belgium, only 17% of the people with alcohol disorder seek a professional help (GP, psychiatrist or psychologist) (Bruffaerts et al., 2004).

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

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3 ALZHEIMER'S DISEASE AND OTHER DEMENTIAS

3.1 Case definition

Dementia is a syndrome due to a brain disease, of progressive and chronic nature, characterized by a deterioration in multiple cortical functions such as memory, thinking, orientation, language, judgment, learning capacities, behavior, and the ability to perform daily activities. A deterioration in the control of emotions, social behavior or motivation is frequently associated with cognitive impairment. It is a major cause of disability and dependency among older people. Alzheimer's disease (AD) is the most common form of dementia, accounting for 50% to 75% of the cases (Hulstaert et al., 2009; World Health Organization, 2006; Vos et al., 2020).

3.1.1 Corresponding disease classification codes

ICD-10 codes

- G30 Alzheimer's disease
- G31.1 Senile degeneration of brain, not elsewhere classified
- G31.8 Other specified degenerative diseases of nervous system
- G32.8 Other specified degenerative disorders of nervous system in diseases classified elsewhere
- F00 Dementia in Alzheimer disease
- F01 Vascular dementia
- F02 Dementia in other diseases classified elsewhere
- F03 Unspecified dementia

ICD-9 codes

- 290 Dementias
- 294 Persistent mental disorders due to conditions classified elsewhere
- 331 Other cerebral degeneration

ICPC-2 codes

- P70 Dementia

ATC codes

- N06D Anti-dementia drugs
- N06DX01 memantine
- N06DA anticholinesterases

Nomenclature codes

- 102933 Diagnostic assessment of dementia performed by a doctor specialised in neurology, psychiatry or geriatrics, with a written report (outpatient).

- 102992 Diagnostic assessment of dementia performed by a doctor specialised in neurology, psychiatry or geriatrics (accredited), with a written report (outpatient).
- 784512 Conventions of functional rehabilitation concluded with memory clinics (dementia): clinic session (outpatient)
- 784523 Conventions of functional rehabilitation concluded with memory clinics (dementia): clinic session (inpatient)
- 784534 Conventions of functional rehabilitation concluded with memory clinics (dementia): home session, first session (outpatient)
- 784556 Conventions of functional rehabilitation concluded with memory clinics (dementia): home session, second session on the same day (outpatient)

3.2 Disease model

3.2.1 Health states

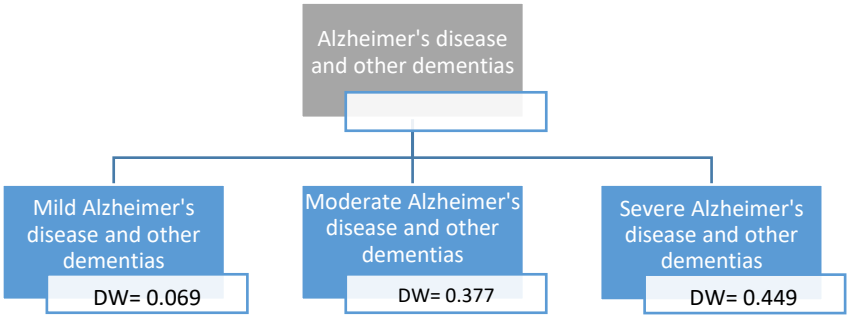

Figure 1. Alzheimer's disease and other dementias disease model

3.2.2 Disability weights

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

Health state	Lay description	DW
Mild Alzheimer's disease and other dementias	Has some trouble remembering recent events, and finds it hard to concentrate and make decisions and plans.	0.069
Moderate Alzheimer's disease and other dementias	Has memory problems and confusion, feels disoriented, at times hears voices that are not real, and needs help with some daily activities.	0.377
Severe Alzheimer's disease and other dementias	Has complete memory loss; no longer recognizes close family members; and requires help with all daily activities.	0.449

3.2.3 Proportion of patients in the considered health states

Table 2. Proportion of patients in the different health states considered in the Alzheimer's disease and other dementias disease model, Belgium.

Health state	Parent	Proportion	Source
Alzheimer's disease and other dementias	N/A	100%	Per definition
Alzheimer's disease and other dementias, mild	Alzheimer's disease and other dementias, parent	<70: 79% 70-79: 71% 80+: 61%	GBD 2016 Dementia Collaborators; CDR stage 1 (Hughes et al., 1982)
Alzheimer's disease and other dementias, moderate	Alzheimer's disease and other dementias, parent	<70: 17% 70-79: 19% 80+: 26%	GBD 2016 Dementia Collaborators; CDR stage 2 (Hughes et al., 1982)
Alzheimer's disease and other dementias, severe	Alzheimer's disease and other dementias, parent	<70: 4% 70-79: 9% 80+: 12%	GBD 2016 Dementia Collaborators; CDR stage 3 (Hughes et al., 1982)

3.2.4 Discussion

The severity distribution in the GBD model is based on data from a systematic review (Nichols et al., 2019; Salomon et al., 2015; Vos et al., 2020) that covered 23/1/2015 to 7/10/2016, reporting the prevalence of AD and other dementias on the Clinical Dementia Rating Scale (CDR). A random-effect meta-analysis was performed to pool the proportions of mild (CDR 1), moderate (CDR 2) and severe (CDR 3) cases. As evidence indicates an age pattern with greater proportions of more severe disease in elder age groups, the analysis was made separately for age groups: 40-69, 70-79 and 80 years or more. Since data are not specific to Belgium, the question of applicability to the Belgian context is raised. However, 63 sources from Western Europe were used in modeling prevalence estimates, allowing extrapolations to Belgium.

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

3.3 Prevalence

3.3.1 Data sources

Different data sources exist for Alzheimer's disease and other dementias, each with a specific case definition:

1. **Hospital Discharge data:** patient with AD or dementia admitted to the hospital during the reference year (before 2015: ICD-9 codes 290,294,331; after 2015 ICD-10 codes: G30,G31.1, G31.8, G32.8, F00, F01, F03).
2. **Health insurance data:** person with a prescription for ATC codes N06DA and N06DX01 or with a nomenclature code referring to dementia (102933, 102992, 784512, 784523, 784534, 784556) during the reference year.
3. **Health Interview Survey:** there are no questions related to Alzheimer's disease and other dementias in the Health interview survey.
4. **Sentinel GP network data (Intego):** Number of individuals with AD and other dementias diagnosis ever recorded by GP (ICPC code P70) who had a GP contact during the reference year.

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

Source	Strengths	Weaknesses	Evaluation
Registry	Not available	Not available	Not available
Hospital discharge data	Exhaustive information on all cases hospitalized for AD or dementia Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on AD or dementia patients who were not admitted to the hospital during the reference year. This may represent a rather large proportion of all cases. Hospitalization rate of patients with dementia: 30% to 43% (Tuppin et al., 2009; Zhu et al., 2015; Motzek 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	Sensitivity: low Specificity: medium
Health insurance data (IMA/EPS) – Pharmaceutical database	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 → False negatives: patients with the condition who do not take this treatment (up to 30% of patients with dementia do not take any medicine; those	Sensitivity: low Specificity: medium

		medications are not recommended for the treatment of some dementias: frontotemporal dementia; vascular dementia) (KCE, 2009; O'Brien et aL, 2017) People who are not insured (e.g. homeless and illegal people, foreigners with their official residence abroad) are not included	
Health insurance data (IMA/EPS) – Nomenclature codes	Case definition based on medication and care Large, representative sample Longitudinal approach	Those nomenclature codes refer mostly to outpatient cases of dementia People who are not insured (e.g. homeless and illegal people, foreigners with their official residence abroad) are not included; however, this comprises a small part of the total population (~2%)	Sensitivity: low Specificity: high
Health Interview Survey	Not applicable: there are no questions related to Alzheimer's disease and other dementias in the Health interview survey.	N/A	N/A
Sentinel GP network data (Intego)	Diagnosis by medical professionals Longitudinal approach	Will not capture patients that bypass the GP (ED, hospitalization, people living in a long-term care facility: 30 to 50% of people with dementia live in institution (KCE, 2009; Prince et al., 2013; Matthews & Dening, 2002)) 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 specific software and interested in registration) For the PP: not possible to identify the reason for consultation, so it might not be related to the condition in question.	Sensitivity: low Specificity: medium

		Recognition rate of dementia is low: only 40-50% of people living with dementia have received a diagnosis (KCE, 2009; Prince et al., 2016). However, 73% of dementia cases in the population are diagnosed by a primary care practitioner (Mitchell et al., 2011).	
Sentinel network GP data (Sciensano)	Not applicable: Dementia has not been registered by the Sciensano SGPs network.	N/A	N/A

3.3.2 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 dementia.

The health insurance dataset (pharmaceutical dataset) is proposed to be the best national estimate for AD and other dementias prevalence since anti-dementia drugs are very specific to these conditions. Evidence has shown that using the pharmaceutical dataset provides reliable estimates of the disease (Chini et al., 2011). However, it has to be noticed that some types of dementias could be underestimated (e.g. anticholinesterases are not recommended in Lewy body dementia or vascular dementia; memantine is not recommended in vascular dementia) (Hulstaert et al., 2009; O'Brien et al., 2017). Using the nomenclature codes referring to dementia would generate a lot of false negatives since those codes refer almost exclusively to outpatients.

3.3.3 Discussion

Given the potentially high burden of AD and other dementias, further studies are needed to quantify the validity (sensitivity/specificity) of the proposed approach for defining the prevalence of these diseases.

The hospital discharge data could be an alternative source of estimate since patients with dementia are more likely to be hospitalized than people with no dementia (hospitalization rate of patients with dementia: 30% to 43%) (Motzek et al., 2018; Tuppin et al., 2009; Zhu et al., 2015). Nevertheless, dementia is rarely a cause for hospitalization and secondary diagnosis data should be used, which is not systematically registered.

The Intego sentinel GP network may underestimate the AD and other dementias prevalence since data are limited to Flanders and to community-dwelling people (45% to 50% of patients with dementia live in institution (Hulstaert et al., 2009; Matthews et al., 2002; Prince et al., 2013)). Furthermore, evidence shows that the recognition rate of dementia in primary care is low, especially in the early stages of the disease (45% for mild dementia and 81% for moderate to severe dementia) (Prince et al., 2016).

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4 AMPHETAMINE DEPENDENCE

4.1 Case definition

Amphetamine use disorders are a group of substance-related conditions affecting the use of amphetamine.

According to the Diagnostic and Statistical Manual of Mental Disorders, version IV, text revised (DSM-IV) (APA, 2000), the distinction is made between amphetamine abuse (AA) and amphetamine dependence (AD), which is the most severe form of amphetamine use disorders.

The case definition used here is also used in the GBD 2017 study (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018), and corresponds to the definition of amphetamine dependence in the DSM IV, and is defined as a "maladaptive pattern of substance use, leading to clinically significant impairment of distress" (Bell, 1994). At least three of the following criteria must have occurred during the past 12 months:

- Tolerance, characterized by either
  - a need for increased amounts of the substance to achieve intoxication; or
  - markedly diminished effect with continued use of the same amount of the substance;
- Withdrawal, characterized by either
  - withdrawal symptoms characteristic to dependence; or
  - the same (or similar) substance is taken to avoid withdrawal symptoms;
- Substance taken in progressively larger amounts or for longer periods;
- Persistent desire or unsuccessful attempts to cut down or reduce substance use;
- Disproportional time spending in obtaining the substance;
- Former social, occupational, or recreational activities are given up or reduced because of the substance use;
- Substance use is continued despite knowledge physical and psychological damages occurring as a result of the substance use.

The choice has been made to use the fourth version of the DSM instead of the most recent version being the fifth (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-5 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 (Peer et al., 2013). 12-month prevalence of amphetamine use disorders were lower when using DSM-5 criteria instead of the fourth version (Goldstein et al., 2015). It has to be noticed that a major change from DSM-IV to DSM-5 is the combination of substance abuse disorder and substance dependence into a single substance use disorder, which requires 2 out of 11 criteria in a 12-month period for diagnosis.

4.1.1 Corresponding disease classification codes

DSM-IV-TR code

- 304.40 Amphetamine dependence

ICD-10 code

- F15.2 Mental and behavioural disorders due to use of other stimulants, including caffeine : dependence syndrome

ICD-9 code

- 304.4 Amphetamine and other psychostimulant dependence

ICPC-2 code

- P19 Drug abuse

ATC code

- Not applicable : there are no drugs sufficiently specific for the treatment of amphetamine dependence.

Nomenclature code

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

4.2 Disease model

4.2.1 Health states

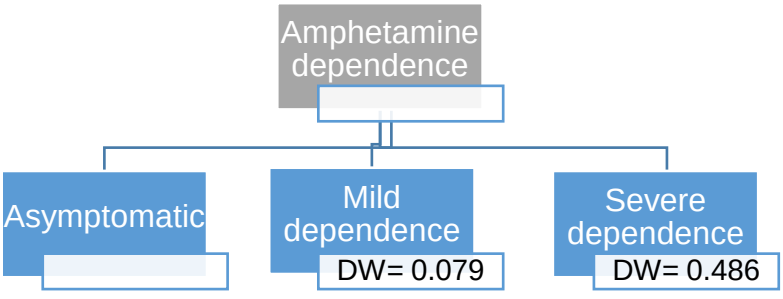

Figure 1. Amphetamine dependence disease model

4.2.2 Disability weights

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

Health state	Lay description	DW
Asymptomatic	Not applicable	Not applicable
Mild dependence	Uses stimulants (drugs) at least once a week and has some difficulty controlling the habit. When not using, the person functions normally.	0.079
Severe dependence	Uses stimulants (drugs) and has difficulty controlling the habit. The person sometimes has depression, hallucinations, and mood swings, and has difficulty in daily activities	0.486

4.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Amphetamine dependence	N/A	100%	Per definition
Asymptomatic	Amphetamine dependence	65%	European Web Survey on Drugs (Matias et al. 2019)
Mild dependence	Amphetamine dependence	18%	European Web Survey on Drugs (Matias et al. 2019)
Severe dependence	Amphetamine dependence	17%	European Web Survey on Drugs (Matias et al. 2019)

4.2.4 Discussion

The distribution of amphetamine dependence cases within the different levels of severity is derived from the European Web Survey on Drugs (EWSD), conducted by the European Monitoring Centre for Drugs and Drugs Addiction (EMCDDA) from 2016 to 2018. The ESWD collected information about patterns of use and purchase of the most commonly used illicit drugs in 14 countries, including Belgium. The categories for the frequency of amphetamine use in the past 12 months was defined as:

- Infrequent use: < 11 days in past year
- Occasional use: between 11-50 days in the past year
- Frequent use: +51 days in the past year

These categories correspond, respectively, to the health states asymptomatic, mild dependence and severe dependence. Although they are not matching perfectly with the definition of the different health states described in Table 1, the choice has been made to prefer local data to avoid using the GBD 2017 study severity distribution, that is determined based on data from the (US) National Epidemiological Survey on Alcohol and Related Conditions (NESARC) (Grant & Dawson, 2006), a representative sample of the non-institutionalized US population aged 18 and older. Indeed, there are cross-cultural differences in drug consumption: in 2017, amphetamine use 12-month prevalence was 4 times higher in North America compared to Western and Central Europe, with respectively 2.1% and 0.5% (UNODC, 2019).

In the GBD study, a category “asymptomatic” represents the percentage of people with the disease or condition and no symptoms. The choice to include a category “asymptomatic” within the severity distribution depends on the source used to produce the prevalence estimates, and on the case definition used. Some sources will include the asymptomatic cases and other not. It is important to ensure that the proxy used for the prevalence estimates matches closely the case definition regarding the presence of symptoms or not, because this will have an influence on the severity distribution and therefore on the average disability weight derived. For the calculation of YLDs, the asymptomatic cases are not taken into account since there are not experiencing any disability.

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

4.3 Prevalence

4.3.1 Data sources

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

1. **Belgian Treatment Demand Indicator Registry (TDI)**: patient in contact with an inpatient or outpatient treatment centre that have started a new treatment for amphetamine dependence during the reference year. Treatment centres are defined as facilities or practitioners providing treatment for drug or alcohol addiction. An episode is defined as a treatment process separated by at least 6 months from a previous one in outpatient settings. In residential settings, an episode occurs each time a patient is admitted and ends when the patient leaves the centre and no further admission is foreseen.
2. **Hospital Discharge data**: patient with amphetamine dependence as primary diagnosis admitted to the hospital during the reference year (before 2015: ICD-9 code 304.4; after 2015 ICD-10 codes: F15.2).

3. **Health insurance data**: not applicable. There are no drugs/nomenclature codes sufficiently specific to amphetamine dependence (Lee et al., 2018).
4. **Health Interview Survey**: number of respondents who have answered “Amphetamine, speed” and “in the past 12 months” to the question: “What other substances did you use, even once, and when did you take them last?”.
5. **Sentinel GP network data (Intego)**: number of individuals with “drug abuse” diagnosis ever recorded by GP (ICPC-2 code P19) who had a GP contact during the reference year.
6. **Sentinel GP network data (Sciensano)**: patient with an amphetamine use problem in contact for the first time with the GP and that begins a new treatment for this problem during the reference year. The treatment is defined as any activity that can be lead in order to enhance the physical, psychological or mental health state of a person with a substance problem. A treatment episode is defined as a treatment process separated by at least 6 months from a previous one.

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

Source	Strengths	Weaknesses	Evaluation
Belgian Treatment Demand Indicator Registry (TDI)	Reliable data on drug users in treatment at a national level Longitudinal approach Mandatory registration in hospitals and specialized centres Registration by professionals National database Possibility to identify 80% of the patients uniquely via the SSIN. Possibility to link these data with other databases through the SSIN (TDI-IMA databases) (Van Baelen et al., 2018)	TDI concerns only new treatment demand: incidence indicator instead of prevalence indicator. → False positives: The registration using the SSIN is not mandatory: about 20% of the patients are anonymous and can be registered several times leading to overestimation of the number of patients (Antoine, 2018). → False-negatives: This number is supposed to be high since in 2017, in Europe, less than 15% of patients with substance dependence have received a treatment for the first time (EMCDDA, 2019). Evidence has shown that in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders patients receive a treatment (either professional	Sensitivity: low Specificity: high

		treatment or self-help group) (Harris et al., 2019). Lack of registration in the non-specialized sector (GP, medical house, centres for mental health, private practice,…). Long-term treatment patients are not reported.	
Hospital discharge data	Exhaustive information on all cases hospitalized for amphetamine dependence Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on patients with AD who were not admitted to hospital during the reference year: this number is assumed to be large as most treatments for drug use are provided by outpatient facilities (EMCDDA, 2019a; 2019b). Furthermore, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007), and in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019). 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: medium
Health insurance data (IMA/EPS)	Not applicable: there are no drug or nomenclature codes sufficiently specific to amphetamine dependence (Lee et al., 2018)	N/A	N/A
Health Interview Survey	Based on information from a representative sample	Self-reported information; it is assumed that there may be many false positives and false negatives	Sensitivity: medium Specificity: medium

		Provides representative results at national and regional levels	→ False positives: the HIS question relates to amphetamine use during the last month, even once, which could lead to an overestimation of amphetamine dependence cases. → False-negatives: drug use is known to be underestimated in household surveys (Gisle et al., 2018; Hickman et al., 2002) Not yearly available (+/- every 5 years) Comparing estimates between subgroups of the sample might lack statistical precision	
Sentinel network (Intego)	**GP data**	Diagnosis by medical professional Longitudinal approach	Case definition used in ICPC-2 code is not enough detailed and encompasses all cases of drug abuse, leading to an overestimation of amphetamine dependence cases. Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP. Evidence has shown a reduced use of primary care in amphetamine dependence (McKetin et al., 2018; O'Toole et al., 2007). Furthermore, the treatment rate in people with substance use disorders is low in Belgium, as in the rest of Europe or high-income countries (EMCDDA, 2019a). Finally, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007). Results are limited to Flanders At the level of Flanders, the representativeness cannot be 100%	Sensitivity: low Specificity: medium

		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 amphetamine dependence.	
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 Evidence has shown a reduced use of primary care in amphetamine dependence (McKetin et al., 2018; O'Toole et al., 2007). Furthermore, the treatment rate of people with substance use disorders is low in Belgium, as in the rest of Europe or high-income countries (EMCDDA, 2019a).	Sensitivity: low Specificity: medium

4.3.2 National best estimate

The Belgian Health Interview Survey (HIS) is assumed to yield the best estimate of amphetamine dependence prevalence.

4.3.3 Discussion

It has to be noticed that the number of amphetamine dependence cases in the general population may be underestimated using the HIS as best estimate, for several reasons:

- Population surveys do not include homeless people, people in mental institutions and prisons, however there is supposed to be a lot of cases of substance dependence in these populations (Gisle et al., 2018).
- Amphetamine dependence may be underreported due to a selection bias: people with a drug dependence are less likely to participate to general population surveys. However, evidence has shown good validity of self-reported substance use compared to biological measures (e.g. blood or urine samples) (Rowe et al., 2018; Hjorthøj et al., 2012).

Another limitation of using the HIS to get the AD prevalence is that the HIS question relates to amphetamine use during the past 12 months, even once, which could lead to an

overestimation of amphetamine dependence cases. However, we take this parameter into account by including asymptomatic cases (i.e. occasional users) in the severity distribution and, therefore, in the average disability weight used to compute the Years Lived with Disability.

Despite these limitations, the HIS has been selected to be the best source to get the amphetamine dependence prevalence, after having considered other possibilities:

The Belgian Treatment Demand Indicator registry does not allow to compute the prevalence of the AD cases in the population, only the incidence of the new started treatments for an amphetamine use problem. Moreover, the treatment rate of people with substance use disorders is low in Belgium, as in the rest of Europe or high-income countries (EMCDDA, 2019a).

The hospital discharge data may miss a lot of cases as most treatments for drug use are provided by outpatient facilities (EMCDDA, 2019a). Furthermore, the treatment rate of people with substance use disorders is low in Belgium, as in the rest of Europe or high-income countries (EMCDDA, 2019a).

Using the health insurance data is to get the AD prevalence is not enough sensitive as there are no drugs or nomenclature codes sufficiently specific to match the case definition of amphetamine dependence (Lee et al., 2018).

Finally, we have decided not to use the sentinel GP networks as a source to compute the AD prevalence since evidence has shown a reduced use of primary care in amphetamine dependence (McKetin et al., 2018; O'Toole et al., 2007), and that in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders (SUD) patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019). This proportion is 7.7% among people with SUD only, and 20.1% among patients with SUD and at least one comorbid mental disorder.

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5 ANGINA PECTORIS

5.1 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 (Vos et al., 2020).

5.1.1 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.

5.2 Disease model

5.2.1 Health states

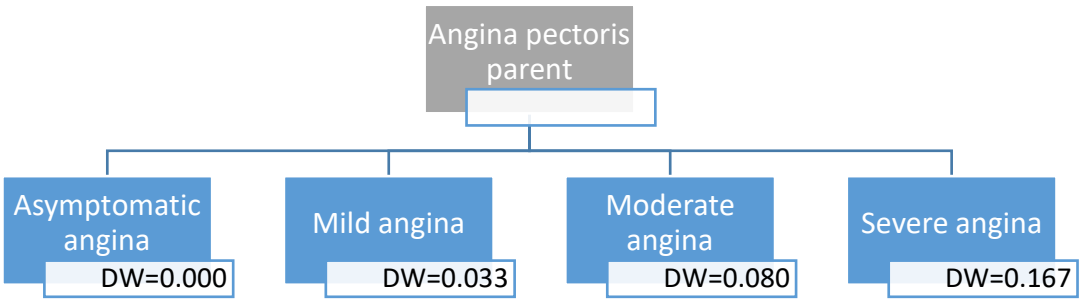

Figure 2. Angina pectoris disease model

5.2.2 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

5.2.3 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)

5.2.4 Discussion

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 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.

5.3 Prevalence

5.3.1 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 Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on angina pectoris patients who were not admitted to hospital during the reference year; this may represent a rather 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	Sensitivity: low Specificity: high
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	Sensitivity: low Specificity: high

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

5.3.2 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.

5.3.3 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.

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6 ANXIETY DISORDERS

6.1 Case definition

Anxiety disorders (AD) cover a range of mental disorders characterized by feelings of worry, anxiety or fear that are severe enough to interfere with the person's daily activities, typically in combination with other physiological symptoms. Are included in the case definition all cases of anxiety disorders reaching diagnostic threshold defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM), or the World Health Organization International Classification of Diseases (ICD-10) (APA, 2000; WHO, 1992).

- Panic disorder
- Agoraphobia
- Specific phobia
- Social phobia
- Obsessive-compulsive disorder
- Post-traumatic stress disorder
- Acute stress disorder
- Generalised anxiety disorder
- Separation anxiety disorder
- Anxiety disorder not otherwise specified

Anxiety disorders due to a general medical condition and substance-induced anxiety disorder have been excluded from the case definition.

As specific anxiety disorders frequently co-occur, anxiety disorders were modelled as a single cause for anxiety disorder to avoid the double-counting of individuals meeting criteria for more than one anxiety disorder. As in the GBD studies, the BeBOD study reports burden for “any” anxiety disorder inclusive of the common anxiety disorders, for example, generalized anxiety disorder, and early-onset disorders such as separation anxiety disorder.

The choice has been made to use the fourth version of the DSM instead of the most recent version being the fifth (published in 2013) for comparability reasons since DSM-IV classification is widely used in research for more than twenty years, and the DSM-IV is also the classification used in the GBD studies. It must be noticed some changes between the fourth and the fifth version of the DSM: in the DSM-5, the category “Anxiety disorders” has been divided into three categories: anxiety disorders; obsessive-compulsive disorders and trauma and stressor-related disorders (Rodríguez-Testal et al., 2014). For that reason, the 12-

month prevalence of anxiety disorders should be higher using the DSM-IV classification instead of the fifth version for the case definition.

