KCE REPORT 348

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

IDENTIFYING PATIENT NEEDS: METHODOLOGICAL APPROACH AND APPLICATION

2021 www.kce.fgov.be

KCE REPORT 348
HEALTH SERVICES RESEARCH

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

IDENTIFYING PATIENT NEEDS: METHODOLOGICAL APPROACH AND APPLICATION

CHARLINE MAERTENS DE NOORDHOUT, JENS DETOLLENAERE, CÉLIA PRIMUS-DE JONG, LAURENCE KOHN, BRECHT DEVLEESSCHAUWER, RANA CHARAFEDDINE, IRINA CLEEMPUT

2021 www.kce.fgov.be

COLOPHON

Title:	Identifying Patient needs: methodological approach and application
Authors:	Charline Maertens de Noordhout (KCE), Jens Detollenaere (KCE), Célia Primus-de Jong (KCE), Laurence Kohn (KCE), Brecht Devleesschauwer (Sciensano), Rana Charafeddine (Sciensano), Irina Cleemput (KCE)
Project facilitator:	Nathalie Swartenbroekx (KCE)
Project coordinator and Senior supervisor:	Irina Cleemput (KCE)
Reviewers	Diego Castanares (KCE), Marijke Eyssen (KCE), Mélanie Lefèvre (KCE)
Advisory committee:	Ann Ceuppens (Onafhankelijke Ziekenfondsen), Sabine Corachan (LUSS - Ligue des Usagers des Services de Santé), Françoise De Wolf (Solidaris), Siska Germonpré (Socialistische Mutualiteit), Wies Kestens (Onafhankelijke Ziekenfondsen), Anneleen Lintermans (former VPP - Vlaams Patiëntenplatform), Murielle Lona (ML – OZ - Mutualités Libres-Onafhankelijke Ziekenfondsen), Karen Mullié (Observatorium Chronische Ziekten), Betty Ryckaert (Observatorium Chronische Ziekten), Katlijn Sanctorum (RaDiOrg – Rare Diseases organisation Belgium), Else Tambuyzer (VPP), Marijke Van Duynslaeger (Socialistische Mutualiteit), Anne Van Meerbeeck (VPP), Lisa Van Wilder (UGent), Rebekka Verniest (CM), Ilse Weeghmans (former VPP)
Stakeholders:	Michael Berntgen (EMA – European Medicines Agency), Robrecht De Schreye (Sciensano), Charles Denonne (FAGG – AFMPS - Federaal agentschap voor geneesmiddelen en gezondheidsproducten – Agence fédérale des medicaments et des produits de santé), Stefanie Devos (BeMedTec), Martine Dewitte (RIZIV – INAMI - Rijksinstituut voor ziekte- en invaliditeitsverzekering – Institut national d'assurance maladie-invalidité), Wim Penninckx (FAGG), Sander Roosens (RIZIV – INAMI), Maelle Van De Walle (Sciensano), René Westhovens (RIZIV – INAMI), Harun Yaras (SPF Santé Publique – FOD Volksgezondheid)
External validators:	Pauline Boeckxstaens (UGent), Juanita Haagsma (Erasmus Universiteit Rotterdam, the Netherlands), Olivier Schmitz (UCL - Université catholique de Louvain)
Acknowledgements:	Jef Adriaenssens (KCE), Finaba Berete (Sciensano), Jan Bogaerts (EORTC), Nicolas Bouckaert (KCE), Cécile Camberlin (KCE), Carl Devos (KCE), Stephan Devriese (KCE), Martine Dewitte (RIZIV – INAMI), Kris Doggen (Sciensano), Dimitri Mortelmans (University of Antwerp), Caroline Obyn (KCE), Johan Van der Heyden (Sciensano), Carine Van de Voorde (KCE), Amélie Van Vyve (Sciensano), Leen Verleye (KCE), all people who contributed to the KCE project on long COVID and by doing so to the pilot study for this project.
Reported interests:	'All experts and stakeholders consulted within this report were selected because of their involvement in the topic of Patient needs. Therefore, by definition, each of them might have a certain degree of conflict of interest to the main topic of this report'

Layout:	Ine Verhulst
Disclaimer:	• **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.** • **Subsequently, a (final) version was submitted to the validators. The validation of the report results from a consensus or a voting process between the validators. The validators did not co-author the scientific report and did not necessarily all three agree with its content.** • **Finally, this report has been approved by common assent by the Executive Board.** • **Only the KCE is responsible for errors or omissions that could persist. The policy recommendations are also under the full responsibility of the KCE.**
Publication date:	13 January 2022
Domain:	Health Services Research (HSR)
MeSH:	Needs assessment, Research Design, Surveys and Questionnaires, Qualitative Research
NLM Classification:	W84.3
Language:	English
Format:	Adobe® PDF™ (A4)
Legal depot:	D/2021/10.273/51
ISSN:	2466-6459

How to refer to this document?

