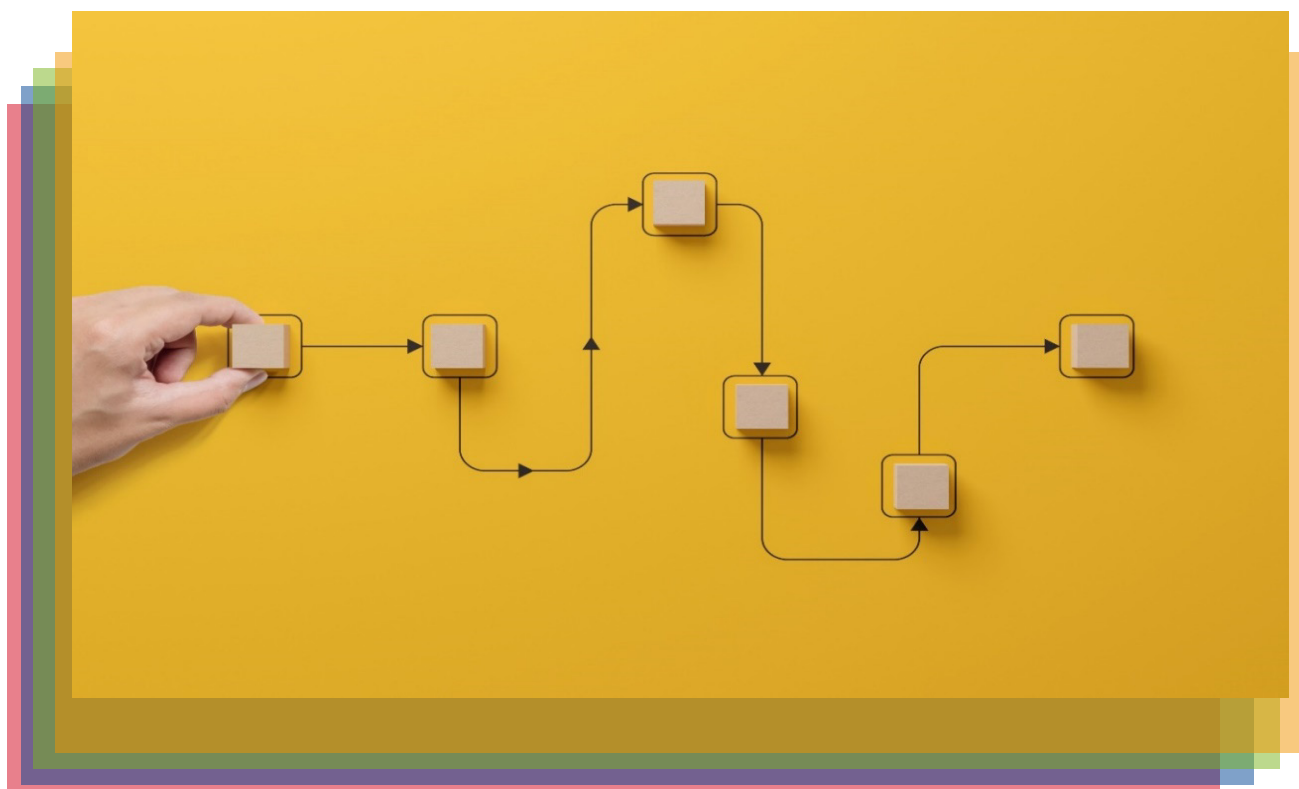


PROTOCOL FOR NEED (NEEDS EXAMINATION, EVALUATION AND DISSEMINATION) RESEARCH PROJECTS



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LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
AI	Artificial Intelligence
APR-DRG	All Patient Refined-Diagnosis Related Group
BCR	Belgian Cancer Registry
BeBOD	Belgian Burden of Disease
COPD	Chronic Obstructive Pulmonary Disease
CPI	Consumer Price Index
CRRD	Central Registry of Rare Disease
DALYs	Disability-Adjusted Life Years
EHIS	European Health Interview Survey
EMA	European Medicines Agency
EN	English
EU	European Union
FAMHP	Federal Agency for Medicines and Health Products
FR	French
GBD	Global Burden of Disease study
GP	General Practitioner
HALE	Healthy Life Expectancy
HBS	Health Budget Survey
HC	Health Condition
HICP	Harmonised Index of Consumer Prices
HIS	Health Interview Survey
HRQoL	Health-Related Quality of Life
ICPC	International Classification of Primary Care
IHME	Institute for Health Metrics and Evaluation
IMA – AIM	Inter-Mutualistic Agency
KSZ – BCSS	Kruispuntbank van de Sociale Zekerheid – Banque Carrefour de la Sécurité Sociale
LE	Life Expectancy
LUSS	Ligues des Usagers des Services de Santé
MMAT	Mixed-Methods Appraisal Tool
NEED	Needs Examination, Evaluation, and Dissemination
NIHDI	National Institute for Health and Disability Insurance
NL	Dutch
OECD	Organisation for Economic Co-operation and Development



OOP	Out-of-pocket payments
PPP	Purchasing Power Parity
PPS	Purchasing Power Standard
QALY	Quality-Adjusted Life Year
R&D	Research and Development
SD	Standard Deviation
TCT	Technische Cel – Cellule Technique
VPP	Vlaams Patiëntenplatform
WHO	World Health Organization
YLDs	Years Lived with Disability
YLLs	Years of Life Lost

1 INTRODUCTION

1.1 Context

Innovation in healthcare is driven by many factors. The state of the scientific knowledge regarding a disease is clearly an important one, but commercial profitability is also an undeniable driver of innovation, especially for private, for-profit companies. As a consequence, private R&D often focuses on areas that promise high financial returns on investment rather than on health problems with particularly high unmet needs but potentially less attractive markets, such as mental health and neglected diseases, or critical public health issues like drug resistance.

Policy decisions regarding the approval and/or reimbursement of healthcare innovations tend to be reactive, often following a request from industry or stakeholders with a vested interest. Systems are historically conceived in this way, assuming that addressing areas of commercial interest would also result in meeting the highest needs, thereby leading to a win-win for companies and society. However, the system has now reached its limits: many innovations focus on areas where only marginal benefits can be obtained for a large population, at prices that become unaffordable for the public healthcare payer and imply inefficient use of public healthcare resources. Although efforts are being made to guide innovation towards health priorities (e.g. in Belgium, a commission defining healthcare priorities was established in 2023), many important health-related needs remain unmet. Compounding the issue, there is a lack of scientific evidence on the most important unmet needs within and across different disease areas. This prevents decision makers to assess the performance of new health interventions in terms of meeting unmet needs and to consider alternative solutions that could potentially better address the needs of patients and society than the current options, such as the development of primary or secondary prevention strategies.

Public steering of innovation could help to address these gaps, but this requires solid evidence on what the actual unmet needs are, as well as prioritisation of these needs. To build a more effective and fair healthcare system, we therefore need a clear, evidence-based process to identify and prioritise these needs. This would ensure that innovation and policy decisions are focused on solving the most pressing health challenges.

1.2 The NEED project

The [NEED initiative](#) was launched at the end of 2022 in the context of the Belgian presidency of the Council of the European Union.

In March 2024, four scientific reports were published based on the work performed in the context of the NEED initiative, including a report on the development of the NEED assessment framework¹, the applicability of the NEED approach to rare diseases², and the application of the NEED framework to Crohn's disease³ and malignant melanoma⁴. In 2025, an updated version of the NEED framework, i.e. "the NEED assessment framework 2025," was published, partly based on EU expert consensus. This publication also included a core version of the framework, incorporating the minimally required criteria for a meaningful health-related unmet needs assessment.⁵

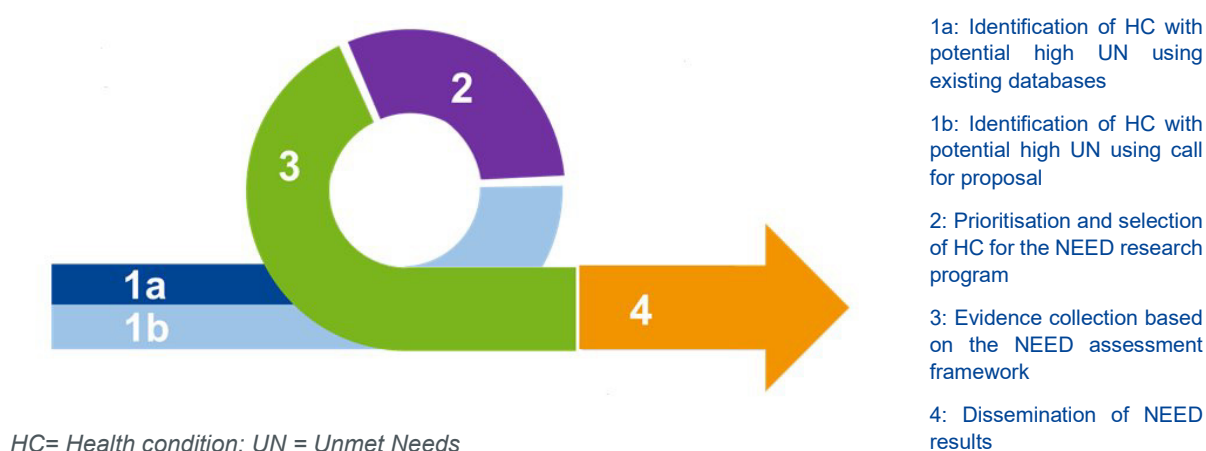
Following this, the first version of the [NEED database](#) was published in 2024.⁶ This database is publicly available online, and users can directly access and download the unmet needs data and the disease descriptive information, currently relating to Crohn's disease, malignant melanoma, and long Covid. Finally, 80 health conditions from the Belgian Burden of Disease (BeBOD^a) for which estimates were

^a **BeBOD (Belgian National Burden of Disease Study)** is a national research initiative led by Sciensano to systematically quantify the burden of diseases, injuries, and risk factors in Belgium using Disability-Adjusted Life Years (DALYs). BeBOD provides coherent, locally grounded, and comparable estimates to support evidence-based public health policy and decision-making.

available for at least three indicators of the NEED framework were also included in the NEED database.

As the objective of the NEED initiative is to standardise the evidence collection regarding health-related unmet patient and societal needs in different health conditions, important methodological work was required. The NEED programme implementation model was published in the very first NEED report.¹ It includes 4 steps: identification of health conditions with potential high unmet needs; selection of health conditions for in-depth research on patient and societal unmet needs, collection of scientific evidence regarding unmet needs in selected health conditions and finally dissemination of the results to the relevant stakeholders (Figure 1).

Figure 1 – The NEED 4-step implementation model



In 2024, a methodological approach for identifying and selecting health conditions with potential high unmet needs (steps 1 and 2 of the implementation model) was published.⁷ The method was also applied to (1) launch a call for proposals in Belgium and in the EU of conditions to examine in the context of the NEED initiative, (2) create a list of proposed health conditions with potential high unmet health-related needs (published on the NEED website: <https://www.unmet-needs.eu/index.php/en/research/call-for-research-topics-en-results>) and (3) select two additional case studies for the NEED research programme.

The current report focuses on step 3 of the NEED implementation model: evidence collection on the different unmet need criteria outlined in the NEED assessment framework. The objective is to develop a standardised protocol for conducting a NEED study. Such a study can be carried out as part of the annual NEED programme or independently by academic researchers, consultants, or industry partners. The protocol is also intended to guide other stakeholders and decision-makers in defining evidence requirements for unmet health-related needs, including the identification of data sources, type of collected data, and appropriate methods for data collection, for example, in response to regulatory or reimbursement requests.

Alongside this report, a **toolbox**⁸ has been published and made available online to enable the evidence collection described in this protocol. This box includes eight instruments and tools for collecting relevant primary and secondary data when performing a NEED study. It includes a standardised search strategy to conduct a systematic literature review for all indicators of the NEED framework in a specific health condition (tool 1), a generic patient questionnaire (tool 2), a generic patient interview guide (tool 3), a generic interview guide for proxies in case patients cannot answer themselves (tool 4), a declaration of conflict of interest form (tool 5), a generic questionnaire for clinical experts (tool 6), a checklist for calculating non-healthcare costs (tool 7) and a R code for performing survey analyses (tool 8).



The **dissemination of NEED results** (step 4 of the implementation model, see Figure 1) mainly occurs through the NEED database as introduced above and is therefore not part of this protocol. The definitions of the various concepts related to unmet health-related needs, as well as the rationale and scope of the NEED approach, can be consulted in KCE report 377.¹

2 AIM AND OBJECTIVES

This protocol aims to establish a standardised and transparent approach for conducting research on unmet health-related needs of patients and society associated with a specific health condition.

The ultimate goal is to populate the NEED database with scientifically valid and standardised data on unmet needs across various health conditions and countries, thereby supporting more needs-driven healthcare policy and innovation. Although comparability of evidence across diseases will always be a challenge, the goal is to create a database with scientific evidence that meets minimal quality criteria by following a validated scientific approach.

The research protocol has two primary objectives:

- To outline the process for conducting a NEED research project;
- To address the most common questions encountered when undertaking a NEED research project.

This protocol is intended to guide researchers interested in conducting a NEED study and contributing to the NEED database. Additionally, it may serve as a source of inspiration for researchers assessing the needs of patients or society, as well as developing methodologies involved in such evaluations.

In parallel with this protocol, the NEED toolbox provides the various instruments required for its implementation and for assessing unmet needs.⁸

3 SCOPE

A NEED research project identifies and measures the patient and societal unmet health-related needs associated with a health condition. It can be conducted at different geographic levels:

- In a single European Union (EU) country,
- Across groups of similar countries (e.g. Benelux, Nordic countries, South EU, Central EU...), or
- Across all EU countries.

This research protocol focuses on the procedures to perform a NEED research project **at the country level**.

4 THE NEED ASSESSMENT FRAMEWORK

The structure of the NEED assessment framework 2025 is outlined in Table 1. This version of the framework includes 26 criteria and 46 indicators to evaluate unmet health-related needs.⁵ A core version of the NEED framework, encompassing the minimally required criteria for a meaningful unmet needs assessment, is also available (indicated by an asterisk (*) in Table 1).

It is important to note that the NEED framework is not static; rather, it is an evolving tool which is regularly being refined to be as comprehensive and robust as possible. Updates are likely in order to make it even more grounded in existing and validated indicators. As such, users are strongly encouraged to consult the NEED website^b for the most up-to-date version before starting a new NEED research project.

Each indicator referenced in the framework is further detailed in chapter 5, where definitions are provided along with proposed measurement methods as well as data collection strategies. The limitations of the various indicators are not detailed in this chapter, as they may depend on their practical application. However, they are thoroughly described in the technical sheets for each indicator included in the NEED database (see the "info" tab in the NEED database^c).

Depending on the nature of each indicator, data collection may involve **primary** or **secondary** sources. Primary data collection includes patient surveys, patient interviews, and expert input. Secondary data sources include reviews of scientific and/or grey literature and existing databases. These data collection methods are explained in more detail in chapter 6.

Where possible, researchers are encouraged to follow the preferred data collection methods described in chapter 5 for each indicator. In addition to the preferred method, a complementary approach is proposed to facilitate a more in-depth analysis of specific indicators. For instance, a literature review is systematically suggested as a complementary method to the primary approach. Nevertheless, we acknowledge that in particular circumstances, it might be justifiable to deviate from the preferred methodology (e.g. due to the patient population or disease characteristics).

^b NEED, <https://health-needs.eu/index.php/en/> (last access: 11 June 2025)

^c NEED database, <https://healthinformation.sciensano.be/shiny/NEED/> (last access: 11 June 2025)



Table 1 – The structure of the NEED assessment framework 2025 with three domains, three dimensions, and 26 needs criteria

Domains	Dimensions		
	Patients	Societal	Future (patient and societal)
Health needs	Impact on: • Life expectancy* • General HRQoL* • Physical health • Psychological health • Autonomy • Sexual and reproductive health	• Frequency* • Transmissibility • Burden on informal caregivers' health	• Forecasted burden of disease*
Healthcare needs	• Effectiveness of treatment* • Burden of treatment • Quality of care* • Access to care* • Availability of scientific research	• Value for money of standard of care* • Preventability*	• Forecasted healthcare costs
Social needs	• Impact on: a. Social life* b. Education* c. Work* • Financial consequences	• Productivity losses* • Environmental impact of standard of care • Burden on informal caregivers' social life	• Forecasted productivity losses

* Criteria included in the core NEED assessment framework 2025⁵; indicators related to the needs criteria are further developed in the chapter 5.

5 DESCRIPTION OF NEED INDICATORS

This chapter provides definitions of the criteria and related indicators included in the NEED assessment framework 2025⁵, as well as guidance for methods and data sources that should preferably be used for evaluating these criteria. Our goal is to standardise, to the largest possible extent, the data presented in the NEED database, to harmonise the used methods, and to ensure comparability across the different health conditions and countries from which the data originate. This document is intended for researchers who want to collect and submit data for the database.

Before diving deeper into each of the indicators separately, **some general remarks** have to be made.

- Before launching a NEED study, the national **ethical regulations** should be verified to determine whether submission to an ethics committee is required for conducting the study. This verification must be performed for each country if the study is multinational.
- All professional study contributors, i.e. researchers, external reviewers of the questionnaire, and clinical experts responding to the expert questionnaire, should complete the **declaration of interest** form before participating. A standardised declaration of interest form is available in the NEED toolbox.⁸
- While the NEED database seeks to be comprehensive, not every indicator will necessarily be relevant to all health conditions. Still, researchers should very carefully evaluate this before deciding to exclude an indicator at the outset. For instance, one indicator is *productivity losses for informal caregivers*. Some conditions may not require significant involvement from informal caregivers and, therefore, may not result in such losses. Similarly, the indicator of *preventability* may not apply to certain conditions, such as certain rare diseases, for which no effective primary prevention strategies exist. Nevertheless, collecting this information is crucial to enable comparability across health conditions. Indeed, while the database aims to highlight areas of highest unmet need, it must also include information on areas of lower unmet need, without which, assessing relative levels of need would not be possible.
- This document is written for an **international public**. Although the creation of the NEED database was initiated by Belgian public healthcare research institutions, its ambition is to be useful at the European level. As a result of its origins, some of the data sources referred to in this guidance document concern the Belgian situation. Nevertheless, researchers from other European countries are also strongly encouraged to submit data for the NEED database.
- For various indicators, we suggest **qualitative data as a complementary source** of information. Importantly, this should be regarded as valuable additional insight rather than a replacement for quantitative data. The NEED database aims to highlight important unmet needs in terms of both severity and frequency (e.g. the percentage of patients with a given health condition who suffer from severe symptoms). Qualitative data offers rich contextual detail, providing concrete examples of the diverse challenges patients face and potential solutions they identify, but it cannot be understood as a quantitatively representative sample of the patient population.
- Although this protocol was designed to be applicable to all types of health conditions, certain aspects still need to be further developed and refined **for rare or ultra-rare diseases**. Upcoming case studies, particularly the one planned on sickle cell disease in 2026, will provide valuable experience and help to clarify specific elements of the protocol within a NEED study for rare conditions. Conducting NEED studies in rare diseases presents unique methodological and operational challenges, including limited scientific literature and a scarcity of clinical trials from which to derive robust evidence, for instance, on treatment effectiveness. Reliable identification and classification of conditions using ORPHAcodes, as well as the grouping of ultra-rare diseases where appropriate, will likely be necessary to facilitate meaningful analysis. In addition, the use of rare diseases registries and Orphanet will be critical for obtaining estimates of prevalence and incidence. Given the typically small and dispersed patient populations, data collection may need



to occur at an international level, potentially employing targeted sampling approaches rather than convenience sampling, which in turn has implications for ethical approval. Finally, ensuring that the study sample is as representative as possible remains a particular challenge in this context. Addressing these complexities will require close collaboration with institutions and patient associations active in the rare disease field, such as Sciensano and RaDiOrg in Belgium, to ensure that methodological adaptations are both feasible and aligned with the realities of rare disease research.

5.1 Impact on life expectancy

5.1.1 Years of life lost per death

A. Definition

The number of years of life lost (YLL) due to the health condition, per death

B. Measurement method

YLL quantifies the burden of premature mortality by estimating the number of healthy life years lost when individuals die before their expected lifespan.