6.1.1 Corresponding disease classification codes

DSM-IV-TR codes

- 300.00 Anxiety disorder, NOS
- 300.02 Generalized anxiety disorder
- 300.21 Panic disorder with agoraphobia
- 300.22 Agoraphobia without history of panic disorder
- 300.23 Social phobia
- 300.29 Specific phobia
- 300.3 Obsessive-compulsive disorder
- 309.21 Separation anxiety disorder
- 309.81 Posttraumatic stress disorder

ICD-10 codes

- F40 Phobic anxiety disorders
- F41 Other anxiety disorders
- F42 Obsessive-compulsive disorder
- F43 Reaction to severe stress, and adjustment disorders
- F93.0 Separation anxiety disorder of childhood
- F93.1 Phobic anxiety disorder of childhood
- F93.2 Social anxiety disorder of childhood

ICD-9 codes

- 300.0 Anxiety states
- 300.2 Phobic disorders
- 300.3 Obsessive-compulsive disorders
- 309.21 Separation anxiety disorder
- 309.81 Posttraumatic stress disorder

ICPC-2 codes

- P02 Acute stress reaction
- P74 Anxiety disorder/anxiety state
- P79 Phobia/compulsive disorder
- P82 Post-traumatic stress disorder

ATC codes

- N05B Anxiolytics
- N05C Hypnotics and sedatives

- N06AB Selective serotonin reuptake inhibitors

Nomenclature codes

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

6.2 Disease model

6.2.1 Health states

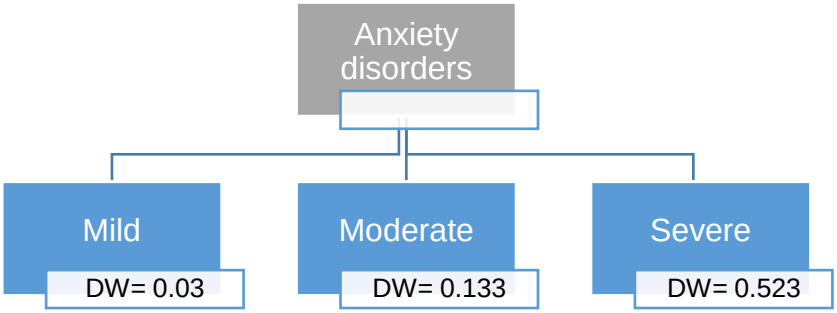

Figure 1. Anxiety disorders disease model

6.2.2 Disability weights

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

Health state	Lay description	DW
Anxiety disorder, mild	Feels mildly anxious and worried, which makes it slightly difficult to concentrate, remember things, and sleep. The person tires easily but is able to perform daily activities.	0.030
Anxiety disorder, moderate	Feels anxious and worried, which makes it difficult to concentrate, remember things, and sleep. The person tires easily and finds it difficult to perform daily activities.	0.133
Anxiety disorder, severe	Constantly feels very anxious and worried, which makes it difficult to concentrate, remember things, and sleep. The person has lost pleasure in life and thinks about suicide.	0.523

6.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Anxiety disorder	N/A	100%	Per definition
Mild	Anxiety disorder	55%	GBD 2017
Moderate	Anxiety disorder	27%	GBD 2017
Severe	Anxiety disorder	18%	GBD 2017

6.2.4 Discussion

The distribution of the anxiety disorders (AD) cases into the different health states has been adapted from the severity splits used in the GBD 2017 study (GBD 2017 Disease and Injury Incidence and Prevalence, 2018). In the GBD 2017 study, 2 population surveys were used to estimate the proportion of AD cases in the asymptomatic; mild; moderate and severe diseases categories:

- The (US) National Epidemiological Survey on Alcohol and Related Conditions (NESARC) (Grant & Dawson, 2006). Wave 1 was conducted in 2000-2001 and Wave 2 was conducted in 2004-2005. NESARC is a representative sample of the non-institutionalized US population aged 18 and older. Information on the occurrence of more than one psychological disorder or substance use disorder in the same person are collected, using definitions from the DSM-IV.
- The Australian National Survey of Mental Health and Wellbeing of Adults (NSMHWB) 1997 (Andrews et al., 1999). NSMHWB is a representative sample of non-institutionalized adults in Australia. They were screened for mental and substance use disorders via the Composite International Diagnostic Interview (CIDI), a standard questionnaire based on criteria from ICD-10 and DSM-IV. Both 1-month and 12-month prevalence are available.

The choice has been made to adapt this distribution of anxiety disorders cases to match the case definition used. In the GBD study, a category “asymptomatic” represents the percentage of people with the disease or condition and no symptoms. For the calculation of YLDs, these cases are not taken into account since there are asymptomatic and are not experiencing any disability. Although in the GBD study, there is a percentage of AD cases in the asymptomatic category, we have made the choice to assume that there are no asymptomatic cases considering the case definitions used, and given that individuals suffering from anxiety disorders are experiencing substantial impairment (Weiller et al., 1998).

It must be noticed that the proportion of the AD cases in the different health states may not be fully representative of the Belgian population because of regional differences in anxiety disorders. The prevalence estimates of AD can be influenced by a wide range of factors, such as gender; environmental factors (urban context); socio-economic status; marital status or exposure to violence and conflict (Baxter et al., 2013). However, the prevalence estimates are similar in the North American, Australian and Western Europe regions (Baxter et al., 2013; Alonso et al., 2018).

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

6.3 Prevalence

6.3.1 Data sources

Different data sources exist for anxiety disorders (AD), each with a specific case definition:

1. **Register**: not applicable: there is no registry for anxiety disorders in Belgium.
2. **Hospital Discharge data (Minimum psychiatric dataset)**: patient with AD admitted to a psychiatric hospital, or a psychiatric service in a general hospital, or an initiative of sheltered living or a psychiatric care home during the reference year (before 2015: ICD-9 codes 300.0., 300.2, 300.3, 309.21, 309.81; after 2015 ICD-10 codes: F40-43, F93.0-2).
3. **Health insurance data**: person with a prescription for ATC codes N05B, N05C or N06AB during the reference year.
4. **Health Interview Survey**: number of respondents aged of 15 and over with a score of 10+ to the 7-item Generalized Anxiety Disorder scale (GAD-7) (Spitzer et al., 2006).
5. **Sentinel GP network data (Intego)**: Number of individuals with a diagnosis of acute stress reaction, or anxiety disorder/anxiety state, or phobia/compulsive disorder, or post-traumatic stress disorder ever recorded by a general practitioner (ICPC-2 codes P02, P74, P79, P82) who had a GP contact during the reference year.
6. **Sentinel GP network data (Sciensano)**: not applicable; anxiety disorders have not been registered by the Sciensano sentinel GP network.

Table 3. Potential sources and methods for the computation of Anxiety disorders (AD) prevalence in Belgium

Source	Strengths	Weaknesses	Evaluation
Registry	Not applicable: there is no registry for anxiety disorders in Belgium	N/A	N/A
Hospital discharge data	Exhaustive information on all cases hospitalised for anxiety disorders Diagnoses by medical doctor Official database, organised and managed by public health authorities National database	No information on patients with AD who were not admitted to hospital during the reference year; this number is supposed to be high since hospitalisation is not the reference treatment for AD. 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 anxiety disorders, treated with anxiolytics, or hypnotics and sedatives, or selective serotonin reuptake inhibitors (SSRI) for other reasons. For instance, SSRI are also used for the treatment of depression. → False negatives: patients with AD who do not take this treatment. This number is supposed to be high since there is a long delay after onset before patients with AD get treatment (Bruffaerts et al., 2007). Furthermore, only 38% with AD seek professional help, and only 40% of those receive medication (Bruffaerts et al., 2004).	Sensitivity: low Specificity: low

		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; it is assumed that there may be many false positives and false negatives → False negatives: the HIS question relates to Generalized Anxiety Disorder (GAD); there are no questions relating to the other anxiety disorders. Not yearly available (+/- every 5 years) Comparing estimates between subgroups of the sample might lack statistical precision	Sensitivity: low 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. In Belgium, only 38% of patients with AD seek professional help (Bruffaerts et al., 2004). 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 AD	Sensitivity: medium Specificity: high
Sentinel GP network data (Sciensano)	Not applicable; anxiety disorders have not been registered by the Sciensano sentinel GP network.	N/A	N/A

6.3.2 National best estimate

The Intego sentinel GP network has been selected as being the best estimate to yield the prevalence of anxiety disorders (AD) in Belgium. As these results only reflect the situation in Flanders, a correction factor is applied, which is calculated as the ratio of the prevalence of generalized anxiety disorder (GAD) in Brussels and in Wallonia, respectively, by sex and by age groups, and the prevalence of GAD in Flanders, using the results of the Belgian Health Interview Survey (Gisle et al., 2018). The Intego sentinel GP network prevalence of AD is therefore multiplied by the different ratios obtained to get the AD prevalence in the two other regions of Belgium.

6.3.3 Discussion

The general practitioner (GP) is often the first contact with the health care system for a patient with mental health problems seeking help. Ansseau et al. (2004) have shown a high prevalence of mental disorders in primary care in Belgium, with 40% of the patients detected with anxiety disorder (as described in the case definition) in a general practice setting. In Belgium, only 38% of people suffering from anxiety disorders is searching for a professional help (Bruffaerts et al., 2004). Among them, 36% consults a GP and 34% contacts a psychiatrist and a GP, which means that GP is involved in 7 out of 10 cases as far as it concerns diagnosis and/or treatment of people with AD. This explains why, despite of low rates of treatment-seeking, despite the fact that the recognition of AD in primary care is pretty low (Weiller et al., 1998; Alonso et al., 2018), and despite the important delays between onset of the disorder and first treatment contact (Bruffaerts et al., 2007; Wang et al., 2007), we have selected the Intego sentinel GP network as being the best source to assess the prevalence of AD in the general population.

However, it should be noted that, in the Intego sentinel GP network dataset, the ICPC-2 codes used for anxiety disorders (see disease classification codes) include some disorders that are not considered as anxiety disorders, such as adjustment disorder or different types of mania, which could lead to an overestimation of the prevalence of AD.

Since a vast majority of people with anxiety disorders is living in the community, assessing the prevalence of this condition using the hospital discharge data, therefore, could lead to underestimation of positive cases.

Using the Health Insurance data to get the AD prevalence via medicine consumption would lead to a large number of false positives, since anxiolytics, hypnotics and sedatives, and selective serotonin reuptake inhibitors (SSRI) are not sufficiently specific to the treatment of AD. For instance, SSRI are also used in the treatment of depression. On another hand, AD

can be treated with off-label treatments (O'Brien et al., 2017), which would, in that case, lead to false negatives.

The Belgian Health Interview Survey has assessed the prevalence of the generalized anxiety disorder in the general population, but using this source of data to get the prevalence of AD in Belgium would not be sufficiently sensitive since the case definition selected for AD is much broader and refers to a large number of other anxiety disorders, i.e. phobia.

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7 ASTHMA

7.1 Case definition

Asthma is a chronic lung disease marked by spasms in the bronchi usually resulting from an allergic reaction or hypersensitivity and causing difficulty in breathing. We define asthma as a doctor's diagnosis and wheezing in the past year (Vos et al., 2020).

7.1.1 Corresponding disease classification codes

ICD-10 codes

- J45 Asthma
- J46 Status asthmaticus

ICD-9 codes

- 493 Extrinsic asthma, unspecified

ICPC-2 codes

- R96 Asthma

ATC codes

- R03DC01 Zafirlukast
- R03DC03 Montelukast
- R03DX05 Omalizumab
- R03A Adrenergics, inhalants
- R03 Drugs for obstructive airway diseases
- R03BA Glucocorticoids

Nomenclature codes

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

7.2 Disease model

7.2.1 Health states

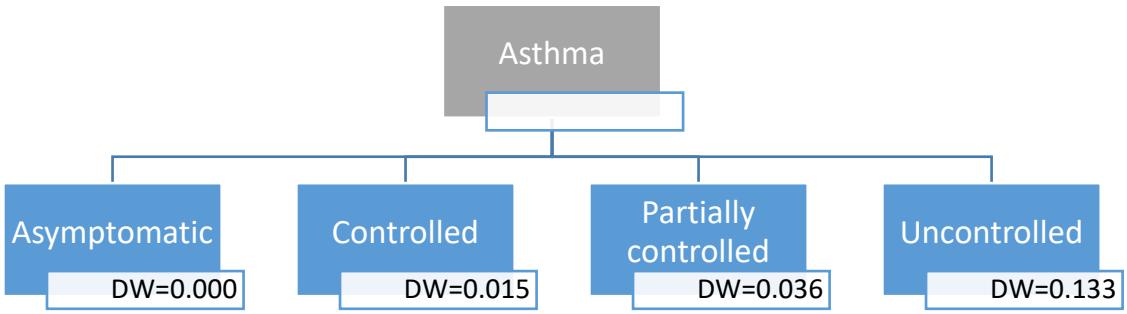

Figure 1. Asthma disease model

7.2.2 Disability weights

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

Health state	Lay description	DW
Asymptomatic Asthma		0.000
Controlled Asthma	This person has wheezing and cough once a month, which does not cause difficulty with daily activities.	0.015
Partially controlled Asthma	This person has wheezing and cough once a week, which causes some difficulty with daily activities.	0.036
Uncontrolled Asthma	This person has wheezing, cough, and shortness of breath more than twice a week, which causes difficulty with daily activities and sometimes wakes the person at night.	0.133

7.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Asthma	N/A	100%	Per definition
Asymptomatic	Asthma	35.9%	Burnstein et al. (2015)
Controlled asthma	Asthma	23.2%	Burnstein et al. (2015)
Partially controlled asthma	Asthma	21.5%	Burnstein et al. (2015)
Uncontrolled asthma	Asthma	19.4%	Burnstein et al. (2015)

7.2.4 Discussion

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. These disability weights are more or less in line with the European disability weights for asthma, which have estimated the disability weight for controlled asthma at 0.020 (0.015-0.024), and for partially controlled asthma at 0.045 (0.035-0.055) (Haagsma et al., 2015).

The severity distribution in the GBD model is based exclusively on data from the USA, raising questions on applicability for the Belgian context (Burstein et al., 2015). 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 asthma being measured in MEPS relates to health care contact. For GBD 2017, data were used from 2000-2014.

The Global Initiative for Asthma (GINA) proposed a questionnaire to rate the severity distribution of asthma. A world-wide study showed that the severity distribution of asthma in Western-Europe is similar to the distribution in the United States (Rabe et al., 2004). One study in the Belgian context applied the GINA methodology to estimate the asthma severity distribution, and reported a similar distribution, except for the severe group, which was estimated at 10% compared to the 18% in the GINA study (Verleden & De Vuyst, 2002). However, based on the available information, it is reasonable to believe that the severity distribution is similar in Western Europe compared to the United States.

7.3 Prevalence

7.3.1 Data sources

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

1. **Hospital discharge data:** patient with asthma admitted to the hospital during the reference year (before 2015: ICD-9 code; after 2015 ICD-10 code).
2. **Health insurance data:** asthma is encoded as a pseudopathology based on the ATC-codes and age < 50 (ATC code: R03DC01, Zafirlukast; R03DC03, Montelukast; R03DX05, Omalizumab; R03A, Adrenergics, inhalants; R03, Drugs for obstructive airway diseases; R03BA, Glucocorticoids).
3. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you had asthma (allergic asthma included)?”.
4. **Sentinel GP network data (Intego):** number of individuals with migraine diagnosis ever recorded by GP (ICPC-2 codes R96) who had a GP contact during the reference year.
5. **Sentinel GP network data (Sciensano):** not applicable; asthma has not been registered by the Sciensano SGPs network.

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

Source	Strengths	Weaknesses	Evaluation
Hospital discharge data	Exhaustive information on all cases hospitalized for asthma Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on asthma patients who were not admitted to hospital during the reference year; this is a substantial proportion of the asthma 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)	Large, representative sample Longitudinal approach	asthma pseudodiagnoses are limited to patients younger than 50 years. 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 condition 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: low 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 induce an overestimation of asthma 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: medium

Sentinel network (Intego)	**GP data**	Diagnosis by medical professional Longitudinal approach	Will not capture patients that bypass the GP (ED, 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) For the PP: not possible to identify the reason for consultation, so might not be related to asthma.	Sensitivity: medium Specificity: high
Sentinel network (Sciensano)	**GP data**	Not applicable. Asthma 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 asthma in Belgium. Although health insurance data is available, an age restriction < 50 years has been put in place for the diagnosis of asthma, which would result in an underestimated proportion (Berete et al., 2020).

7.3.3 Discussion

Asthma is a prevalent disease, which is more often reported in children and adolescents compared to adults (Stern et al., 2020). Although pharmaceutical treatments are available to reduce the burden of asthma by reducing the probability for and number of exacerbations (Sin et al., 2004), a proportion of asthma patients remain untreated (Dow et al., 2001), and another proportion is not compliant with the prescribed treatment regime (Darbà et al., 2016). Therefore, we decided to estimate the prevalence of asthma based on the self-reported health interview survey (HIS). A study by Berete et al. (2020) showed an absolute difference of 2.71% and relative difference of 165.82 for asthma when comparing the Belgian HIS to the health insurance data.

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

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8 BIPOLAR DISORDER

8.1 Case definition

Bipolar disorder (BD) is a chronic mood disorder characterised by two or more episodes in which the patient mood and activity levels are significantly disturbed, this disturbance consisting on some occasions of an elevation of mood and increased energy and activity (hypomania or mania) and on others of a lowering of mood and decreased energy and activity (depression). Those disturbances can be accompanied or not by psychotic symptoms (hallucinations, delusions).

According to the Diagnostic and Statistical Manual of Mental Disorders, version IV, text revised (DSM-IV-TR) (APA, 2000), a **manic episode** involves the experience of elevated, expansive, or irritable mood lasting for at least one week. During this period, at least three (or four if mood is only irritable) of the following symptoms must also be experienced:

- Inflated self-esteem or grandiosity;
- Decreased need for sleep;
- More talkative;
- Flight of ideas or experience that thoughts are racing;
- Distractibility;
- Increase in goal-directed activity; and
- Excessive involvement in pleasurable activities with high potential for painful consequences.

A **hypomanic episode** involves the experience of elevated, expansive, or irritable mood lasting for at least four days. During this period, at least three (or four if mood is only irritable) of the symptoms previously listed for a manic episode must also be experienced.

A **major depressive episode** involves the experience of depressed mood almost all day, every day, for at least two weeks. A total of five of nine criteria must be met to make a diagnosis and at least one of the five criteria should either be:

- “Depressed mood” for most of every day; or
- “Loss of interest in nearly all activities” for most of every day.

The other seven criteria are:

- Change in eating, appetite, or weight;
- Excessive sleeping or insomnia;

- Agitated or slow motor activity;
- Fatigue;
- Feeling worthless or inappropriately guilty;
- Trouble concentrating; and
- Repeated thoughts about death.

Bipolar disorder (BD) includes three different types: bipolar I, bipolar II, and bipolar III. Bipolar I is characterised by an alternation of manic and depressive episodes, where manic episodes are the dominant feature, between which there are often episodes with normal mood. Bipolar II is characterised by the occurrence of at least one major depressive episode and at least one hypomanic episode. Bipolar III actually groups 2 subtypes: subjects presenting only manic or hypomanic episodes induced by antidepressant treatments on the one hand; and on the other hand those presenting only depressive episodes but associated with a family history of bipolar disorder.

Cyclothymic disorder and bipolar disorder not otherwise specified (NOS) are also included in the case definition of BD. Cyclothymic disorder is a milder form of bipolar disorder and is characterised by hypomania and depressive symptoms that occur often and fairly constantly but with less severe symptoms than bipolar I or II. Finally, bipolar disorder NOS is characterised by clinically significant symptoms of bipolar disorder which do not meet criteria for the other diagnoses (APA, 2000; WHO, 1992).

Are excluded from the case definition the cases due to a general medical condition or substance-induced cases.

The choice has been made to use the fourth version of the DSM instead of the most recent version being the fifth (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 Global Burden of Disease studies (GBD 2017 Disease and Injury Incidence and Prevalence, 2018). Finally, changes made in the DSM-5 mostly concern the introduction of a new specifier “with mixed features” that can apply to episodes of mania or hypomania when depressive features are present and also to episodes of depression when features of mania or hypomania are present (Murphy & Hallahan, 2016), with a subsequent increase in prevalence rates of mixed features among bipolar disorder patients (Shim et al., 2015). Since in the BeBOD study, as well as in the GBD 2017 study, burden is calculated for the entire spectrum of bipolar disorder simultaneously, rather than individually for each subtype of the disorder, this increase in prevalence will not have any consequence on the burden of bipolar disorder as a whole.

8.1.1 Corresponding disease classification codes

DSM-IV-TR codes

- 296.00-06 Bipolar I disorder, single manic episode
- 296.40 Bipolar I disorder, most recent episode hypomanic
- 296.40-46 Bipolar I disorder, most recent episode manic
- 296.50-56 Bipolar I disorder, most recent episode depressed
- 296.60-66 Bipolar I disorder, most recent episode mixed
- 296.7 Bipolar I disorder, most recent episode unspecified
- 296.80 Bipolar disorder NOS
- 296.89 Bipolar II disorder
- 301.13 Cyclothymic disorder

ICD-10 codes

- F30 Manic episode
- F31 Bipolar affective disorder
- F34.0 Cyclothymia

ICD-9 codes

- 296.0 Bipolar I disorder, single manic episode
- 296.1 Manic disorder recurrent episode
- 296.4 Bipolar I disorder, most recent episode (or current) manic
- 296.5 Bipolar I disorder, most recent episode (or current) depressed
- 296.6 Bipolar I disorder, most recent episode (or current) mixed
- 296.7 Bipolar I disorder, most recent episode (or current) unspecified
- 296.8 Other and unspecified bipolar disorders
- 301.13 Cyclothymic disorder

ICPC-2 code

- P73 Affective psychosis

ATC codes

- *N03A Antiepileptics*
- N03AF01 Carbamazepine
- N03AG01 Valproic acid (Sodium valproate)
- N03AG02 Valpromide
- N03AX09 Lamotrigine
- *N05A Antipsychotics*
- N05AD01 Haloperidol
- N05AE04 Ziprasidone

- N05AE05 Lurasidone
- N05AH03 Olanzapine
- N05AH04 Quetiapine
- N05AF05 Asenapine
- N05AX08 Risperdone
- N05AX12 Aripiprazole
- N05AX13 Paliperidone
- N05AN Lithium
- *N06A Antidepressants*
- N06AB Selective serotonin reuptake inhibitors

Nomenclature codes

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

8.2 Disease model

8.2.1 Health states

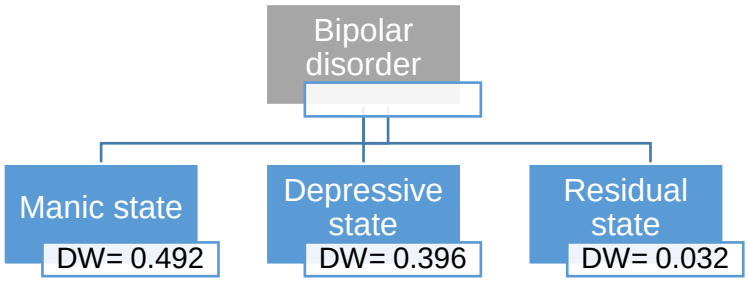

Figure 1. Bipolar disorder disease model

8.2.2 Disability weights

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

Health state	Lay description	DW
Bipolar disorder, manic state	Is hyperactive, hears and believes things that are not real, and engages in impulsive and aggressive behavior that endanger the person and others.	0.492
Bipolar disorder, depressive state	Has constant sadness and has lost interest in usual activities. The person has some difficulty in daily life, sleeps badly, has trouble concentrating, and sometimes thinks about harming himself (or herself).	0.396
Bipolar disorder, residual state	Has mild mood swings, irritability, and some difficulty with daily activities.	0.032

8.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Bipolar disorder	N/A	100%	Per definition
Bipolar disorder, manic state	Bipolar disorder	17%	Vieta et al. (2013)
Bipolar disorder, depressive state	Bipolar disorder	33%	Vieta et al. (2013)
Bipolar disorder, residual state	Bipolar disorder	50%	Ferrari et al. (2012)

8.2.4 Discussion

The proportion of the cases in the manic and depressive states has been adapted from a multinational observational cohort study (Vieta et al., 2013) including 2876 patients with bipolar I and bipolar II from 10 countries. In Belgium, the proportion of cases in manic and hypomanic, depressive, mixed and NOS states was, respectively, 30%, 63% and 7%. The choice has been made to group the manic and hypomanic states into a single “manic state” category, and to redistribute 50% of the mixed and NOS cases in the manic category, and the remaining 50% in the depressive state category.

In absence of Belgian data, the proportion of cases in the residual state is derived from a systematic literature review performed in the framework of the Global Burden of Disease study (Ferrari et al., 2012). A meta-analysis was carried out to pool the estimates of bipolar disorder (BD) cases in each health states across studies, which were performed in different countries: USA, Australia, Ethiopia, and in multiple European countries. However, given the need to include studies reporting cases of BD as described in the case definition, the number of studies included is limited. Despite the fact that one of the studies included used a Belgian sample, the choice has been made to use the pooled estimation of residual cases instead of local data given that this sample referred to bipolar I only and was thus less representative of the spectrum of bipolar disorder that was assessed in the other studies included. For that reason, and also because it is expected that the treatment rate, which varies across the countries, has an impact on the proportion of cases in each health state, the proportion of cases in the residual state may not be fully representative of the Belgian population.

8.3 Prevalence

8.3.1 Data sources

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

1. **Register:** not applicable: there is no registry for bipolar disorder in Belgium.
2. **Hospital Discharge data (Minimum psychiatric dataset)**: patient with bipolar disorder admitted to a psychiatric hospital, or a psychiatric service in a general hospital, or an initiative of sheltered living or a psychiatric care home during the reference year (before 2015: ICD-9 codes 296.0-1, 296.4-8, 301.13; after 2015 ICD-10 codes: F30, F31, F34.0).
3. **Health insurance data:** person with a prescription for ATC codes N03AF01, N03AG01, N03AG02, N03AX09, N05AD01, N05AE04, N05AE05, N05AH03, N05AH04, N05AF05, N05AX08, N05AX12, N05AX13, N05AN, N06AB during the reference year.
4. **Health Interview Survey:** not applicable: there is no question related to bipolar disorder in the Belgian Health Interview Survey.
5. **Sentinel GP network data (Intego):** Number of individuals with affective psychosis diagnosis ever recorded by GP (ICPC-2 code P73) who had a GP contact during the reference year.
6. **Sentinel GP network data (Sciensano):** not applicable: bipolar disorder has not been registered by the Sciensano sentinel GP network.

Table 3. Potential sources and methods for the computation of bipolar disorder (BD) prevalence in Belgium

Source	Strengths	Weaknesses	Evaluation
Registry	Not applicable: there is no registry for bipolar disorder in Belgium	N/A	N/A
Hospital discharge data (Minimum psychiatric dataset)	Exhaustive information on all cases hospitalized for bipolar disorder Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on patients with BD who were not admitted to hospital during the reference year. This number is supposed to be high, i.e., in 2003, in Belgium, only 9% of the patients admitted to a psychiatric hospital, or a psychiatric service in a general hospital, or an initiative of sheltered living or a	Sensitivity: low Specificity: high

		psychiatric care home suffered from mood disorder (Verniest et al., 2008). 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 are based on the prescription of medicines, not on a medical diagnosis, which generates false positives and false negatives → False positives: patients without BD, treated with above-mentioned medicines (see 11.3.1.) for other reasons, for instance the primary use of antiepileptics is the treatment of epilepsy, and antipsychotics are frequently prescribed in psychosis such as schizophrenia. → False negatives: the treatment adherence in BD is low. Up to 48% of patients with BD do not take their treatment or take it partially (Sajatovic et al., 2006; Forma et al., 2020) People who are not insured (e.g. homeless and illegal people, foreigners with their official residence abroad) are not included	Sensitivity: medium Specificity: low
Health Interview Survey	Not applicable: there is no question related to bipolar disorder in the Belgian Health interview Survey	N/A	N/A
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	Sensitivity: medium Specificity: medium

		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 bipolar disorder.	
Sentinel GP network data (Sciensano)	Not applicable: bipolar disorder has not been registered by the Sciensano sentinel GP network	N/A	N/A

8.3.2 National best estimate

The Intego sentinel GP network has been selected as the best estimate to yield the prevalence of bipolar disorder in Belgium. As these results only reflect the situation in Flanders, a correction factor can be applied, which is calculated as the ratio of the use of lithium, in Belgium and the use of lithium in Flanders, using the health insurance data. In that case, the assumption is made that there are no regional differences in the consumption of lithium among people suffering from bipolar disorder.

According to Vieta et al. (2013), lithium is prescribed in about 30% of the bipolar disorder cases, irrespective of disease phase; antipsychotics are the most commonly used drug class in all episode types except depressive episodes, where antidepressants are more commonly prescribed.

8.3.3 Discussion

Despite the fact that bipolar disorder (BD) is commonly underdiagnosed or misdiagnosed, mainly as major depressive disorder (Hu et al., 2014; Angst, 2013), the generalist practitioner (GP) is a key player in the management of bipolar disorder (Forma et al., 2020; Piterman et al., 2010), and is the third healthcare resource used by patients with BD after the psychiatrist and the psychologist, and before hospitalizations and visits to the emergency room (Vieta et al., 2013). According to a systematic review, the global prevalence of bipolar disorder in primary care is 1.9% (Stubbs et al., 2016).

Since a vast majority of people with bipolar disorder is living in the community, assessing the prevalence of this disease using the hospital discharge data, therefore, could lead to underestimation. Indeed, in 2003, in Belgium, only 9% of the patients admitted to a psychiatric

hospital, or a psychiatric service in a general hospital, or an initiative of sheltered living or a psychiatric care home suffered from mood disorder (Verniest et al., 2008).

Finally, antipsychotics, mood stabilizers such as lithium, antidepressants and antiepileptics play an important role in the symptomatic treatment of bipolar disorder and in preventing relapse. There are often used in combination, the mean number of drugs per patient being about three (Vieta et al., 2013). However, the treatment adherence in BD is low. Up to 48% of patients with BD do not take their treatment or take it partially (Sajatovic et al., 2006; Format et al., 2020). Moreover, using the number of reimbursed antipsychotics, antiepileptics or antidepressants as a proxy to assess the BD prevalence in Belgium is not specific enough and would lead to a large number of false positives as they are frequently prescribed for a wide range of psychiatric and non-psychiatric diseases (Morrens et al., 2015). Health insurance data source, therefore, has not been selected to get the prevalence of bipolar disorder in Belgium.

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9 BLINDNESS AND VISION IMPAIRMENT

9.1 Case definition

Vision loss is defined as visual acuity <6/18 according to the Snellen chart. Near vision loss describes the progressive inability to focus on near objects as individuals age (presbyopia). This impairs the ability to read. The majority of presbyopia can be corrected by the use of reading glasses, contact lenses, or refractive surgery. Vision loss as can be caused by: uncorrected refractive error, cataract, glaucoma, macular degeneration, diabetic retinopathy, trachoma, vitamin A deficiency, retinopathy of prematurity, meningitis, encephalitis, onchocerciasis, and a residual category of other vision loss. The following severity levels are included (Vos et al., 2020):

CONDITION	CASE DEFINITION
Blindness	Visual acuity of <3/60 or <10% visual field around central fixation
Severe vision loss	≥3/60 and <6/60
Moderate vision loss	≥6/60 and <6/18
Mild vision loss	≥6/18 and <6/12
Near vision loss	Near visual acuity of <6/12 distance equivalent

9.1.1 Corresponding disease classification codes

ICD-10 codes

- H25 Senile cataract
- H26 Other cataract
- H27 Other disorders of lens
- H28 Cataract and other disorders of lens in diseases classified elsewhere
- H31 Other disorders of choroid
- H32 Chorioretinal disorders in diseases classified elsewhere
- H33 Retinal detachments and breaks
- H34 Retinal vascular occlusions
- H35 Other retinal disorders
- H36 Retinal disorders in diseases classified elsewhere
- H40-H42 Glaucoma
- H46-H48 Disorders of optic nerve and visual pathways
- H49 Paralytic strabismus
- H50 Other strabismus
- H51 Other disorders of binocular movement

- H53-H54 Visual disturbances and blindness

ICD-9 codes

- 360.8 Other disorders of globe
- 361 Retinal detachments and defects
- 362 Other retinal disorders
- 363 Chorioretinal inflammations scars and other disorders of choroid
- 365 Glaucoma
- 366 Cataract
- 368 Visual disturbances
- 369 Blindness and low vision
- 377 Disorders of optic nerve and visual pathways
- 378 Strabismus and other disorders of binocular eye movements

ICPC-2 codes

- F82 Detached retina
- F83 Retinopathy
- F84 Macular degeneration
- F91 Refractive error
- F92 Cataract
- F93 Glaucoma
- F94 Blindness
- F95 Strabismus

ATC codes

- Not applicable : there is no drug sufficiently specific to match the case definition of vision impairment.

Nomenclature codes

- Not applicable: there are different nomenclature codes available for vision loss, but none are sufficiently specific to match the case definition of vision impairment.

9.2 Disease model

9.2.1 Health states

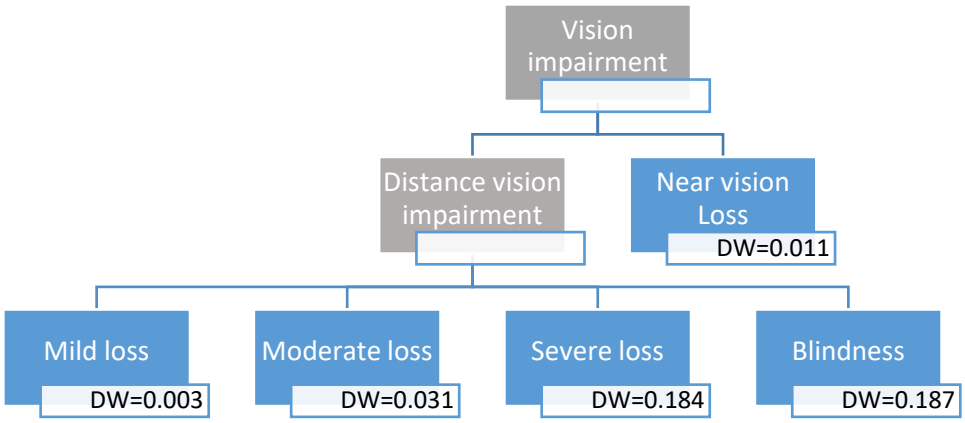

Figure 1. Vision impairment disease model

9.2.2 Disability weights

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

Health state	Lay description	DW
Distance vision, mild loss	This person has some difficulty with distance vision, for example reading signs, but no other problems with eyesight.	0.003
Distance vision, moderate loss	This person has vision problems that make it difficult to recognize faces or objects across a room.	0.031
Distance vision, severe loss	This person 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
Distance vision, blindness	This person 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
Near vision loss	This person has difficulty seeing things that are nearer than 3 feet if uncorrected by reading glasses, but has no difficulty with seeing things at a distance.	0.011

9.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Vision impairment	N/A	100%	Per definition
Distance vision, mild loss	Vision impairment	36.0%	Bourne et al. (2021)
Distance vision, moderate loss	Vision impairment	43.8%	Bourne et al. (2021)
Distance vision, severe loss	Vision impairment	5.9%	Bourne et al. (2021)
Distance vision, blindness	Vision impairment	3.7%	Bourne et al. (2021)
Near vision loss	Vision impairment	10.6%	Bourne et al. (2021)

Estimates for proportions were derived from Bourne et al. (2021) for the population of Western Europe. They reported that 1.78 per 1000 suffered from blindness, 23.9 per 1000 suffered from moderate and severe vision loss, 17.3 per 1000 from mild vision loss, and 5.1 per 1000 from uncorrected near vision loss. Within the category of moderate and severe vision loss, it was estimated that 88.1% suffered from moderate loss, whereas 11.9% suffered from severe loss in the global population.

9.2.4 Discussion

Disability weights for the Belgian national burden of disease study are adapted from the Global Burden of Disease study (Vos et al., 2020), as these provide an exhaustive set of internally consistent disability weights.

These disability weights are similar as those reported in a European context. Haagsma et al. (2015) reported disability weight estimates of 0.012 (0.008-0.015) for near vision impairment, 0.004 (0.002-0.005) for distance vision, mild impairment, 0.034 (0.027-0.042) for distance vision, moderate impairment, 0.158 (0.13-0.193) for distance vision, severe impairment, and 0.173 (0.145-0.213) for distance vision blindness (Haagsma et al., 2015).

Vision impairment, and more specifically, vision impairment due to retinopathy is an often diagnosed sequela of diabetes (Fong et al., 2004). As diabetic retinopathy is modelled in the diabetic envelope, ideally it should be removed from the vision impairment envelope. However, the impact of removing and adjusting the estimates based on the potential overlap was rather small. Therefore, it was decided to not correct for this overlap in the current disease model.

9.3 Prevalence

9.3.1 Data sources

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

1. **Hospital discharge data:** patient with vision impairment admitted to the hospital during the reference year (before 2015: ICD-9 code; after 2015 ICD-10 code).
2. **Health insurance data:** not applicable.
3. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you had an eye disease such as cataract, glaucoma or macular degeneration?”.
4. **Sentinel GP network data (Intego):** number of individuals with vision loss diagnosis ever recorded by GP (ICPC-2 codes F82, F83, F84, F91, F92, F93, F94, F95) who had a GP contact during the reference year.
5. **Sentinel GP network data (Sciensano):** not applicable; vision impairment has not been registered by the Sciensano SGPs network.

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

Source	Strengths	Weaknesses	Evaluation
Hospital discharge data	Exhaustive information on all cases hospitalized for vision impairment Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on vision impairment patients who were not admitted to hospital during the reference year; this is a substantial proportion of 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)	Not applicable: there are no (reimbursed) medications or health care usages that would allow a sufficiently specific diagnosis of vision impairment		
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 vision impairment; integration with information on disability or health-related quality of life may increase specificity	Sensitivity: high Specificity: medium

			Not yearly available (+/- every 5 years) Comparing estimates between subgroups of the sample might lack statistical precision Vision problems for which glasses or contact lenses are used, are not taken into account.	
Sentinel network (Intego)	**GP data**	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 vision impairment.	Sensitivity: medium Specificity: high
Sentinel network (Sciensano)	**GP data**	Not applicable. Vision impairment has not been registered by the Sciensano SGPs.		

9.3.2 National best estimate

The national best estimates are based on two different data-sources. The Health Interview Survey appears to be the most complete source of information on the prevalence of vision impairment (macular degeneration, cataract and glaucoma), which is representative for the entire Belgium. Intego appears to be the most complete source of information on the prevalence of vision impairment for near vision loss, and refractive error.

9.3.3 Discussion

Vision impairments are diverse in nature. We evaluated that hospital discharge data would yield a substantial underestimation of vision impairment in Belgium, as hospital admissions are rather limited for vision impairments.

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

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10 CANNABIS DEPENDENCE

10.1 Case definition

Cannabis use disorders are a group of substance-related conditions affecting the use of cannabis. According to the Diagnostic and Statistical Manual of Mental Disorders, version IV, text revised (DSM-IV) (APA, 2000), the distinction is made between cannabis abuse (CA) and cannabis dependence (CD), which is the most severe form of cannabis use disorders.

The case definition used here is also used in the GBD 2017 study (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018), and corresponds to the definition of cannabis dependence in the DSM IV, and is defined as a "maladaptive pattern of substance use, leading to clinically significant impairment of distress" (Bell, 1994). At least three of the following criteria must have occurred during the past 12 months:

- Tolerance, characterized by either
  - a need for increased amounts of the substance to achieve intoxication; or
  - markedly diminished effect with continued use of the same amount of the substance;
- Withdrawal, characterized by either
  - withdrawal symptoms characteristic to dependence; or
  - the same (or similar) substance is taken to avoid withdrawal symptoms;
- Substance taken in progressively larger amounts or for longer periods;
- Persistent desire or unsuccessful attempts to cut down or reduce substance use;
- Disproportional time spending in obtaining the substance;
- Former social, occupational, or recreational activities are given up or reduced because of the substance use;
- Substance use is continued despite knowledge physical and psychological damages occurring as a result of the substance use.

This definition excludes cannabis dependence cases due to a general medical condition (e.g. chemotherapy side effects, loss of appetite, chronic pain management).

The choice has been made to use the fourth version of the DSM instead of the most recent version being the fifth (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-5 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 (Peer et al., 2013). 12-month prevalence of cannabis use disorders were lower when using DSM-5 criteria instead of the fourth version (Goldstein et al., 2015). It has to be noticed that a major change from DSM-IV to DSM-5 is the combination of substance abuse disorder and substance dependence into a single substance use disorder, which requires 2 out of 11 criteria in a 12-month period for diagnosis.

10.1.1 Corresponding disease classification codes

DSM-IV-TR code

- 304.30 Cannabis dependence

ICD-10 codes

- F12.2 Mental and behavioral disorders due to use of cannabinoids: dependence syndrome

ICD-9 codes

- 304.3 Cannabis dependence

ICPC-2 code

- P19 Drug abuse

ATC codes

- Not applicable : there are no drugs sufficiently specific for the treatment of cannabis dependence.

Nomenclature codes

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

10.2 Disease model

10.2.1 Health states

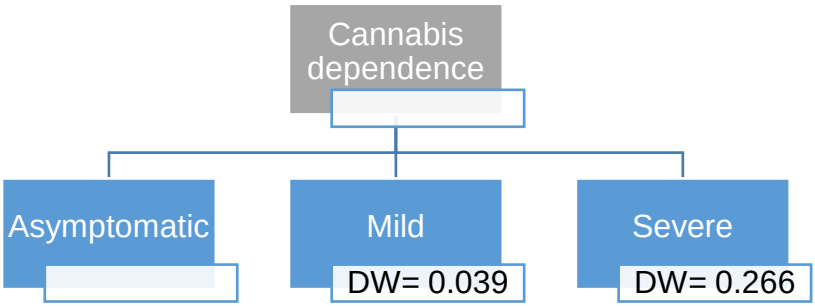

Figure 1. Cannabis dependence disease model

10.2.2 Disability weights

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

Health state	Lay description	DW
Asymptomatic	Not applicable.	Not applicable
Mild dependence	Uses marijuana at least once a week and has some difficulty controlling the habit. When not using, the person functions normally.	0.039
Severe dependence	Uses marijuana daily and has difficulty controlling the habit. The person sometimes has mood swings, anxiety, and hallucinations, and has some difficulty in daily activities.	0.266

10.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Cannabis dependence	N/A	100%	Per definition
Asymptomatic	Cannabis dependence	62.2%	HIS 2018 (Gisle & Drieskens, 2018)
Mild dependence	Cannabis dependence	24.8%	HIS 2018 (Gisle & Drieskens, 2018)
Severe dependence	Cannabis dependence	13%	HIS 2018 (Gisle & Drieskens, 2018)

10.2.4 Discussion

The distribution of cannabis dependence cases within the different levels of severity is derived from the Belgian Health Interview Survey 2018 (HIS) (Gisle & Drieskens, 2018). Last month cannabis users were asked about frequency of use in past month. They have been divided in 3 categories: cannabis use for 1 to 3 days; cannabis use for 4 to 29 days and cannabis use every day in the past month, which corresponds to the asymptomatic, mild and severe dependence, respectively.

The HIS data show a 12-month prevalence of 7% and a last-month prevalence of 4.3%. This implies that among the 7% of 12-month users, 2.7% did not use in the last month and are therefore in the asymptomatic category. We distributed the remaining 4.3% among the different health states according to the HIS severity distribution.

Although these categories are referring to past month use and not 12-month use, and are not matching perfectly with the different health states described in Table 1 (i.e., they only refer to frequency), we have made the choice to use the HIS data instead of using the Belgian data of the European Web Survey on Drugs (EWSD) (Mathias et al., 2019) severity distribution, used in amphetamines and cocaine dependence, or that of the GBD 2017 study:

- According to Matias et al. (2019), with regard to cannabis use, it is preferable to use data from general population surveys (GPS) rather than the EWSD data. Indeed, EWSD attracts more people reporting frequent drug use than in the GPS, and the distribution of frequency of cannabis use in the web survey samples is very different to that in the GPS, in which the majority are infrequent or occasional users. Using the severity distribution of EWSD would, therefore, overestimate the number of severe cannabis dependence cases leading to an overestimation of the Years Lived with Disability. On the other hand, there is a possibility that the prevalence (see 15.3.3) and the severity distribution of cannabis dependence will be underestimated using the HIS data.
- The GBD 2017 severity distribution is determined based on data from the (US) National Epidemiological Survey on Alcohol and Related Conditions (NESARC) (Grant & Dawson, 2006), a representative sample of the non-institutionalized US population aged 18 and older. There are cross-cultural differences in drug consumption: in 2017, past-year cannabis use was more than twice higher in North America compared to Western and Central Europe, with respectively 15.3% and 7% (UNODC, 2019). Therefore, local data is preferred.

In the GBD study, a category “asymptomatic” represents the percentage of people with the disease or condition and no symptoms. The choice to include a category “asymptomatic” within the severity distribution depends on the source used to produce the prevalence

estimates, and on the case definition used. Some sources will include the asymptomatic cases and other not. It is important to ensure that the proxy used for the prevalence estimates matches closely the case definition regarding the presence of symptoms or not, because this will have an influence on the severity distribution and therefore on the average disability weight derived. For the calculation of YLDs, the asymptomatic cases are not taken into account since there are not experiencing any disability.

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

10.3 Prevalence

10.3.1 Data sources

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

1. **Belgian Treatment Demand Indicator Registry (TDI)**: patient in contact with an inpatient or outpatient treatment centre that have started a new treatment for cannabis dependence during the reference year. Treatment centres are defined as facilities or practitioners providing treatment for drug or alcohol addiction. An episode is defined as a treatment process separated by at least 6 months from a previous one in outpatient settings. In residential settings, an episode occurs each time a patient is admitted and ends when the patient leaves the centre and no further admission is foreseen.
2. **Hospital Discharge data**: patient with cannabis dependence admitted to the hospital during the reference year (before 2015: ICD-9 code 304.3; after 2015: ICD-10 code: F12.2).
3. **Health insurance data**: not applicable: there are no drugs/nomenclature codes sufficiently specific to match the case definition of cannabis dependence.
4. **Health Interview Survey**: number of respondents with positive answer to the question “during the past 12 months, have you used cannabis?”.
5. **Sentinel GP network data (Intego)**: number of individuals with “drug abuse” diagnosis ever recorded by GP (ICPC-2 code P19) who had a GP contact during the reference year.
6. **Sentinel GP network data (Sciensano)**: patient with an cannabis use problem in contact for the first time with the GP and that begins a new treatment for this problem during the reference year. The treatment is defined as any activity that can be lead in order to enhance the physical, psychological or mental health state of a person with a substance problem. A treatment episode is defined as a treatment process separated by at least 6 months from a previous one.

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

Source	Strengths	Weaknesses	Evaluation
Belgian Treatment Demand Indicator Registry (TDI)	Reliable data on drug users in treatment at a national level Longitudinal approach Mandatory registration in hospitals and specialized centres Registration by professionals National database Possibility to identify 80% of the patients uniquely via the SSIN. Possibility to link these data with other databases through the SSIN (TDI-IMA databases) (Van Baelen et al., 2018)	TDI concerns only new treatment demand: incidence indicator instead of prevalence indicator. → False positives: The registration using the SSIN is not mandatory: about 20% of the patients are anonymous and can be registered several times leading to overestimation of the number of patients (Antoine, 2018). →False negatives: This number is supposed to be high since, in 2017 in Europe, less than 15% of patients with substance dependence have received a treatment for the first time (EMCDDA, 2019a). Evidence has shown that in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019). Finally, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007). Lack of registration in the non-specialized sector (GP, medical house, centres for mental health, private practice,…). Long-term treatment patients are not reported.	Sensitivity: low Specificity: high
Hospital discharge data	Exhaustive information on all cases hospitalized for	No information on patients with cannabis dependence who were not admitted to hospital	Sensitivity: low Specificity: medium

	cannabis dependence Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	during the reference year; this number is assumed to be large as most treatments for drug use is provided by outpatient facilities (EMCDDA, 2019a; 2019b). Furthermore, the treatment rate of people with substance use disorders is low in Belgium, as in the rest of Europe or high-income countries (EMCDDA, 2019a). 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)	Not applicable: there a no drugs/nomenclature codes sufficiently specific to match the case definition of cannabis dependence.	N/A	N/A
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 → <u>False positives</u>: the HIS question relates to cannabis use during the last month, even once, which could lead to an overestimation of cannabis dependent cases by taking into account recreative use. → <u>False negatives</u>: drug use is known to be underestimated in household surveys (Gisle & Drieskens, 2018; Hickman et al., 2002). Not yearly available (+/- every 5 years) Comparing estimates between subgroups of	Sensitivity: medium Specificity: medium

			the sample might lack statistical precision	
Sentinel network (Intego)	**GP data**	Diagnosis by medical professional Longitudinal approach	Case definition used in ICPC-2 code is not enough detailed and encompasses all cases of drug abuse, leading to an overestimation of cannabis dependence cases. Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP. Moreover, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007). 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 cannabis dependence	Sensitivity: low Specificity: medium
Sentinel network (Sciensano)	**GP data**	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 There is supposed to be a large number of <u>false negatives</u>: in 2017 in Europe, less than 15% of patients with substance dependence have received a treatment for the first time (EMCDDA, 2019a). Evidence has shown that in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders patients receive a treatment (either professional	Sensitivity: low Specificity: medium

treatment or self-help group) (Harris et al., 2019). Finally, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007).

10.3.2 National best estimate

The **Belgian Health Interview Survey (HIS)** is assumed to yield the best estimate of cannabis dependence prevalence.

10.3.3 Discussion

It has to be noticed that the number of cannabis dependence (CD) cases in the general population may be underestimated using the HIS as best estimate, for several reasons:

- Population surveys do not include homeless people, people in mental institutions and prisons, however there is supposed to be a lot of cases of substance dependence in these populations (Gisle & Drieskens, 2018).
- Cannabis dependence may be underreported in population surveys due to a denial or underestimation of the substance use, and a bias of selection: people with drug dependence are less likely to participate to general population surveys. However, it seems that with regard to cannabis dependence, this bias is less marked than for other substances (Matias et al., 2019). Moreover, evidence has shown good validity of self-reported substance use compared to biological measures (e.g. blood or urine samples) (Hjorthøj et al., 2012).

Another limitation of using the HIS to get the CD prevalence is that the HIS question relates to the cannabis use during the past 12 months, which could lead to an overestimation of cannabis dependence cases by taking into account the “recreative use”. However, we take this parameter into consideration by including asymptomatic cases (i.e. occasional users) in the severity distribution and, therefore, in the average disability weight used to compute the Years Lived with Disability.

Despite these limitations, the HIS has been selected to be the best source to get the cannabis dependence prevalence, after having considered other possibilities:

The Belgian Treatment Demand Indicator Registry does not allow to compute the prevalence of the cannabis dependence cases in the population, only the incidence of the new started treatments for a cannabis use problem. A pretty large number of CD cases could be missed

as in 2017 in Europe, less than 15% of patients with substance dependence have received a treatment for the first time (EMCDDA, 2019a). Evidence has shown that in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019).

Using the hospital discharge data could lead to a large number of false-negatives as most treatments for drug use are provided by outpatient facilities (EMCDDA, 2019a; 2019b). Furthermore, the treatment rate of people with substance use disorders is low in Belgium, as in the rest of Europe or high-income countries (EMCDDA, 2019a).

Using the health insurance data is to get the CD prevalence is not enough sensitive as there are no drugs or nomenclature codes sufficiently specific to match the case definition of cannabis dependence.

Finally, we have decided not to use the sentinel GP networks as a source to compute the CD prevalence since the treatment rate of people with substance use disorders is low in Belgium, as in the rest of Europe or high-income countries (EMCDDA, 2019a): only 12.5% of 12-month substance use disorders (SUD) patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019). This proportion is 7.7% among people with SUD only, and 20.1% among patients with SUD and at least one comorbid mental disorder.

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11 CEREBROVASCULAR DISEASE

11.1 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.

11.1.1 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)

11.2 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).

11.2.1 Health states

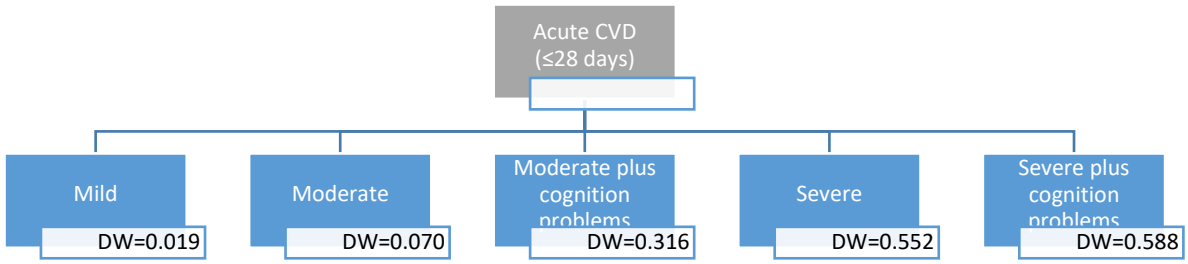

Figure 1. Acute cerebrovascular disease (stroke) disease model

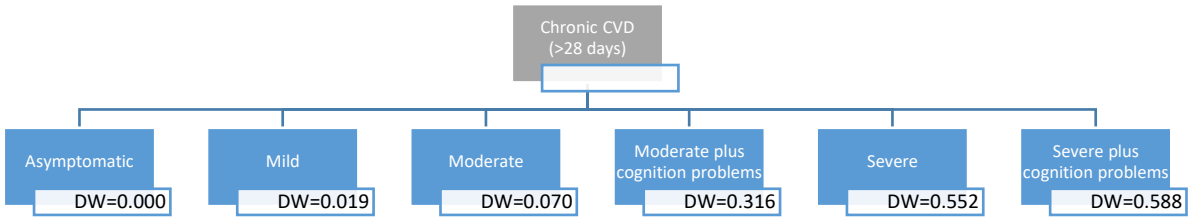

Figure 2. Chronic cerebrovascular disease (stroke) disease model

11.2.2 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

11.2.3 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

11.2.4 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.

11.3 Prevalence

11.3.1 Data sources

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

1. **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).
2. **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.

3. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you had stroke?”.
4. **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.
5. **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 be many false positive and false negatives	Sensitivity: medium Specificity: medium

		Provides representative results at national and regional levels	Not yearly available (+/- every 5 years) Comparing estimates between subgroups of the sample might lack statistical precision	
Sentinel network (Intego)	**GP data**	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 network (Sciensano)	**GP data**	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

11.3.2 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.

11.3.3 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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12 CHRONIC KIDNEY DISEASE

12.1 Case definition

Chronic kidney disease (CKD) is a general term for heterogeneous disorders affecting kidney structure and function, characterized by a decrease of the blood filtration by the kidneys. While the early stages of the disease are asymptomatic and, therefore, difficult to detect, the most severe stage (end-stage chronic kidney disease) is associated with high morbidity and can only be treated by dialysis or transplantation. Major outcomes of CKD include progression to kidney failure, development of complications of impaired kidney function, and increased risk for cardiovascular disease.

The prevalence of the disease, all stages combined, is high: 5%-8% in Europe (Zhang & Rothenbacher, 2008). It increases sharply with age and is higher in women. The age and sex-adjusted prevalence of end-stage CKD is much lower: 0.12%-0.15% in Belgium (ERA-EDTA Registry, 2017).

We have used the case definition described in the Global Burden of Disease study (GBD Chronic Kidney Disease Collaboration, 2020), in which CKD is defined as elevated urinary albumin to creatinine ratio (ACR), decreased estimated glomerular filtration rate (eGFR), or end-stage kidney disease (ESRD). The GBD study considers six stages of CKD:

1. CKD stages I-II (eGFR > 60ml/min/1.73m^2 and ACR > 30 mg/g)
2. CKD stage III (eGFR 30-59ml/min/1.73m^2)
3. CKD Stage IV (eGFR 15-29ml/min/1.73m^2)
4. CKD Stage V (eGFR<15ml/min/1.73m^2) not on renal replacement therapy
5. End-stage renal disease (ESRD) on dialysis
6. ESRD with kidney transplant

These six stages differ slightly from those described in the literature (Levey et al., 2003) since stages I and II are grouped in one single stage and ESRD on renal replacement therapy (dialysis or kidney transplant) is accounted for a stage instead of being part of stage V.

The etiologies of CKD are diabetes mellitus type 1, diabetes mellitus type 2, glomerulonephritis, hypertension, and other and unknown causes. Therefore, the codes referring to kidney complications due to those diseases are included in the case definition of CKD (e.g. ICD-10 code E13.2 Other specified diabetes mellitus with renal complications is not attributed to diabetes but to CKD).