YLLs caused by a health condition (HC) are calculated as follows:

$$YLL_{HC} = \sum_i (N_i \times L_i)$$

Where:

N_i = Number of deaths caused by the health condition in a given year (or in a given period) in age-group i

L_i = “Standardised expectation of remaining life expectancy” at the age of death (i.e. how many years that person would, on average, have lived had they not died then) using a standard life expectancy table.

One YLL_{HC} represents one year of life lost due to early death caused by the health condition.⁹

Example: If a health condition causes 50 deaths among the population with an age of 60 years in 2025, i.e. where the standardised expectation of remaining life expectancy is 20 years, then total YLL in 2025 = $50 \times 20 = 1\,000$ for the population with an age of 60 years. The YLL for the total population in 2025 is calculated as the sum of all age-specific YLL.

YLLs per death caused by a health condition (HC) are calculated as follows

$$YLL_{perdeath} = \frac{YLL_{HC}}{\sum_i N_i} = L$$

Where:

$YLL_{HC} = \sum_i (N_i \cdot L_i)$ = total years of life lost due to the health condition in a given period

$\sum_i N_i$ = total number of deaths caused by the health condition in that period

L = the average standardised remaining life expectancy across all deaths caused by the health condition.

C. Data collection method

Database analysis, see section 6.2.2.

Example of data sources: Belgian national Burden of Disease study (BeBoD) (see chapter 7) and Global Burden of Disease (GBD) study (see chapter 8).

5.1.2 *Years of life lost per case*

A. Definition

The number of years of life lost (YLL) due to the health condition, per case

B. Measurement method

YLL quantifies the burden of premature mortality by estimating the number of healthy life years lost when individuals die before their expected lifespan.

YLLs per case are calculated as follows:

$$YLL_{\text{per case}} = \frac{YLL_{HC}}{P_{HC}}$$

Where:

YLL_{HC} = Total YLLs caused by a health condition in a period of one year.

P_{HC} = the number of prevalent cases (the number of people living with that health condition in a period of one year).

C. Data collection method

Database analysis, see section 6.2.2.

Example of data sources: Belgian national Burden of Disease study (BeBoD) (see chapter 7) and Global Burden of Disease (GBD) study (see chapter 8).

5.2 Impact on general health-related quality of life

5.2.1 *Years of life lived with disability per case*

A. Definition

The part of the year of life in perfect health lost due to disability or ill-health caused by the health condition, per case, over a period of one year.

B. Measurement method

Years Lived with Disability (YLD), taking the prevalence perspective, are calculated by multiplying the number of prevalent cases (P) in a given year by a severity-weighted disability weight (DW). A DW reflects the time in perfect health lost due to a reduction in quality of life caused by a given health state or sequela.⁹

The DW is a value on a scale from 0 to 1, whereby a DW of 0 reflects a health state that is equivalent to full health, whereas a DW equal to 1 means that the health state is equivalent to death. The DW value can be derived from the valuations of a panel of judges (patients, experts, etc) stated toward a set of hypothetical health states expressing the relative undesirability of the health states. Different valuation methods exist, e.g. trade-off methods such as the time trade-off and the person trade-off, the discrete choice experiments or the scales such as the Visual Analogue Scale or a combination of these. The DWs used in the Global Burden of Disease (GBD) are based on an ordinal health state valuation methodology based on paired comparisons questions, a type of discrete choice question,



and a population health equivalence technique, a type of trade-off method, to anchor DWs to scale from zero to one.¹⁰

In principle, YLDs should be calculated separately for each sequela j (or severity stage) associated with a health condition:

$$YLD_j = P_j * DW_j$$

Where:

P_j = number of prevalent cases in sequela j

DW_j = disability weight for sequela j (a value between 0 = full health and 1 = death)

The total YLD for a health condition is then obtained by summing across sequelae:

$$YLD_{HC} = \sum YLD_j$$

In practice, however, prevalence data are often not available at the sequela level (P_j). In such cases, the calculation is simplified by applying a severity-weighted average DW across all sequela:

$$YLD_{HC} = P_{HC} * \overline{DW_j}$$

Where:

P_{HC} = Total prevalent cases with the health condition

$\overline{DW_j}$ = Average DW across sequelae, weighted by estimated severity distribution

The severity-weighted **YLD per case** can then be expressed as:

$$YLD_{\text{per case}} = \frac{YLD_{HC}}{P_{HC}}$$

For example, in the case of Crohn's disease, a disability weight (DW) of 0.14 indicates that individuals experience a 14% reduction in health-related quality of life relative to a state of full health. Expressed in terms of years lived with disability (YLD), this translates to 0.14 YLD per case, meaning that each affected individual loses the equivalent of 0.14 years (approximately 51 days) of healthy life per year as a consequence of living with the condition.

C. Data collection method

Database analysis, see section 6.2.2.

Example of data sources: Belgian Burden of Disease study (BeBoD) (see chapter 7) and the Global Burden of Disease (GBD) study (see chapter 8).

5.2.2 EQ-5D-5L score

A. Definition

A score measuring health-related quality of life along five dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression.¹¹

B. Measurement method

- EQ-5D-5L average score before the onset of the first symptoms
- EQ-5D-5L average score today
- Average difference in EQ-5D-5L scores today versus before the onset of the first symptoms

If available, the national value set for the EQ-5D-5L health states should be used to assign a utility score to each individual health state description.¹² The utility score is calculated as:

$$Utility(state) = 1 - \left[\text{Intercept} + \sum_{\text{dimensions}} (\beta_{\text{dimension}} \times \text{severity multiplier for level of that dimension}) \right]$$

As an example, consider health state **15342**, defined as: mobility (MO) = 1, self-care (SC) = 5, usual activity (UA) = 3, pain/discomfort (PD) = 4, and anxiety/depression (AD) = 2, with an intercept of 0.038. The utility is calculated as follows:

$$\begin{aligned} Utility_{15342} &= 1 - (\text{Intercept} + \beta_{MO} * 0 + \beta_{SC} * 1 + \beta_{UA} * 3 + \beta_{PD} * 4 + \beta_{AD} * 2) \\ &= 1 - (0.038 + 0 + 0.166 + 0.047 + 0.380 + 0.061) = 1 - 0.691 = 0.309 \end{aligned}$$

Thus, the utility score of health state 15342 in Belgium is **0.39**.

If no national value set is available, one from a culturally similar country may be used.

The **average EQ-5D-5L score** (for “before” and “today”) is calculated as:

$$\text{Average score} = \frac{\text{Sum of individual EQ-5D-5L scores}}{N}$$

where N is the number of respondents with a valid score.

The average difference between scores (“today” vs. “before”) is obtained by first calculating each individual’s score difference, and then averaging these differences across all respondents with valid data.

C. Data collection method

Patient survey (calculated with questions H1, H2, H3, H4, H5, H7, H8, H9, H10, H11) see section 6.1.1.

5.3 Impact on physical health

5.3.1 Experienced burden of physical symptoms related to the health condition

A. Definition

The level of burden of physical symptoms experienced by patients over the last 2 years.

B. Measurement method

- For each reported symptom over the last 2 years, the percentage of participants who report it as moderately, very, or extremely burdensome.

C. Data collection method

Preferred: Patient survey (H13, H13B questions), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2)

5.3.2 Pain/discomfort before disease vs today

A. Definition

The level of pain or discomfort due to the health condition, and the difference in the level of pain or discomfort today compared to before the onset of the first symptoms.

B. Measurement method

- % of participants who report moderate, severe or extreme problems with pain/discomfort today (EQ-5D-5L tool)



- Difference in % of participants who report moderate, severe or extreme problems with pain/discomfort before vs today (EQ-5D-5L tool)

C. Data collection method

Preferred: Patient survey (H4, H10 questions), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2)

5.4 Impact on psychological health

5.4.1 Experienced burden of psychological symptoms related to the health condition

A. Definition

The level of burden of psychological symptoms experienced by the patients over the last 2 years.

B. Measurement method

- % of participants who report the psychological symptom over the last 2 years as moderately, very or extremely burdensome, for each psychological symptom listed in the survey

C. Data collection method

Preferred: Patient survey (H13, H13B questions), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2)

5.4.2 Anxiety/depression before disease vs today

A. Definition

The level of anxiety/depression due to the health condition and the difference in the level of anxiety or depression today compared to before the onset of the first symptoms.

B. Measurement method

- % of participants who report moderate, severe or extreme problems with anxiety/depression today (EQ-5D-5L tool)
- Difference in % of participants who report moderate, severe or extreme problems with anxiety/depression before vs today (EQ-5D-5L tool)

C. Data collection method

Preferred: Patient survey (H5, H11 questions), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2).

5.5 Impact on autonomy

5.5.1 Mobility before disease vs today

A. Definition

The level of problems with mobility due to the health condition, and the difference in the extent of mobility problems today compared to before the onset of the first symptoms.

B. Measurement method

- % of participants who report moderate, severe or extreme problems with mobility today (EQ-5D-5L tool)
- Difference in % of participants who report moderate, severe or extreme problems with mobility before vs today (EQ-5D-5L tool)

C. Data collection method

Preferred: Patient survey (H1, H7 questions), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2).

5.5.2 Self-care before disease vs today

A. Definition

The level of problems with self-care due to the health condition, and the difference in the extent of self-care problems today compared to before the onset of the first symptoms.

B. Measurement method

- % of participants who report moderate, severe or extreme problems with self-care today (EQ-5D-5L tool)
 - Difference in % of participants who report moderate, severe or extreme problems with self-care before vs today (EQ-5D-5L tool)

C. Data collection method

Preferred: Patient survey (H2, H8 questions), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2).

5.5.3 Usual activities before disease vs today

A. Definition

The level of problems with performing usual activities due to the health condition, and the difference in the extent of problems performing usual activities today compared to before the onset of the first symptoms.

B. Measurement method

- % of participants who report moderate, severe or extreme problems with usual activities today (EQ-5D-5L tool)
- Difference in % of participants who report moderate, severe or extreme problems with usual activities before vs today (EQ-5D-5L tool)

Data collection method

Preferred: Patient survey (H3, H9 questions), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2).



5.6 Impact on sexual and reproductive health

5.6.1 *Impact on sexual health*

A. Definition

The extent to which the health condition interferes with the patients' sexual life.

B. Measurement method

- % of participants who report that the disease interferes moderately, a lot, or extremely with their sexual life.

C. Data collection method

Preferred: Patient survey (H14 question), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2).

5.6.2 *Impact on reproductive health*

A. Definition

The extent to which the health condition interfered with the patients' reproductive life.

B. Measurement method

- % of participants who report that the disease interfered moderately, a lot, or extremely with their reproductive life.

C. Data collection method

Preferred: Patient survey (H15 question), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2).

5.7 Treatment effectiveness

5.7.1 *Effectiveness of current overall treatment (standard of care)*

A. Definition

The overall effectiveness level of the current treatment. Treatment may include various interventions such as medications, surgery, medical procedures, medical devices, physical therapy, psychological therapy, and other forms of (clinical) interventions to cure the specific health condition, to target symptoms caused by the condition, or to prevent complications.

B. Measurement method

Treatment effectiveness in patient population: not effective, somewhat, moderately, or very effective

C. Data collection method

Clinical expert survey (see section 6.1.3) and literature review (see section 6.2.1).

5.8 Burden of treatment

5.8.1 *Experienced burden of treatment side-effects*

A. Definition

The level of burden of side-effects associated with the treatment or management of the health condition over the last 2 years.

B. Measurement method

For each side-effect listed in the survey, the % of participants experiencing the side-effect, who reported it as moderately, very, or extremely burdensome

C. Data collection method

Preferred: Patient survey (HC4, HC4B, HC5 questions), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2).

5.8.2 *Experienced burden of treatment*

A. Definition

The burden associated with the treatment or management of the health condition over the last 2 years, excluding treatment side-effects.

B. Measurement method

% of participants under treatment who report that the treatment, over the last 2 years and apart from its possible associated side-effects, was moderately, very, or extremely burdensome

C. Data collection method

Preferred: Patient survey (HC6 question), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2).

5.9 Quality of care

5.9.1 *Coordination and continuity of care*

A. Definition

Coordination and continuity of care refer to patient care that is well-organised and planned over time, having a healthcare professional responsible for coordinating the care, as well as having continuity in the healthcare professionals who attend to the patient.

B. Measurement method

- % of participants who feel that their care has sometimes, rarely, or never been well organised and planned over time
- % of participants who do not have a single professional (or several professionals) who takes responsibility for coordinating their care
- % of participants who report that they sometimes, rarely, or never see the same healthcare provider for their regular check-ups or appointments

C.

**Data collection method**

Preferred: Patient survey (HC7, HC8, HC9 questions), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2).

5.9.2 Received information**A. Definition**

The extent to which patients receive useful and understandable information. By 'useful' we mean information which is up to date and coherent, and which helps patients better understand and better manage their health condition.

B. Measurement method

% of participants who report sometimes, rarely, or never receiving useful and understandable information

C. Data collection method

Preferred: Patient survey (HC10 question), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2).

5.9.3 Involvement in treatment decisions**A. Definition**

The extent to which patients would like to be more involved in the choices about the treatment for their health condition

B. Measurement method

% of participants who report not really or certainly not being as involved as they would like in treatment decisions

C. Data collection method

Preferred: Patient survey (HC11 question), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2).

5.9.4 Time from first presentation to diagnosis**A. Definition**

The amount of time that has passed between a patient's first medical appointment for the health condition and the diagnosis.

B. Measurement method

% of participants who received a diagnosis >2 months (for chronic diseases) and >1 week (for acute diseases) after first appointment for the health condition

C. Data collection method

Preferred: Patient survey (HC1 question), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2).

5.9.5 *Appropriateness of diagnostic timing*

A. Definition

For diseases with an identifiable optimal diagnostic timing in the disease course, this indicator measures to what extent diagnosis tends to occur too late (causing avoidable disease progress or complications) or too early (leading to overdiagnosis).

B. Measurement method

- Frequency of delayed diagnosis: rare, occasional, moderate, frequent, very frequent, N/A
- Too early diagnosis (over-diagnosis): no concern, slight concern, moderate concern, considerable concern, major concern, N/A
- N/A= Does not apply because there is no optimal timing for diagnosis or it is highly context-dependent

C. Data collection method and data sources

Clinical expert survey, see section 6.1.3

5.10 Access to care

5.10.1 *Treatment availability*

A. Definition

The extent to which patients can access medical treatments for a given disease. It encompasses not only the existence of treatments, but also their authorisation, commercialisation, affordability and practical accessibility for patients within a specific country.

B. Measurement method

Extent to which current treatment/management of [health condition] is available for the patient population: not available, important availability problems, some availability problems, no availability problems.

C. Data collection method

Clinical expert survey, see section 6.1.3

5.10.2 *Foregone care*

A. Definition

Foregone care refers to not receiving health care (e.g. treatment, consultations, medical tests, rehabilitation, or other) despite patients perceiving a need for it. This can be due to several reasons, including costs, waiting lists, or transport difficulties.

B. Measurement method

% of participants who reported not receiving care when needed, excluding responses where lack of time was cited as the reason

C. Data collection method

Preferred: Patient survey (HC12, HC13 questions), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2)



5.11 Scientific research

5.11.1 Research gaps

A. Definition

The extent to which research gaps exist in the following areas: pathophysiology, diagnosis, pharmacopredictive biomarkers, prognostic biomarkers, treatment, primary prevention, inequities, and other possible additional areas.

B. Measurement method

The extent to which **moderate** or **major** research gaps exist in pathophysiology, diagnosis, pharmacopredictive biomarkers, prognostic biomarkers, treatment, primary prevention, inequities, and other possible additional areas (mentioned by the expert). The result is expressed as a categorical variable. For instance, “moderate” or “major”.

- **C. Data collection method**

Clinical expert survey (section 6.1.3) and scientific literature review (section 6.2.1).

5.12 Impact on social life

5.12.1 Foregone social support

A. Definition

The extent to which patients need additional social support (e.g. administrative, logistical, social help) because of their health condition, without getting it.

B. Measurement method

% of participants who report needing social support in at least one area but not receiving it.

C. Data collection method

Preferred: Patient survey (S7 question), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2)

5.12.2 Impact on personal relationships

A. Definition

The level of impact a health condition has on patients' personal relationships, encompassing relationships with their family, partner, friends or neighbours.

B. Measurement method

% of participants who report that their disease interferes moderately, a lot, or extremely with their relationships with their family, partner, friends or neighbours.

C. Data collection method

Preferred: Patient survey (S6 question), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2)

5.13 Impact on education

5.13.1 Impact on education

A. Definition

The extent to which the health condition has affected patients' schooling or studies, in terms of attendance, performance, success, or study choices.

B. Measurement method

% of participants who report that their schooling or studies have been moderately, a lot, or extremely affected by their disease.

C. Data collection method

Preferred: Patient survey (S1 question), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2)

5.14 Impact on work

5.14.1 Reduction in working time

A. Definition

The extent to which the health condition has impacted patients' ability to remain professionally active, causing a reduction in working hours.

B. Measurement method

% of participants with remunerated employment since diagnosis who reduced their working hours or stopped working because of their disease.

C. Data collection method

Preferred: Patient survey (S2 question), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2)

5.15 Financial consequences

Box 1 – Categorisation of costs included in the economic indicators

In the context of diseases, their treatment and consequences, associated costs can be grouped into the following categories: (adapted from Drummond, Methods for the economic evaluation of health care programs – Third edition¹³).

- **Healthcare sector resources:** this category includes all inputs required for the treatment, follow-up, and overall management of a disease. It encompasses both hospital-based and ambulatory (outpatient) care. The expenditures for these resources are typically covered either by the public healthcare payer or directly by the patient, including any contributions from private health insurance.
- **Resources from other publicly supported sectors,** such as home help services (e.g. assistance with daily living activities), social worker visits, ... While the public sector often subsidises these services, patients may still incur costs.
- **Personal resources** (of the patients and their families): this category refers to non-healthcare expenses that patients and their families incur as a direct consequence of managing a disease, but which fall outside the healthcare or social care systems. Some examples are the travel to the hospital, the adaptations made



at home (structural changes or equipment purchases made to accommodate a patient's medical needs at home), etc. In this category, it concerns resources other than time, which will be considered in the next category.

- **Time resources of the patient/family/other informal carers:** this category captures the time lost due to the disease and its treatment, whether spent attending medical appointments, receiving care, or providing informal care. The economic value of this time loss, particularly when it interferes with paid employment, is referred to as productivity losses.