12.1.1 Corresponding disease classification codes

ICD-10 codes

- E08.2 Diabetes mellitus due to underlying condition with kidney complications
- E10.2 Type 1 diabetes mellitus with renal complications
- E11.2 Type 2 diabetes mellitus with renal complications
- E12.2 Malnutrition-related diabetes mellitus with renal complications
- E13.2 Other specified diabetes mellitus with renal complications
- E14.2 Unspecified diabetes mellitus with renal complications
- I12 Hypertensive renal failure
- I13 Hypertensive heart and renal failure
- N02 Recurrent and persistent haematuria
- N03 Chronic nephritic syndrome
- N04 Nephrotic syndrome
- N05 Unspecified nephritic syndrome
- N06 Isolated proteinuria with specified morphological lesion
- N07 Hereditary nephropathy, not elsewhere classified
- N08 Glomerular disorders in diseases classified elsewhere
- N18.1 Chronic kidney disease, stage 1
- N18.2 Chronic kidney disease, stage 2
- N18.3 Chronic kidney disease, stage 3
- N18.4 Chronic kidney disease, stage 4
- N18.5 Chronic kidney disease, stage 5
- N18.6 End-stage renal disease
- N18.9 Chronic kidney disease, unspecified
- N19 Renal failure, unspecified
- Q60 Renal agenesis and other reduction defects of kidney
- Q61 Cystic kidney disease
- Q62 Congenital obstructive defects of renal pelvis and congenital malformations of ureter
- Q63 Other congenital malformations of kidney (excepted Q63.3 Hyperplasic and giant kidney)
- Q64 Other congenital malformations of urinary system (excepted Q64.0 Epispadias and Q64.1 Exstrophy of urinary bladder)
- Z49 Care involving dialysis
- Z99.2 Dependence on renal dialysis

ICD-9 codes

- 249.4 Secondary diabetes mellitus with renal manifestations
- 250.4 Diabetes with renal manifestations
- 403 Hypertensive chronic kidney disease
- 404 Hypertensive heart and chronic kidney disease
- 581 Nephrotic syndrome
- 582 Chronic glomerulonephritis
- 583 Nephritis and nephropathy not specified as acute or chronic
- 585.1 Chronic kidney disease, stage I
- 585.2 Chronic kidney disease, stage II (mild)
- 585.3 Chronic kidney disease, stage III (moderate)
- 585.4 Chronic kidney disease, stage IV (severe)
- 585.5 Chronic kidney disease, stage V
- 585.6 End-stage renal disease
- 585.9 Chronic kidney disease, unspecified
- 586 Renal failure, unspecified
- 589 Small kidney of unknown cause
- 753 Congenital anomalies of urinary system (excepted 753.5 Exstrophy of urinary bladder)
- V45.1 Postsurgical renal dialysis status
- V56 Encounter for dialysis and dialysis catheter care

ICPC-2 code

- U99 Urinary disease, other

ATC codes

- Not applicable: there are no drugs sufficiently specific for the treatment of chronic kidney disease.

Nomenclature codes

Nomenclatures codes related to dialysis

- 470293 Hospital hemodialysis (outpatient). Date of creation: 1/08/2016
- 470304 Hospital hemodialysis (inpatient). Date of creation: 1/08/2016
- 470315 Overnight hospital dialysis (outpatient). Date of creation: 1/08/2016
- 470326 Overnight hospital dialysis (inpatient). Date of creation: 1/08/2016
- 470330 Self-dialysis (outpatient). Date of creation: 1/08/2016
- 470341 Self-dialysis (inpatient). Date of creation: 1/08/2016
- 470352 Home dialysis (outpatient). Date of creation: 1/08/2016

- 470875 Peritoneal dialysis (outpatient). Date of creation: 1/08/2016
- 470890 Children: hemodialysis (outpatient). Date of creation: 1/08/2016
- 470901 Children: hemodialysis (inpatient). Date of creation: 1/08/2/016
- 470912 Children: peritoneal dialysis (outpatient). Date of creation 1/08/2016
- 470934 Hemodialysis self-care (outpatient). Date of creation 1/01/2018
- 470945 Hemodialysis self-care (inpatient). Date of creation: 1/01/2018
- 767594 Outpatient hospital hemodialysis. Date of creation: 1/08/2016
- 767616 Outpatient overnight hospital hemodialysis. Date of creation: 1/08/2016
- 767631 Outpatient hospital hemodialysis, children. Date of creation: 1/08/2016
- 767664 Hemodialysis of patients hospitalised elsewhere. Date of creation: 1/08/2016
- 767686 Hemodialysis of children hospitalised elsewhere. Date of creation: 1/08/2016
- 767701 Hemodialysis of patients hospitalised in the same hospital. Date of creation: 1/08/2016
- 767723 Hemodialysis of children hospitalised in the same hospital. Date of creation: 1/08/2016
- 767734 Home hemodialysis (outpatient). Date of creation: 1/08/2016
- 767782 Self-dialysis of patients hospitalised in the same hospital. Date of creation: 1/08/2016
- 767804 Self-dialysis of patients hospitalised elsewhere. Date of creation 1/08/2016
- 767815 Home peritoneal dialysis (outpatient). Date of creation: 1/08/2016
- 767826 Home peritoneal dialysis (inpatient). Date of creation: 1/08/2016
- 767830 Home peritoneal dialysis, children (outpatient). Date of creation: 1/08/2016
- 767841 Home peritoneal dialysis, children (inpatient). Date of creation: 1/08/2016
- 767955 Hemodialysis self-care (outpatient). Date of creation: 1/01/2018
- 767756 Self-dialysis (outpatient). Date of creation: 1/08/2016
- 767966 Hemodialysis self-care (inpatient). Date of creation 1/01/2018

Nomenclature codes related to a CKD care trajectory

- 107096 fees payable to the general practitioner for the first year of a care trajectory concluded with a beneficiary suffering from chronic renal failure (outpatient). Date of creation 1/06/2009
- 107111 fees payable to the specialist for the first year of a care trajectory concluded with a beneficiary suffering from chronic renal failure (outpatient). Date of creation 1/06/2009
- 107133 fees payable to the general practitioner for the second, third and fourth years of a care trajectory concluded with a beneficiary suffering from chronic renal failure (outpatient). Date of creation 1/06/2009

- 107155 fees payable to the specialist for the second, third and fourth years of a care trajectory concluded with a beneficiary suffering from chronic renal failure (outpatient). Date of creation 1/06/2009

12.2 Disease model

12.2.1 Health states

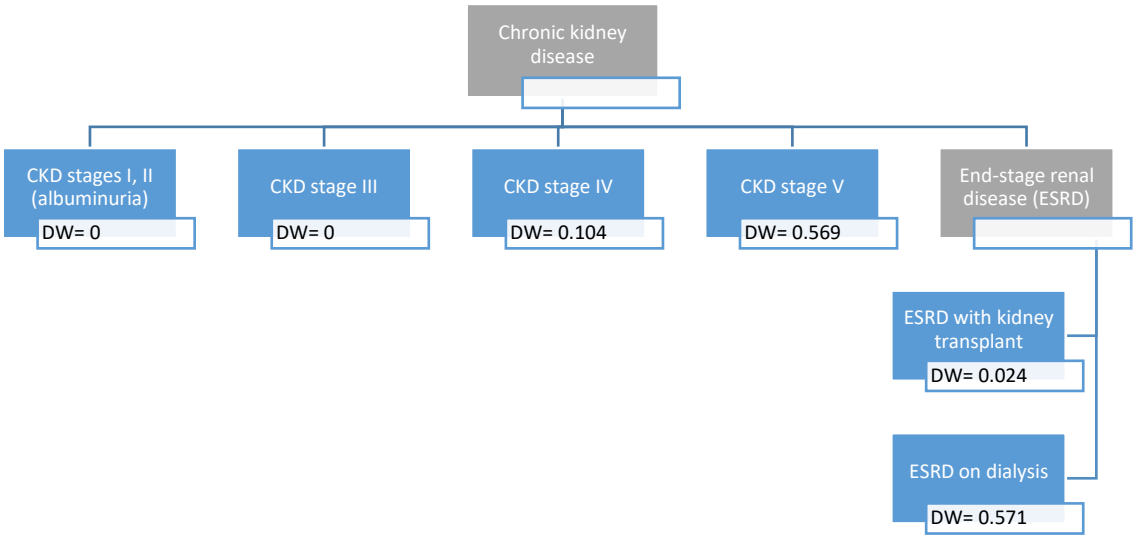

Figure 1. Chronic kidney disease (CKD) disease model

12.2.2 Disability weights

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

Health state	Lay description	DW
CKD stages I-II	Asymptomatic	0
CKD stage III	Asymptomatic	0
CKD stage IV	Tires easily, has nausea, reduced appetite, and difficulty sleeping	0.104
CKD stage V	Has lost a lot of weight and has constant pain. The person has no appetite, feels nauseated, and needs to spend most of the day in bed	0.569
End-stage renal disease, with kidney transplant	Sometimes feels tired and down, and has some difficulty with daily activities	0.024
End-stage renal disease, on dialysis	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

12.2.3 Proportion of patients in the considered health states

Table 2. Proportion of patients in the different health states considered in the Chronic kidney disease (CKD) disease model, Belgium.

Health state	Parent	Proportion	Source
Chronic kidney disease (CKD)	N/A	100%	Per definition
CKD stages I-II	Chronic kidney disease		
CKD stage III	Chronic kidney disease		
CKD stage IV	Chronic kidney disease		
CKD stage V	Chronic kidney disease		
End-stage disease	Chronic kidney disease	100%	Per definition
End-stage renal disease, with kidney transplant	End-stage renal disease		ERA-EDTA Registry (2019)
End-stage renal disease, on dialysis	End-stage renal disease		ERA-EDTA Registry (2019)

12.2.4 Discussion

The proportion of people with end-stage renal disease (ESRD) being treated with kidney transplant or with dialysis is extracted from the latest ERA-EDTA Registry report (2019) using the prevalent counts by treatment modality, the prevalent counts by age and sex, and the treatment modality distribution by age, sex, and primary renal disease.

The proportions are computed as followed:

For both the Dutch-speaking and French-speaking communities, the number of prevalent cases with a kidney transplant or on dialysis is extracted from the ERA-EDTA Registry, and combined with the distribution of modality proportion by sex, and age. To calculate the joint modality distribution by age and sex, the marginal modality distributions were multiplied and standardized. For example, the probability of a kidney transplant in women aged 75 years and older was calculated based on the probability of a kidney transplant in women (e.g., 42%) and the probability of a kidney transplant in people aged 75+ (e.g., 10%). The joint probability of a kidney transplant in women aged 75+ was then calculated as 42% times 10% or 4.2% assuming that there is no association between sex and age for the different treatment modalities. The joint probabilities were afterward standardized to ensure their sum would equal 100%. The proportions for the Brussels Capital Region and the Walloon Region were

calculated based on the data for the French-speaking community, whereas the proportion for the Flemish region was calculated based on the data for the Dutch-speaking community.

12.3 Prevalence

12.3.1 Data sources

Different data sources exist for chronic kidney disease (CKD), each with a specific case definition:

1. **European Renal Association - European Dialysis and Transplant Association (ERA-EDTA) Registry:** patients in dialysis or having had a renal transplant and still alive (end stage renal failure), registered by the Dutch speaking and French speaking societies of nephrology.
2. **Hospital Discharge data:** patient with CKD admitted to the hospital during the reference year (for corresponding ICD-10 and ICD-9 codes, see 18.1.1.).
3. **Health insurance data:** person with a specific nomenclature code referring to dialysis or with a care trajectory related to CKD during the reference year (see 18.1.1.).

   Several conditions are needed to enter into a CKD care trajectory contract:

   - have a CKD with a severe stage (GFR <45ml/min/1.73m^2), defined twice by a blood test and/or
   - have a proteinuria of >1g/day, defined twice by a urine analysis
   - be over 18 years
   - not to be on dialysis or have had a kidney transplant
4. **Health Interview Survey:** percentage of persons of 15 years and older who have answered “yes” to the question: “ in the past 12 months, have you suffered from severe kidney disease other than kidney stones?”.
5. **Sentinel GP network data (Intego):** number of individuals with a urinary disease diagnosis ever recorded by GP (ICPC-2 code U99) who had a GP contact during the reference year.
6. **Sentinel GP network data (Sciensano):** number of individuals with chronic kidney disease diagnosis recorded by a sentinel GP during the reference year.

Table 3. Potential sources and methods for the computation of chronic kidney disease (CKD) prevalence in Belgium

Source	Strengths	Weaknesses	Evaluation
ERA-EDTA Registry	National and European database Diagnoses by medical doctor Case definition internationally defined	Data are limited to End-Stage Renal Disease (ESRD) Only patients >20 years are included	Sensitivity: low Specificity: high
Hospital discharge data	Exhaustive information on all cases hospitalized for CKD Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on patients with CKD who were not admitted to hospital during the reference year; since early stages of the disease are asymptomatic, this could be a large number of patients. Recognition rate of CKD in hospitalized patients is low, especially in the early stages (De Wilde 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	Sensitivity: low Specificity: high
Health insurance data (IMA/EPS)	Case definition based on medication and care Large, representative sample Longitudinal approach	There are two possible case definitions: - Case definition based on the presence of a nomenclature code related to dialysis, which is one of the treatments for ESRD. Patients with CKD stages I to V are not included. For that reason, this case definition is excluded. - Case definition based on the presence of a care trajectory related to CKD. In that case, only patients over 18 years with a severe stage of CKD (stages IIIb to V) and who have	Sensitivity: medium Specificity: high

		signed a care trajectory contract are included. 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; it is assumed that there may be many false positives and false negatives → False positives: people who have declared suffering from CKD without being affected by the disease (e.g. people with renal colic) → False negatives: people who are not aware suffering from CKD, or people suffering from CKD who have not been diagnosed yet Not yearly available (+/- every 5 years) Comparing estimates between subgroups of the sample might lack statistical precision	Sensitivity: low Specificity: medium
Sentinel network (Intego) GP data	Diagnosis by medical professional Longitudinal approach	Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP Because the early stages are asymptomatic, a significant proportion of patients with CKD may be undiagnosed The recognition rate of CKD (all stages) in primary care is low: about 30% (Van Gelder et al., 2016; Ryan et al., 2007) 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	Sensitivity: medium Specificity: high

		software and interested in registration) For the PP: not possible to identify the reason for consultation, so might not be related to CKD	
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, hospitalisation) unless the information is transmitted to the GP Because the early stages are asymptomatic, a significant proportion of patients with CKD may be undiagnosed The recognition rate of CKD (all stages) in primary care is low: about 30% (Van Gelder et al., 2016; Ryan et al., 2007) Only periodic registration Last registration: 2011-2012	Sensitivity: low Specificity: high

12.3.2 National best estimate

The Intego sentinel GP network have been selected as the best estimate to yield the prevalence of chronic kidney disease (CKD) stages IIIb to V in Belgium. The ERA-EDTA registry has been selected as the best source to get the prevalence of End-stage renal disease.

Since the Intego sentinel GP network is regional and only reflects the situation in Flanders, a correction factor is applied, which is calculated as the ratio of the prevalence of serious kidney disease other than kidney stones in Brussels and in Wallonia, respectively, by sex and by age groups, and the prevalence of serious kidney disease other than kidney stones in Flanders, using the results of the Belgian Health Interview Survey. The Intego sentinel GP network prevalence of CKD is therefore multiplied by the different ratios obtained to get the CKD prevalence in the two other regions of Belgium.

12.3.3 Discussion

Despite the fact that the generalist practitioner (GP) plays a privileged role in the detection and the management of the chronic kidney disease, the recognition rate in the primary care is low, with about 30% of all stages CKD cases diagnosed (Van Gelder et el., 2016; Ryan et al., 2007). This may lead to a lack or a delay of referral to a nephrologist (De Wilde et al., 2018;

van Dipten et al., 2017) and can delay the diagnosis. However, since symptoms of severe stages are very disabling, patients concerned are more likely to seek professional help. Furthermore, as patients suffering from early stages of CKD (stages I to III) are asymptomatic (see Disability weights point 18.2.2.), they will not be included in the YLD calculation, since their disability weight equals to 0. For that reason, it is not necessary that the source selected to obtain the prevalence of CKD in Belgium includes mild stage cases.

Despite the fact the ICPC-2 code U99 (urinary disease, other) used in the Intego sentinel GP network to encode the diagnose of CKD is broad and include others diseases, e.g. acute kidney insufficiency or uretero-vesical reflux, which could induce an overestimation of CKD prevalence, diagnosis data are linked to biological measures, via the calculation of the estimated glomerular filtration rate (eGFR), in order to get the prevalence of CKD cases in the different health stages, allowing to refine the case definition.

Despite these limitations, the Intego sentinel GPs data have been selected to get the prevalence of severe stages of CKD after having considered other possibilities:

The Belgian Health Interview Survey provides self-reported data which can lead to false positives and to a substantial number of false negatives. Furthermore, the HIS question relates to a pretty broad case definition that could be not sufficiently specific with the one used in this study.

The Sciensano GP network registration of CKD is periodic, which does not ensure the most recent data possible.

The recognition rate of chronic kidney disease in the hospitals is low, especially in the early stages (De Wilde et al., 2018). Using the hospital discharge data to get the prevalence of CKD would lead to a substantial underestimation of the cases.

The Health insurance database includes patients with a CKD care trajectory. Those patients benefit from more regular follow-up with the GP and the specialist compared to patient without a CKD care trajectory (Van Casteren et al., 2013).

Despite the fact that both the GP and the specialist can register the patient on a CKD care trajectory, and despite the fact that patients living in nursing homes, if they meet the criteria, can also sign a care trajectory contract, it should be noted that not all patients with severe renal failure sign such a contract. Therefore, the use of the Health insurance data related to CKD care trajectories may lead to an underestimation of the “true” prevalence of patients with severe CKD in Belgium.

Furthermore, it should be noted that there are considerable discrepancies in enrollment in care trajectories between the regions, with a majority of patients on care trajectory in Flanders (Van Casteren et al., 2013), this may hamper comparisons between regions.

Since the data of the ERA-EDTA registry are not open-source, the prevalent cases and modality distributions are extracted from the tables in the reports that our published yearly. Consequently, only larger age groups (< 20 years, 20-44 years, 45-64 years, and >74 years) can be used to calculate the prevalent counts.

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13 CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

13.1 Case definition

COPD is defined as in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification: a measurement of <0.7 FEV1/FVC (one second of forceful exhalation/total forced expiration) on spirometry after bronchodilation. The severity grading of COPD follows this GOLD class definition (Vos et al., 2020).

GOLD CLASS	FEV1 Score
I: Mild	≥ 80% of normal
II: Moderate	50-79% of normal
III & IV: Severe	< 50% of normal

13.1.1 Corresponding disease classification codes

ICD-10 codes

- J41 Simple and mucopurulent chronic bronchitis
- J42 Unspecified chronic bronchitis
- J43 Emphysema
- J44 Other chronic obstructive pulmonary disease
- J47 Bronchiectasis

ICD-9 codes

- 491 Chronic bronchitis
- 492 Emphysema

ICPC-2 codes

- R95 Chronic obstructive pulmonary disease

ATC codes

- R03BB Anticholinergics
- R03DA04 Theophylline
- R03A Adrenergics, inhalants
- R03BA Glucocorticoids

Nomenclature codes

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

13.2 Disease model

13.2.1 Health states

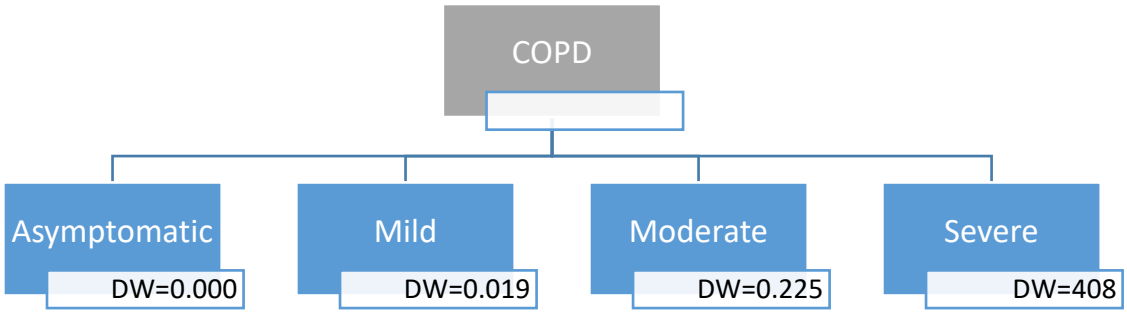

Figure 1. COPD disease model

13.2.2 Disability weights

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

Health state	Lay description	DW
Asymptomatic COPD		0.000
Mild COPD	This person has cough and shortness of breath after heavy physical activity, but is able to walk long distances and climb stairs.	0.019
Moderate COPD	This person has cough, wheezing, and shortness of breath, even after light physical activity. The person feels tired and can walk only short distances or climb only a few stairs.	0.225
Severe COPD	This person has cough, wheezing, and shortness of breath all the time. The person has great difficulty walking even short distances or climbing any stairs, feels tired when at rest, and is anxious.	0.408

13.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
COPD	N/A	100%	Per definition
Asymptomatic	COPD	19.7%	Burnstein et al. (2015)
Mild COPD	COPD	45.4%	Burnstein et al. (2015)
Moderate COPD	COPD	13.3%	Burnstein et al. (2015)
Severe COPD	COPD	21.6%	Burnstein et al. (2015)

13.2.4 Discussion

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. These disability are in line with those estimated in the European context, where disability weights of 0.025 (0.019-0.031), 0.284 (0.242-0.329), and 0.418 (0.367-0.468) were reported for the mild, moderate and severe health states of COPD, respectively (Haagsma et al., 2015).

The severity distribution in the GBD model is based exclusively on data from the USA, raising questions on applicability for the Belgian context (Burstein et al., 2015). 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”, 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 COPD being measured in MEPS relates to health care contact. For GBD 2017, data were used from 2000-2014.

An international study showed a similar distribution in Belgium, with 66.9% being diagnosed with mild COPD, 19.4% with moderate COPD, and 13.7% with severe COPD following the GOLD severity stages for COPD (De Marco et al., 2004). Therefore, we decided to comply with the GDB-distribution to facilitate international comparisons.

13.3 Prevalence

13.3.1 Data sources

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

1. **Hospital discharge data:** patient with migraine admitted to the hospital during the reference year (before 2015: ICD-9 code; after 2015 ICD-10 code).
2. **Health insurance data:** COPD is encoded as a pseudopathology based on the ATC-codes and age ≥ 50 (ATC code: R03BB, Anticholinergics; R03DA04; Theophylline, R03A Adrenergics, inhalants; R03BA, Glucocorticoids).

3. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you had a chronic bronchitis, chronic obstructive pulmonary disease or emphysema?”.
4. **Sentinel GP network data (Intego):** number of individuals with migraine diagnosis ever recorded by GP (ICPC-2 codes R95) who had a GP contact during the reference year.
5. **Sentinel GP network data (Sciensano):** not applicable; COPD 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 COPD Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on COPD patients who were not admitted to hospital during the reference year; this is a substantial proportion of the COPD 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)	Large, representative sample Longitudinal approach	COPD pseudodiagnoses are limited to patients older than 50 years. 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 condition 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: low 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 induce an overestimation of COPD 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: 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 Migraine.	Sensitivity: medium Specificity: high
Sentinel GP network data (Sciensano)	Not applicable. COPD has not been registered by the Sciensano SGPs.		

13.3.2 National best estimate

The national best estimate for the prevalence of COPD is the Belgian Health Interview Survey, which provides national representative prevalence numbers.

13.3.3 Discussion

Although hospital admissions are possible in case of acute severe COPD exacerbations, not all patients will require hospitalization (Donaldson & Wedzicha, 2006; Søgaard et al., 2016). Therefore, relying on hospital discharge data will yield an underestimated prevalence of COPD. There are several pharmaceutical interventions possible in case of COPD, of which glucocorticoids form an important group. However, there exists an overlap in pharmaceutical treatment between COPD and asthma, making a strict distinction in the prevalence of these

disorders based on health insurance data impossible (Lakshmi et al., 2017; Niewoehner et al., 1999). Moreover, approximately 15% of patients do not fill a new prescription and generally discontinue therapy after about six months, making non-adherence, and non-compliance with treatments a serious problem in COPD (Sanduzzi et al., 2014). These patients would not be identified in health insurance data or in the nomenclature data.

As the COPD according to the GOLD-classification requires a diagnosis by a medical doctor, the Sentinel GP network data of Intego might be a valuable source. However, as this dataset is currently not representative for the country, and not all COPD patients might have yearly follow-up visits, we decided to use the Health Interview Survey to estimate the prevalence of COPD in Belgium. Although health insurance data is available, an age restriction ≥ 50 years has been put in place for the diagnosis of COPD, which would result in an underestimated proportion (Berete et al., 2020). In a recent study, Berete et al. (2020) identified an absolute difference in COPD prevalence of 1.19 (0.47 to 1.90), and relative difference of 42.10 (11.85 to 72.35) when comparing the prevalence based on the Belgian HIS to the prevalence based on health insurance data. Given the high burden of COPD, further studies are needed to quantify the validity (sensitivity/specificity) of the proposed approach for defining the prevalence of COPD.

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14 CIRRHOSIS AND OTHER CHRONIC LIVER DISEASES

14.1 Case definition

Cirrhosis and other chronic liver diseases (collectively referred to as cirrhosis in this document) are a major cause of morbidity and mortality. Cirrhosis is the end stage of hepatic fibrosis, in which the liver does not function properly. In the early stages, cirrhosis is compensated and asymptomatic. Decompensated cirrhosis is defined by an acute deterioration in liver function in patients with cirrhosis, with the occurrence of disabling symptoms such as icterus (jaundice), ascites, bleeding oesophageal varices, hepatic encephalopathy and hepatorenal syndrome (Mansour & McPherson, 2018). Almost all the mortality and morbidity linked to cirrhosis is caused by the decompensated type (GBD 2017 Cirrhosis Collaborators, 2020). The most common causes of cirrhosis are alcohol-related liver diseases, hepatitis B and C, and non-alcoholic steatohepatitis (NASH).

14.1.1 Corresponding disease classification codes

ICD-10 codes

- B18 Chronic viral hepatitis
- I85 Oesophageal varices
- K70.0 Alcoholic fatty liver
- K70.1 Alcoholic hepatitis
- K70.2 Alcoholic fibrosis and sclerosis of liver
- K70.3 Alcoholic cirrhosis of liver
- K71.7 Toxic liver disease with fibrosis and cirrhosis of liver
- K72.1 Chronic hepatic failure
- K73 Chronic hepatitis, not elsewhere classified
- K74 Fibrosis and cirrhosis of liver
- K75.2 Nonspecific reactive hepatitis
- K75.4 Autoimmune hepatitis
- K75.8 Other specified inflammatory liver diseases
- K75.9 Inflammatory liver disease, unspecified
- K76.1 Chronic passive congestion of liver
- K76.2 Central haemorrhagic necrosis of liver
- K76.4 Peliosis hepatis
- K76.5 Hepatic veno-occlusive disease
- K76.6 Portal hypertension
- K76.7 Hepatorenal syndrome

- K76.8 Other specified diseases of liver
- K76.9 Liver disease, unspecified
- K77.8 Liver disorders in other diseases classified elsewhere
- P78.81 Congenital cirrhosis of the liver

ICD-9 codes

- 456.0 Oesophageal varices with bleeding
- 456.1 Oesophageal varices without mention of bleeding
- 456.2 Oesophageal varices in diseases classified elsewhere
- 571 Chronic liver disease and cirrhosis
- 572.3 Portal hypertension
- 572.4 Hepatorenal syndrome
- 572.8 Other sequelae of chronic liver disease
- 573.0 Chronic passive congestion of liver
- 573.3 Hepatitis, unspecified
- 573.5 Hepatopulmonary syndrome
- 573.8 Other specified disorders of liver
- 573.9 Unspecified disorder of liver

ICPC-2 code

- D97 Liver disease, NOS

ATC codes

- There are no drugs sufficiently specific for the treatment of cirrhosis.

Nomenclature codes

- There are no nomenclature codes sufficiently specific to match the case definition of cirrhosis.

14.2 Disease model

14.2.1 Health states

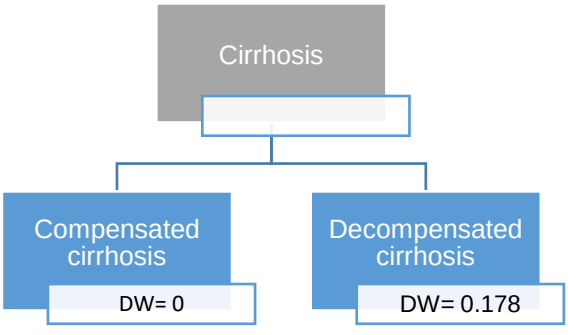

Figure 1. Cirrhosis disease model

14.2.2 Disability weights

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

Health state	Lay description	DW
Compensated cirrhosis	N/A	0
Decompensated cirrhosis	Has swollen belly and swollen legs. The person feels weakness, fatigue and loss of appetite	0.178

14.2.3 Proportion of patients in the considered health states

Given the asymptomatic nature of compensated cirrhosis, and given that there is no disability related to this health state (DW=0), the asymptomatic cases are not part of the YLDs calculation. There is, therefore, no necessity to get the prevalence of compensated cirrhosis, but only the prevalence of decompensated cirrhosis to compute the YLDs related to cirrhosis. For that reason, the choice of the source to get the cirrhosis prevalence should include as much as possible decompensated cases (100% or the nearest of the cirrhosis cases).

14.3 Prevalence

14.3.1 Data sources

Different data sources exist for cirrhosis of the liver, each with a specific case definition:

1. **Register:** not applicable: there is no registry related to cirrhosis.
2. **Hospital Discharge data:** patient with cirrhosis admitted to the hospital during the reference year (see 4.1.1. for the corresponding ICD codes).
3. **Health insurance data:** not applicable: there are no drugs or nomenclature codes sufficiently specific to match the definition of cirrhosis.
4. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you had cirrhosis?”.
5. **Sentinel GP network data (Intego):** number of individuals with cirrhosis diagnosis ever recorded by GP (ICPC-2 code D97) who had a GP contact during the reference year.
6. **Sentinel GP network data (Sciensano):** not applicable: cirrhosis have not been registered by the Sciensano sentinel GP network.

Table 2. Potential sources and methods for the computation of cirrhosis prevalence in Belgium

Source	Strengths	Weaknesses	Evaluation
Registry	Not applicable: there is no registry related to cirrhosis.	N/A	N/A
Hospital discharge data	Exhaustive information on all cases hospitalized for cirrhosis Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on patients with cirrhosis who were not admitted to hospital during the reference year; Since in the early stages, cirrhosis is asymptomatic, patients are more commonly admitted in hospital for decompensated cirrhosis with an acute deterioration of the liver functions that requires complex medical care[1]. Hospital discharge data for cirrhosis are therefore incidence data for decompensated cirrhosis rather than prevalence data for cirrhosis as a whole. HDD is primarily used for administrative purposes, which could result in some problems when data have to be used for epidemiological purposes	Sensitivity: medium Specificity: high
Health insurance data (IMA/EPS)	Not applicable: there are no drugs or nomenclature codes sufficiently specific to match the definition of cirrhosis.	N/A	N/A
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 positives and false negatives. → False positives: people who have reported to have cirrhosis, and who are not suffering from this disease. This number is supposed to be low. → False negatives: people with cirrhosis who are not aware of having the	Sensitivity: low Specificity: medium

			disease and have not reported it. This number could be high as compensated cirrhosis is asymptomatic for a long time before becoming symptomatic. Not yearly available (+/- every 5 years) Comparing estimates between subgroups of the sample might lack statistical precision	
Sentinel network (Intego)	**GP data**	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 cirrhosis	Sensitivity: low Specificity: high
Sentinel network (Sciensano)	**GP data**	Not applicable: cirrhosis have not been registered by the Sciensano sentinel GP network.	N/A	N/A

14.3.2 National best estimate

The **hospital discharge data** have been assessed as the best estimate to yield the prevalence of cirrhosis in Belgium.

14.3.3 Discussion

To get the true prevalence of cirrhosis in Belgium is a difficult exercise since a lot of cases are asymptomatic. Indeed, the liver is an organ with the ability to continue to work normally until 10% of its capacity, which is called compensated cirrhosis, that can last several years without any symptoms. When the disease has progressed to <10% of the liver function, cirrhosis is decompensated, symptoms appear that are very disabling, and medical care is needed.

However, given the asymptomatic nature of compensated cirrhosis, and given that there is no disability related to this health state (DW=0), the asymptomatic cases are not part of the YLDs calculation. There is, therefore, no necessity to get the prevalence of compensated cirrhosis, but only the prevalence of decompensated cirrhosis to compute the YLDs related to cirrhosis.

Patients with cirrhosis are frequently hospitalized (Ge & Runyon, 2016), this concerns mainly patients with decompensated cirrhosis that require acute specialized care.

Since hospital discharge data of patients with an acute decompensated cirrhosis are more incidence data rather than prevalence data, it is necessary to know how long lasts the decompensated health state to derive prevalence data by using this formula:

Prevalence = Incidence x duration

The median survival of compensated vs. decompensated cirrhosis is, respectively >12 years vs. about 2 years (D'Amico et al., 2006). Therefore, prevalence of decompensated cirrhosis is obtained by multiplying by 2 the number of patients hospitalized with cirrhosis in a given year using the hospital discharge data.

The prevalence of cirrhosis would be slightly overestimated, given that there is a possibility that some compensated cases would be included. However, this number is assumed to be low, as only primary diagnosis of cirrhosis are included in the case definition, and compensated cirrhosis is usually not a cause of hospitalization as itself. Indeed, the management of compensated cirrhosis mainly requires preventive examinations in outpatient settings to avoid the progression of the disease to a decompensated state (Shetty et al., 2019).

Therefore, the hospital discharge data have been selected as the best source to get the cirrhosis prevalence after having considered other possibilities:

General practitioners are in first line for prevention, recognition and diagnosis of cirrhosis (Flamm, 2018). They are more likely to diagnose compensated cirrhosis than in the secondary health care (hospital or specialist) through routine check-ups, blood tests or because they know the history of the patients and the risk factors to which they are exposed. This implies that it is necessary to know the proportion of compensated and decompensated cirrhosis in the Intego sentinel GP network to compute the YLDs related to the decompensated health state, which is complicated. Moreover, the Intego data refers to the situation in Flanders and not in the whole country. Therefore, the Intego sentinel GP network has not been selected to get the prevalence of cirrhosis in Belgium.

Finally, the prevalence of cirrhosis has been assessed in the Belgian Health Interview Survey, but given that it is reported data, the number of false negatives could be important and would

lead to an underestimation of the prevalence of cirrhosis cases in Belgium. Moreover, there is no possibility to know the proportion of compensated and decompensated cases.

Currently, the aggregated prevalence estimates for liver cirrhosis based on the hospital discharge data yield small cells (i.e. cells with counts less than 5) for some combinations of age, sex, and region. Consequently, information on prevalent cases and the associated YLD is not yet included in the BeBOD results.

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15 COCAINE DEPENDENCE

15.1 Case definition

Cocaine use disorders are a group of substance-related conditions affecting the use of cocaine.

According to the Diagnostic and Statistical Manual of Mental Disorders, version IV, text revised (DSM-IV) (APA, 2000), the distinction is made between cocaine abuse (CA) and cocaine dependence (CD), which is the most severe form of cocaine use disorders.

The case definition used here is also used in the GBD 2017 study (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018), and corresponds to the definition of cocaine dependence in the DSM IV, and is defined as a "maladaptive pattern of substance use, leading to clinically significant impairment of distress" (Bell, 1994). At least three of the following criteria must have occurred during the past 12 months:

- Tolerance, characterized by either
  - a need for increased amounts of the substance to achieve intoxication; or
  - markedly diminished effect with continued use of the same amount of the substance;
- Withdrawal, characterized by either
  - withdrawal symptoms characteristic to dependence; or
  - the same (or similar) substance is taken to avoid withdrawal symptoms;
- Substance taken in progressively larger amounts or for longer periods;
- Persistent desire or unsuccessful attempts to cut down or reduce substance use;
- Disproportional time spending in obtaining the substance;
- Former social, occupational, or recreational activities are given up or reduced because of the substance use;
- Substance use is continued despite knowledge physical and psychological damages occurring as a result of the substance use.

The choice has been made to use the fourth version of the DSM instead of the most recent version being the fifth (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-5 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 (Peer et al., 2013). 12-month prevalence of cocaine use disorders were

lower when using DSM-5 criteria instead of the fourth version (Goldstein et al., 2015). It has to be noticed that a major change from DSM-IV to DSM-5 is the combination of substance abuse disorder and substance dependence into a single substance use disorder, which requires 2 out of 11 criteria in a 12-month period for diagnosis.

15.1.1 Corresponding disease classification codes

DSM-IV-TR code

- 304.20 Cocaine dependence

ICD-10 codes

- F14.2 Mental and behavioral disorders due to use of cocaine : dependence syndrome

ICD-9 codes

- 304.2 Cocaine dependence

ICPC-2 code

- P19 Drug abuse

ATC codes

- Not applicable : there are no drugs sufficiently specific for the treatment of cocaine dependence.

Nomenclature codes

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

15.2 Disease model

15.2.1 Health states

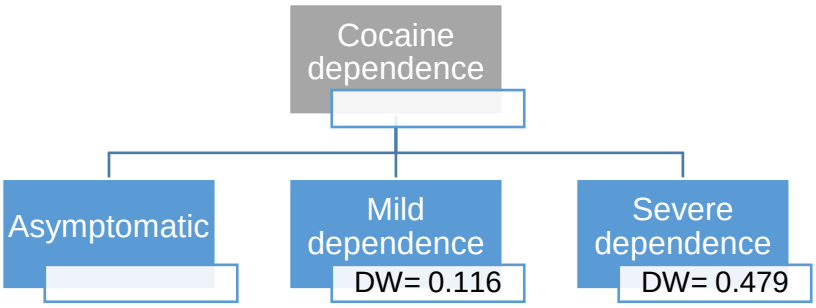

Figure 1. Cocaine dependence disease model

15.2.2 Disability weights

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

Health state	Lay description	DW
Asymptomatic	Not applicable	Not applicable
Mild dependence	Uses cocaine at least once a week and has some difficulty controlling the habit. When not using, the person functions normally.	0.116
Severe dependence	Uses cocaine daily and has difficulty controlling the habit. The person sometimes has mood swings, anxiety, paranoia, hallucinations and sleep problems, and has some difficulty in daily activities.	0.479

15.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Cocaine dependence	N/A	100%	Per definition
Asymptomatic	Cocaine dependence	61%	European Web Survey on Drugs (Matias et al., 2019)
Mild dependence	Cocaine dependence	27%	European Web Survey on Drugs (Matias et al., 2019)
Severe dependence	Cocaine dependence	12%	European Web Survey on Drugs (Matias et al., 2019)

15.2.4 Discussion

The distribution of cocaine dependence cases within the different levels of severity is derived from the European Web Survey on Drugs (EWSD), conducted by the European Monitoring Centre for Drugs and Drugs Addiction (EMCDDA) from 2016 to 2018. The ESWD collected information about patterns of use and purchase of the most commonly used illicit drugs in 14 countries, including Belgium. The categories for the frequency of cocaine use in the past 12 months was defined as:

- Infrequent use: < 11 days in past year
- Occasional use: between 11-50 days in the past year
- Frequent use: +51 days in the past year

These categories correspond, respectively, to the health states asymptomatic, mild dependence and severe dependence. Although they are not matching perfectly with the

definition of the different health states described in Table 1, the choice has been made to prefer local data to avoid using the GBD 2017 study severity distribution, that is determined based on data from the (US) National Epidemiological Survey on Alcohol and Related Conditions (NESARC) (Grant & Dawson, 2006), a representative sample of the non-institutionalized US population aged 18 and older. Indeed, there are cross-cultural differences in drug consumption, e.g. in 2017, cocaine use 12-month prevalence was higher in North America compared to Western and Central Europe, with respectively 2.2% and 1.3% (UNODC, 2019).

In the GBD study, a category “asymptomatic” represents the percentage of people with the disease or condition and no symptoms. The choice to include a category “asymptomatic” within the severity distribution depends on the source used to produce the prevalence estimates, and on the case definition used. Some sources will include the asymptomatic cases and other not. It is important to ensure that the proxy used for the prevalence estimates matches closely the case definition regarding the presence of symptoms or not, because this will have an influence on the severity distribution and therefore on the average disability weight derived. For the calculation of YLDs, the asymptomatic cases are not taken into account since there are not experiencing any disability.

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

15.3 Prevalence

15.3.1 Data sources

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

1. **Belgian Treatment Demand Indicator Registry (TDI)**: patient in contact with an inpatient or outpatient treatment centre that have started a new treatment for cocaine dependence during the reference year. Treatment centres are defined as facilities or practitioners providing treatment for drug or alcohol addiction. An episode is defined as a treatment process separated by at least 6 months from a previous one in outpatient settings. In residential settings, an episode occurs each time a patient is admitted and ends when the patient leaves the centre and no further admission is foreseen.
2. **Hospital Discharge data**: patient with cocaine dependence admitted to the hospital during the reference year (before 2015: ICD-9 code 304.2; after 2015: ICD-10 code F14.2).
3. **Health insurance data**: not applicable: there are no drugs or nomenclature codes sufficiently specific to match the case definition of cocaine dependence.

4. **Health Interview Survey**: number of respondents who have answered “Cocaine” and “in the past 12 months” to the question: “What other substances did you use, even once, and when did you take them last?”.
5. **Sentinel GP network data (Intego)**: Number of individuals with “drug abuse” diagnosis ever recorded by GP (ICPC-2 code P19) who had a GP contact during the reference year.
6. **Sentinel GP network data (Sciensano)**: patient with a cocaine use problem in contact for the first time with the GP and that begins a new treatment for this problem during the reference year. The treatment is defined as any activity that can be lead in order to enhance the physical, psychological or mental health state of a person with a substance problem. A treatment episode is defined as a treatment process separated by at least 6 months from a previous one.

Table 3. Potential sources and methods for the computation of cocaine dependence (CD) prevalence in Belgium

Source	Strengths	Weaknesses	Evaluation
Belgian Treatment Demand Indicator Registry (TDI)	Reliable data on drug users in treatment at a national level Longitudinal approach Mandatory registration in hospitals and specialized centres Registration by professionals National database Possibility to identify 80% of the patients uniquely via the SSIN. Possibility to link these data with other databases through the SSIN (TDI-IMA databases) (Van Baelen et al., 2018)	TDI concerns only new treatment demand: incidence indicator instead of prevalence indicator. → False positives: The registration using the SSIN is not mandatory: about 20% of the patients are anonymous and can be registered several times leading to overestimation of the number of patients (Antoine, 2018). → False negatives: This number is supposed to be high since in 2017, in Europe, less than 15% of patients with substance dependence have received a treatment for the first time (EMCDDA, 2019a). Evidence has shown that in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019).	Sensitivity: low Specificity: high

		Lack of registration in the non-specialized sector (GP, medical house, centres for mental health, private practice,…). Long-term treatment patients are not reported.	
Hospital discharge data	Exhaustive information on all cases hospitalized for cocaine dependence Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on patients with cocaine dependence who were not admitted to hospital during the reference year. This number is supposed to be large as most treatments for drug use are provided by outpatient facilities (EMCDDA, 2019a; 2019b). Furthermore, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007), and in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019). 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: medium
Health insurance data (IMA/EPS)	Not applicable: there are no drugs or nomenclature codes sufficiently specific to match the case definition of cocaine dependence.	N/A	N/A
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 positives and false negatives → False positives: the HIS question relates to cocaine use during the	Sensitivity: medium Specificity: medium

			last month, even once, which could lead to an overestimation of cocaine dependence cases. → False negatives: drug use is known to be underestimated in household surveys (Gisle & Drieskens, 2018; Hickman et al., 2002) Not yearly available (+/- every 5 years) Comparing estimates between subgroups of the sample might lack statistical precision	
Sentinel network (Intego)	**GP data**	Diagnosis by medical professional Longitudinal approach	Case definition used in ICPC-2 code is not enough detailed and encompasses all cases of drug abuse, leading to an overestimation of CD cases. Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP. Furthermore, the treatment rate of people with substance use disorders is low in Belgium, as in the rest of Europe or high-income countries (EMCDDA, 2019a). Finally, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007). 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	Sensitivity: low Specificity: medium

		not be related to cocaine dependence cases.	
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. Furthermore, the treatment rate of people with substance use disorders is low in Belgium, as in the rest of Europe or high-income countries (EMCDDA, 2019a). Finally, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007).	Sensitivity: low Specificity: medium

15.3.2 National best estimate

The **Belgian Health Interview Survey (HIS)** is assumed to yield the best estimate of cocaine dependence prevalence.

15.3.3 Discussion

It has to be noticed that the number of cocaine dependence (CD) cases in the general population may be underestimated using the HIS as best estimate, for several reasons:

- Population surveys do not include homeless people, people in mental institutions and prisons, however there is supposed to be a lot of cases of substance dependence in these populations (Gisle & Drieskens, 2018).
- Cocaine dependence may be underreported due to a selection bias: people with drug dependence are less likely to participate to population surveys. However, evidence has shown good validity of self-reported substance use compared to biological measures (e.g. blood or urine samples) (Hjorthøj et al., 2012).

Another limitation of using the HIS to get the CD prevalence is that the HIS question relates to the cocaine use during the past 12 months, even once, which could lead to an overestimation of cocaine dependence cases. However, we take this parameter into account by including asymptomatic cases (i.e. occasional users) in the severity distribution and, therefore, in the average disability weight used to compute the Years Lived with Disability.

Despite these limitations, the HIS has been selected to be the best source to get the opioid dependence prevalence, after having considered other possibilities:

The Belgian Treatment Demand Indicator Registry does not allow to compute the prevalence of the CD cases in the population, only the incidence of the new started treatments for a cocaine use problem. A pretty large number of CD cases could be missed as in 2017 in Europe, less than 15% of patients with substance dependence have received a treatment for the first time (EMCDDA, 2019a). Moreover, evidence has shown that in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019).

Using the hospital discharge data could lead to a large number of false-negatives as most treatments for drug use are provided by outpatient facilities (EMCDDA, 2019a; 2019b). Furthermore, the treatment rate of people with substance use disorders is low in Belgium, as in the rest of Europe or high-income countries (EMCDDA, 2019a).

Using the health insurance data is to get the CD prevalence is not enough sensitive as there are no drugs or nomenclature codes sufficiently specific to match the case definition of cocaine dependence.

Finally, we have decided not to use the sentinel GP networks as a source to compute the CD prevalence since the treatment rate of people with substance use disorders is low in Belgium, as in the rest of Europe or high-income countries (EMCDDA, 2019a): only 12.5% of 12-month substance use disorders (SUD) patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019). This proportion is 7.7% among people with SUD only, and 20.1% among patients with SUD and at least one comorbid mental disorder.

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16 DIABETES

16.1 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.

16.1.1 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); except E10.2
- 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); except E11.2.
- E12 Malnutrition-related diabetes mellitus (both insulin-dependent and non-insulin-dependent; except E12.2
- E13 Other specified diabetes mellitus; except E13.2
- E14 Unspecified diabetes mellitus (including diabetes NOS); except E14.2

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.

E10.2, E11.2, E12.2, E13.2 and E14.2 are attributed to “chronic kidney disease”, diabetes mellitus being considered as the primary renal disease.

ICD-9 codes

- 249 Secondary diabetes mellitus
- 250 Diabetes mellitus, except 250.4 (diabetes with renal manifestations)

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, except code 250.4 that is attributed to “chronic kidney disease”, diabetes mellitus being considered as the primary renal disease.

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

- ~~770033~~ Code deleted on 1/11/2016
- ~~770055~~ Code deleted on 1/11/2016
- 770070 Compensation for the referral of a patient to a third-line diabetic foot clinic
- ~~771573~~ Code deleted on 1/11/2016
- ~~771595~~ Code deleted on 1/11/2016
- 772450 Functional re-education agreement for insulin therapy by continuous infusion at home using a portable insulin pump: One-day performance of the re-education program (daily flat rate, outpatient).
- 772641 Functional re-education agreement for insulin therapy by continuous infusion at home using a portable insulin pump: One-day performance of the re-education program (daily flat rate, inpatient).
- ~~773113~~ Code deleted on 1/12/2016
- ~~773231~~ Code deleted on 1/10/2008
- ~~773253~~ Code deleted on 1/11/2016
- ~~773275~~ Code deleted on 31/12/2007
- 773393 Functional rehabilitation - accredited third-line diabetic foot clinics (786): interdisciplinary outpatient foot clinic consultation

- 773496 Functional rehabilitation: Accredited third-line diabetic foot clinics: Support session (outpatient).
- ~~773592~~ Code deleted on 1/01/2017
- ~~774115~~ Code deleted on 1/12/2016
- ~~774130~~ Code deleted on 1/12/2016
- ~~774152~~ Code deleted on 1/12/2016
- ~~775456~~ Code deleted on 1/12/2016
- ~~775471~~ Code deleted on 1/12/2016
- 789751 Insulin pump program delivery day (previous agreement) for a beneficiary <18 years of age with an existing agreement - with insulin pump (outpatient).
- 789935 Insulin pump program delivery day (previous agreement) for a beneficiary >=18 years of age with an existing agreement – group 3 adult agreement - with insulin pump (outpatient).
- ~~794076~~ Code deleted on 1/01/2019
- 102852 Follow-up of a patient with type 2 diabetes according to the care protocol established by the Insurance Committee (outpatient).
- 109594 Medical Homes: Follow-up of a type 2 diabetic patient according to the care protocol established by the Insurance Committee (outpatient).
- 107015 Flat fees payable to the general practitioner for the first year of a care trajectory concluded with a beneficiary suffering from type 2 diabetes mellitus (outpatient).
- 107030 Flat fees payable to the specialist physician for the first year of a care trajectory concluded with a beneficiary suffering from type 2 diabetes mellitus (outpatient).
- 107052 Flat fees payable to the general practitioner for the second, third and fourth years of a care trajectory concluded with a beneficiary suffering from type 2 diabetes mellitus (outpatient).
- 107074 Flat fees payable to the specialist physician for the second, third and fourth years of a care trajectory concluded with a beneficiary suffering from type 2 diabetes mellitus (outpatient).
- 788756 Group A multidisciplinary care program delivery day - Finger prick method (outpatient).
- 788852 Group C multidisciplinary care program delivery day - Sensor method of measurement (outpatient).

16.2 Disease model

16.2.1 Health states

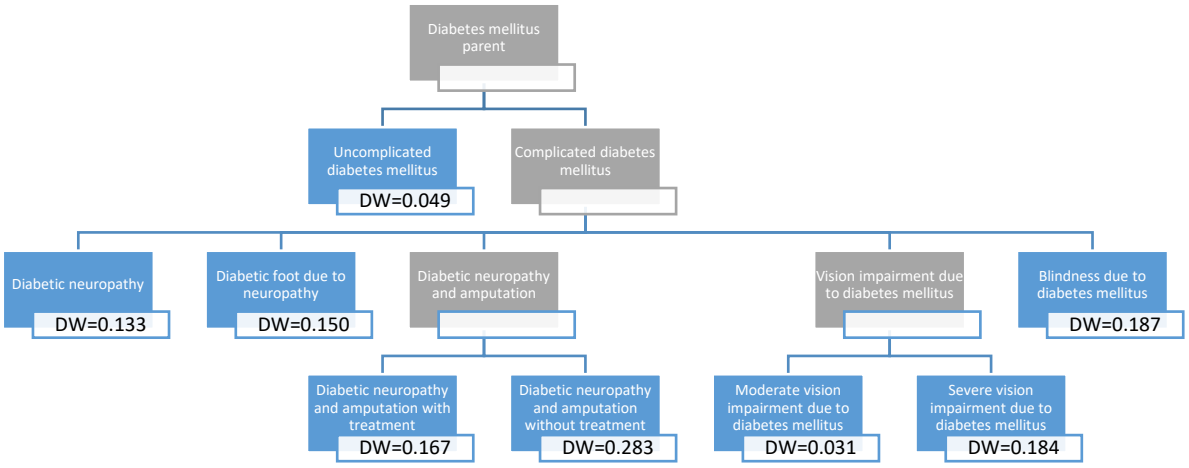

Figure 1. Diabetes disease model

16.2.2 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

†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)

16.2.3 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. The assumption was then made that patients were 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)

16.2.4 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.

Vision impairment, and more specifically, vision impairment due to retinopathy is an often diagnosed sequela of diabetes (Fong et al., 2004). As diabetic retinopathy is modelled in the diabetic envelope, ideally it should be removed from the vision impairment envelope. However, the impact of removing and adjusting the estimates based on the potential overlap was rather small. Therefore, it was decided to not correct for this overlap in the current disease model.

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 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.

16.3 Prevalence

16.3.1 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 diabetes 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 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)	Sensitivity: low Specificity: high
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	Sensitivity: high Specificity: high

		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: high (90%; Vaes et al. (2018)) 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 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

16.3.2 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.

16.3.3 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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17 EPILEPSY

17.1 Case definition

The case definition for epilepsy encompasses (Vos et al., 2020):

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., 2021).
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.

17.1.1 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.

17.2 Disease model

17.2.1 Health states

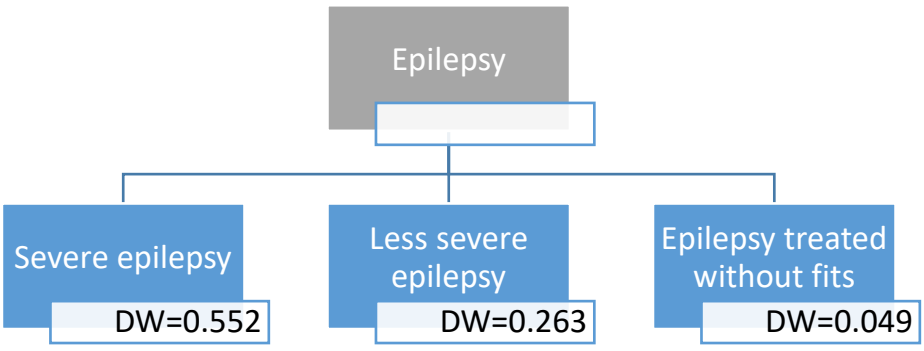

Figure 1. Epilepsy disease model

17.2.2 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

17.2.3 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

17.2.4 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.

Disability weights for epilepsy were retrieved from the GBD, and are consistent with those reported in the European context (Haagsma et al., 2015).

17.3 Prevalence

17.3.1 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 prescribed for another	Sensitivity: high Specificity: low

		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.		

17.3.2 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).

17.3.3 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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18 HEARING IMPAIREMENT

18.1 Case definition

Hearing impairment is an estimation of the prevalence of hearing loss at a range of severities, as measured by the softest sound that an individual can hear in their better ear, taken as the average across frequencies from 500 to 4000 Hertz.

CONDITION	CASE DEFINITION (Threshold in decibels)
None	0–19
Mild	20–34
Moderate	35–49
Moderately severe	50–64
Severe	65–79
Profound	80–94
Complete	95+

The following causes of hearing loss are included: congenital, meningitis, otitis, and age-related and other. Congenital hearing loss is defined as hearing loss present at birth. Age-related and other hearing loss includes causes not identified as meningitis, otitis, or congenital. This includes presbycusis, the gradual loss of hearing with age, caused by breakdown of neurons in the inner ear. For all causes, hearing loss with and without tinnitus, the perception of noise or ringing in the ears, was modelled separately (Vos et al., 2020).