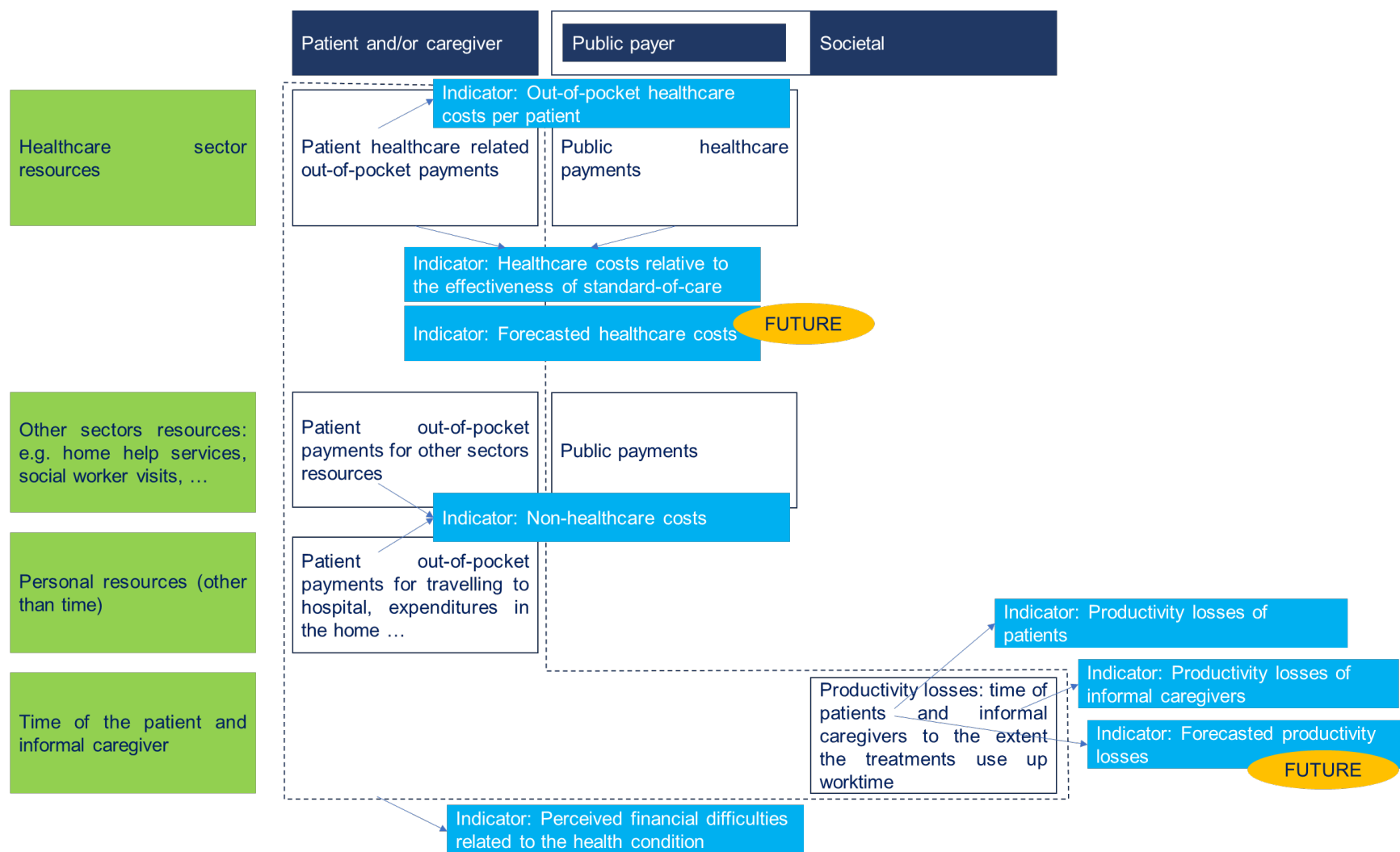
Figure 2 illustrates how different cost components associated with diseases are distributed across three stakeholder groups: patients and/or their informal caregivers, public payers, and society as a whole. The figure organises the costs according to the type of resources consumed, as listed above, and the stakeholder groups paying for them and links these combinations to specific indicators. As such, the different economic indicators capture different dimensions of economic burden:

- Out-of-pocket healthcare costs per patient (see section 5.15.1): focuses solely on the direct healthcare expenses paid by the patient.
- Value-for-money of standard of care (see section 5.19.1): considers two types of healthcare costs:
 1. Public healthcare payments, and
 2. Patient healthcare-related out-of-pocket payments.

These combined costs are evaluated relative to the effectiveness of the standard of care to assess how efficiently healthcare resources are being used. Importantly, this indicator does not include productivity losses, which are addressed through separate indicators.

- Forecasted healthcare costs (see section 5.25.1): reflect the same costs as the indicator 'Value-for-money of standard of care'
- Non-healthcare costs per patient (see section 5.15.3): includes out-of-pocket expenditures for the patient for the use of services from other publicly supported sectors (e.g., home help) as well as expenditures outside healthcare, though still related to the disease and borne by the patient.
- Perceived financial difficulties related to the health condition (see section 5.15.2): reflects the subjective financial strain experienced by patients or caregivers and considers all cost components born by the patient, as well as the impact of the potential productivity loss.
- Productivity losses (see section 5.21) and forecasted productivity losses (see section 5.26.1) are considered a cost to society as a whole in terms of reduced labour productivity.

Figure 2 – Categorisation of possible resources used in the treatment and management of a disease, the payer perspectives and the corresponding economic indicators in the NEED database





5.15.1 Out-of-pocket healthcare costs (per patient)

A. Definition

Healthcare costs that patients must pay themselves when accessing healthcare, due to incomplete coverage by public health insurance for certain medical goods and services. Depending on the country, these may include the following components:

- **co-payments** related to reimbursed services: the part of the official tariff for a healthcare service that is not covered by compulsory health insurance schemes through third party payments or reimbursement
- supplements: extra billings related to reimbursed services: additional charges billed on top of the official tariff for reimbursed services, typically when providers are allowed to charge more than the official tariff established by public insurance.
- payments for non-reimbursed **goods and services**: this includes costs for healthcare items and services not covered at all by public schemes, such as over-the-counter (OTC) medicines, non-reimbursed procedures, ...

Out-of-pocket (OOP) healthcare costs concern payments made across the different healthcare sectors. All of the following healthcare sectors should thus be considered:

- Ambulatory (i.e. outpatient) care, including primary care as well as specialists' outpatient care
- Inpatient care: costs incurred during hospital admissions
- Pharmaceuticals both in ambulatory and inpatient settings
- Dental care
- Long-term care: including home care and institutional care services.

When analysing OOP healthcare costs, the financial protection mechanisms in place should be taken into account if possible and applicable. Depending on the country, such protection mechanisms could encompass increased reimbursement to reduce co-payments, or maximum billing to cap co-payments for low income households or patients with high healthcare expenditures.

Note that this indicator only represents OOP payments that are **specifically associated with the disease in question**. In other words, it represents the additional (incremental) costs beyond those typically borne by individuals without the disease.

B. Measurement method

- Average annual OOP cost per patient in Euros
- For the standardisation of the currency and inflation, see chapter 9

C. Data collection methods and data sources

Preferred: database analysis (see section 6.2.2). If data from national databases of a European country are available, these should be used as the primary source.

- Complementary: literature search (see section 6.2.1), patient interviews (see section 6.1.2), particularly for payments for non-reimbursed healthcare services and products.

5.15.2 Perceived financial difficulties related to the health condition

A. Definition

The extent to which patients experience financial difficulties due to the health condition or its medical treatment.

B. Measurement method

% of participants who report that the disease or medical treatment causes 'moderate', 'a lot' or 'extreme' financial difficulties.

C. Data collection method

Preferred: Patient survey (S5 question), see section 6.1.1.

Complementary: Patient interviews (see section 6.1.2)

5.15.3 Non-healthcare costs

A. Definition

Costs that patients must cover for aspects other than medical care, but that are nevertheless a consequence of the disease. This indicator covers several types of costs, such as

- **Transportation** to and from healthcare facilities using various modes of transportation, including private vehicle (including costs such as parking and tolls), shared car, bus, train, airplane, and ferry. Also includes taxis if public transport is inaccessible, as well as adapted transport services for people with reduced mobility.
- **Accommodation** nearby the healthcare facility if the healthcare facility is a long way from home. This concerns accommodation outside the healthcare facility, as this indicator concerns non-medical costs. Accommodation outside the healthcare facility may, for instance, be required when the treatment takes place abroad.
- **Adaptations of the home, the workplace or the car.** These adaptations can take form in many ways, e.g. adapting a room to accommodate a home dialysis machine, making doors wider so that a wheelchair can pass through, installing a stair lift, ergonomic furniture, etc. Adaptations may be required in different parts of the house: kitchen, bathroom, toilet, living room, bedroom....
- **Support and assistance for day-to-day activities** when provided by professional (paid) caregivers, for example, for
 - Personal care: washing, dressing, toilet
 - House maintenance, cleaning, laundry, meal preparation, gardening, ...
 - Activities in the community: shopping, transport outside the house
 - *Note that when this support is provided by family or friends (i.e. informal caregivers), then this often does not lead to expenditures for the patient. Productivity losses incurred by informal caregivers are also a cost, but these are considered in a separate indicator (see section 5.21.4).*
- **Institutionalisation** in case the patient needs to be institutionalised (e.g. persons with young dementia who are in a residential care centre).
- **Specialised equipment:** e.g. wheelchair, scoot mobile, assistive devices for communication, insoles, walker (rollator).
- **Technology and subscriptions:** devices or software to assist with daily tasks, such as voice-activated systems, health-monitoring apps or personal alarms.



- Education, training or work reintegration programme: to learn new skills to adapt to limitations or to re-enter the workforce.
- **Personal hygiene items:** e.g. incontinence products, bandages, wound care material.
- Specific diets or nutritional supplements: these should only be considered when they pose supplemental costs compared to a regular diet.
- Prescribed sporting activities: e.g. cardiac rehabilitation after a cardiovascular event.
- Adapted clothing or shoes
- Increased energy costs: heating, electricity or water costs, if someone's condition requires an above average temperature maintained in the home, for example, or for charging wheelchairs, ...
- **Increased waste costs:** e.g. when using certain medical devices
- Additional insurance costs: insurers may demand higher insurance premiums or reject applications for mortgages, life insurance, health insurance, travel insurance, etc.
- Additional costs for leisure activities or travel: e.g. because a patient has to pay extra to bring medical equipment, has to use adapted facilities,...

B. Measurement method

- Checkmark list: see NEED toolbox (tool 7)⁸

In the NEED database, no amounts of expenditures are included, because these costs are very often hard to calculate (for further considerations on this indicator, see Appendix).

For each cost group listed in the checklist in the toolbox, it should be assessed whether they are applicable, either for most or a minority of patients, or not. The imputed values for each cost group can be:

- Applicable to most patients: One-off costs
- Applicable to most patients: Recurring costs short-term (<1 year)
- Applicable to most patients: Recurring costs long-term (>1 year)
- Applicable to a minority of patients: One-off costs
- Applicable to a minority of patients: Recurring costs short-term (<1 year)
- Applicable to a minority of patients: Recurring costs long-term (>1 year)
- Not applicable.
- At the end, there is an open field for 'Other costs', which allows researchers to specify any additional costs not already covered by the predefined cost groups.

Some of the costs listed in the cost groups may be partially or fully reimbursed, e.g. specialised equipment or personal hygiene items. Only when they are not fully reimbursed should they be mentioned as applicable for this indicator.

C. Data collection methods and data sources

Preferred: The evaluation of the checklist can be based on any or a combination of the following methods.

- Expert consultation, including patient representatives
- Literature research (see section 6.2.1)
- Patient interviews (see section 6.1.2)

These sources are considered equivalent, and there is no order of priority to follow.

5.16 Frequency

5.16.1 Prevalence or incidence

A. Definition

Prevalence: the total number of individuals in the population who have the health condition in a given time period.

Incidence: the number of individuals who develop the health condition during a particular time period.

B. Measurement method

- Prevalence: number of cases at a specific time per 100 000 population
- Incidence: number of new cases within one year per 100 000 population

C. Data collection method

Database analysis, see section 6.2.2. Possible data sources can be, for instance, disease-specific and central registries, BeBOD or the GBD (see chapter 8).

5.17 Transmissibility

5.17.1 Contagiousness

A. Definition

The extent to which an infectious disease can be directly or indirectly transmitted from one person to another. This is measured by the basic reproduction number (average number of secondary infections produced by a typical case of an infection in a population where everyone is susceptible).

B. Measurement method

- Basic reproduction number (R_0)

C. Data collection method

Scientific literature reviews, see section 6.2.1

5.18 Burden on informal caregivers' health

5.18.1 Impact on informal caregivers' health

A. Definition

The extent to which the health condition negatively impacts the physical and psychological health of informal caregivers.

B. Measurement method

% of proxy respondents who consider that their health is 'moderately', 'a lot', or 'extremely' affected by their role as carers.

C. Data collection method

Preferred: Patient survey (CG6 question), see section 6.1.1. Complementary: patient interviews (for proxy respondents), see section 6.1.2



5.19 Value for money of standard of care

5.19.1 Healthcare costs relative to the effectiveness of standard of care

This indicator represents a disaggregated presentation of healthcare costs of standard of care and the effectiveness of standard of care.

HEALTHCARE COSTS OF STANDARD OF CARE

A. Definition

Healthcare costs of standard of care refer to those costs borne by the healthcare payers (including the public healthcare payer and patients), per year and per patient, for standard of care. Standard of care refers to the clinical management of the disease, including the diagnostic approach and treatment that is widely accepted by medical experts as appropriate for managing a specific disease and is commonly used in clinical practice, also known as best practice, standard medical care, or standard therapy.

B. Measurement method

- Annual costs per patient for the healthcare payer (public healthcare payer and patient)
- For instructions on currency conversion and inflation, see chapter 9. See the appendix for further considerations on this indicator.

C. Data collection method

Preferred: database analysis (see 6.2.2).

Complementary: scientific literature review (see 6.2.1).

Also see section 6.2.2 for adjustments to be made for 'baseline healthcare costs'.

EFFECTIVENESS OF STANDARD OF CARE

The evaluation of the effectiveness of standard of care / current treatment is based on the following indicators in the database:

- Effectiveness of current overall treatment/management (see section 5.7.1)
- Years of life lived with disability per case (see section 5.2.1)
- YLL (per year) per case (see section 5.1.1)
- Years of life lost per death (see section 5.1.2)
- For the definition, measurement and data collection method of these indicators, we refer to the corresponding sections of the report. No separate calculations need to be made to assess the effectiveness of current treatment.

5.20 Preventability

5.20.1 Implementation of effective primary prevention strategies

A. Definition

The extent to which effective primary prevention strategies are implemented for the given health condition.

B. Measurement method

Implementation of effective primary prevention strategies: not at all, minimally, moderately, or fully implemented, N/A.

C. Data collection method and data sources

Clinical expert survey, see section 6.1.3

5.21 Productivity losses

Productivity losses represent the economic consequences of absence from work or reduced work performance due to a health condition. They can be categorised into three main types: **absenteeism** (time off work due to a health condition; indicator 5.21.1), **presenteeism** (working while ill but at reduced productivity; indicator 5.21.2), and **work reduction or labour force exits** (reducing or leaving participation in the workforce because of a health condition, or never entering it due to it; indicator 5.21.3). Productivity losses may occur not only for patients but also for **informal carers** (indicator 5.21.4).

Within the context of the NEED database, it was chosen to measure the productivity losses, not to assign a monetary value to them. The rationale for this choice can be found in the Appendix.

5.21.1 Absenteeism of patients

A. Definition

Patients' absence from work due to illness.

B. Measurement method

Productivity losses through absenteeism of patients are measured (in average absence duration and number of persons absent) but not valued in Euros in the NEED database (see Appendix for further considerations on this choice).

- Measurement method 1: average annual absence per patient since the diagnosis, based on two questions from the patient survey
- Measurement method 2: average duration of absence per disease and number of persons absent per disease, based on database analysis

MEASUREMENT METHOD 1 (PATIENT SURVEY)

This indicator is measured as the total duration of absence from work since the start of the disease (in years), divided by the time elapsed since diagnosis (in years). So the indicator is measured as a fraction:

'Total period of absence since start of the disease' (in years) (S3, S3B questions)

÷ 'How long ago did the patient receive the diagnosis' (in years) (D13, D13B questions)



EXCLUSION OF PATIENTS RECENTLY DIAGNOSED

For the calculation of this indicator, only data from patients who reported that the diagnosis was more than 6 months ago. This is to avoid potential instability in the indicator for patients who were only recently diagnosed, since the time since diagnosis is used as the denominator.

CONVERSION OF CATEGORICAL RESPONSES TO NUMERIC VALUES

For the calculation of the fraction, the categorical responses should be converted to estimated numeric values (in years). For this, a midpoint estimate can be used: the average of the lower and upper limit of the response category. E.g. for respondents who selected "6 months to 2 years ago", the midpoint estimate is 1.25 years, which is the average of 0.5 and 2 years.

EXAMPLE CALCULATION: AVERAGE ANNUAL ABSENCE PER PATIENT SINCE DIAGNOSIS

The following example in the Table 2 illustrates how indicator 1 can be calculated using data from the patient questionnaire.

Table 2 – Example outcome for annual absence per patient since diagnosis

Patient ID	Estimated total absence (years)	Time since diagnosis (years)	Annual absence (Absence ÷ Time since diagnosis) (years)
P001	0.50 (1 - 3 months)	1.25 (6 months - 2 years)	0.40
P002	0.50 (1 - 3 months)	3.50 (2 - 5 years)	0.14
P003	0.67 (4 months - 1 year)	7.5 (5 - 10 years)	0.09
P004	2	15	0.13

Based on the results from the four patients (Table 3), the calculated value for indicator 1 equals $(0.40 + 0.14 + 0.09 + 0.13) \div 4 = 0.19$ years = 2,3 months.

This means that on average, patients who were diagnosed minimum 6 months to 2 years ago reported being absent from work for about 2.3 months per year since their diagnosis.

MEASUREMENT METHOD 2 (DATABASE ANALYSIS)

Average duration of absence per disease and number of persons absent per disease, based on database analysis.

The precise measurement of this indicator can vary depending on the database used. E.g. for Belgium, at the time of writing, data from the 'Kenniscentrum Arbeidsongeschiktheid – Centre de connaissances en matière d'incapacité de travail' are available over a period of five years.

Productivity losses through absenteeism of patients are measured (in average absence duration and number of persons absent) but not valued in Euros in the NEED research (see Appendix for further considerations on this choice).

C. Data collection method and data sources

- Measurement method 1: Patient survey (S3, S3B, D13, D13B questions)(see section 6.1.1)
- Measurement method 2: Database analysis (see section 6.2.2).

5.21.2 Presenteeism of patients

A. Definition

Patients' presence at work without being fully productive due to illness.

B. Measurement method



- For the patients who are currently working, the mean score of how the disease affects their productivity at work ranging from 0 (the disease has no effect on work) to 10 (the disease completely prevents them from working).
- Note that only patients who are currently working are requested to answer this question.

C. Data collection method and data sources

Patient survey (S4 question) (see section 6.1.1).

5.21.3 Work reduction or early labour force exits of patients

See indicator in section 5.14.1.

5.21.4 Informal caregiving time burden

A. Definition

The time informal caregivers spend caring for a person affected by the disease. This care can involve for example personal care (such as dressing/undressing, going to the toilet...), household tasks (such as preparing meals, cleaning...), or practical support (such as accompanying patients to medical or other appointments...).

B. Measurement method

- Average number of hours spent on informal care in the previous week, per patient.
- Similar to the productivity losses of patients, productivity losses of informal caregivers are only measured (in time spent caring) and not valued (in Euros) in the NEED research.

C. Data collection method and data sources

Preferred: patient survey (CG5 question) (see section 6.1.1), when filled out by the informal caregiver acting as proxy respondent.

- If the patient him/herself fills out the questionnaire, no data on this question is available from the survey. If the survey does not result in a sufficient number of answers, complementary information sources should be considered.

Complementary: patient interviews (for proxy respondents) (see section 6.1.2)

5.22 Burden on informal caregivers' social life

5.22.1 Impact on informal caregivers' social life

A. Definition

The extent to which the health condition negatively impacts the informal caregiver's social life.

B. Measurement method

% of proxy respondents who consider that their social life was 'moderately', 'a lot', or 'extremely' affected by their role as carers

C. Data collection method

Preferred: Patient survey (CG7 question), see section 6.1.1, when filled out by the informal caregiver acting as proxy respondent.



If the patient him/herself fills out the questionnaire, no data on this question is available from the survey. If the survey does not result in a sufficient number of answers, complementary information sources should be considered.

Complementary: patient interviews (for proxy respondents), see section 6.1.2.

5.23 Environmental impact of standard of care

5.23.1 Greenhouse gas emissions related to the standard of care

A. Definition

The estimated amount of direct greenhouse gas emissions (scope 1: emitted by healthcare providers), and indirect greenhouse gas emissions (scope 2: derived from primary resources, and scope 3: derived from products used by healthcare providers) related to the standard of care for the health condition.

B. Measurement method

- Estimated amount of direct greenhouse gas emissions of standard of care (per patient: tCO₂e/capita or total) (from sources that are owned or controlled by care providers; Scope 1 emissions)
- Estimated amount of indirect greenhouse gas emissions (off-site) of standard of care (per patient: tCO₂e/capita or total) (e.g. patient travel, general disease management, procurement of pharmaceuticals; Scope 2 and 3 emissions)

C. Data collection method

Scientific and/or grey literature review, see section 6.2.1

5.23.2 Hazardous waste related to standard of care

A. Definition

The estimated volume of hazardous (e.g. radioactive, infectious) waste generated as part of the standard of care for the health condition.

B. Measurement method

- Estimated volume of hazardous (e.g. radioactive, infectious) waste per year. Includes waste at the care provision level and production level
- Estimated volume of non-hazardous waste per year. Includes waste at the care provision level and production level

C. Data collection method

Scientific and/or grey literature reviews, see section 6.2.1

5.23.3 Use of natural resources and raw materials related to standard of care

A. Definition

The estimated volume of natural resources and raw materials utilised in the standard of care for the health condition.