18.1.1 Corresponding disease classification codes

ICD-10 codes

- H60 Otitis externa
- H61 Other disorders of external ear
- H65 Nonsuppurative otitis media
- H66 Suppurative and unspecified otitis media
- H68 Eustachian salpingitis and obstruction
- H69 Other disorders of Eustachian tube
- H70 Mastoiditis and related conditions
- H72 Perforation of tympanic membrane
- H73 Other disorders of tympanic membrane
- H74 Other disorders of middle ear and mastoid
- H80 Otosclerosis
- H83 Other diseases of inner ear

- H90 Conductive and sensorineural hearing loss
- H91 Other hearing loss
- H93 Other disorders of ear, not elsewhere classified
- H95 Postprocedural disorders of ear and mastoid process, not elsewhere classified

ICD-9 codes

- 380 Disorders of external ear
- 381 Nonsuppurative otitis media and Eustachian tube disorders
- 382 Suppurative and unspecified otitis media
- 383 Mastoiditis and related conditions
- 384 Other disorders of tympanic membrane
- 385 Other disorders of middle ear and mastoid
- 387 Otosclerosis
- 388 Other disorders of ear
- 389 Deafness

ICPC-2 codes

- H02 Hearing complaint
- H03 Tinnitus, ringing/buzzing ear
- H28 Limited function/disability ear
- H74 Chronic otitis media
- H77 Perforation ear drum
- H80 Congenital anomaly of ear
- H83 Otosclerosis
- H84 Presbyacusis
- H86 Deafness

ATC codes

- Not applicable : there is no drug sufficiently specific to match the case definition of hearing impairment.

Nomenclature codes

- Not applicable: there are difference nomenclature codes available for hearing loss, but none are sufficiently specific to match the case definition of hearing impairment.

18.2 Disease model

18.2.1 Health states

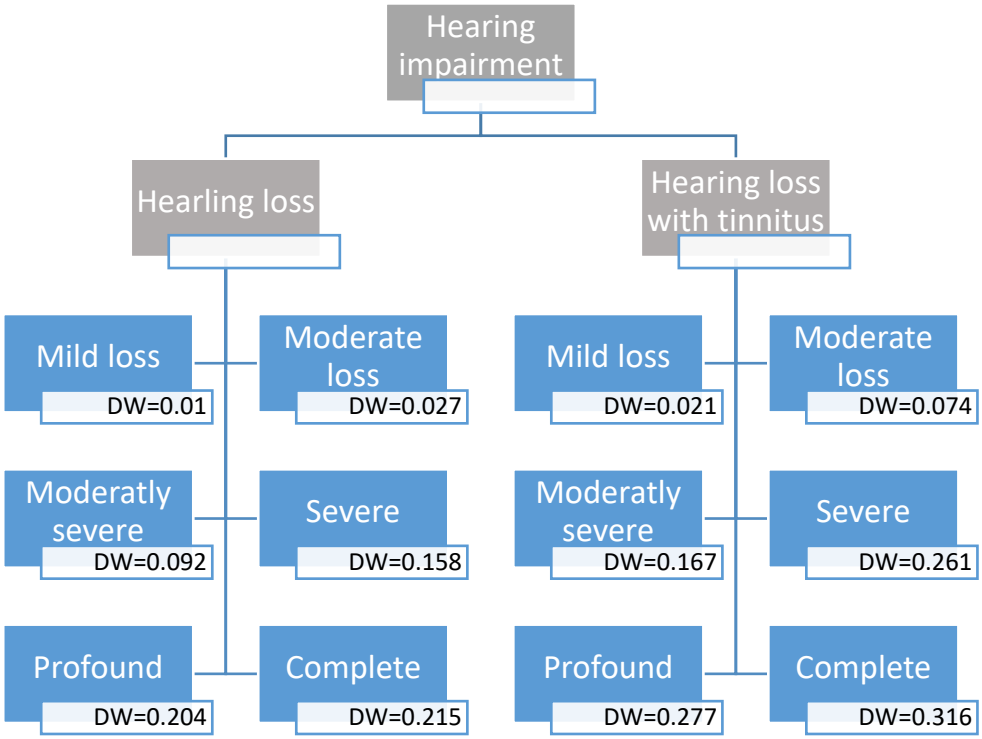

Figure 1. Hearing impairment disease model

18.2.2 Disability weights

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

Health state	Lay description	DW
Hearing loss, mild	This person has great difficulty hearing and understanding another person talking in a noisy place (for example, on an urban street).	0.01
Hearing loss, mild, with ringing	This person has great difficulty hearing and understanding another person talking in a noisy place (for example, on an urban street), and sometimes has annoying ringing in the ears.	0.021
Hearing loss, moderate	This person is unable to hear and understand another person talking in a noisy place (for example, on an urban street), and has difficulty hearing another person talking even in a quiet place or on the phone.	0.027
Hearing loss, moderate, with ringing	This person is unable to hear and understand another person talking in a noisy place (for example, on an urban street), and has difficulty hearing another person talking even in a quiet place or on the phone,	0.074

	and has annoying ringing in the ears for more than 5 minutes at a time, almost every day.	
Hearing loss, moderately severe	(custom DW from hearing loss impairment envelope)	0.092
Hearing loss, moderately severe, with ringing	(custom DW from hearing loss impairment envelope)	0.167
Hearing loss, severe	This person is unable to hear and understand another person talking, even in a quiet place, and unable to take part in a phone conversation. Difficulties with communicating and relating to others cause emotional impact at times (for example worry or depression).	0.158
Hearing loss, severe, with ringing	This person is unable to hear and understand another person talking, even in a quiet place, and unable to take part in a phone conversation, and has annoying ringing in the ears for more than 5 minutes at a time, almost every day. Difficulties with communicating and relating to others cause emotional impact at times (for example worry or depression).	0.261
Hearing loss, profound	This person is unable to hear and understand another person talking, even in a quiet place, is unable to take part in a phone conversation, and has great difficulty hearing anything in any other situation. Difficulties with communicating and relating to others often cause worry, depression, and loneliness.	0.204
Hearing loss, profound, with ringing	This person is unable to hear and understand another person talking, even in a quiet place, is unable to take part in a phone conversation, has great difficulty hearing anything in any other situation, and has annoying ringing in the ears for more than 5 minutes at a time, several times a day. Difficulties with communicating and relating to others often cause worry, depression, or loneliness.	0.277
Hearing loss, complete	This person cannot hear at all in any situation, including even the loudest sounds, and cannot communicate verbally or use a phone. Difficulties with communicating and relating to others often cause worry, depression or loneliness.	0.215
Hearing loss, complete, with ringing	This person cannot hear at all in any situation, including even the loudest sounds, and cannot communicate verbally or use a phone, and has very annoying ringing in the ears for more than half of the day. Difficulties with communicating and relating to others often cause worry, depression or loneliness.	0.316

18.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Hearing impairment	N/A	100%	Per definition
Hearing loss, mild	Hearing impairment	71.7%	Haile et al. (2021)
Hearing loss, mild, with ringing	Hearing impairment	4.4%	Haile et al. (2021)
Hearing loss, moderate	Hearing impairment	15.9%	Haile et al. (2021)
Hearing loss, moderate, with ringing	Hearing impairment	1.0%	Haile et al. (2021)
Hearing loss, moderately severe	Hearing impairment	4.6%	Haile et al. (2021)
Hearing loss, moderately severe, with ringing	Hearing impairment	0.3%	Haile et al. (2021)
Hearing loss, severe	Hearing impairment	0.7%	Haile et al. (2021)
Hearing loss, severe, with ringing	Hearing impairment	0.01%	Haile et al. (2021)
Hearing loss, profound	Hearing impairment	0.7%	Haile et al. (2021)
Hearing loss, profound, with ringing	Hearing impairment	0.01%	Haile et al. (2021)
Hearing loss, complete	Hearing impairment	0.7%	Haile et al. (2021)
Hearing loss, complete, with ringing	Hearing impairment	0.01%	Haile et al. (2021)

Proportion estimates were retrieved from Haile et al. (2021). The proportion of patients with hearing loss with a tinnitus component, i.e. with ringing, was estimated using the Intego-dataset based on the amount of patients that reported tinnitus complaints over the total amount of patients with hearing complaints, i.e. with or without a component of tinnitus. These estimates were afterwards age- and gender standardized according to the Belgian population structure of 2018, which yielded an estimate of 5.7% for patients with hearing loss, who also suffer from tinnitus (Haile et al., 2021). This estimate is lower compared to the reported overall prevalence of tinnitus of 9.6% in the general population (Bhatt et al., 2016).

18.2.4 Discussion

Disability weights for the Belgian national burden of disease study are adapted from the Global Burden of Disease study (Salomon et al., 2015; Vos et al., 2020), as these provide an exhaustive set of internally consistent disability weights. In contrast to the GBD study, in which the identified fraction of people in each severity category that used a hearing aid are shifted to the category directly below, hearing aids were not taken into account for the current study.

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 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”, i.e. days out of role due to illness. Professional coders translate the verbatim text into three-digit ICD-9 codes. For GBD 2017, data were used from 2000-2014 (Burstein et al., 2015).

The disability weights for hearing impairment based on the US population is similar to the disability weights that were estimated in a European sample (Haagsma et al., 2015).

18.3 Prevalence

18.3.1 Data sources

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

1. **Hospital discharge data:** patient with hearing impairment admitted to the hospital during the reference year (before 2015: ICD-9 code; after 2015 ICD-10 code).
2. **Health insurance data:** not applicable.
3. **Health Interview Survey:** not applicable.
4. **Sentinel GP network data (Intego):** number of individuals with hearing loss diagnosis ever recorded by GP (ICPC-2 codes H02, H03, H28, H70, H71, H72, H73, H74, H77, H80, H83, H84, H86, H99) who had a GP contact during the reference year.
5. **Sentinel GP network data (Sciensano):** not applicable; hearing impairment has not been registered by the Sciensano SGPs network.

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

Source	Strengths	Weaknesses	Evaluation
Hospital discharge data	Exhaustive information on all cases hospitalized for hearing impairment Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on hearing impairment patients who were not admitted to hospital during the reference year; this is a substantial proportion of 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)	Not applicable: there are no (reimbursed) medications or health care usages that would allow a sufficiently specific diagnosis of vision impairment		
Health Interview Survey	Not applicable. Hearing impairment has not been registered in the HIS.		
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 hearing impairment.	Sensitivity: medium Specificity: medium
Sentinel GP network data (Sciensano)	Not applicable. Vision impairment has not been registered by the Sciensano SGPs.		

18.3.2 National best estimate

Intego appears to be the most complete source of information on the prevalence of hearing impairment in Belgium, since prevalence numbers regarding hearing impairment are lacking in the Belgian HIS, and no clear nomenclature codes could be retrieved for hearing impairment.

18.3.3 Discussion

Given the complexity of hearing disorders, estimating precise prevalence estimates is challenging. Hospital admissions for hearing impairments are rather rare, and would give an underestimation of the prevalence of hearing impairment. Although the use of hearing aids is a question within the health interview survey, only a minority of patients will rely on hearing aids. Hence, estimating the prevalence based on the health interview survey would also yield underestimated prevalence estimates. Therefore, we decided to use the Sentinel GP network data (Intego) to estimate the prevalence of hearing impairment in Belgium. One major limitation of this dataset is that not all patients with a hearing impairment will yearly visit their GP. Consequently, these patients will not be registered and will not be included in the prevalence.

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

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19 LOW BACK PAIN

19.1 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.

19.1.1 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.

19.2 Disease model

19.2.1 Health states

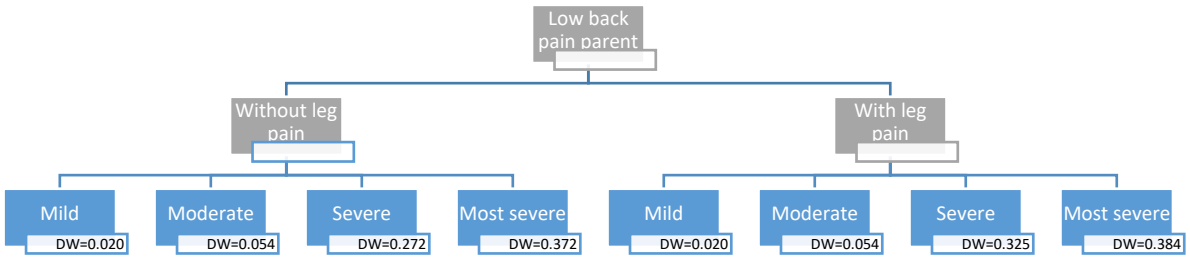

Figure 1. Low back pain disease model

19.2.2 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

19.2.3 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		

19.2.4 Discussion

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 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”, 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 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.

19.3 Prevalence

19.3.1 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 network (Sciensano)	**GP data**	Not applicable. Low back pain has not been registered by the Sciensano SGPs.

19.3.2 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.

19.3.3 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.

19.4 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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20 MIGRAINE

20.1 Case definition

Migraine is a disabling primary headache disorder, typically characterized by recurrent moderate or severe unilateral pulsatile headaches. The two major types are migraine without aura and migraine with aura (transient neurological symptoms).

The reference diagnostic criteria for migraine are from the International Classification of Headache Disorders **ICHD-3**, which describe five criteria:

1. At least five attacks fulfilling criteria 2-5
2. Headache attacks lasting 4-72 hour (untreated or unsuccessfully treated)
3. Headache has at least two of the following four characteristics:
    a. Unilateral location
    b. Pulsating quality
    c. Moderate or severe pain intensity
    d. Aggravation by or causing avoidance of routine physical activity
4. During headache at least one of the following:
    a. Nausea and/or vomiting
    b. Photophobia and phonophobia
5. Not better accounted for by another ICHD-3 diagnosis

Definite migraine is headache that satisfies all the criteria outlined above, while probable migraine satisfies all of the above criteria except one.

20.1.1 Corresponding disease classification codes

ICD-10 codes

- G43.0 Migraine without aura
- G43.1 Migraine with aura

ICD-9 codes

- 346.12 Migraine without aura
- 346.03 Migraine with aura

ICPC-2 codes

- N89 Migraine

ATC codes

- N02C Antimigraine preparations

Nomenclature codes

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

20.2 Disease model

20.2.1 Health states

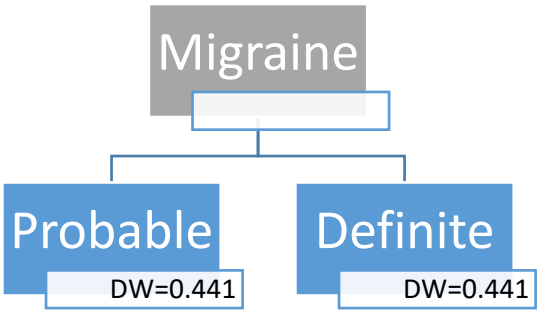

Figure 1. Migraine disease model

The proportion of time symptomatic is 0.093 for definite migraine and 0.066 for probable migraine (Vos et al., 2020). However, precise and valid estimates for the proportion of definite and probable migraine are lacking for Belgium. Therefore, the estimated proportion of time symptomatic for the entire migraine population was inferred from the pooled data analysis in the GBD-2016, which estimated the proportion of time symptomatic at 0.085 for the entire migraine population (Stovner et al., 2018).

20.2.2 Disability weights

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

Health state	Lay description	DW
Migraine, probable	This person has migraine, with or without aura that is perfectly matching all diagnostic criteria	0.441
Migraine, definite	This person has migraine, with or without aura that is imperfectly matching all diagnostic criteria	0.441

20.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Migraine	N/A	100%	Per definition
Migraine, probable		NA	
Migraine, definite		NA	

20.2.4 Discussion

Disability weights for the Belgian national burden of disease study are adapted from the Global Burden of Disease study (Stovner et al., 2018; Vos et al., 2020), as these provide an exhaustive set of internally consistent disability weights.

Two states are described in the GBD-study, which were given an identical disability weight, but differed in their estimated proportion of time symptomatic. Based on 16 studies, the pooled overall proportion of time symptomatic was estimated at 0.085 (Stovner et al., 2018). An important difference in the current disease model compared to the GBD-model is the handling of medication-overuse headache (MoH) data. Up to 50% of chronic migraine cases could show signs of MoH (Negro & Martelletti, 2011). In the disease model of the GBD-study a substantial part of the MoHs are attributed to migraine. Consequently, the estimated total disability for migraine in the current study will be lower compared to the disability reported by the GBD-study. Due to the heterogeneity of MoH and unavailability of diagnostic codes, it was decided to currently exclude MoH from the Belgian model.

20.3 Prevalence

20.3.1 Data sources

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

1. **Hospital discharge data:** patient with migraine admitted to the hospital during the reference year (before 2015: ICD-9 code; after 2015 ICD-10 code).
2. **Health insurance data:** migraine-specific medications are available as “Antimigraine preparations (ATC code N02C)”.
3. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you had a severe headache such as migraine?”.
4. **Sentinel GP network data (Intego):** number of individuals with migraine diagnosis ever recorded by GP (ICPC-2 codes N89) who had a GP contact during the reference year.
5. **Sentinel GP network data (Sciensano):** not applicable; migraine has not been registered by the Sciensano SGPs network.

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

Source	Strengths	Weaknesses	Evaluation
Hospital discharge data	Exhaustive information on all cases hospitalized for migraine Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on migraine patients who were not admitted to hospital during the reference year; this is a substantial proportion of the migraine 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)	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 migraine 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: low 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 induce an overestimation of migraine prevalence; integration with information on disability or health-related quality of life may increase specificity Question includes all headaches that could be perceived migraine-like. Not yearly available (+/- every 5 years) Comparing estimates between subgroups of the	Sensitivity: high Specificity: medium

			sample might lack statistical precision	
Sentinel network (Intego)	**GP data**	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 migraine.	Sensitivity: medium Specificity: high
Sentinel network (Sciensano)	**GP data**	Not applicable. Migraine has not been registered by the Sciensano SGPs.		

20.3.2 National best estimate

Intego appears to be the most appropriate source of information on the prevalence of migraine in Belgium, but only covers the region of Flanders. The health interview survey only takes into account severe cases, resulting in an underestimation of the proportion of patients that suffer from migraine. Similarly, the hospital discharge data will result in underestimated prevalence estimates, since hospitalization due to migraine is rare.

20.3.3 Discussion

Migraine diagnoses are often underdiagnosed, thus appropriate treatment is often lacking (Bigal et al., 2008). When correctly diagnosed, different pharmaceutical anti-migraine and preventive treatments are available categorized as acute abortive and prophylactic medications. Common prophylactic medications used are β-blockers, antiepileptic medications (topiramate and divalproex sodium), and tricyclic antidepressants. Common acute abortive and analgesic medications include triptans, ergotamines, antiemetics, nonsteroidal anti-inflammatory drugs, and combination opioids, which have a wide array of mechanisms that target different pathways and biological factors in headache generation including such neurotransmitter pathways as serotonin, dopamine, norepinephrine,

cyclooxygenase, opioid pain receptors, and calcitonin gene-related peptide (CGRP) (Ong & De Felice, 2018). However, these treatments could also be offered for other disorders.

Although hospital admission for migraine are increasing (Law et al., 2020), only a minority of migraine patients is ever hospitalized. Therefore, hospital discharge data would give a substantial underestimation of migraine patients.

Not all patients with mild forms of migraine will contact a medical specialist, and if they do, the diagnosis of migraine by the clinician is a challenging task, which require substantial knowledge of the ICHD-criteria (listed under 1.1). Moreover, migraineurs often experience varying prodrome symptoms including tension and neck pain before having a migraine attack. This often leads to misdiagnosis of migraine or attribution of the headache as a secondary symptom of neck pain or tension (Kelman, 2004). A correct diagnosis often requires keeping a diary and an in-depth interview by a medical specialist. Due to these challenges, migraine is often underdiagnosed in the population (Lipton et al., 2001), and the prevalence estimates based on the ICPC-2 codes encoded by general practitioners might be an underestimation of the prevalence of migraine in the population. Given the high burden of migraine, further studies are urgently needed to quantify the validity (sensitivity/specificity) of the proposed approach for defining the prevalence of migraine.

20.4 References

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injuries in 204 countries and territories, 1990–2019: A systematic analysis for the Global Burden of Disease Study 2019. The Lancet, 396(10258), 1204–1222.

21 NECK PAIN

21.1 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.

21.1.1 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.

21.2 Disease model

21.2.1 Health states

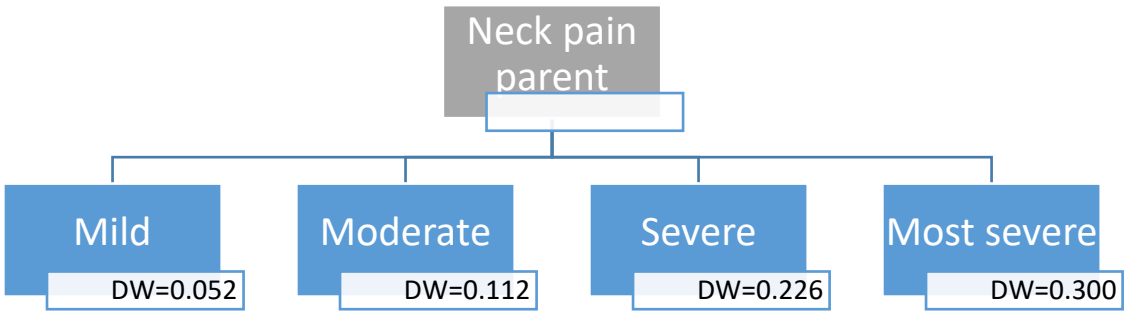

Figure 1. Neck pain disease model

21.2.2 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

21.2.3 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)

21.2.4 Discussion

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 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”, 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 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.

21.3 Prevalence

21.3.1 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 network (Sciensano)	**GP data**	Not applicable. Neck pain has not been registered by the Sciensano SGPs.

21.3.2 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.

21.3.3 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.

21.4 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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22 OSTEOARTHRITIS

22.1 Case definition

The Osteoarthritis (OST) reference case definition is symptomatic osteoarthritis of the hip or knee radiologically confirmed as Kellgren-Lawrence grade 2-4. Grade 2 symptomatic requires one defined osteophyte in hip or knee and pain for at least one month out of the last 12. Grade 3-4 symptomatic requires osteophytes and joint space narrowing in hip or knee with deformity also present for grade 4, and pain for at least one month out of the last 12 months.

OST is the most common form of arthritis, involving inflammation and breakdown of joints. For the purposes of OST estimates for this study, only hip and knee sites were reviewed. The hip and knee are the common sites of OST in the larger joints and are considered to produce the greatest disability. OST of the spine is also common; however, it was considered that any symptoms and disability related to the cervical and/or lumbar spine would be captured in the estimates of low back pain and neck pain. Hand OST involving the fingers and thumbs is another common site for OST, but as it often overlaps with knee OST and could also be captured in the Other musculoskeletal disorders category, it was not considered as a separate entity.

22.1.1 Corresponding disease classification codes

ICD-10 codes

- M16 Coxarthrosis [arthrosis of hip]
- M17 Gonarthrosis [arthrosis of knee]

ICD-9 codes

- 715 Other and unspecified disorders of back

ICPC-2 codes

- L89 Osteoarthritis of hip
- L90 Osteoarthritis of knee
- L91 Osteoarthritis, other

ATC codes

- MA1AH02 Rofecoxib – anti-inflammatory and anti-rheumatic product

Nomenclature codes referring to osteoarthritis

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

22.2 Disease model

22.2.1 Health states

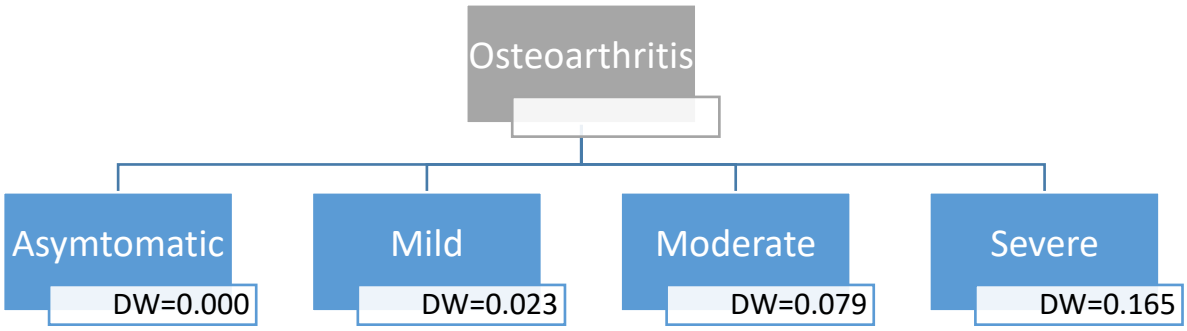

Figure 1. Osteoarthritis disease model

22.2.2 Disability weights

Table 1. Disability weights (DW) by severity levels for osteoarthritis according to the Global Burden of Disease study (Salomon et al., 2015)

Severity level	Lay description	DW
Asymptomatic	N/A	N/A
Osteoarthritis, mild	This person has pain in the leg, which causes some difficulty running, walking long distances, and getting up and down.	0.023
Osteoarthritis, moderate	This person has moderate pain in the leg, which makes the person limp, and causes some difficulty walking, standing, lifting and carrying heavy things, getting up and down, and sleeping.	0.079
Osteoarthritis, severe	This person has severe pain in the leg, which makes the person limp and causes a lot of difficulty walking, standing, lifting and carrying heavy things, getting up and down, and sleeping.	0.165

22.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Osteoarthritis parent		100%	Per definition
Asymptomatic osteoarthritis	Osteoarthritis parent	N/A	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Osteoarthritis, mild	Osteoarthritis parent	47.0%	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)

Osteoarthritis, moderate	Osteoarthritis parent	35.9%	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Osteoarthritis, severe	Osteoarthritis parent	17.1%	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)

22.2.4 Discussion

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

The severity distribution in the GBD model is based on polled estimates of four studies from three regions. Severity was classified based on the Western Ontario and McMaster Universities Arthritis Index (WOMAC) with scores 0-5 taken as mild, 6-13 as moderate, and 14 and higher as severe. It is reasonable to assume that Belgium will have estimates similar to the high-income countries.

22.3 Prevalence

Different data sources exist for osteoarthritis, 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: M16 and M17).
2. **Health insurance data:** Not applicable
3. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you suffered from osteoarthritis ?”.
4. **Sentinel GP network data (Intego):** Number of individuals with low back pain diagnosis ever recorded by GP (ICPC-2 codes L89, L90 and L91) who had a GP contact during the reference year.
5. **Sentinel GP network data (Sciensano):** not applicable. OST has not been registered by the Sciensano SGPs.

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

Source	Strengths	Weaknesses	Evaluation
Registry	N/A	N/A	N/A
Hospital discharge data	Exhaustive information on all cases hospitalized for OST Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on OST patients who were not admitted to hospital during the reference year; this might be a substantial proportion of the OST 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 is only one reimbursed medication that that would not allow a sufficiently specific diagnosis of low back pain	N/A	N/A
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 underestimation of OST prevalence 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	Sensitivity: low Specificity: high

		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 OST.	
Sentinel GP network data (Sciensano)	N/A	N/A	N/A

22.3.1 National best estimate

The **Health Interview Survey** appears to be the most complete source of information on the prevalence of OST in Belgium.

22.3.2 Discussion

Given the potentially high burden of OST, further studies are needed to quantify the validity (sensitivity/specificity) of the proposed approach. Identification through nomenclature codes could be explored together with medical experts.

22.4 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;392:1789-858.

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.

23 OPIOID DEPENDENCE

23.1 Case definition

Opioid use disorders are a group of substance-related conditions affecting the use of opioids. “Opioids” is a generic term that refers both to opiates (including natural opiates: morphine, codeine, thebaine, and semi-synthetic opiates: heroin, hydrocodone, oxycodone, buprenorphine) and to synthetic opioids (tramadol, methadone, fentanyl, …) (UNODC, 2019).

According to the Diagnostic and Statistical Manual of Mental Disorders, version IV, text revised (DSM-IV) (APA, 2000), the distinction is made between opioid abuse (OA) and opioid dependence (OD), which is the most severe form of opioid use disorders.

The case definition used here is also used in the GBD 2017 study (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018), and corresponds to the definition of opioid dependence in the DSM IV, and is defined as a “maladaptive pattern of substance use, leading to clinically significant impairment of distress” (Bell, 1994). At least three of the following criteria must have occurred during the past 12 months:

- Tolerance, characterized by either
  - a need for increased amounts of the substance to achieve intoxication; or
  - markedly diminished effect with continued use of the same amount of the substance;
- Withdrawal, characterized by either
  - withdrawal symptoms characteristic to dependence; or
  - the same (or similar) substance is taken to avoid withdrawal symptoms;
- Substance taken in progressively larger amounts or for longer periods;
- Persistent desire or unsuccessful attempts to cut down or reduce substance use;
- Disproportional time spending in obtaining the substance;
- Former social, occupational, or recreational activities are given up or reduced because of the substance use;
- Substance use is continued despite knowledge physical and psychological damages occurring as a result of the substance use.

This definition excludes opioid dependence cases due to a general medical condition (e.g. pain management).

The choice has been made to use the fourth version of the DSM instead of the most recent version being the fifth (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-5 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 (Peer et al., 2013). 12-month prevalence of opioid use disorder were slightly higher when using DSM-5 criteria instead of the fourth version (Goldstein et al., 2015). It has to be noticed that a major change from DSM-IV to DSM-5 is the combination of substance abuse disorder and substance dependence into a single substance use disorder, which requires 2 out of 11 criteria in a 12-month period for diagnosis.

23.1.1 Corresponding disease classification codes

DSM-IV-TR code

- 304.00 Opioid dependence

ICD-10 code

- F11.2 Mental and behavioral disorders due to use of opioids: dependence syndrome

ICD-9 code

- 304.0 Opioid type dependence

ICPC-2 code

- P19 Drug abuse

ATC codes

- N07BC01 buprenorphine
- N07BC02 methadone
- N07BC03 levacetylmethadol
- N07BC04 lofedixine
- N07BC05 levomethadone
- N07BC06 diamorphine
- N07BC51 buprenorphine, combinations
- N02AE buprenorphine (< 0.4mg)
- N07BB04 naltrexone
- N02AA01 morphine
- Pharmaceutical preparation containing methadone

Nomenclature codes

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

23.2 Disease model

23.2.1 Health states

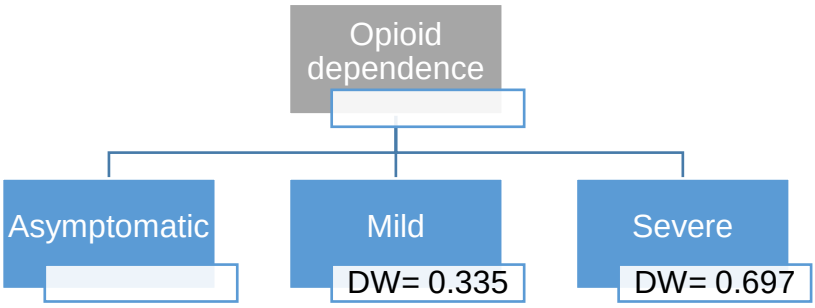

Figure 1. Opioid dependence disease model

23.2.2 Disability weights

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

Health state	Lay description	DW
Asymptomatic	Not applicable	Not applicable
Mild dependence	Uses heroin (or methadone) daily and has difficulty controlling the habit. When not using, the person functions normally.	0.335
Severe dependence	Uses heroin daily and has difficulty controlling the habit. When the effects wear off, the person feels severe nausea, agitation, vomiting, and fever. The person has a lot of difficulty in daily activities.	0.697

23.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Opioid dependence	N/A	100%	Per definition
Asymptomatic	Opioid dependence	16%	GBD 2017
Mild dependence	Opioid dependence	37%	GBD 2017
Severe dependence	Opioid dependence	47%	GBD 2017

23.2.4 Discussion

The distribution of opioid dependence cases within the different levels of severity is derived from the GBD 2017 study, in absence of Belgian data, and is determined based on data from

the (US) National Epidemiological Survey on Alcohol and Related Conditions (NESARC) (Grant & Dawson, 2006), and the Comorbidity and Trauma study conducted in 2005-2008 (EMCDDA, 2019; Wang et al., 2007).

The NESARC study Wave 1 was conducted in 2000-2001 and Wave 2 was conducted in 2004-2005. NESARC is a representative sample of the non-institutionalized US population aged 18 and older. Information on the occurrence of more than one psychological disorder or substance use disorder in the same person are collected, using definitions from the DSM-IV.

In the GBD study, a category “asymptomatic” represents the percentage of people with the disease or condition and no symptoms. The choice to include a category “asymptomatic” within the severity distribution depends on the source used to produce the prevalence estimates, and on the case definition used. Some sources will include the asymptomatic cases and other not. It is important to ensure that the proxy used for the prevalence estimates matches closely the case definition regarding the presence of symptoms or not, because this will have an influence on the severity distribution and therefore on the average disability weight derived. For the calculation of YLDs, the asymptomatic cases are not taken into account since there are not experiencing any disability.

It has to be noticed that the proportion of the opioid dependence cases in the different health states may not be fully representative of the Belgian population because of cross-cultural differences in drug consumption: in 2017, opioids dependence 12-month prevalence was 6.6 times higher in North America compared to Western and Central Europe, with respectively 4% and 0.6% (UNODC, 2019). Since the health states are not defined in terms of clinical grading scales, comparability with available epidemiological and clinical evidence is hampered.

23.3 Prevalence

23.3.1 Data sources

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

1. **Belgian Treatment Demand Indicator Registry (TDI)**: patient in contact with an inpatient or outpatient treatment centre that have started a new treatment for opioid dependence during the reference year. Treatment centres are defined as facilities or practitioners providing treatment for drug or alcohol addiction. An episode is defined as a treatment process separated by at least 6 months from a previous one in outpatient settings. In residential settings, an episode occurs each time a patient is admitted and ends when the patient leaves the centre and no further admission is foreseen.
2. **Opiates Substitution Treatment Registry (OST)**: patient with a reimbursed prescription of methadone or buprenorphine, prescribed by a medical practitioner and delivered in a

public pharmacy, in an hospital pharmacy or in a specialized centre during the reference year.

3. **Hospital Discharge data**: patient with opioid dependence admitted to the hospital during the reference year (before 2015: ICD-9 codes 304.0; after 2015 ICD-10 codes: F11.2).
4. **Health insurance data**: person with a prescription for one of the following ATC codes N07BC01, N07BC02, N07BC03, N07BC04, N07BC05, N07BC06, N07BC51, N02AE, N07BB04, N02AA01 during the reference year.
5. **Health Interview Survey**: number of respondents who have answered "opioids not prescribed for you by a doctor (e.g., fentanyl, buprenorphine, oxycodone), codeine,...)" and "during the past 12 months" to the question: "What other substances did you use, even once, and when did you take them last?".
6. **Sentinel GP network data (Intego)**: Number of individuals with "drug abuse" diagnosis ever recorded by GP (ICPC-2 code P19) who had a GP contact during the reference year.
7. **Sentinel GP network data (Sciensano)**: patient with an opioid use problem in contact for the first time with the GP and that begins a new treatment for this problem during the reference year. The treatment is defined as any activity that can be lead in order to enhance the physical, psychological or mental health state of a person with a substance problem. A treatment episode is defined as a treatment process separated by at least 6 months from a previous one.

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

Source	Strengths	Weaknesses	Evaluation
Belgian Treatment Demand Indicator Registry (TDI)	Reliable data on drug users in treatment at a national level Longitudinal approach Mandatory registration in hospitals and specialized centres Registration by professionals National database Possibility to identify 80% of the patients uniquely via the SSIN. Possibility to link these data with other databases through the SSIN (TDI-IMA databases) (Van Baelen et al., 2018)	TDI concerns only new treatment demand: incidence indicator instead of prevalence indicator. → False-positives: The registration using the SSIN is not mandatory: about 20% of the patients are anonymous and can be registered several times leading to overestimation of the number of patients (Antoine, 2018). → False-negatives: This number is supposed to be high as the register does not collect data from the GP's who are the main providers of opiates substitution treatment in the French	Sensitivity: low Specificity: high

		Community (EMCDDA, 2019a). Moreover, in 2017 in Europe, less than 15% of patients with substance dependence have received a treatment for the first time (EMCDDA, 2019b). Evidence has shown that in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019). Furthermore, in Europe, the use of opioids is also linked to OD people who seek alternatives to heroin, with a diversion of the use of methadone or buprenorphine for non-medical use, including self-medication outside treatment settings (UNODC, 2019); this OD cases are not registered. Finally, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007). Lack of registration in the non-specialized sector (GP, medical house, centres for mental health, private practice,…). Long-term treatment patients are not reported.	
Opiate Substitution Treatment Registry (OST)	Reliable data on opioid dependent patient in treatment (prevalence data) National database Longitudinal approach Unique coding of patients allowing to follow the dynamics of treatment (retention in	Case definitions are based on the prescription of medicines, not on a medical diagnosis, which generates false positives and false negatives. → <u>False positives</u>: patients without OD, treated with drugs used in opioid dependence for other reasons: for instance	Sensitivity: low Specificity: high

	treatment, type of treatment settings) Unique coding of professionals allowing to follow "doctor shopping"	chronic pain management. However, this number is assumed to be low since OST (methadone and buprenorphine) are mainly prescribed in case of opioid addiction. → False negatives: patients with opioid dependence who do not take this treatment. This number is assumed to be large since there is a large unmet need for OST (Fraeyman et al., 2016). OST delivered in prisons are not registered (Ledoux et al., 2008). OST delivered to non-residents or to patients with no health insurance are not fully registered (Ledoux et al., 2008).	
Hospital discharge data	Exhaustive information on all cases hospitalized for opioid dependence Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on patients with OD who were not admitted to hospital during the reference year: this number is assumed to be large as most treatments for drug use are provided by outpatient facilities (EMCDDA, 2019b). Furthermore, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007). 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: medium
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 OD, treated with drugs used in opioid	Sensitivity: low Specificity: low

		dependence for other reasons: for instance naltrexone is also used in the treatment of alcohol dependence. → False negatives: patients with opioid dependence who do not take this treatment. This number is supposed to be high as in 2017, in Europe, less than 15% of people with substance dependence have received a treatment for the first time (EMCDDA, 2019b), and evidence has shown that in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019). 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; it is assumed that there may be many false positive and false negatives → False positives: the HIS question relates to opioids use during the last month, even once, which leads to an overestimation of OD cases. → False negatives: drug use is known to be underestimated in household surveys (Gisle et al., 2018; Hicman et al., 2002). Not yearly available (+/- every 5 years) Comparing estimates between subgroups of the sample might lack statistical precision	Sensitivity: medium Specificity: medium

Sentinel network (Intego)	**GP data**	Diagnosis by medical professional Longitudinal approach	Case definition used in ICPC-2 code is not enough detailed and encompasses all cases of drug abuse, leading to an overestimation of opioid dependence cases. Will not capture patients that bypass the GP (ED, hospitalisation) unless the information is transmitted to the GP. While GP's are the main providers of opiates substitution treatment (OST) in the French Community, it is not the case in Flanders (EMCDDA, 2019a; Ledoux et al., 2005), and there is a considerable unmet demand for OST (UNODC, 2019). 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 opioid dependence.	Sensitivity: low Specificity: medium
Sentinel network (Sciensano)	**GP data**	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, hospitalisation) unless the information is transmitted to the GP. While GP's are the main providers of opiates substitution treatment (OST) in the French Community, it is not the case in Flanders (EMCDDA, 2019a; Ledoux et al., 2005), and there is a considerable unmet demand for OST (UNODC, 2019).	Sensitivity: low Specificity: medium

There is supposed to be a large number of false negatives: in 2017 in Europe, less than 15% of patients with substance dependence have received a treatment for the first time (EMCDDA, 2019b). Evidence has shown that in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019). Furthermore, in Europe, the use of opioids is also linked to OD people who seek alternatives to heroin, with a diversion of the use of methadone or buprenorphine for non-medical use, including self-medication outside treatment settings (UNODC, 2019); this OD cases are not registered. Finally, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007).

23.3.2 National best estimate

The **Belgian Health Interview Survey (HIS)** is assumed to yield the best estimate of opioid dependence prevalence.

23.3.3 Discussion

It has to be noticed that the number of opioid dependence (OD) cases in the general population may be underestimated using the HIS as best estimate, for several reasons:

- Population surveys do not include homeless people, people in mental institutions and prisons, however there is supposed to be a lot of cases of substance dependence in these populations (Gisle et al., 2018).
- Opioid dependence may be underreported in population surveys due to a selection bias: people with a drug dependence, especially with opioid dependence, are less likely to participate to general population surveys. However, evidence has shown good validity of self-reported substance use compared to biological measures (e.g. blood or urine samples) (Hjorthøj et al., 2012).

Another limitation of using the HIS to get the OD prevalence is that the HIS question relates to the opioid use during the past 12 months, even once, which could lead to an overestimation of opioid dependence cases. However, we take this parameter into account by including asymptomatic cases (i.e. occasional users) in the severity distribution and, therefore, in the average disability weight used to compute the Years Lived with Disability.

Despite these limitations, the HIS has been selected to be the best source to get the opioid dependence prevalence, after having considered other possibilities:

The Belgian Treatment Demand Indicator Registry does not allow to compute the prevalence of the OD cases in the population, only the incidence of the new started treatments for an opioid use problem. A pretty large number of OD cases could be missed as in Europe, the use of opioids is also linked to OD people who seek alternatives to heroin, including self-medication outside treatment settings (UNODC, 2019). Furthermore, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007), and the treatment rate for substance dependence is low: in 2017 in Europe, less than 15% of patients with substance dependence have received a treatment for the first time (EMCDDA, 2019b), and in high-income countries, Belgium included, only 12.5% of 12-month substance use disorders patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019).

The Belgian Opiate Substitution Treatment (OST) registry allows to get the prevalence of people on OST, but the number of people with opioid dependence in the population would be underestimated since the treatment rate and the demand for treatment are low.

Hospital discharge data may miss many cases as most treatments for drug use are provided by outpatient facilities (EMCDDA, 2019b). Furthermore, in Belgium, only 13% of people with substance use disorder make treatment contact in year of onset (Wang et al., 2007).

Using the health insurance data to get the OD prevalence is not enough sensitive as the treatment rate for drug dependence in Europe and in high-income countries is low (12.5%-15%) (EMCDDA, 2019b). Moreover, the specificity of this source has been assessed to be low as treatment used in opioid dependence are also prescribed for other reasons: for instance naltrexone is also used in the treatment of alcohol dependence.

Finally, we have decided not to use the sentinel GP networks as a source to compute the OD prevalence since, while GP's are the main providers of opiates substitution treatment (OST) in the French Community, it is not the case in Flanders (EMCDDA, 2019a; Ledoux et al., 2005), and there is a considerable unmet demand for OST (Fraeyman et al., 2016). Furthermore, the treatment rate of people with substance use disorders is low in Belgium, as in the rest of Europe or high-income countries (EMCDDA, 2019b): only 12.5% of 12-month substance use disorders (SUD) patients receive a treatment (either professional treatment or self-help group) (Harris et al., 2019). This proportion is 7.7% among people with SUD only, and 20.1% among patients with SUD and at least one comorbid mental disorder.

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24 PARKINSON'S DISEASE

24.1 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.

24.1.1 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.

24.2 Disease model

24.2.1 Health states

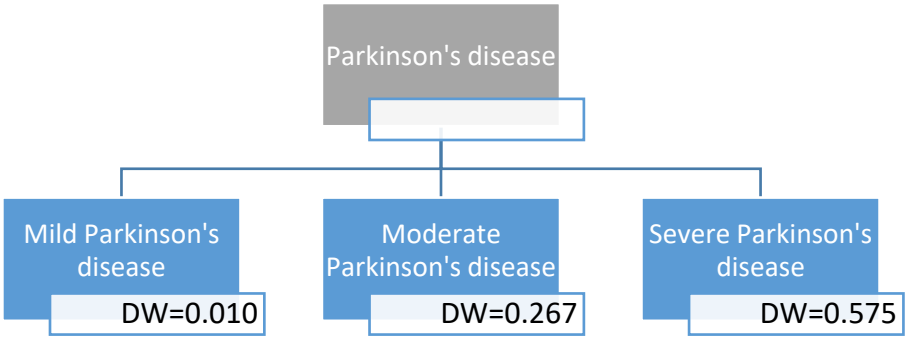

Figure 1. Parkinson's disease disease model

24.2.2 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	0.575

talking, swallowing, sleeping, and remembering things.

24.2.3 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

24.2.4 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.

24.3 Prevalence

24.3.1 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	Sensitivity: medium Specificity: high

		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. 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.		

24.3.2 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.

24.3.3 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.

24.4 References

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25 RHEUMATOID ARTHRITIS

25.1 Case definition

Rheumatoid arthritis (RHE) is a systemic autoimmune disorder that causes pain and swelling of the joints. While RHE is known to affect internal organs in addition to the joints, these extra-articular effects are not factored into the disability weights (DW) used in GBD. The reference case definition for RHE is based on the 1987 criteria by the American College of Rheumatology (ACR 1987).

25.1.1 Corresponding disease classification codes

ICD-10 codes

- M05 Rheumatoid arthritis with rheumatoid factor
- M06 Other rheumatoid arthritis
- M08 Juvenile arthritis

ICD-9 codes

- 714 Rheumatoid arthritis and other inflammatory polyarthropathies

ICPC-2 codes

- L88 Rheumatoid arthritis

ATC codes

- M01 Anti-inflammatory and anti-rheumatic products

Nomenclature codes referring to rheumatoid oarthritis

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

25.2 Disease model

25.2.1 Health states

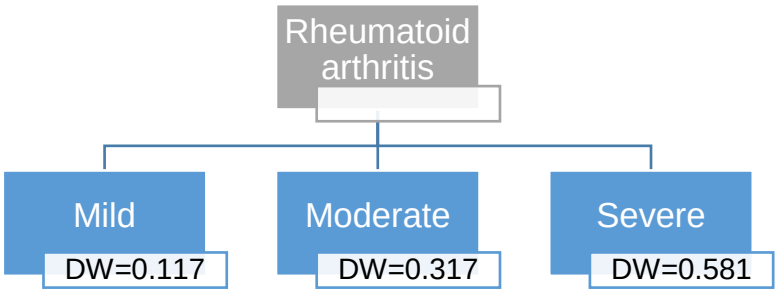

Figure 1. Rheumatoid arthritis disease model

25.2.2 Disability weights

Table 1. Disability weights (DW) by severity levels for rheumatoid arthritis according to the Global Burden of Disease study (Salomon et al., 2015)

Severity level	Lay description	DW
Rheumatoid arthritis, mild	This person has moderate pain and stiffness in the arms and hands which causes difficulty lifting, carrying, and holding things, and trouble sleeping because of the pain.	0.117
Rheumatoid arthritis, moderate	This person has moderate pain and stiffness in the arms and hands which causes difficulty lifting, carrying, and holding things, and trouble sleeping because of the pain.	0.317
Rheumatoid arthritis, severe	This person has severe, constant pain, and deformity in most joints, causing difficulty moving around, getting up and down, eating, dressing, lifting, carrying, and using the hands. The person often feels sadness, anxiety, and extreme fatigue.	0.581

25.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Rheumatoid arthritis parent		100%	Per definition
Asymptomatic rheumatoid arthritis	Rheumatoid arthritis parent	N/A	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Rheumatoid arthritis, mild	Rheumatoid arthritis parent	47.0%	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Rheumatoid arthritis, moderate	Rheumatoid arthritis parent	35.9%	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)
Rheumatoid arthritis, severe	Rheumatoid arthritis parent	17.1%	GBD 2017 Disease and Injury Incidence and Prevalence Collaborators (2018)

25.2.4 Discussion

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

25.3 Prevalence

Different data sources exist for rheumatoid arthritis, 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 714; after 2015 ICD-10 codes: M05, M06 and M08).
2. **Health insurance data:** Not applicable
3. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you suffered from rheumatoid arthritis ?”.
4. **Sentinel GP network data (Intego):** Number of individuals with RHE diagnosis ever recorded by GP (ICPC-2 codes L88) who had a GP contact during the reference year.
5. **Sentinel GP network data (Sciensano):** not applicable. RHE has not been registered by the Sciensano SGPs.

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

Source	Strengths	Weaknesses	Evaluation
Registry	N/A	N/A	N/A
Hospital discharge data	Exhaustive information on all cases hospitalized for RHE Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on RHE patients who were not admitted to hospital during the reference year; this might be a substantial proportion of the RHE 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 is only one reimbursed medication that that would not allow a sufficiently specific diagnosis of rheumatoid arthritis	N/A	N/A
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 underestimation of RHE prevalence Not yearly available (+/- every 5 years) Comparing estimates between subgroups of the sample might	Sensitivity: high Specificity: high

		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 RHE.	Sensitivity: low Specificity: high
Sentinel GP network data (Sciensano)	N/A	N/A	N/A

25.3.1 National best estimate

The **Health Interview Survey** appears to be the most complete source of information on the prevalence of RHE in Belgium.

25.3.2 Discussion

Given the potentially high burden of RHE, further studies are needed to quantify the validity (sensitivity/specificity) of the proposed approach. Identification through nomenclature codes could be explored together with medical experts.

25.4 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;392:1789-858.

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.

26 SCHIZOPHRENIA

26.1 Case definition

Schizophrenia is a severe mental disorder characterised by fundamental disturbances in thinking, perception and emotions. According to the Diagnostic and Statistical Manual of Mental Disorders, version IV, text revised (DSM-IV-TR) (APA, 2000), several diagnostic criteria are to be fulfilled to meet the case definition of schizophrenia:

A. Characteristic symptoms: Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):
   - Delusions
   - Hallucinations
   - Disorganized speech
   - Grossly disorganized or catatonic behavior
   - Negative symptoms, i.e. loss of interest, affective flattening

B. Social/occupational dysfunction

C. Continuous signs of disturbance persisting for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms.

D. Are excluded of the case definition: mood disorders, condition due to substance use or general medical condition and disorder in relationship to a pervasive developmental disorder (e.g. autistic disorder).

The choice has been made to use the fourth version of the DSM instead of the most recent version being the fifth (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-5 have a minimal impact on the prevalence of schizophrenia diagnoses, as only modest changes of diagnostic criteria has been incorporated since the DSM-IV criteria have shown high reliability and fair validity (Tandon et al., 2013).

26.1.1 Corresponding disease classification codes

DSM-IV-TR

- 295.10 Schizophrenia, disorganized type
- 295.20 Schizophrenia, catatonic type
- 295.30 Schizophrenia, paranoid type
- 295.60 Schizophrenia, residual type

- 296.70 Schizoaffective disorder
- 295.90 Schizophrenia, undifferentiated type

ICD-10 codes

- F20 Schizophrenia
- F25 Schizoaffective disorders

ICD-9 codes

- 295.0 Simple type schizophrenia
- 295.1 Disorganized type schizophrenia
- 295.2 Catatonic type schizophrenia
- 295.3 Paranoid type schizophrenia
- 295.5 Latent schizophrenia
- 295.6 Schizophrenic disorder, residual type
- 295.7 Schizoaffective disorder
- 295.8 Other specified types of schizophrenia

ICPC-2 code

- P72 Schizophrenia

ATC codes

- N05A Antipsychotics

Nomenclature codes

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

26.2 Disease model

26.2.1 Health states

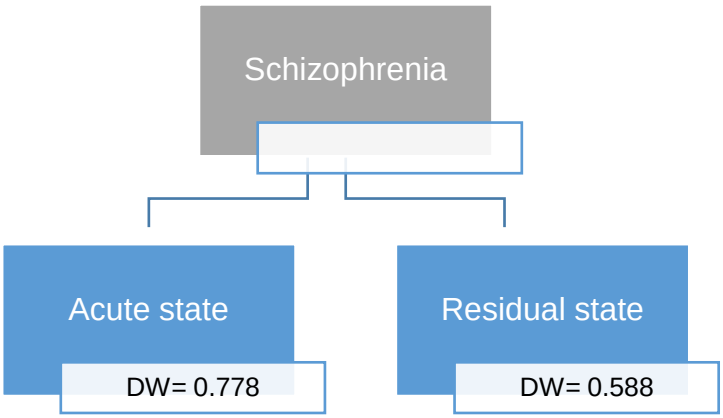

Figure 1. Schizophrenia disease model

26.2.2 Disability weights

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

Health state	Lay description	DW
Acute state	Hears and sees things that are not real and is afraid, confused, and sometimes violent. The person has great difficulty with communication and daily activities, and sometimes wants to harm or kill himself (or herself).	0.778
Residual state	Hears and sees things that are not real and has trouble communicating. The person can be forgetful, has difficulty with daily activities, and thinks about hurting himself (or herself).	0.588

26.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
Schizophrenia	N/A	100%	Per definition
Schizophrenia, acute state	Schizophrenia	63%	Ferrari et al. 2012
Schizophrenia, residual state	Schizophrenia	37%	Ferrari et al. 2012

26.2.4 Discussion

In absence of Belgian data, the proportion of cases in the acute and residual health states is derived from a systematic literature review performed in the framework of the Global Burden of Disease study (Ferrari et al., 2012). A meta-analysis was carried out to pool the estimates of schizophrenia cases in each health states across studies. However, given the need to include studies reporting cases of schizophrenia as described in the case definition, as well the different health states similar to those used in the GBD methodology, the number of studies included is limited. For that reason, and also because the DSM-IV diagnosis criteria for schizophrenia are dependent of the environmental context, the proportion of cases in the different health states may not be fully representative of the Belgian population.

26.3 Prevalence

26.3.1 Data sources

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

1. **Register**: not applicable: there is no registry for schizophrenia in Belgium.

2. **Hospital Discharge data (Minimum psychiatric dataset)**: patient with schizophrenia admitted to a psychiatric hospital, or a psychiatric service in a general hospital, or an initiative of sheltered living or a psychiatric care home during the reference year (before 2015: ICD-9 codes 295.0-3, 295.5, 295.6, 295.8; after 2015 ICD-10 code: F20).
3. **Health insurance data**: person with a prescription for ATC codes of the group N05A during the reference year.
4. **Health Interview Survey**: not applicable: there is no question related to schizophrenia in the Belgian Health Interview Survey.
5. **Sentinel GP network data (Intego)**: number of individuals with schizophrenia diagnosis ever recorded by GP (ICPC-2 code P72) who had a GP contact during the reference year.
6. **Sentinel GP network data (Sciensano)**: not applicable: schizophrenia has not been registered by the Sciensano sentinel GP network.

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

Source	Strengths	Weaknesses	Evaluation
Registry	Not applicable: there is no registry for schizophrenia in Belgium.	N/A	N/A
Hospital discharge data (Minimum psychiatric dataset)	Exhaustive information on all cases hospitalized for schizophrenia Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on patients with schizophrenia who were not admitted to hospital during the reference year. This number could be high since the World Mental Health and ESEMeD studies have shown a poor treatment rate (inpatient or outpatient professional help) in mental disorders in Belgium: 46.1% of serious cases were untreated during the last 12-months (Demyttenaere et al., 2004). HDD is primarily used for administrative purposes, which could result in some problems when data have to be used for epidemiological purposes	Sensitivity: medium Specificity: high
Health insurance data (IMA/EPS)	Case definition based on medication and care	Case definitions are based on the prescription of medicines, not on a	Sensitivity: low Specificity: low

	Large, representative sample Longitudinal approach	medical diagnosis, which generates false positives and false negatives: → False positives: patients without schizophrenia, treated with antipsychotics for other reasons, for instance dementia, bipolar disorder or for sedative effect. Antipsychotics are frequently prescribed for a wide range of psychiatric and non-psychiatric diseases (Morrens et al., 2015). → False negatives: patients with schizophrenia who don't take the treatment. Evidence has shown a high rate of non-adherence in prescribed drugs: from 30% to 61% of the patients with schizophrenia don't take their treatment or take it irregularly (Velligan et al., 2010; Haddad et al., 2014). People who are not insured (e.g. homeless and illegal people, foreigners with their official residence abroad) are not included	
Health Interview Survey	Not applicable: there is no question related to schizophrenia in the Belgian Health Interview Survey	N/A	N/A
Sentinel network GP data (Intego)	Diagnosis by medical professional Longitudinal approach	Will not capture patients that bypass the GP (directly consulting a specialist, ED, hospitalisation) unless the information is transmitted to the GP. In Belgium, only 33% of people suffering from a mental health problem is searching for a professional help (Bruffaerts et al., 2004),	Sensitivity: medium Specificity: high

		which means that the number of positive cases in the population could be underestimated. However, in more than 70% of the cases, this professional help is provided by GPs (Bruffaerts et al., 2004). 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 schizophrenia	
Sentinel network data (Sciensano)	GP Not applicable: schizophrenia has not been registered by the Sciensano sentinel GP network.	N/A	N/A

26.3.2 National best estimate

The Intego sentinel GP network has been selected as the best estimate to yield the prevalence of schizophrenia in Belgium. As these results only reflect the situation in Flanders, a correction factor is applied, which is calculated as the ratio of the use of antipsychotics in Brussels and Wallonia, respectively, by sex and by age groups, and the use of antipsychotics in Flanders, using the health insurance data (minimal treatment duration of 3 months). The Intego sentinel GP network prevalence of schizophrenia is therefore multiplied by the different ratios obtained to get the prevalence of schizophrenia in the regions of Brussels and Wallonia.