B. Measurement method

- Estimated volume of natural resources used per year, including rare earth elements, helium, etc

C. Data collection method

Scientific and/or grey literature reviews, see section 6.2.1

5.24 Forecasted burden of disease

5.24.1 Forecasted incidence or prevalence

A. Definition

The total number of individuals in the population who are estimated to have the health condition at a specific period of time in the future.

B. Measurement method

Different projection techniques can be used to forecast the future prevalence or incidence of a disease. In general, the main methodologies include statistical extrapolations, risk-factor-based models and transmission models. Each model features specific pros and cons, and for more information about these different models, we refer the reader to the '*Methodological framework for the projections of the non-fatal burden of disease of non-communicable diseases in Belgium*'^d. In this Belgian study, an extrapolation method is used, whereby trends from the past are projected towards the future (up to 2050), considering important socio-demographic factors as sex, age, and the region of residence in the occurrence of a particular health condition. In addition, the model includes demographic shifts based on the population projections extracted from the federal planning bureau (<https://www.plan.be/en/data/population-projections-2024-2070>). Important to notice is that these extrapolation models do not aim to predict the future but rather project a reference trend from the past into the future under similar conditions.

C. Data collection method

Database analysis, see section 6.2.2. Possible data sources can be the Belgian National Burden of Disease study or the Global Burden of Disease study.

5.24.2 Forecasted years of life lost per death

A. Definition

The future number of years of life lost (YLL) due to the health condition, per death

B. Measurement method

See section 5.1.1.

- In the GBD, forecasting of mortality and YLL was done using a three-component approach: (1) mortality was modelled in function of SDI, time, and other covariates; (2) a risk factor scalar was used for combined effects; (3) and a smoother was used to attenuate drift. Cause-specific mortality estimates were scaled to 1 to fit the all-cause mortality envelope.¹⁴ Forecasted YLLs were calculated by multiplying projected cause-specific death rates by standard life expectancy.

C. Data collection method

Database analysis, see section 6.2.2. Possible data sources can be the Belgian National Burden of Disease or the Global Burden of Disease study.

^d For further information see: <https://www.sciensano.be/en/biblio/belgian-national-burden-disease-study-methodological-framework-projections-non-fatal-burden-disease>



5.24.3 Forecasted years of life lost per case

A. Definition

The future number of years of life lost (YLL) due to the health condition, per case

B. Measurement method

See section 5.1.2.

- In the GBD, forecasting of mortality and YLL was done using a three-component approach: (1) mortality was modelled in function of SDI, time, and other covariates; (2) a risk factor scalar was used for combined effects; (3) and a smoother was used to attenuate drift. Cause-specific mortality estimates were scaled to 1 to fit the all-cause mortality envelope.¹⁴ Forecasted YLLs were calculated by multiplying projected cause-specific death rates by standard life expectancy.

C. Data collection method

Database analysis, see section 6.2.2. Possible data sources can be the Belgian National Burden of Disease or the Global Burden of Disease study.

5.24.4 Forecasted years lived with disability per case

A. Definition

The future part of the year of life in perfect health lost due to disability or ill-health caused by the health condition, per case, over a period of one year

B. Measurement method

- See section 5.2.1.
- To estimate the forecasted years lived with disability, the forecasted prevalence of a specific health condition is multiplied by the severity-weighted DW as specified in section 5.2.1. The severity distribution among patients and associated impact is assumed to be constant over time.

C. Data collection method and data sources

Database analysis, see section 6.2.2. Possible data sources can be the Belgian National Burden of Disease or the Global Burden of Disease study.

5.25 Forecasted healthcare costs

5.25.1 Forecasted healthcare costs attributable to the health condition

A. Definition

This indicator reflects the projected healthcare costs associated with the specified health condition, covering costs borne by both public healthcare payers and patients in future years. For this indicator, the perspective from society is taken, and it is presented as a cost in Euros per 100 000 inhabitants.

B. Measurement method

- Annual cost in Euros per 100 000 inhabitants, considering the prevalence of the disease as well as an average annual cost per patient with the disease.

The calculation of forecasted healthcare costs incorporates the anticipated prevalence of the condition (see section 5.24.1), accounting for expected changes in epidemiology and demographics. Future per-patient healthcare costs, on the other hand, are assumed to remain constant - equal to current levels - due to the difficulty of accurately forecasting such changes.

If attributable costs cannot be calculated, incremental costs can serve as an alternative. Incremental costs can be calculated using a causal inference framework as described by Gorasso et al. (2023)¹⁵ in the Belgian context. In short, incremental costs reflect the difference in costs that have been made by people with a certain health condition compared to those without this health condition, corrected for potential confounding factors.¹⁵

For the currency and inflation, we refer to chapter 9.

C. Data collection method and data sources

Preferred: database analysis (see section 6.2.2)

Complementary: scientific literature research (see section 6.2.1)

5.26 Forecasted productivity losses

5.26.1 Forecasted productivity losses attributable to the health condition

A. Definition

This indicator reflects the projected productivity losses attributable to the specified health condition. Productivity losses may occur due to absenteeism, presenteeism, as well as through early labour force exits and work reduction. In the context of the indicator on forecasted productivity losses, the focus lies on those losses linked to absenteeism.

To be coherent with the indicator in section 5.21.1 (absenteeism), this indicator is measured (in days absence) but not valued (in Euros), for the same reasoning as explained in the Appendix.

Since, for this indicator on forecasted productivity losses, the perspective from the society is taken, it is presented per 100 000 inhabitants in a given year.

B. Measurement method

- Average number of days absence due to the disease per year per 100 000 inhabitants

C. Data collection method and data sources

Preferred: database analysis (see section 6.2.2)

Complementary: scientific literature research (see section 6.2.1)



6 EVIDENCE COLLECTION BASED ON THE NEED ASSESSMENT FRAMEWORK

6.1 Primary data collection

6.1.1 Patient survey

A patient survey is the preferred method of data collection for 28 indicators included in the NEED framework (see Table 3). If the patient is unable to respond, a proxy may complete the survey on their behalf. Three indicators require input from proxies who are informal carers.

Table 3 – NEED indicators that have patient survey as preferred data collection method

	Indicator	Respondent
1	EQ-5D-5L	Patient or Proxy*
2	Experienced burden of physical symptoms related to the health condition	Patient or Proxy
3	Pain/discomfort before disease vs today	Patient or Proxy
4	Experienced burden of psychological symptoms related to the health condition	Patient or Proxy
5	Anxiety/depression before disease vs today	Patient or Proxy
6	Mobility before disease vs today	Patient or Proxy
7	Self-care before disease vs today	Patient or Proxy
8	Usual activities before disease vs today	Patient or Proxy
9	Impact on sexual health	Patient or Proxy
10	Impact on reproductive health	Patient or Proxy
11	Experienced burden of treatment side-effects	Patient or Proxy
12	Experienced burden of treatment	Patient or Proxy
13	Coordination and continuity of care	Patient or Proxy
14	Received information	Patient or Proxy
15	Involvement in treatment decisions	Patient or Proxy
16	Time from first presentation to diagnosis	Patient or Proxy
17	Forgone care	Patient or Proxy
18	Forgone social support	Patient or Proxy
19	Impact on personal relationships	Patient or Proxy
20	Impact on education	Patient or Proxy
21	Reduction in working time	Patient or Proxy
22	Perceived financial difficulties related to the health condition	Patient or Proxy
23	Absenteeism of patients	Patient or Proxy
24	Presenteeism of patients	Patient or Proxy
25	Work reduction of patients or early labour force exits	Patient or Proxy
26	Impact on informal caregiver's health	Informal caregiver° (Proxy)
27	Impact on informal caregivers' social life	Informal caregiver °(Proxy)
28	Informal caregiving time burden	Informal caregiver° (Proxy)

*Proxy is defined in Table 7.

6.1.1.1 *Generic patient questionnaire*

A generic questionnaire to survey adult patients with a given health condition (or their proxies) has been developed and is available in the NEED toolbox in Excel and Limesurvey format.⁸ The development and validation process is further explained in the NEED toolbox.⁸ This questionnaire aims to evaluate selected indicators from the NEED framework, addressing dimensions of patient and societal needs. The latest version of the questionnaire consists of 55 items addressed to patients and an additional 7 items addressed to informal caregivers participating on behalf of an affected person. The items capture patients' socioeconomic background information, the impact of their health condition on their health status and quality of life, their healthcare-related needs, their unmet social support needs and the repercussions of the condition on their social life, including education, work, finances, and relationships. In addition to these dimensions, open-ended questions are included to capture unmet needs not covered by previous questions, as well as the unmet needs the patient considers to be the highest priority. When the respondent is an informal caregiver, additional items are provided to assess the impact of the patient's health condition on the caregiver's own health and their social life, and the time burden associated with caregiving.

A distinctive feature of this questionnaire is that it includes both generic items directly applicable across various health conditions and items that require adaptation (or removal) depending on the particular pathology under study. Accordingly, a preliminary adaptation phase is essential prior to its deployment in the context of this study.

ADAPTATION PROCEDURE

The items requiring adaptation are listed in the table below as "disease-specific" or "country-specific" (Table 4), along with a description of the modifications that should be implemented. The revision process may involve changes to the content (e.g., removing questions that are not relevant to the disease under study, adapting examples provided in certain items) and/or adjustments to wording (e.g., terminology used to describe symptoms or side effects). This adaptation must be based on a literature review of the health condition in question, validated by at least two clinical experts in the field, and followed by a pilot study involving patients.

Unless the patient population is too small, such as in the case of ultra rare diseases, the survey should be piloted with a few patients (e.g. five patients), and additional feedback should be collected from them. This allows us to assess patients' understanding and interpretation of the questions, the acceptability of questions, the time it takes them to complete the survey, and any additional comments they may have. Alternatively, if recruiting patients for the pilot is challenging, a small group of individuals from diverse backgrounds and age groups, representative of the patient population and without a scientific background, can be invited to test the survey. These can help evaluate the clarity of the questions and the user-friendliness of the online platform.

With regard to generic items, the original wording should always be retained, unless clearly irrelevant to the condition under study. The wording of standard validated tools (e.g. EQ-5D-5L, VAS) should not be modified.



Table 4 – Overview of the NEED patient questionnaire

Section	Item theme	Item code	Generic specific /	Adaptations to be made	Descriptive Framework indicator / NEED	Respondent
General information	Gender, birth year, level of education, birth country (if other), financial situation	D1, D1b, D2, D3, D5, D8, D12	Generic		Descriptive	Patient or Proxy*
	Place of residence, country of birth	D4, END1, D7	Country-specific answer options	Adapt responses within [...] to the studied country	Descriptive	Patient or Proxy*
	Housing situation	D6	Disease-specific answer options	Adapt response to the studied disease	Descriptive	Patient or Proxy*
	Employment status (before and after onset of disease)	D9, D11	Country-specific answer options	Adapt the example in [...] of country-specific unemployment benefits	Descriptive	Patient or Proxy*
	Employment status	D10	Generic		Used for indicators: Reduction in working time; Work reduction or early labour force exits of patients; Absenteeism of patients	Patient or Proxy*
Diagnosis	Specific diagnosis	DSD1, END2	Disease-specific	Keep this question only when studying a disease with different subtypes or a group of diseases. Adapt diagnostic subtype/group in the response options in [...].	Descriptive	Patient or Proxy*
	Time to diagnosis	HC1	Generic		Time from first presentation to diagnosis	Patient or Proxy*



	Time since diagnosis	D13, D13b	Generic		Used for indicator : Absenteeism of patients	Patient Proxy*	or
	Hospitalisation for health condition	DSD2	Disease-specific	Keep only in diseases for which relevant (i.e. where hospitalisation is a proxy of disease severity: e.g. acute Covid, hyperemesis gravidarum)	Descriptive	Patient Proxy*	or
Associated health condition(s)	Associated health conditions	DSD3	Disease-specific	Delete if irrelevant for the disease studied. Response options in [...] need to be adapted: add specific associated health conditions (e.g. in the case of Crohn's disease: ankylosing spondylitis, erythema nodosum, (epi)scleritis or uveitis, erythema nodosum,...)	Descriptive	Patient Proxy*	or
	Other health conditions	D14	Generic		Descriptive	Patient Proxy*	or
		D15	Disease-specific answer options	For each answer category, add in (...) some examples for the most common comorbidities of the studied disease	Descriptive	Patient Proxy*	or
General Health-related quality of life (before first symptoms and today)	Mobility level	H1, H2, H3, H4, H5, H7, H8, H9, H10, H11	Generic		Mobility before disease vs today	Patient Proxy*	or
	Self-care level				Self-care before disease vs today		
	Usual activities level				Usual activities before disease vs today		
	Pain/discomfort level				Pain/discomfort before disease vs today		
	Anxiety level				Anxiety/depression before disease vs today		
	Today and before the onset of the first symptoms (EQ-5D-5L)				EQ-5D-5L		

	self-reported health status (VAS-EQ-5D-5L)	H6PROXY, H6, H12PROXY, H12	Generic		Descriptive	Patient Proxy*	or
Disease-related treatment	Received treatments, side-effects and their burden	HC3, HC4	Disease-specific answer options	Response options in [...] are to be adapted. Response options not in [...] are to be kept.	Experienced burden of treatment side-effects	Patient Proxy*	or
		HC2, HC4b, HC5	Generic		Experienced burden of treatment side-effects	Patient Proxy*	or
	Burden of treatment aside from side-effects	HC6	Generic		Experienced burden of treatment	Patient Proxy*	or
Disease-related symptoms	Symptoms (physical and psychological) and effects of the disease (sleep, concentration, mood, and self-esteem; perceived stigma) and their burden	H13, H13b	Disease-specific answer options	Response options in [...] are to be adapted. Response options not in [...] are to be kept.	Experienced burden of physical symptoms related to the health condition Experienced burden of psychological symptoms related to the health condition	Patient Proxy*	or
	Impact on sexual life	H14	Generic		Impact on sexual life	Patient Proxy*	or
	Impact on reproductive life	H15	Disease-specific examples	Adapt the example in [...] only if irrelevant	Impact on reproductive life	Patient Proxy*	or
Care management	Organisation, coordination, continuity of care	HC7, HC8, HC9	Generic		Coordination and continuity of care	Patient Proxy*	or
	Received information	HC10	Generic		Received information	Patient Proxy*	or
	Involvement in decision-making	HC11	Generic		Involvement in treatment decisions	Patient Proxy*	or
Access to care	Forgone care	HC12, HC13	Generic		Foregone care	Patient Proxy*	or

Impact on education and work	Impact on education	S1	Generic		Impact on education	Patient Proxy*	or
	Reduction of working time	S2	Generic		Reduction in working time Work reduction or early labour force exits of patients Used for indicator: Presenteeism of patients	Patient Proxy*	or
	Productivity loss	S4, S4PROXY	Generic		Presenteeism of patients	Patient Proxy*	or
	Productivity loss	S3, S3b	Generic		Absenteeism of patients	Patient Proxy*	or
Financial impact	Financial impact	S5	Generic		Perceived financial difficulties related to the health condition	Patient Proxy*	or
Impact on relationships	Impact on social connection	S6	Generic		Impact on personal relationships	Patient Proxy*	or
	Forgone social support	S7	Generic		Foregone social support	Patient Proxy*	or
Priority needs	Unmet needs to be addressed as a priority	P1	Generic		Descriptive	Patient Proxy*	or
General	Additional unmet needs	G1, G2	Generic		Descriptive	Patient Proxy*	or
Impact on informal caregiver	Proxy respondent type	CG1	Generic		Descriptive Used for all indicators related to informal caregivers	Proxy*	
	Proxy relationship with the patient, gender, date of birth	CG2, CG3, CG4	Generic		Descriptive	Informal caregiver°	



	Informal caregiving time burden	CG5	Generic		Informal caregiving time burden	Informal caregiver°
	Impact on informal caregiver's physical and psychological health	CG6	Generic		Impact on informal caregiver's health	Informal caregiver°
	Impact on informal caregiver's social life	CG7	Generic		Impact on informal caregiver's social life	Informal caregiver°

*D=descriptive, DS=disease-specific question H=Health, HC=Healthcare, S=Social, P=Prioritisation, G=General, CG=Informal caregiver. *Proxy is defined as: as the person who provides information on behalf of the patient. In order to participate, the proxy must have a close relationship with the patient (e.g., family member, volunteer, neighbour) and spend significant time with him/her, and be familiar with the patient's situation, experiences, and preferences. In the NEED project, formal caregivers, i.e. caregivers that are paid to provide care services (e.g., healthcare professionals) are not eligible to act as a proxy. Close people with a recognised legal status as a 'carer' are considered proxies, provided they meet the above criteria; °Informal caregiver is defined as a person that provides continuous or regular help and support to the patient without financial compensation. This support may include personal care (e.g., dressing/undressing, assistance with toileting), mobility support (help with moving around), household tasks (e.g., meal preparation, cleaning), practical assistance (e.g., health monitoring, accompanying the patient to medical or other appointments), emotional or psychological support (spending time with the patient to provide emotional comfort), and help with administrative tasks (e.g., managing finances). *Proxy is defined in Table 7*

ADMINISTRATION PROCEDURE

The questionnaire starts with an introduction to the study, consisting of the aim, requirements for participation, and confidentiality policy. Respondents are asked to provide their informed consent by ticking a box at the end of the introductory text before proceeding. The estimated completion time is approximately 40 minutes. Participants have the option to complete the questionnaire in multiple sessions using the same link.

- **Availability:** The generic questionnaire (in French, Dutch, and English) is available in an Excel sheet and in Limesurvey:
 - <https://survey.kce.be/index.php/632819?newtest=Y&lang=fr> (FR)
 - <https://survey.kce.be/index.php/632819?newtest=Y&lang=nl> (NL)
 - <https://survey.kce.be/index.php/632819?newtest=Y&lang=en> (EN)
- The Excel sheet also contains an explanation of the LimeSurvey structure to facilitate both the development of the disease-specific questionnaire and its integration into the LimeSurvey platform.

Target population: This questionnaire can be used with adult patients from any disease, provided that adaptations are made to the disease-specific questions. A version of the generic questionnaire that can be used for studies in paediatric populations is under development (expected publication 2026). The adult questionnaire is designed to be completed by the patient or, if the patient is unable to respond, by a proxy on their behalf (see the definition of proxy in Table 7). A proxy may also assist a patient who is physically present and able to respond, for example, by reading questions aloud and recording the patient's responses in the questionnaire. In such cases, the proxy must remain neutral and must not influence the patient's answers.

Scoring: No global score is calculated. Responses to the items contribute to the assessment of specific indicators. These measurement approaches are detailed for each indicator in Chapter 5 of this protocol.

Follow-up interview: At the end of the questionnaire, participants are asked whether they are willing to take part in an individual interview. If so, they are asked to provide their contact details. More information about the interviews can be found in the section 6.1.2.

Updates: Note that the generic questionnaire is likely to evolve as the NEED framework evolves. It is therefore important to always check for the latest version of the questionnaire before starting a NEED study. A version of the generic questionnaire that can be used for studies in paediatric populations is under development (expected publication 2026).

6.1.1.2 Defining the survey sample

When developing the NEED research project, the scope must be carefully defined because it might have an impact on the patient recruitment strategy. It is advised to involve patient organisations and clinical experts with experience in conducting research in the specific patient population, as they may identify potential caveats and highlight specific points of attention. For instance, the scope may be broadened to include closely related health conditions or narrowed to a specific subtype, and might therefore somewhat differ from the initially selected health condition. Patient-related inclusion criteria to consider include: age range (mainly to consider which NEED questionnaire is more appropriate-adult or paediatric), specific sub-diagnoses, and country of residence. Exclusion criteria, if any, must be clearly defined and justified.

Additionally, it is important to consider whether the questionnaire should be translated into other languages, whether official or minority languages, in order to avoid excluding population groups and ensure full understanding of the questions. Translation should follow the TRAPD model and involve, at a minimum, one bilingual translator, one bilingual reviewer, a discussion to resolve discrepancies,



testing by a native-speaker, and documentation. Throughout the process, cultural appropriateness must be carefully considered. Questionnaire translation guidelines should be followed as far as the available budget allows (e.g. the TRAPD approach¹⁶).