26.3.3 Discussion

The general practitioner (GP) is often the first contact with the health care system for a patient with mental health problems seeking help. In Belgium, only 33% of people suffering from a mental health problem is searching for a professional help. Among them, 34% consults a GP and 43% contacts a psychiatrist and a GP, which means that GP is involved in 7 out of 10 cases as far as it concerns diagnosis and/or treatment of people with mental health disorders (Bruffaerts et al., 2004). This explains why, despite of pretty low rates of treatment-seeking,

and despite the fact that the recognition of the disease may be less easy for the GPs than for a psychiatrist, we have selected the Intego sentinel GP network as best source to assess the schizophrenia prevalence in the general population.

However, it must be noted that the ICPC-2 code P72 used for schizophrenia in the Intego dataset includes conditions and disorders that go beyond the strict definition of schizophrenia such as different kind of delusions, delusional disorder, paranoia, etc. which could lead to an overestimation of the prevalent cases of schizophrenia.

The World Mental Health and ESEMeD studies have shown a poor treatment rate (inpatient or outpatient professional help) in mental disorders in Belgium: 46.1% of serious cases were untreated during the last 12-months (Demyttenaere et al., 2004). This can be partly explained by the poor rate of help-seeking in people with mental health problems (Alonso et al., 2004) and also by a suboptimal accessibility of mental health care, which is complicated in Belgium given the large diversity of services offered and the fragmentation of the offer (Mistiaen et al., 2019). Since a vast majority of people with schizophrenia is living in the community, assessing the prevalence of this disease using the hospital discharge data, therefore, could lead to underestimation. However, evidence also showed that serious mental health cases are more likely to be treated than less severe cases and to get help via the specialized health care sector versus via the primary health care (Demyttenaere et al., 2004; Bijl et al., 2003). Indeed, in 2003, in Belgium, about 50% of the patients admitted to a psychiatric hospital, or a psychiatric service in a general hospital, or an initiative of sheltered living or a psychiatric care home suffered from schizophrenia (Verniest et al., 2008).

In Belgium, the organization of mental health care delivery system has been transformed by several reforms over the last decennia, the last one being the “Article 107 project” in 2010 which aims to reduce residential treatment (deinstitutionalisation, shortened length of stay), and to reinforce ambulatory psychiatric care, integrated and continued care, and coordination between health care providers (Mistiaen et al., 2019). Despite these measures, Belgium has the second highest number of psychiatric beds compared to the number of inhabitants among OECD countries (OECD, 2013), and evidence has shown a low effect of the reform on the hospitalisation rate, and a continued influence of hospitals despite the goal of deinstitutionalisation (Lorant et al., 2019; Nicaise et al., 2014). Therefore, the hospital discharge data, which contains all admissions in psychiatric hospitals, psychiatric service in general hospitals, initiative of sheltered living and psychiatric care, could be an alternative source to estimate the prevalence of schizophrenia in the general population.

Finally, antipsychotics play an important role in the symptomatic treatment of schizophrenia and in preventing relapse. With psychosocial interventions and rehabilitation, they are one of

the three pillars of the treatment. However, using the number of reimbursed antipsychotics as a proxy to assess the schizophrenia prevalence in Belgium is not specific enough and would lead to a large number of false positives as antipsychotics are frequently prescribed for a wide range of psychiatric and non-psychiatric diseases (Morrens et al., 2015), for instance in bipolar disorder or dementia. Morrens et al. (2015) have shown a large amount of off-labels use in antipsychotics over a 15-years period in Belgium: only 29.5% of prescriptions for antipsychotics were for psychotic disorders. Furthermore, evidence has shown a high rate of non-adherence in prescribed drugs: from 30% to 61% of the patients with schizophrenia do not take their treatment or take it irregularly (Velligan et al., 2010; Haddad et al., 2014). Health insurance data source, therefore, has not been selected to get the schizophrenia prevalence in Belgium.

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27 TENSION TYPE HEADACHE (TTH)

27.1 Case definition

Tension-type headache (TTH) is characterized by a dull, non-pulsatile, diffuse, band-like (or vice-like) pain of mild to moderate intensity in the head or neck. The reference diagnostic criteria for migraine are from the International Classification of Headache Disorders **ICHD-3**, which describe five criteria:

1. At least 10 attacks fulfilling criteria 2-5
2. Lasing from 30 minutes to 7 days
3. At least two of the following four characteristics:
    a. Bilateral location
    b. Pressing or tightening (non-pulsating) quality
    c. Mild or moderate intensity
    d. Not aggravated by routine physical activity such as walking or climbing stairs
4. Both of the following:
    a. No nausea or vomiting
    b. No more than one of photophobia or phonophobia
5. Not better accounted for by another ICHD-3 diagnosis Definite migraine is headache that satisfies all the criteria outlined above, while probable migraine satisfies all of the above criteria except one.

Definite tension-type headache is headache that satisfies all criteria outlined above, while probable tension-type headache satisfies all of the above criteria except one.

27.1.1 Corresponding disease classification codes

ICD-10 codes

- G44.2 Tension-type headache

ICD-9 codes

- 339.1 Tension type headache

ICPC-2 codes

- N95 Tension headaches

ATC codes

- Not applicable: there are no nomenclature codes sufficiently specific for Tension type headache.

Nomenclature codes

- Not applicable: there are no nomenclature codes sufficiently specific for Tension type headache.

27.2 Disease model

27.2.1 Health states

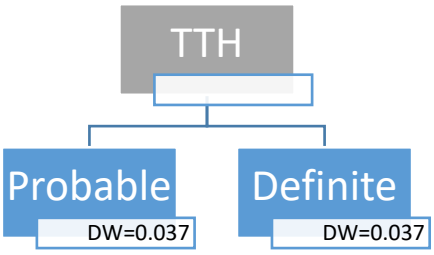

Figure 1. TTH disease model

The proportion of time symptomatic is 0.029 for definite TTH and 0.021 for probable TTH (Vos et al., 2020). However, precise and valid estimates for the proportion of definite and probable migraine are lacking for Belgium. Therefore, the estimated proportion of time symptomatic for the entire migraine population was inferred from the pooled data analysis in the GBD-2016, which estimated the proportion of time symptomatic at 0.047 for the entire migraine population (Stovner et al., 2018).

An important difference in the current disease model compared to the GBD-model is the handling of medication-overuse headache (MoH) data. Up to 20% of chronic TTH cases could show signs of MoH (Monteith & Oshinsky, 2009), which is lower compared to migraine, but still substantial. In the disease model of the GBD-study a substantial part of the MoHs are attributed to TTH. Consequently, the estimated total disability for TTH in the current study will be lower compared to the disability reported by the GBD-study. Due to the heterogeneity of MoH and unavailability of diagnostic codes, it was decided to currently exclude MoH from the Belgian model.

27.2.2 Disability weights

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

Health state	Lay description	DW
TTH, probable	This person has tension type headache that is perfectly matching all diagnostic criteria	0.037
TTH, definite	This person has tension type headache that is imperfectly matching all diagnostic criteria	0.037

27.2.3 Proportion of patients in the considered health states

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

Health state	Parent	Proportion	Source
TTH	N/A	100%	Per definition
TTH, probable		NA	
TTH, definite		NA	

27.2.4 Discussion

Disability weights for the Belgian national burden of disease study are adapted from the Global Burden of Disease study (Vos et al., 2020), as these provide an exhaustive set of internally consistent disability weights.

Two states are described in the GBD-study, which were given an identical disability weight, but differed in their estimated proportion of time symptomatic. Based on 7 studies, the pooled overall proportion of time symptomatic was estimated at 0.047 (Salomon et al., 2015).

27.3 Prevalence

27.3.1 Data sources

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

1. **Hospital discharge data:** patient with TTH admitted to the hospital during the reference year (before 2015: ICD-9 code; after 2015 ICD-10 code).
2. **Health insurance data:** TTH-specific medication are not available.
3. **Health Interview Survey:** number of respondents with positive answer to the question “in the past 12 months, have you had a severe headache such as migraine?”.
4. **Sentinel GP network data (Intego):** number of individuals with TTH diagnosis ever recorded by GP (ICPC-2 codes N95) who had a GP contact during the reference year.
5. **Sentinel GP network data (Sciensano):** not applicable; TTH has not been registered by the Sciensano SGPs network.

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

Source	Strengths	Weaknesses	Evaluation
Hospital discharge data	Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	Only information available on other headache disorders that are not TTH. 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: medium
Health insurance data (IMA/EPS)	Not applicable		
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 TTH prevalence; integration with information on disability or health-related quality of life may increase specificity Question includes all headaches that could be perceived migraine-like. Not yearly available (+/- every 5 years) Comparing estimates between subgroups of the sample might lack statistical precision	Sensitivity: high 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 TTH.	Sensitivity: medium Specificity: high
Sentinel GP network data (Sciensano)	Not applicable. TTH has not been registered by the Sciensano SGPs.		

27.3.2 National best estimate

Intego appears to be the most appropriate source of information on the prevalence of TTH in Belgium, but only covers the region of Flanders. However, the ICPC-2 code for tension headaches might constitute more headache forms compared to those defined under the case definition (1.1).

27.3.3 Discussion

There is currently only one dataset available that can be used to give an estimate on the prevalence of TTH in Belgium with reasonable sensitivity and specificity. However, patients with tension-type headache might never contact their general practitioner, and might treat their TTH by self-care with or without non-prescribed drugs (Loder & Rizzoli, 2008), which has been proven to be an effective treatment strategy (Probyn et al., 2017).

Given the high burden and prevalence of TTH and tension-like headaches, further studies are needed to quantify the validity (sensitivity/specificity) of the proposed approach for defining the prevalence of TTH.

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28 UNIPOLAR DEPRESSIVE DISORDERS

28.1 Case definition

Unipolar depressive disorders cover a range of common mental disorders that causes impairment in social and occupational functioning, associated with a higher risk of death, through suicide in the most severe form but also from physical illness such as cardiovascular diseases. Unipolar depression occurs in absence of history of mood elevation that occurs in bipolar disorders (Symonds & Anderson, 2016).

Unipolar depressive disorders (UDD) include two main sub-categories, depending on severity and on whether it is episodic or persistent: **major depressive disorder (MDD), or major depression** and **dysthymia**, a persistent, mild depressive disorder.

According to the Diagnostic and Statistical Manual of Mental Disorders, version IV, text revised (DSM-IV-TR) (APA, 2000), the following diagnostic criteria must be fulfilled to meet the case definition of the unipolar depressive disorders:

- **Major depression**: over the previous 2 weeks, five or more of the following have been present most of the time (must include at least one of the first two 'core' symptoms):
  - depressed mood most of the day (e.g. sad, empty, hopeless)
  - loss of interest or pleasure in almost all activities nearly every day
  - significant appetite/weight loss or gain
  - insomnia or hypersomnia
  - psychomotor agitation or retardation (observable by others)
  - fatigue or loss of energy
  - feelings of worthlessness or excessive guilt
  - diminished concentration or indecisiveness
  - recurrent thoughts of death, or suicidal thoughts, plans or attempts

Severity can be mild, moderate or severe, and the depressive episode can be classified as single or recurrent.

- **Dysthymia**: depressed mood for most of the day, for more days than not, for at least 2 years, together with two or more of:
  - poor appetite or overeating
  - insomnia or hypersomnia
  - low energy or fatigue
  - low self-esteem
  - impaired concentration or indecisiveness
  - hopelessness

Seasonal depression and postnatal depression are included in these case definitions.

Are excluded of these case definitions: psychotic depression, bipolar depression, bereavement depression, and symptoms of depression in relation with a medical condition (e.g. neurological causes; medication).

The choice has been made to use the fourth version of the DSM instead of the most recent version being the fifth (published in 2013) for comparability reasons since DSM-IV classification is widely used in research for more than twenty years, and the DSM-IV is also the classification used in the GBD studies. It should be noticed that using the DSM-V classification for the case definition of depressive disorders would increase the number of positive cases compared to using the DSM-IV-TR due to different changes (Rodríguez-Testal et al., 2014): first, the incorporation of the specifier "with anxious distress" in the depressive disorders acknowledges the existence of an anxio-depressive emotional combination, which was former included under "unspecified anxiety disorders" in the DSM-IV-TR. Second, in the category of Major depressive disorder (MDD), the differentiation between single and recurrent episode disappears; chronic forms of MDD and Dysthymic disorder are now integrated in the new Persistent depressive disorder. Finally, if the bereavement depression was clearly excluded in the DSM-IV-TR, to avoid the medicalization of the natural course of grief, it is not the case in the DSM-V, which could lead to an increase of the MDD cases diagnosed.

28.1.1 Corresponding disease classification codes

DSM-IV-TR codes

Major depressive disorder

- 296.20 Major depressive disorder, single episode, unspecified
- 296.21 Major depressive disorder, single episode, mild
- 296.22 Major depressive disorder, single episode, moderate
- 296.23 Major depressive disorder, single episode, severe without psychotic features
- 296.24 Major depressive disorder, single episode, severe with psychotic features
- 296.25 Major depressive disorder, single episode, in partial remission
- 296.26 Major depressive disorder, single episode, in full remission
- 296.30 Major depressive disorder, recurrent, unspecified
- 296.31 Major depressive disorder, recurrent, mild
- 296.32 Major depressive disorder, recurrent, moderate
- 296.33 Major depressive disorder, recurrent, severe without psychotic features
- 296.34 Major depressive disorder, recurrent, severe with psychotic features
- 296.35 Major depressive disorder, recurrent, in partial remission

- 296.36 Major depressive disorder, recurrent, in full remission
- 311 Depressive disorder, NOS

Dysthymia

- 300.4 Dysthymic disorder

ICD-10 codes

Major depressive disorder

- F32 Depressive episode
- F33 Recurrent depressive disorder

Dysthymia

- F34.1 Dysthymia

ICD-9 codes

Major depressive disorder

- 296.2 Major depressive disorder, single episode
- 296.3 Major depressive disorder, recurrent episode
- 311 Depressive disorder, not elsewhere classified

Dysthymia

- 300.4 Dysthymic disorder

ICPC-2 code

- P76 Depressive disorder

ATC codes

- N06A Antidepressants
- N06C Psycholeptics and psychoanaleptics in combination

Nomenclature codes

- Not applicable: there are no nomenclature codes sufficiently specific for the treatment of unipolar depressive disorder.

28.2 Disease model

28.2.1 Health states

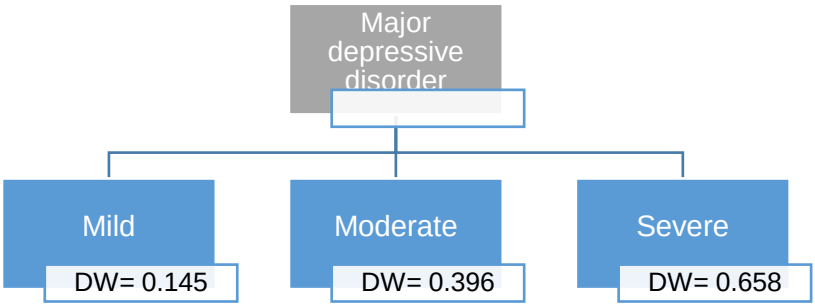

Figure 1. Major depressive disorder disease model

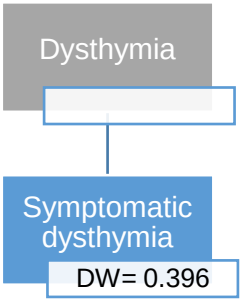

Figure 2. Dysthymia disease model

28.2.2 Disability weights

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

Health state	Lay description	DW
Major depressive disorder, mild	Feels persistent sadness and has lost interest in usual activities. The person sometimes sleeps badly, feels tired, or has trouble concentrating but still manages to function in daily life with extra effort.	0.145
Major depressive disorder, moderate	Has constant sadness and has lost interest in usual activities. The person has some difficulty in daily life, sleeps badly, has trouble concentrating, and sometimes thinks about harming himself (or herself).	0.396
Major depressive disorder, severe	Has overwhelming, constant sadness and cannot function in daily life. The person sometimes loses touch with reality and wants to harm or kill himself (or herself).	0.658

Table 2. Disability weights (DW) by health state for Dysthymia according to the Global Burden of Disease study (Salomon et al., 2015)

Health state	Lay description	DW
Symptomatic dysthymia	Feels persistent sadness and has lost interest in usual activities. The person sometimes sleeps badly, feels tired, or has trouble concentrating but still manages to function in daily life with extra effort.	0.145

28.2.3 Proportion of patients in the considered health states

Table 3. Proportion of patients in the different health states considered in the Major depressive disorder disease model, Belgium.

Health state	Parent	Proportion	Source
Major depressive disorder	N/A	100%	Per definition
Major depressive disorder, mild	Major depressive disorder	69%	GBD 2017
Major depressive disorder, moderate	Major depressive disorder	20%	GBD 2017
Major depressive disorder, severe	Major depressive disorder	12%	GBD 2017

Table 4. Proportion of patients in the different health states considered in the Dysthymia disease model, Belgium.

Health state	Parent	Proportion	Source
Dysthymia	N/A	100%	Per definition
Dysthymia, symptomatic	Dysthymia	100%	GBD 2017

Given the milder and more stable presentation of dysthymia, it was assigned the same disability weight as that for mild major depressive disorder.

28.2.4 Discussion

The distribution of the unipolar depressive disorders (UDD) cases into the different health states has been adapted from the severity splits used in the GBD 2017 study (Salomon et al., 2015). In the GBD 2017 study, two population surveys were used to estimate the proportion of major depressive disorder (MDD) cases in the asymptomatic; mild; moderate and severe diseases categories, and the proportion of dysthymia cases in the asymptomatic and symptomatic categories:

The (US) National Epidemiological Survey on Alcohol and Related Conditions (NESARC) (Grant & Dawson, 2006). Wave 1 was conducted in 2000-2001 and Wave 2 was conducted in 2004-2005. NESARC is a representative sample of the non-institutionalized US population

aged 18 and older. Information on the occurrence of more than one psychological disorder or substance use disorder in the same person are collected, using definitions from the DSM-IV.

The Australian National Survey of Mental Health and Wellbeing of Adults (NSMHWB) 1997 (Andrews et al., 1999). NSMHWB is a representative sample of non-institutionalized adults in Australia. They were screened for mental and substance use disorders via the Composite International Diagnostic Interview (CIDI), a standard questionnaire based on criteria from ICD-10 and DSM-IV. Both 1-month and 12-month prevalence are available.

The choice has been made to adapt this distribution of UDD cases to match the case definition used. In the GBD study, a category “asymptomatic” represents the percentage of people with the disease or condition and no symptoms. For the calculation of YLDs, these cases are not taken into account since there are asymptomatic and are not experiencing any disability. Although in the GBD study, there is a percentage of MDD and dysthymia cases in the asymptomatic category, we have made the choice to assume that there are no asymptomatic cases considering the case definitions used, given that individuals suffering from depressive disorders are experiencing significant distress and disability, and are thus not asymptomatic (Wakefield et al., 2010).

It must be noticed that the proportion of the unipolar depressive disorders cases in the different health states may not be fully representative of the Belgian population because of regional differences in depressive disorders. However, evidence has shown similar prevalence of depressive disorders in Western Europe, North America and Australia, with a slightly higher trend in Europe (Ferrari et al., 2013).

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

28.3 Prevalence

28.3.1 Data sources

Different data sources exist for unipolar depressive disorders (UDD), each with a specific case definition:

1. **Register**: not applicable: there is no registry for UDD in Belgium.
2. **Hospital Discharge data (Minimum psychiatric dataset)**: patient with UDD admitted to a psychiatric hospital, or a psychiatric service in a general hospital, or an initiative of sheltered living or a psychiatric care home during the reference year (before 2015: ICD-9 codes 296.2-3, 300.4, 311; after 2015 ICD-10 codes: F32-33-34.1).

3. **Health insurance data**: person with a prescription for ATC codes N06A and/or N06C during the reference year.
4. **Health Interview Survey**: the prevalence of UDD has been assessed via the “Patient Health Questionnaire 9-item depression scale” (PHQ-9) (Kroenke et al., 2001), with the following question and items: “Over the last 2 weeks, how often have you been bothered by any of the following problems (0:Not at all; 1: Several days; 2: More than half the days; 3: Nearly every day)?”:
    1. Feeling down, depressed or hopeless
    2. Little interest or pleasure in doing things
    3. Trouble falling or staying asleep, or sleeping too much
    4. Feeling tired or having little energy
    5. Poor appetite or overeating
    6. Feeling bad about yourself – or that you are a failure – or have let yourself or your family down
    7. Trouble concentrating on things, such as reading the newspaper or watching television
    8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual
    9. Thoughts that you would be better off dead or of hurting yourself in some way
    - *Major depressive disorder*: the case definition is based on an algorithm in which 5 items out of the first 8 must be present at least "more than half of the days" of which one of the first two items must be present (1 or 2). Item 9 (thoughts of death) is taken into account as soon as it is present "several days".
    - *Dysthymia*: the case definition is based on an algorithm in which 2 or more items out of the 3 to 7 must be present at least "more than half of the days”, in addition to the first item that must be present at this frequency (feeling depressed).

5. **Sentinel GP network data (Intego)**: number of individuals with a depressive disorder diagnosis ever recorded by GP (ICPC-2 code P76) who had a GP contact during the reference year.
6. **Sentinel GP network data (Sciensano)**: number of individuals of ≥18 years who were diagnosed by their GP with a new episode of depression in Belgian sentinel general practices (SGP) during 2008.

Table 5. Potential sources and methods for the computation of unipolar depressive disorders (UDD) prevalence in Belgium

Source	Strengths	Weaknesses	Evaluation
Registry	Not applicable: there is no registry for UDD in Belgium.	N/A	N/A
Hospital discharge data	Exhaustive information on all cases hospitalized for unipolar depressive disorders Diagnoses by medical doctor Official database, organized and managed by public health authorities National database	No information on patients with UDD who were not admitted to hospital during the reference year; this number is supposed to be high since most of mild and moderate cases of depression are not requiring an hospitalization (Moraska et al., 2013; Birnbaum et al., 2010). 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 with unipolar depressive disorders treated with psychotherapy only, or who have decided to stop their treatment; Patients without UDD treated with antidepressants or psycholeptics and psychoanaleptics in combination for other reasons, for instance anxiety disorder. → False negatives: patients with UDD who don't take this treatment. They are supposed to be few as in Belgium, 79% of patients with a mood disorder who have been seeking professional help have received a medicinal treatment	Sensitivity: medium Specificity: low

		(Bruffaerts et al., 2004), but they were only 43% to seek help. 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; it is assumed that there may be many false positives 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 be related to UDD	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)	Only the new episodes of depression are registered (incidence rates), not possible to get prevalence data. Will not capture patients that bypass the GP (ED, hospitalization) unless the information is transmitted to the GP Only one registration in 2008.	Sensitivity: low Specificity: high

28.3.2 National best estimate

The **Belgian Health Interview Survey (HIS)** is assumed to yield the best estimate of unipolar depressive disorders prevalence.

28.3.3 Discussion

It has to be noticed that the number of unipolar depressive disorders (UDD) cases in the general population may be underestimated using the HIS as best estimate, for several reasons:

Population surveys do not include homeless people, people in mental institutions and prisons, however there is supposed to be a lot of cases of depression in these populations (Fazel et al., 2008; Majekodunmi et al., 2017).

UDD may be underreported in population surveys due to a denial of the disease or underestimation of the symptoms, and a bias of low social desirability, i.e. the fact that people are less likely to report diseases or conditions that are not socially accepted. However, in addition to a self-reported indicator of depression, the Belgian health interview survey assess the prevalence of UDD using an internationally validated diagnostic instrument (PHQ-9), which has showed good sensitivity (88%) and specificity (88%) (Kroenke et al., 2001).

Another limitation of using the HIS to get the UDD prevalence is that the HIS question relates to symptoms of depression that occurred “over the last two weeks”, but the case definition of dysthymia implies that symptoms must have occurred for at least two years. This could lead to a possible overestimation of dysthymic cases.

Despite these limitations, the HIS has been selected to be the best source to get the unipolar depressive disorders prevalence, after having considered other possibilities:

Using the sentinel GP network data as a source to yield the prevalence of unipolar depressive disorders (UDD) could be an alternative, as Ansseau et al. (2004) have shown a high prevalence of mental disorders in primary care in Belgium, with 31% of the patients detected with a mood disorder in a general practice setting. Moreover, in Belgium, 85% of people with a mood disorder (defined as major depression and dysthymia) who seeking health care consulted a GP (Bruffaerts et al., 2004). However, they were only 43% to actually seek health care. The treatment seeking is getting better over time, since 94% of people with a mood disorder making treatment contact 50 years after the onset of disorder, with a median duration of delay of 1 year (Bruffaerts et al., 2007). Regarding self-reported data, in 2018 in Belgium, 81% of the people who have declared suffering from depression consulted a professional of

health (Gisle et al., 2018). It must be noted that identification of mild depression in primary care is not easy, and a lot of less severe UDD cases could be missed (Mitchell et al., 2011).

Given that the Intego Sentinel GP network has only a partly cover of the country and does not allow to make the distinction between the major depressive disorder and the dysthymia (which is necessary because the two diseases are not following the same disease model and don't have the same disability weights), and given that the Sciensano sentinel GP network does have a national cover but has only collected incidence data in 2008, the sentinel GP networks have not been selected as best estimate to get the prevalence of UDD.

Assessing the prevalence of unipolar depressive disorder using the health insurance data has not been considered as an option given the lack of specificity: it is assumed to have a substantial number of false positives since more than a third of patients discontinues treatment after a new antidepressants prescription (Pradier et al., 2020), since 20% of patients with a mood disorder who have been seeking professional help received no treatment or psychological help only (Bruffaerts et al., 2004), and since only 54% of antidepressants prescriptions are associated with a diagnosis of depression (Schwalm et al., 2017). It is true that antidepressants are commonly prescribed for the treatment of depression, however, if 79% of patients with a mood disorder who have been seeking professional help have received a medicinal treatment, they were only 43% to seek help for the past 12 months preceding the study (Bruffaerts et al., 2004). This proportion is higher when looking at self-reported data: in 2018, 81% of the people who have declared suffering from depression consulted a professional of health, and among them, 67% received a medicinal treatment (Gisle et al., 2018). Finally, international guidelines recommend the prescription of an antidepressant medication only for severe cases of depression (Fournier et al., 2010), which involves to miss a lot of mild and moderate cases using the health insurance data as best estimate.

Finally, since the hospitalisation rate of people suffering from depression increases significantly with the severity of the symptoms (Moraska et al., 2013; Birnbaum et al., 2010), using the hospital discharge data to assess the prevalence of UDD would lead to an underestimation of the mild and moderate cases, which are the majority of all UDD cases.

28.4 References

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