The minimum sample size of completed patient surveys is calculated based on an error margin of 5%, a confidence level of 95%, and the estimated prevalence of the health condition in the country (and potentially, the prevalence of specific sub-diagnoses if stratified sub-analyses are planned). Potential dropouts should also be taken into account in the sample size calculation, as for some health conditions, there might be a high risk that participants start but do not complete the survey.

For cases in which patients might be unable to complete a questionnaire themselves, the possibility of including patient proxies should be considered. The proxy must be someone who has a close relationship with the patient (e.g., family members, legal representative, neighbour), who spends a significant amount of time with him/her, and who has a good understanding of the patient's situation, experiences, and preferences. In the NEED project, formal caregivers, i.e. caregivers that are paid to provide care services (e.g., healthcare professionals), are not eligible to act as a proxy.

6.1.1.3 Recruitment of survey participants

The recruitment strategy for survey participants aims to gather a sample that accurately represents the patient population in the targeted country (or countries), considering factors such as gender, age group, socioeconomic context, disease stage or severity, disease subtypes, outpatient vs inpatient, and treatment options.

The patient survey can be auto-administered online or on paper, depending on the patient population and patients' preferences. When a paper version is preferred, a pre-stamped envelope should be provided to participants.

Drawing on our experience from previous NEED case studies, we offer several recommendations. A comprehensive, multichannel recruitment approach should be implemented, incorporating social media, the NEED website, press releases, healthcare settings, community centres, targeted e-mails (to patient organisations, disease advocacy groups, healthcare settings, etc), and sometimes direct outreach. Recruitment materials may include both physical and digital posters, flyers, and social media posts with links to a dedicated webpage and a QR code leading directly to the survey. Figure 3 gives an example of a poster developed for a NEED survey on psychotic disorders. Furthermore, collaboration with sickness funds, umbrella patient organisations, disease-specific and general patient organisations, hospitals, universities, and healthcare professionals can help disseminate the call for participation. It may also be beneficial to present the research directly to patient organisations and healthcare settings to raise awareness.

Figure 3 – Example of recruitment material (poster) for NEED study



The recruitment period typically lasts around three months, with ongoing monitoring and adjustment to the strategy as needed to obtain a representative sample. However, this duration may vary depending on the expected sample size and the challenges encountered in reaching the target study population. While the strategy aims to capture a diverse range of patient profiles as described above (e.g., socioeconomic status, disease stage), the voluntary nature of recruitment introduces potential bias (such as volunteer bias), which could limit the generalisability of findings on the unmet needs associated with the health condition. Therefore, particular attention must be placed on the representativity of the sample, particularly so in the case of small samples (i.e. rare diseases).

Additionally, depending on the health condition and patient population, recruitment materials and strategy may also target adult proxies, in addition to patients themselves.

6.1.1.4 Survey data storage and analysis

Pseudoanonymised survey data must be stored on a secure server. Personal identifiers (name, phone number, and e-mail address) are collected only from participants who volunteer for an interview and are stored separately. The link between survey responses and contact information is managed exclusively by a third party to ensure confidentiality.

Data analysis is conducted primarily through quantitative methods, using descriptive and inferential statistics.

The study's inclusion criteria must be verified, and patients who do not meet these criteria should be excluded from the analysis. It is also necessary to check whether any participants responded to the questionnaire more than once. If this is the case, we recommend keeping the last completed questionnaire and removing the first.

Responses categorised as "other" must be carefully reviewed. Some of them may need to be reassigned to existing categories, which could require input from a clinician.



In addition, responses such as “I don’t know,” “Not applicable,” and “I don’t want to answer” must be carefully assessed and handled appropriately. For most indicators, it is recommended that these responses be excluded from the denominator; however, for some, they may be relevant and should be kept (e.g. “I don’t know” in the question on involvement in treatment decisions). Detailed calculation methods are provided in the technical sheets available in the NEED database and should be reviewed thoroughly before analysis (see info tab on the NEED database website).

A standardised R script, available in the NEED toolbox⁸, supports consistent analysis of the patient questionnaire and also generates figures and tables that facilitate the preparation of scientific reports or publications.

This script generates the indicator values to be included in the NEED database. These indicator values should be entered into the single-disease *NEED database Excel template* (see supplementary material) and submitted to the NEED team for review. After validation, the data are published in the online NEED database. Where sample size permits, results should be disaggregated by gender, age group, socioeconomic status, and, when relevant, by disease severity or subtype (see the NEED Excel template for category definitions).

MISSING DATA

- Missing data are common in patient surveys and can bias results if not properly handled. It is important to plan how to address missing responses in the NEED questionnaire analysis. According to Rubin’s framework, there are three mechanisms under which data may be missing: missing completely at random (MCAR), missing at random (MAR), and missing not at random (MNAR). The appropriate method for handling missing data depends on which of these scenarios is most plausible for a given dataset, and multiple strategies may be necessary. When data are **MCAR**, missing responses occur randomly, so complete-case analysis yields unbiased results; however, this assumption is rarely realistic. For **MAR**, missingness depends on observed factors, making multiple imputation the preferred method, as it preserves incomplete records and improves accuracy when auxiliary variables are included. In **MNAR**, missingness depends on unobserved values themselves, making standard methods inadequate; instead, sensitivity analyses are essential to test how results change under different assumptions. If imputation or sensitivity analyses are not feasible, the extent of missing data should at least be reported.¹⁷
- For the two scenarios outlined below, we advise the following steps:
 - **Participant starts but does not complete the questionnaire:** Unless a participant explicitly asks that his/her data be excluded, responses may be included in the dataset if the participant has answered all questions from D1 to H12. Nevertheless, the decision to include partially completed questionnaires should be made on a case-by-case basis, taking into account factors such as the representativeness of the patient sample and whether the health condition under study is rare or more common. The total number of initial participants should be clearly reported in the participant flowchart (CONSORT diagram), along with the number of participants contributing data per item.
 - **Questionnaire submitted with incomplete responses:** If the missingness mechanism is assumed to be *Missing Completely at Random (MCAR)*, the missing responses can be ignored. If the mechanism is assumed to be *Missing at Random (MAR)*, the missing responses should be imputed. If the mechanism is assumed to be *Not Missing at Random (NMAR)*, or if imputation is not feasible, “missing” should be explicitly reported as a category in both tables and figures.

6.1.2 Patient interviews

For the 24 indicators listed in Table 5, it can be useful to conduct individual patient interviews in addition to the patient survey. Interviews enable the collection of in-depth information on the context, experiences, and underlying mechanisms of unmet needs reported in the patient survey. The benefits of the qualitative data collection are the deeper insight into the unmet needs, such as descriptions of the burden of disease and its impacts on patients' lives, allowing for potential identification of additional aspects that did not emerge from the survey. The interviews can also help identify the causes for unmet healthcare and social needs, which is useful to generate hypotheses to develop targeted solutions.

Table 5 – NEED indicators with patient interview as a complementary data collection method

Indicators	Respondent
Experienced burden of physical symptoms related to the health condition	Patient or Proxy*
Pain/discomfort before disease vs today	Patient or Proxy*
Experienced burden of psychological symptoms related to the health condition	Patient or Proxy*
Anxiety/depression before disease vs today	Patient or Proxy*
Mobility before disease vs today	Patient or Proxy*
Self-care before disease vs today	Patient or Proxy*
Usual activities before disease vs today	Patient or Proxy*
Impact on sexual health	Patient or Proxy*
Impact on reproductive health	Patient or Proxy*
Experienced burden of treatment	Patient or Proxy*
Experienced burden of treatment side-effects	Patient or Proxy*
Coordination and continuity of care	Patient or Proxy*
Received information	Patient or Proxy*
Involvement in treatment decisions	Patient or Proxy*
Time from first presentation to diagnosis	Patient or Proxy*
Forgone care	Patient or Proxy*
Forgone social support	Patient or Proxy*
Impact on personal relationships	Patient or Proxy*
Impact on education	Patient or Proxy*
Reduction in working time	Patient or Proxy*
Perceived financial difficulties related to the health condition	Patient or Proxy*
Non-healthcare costs	Patient or Proxy*
Impact on informal caregiver's health	Informal caregiver° (Proxy)
Impact on informal caregivers' social life	Informal caregiver° (Proxy)
Informal caregiving time burden	Informal caregiver° (Proxy)

*Proxy is defined in Table 7.



To conduct a patient interview effectively, the interviewer must have training in qualitative interview techniques, as well as solid past experience conducting such interviews. The interview must not be conducted by a healthcare professional involved in the patient's care.

Each interview should not last more than 1.5 hours in total. It may be divided into shorter segments if needed or adapted to the specific needs of the patient population—for example, allowing patients to respond via chat while the interviewer speaks orally. The first few interviews can be used as a pilot to adapt the interview guide.

After completing the questionnaire and volunteering for the interview, patients and proxies may choose to attend the interview either individually or together. This choice is entirely theirs and is clearly explained when the appointment is scheduled. If the patient opts to attend alone or with a proxy for a joint interview, we recommend using the generic patient interview guide. Conversely, if the proxy chooses to attend alone, we recommend using the generic proxy interview guide.

In joint interviews with both patient and proxy, the interviewer should initially direct questions to the patient. The proxy should provide assistance only when the patient is unable to respond or explicitly requests their input. One specific challenge for the interviewer in this type of interview concerns the handling of disagreements, for which guidance can be found in the literature.^{18, 19}

6.1.2.1 Generic patient interview guide

The NEED toolbox contains a generic interview guide that is adaptable to the health condition under consideration.⁸ The generic interview guide is currently available in English, French, and Dutch. The topics covered during the interviews draw on the adult NEED framework, completed with aspects identified in previous case studies.^{3, 4, 20}

The themes included in the interview guide are presented in Table 6.

Table 6 – Themes included in the patient interview guide

Theme	Sub-themes
Health	- Impact on psychological and physical health* - Symptoms* - Daily life functioning, including sexual and reproductive life - Interaction with other health problems*
Healthcare	- Patient journey leading up to diagnosis* - Experience with treatment* (received, refusal, administration) - Therapeutic needs: information needs, forgone care, accessibility, care network - Perception of quality of care: coordination, continuity, relationship with care providers - Financial burden - Administrative burden
Social impact	- Impact of the disease on social activities, relationships, work, education, and finance
Support identified	- Identification of formal and informal support networks: received and forgone support
Solutions	- Identification of potential solutions to address unmet needs in healthcare themes
Priority needs	- Unmet needs expressed throughout the interview that should be addressed as a priority

**Items or response options that may need to be adapted to the health condition under study*

The purpose of the interview is to gain a better understanding of the unmet needs identified in the survey. We therefore recommend retaining all themes and sub-themes in Table 6 and adapting them if necessary to reflect disease-specific issues and individual factors identified in the survey.

6.1.2.2 Generic proxy interview guide

Table 7 – Definitions of proxy respondent and proxy informal caregiver

Proxy respondent: someone who provides information on behalf of the patient. In order to participate, the proxy must meet three criteria: be an adult with a close relationship with the patient (e.g., family member, volunteer, neighbour); spend significant time with him/her; and be familiar with the patient's situation, experiences, and preferences (adapted from ²¹ and ²²). Close people with a recognised legal status as a 'carer' are considered proxies, provided they meet the above criteria. In the NEED project, formal caregivers, i.e. caregivers that are paid to provide care services (e.g., healthcare professionals) are not eligible to act as a proxy.

Proxy informal caregiver: someone who provides continuous or regular help and support to the patient without financial compensation. This support may include personal care (e.g., dressing/undressing, assistance with toileting), mobility support (help with moving around), household tasks (e.g., meal preparation, cleaning), practical assistance (e.g., health monitoring, accompanying the patient to medical or other appointments), emotional or psychological support (spending time with the patient to provide emotional comfort), and help with administrative tasks (e.g., managing finances) (adapted from ²³). A filter question at the start of this interview serves to determine whether the person meets the criteria for being considered an informal caregiver.

The generic interview guide for proxy respondents draws on the generic patient interview guide, and both aim to assess the unmet needs of patients. Questions from the generic patient interview guide were rephrased with a proxy-patient perspective, meaning the proxy should answer based on what they think the patient would say.^{24, 25} This perspective was preferred as it aligns more closely with the patient's self-report.²⁵ Here is an example of a question framed with the proxy-patient perspective: *"How do you think your loved one would describe their relationship with the caregivers they see for [the illness]?"* When proxies cannot report patients' perspectives due to lack of knowledge, they should inform the interviewer and decline to answer. However, for questions concerning healthcare quality and the patient's support needs, when the patient's perspective cannot be obtained but the proxy's viewpoint seems relevant, the interviewer may invite the proxy to provide their own opinion.

In addition to the topics covered in the patient interview guide, the proxy guide includes a dedicated section for proxies who serve as informal caregivers. At the beginning of this additional section, a filter question is used to determine whether the participant meets the criteria for being considered an informal caregiver.

The final version of the proxy interview guide is presented in the NEED toolbox.⁸ This guide is currently available in English, French and Dutch. The topics of the proxy interview guide are the same as the topics of the generic patient interview guide, with the addition of the following topics on the section "informal caregivers":

- Impact on informal caregivers' health
- Impact on informal caregivers' time
- Impact on informal caregivers' social life
- Informal caregivers' support and information needs

Any disease-specific adaptations applied to the generic patient interview guide must also be applied to the proxy respondent interview guide. The section "informal caregivers" is not disease-specific and should therefore not be adapted.



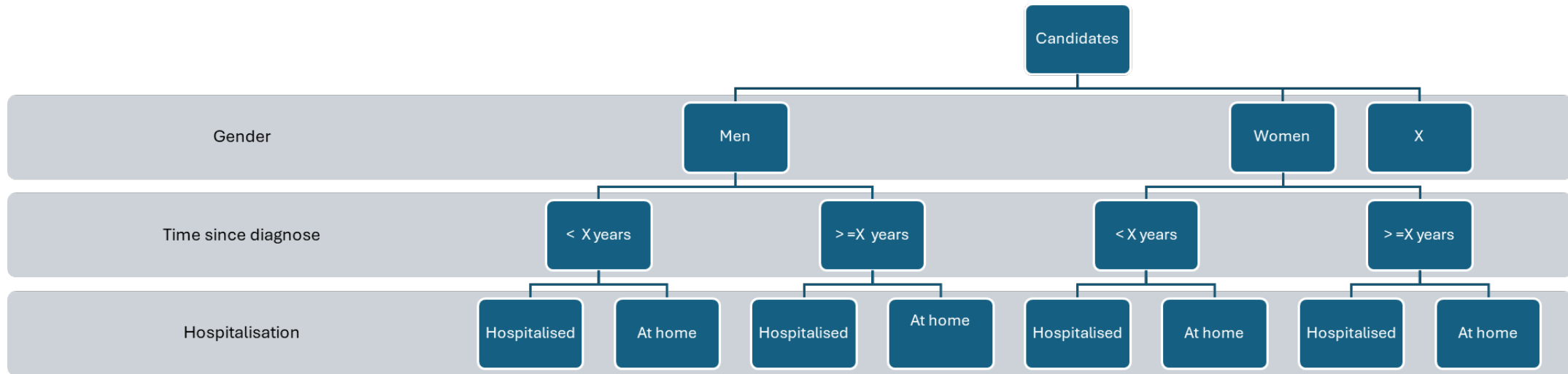
6.1.2.3 *Recruitment and selection of interviewees*

The aim of interview sampling is to ensure a heterogeneous sample of patients in order to obtain a comprehensive range of all types of unmet needs associated with the health condition. This sampling strategy is characteristic of qualitative research and differs from quantitative sampling, which aims to select a representative portion of patients.

Patients willing to be interviewed are invited to leave their contact details in the questionnaire so that they can be contacted by the research team if they meet the inclusion criteria. Ideally, a minimum of 20 individual interviews should be conducted. To ensure a broad representation of respondent profiles, the recruitment of participants should be based on segmentation criteria, such as gender, age, socioeconomic context, specific diagnosis, disease stage or severity, treatment type, or other relevant clinical criteria (e.g. outpatient vs. hospitalised, time since diagnosis) (see Figure 4). Then, in each segment of the volunteering population, the same number of participants are randomly selected. In cases where there are insufficient candidates in a specific segment, additional candidates are contacted in adjacent categories.



Figure 4 – Example of a segmentation tree to select participants for the interviews





Participants selected to participate in the interviews are called to confirm their willingness to participate and to set the date and mode (online or in-person, presence of proxy) for the interview. Once they agree, participants receive the confirmation and informed consent form by e-mail, followed by logistical information. If a selected candidate does not respond to three phone call attempts or emails or refuses to participate, another candidate within the same segment should be randomly selected. Non-selected candidates are informed of their status via email to ensure transparency and communication regarding the selection process.

At the beginning of the interview, participants will have the opportunity to ask the researchers any questions they may have with respect to the informed consent, the interview and the study. Once the participants have received sufficient information, they will be able to sign the informed consent form (either electronically using a specific software -such as Adobe sign- if the interview is online, or in paper if the interview is in-person). If needed, the researcher can provide support in doing this. The document will then be countersigned by the researcher, and the participant will receive the final document by email.

Respondents can choose between an online interview or in person. If online, the interviews are conducted via videoconferencing, with both the interviewer and interviewee having their cameras on, whenever possible. The interviewer will ask questions and react to the interviewee's responses verbally. Participants who have difficulty speaking, but are able to type, can respond in writing using the chat feature of the videoconferencing platform. Additionally, participants who experience high levels of fatigue should be offered the option to complete the interview in shorter segments.

6.1.2.4 Interview data storage and analysis

Data collected through the interviews should be stored in a secure server.

Each interview should be recorded and transcribed verbatim. All names of participants, institutions, locations or healthcare providers should be anonymised during transcription, so that results can be presented anonymously. The transcription serves as material for the data analysis. The verbatim interview transcripts are analysed thematically using a method that combines both deductive approaches (based on the interview guide questions and the survey results) and inductive approaches.

A qualitative data analysis software, such as NVIVO®, should be used to develop a coding tree. The quotes should be anonymised by replacing any information that could identify the patient with a generic descriptor that reflects the person or feature (e.g., "Dr Maertens" could be replaced by "the physician", "Brussels" could be replaced by place of residence", "Erasmus Hospital" could be replaced by "treatment hospital", etc). The key points emerging from the interviews, as well as the supporting quotes, should be entered into the *NEED database Excel template* (see supplementary material) to be published on the NEED database.

6.1.3 Clinical expert input

For five indicators of the NEED assessment framework 2025, the input of clinical experts is the preferred source of information (see Table 8).

A systematic literature review for each indicator in Table 6 would make NEED studies overly burdensome, and the available literature may not fully reflect the national context. We therefore recommend surveying clinical experts to gather their assessments. These expert inputs should be validated against high-quality scientific or grey literature, even if not systematically identified (e.g. evidence on the clinical effectiveness of current treatments).

Table 8 – NEED indicators estimated with a clinical expert survey

Indicators
Implementation of effective primary prevention strategies
Appropriateness of diagnostic timing
Treatment availability
Treatment effectiveness*
Research gaps

*to be estimated using both expert survey and scientific literature review

6.1.3.1 Generic expert questionnaire

A questionnaire to collect expert input on the indicators mentioned above Table 8 is available in the NEED toolbox, both in Word and Limesurvey format (tool 6).⁸

Clinical experts are asked to base their ratings as much as possible on evidence and to support their answers by providing comments or references to scientific articles in an open comment box.

For each health condition, the aim should be to consult at least five carefully-selected clinical experts, who represent the different specialties involved in the care of patients with the selected health condition.

- **Availability:** The generic expert questionnaire is available in English in a Word document and in Limesurvey:
 - <https://survey.kce.be/index.php/695183?lang=en> (EN)
- A separate LimeSurvey structure document available in the Toolbox contains explanations to facilitate the direct integration of the questionnaire into the LimeSurvey platform.

6.1.3.2 Recruitment and selection of clinical experts

The clinical experts invited to complete the questionnaire should be selected among academics with extensive expertise in the health condition under study. They should be healthcare professionals by training, primarily doctors, but depending on the health condition, may also include midwives, nurses, clinical psychologists, or others, with extensive experience in caring for patients affected by the condition. A declaration of interest form (see Supplementary tool 5 in the NEED toolbox⁸) should be completed by experts, and those with a significant conflict of interest should be excluded.

6.1.3.3 Expert questionnaire data storage and analysis

Data collected through the survey should be stored in a secure server.

In order to present a single answer category in the NEED database for each indicator assessed through the expert survey, the following analysis method will be used: the distribution of responses will be examined to determine the proportion falling within the same category, as well as the proportion falling in adjacent or more divergent categories.

- **Strong Majority with Adjacent Disagreement**
If 75% or more of respondents select the same category, and the remaining responses are in an adjacent category (e.g. three out of four say *Major gap*, one says *Moderate gap*), the majority category is retained as the consensus.
- **Non-Adjacent Disagreement**
If a respondent selects a category that differs substantially from the majority (e.g., three rate it as a *Major gap* while one rates it as a *Minor gap*), the item is flagged for further discussion. The outlying response is then reviewed alongside any qualitative comments from other participants to



better understand the reasoning and, if needed, to revise the consensus. In such cases, conducting a Delphi process may also be appropriate.

- **No Clear Majority or Mixed Responses**

In cases where no clear majority exists (e.g., responses are evenly split or span multiple categories), a weighted scoring technique is applied:

- Each category is assigned a numerical weight:
 - No gap = 0
 - Minor gap = 1
 - Moderate gap = 2
 - Major gap = 3
 - Don't know = excluded from scoring
- The average score is calculated from included responses.
- The average is then mapped back to a category using predefined ranges:
 - 0.0–0.49 → *No gap*
 - 0.5–1.49 → *Minor gap*
 - 1.5–2.49 → *Moderate gap*
 - 2.5–3.0 → *Major gap*

If discrepancies arise in the use of the 'Not Applicable' category, that is when more than one respondent selects '*not applicable*' for a given category while others provide a categorical assessment (e.g. three identify *minor gaps* in biomarkers while two consider the category '*not applicable*') this divergence must be discussed with respondents, as it reflects a fundamental difference in perspectives. If only one respondent selects the 'not applicable' category, this response can be excluded while the other responses are treated according to the criteria specified above.

6.2 Secondary data collection

6.2.1 Scientific and/or grey literature reviews

The review of the scientific (and grey) literature in the context of a NEED research project has two distinct objectives: (i) to describe the health condition and key background information, and (ii) to identify existing evidence on the indicators of the NEED assessment framework

To achieve the first objective, a pragmatic literature review should be conducted prior to the primary data collection. This review should gather disease-specific information on the epidemiology, pathophysiology, aetiology, clinical presentation, comorbidities, diagnostic methods, treatment and management (including side-effects and wider support options), long-term outcomes, prevention, and socioeconomic (or other relevant) inequities. The disease description generated from this review will be used to tailor the generic patient questionnaire to the specific condition (see above), and a polished version will be published in the NEED database alongside the collected data, providing a context for the interpretation of results. At least one clinical expert in the disease should review the disease description for accuracy.

To address the second objective, a systematic review of the literature should be performed using the NEED standardised search strategy. The strategy is available in the NEED toolbox.⁸ This literature review gathers evidence related to the NEED framework criteria and indicators, particularly in cases where they are not estimated through patient surveys, interviews, expert opinions, or database analyses, or when additional information is required (e.g., to estimate the indicator

transmissibility) This literature review provides a consistent structure with NEED indicator-specific terms that enable reviews to be conducted on individual indicators, on specific dimensions of the framework, or across all dimensions. Terms can be combined using either a moderately specific or a highly specific approach, the latter further narrowing the number of results. The strategies to refine search results are available in the toolbox⁸.

These generic strategies can be easily combined with terms specific to the health condition under study, enabling the creation of targeted and consistent literature searches across different NEED studies. An example of a condition-specific strategy for psychotic disorder, combined with the other generic strategies, can be found in Table 9.

Table 9 – Disease-specific literature review used in the NEED psychotic disorder study (publication expected March 2026)

No.	Search terms	Results	
1	exp Schizophrenia/	118581	Terms related to schizophrenia/psychotic disorders
2	schizophrenia.ti,kf.	91857	
3	exp Psychotic Disorders/	60658	
4	Psychotic Disorders.ti,kf.	3271	
5	1 or 2 or 3 or 4	182243	Disease-specific strategy to be combined with generic strategy

We encourage researchers to use software to manage and streamline the literature review process, such as Covidence^e, ASReview^f or DistillerSR^g.

Studies should be evaluated using a standardised quality assessment tool, such as the Mixed-Methods Appraisal Tool (MMAT) or the CASP Systematic Review Checklist. Those deemed to be of very low quality should be excluded from the analysis.

When selecting evidence for inclusion in the NEED database, national-level data should be prioritised, followed by data from other European countries. All evidence meeting at least a low-quality threshold should be reported. If multiple estimates of the same quality are available for a given indicator, each should be presented. When data for a specific health condition are unavailable, proxy data may be used, for example, information on a broader disease category or a relevant subtype.

6.2.2 Database analysis

For 13 indicators of the NEED assessment, evidence must be collected through existing national or international databases, and estimates can be complemented by scientific literature reviews (see Table 10).

^e Covidence, <https://www.covidence.org/> (last access 27 February 2025)

^f ASReview, <https://asreview.nl/> (last access 27 February 2025)

^g DistillerSR, <https://www.distillersr.com/products/distillersr-systematic-review-software> (last access 27 February 2025)

**Table 10 – NEED indicators estimated with database analysis as primary data source**

Indicators
Years of life lost per case
Years of life lost per death
Years of life lived with disability per case
Prevalence or incidence
Forecasted years of life lost per case
Forecasted years of life lost per death
Forecasted years of life lived with disability per case
Forecasted prevalence or incidence
Out-of-pocket healthcare costs (per patient)
Annual healthcare costs per patient
Absenteeism*
Forecasted healthcare costs attributable to the health condition
Forecasted productivity losses attributable to the health condition

*Also estimated from patient survey

Accessing databases often takes time, and estimating indicators may require combining several of them. Therefore, we recommend identifying the relevant databases and requesting access early in the process of conducting a NEED research project. In Belgium, the Health Data Agency^h provides a catalogue of health(care) data and facilitates access to quality data related to health(care).

Some general remarks concerning the economic indicators of the NEED database should be noted.

- The primary emphasis of the NEED database is on European countries. For the economic indicators, healthcare cost data from the United States, for example, should generally not be used as the main source.
- Economic data are often highly country-specific, making it difficult to compare them across countries, even European countries. To address this, we provide guidance on using Purchasing Power Parities to convert national cost data into a Euro standard, accounting for price level differences across the European Union. For this, we refer to Chapter 9.
- To serve as an example for other countries and guide researchers interested in evaluating economic indicators at the Belgian level, we provide additional information about databases in Belgium that may be useful for developing the economic indicators based on Belgian data (see Chapter 7).

6.2.1.1 Methods for calculating healthcare costs attributable to the specific health condition (if data from national databases are available)

This section is applicable if national administrative databases that include data on economic indicators (out-of-pocket healthcare costs, healthcare costs) are available. The aim for these indicators is to calculate the annual weighted average cost per patient, which is attributable to the health condition. The objective indeed is to estimate only the costs attributable to the studied health condition. Healthcare costs which are unrelated to the condition under consideration (e.g. patients visiting their

^h Belgian Health Data Agency; <https://www.hda.belgium.be/en> (last access: 19 September 2025)

GP for an unrelated health condition) should not be considered for the analysis. Therefore, adjustments need to be made for such 'baseline healthcare costs', i.e. costs that also occur in the general population without the studied health condition. These adjustments should be based on relevant factors which are available in the data, such as age, gender, reimbursement status (which gives an idea of income or disability), and/or the region where a person lives. All these factors can also notably affect the height of the 'baseline healthcare costs'.¹⁵

Consider an administrative database that has for each individual in the dataset (a) total out-of-pocket costs and (b) information on whether an individual has a particular diagnosis or health condition of interest. In this particular database, it is not possible to directly connect a single out-of-pocket payment to a particular health condition, as this information is not recorded. Therefore, to estimate the average out-of-pocket costs that can be attributed to the diagnosis or health condition, the total out-of-pocket costs for individuals with the diagnosis or health condition are compared to the total out-of-pocket costs for individuals without the diagnosis, while controlling for other factors that can influence out-of-pocket costs, such as age, sex, socio-economic status, and region of residence.

A suitable method for this is G-computation, a method within causal inference that involves modelling the relationship between variables and simulating or "re-computing" outcomes under different scenarios to estimate causal effects. This method was developed at Harvard University.²⁶

The method involves the following steps:

1. Model fitting

In a first step, the data in the administrative database are used to fit a multiple linear regression model, with the out-of-pocket payments being the dependent variable (Y) and all influencing factors (including the health condition in question) as independent variables.

Then, the coefficients of this multiple linear regression model are used for the following steps.

2. Prediction under observed conditions

The out-of-pocket payments are predicted for each individual in the dataset. This means that from this point onwards, instead of using the "real" out-of-pocket payments, predicted out-of-pocket payments per patient based on the regression analysis are used.

2. Counterfactual prediction

The same regression model is then used again to predict average out-of-pocket payments per patient in a scenario where none of the individuals have the health condition of interest, keeping all other characteristics (age, sex, ...) as observed.

3. Estimation of attributable costs

The average out-of-pocket payments attributable to the health condition are calculated as the difference between an individual's predicted out-of-pocket payments with their actual health status from the original dataset (output of step 2) and the individual's predicted out-of-pocket payments assuming none of the individuals are affected by the health condition (output of step 3).

4. Survey weighting (if applicable)

Depending on the administrative database, it may be necessary to survey-weight the average out-of-pocket payments attributable to the health condition.

See Gorasso et al.¹⁵ for an example of the methodology used.



7 BELGIAN DATA SOURCES

The main Belgian databases that can be used are: the Belgian National Burden of Disease, the Health Interview Survey (HIS), disease-specific and central registries, Intego, the Inter-Mutualistic Agency (IMA-AIM) database and EPS, the 'Kruispuntbank van de Sociale Zekerheid – Banque Carrefour de la Sécurité Sociale (KSZ-BCSS) data, hospital discharge data, kenniscentrum arbeidsongeschiktheid – centre de connaissances en matière d'incapacité de travail, Belgian household budget survey (HBS) data.

7.1 The Belgian National Burden of Disease (BeBOD) study

The BeBOD study, launched in 2016, aims to establish a coherent framework for routinely quantifying the burden of disease in Belgium.ⁱ To date, estimates of mortality and years of life lost for 138 causes of death, estimates of the non-fatal burden of 56 cancer types, and estimates of the burden of 37 key diseases are available.^{27, 28} BeBOD relies on routine data sources to estimate the true disease burden and quantify related uncertainties. BeBOD estimates of the

burden of disease include: Disability-Adjusted Life Years (DALYs), Years Lived with Disability (YLDs), Years of Life Lost (YLLs), number of prevalent cases, and causes of death. Other European countries, such as Germany and the Netherlands, have also developed their own national burden of disease study.

In the NEED context, the BeBOD could be useful to get Belgian estimates of :

- Years of life lost (per death/per case)
- Years of life lived with disability (per case)
- Prevalence or Incidence
- Forecasted Years of life list
- Forecasted Years of life lived with disability

7.2 The Health Interview Survey (HIS)

The HIS^j collects information on eight main health domains (i.e. health and quality of life, lifestyle, preventive knowledge and practices, mental health and well-being, use of health services, health and society, and dental health) of a representative sample of the general Belgian population, including the elderly staying in a nursing 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 paper-and-pencil self-administered questionnaire.²⁹ The basic sample consists of 10 000 persons but oversampling of specific population groups (e.g. German community, older people) is possible to obtain more precise estimates. By using weighting factors, representative results can be calculated at the level of the total population. To date, a HIS has been conducted in Belgium in 1997, 2001, 2004, 2008, 2013, 2018 and 2023. The detailed methodology of the survey is described elsewhere.³⁰ Furthermore, since 2013, the HIS is part of the European Health Interview Survey (EHIS)- see Section 8.3.

In the NEED context, the HIS could be useful to get Belgian estimates of :

- EQ-5D-5L average score (for some chronic conditions)

ⁱ The Belgian National Burden of Disease Study, <https://www.sciensano.be/en/projects/belgian-national-burden-disease-study> (last access: 29 January 2024)

^j Health Interview Survey , <https://www.sciensano.be/en/projects/health-interview-survey> (last access: 29 January 2024)

- Pain/discomfort at the time of survey completion
- Anxiety/depression at the time of survey completion
- Mobility at the time of survey completion
- Self-care at the time of survey completion
- Usual activities at the time of survey completion
- Received information
- Involvement in treatment decisions
- Impact in social life
- Prevalence or incidence (for some chronic conditions)

7.3 Disease-specific and central registries

In Belgium, disease-specific and central registries exist only for a very limited number of diseases. Nationally representative registries include the Belgian Cancer Registry (BCR) and some registries for rare diseases (e.g. the Central Registry of Rare Disease^k (CRRD)). Other registries are of a regional or local scale. The data collection methods for registries vary. For the CRRD, a database holding a limited set of data from patients affected by a rare disease who have consulted a specialist in Belgium about their disease, data are collected by registering centres (genetic centres, university hospitals) through manual input via web-based forms or via automated data extraction from EHR (CSV or API upload). In the case of the BCR, hospitals operating oncology care programs are required by law to participate in cancer registration by providing data to the BCR.³¹ The BCR collects, amongst others, data on the incidence and stage of cancer, the localisation of the tumour and the survival rate of patients suffering from cancer. The full list of variables available in BCR databases is available at <https://kankerregister.org/tumourbank.aspx?Pageld=212>. Some results are freely available through an online tool^l and publications.

Other disease-specific and central registries in Belgium include: the registries of congenital anomalies (Antwerp and Hainaut, and Namur)^m, the Belgian Cystic Fibrosis Registryⁿ, the Belgian Neuromuscular Disease Registry (-Spinal Muscular Atrophy)^o and the Belgian Rare Bleeding Disorders Registry (under development). It would also be worthwhile to engage with patient associations, which may possess relevant disease-specific data.

In the NEED context, the disease-specific and central registries could be useful to get Belgian estimates of :

- Prevalence or Incidence
- Diagnostic timing
- Treatment effectiveness

^k Central Registry of Rare Diseases, [Central Registry Rare Diseases | sciensano.be](https://www.sciensano.be/en/projects/central-registry-rare-diseases) (last access: 10 October 2025)

^l Belgian Cancer Registry online tool, <https://kankerregister.org/default.aspx?Pageld=344> (last access: 10 October 2025)

^m Eurocat, https://eu-rd-platform.jrc.ec.europa.eu/eurocat_en (last access: 10 October 2025)

ⁿ Belgian Cystic Fibrosis Registry, <https://www.sciensano.be/en/projects/belgian-cystic-fibrosis-registry> (last access: 10 October 2025)

^o Belgian Neuromuscular Disease Registry, <https://www.sciensano.be/en/belgian-neuromuscular-diseases-registry-bnmdr> (last access: 10 October 2025)



7.4 Intego

Intego is an electronic patient record (EPR)-based network of 54 voluntarily participating general practitioner (GP) practices in Flanders, which all use the same EPR software. This network has been operational since 1994 and is coordinated by the Academic Centre for General Practice at the KU Leuven and covers approximately 2% of the Flemish population.³² The Intego database^p includes information on diagnoses (primarily based on the International Classification of Primary Care (ICPC) coding system) and prescribed drugs. For diseases that are well-recognised in primary care, and for which people are frequently in contact with GPs, the Intego database is the most appropriate source of information for diagnosis.³³ Sciensano is currently preparing a linkage scheme for an Intego-IMA linkage.³³

In the NEED context, Intego could be useful to get Belgian estimates of :

- Prevalence or Incidence
- Diagnostic timing

7.5 The Inter-Mutualistic Agency (IMA – AIM) database and permanent sample (EPS)

The IMA – AIM database is a partnership of the seven Belgian sickness funds which continuously collects detailed administrative health insurance data of the different sickness funds in a common format. Only data on healthcare covered by the public health insurance or used by residents insured in the public health insurance are registered. The IMA – AIM database combines three main types of data^q: (1) Population, including socio-demographic information on the members of sickness funds (e.g. chronic illness reimbursement status, work incapacity, invalidity, increased reimbursement category, unemployment), (2) reimbursed healthcare expenses including procedures, services, admissions, reimbursed prescription drugs in hospitals pharmacies (i.e. Gezondheidszorg – Soins de Santé), and (3) reimbursed expenses on pharmaceutical products in public pharmacies (i.e. the NIHDI Pharmanet). Pharmanet contains data on: pharmaceutical specialties (drugs produced by the pharmaceutical industry), magistral preparations (medicines prepared by the pharmacist himself from a prescription), the various fees (on-call fees, fees for dispensing methadone, oxygen, etc.), medical nutrition (foods with special composition intended for people with certain diseases, to be used in case of (risk of) malnutrition or in a perioperative context), services within the framework of diabetes and chronic renal failure care pathways (sticks and lancets, glucometer, blood pressure monitor).³⁴

As information on patients' diagnosis is not recorded in the IMA – AIM database, "pseudo-diagnosis" or "pseudo-pathologies" based on Pharmanet data were developed starting in 2016 as a proxy for patient diagnosis. Pseudo-pathologies are determined by IMA – AIM on the basis of medicines dispensed in public pharmacies. A pseudo-pathology group is assigned to an individual only to the extent that the total number of Defined Daily Doses (DDD) for all Anatomical Therapeutic Chemical (ATC) Classification codes in that group is greater than or equal to 90 during the reference year. For some pseudo-pathologies there are also restrictions on age and type of prescriber.³⁵ The pseudo-pathologies have been updated and improved at various times by a guidance group and extended with NIHDI nomenclature codes. In 2019, 31 pseudo-pathologies were available in the IMA – AIM database.

Sciensano performed a linkage between IMA – AIM data and HIS 2013 and 2018 (HISLink project^r), partly to verify the HIS reporting on the use of care, but also to overcome the shortcomings of the health insurance data (e.g. information on non-reimbursed healthcare use is lacking, no link between

^p INTEGO, <https://www.intego.be/resultaten> (last access: 29 January 2024)

^q IMA – AIM, <https://aim-ima.be/-Nos-banques-de-donnees-?lang=fr> (last access: 29 January 2024)

^r HISLink project, <https://www.sciensano.be/en/projects/linkage-health-interview-survey-data-health-insurance-data> (last access: 29 January 2024)

healthcare use and health needs, information on socio-demographic background characteristics is scarce). Data extracted from the HIS are covering the following topics: socio-demographic characteristics (i.e. age, gender, education, place of residence, income, employment, household composition, nationality/country of birth), health status, lifestyle and health behaviour and use of health care and other services.

Furthermore, IMA – AIM data can be coupled at the individual level to all respondents surveyed in one of the selected waves of the EU-SILC. This provides complementary information on, for instance, the receipt of a disability or invalidity allowance, and the take-up and use of protection measures in healthcare insurance, such as increased reimbursement status or the system of maximum billing.

The IMA – AIM data could also be coupled with micro-data from the HBS to obtain certain socioeconomic information and data on healthcare expenses, including expenses not covered by the public health insurance.

The IMA – AIM also compiles and manages a representative dataset known as the Permanent Sample (EPS). This sample consists of randomly selected members from the Sickness Funds, stratified by age and gender. Approximately 1 in 40 members under the age of 65 are included, while the sampling rate increases to 1 in 20 for those aged 65 and older. The larger sample size for the older population enhances the precision of estimates for this group, which typically incurs higher healthcare costs and which would otherwise be underrepresented. The EPS data, however, are only sufficiently robust when analysing conditions that are highly prevalent and affect large segments of the population.³⁴

Data available at IMA – AIM also include data on **co-payments** (see section on the indicator on out-of-pocket healthcare costs for the patient). Regarding **supplements**, a distinction has to be made for hospital and ambulatory settings. Data on supplements paid in hospital setting are also collected by the sickness funds and available at IMA-AIM. In ambulatory setting, data on supplements are collected only partially by the sickness funds; these partial data are also available at IMA – AIM.

In the NEED context, the IMA – AIM could be useful to get Belgian estimates of :

- Out-of-pocket healthcare costs per patient
- Healthcare costs relative to the effectiveness of the standard of care
- Forecasted healthcare costs attributable to the health condition

7.6 Kruispuntbank van de Sociale Zekerheid – Banque Carrefour de la Sécurité Sociale (KSZ-BCSS) data

The KSZ-BCSS^s routinely collects administrative information from the different branches of the Belgian social security system that can all be linked at the individual level. This dataset provides information on healthcare financing, namely the social security contributions from employer and employees and can be linked to all respondents surveyed in one of the selected waves of the EU-SILC. The KSZ-BCSS also includes data on work incapacity/invalidity and unemployment.

In the NEED context, the KSZ-BCSS could be useful, when linked with a database in which patients with the concerned condition can be identified, to get Belgian estimates of :

- Absenteeism of patients

^s KSZ-BCSS, https://www.ksz-bcss.fgov.be/fr/dwh/dwh_page/content/websites/datawarehouse/about/mission.html (last access: 10 October 2025)



7.7 Hospital discharge data

All general hospitals are required to submit biannually data on all inpatient and day-care hospital stays and emergency room contacts: the “Minimale Ziekenhuis Gegevens – Résumé Hospitalier Minimum” or MZG – RHM defined in the Royal Decree of 27 April 2007).³⁴ These data are transferred to the FPS Public Health. The MZG – RHM database includes variables related to demographics, clinical information such as diagnoses, comorbidities, treatments and complications, length of stay, nursing units involved, discharge status and readmission in the same hospital. The clinical data also contain the All Patient Refined-Diagnosis Related Group (APR-DRG), severity of illness and risk of mortality output by the 3M™ APR-DRG Grouper software for each hospital stay, based on the principal diagnosis, secondary diagnoses and procedures, age and sex of the patient and, for some APR-DRGs (for neonates) birth weight. The MZG – RHM data are mainly collected for the measurement of hospital needs for public financing, and for the evaluation of the effectiveness and quality of hospital care. The data can also be used to determine population healthcare needs through epidemiological studies.

The Technische Cel – Cellule Technique (TCT) from NIHD and FPS Public Health^t is responsible for the management and processing of the hospital data. Each year, the TCT links the MZG – RHM data with Hospital Billing Data to analyse the relationship between health insurance expenditures and the treated condition and to elaborate financing rules, accreditation standards and quality conditions.³⁴ The Hospital Billing Data includes all reimbursements by the NIHD related to general hospital stays: fees charged by physicians and other healthcare providers, pharmaceuticals and implants/invasive medical devices, per admission and per diem lump sum payments, etc. The TCT publishes the average expenditures per hospital stay (minimum one overnight stay) for the different APR – DRGs, which include costs reimbursed by the mandatory health insurance scheme and excludes patients' co-payments (with a few exceptions), supplements, and costs reimbursed by additional insurances.

In the NEED context, this database can be used to get Belgian estimates of:

- Healthcare costs of standard of care

7.8 Kenniscentrum arbeidsongeschiktheid – Centre de connaissances en matière d'incapacité de travail

The Knowledge Centre for Work Incapacity ('Kenniscentrum Arbeidsongeschiktheid' – 'Centre de connaissances en matière d'incapacité de travail') from NIHD has data on work incapacity, invalidity and 'adapted work'. Data on diagnostic codes (ICD-10) are available for work absences longer than 6 months.

In the NEED context, this database could be useful to get Belgian estimates of:

- Absenteeism of patient

7.9 Belgian Household Budget Survey (HBS) data

The Belgian HBS^u is conducted every two years since 2010 with the primary aim to collect data on households' consumption expenditure on goods and services and calculate weights for the Consumer Price Index and national accounts. Micro-data are collected by Statistics Belgium through a combination of interview questions and detailed consumption logs maintained by households on a daily basis. The HBS data contain individual and household information for a representative sample of 6 000 households residing in Belgium. More information on the survey design can be found elsewhere.³⁶ HBS data include very detailed information on consumption expenditures, basic sociodemographic (e.g. age, sex, household size, region of residence) and socioeconomic (e.g.

^t Technische Cel – Cellule Technique, <https://tct.fgov.be/webetct/etct-web/> (last access: 10 October 2025)

^u Household Budget Survey, <https://statbel.fgov.be/en/themes/households/household-budget-survey-hbs#documents> (last access: 10 October 2025)

income, educational attainment) information. All annual healthcare expenses are registered, including expenses that are not covered by the public health insurance, such as certain medicines, glasses, etc. and valued at the amount paid at consumption (prior to reimbursement if applicable). Despite this extensive registration of healthcare consumption, a number of expenses related to healthcare (e.g. own transport costs to a healthcare provider) are not registered as a separate category and hence cannot be identified.³⁷ Household budget surveys are conducted in all EU Member States, and despite harmonisation efforts within the EU, each Member State decides the objectives, methodology and frequency of surveying.

In the NEED context, the HBS could be useful to get input on healthcare costs borne by the patients, but only when the data can be linked to another database in which patients with the concerned disease can be identified. The HBS also reports total health expenditures which are not necessarily all related to the concerned disease. Taking these concerns into consideration, the HBS can provide input for:

- Out-of-pocket healthcare costs per patient

8 INTERNATIONAL DATA SOURCES

The main databases that can be used are the GBD study^v, Orphanet, the European health interview survey (EHIS)^w, and the Household Budget Survey (HBS). The European Health Information portal^x can be used to identify and access relevant population health and health care data in Europe.

8.1 The Global Burden of Disease (GBD) study

The GBD study, which started in the early 1990s, presented an important set of comparative findings on the impact of different diseases, injuries and risk factors on population health. Since 2018, the Institute for Health Metrics and Evaluation (IHME) and the World Health Organisation work together on the annual GBD study.³⁸ The GBD 2019 study provides updated estimates of the world's health for 369 diseases and injuries and 87 risk factors from 1990 to 2019.³⁹ The metrics used to quantify health impact of specific diseases include: Deaths, YLLs, YLDs, DALYs, Incidence, Prevalence, Maternal mortality ratio, Probability of death, Life expectancy, Healthy life expectancy (HALE). These estimates have to be interpreted carefully and cannot replace estimates from a national burden of disease study because they suffer from several important limitations already discussed elsewhere.^{40, 41} Detailed information about data^y, approaches, statistical modelling, and metrics for the GBD 2019 study have also been reported elsewhere.³⁹

In the NEED context, the GBD could be useful to get estimates of :

- Years of life lost
- Years of life lived with disability
- Prevalence or Incidence
- Forecasted Years of life lost
- Forecasted Years of life lived with disability

^v Burden of Disease database, <https://www.healthdata.org/research-analysis/gbd> (last access: 11 June 2025)

^w European health survey, <https://ec.europa.eu/eurostat/web/microdata/european-health-interview-survey> (last access: 11 June 2025)

^x European Health Information Portal; <https://www.healthinformationportal.eu/health-information-portal> (last access: 11 June 2025)

^y GBD Compare, <https://vizhub.healthdata.org/gbd-compare/> (last access: 11 June 2025)



8.2 Orphanet

Orphanet^z is an international database dedicated to rare diseases and orphan drugs. Initially created in France in 1997, it has since grown into a collaborative project involving over 40 countries, mainly in Europe. The database provides detailed, structured information on more than 6 500 rare diseases, including their clinical features, prevalence, and classification. Orphanet also maintains the Orphanet rare disease nomenclature (ORPHAcodes), essential in improving the visibility of rare diseases in health and research information systems.

In the NEED context, Orphanet could be useful to get estimates of :

- Prevalence or Incidence of rare diseases

8.3 The European health interview survey (EHIS)

The European Health Interview Survey (EHIS) provides an overall picture of the health status of the population and allows to identify the main health problems, as well as the social and behavioural factors that influence them. This information enables health authorities to pursue a proactive health policy aimed at improving public health and addressing the needs of groups at risk. The first EHIS was carried out in 2007, and then in 2014 and 2019. The next EHIS will be conducted in 2025 (in line with EU Regulation). The EHIS collects information on a wide range of health topics: physical and mental health, lifestyle, use of health care and preventive services, perception of the physical and social environment, etc.

In the NEED context, the EHIS could be useful to get estimates of :

- EQ-5D-5L score (for some chronic conditions)
- Pain/discomfort
- Usual activities
- Received information
- Involvement in treatment decisions
- Prevalence or incidence (for some chronic conditions)

8.4 The Household Budget Survey (HBS)

The Household Budget Survey (HBS) is conducted every two years with the primary aim to track (changes in) consumer behaviour and calculate weights for the Consumer Price Index and national accounts. Micro-data are collected through a combination of interview questions and detailed consumption logs maintained by households on a daily basis. Household budget surveys are conducted in all EU Member States, and despite efforts towards harmonisation within the EU, each Member State decides the objectives, methodology and frequency of conduction of the survey. Hence, differences remain, which means that international comparisons should be interpreted with caution. The HBS data contain individual and household information for a representative sample of the population residing in a specific country. Usually, they include very detailed information on consumption expenditures, next to basic sociodemographic (e.g. age, sex, household size, region of residence) and socioeconomic information (e.g. income, educational attainment).

In the NEED context, the HBS could be useful to get input on healthcare costs borne by the patients, but only when the data can be linked to another database in which patients with the concerned disease

^z Orphanet, <https://www.orpha.net/> (last access: 10 October 2025)

can be identified. The HBS also reports total health expenditures, which are not necessarily all related to the concerned disease. Taking these concerns into consideration, the HBS can provide input for:

- Out-of-pocket healthcare costs per patient

9 COST STANDARDIZATION PROCEDURE: CURRENCY AND INFLATION

9.1 Currency

All cost data in the NEED database should be expressed in euro.

When cost data originate from a country where the euro is the official currency, then there are two options, both of which can be followed to present cost data in the database:

- The original cost data in euro are presented as such (without adjusting for purchasing power to the EU-27 area) (option 1)
- The original cost data in euro are converted to “EU-27 euro” as **Purchasing Power Standard (PPS)** (option 2). One PPS corresponds to the average purchasing power of one euro across the 27 Member States of the European Union. This artificial currency adjusts for differences in national price levels and reflects the weighted average price level within the EU-27.⁴² Cost data should be **converted to EU-27 euro** using the **Purchasing Power Parity (PPP)** index, where **EU-27 = 1**. PPP indices can be obtained from Eurostat’s publicly available database^{aa}.

When cost data originate from a country which has another currency than euro, then the data should be converted to “EU-27 euro” (option 2).

E.g. **Original cost:** 5 000 Polish Zloty (PLN) in 2024

From Eurostat’s PPP data:

- PPP Poland (2024) = 3.02205
- PPP EU-27 = 1

Cost converted to EU-27 PPS euro = Cost in national currency x (PPP EU-27 ÷ PPP national currency)

= 5 000 PLN x (1 ÷ 3.02205) = 1 654.5 EU-27 PPS euro

9.2 Inflation to the current year

If historical cost data are used, then these should first be inflated to current costs using the Consumer Price Index (CPI) from the origin country, before converting to EU-27 PPS euro. The international CPIs are available on the website of the OECD^{bb}. For consistency it is recommended to use the ‘Eurostat Harmonised index of consumer prices (HICP)’.

It is recommended to inflate the historical cost data to the year in which the NEED study for the concerned disease is published.

^{aa} Purchasing Power Standard, Eurostat database: https://ec.europa.eu/eurostat/databrowser/view/prc_ppp_ind/default/table?lang=en&category=prc.prc_ppp. (last access: 19 August 2025)

^{bb} the Consumer Price Index, OECD database: <https://www.oecd.org/en/data/indicators/inflation-cpi.html> (last access: 19 August 2025)



10 REPORTING

10.1 Technical sheets and disease description

For each indicator in the NEED database, a **technical sheet** is prepared to ensure result transparency. Each sheet provides key details on data collection methods, such as literature reviews, patient surveys and interviews, expert input, and database analyses. It also specifies the calculation methods, units of measurement, any proxy indicators used, the data's reference year, coverage, consulted sources, and any limitations associated with the indicator (see Figure 5).

Figure 5 – Technical sheet developed for the EQ-5D-5L average score indicator

INDICATOR	EQ-5D-5L AVERAGE SCORE
DESCRIPTION	The EuroQol 5-Dimension 5-level (EQ-5D-5L) questionnaire asks respondents to describe their health status on five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each item has five response categories, reflecting the level of problems experienced in each dimension (no problems, slight problems, moderate problems, severe problems, extreme problems).{Feng, 2021 #2824}{Herdman, 2011 #2825}{Janssen, 2013 #2826} The EQ-5D-5L is a simple, standardized and widely used tool, that provides a comparable measure of health-related quality of life. Such a measure facilitates comparisons across different populations, regions, and countries. This comparability is crucial for: benchmarking health outcomes, conducting cross-country health research, and informing international health policy and resource allocation.{Feng, 2021 #2824}{Herdman, 2011 #2825}{Janssen, 2013 #2826}
DIMENSION	Patient needs
DOMAIN	Health needs
CRITERION	Impact on general health-related quality of life
DATA TYPE	Numerical; continuous
CALCULATION	Calculation of: - The average EQ-5D-5L score: - Numerator: sum of EQ-5D-5L scores of the participants to the survey - Denominator: number of survey participants Patients were asked to rate their QoL BEFORE the onset of the health condition and at the time of survey completion (TODAY). The difference between both: [(average BEFORE) – (average TODAY)] was also calculated (DIFFERENCE). Individual subjective health states described with the EQ-5D-5L tool (e.g. 11111 for perfect health and 55555 for the worst health conditions) were valued using the most recent Belgian valuation set (2021).{Bouckaert, 2021 #2726}
UNIT	EQ5D utility score (For Belgium - range: – 0.532; 1)
PROXY	Example - EQ5D – 3L
DATA COLLECTION METHOD	Patient survey{De Jaeger, 2024 #2749}
YEAR DATA REFERS TO	2023
DISEASE PROXY USED	
DATA SOURCE	Patient survey described in the following report: “Needs Examination, Evaluation and Dissemination (NEED): Identification of unmet health-related needs associated with Crohn’s disease.” {De Jaeger, 2024 #2749}
LAST UPDATE	2024

In addition, a **description of the health condition** should be included in the NEED database in parallel with the technical sheet. Ideally, information should be provided on:

- Epidemiology
- Pathophysiology (aetiology, clinical presentation, natural history, comorbidities)
- Diagnosis
- Treatment and management (available treatment options, side-effects, organisation of care and support)
- Long-term outcomes (complications, prognosis, survival)
- Prevention

- Inequities (socioeconomic or other)

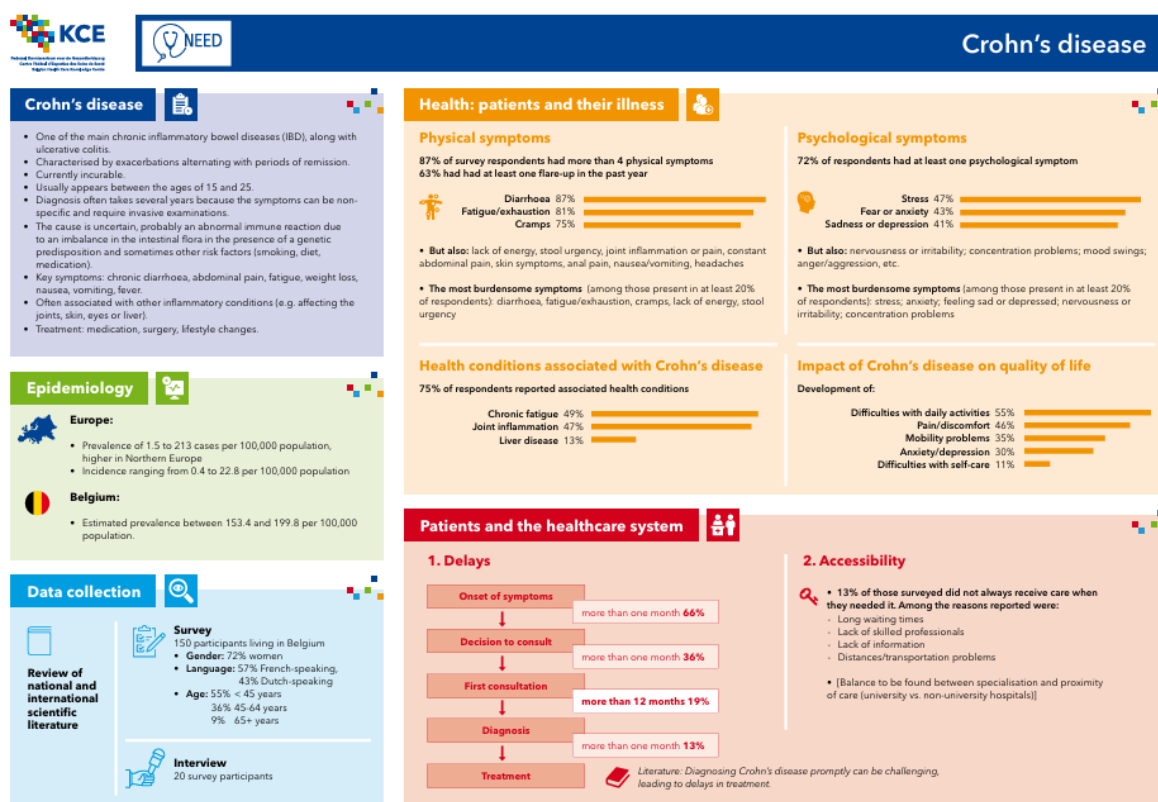
10.2 Reporting of data in a single-disease database

Once the research is complete, all collected estimates, both qualitative and quantitative, must be documented in an Excel spreadsheet. This file can then be imported into the NEED database by the database webmaster. An Excel template, along with detailed instructions for completing it, is available in the supplementary material. Before results are added to the NEED database, they undergo quality control and must be approved by the NEED team to ensure that data were collected in accordance with the NEED protocol.

10.3 Additional publications

- A **report** can be written to summarise the methods and results of the NEED research project, using the NEED reporting layout (see for instance, KCE report 377³). A Word version of the layout can be provided upon request. The publication of NEED reports is usually shared with study participants (patients, proxies, and experts), stakeholders who contributed to the recruitment, and the NEED steering and advisory committees.
- A **fact sheet** can also be developed to share results with relevant stakeholders in a more user-friendly manner (see Figure 6)

Figure 6 – Example of fact sheet developed for NEED study on Crohn's disease



- Alternatively, a **brochure** summarising the key findings from the scientific report can be considered (see for instance: <https://health-needs.eu/index.php/en/research/publications-research-en/eu-high-level-conference-brochure>)
- **Publication** in a scientific journal (preferably in open access) is also strongly encouraged.



- Furthermore, it is recommended to present the results of the NEED research project **at national and international conferences** related to public health or health economics and outcomes research.

11 QUESTIONS AND ANSWERS

Who can lead NEED research?

The NEED database is open to be populated by researchers from diverse fields, including the public sector, academia, and the private sector, provided they adhere to the NEED research protocol, disclose any conflicts of interest, and do not hold any significant ones. Collaborations with researchers from other EU countries are highly encouraged.

Researchers with prior experience in needs assessments, patient preference studies, or research involving PREMs and PROMS are particularly well-suited to lead NEED research projects.

Conducting a NEED research project requires researchers to have expertise in quantitative research, and possibly in qualitative research if a qualitative study is also planned. Essential competencies include knowledge of recruitment strategies and survey data collection, proficiency in analysing survey results and health-related databases, and strong skills in literature review. In the case of a qualitative study, additional expertise in qualitative methods, such as conducting interviews and analysing qualitative data, is also required.

Furthermore, successful projects require close collaboration with disease-specific patient associations, expert patients, and clinical experts, along with the involvement of a dedicated project manager.

How long does it take to complete a NEED study?

The average time it takes to carry out a NEED study for one health condition (or group of health conditions) in one country is 18 months. Table presents the approximate time required for each specific task.

Of course, this timeline can be affected by various factors, such as the availability of human and financial resources or the type of health condition being studied. For example, patient recruitment in the case of rare diseases or certain psychiatric disorders can be more challenging and may take longer. The time required to obtain ethical committee approval can also vary significantly. Additionally, conducting the study across multiple countries may further extend timelines due to differing regulatory procedures in each country.

Table 11 – Approximate time period required to perform a NEED study for one health condition in one country

Step of NEED study		Task	Time period
<i>Evidence collection on the indicators of the NEED assessment framework</i>			
	Literature reviews	Pragmatic literature review	2 weeks
		Systematic literature review	3 months
	Patient survey	Preparation of research protocol and submission to ethics committee	2 months
		Adaptation of the NEED generic questionnaire to a health condition	2 months
		Recruitment of patients/Open Survey	4 months
		Analysis of survey results	3 months

	Patient interviews	Adaptation of generic interview guide	1 month
		Interviews with patients	1 month
		Analysis of interviews	2 months
	Expert questionnaire	Adaptation of expert questionnaire	1 week
		Recruitment of experts for the survey and analysis of the results	4 weeks
	Databases analysis	Database identification and access request	1 month
		Analysis of databases	3 months
Reporting			
	NEED report & fact sheets	2 months	
	Technical sheets for the NEED database	2 weeks	
	Excel file with aggregated results for the NEED database	1 week	

These durations should not be interpreted as a linear timelines, as many tasks are performed concurrently. Additionally, the time estimates do not imply continuous full-time work; certain phases may involve unavoidable delays, such as waiting for input from external experts. The figures are based on the assumption that a single individual is responsible for each task, so overall timelines may vary depending on team size and resource availability.

Can we modify the NEED generic data collection tools (e.g. patient questionnaire, interview guide) included in the NEED toolbox?

Patient questionnaire, interview guide, and expert opinion questionnaire:

Aside from adapting these tools to the selected health condition, we do not recommend modifying them, as they were developed to collect data on specific indicators of the NEED framework which must remain comparable across diseases.

In addition, the patient questionnaire incorporates several questions from validated questionnaires (e.g. EQ5D-5L). If you are planning to modify the patient questionnaire beyond what is described in section 6.1.1. We encourage you to contact the NEED research team (contacts and emails are available below), as they can advise you on how best to proceed.

Adding questions to the patient questionnaire, such as disease-specific tools to measure health-related quality of life, is possible, but it is important to ensure that the questionnaire remains manageable for patients in terms of length and time needed for completion, for instance.

Literature review strategy:

For the literature review search strategy, researchers are free to modify the NEED standardised search strategy.

I have collected unmet needs data on a health condition, but without following the NEED protocol. Can the unmet needs data for the indicators I studied be integrated into the NEED database?

If the methodology you used to collect data on specific indicators included in the NEED assessment framework aligns with the recommendations included in this guidance report, your data can be incorporated into the NEED database. The NEED team will assess the scientific quality of your study and its compliance with the NEED study guidance before including the data in the database.



Table 12 – Decision process for integrating unmet health-related needs data into the NEED database

Outcome	Process description
Data collected following the NEED protocol	• If the data you collected is eligible for inclusion in the NEED database, please complete a <i>technical sheet</i> detailing the measurement and data collection methods used for each indicator, and input the data into the <i>NEED database Excel template</i> (see supplementary material). • If the health condition is not yet included in the NEED database, submit a description of the disease. A disease description template can be provided under request. • The NEED team will check the quality of the measurement and data collection methods before including them in the NEED database.
Data collected without following the NEED protocol → The NEED team has to evaluate the methods used	• If unmet needs data were collected from patients through means other than the NEED patient questionnaire (e.g., from a clinical trial), please submit information about the research protocol and results obtained. • The NEED team will assess whether the methods used are compatible, robust, and reliable for the data to be included in the NEED database. If this is the case, data can be included in the NEED database.

In any case, data will be rejected if they:

- Do not align with any of the criteria or indicators defined in the NEED database;
- Are based on patient needs collected from a sample that is not representative of the overall patient population;
- Were not collected in a European country;
- Do not meet quality standards (e.g. reliability)

What if the data were collected as part of a clinical trial or a different study?

The NEED team will evaluate the data on a case-by-case basis.

Where can I find funding to perform a NEED research project?

A list of the main EU funding opportunities for a NEED project is available in Table 13. However, national funding sources, whether public or private, may also be sufficient to support the development of a NEED study.

Table 13 – List of European Fundings

Funding	Short description/amount	Website
COST Actions	COST funds interdisciplinary research networks called COST Actions that bring researchers and innovators together to investigate a topic of their choice for four years.	https://www.cost.eu/funding/documents-guidelines/
EC Horizon Europe – Cluster 1: Health	Horizon Europe is the EU's key funding programme for research and innovation, with Cluster 1 focusing on health	https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe/cluster-1-health_en



EU4Health programme	Budget of €4.4 billion, EU4Health (2021-2027) is the EU's largest health programme	https://hadea.ec.europa.eu/programmes/eu4health_en
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The **EU funding and tenders portal** of the European Commission^{cc} regroups funding opportunities issued by the European Union institutions, agencies, and bodies. These are direct financial contributions, known as grants, that are awarded to third-party beneficiaries (e.g., research organisations, public entities, non-governmental organisations, and private companies) to engage in activities that serve EU policies.

In all cases, the sources of funding and, if applicable, the funding reference must be clearly stated in the project.

Must I collect information concerning one specific country?

Ideally, all collected data should consistently concern the same country (or group of countries) across all indicators. In any case, it should be clearly stated which country the collected data refers to. In some situations, a proxy country may be referenced. For example, when a study involving primary data collection is conducted in one country, but literature data for a specific criterion is only available from another country with comparable population and health system characteristics.

Can I collect data on a group of diseases rather than on a specific health condition?

Health conditions should be defined carefully—neither too broadly nor too narrowly in order to remain comparable across diseases within the database. If a disease category is too broad, encompassing heterogeneous conditions, the range of unmet needs may also be highly diverse, limiting the usefulness of findings for concrete decision-making. Conversely, if defined too narrowly, such as sub-diagnoses within a specific patient population, the target group may become very small, difficult to identify in practice, and less actionable in terms of addressing health-related needs. As a reference, health conditions are generally defined at the level of single diagnoses as classified in ICD-11 or DSM-V, for example, type 2 diabetes mellitus (ICD-11: 5A11) or major depressive disorder (DSM-V: 296.2x).

In certain cases, as demonstrated in previous projects (e.g., unmet needs related to psychotic disorders (expected publication March 2026)), it may be advantageous to adopt a broader classification, such as grouping schizophrenia spectrum disorders in DSM-V (e.g., schizophrenia, schizoaffective disorder, schizophreniform disorder) because of the important overlap which exists in clinical practice between these conditions. Indeed, limiting recruitment to individuals with one specific diagnosis (e.g. schizophrenia) would risk being biased because of various factors: a discrepancy between the diagnoses recorded by healthcare professionals and those communicated to patients, changes in diagnoses over time, clinical uncertainty (e.g. differentiating schizoaffective disorder, schizophrenia, and schizophreniform disorder). When studying a broader disease category, more granular data can still be captured by stratifying the analyses. This approach allows practical recruitment while preserving the ability to generate meaningful, comparable, condition-specific insights, particularly when there is significant diagnostic overlap among related health conditions.

^{cc} <https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/calls-for-proposals>
(last access: 28 July 2025)



12 CONCLUSION

This protocol provides a structured overview of NEED framework indicators and primary and secondary data collection methodologies applicable to the implementation of a NEED study. These methods are intended to evolve, accounting for the emergence of new data sources and tools, technological advancements (e.g. Artificial Intelligence (AI), and the experiential insights gained by researchers for conducting NEED studies. We hope that this protocol will serve as both a reference for researchers interested in investigating the unmet health-related needs of patients and society, and as a step forward in refining research practices in this field.

13 USEFUL CONTACTS

Name of the contact	Affiliation	Email
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■ APPENDICES

APPENDIX 1. CONSIDERATIONS ON THE ECONOMIC INDICATORS

Appendix 1.1. Out-of-pocket healthcare costs

Rationale for presenting annual out-of-pocket costs

In the NEED assessment framework, we use **annual out-of-pocket healthcare payments** as the standard metric because estimating lifetime expenses poses significant methodological challenges. Lifetime calculations require long-term projections and rely on numerous assumptions about disease progression, treatment patterns, life expectancy, and future healthcare costs, all of which introduce uncertainty. In contrast, annual costs are more readily measurable and based on observable data, making them a more practical and reliable basis for analysis within this context. They can be deduced top-down from national databases, where total payments in a year can be divided by the number of patients, thereby obtaining an average annual cost per patient.

Considerations on presenting annual versus lifetime out-of-pocket healthcare costs

The choice between calculating annual OOP healthcare costs and estimating total costs accumulated over a patient's lifetime has implications for interpreting the financial burden of a disease, especially when comparing chronic and acute conditions from the perspective of the patient.

- Underestimation of long-term burden for patients with chronic diseases

For chronic diseases, such as diabetes, multiple sclerosis, or rheumatoid arthritis, the financial burden for a patient extends over many years or even decades. Calculating OOP costs on an annual basis may significantly underestimate the cumulative burden that these patients face over their lifetimes. While the yearly costs might appear manageable in isolation, the total financial impact becomes substantial when aggregated over time.

- Overemphasis on disease burden for patients with acute diseases

In contrast, acute diseases, such as appendicitis, fractures, or short-term infections, typically involve a short, intense period of healthcare use and related OOP spending. When measured on an annual basis, these costs may appear disproportionately high relative to their long-term burden.

This limitation should be kept in mind when comparing the financial burden of acute and chronic diseases, from the perspective of the patient, as focusing on annual costs may distort the comparison and resulting burden-of-disease rankings or priority-setting frameworks.

- Adjustment through prevalence data and shift to a population or national perspective

While annual per-patient OOP cost estimates may distort comparisons between chronic and acute diseases at the individual level, this limitation can be addressed by incorporating prevalence data, which shifts the analysis from the patient perspective to the population or national level. Prevalence captures the total number of individuals living with a disease at a given point in time. For chronic conditions, even those with relatively low annual incidence rates, prevalence remains high due to the long duration of illness. In contrast, for acute conditions that resolve quickly, prevalence remains close to incidence because individuals generally recover and exit the pool of prevalent cases.

By combining the annual per patient OOP cost with disease prevalence, the total national cost burden (for all patients) can be calculated. So this approach corrects for the distortions seen when comparing per patient costs alone and provides a more comprehensive view of the overall economic burden at the country level.



Appendix 1.2. Non-healthcare costs

For this indicator, a non-quantitative assessment is done, by use of a checkmark list. The costs represented by this indicator are generally not recorded in national administrative databases and can vary widely between patients, depending on their individual circumstances. Collecting reliable cost data on these aspects would require a detailed questionnaire for patients or their caregivers, focusing specifically on expenses. Respondents would need to prepare the questionnaire thoroughly, providing information on the types and quantities of products used, as well as unit prices. Baseline costs (costs which also occur when the patient is in good health) would need to be deducted. Any reimbursements or lump sum allowances intended to cover these costs would also need to be subtracted. Taking these factors into account, and given that this indicator is not part of the core NEED framework, we opted not to include detailed questions about quantified costs in the patient NEED survey.

Furthermore, since referencing cost data from the literature would likely result in inconsistent and not fully comparable data, given the possible variability in included cost components and their valuation, we instead chose to use a checklist approach. This checklist allows the researcher to indicate whether certain cost types are present in the disease studied and, for recurring costs, whether they have a short-term (<1 year) or long-term (>1 year) impact (see Table 2). For some of these costs, patients may be eligible for reimbursements or allowances. In such cases, the cost group should only be marked if there are remaining net costs to the patient, as the goal is to identify unmet (non-healthcare) financial needs associated with the disease.

Appendix 1.3. Value for money of standard of care

The criterion “*Value for money of standard of care*” is included in the framework because it provides insight into how effectively healthcare resources are being utilised. By evaluating whether the standard of care delivers outcomes that are commensurate with its costs, this criterion helps identify areas where the healthcare system may be underperforming. When the value for money is low, it suggests that significant resources are being allocated to interventions or services that do not yield proportional health benefits. This inefficiency not only reflects suboptimal use of limited healthcare budgets but also results in opportunity costs for society, meaning that the resources spent on low-value care could have been directed toward more effective treatments or services, potentially generating greater health gains or societal benefits. Recognising and addressing such inefficiencies is crucial for improving overall system performance and maximising the impact of public health investments.

A.1 Healthcare costs of standard of care

Perspective of the healthcare payer

Costs for this indicator are measured from the healthcare payers' perspective. As the perspective of the healthcare payers is adopted, costs comprise the total healthcare expenditures paid for by the public healthcare payer as well as by the patients (or their private insurance).

Total costs of standard of care compared to no treatment

In conventional health economic evaluations, the goal is to assess whether a new intervention offers good value for money - in other words, whether its health benefits justify the additional costs. This is commonly done by calculating the incremental cost per quality-adjusted life year (QALY) gained, comparing the costs and health outcomes of the new intervention to those of an existing comparator (often the current standard of care).

In the context of the NEED project, however, a different perspective is adopted. Rather than comparing a new intervention to the standard of care, the project evaluates whether the current standard of care itself represents good value for money. To do this, standard of care is compared to a hypothetical ‘no treatment’ scenario, both in terms of costs and health outcomes.

The aim is to estimate the incremental healthcare costs associated with the standard of care, that is, the additional costs incurred relative to providing no treatment at all. This approach allows for a baseline assessment of the economic and clinical value of existing treatment practices.

Annual cost versus total cost over lifetime

In the context of an economic evaluation, total incremental costs of a new intervention (compared to the comparator treatment) are weighed against the total health impact (also compared to the comparator treatment). On the cost side, total costs are calculated for current as well as future costs. The considered time horizon spans the period in which the studied new intervention leads to differential costs compared to the comparator treatment. This means that for chronic diseases and acute diseases with longer term sequelae, a longer time horizon is considered, sometimes up to the full lifetime of the patients. Costs in future years are discounted to present values and then totalled.

In the context of the NEED project, however, a different approach is taken. If we would want to calculate the total costs over a longer time horizon, then we would need to make multiple assumptions about the age of onset of a disease (average age or the distribution parameters), the evolution of the disease (average, or probabilities when using a decision-tree, or transition probabilities when using a Markov model), the costs in the different stages of the disease, etc. This would be very resource-consuming, and given that the goal of the NEED database is to provide data about many health conditions, a more pragmatic approach was needed. The use of annual costs allows for greater feasibility but also consistency across a large set of diseases, given that considerable assumptions would be required for long-term modelling. Annual costs can more easily be deducted top-down from national databases, where total costs in a year can be divided by the number of patients, thereby obtaining an average annual cost per patient.

To support meaningful comparison of this indicator, users of the NEED database should consider the average duration of a condition when comparing this indicator across diseases, especially when comparing chronic with acute diseases.

Implications of reporting annual costs per patient for chronic versus acute diseases

The decision to report **annual per patient costs**, rather than **total lifetime costs**, has implications for how diseases should be assessed and compared within the NEED framework, particularly when distinguishing between chronic and acute conditions.

For **chronic diseases**, such as diabetes, multiple sclerosis, or chronic obstructive pulmonary disease (COPD), healthcare needs and associated costs **persist over many years**, often for the remainder of the patient's life. Reporting costs on an annual basis captures only a snapshot of the total economic burden these conditions impose. As a result, chronic diseases may appear less costly than they truly are when compared to acute diseases, simply because the cumulative lifetime impact is not reflected.

In contrast, **acute diseases**, such as appendicitis or a mild infectious illness, typically involve short-term but potentially high-intensity costs that are largely concentrated within a single episode of care. In these cases, annual costs can closely approximate the total disease-related expenditure, providing a more accurate representation of the full economic impact.

This methodological choice may therefore understate the true cost burden of chronic diseases relative to acute conditions when looking at a per-patient level.



Appendix 1.4. Productivity losses

Appendix 1.4.1. Productivity losses of the patient

Productivity losses refer to the economic impact of patients being unable to work or being less productive due to their disease. Different definitions exist for productivity losses, but in general, a distinction can be made between the following subcomponents:

- **Absenteeism** refers to patients being absent from work due to illness, i.e. time taken off work. People who were previously at work receive sickness or invalidity benefits if they are no longer able to work due to illness or an accident.^{dd}
- **Presenteeism** refers to patients who are at work while being ill but who are not fully productive because of their illness. Even though the employee may be physically at work, he or she may not be able to fully perform his or her duties.
- **Labour force exits:**
 - Patients who were previously at work may **leave the workforce** because of health issues. This can be unwanted or wanted 'unemployment'.
 - Some patients may reduce their time at work because of health issues.
 - Some patients may never enter the workforce. People with a handicap may be entitled to an income replacement, which differs from the unemployment benefits mentioned above.
 - Note that labour force exits can be considered part of absenteeism but can also be considered a separate category of productivity losses. In some definitions, absenteeism or labour force exits will also account for patients who **die before the statutory retirement age**.

There are three corresponding indicators for productivity losses of patients in the NEED database:

- Absenteeism of patients:
 - Based on the patient survey: average annual absence from the work floor per patient since the diagnosis
 - Based on database analysis: average duration of absence per disease and number of persons absent per disease
- Presenteeism of patients: based on the patient survey
- Labour force exits or work reduction due to the health condition: based on the patient survey

Measurement versus valuation of productivity losses

- Within the context of the NEED database, it was chosen to measure the productivity losses, not to assign a monetary value to them. This means that the database captures and quantifies the extent of productivity losses in time-related units, such as months of work lost per year since the diagnosis, or physical units, such as the number of persons per 100 000 inhabitants absent from work, without translating these losses into monetary terms. This decision was made for several reasons:
- Avoiding distortions in cross-disease comparisons

The NEED database includes data from multiple countries, and data on different diseases may originate from different countries. Although monetary values in the NEED database are standardised

^{dd} In Belgium, work incapacity refers to an absence from work of less than a year and invalidity refers to an absence from work of more than a year.

to the EU-27 Euro, this does not fully account for variations in labour costs between countries. Valuing productivity losses in monetary terms could therefore introduce systematic biases, making comparisons across diseases unreliable.

- Valuation methods differ

In health economics, productivity losses during paid work are often valued using one of two methods:

1. **Human Capital Approach:** This approach calculates productivity costs by multiplying the entire period of work absence by the national average labour cost per day.
2. **Friction Cost Method:** This method takes into account that vacant positions due to an absent employee can be filled again within a certain period. In that case, only the period until a replacement is found, the so-called *friction period*, is valued. However, this method underestimates the financial burden on incapacity and invalidity allowance payers, who continue to bear costs after the friction period ends. This method also does not reflect the burden on the patient, who continues to be impacted by the work absence after the friction period.

So another reason for choosing to measure rather than value productivity losses is to avoid the use of different valuation methods as well as country-specific inputs, other than national labour costs as mentioned above, such as national estimates for the friction period. Using the above-mentioned valuation methods across a multi-country database would introduce additional complexity and potential inconsistencies. By choosing to measure productivity losses without converting them into monetary values, we ensure greater transparency in the data and leave room for users to apply their own valuation models if desired.

Appendix 1.4.2. Productivity losses of the informal caregiver

In the calculation of productivity losses of informal caregivers, the process generally follows three conceptual steps:

Step 1. Measurement of time spent on caregiving

This refers to the number of hours or days per week an informal caregiver dedicates to caring for a person affected by the disease.

Step 2. Impact on work time (time not spent working)

The second step is to determine how that caregiving time affects the caregiver's paid working time. Caregiving responsibilities may result in a reduction of work hours or in quitting a job. However, not all caregiving time leads to lost work hours - some caregivers provide support outside of working hours. This step quantifies the reduction in labour market participation due to caregiving.

Step 3. Valuation of lost productivity: monetary transformation

Finally, the lost work time is converted into a monetary value, usually by multiplying the hours or days not worked by an average labour cost rate. This produces an estimate of the economic cost of productivity loss due to caregiving.

In the NEED analysis, we stop at the first step. This means we measure the time caregivers spend providing care, without estimating how much of this time results in reduced work participation (step 2), or converting it into a productivity loss (step 3).

The completion of step 2 would either require an extensive set of additional questions in the patient (or proxy) questionnaire or involve making numerous assumptions - such as on the starting position of the informal carer (are they part of the active labour force, or are they retired or student or child...); if they were working, the proportion of informal caregivers who remain employed, stop working, reduce their working hours by x hours because of caregiving; the duration of this impact; etcetera.

Regarding the choice not to complete step 3, we refer to the arguments raised in the section on productivity losses in patients. Indeed, the choices on how to operationalise the indicator on



productivity losses in informal caregivers align with how we handle the indicators on productivity losses in patients.

The criterion 'productivity losses of informal carers' is correspondingly operationalised through the indicator 'Informal caregiving time burden'.

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