Maertens de Noordhout C, Detollenaere J, Primus-de Jong C, Kohn L, Devleesschauwer B, Charafeddine R, Cleemput I. Identifying Patient needs: methodological approach and application. Health Services Research (HSR) Brussels: Belgian Health Care Knowledge Centre (KCE). 2021. KCE Reports 348. D/2021/10.273/51.

This document is available on the website of the Belgian Health Care Knowledge Centre.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
ADL	Activities of Daily Living
AFMPS	Agence fédérale des médicaments et des produits de santé
BCoDE	Burden of Communicable Diseases in Europe
BCR	Belgian cancer registry
BDI	Beck Depression Inventory
BE	Belgium
BeBOD	Belgian National Burden of Disease Study
BSI	Brief Symptom Inventory
BXL	Brussels
CAHPS	Consumer Assessment of Healthcare Providers and Systems
CAN	Camberwell Assessment of Need
CAN-C	Camberwell Assessment of Need for Clinicians
CANDID	Camberwell Assessment of Need for Adults with Developmental and Intellectual Disabilities
CANE	Camberwell Assessment of Need for the Elderly
CANFOR	Camberwell Assessment of Need – Forensic version
CAN-R	Camberwell Assessment of Need for Research
CANSAS	Camberwell Assessment of Need Short Assessment Schedule
CANSAS-P	Camberwell Assessment of Need Short Assessment Schedule for Patients
CARENAPD	Care Needs Assessment Pack For Dementia
CARES	Cancer Rehabilitation Evaluation Systems

CATT – CAIT	Commissie voor advies in geval van tijdelijke tegemoetkoming voor het gebruik van een geneesmiddel – Commission d'avis en cas d'intervention temporaire dans l'usage d'un medicament – Advisory Committee on Temporary Reimbursement for the use of a medicinal product
CCM	Cancer Care Monitor
CHOICE	Creating better Health Outcomes by Improving Communication about patients' Experiences
CI	Confidence Interval
CIPS	Cancer Inventory of Problem Situations
CNQ	Cancer Needs Questionnaire
COPD	Chronic Obstructive Pulmonary Disease
CTIIM – CRIDMI	Commissie Tegemoetkoming Implantaten en Invasieve Medische Hulpmiddelen – Commission de remboursement des implants et des dispositifs médicaux invasifs
DALY	Disability Adjusted Life Year
DAS	Dyadic Adjustment Scale
DW	Disability weight
EHC-NAQ	Elderly Health Care Needs Assessment Questionnaire
EMA	European Medicines Agency
EORTC	European Organization for Research and Treatment of Cancer
EQ-5D	EuroQoL-5D
EQ-5D-3L	EuroQoL 5 dimensions 3 levels questionnaire
EQ-5D-5L	EuroQoL 5 dimensions 5 levels questionnaire
EU-SILC	EU Statistics on Income and Living Condition
EVMPD	EudraVigilance Medicinal Product Dictionary
FAGG	Federaal agentschap voor geneesmiddelen en gezondheidsproducten

FAMHP	Federal Agency for Medicines and Health Products
F2F	Face-to-face
FAMHP	Federal Agency for Medicines and Health Products
FL	Flanders
GAIS	Global Adjustment to Illness Scale
GBD	Global Burden of Disease study
GERD	Gastroesophageal Reflux Disease
HADS	Hospital Anxiety and Depression Scale
HESPER	Humanitarian Emergency Settings Perceived Needs Scale
HIS	Health Interview Survey
HRQoL	Health-Related Quality of Life
ICF	International Classification of Functioning, Disability and Health
ICHOM	International Consortium for Health Outcomes Measurement
IHME	Institute for Health Metrics and Evaluation
IMA – AIM	Intermutualistisch Agentschap – Agence Intermutualiste
INAMI	Institut national d'assurance maladie-invalidité
ISEL	Interpersonal Support Evaluation List
IQR	Interquartile range
JLA	James Lind Alliance Priority Setting Partnerships (PSPs)
KPS	Kanorfsky Performance Scale
LSI	Life Satisfaction Index
LUSS	Ligue des Usagers des Services de Santé
MA	Marketing Authorization
MCDA	Multi-criteria decision analysis

MedDRA	Medical for Regulatory Activities
MPAC	Memorial Pain Assessment Scale
MSAS	Memorial Symptom Assessment Scale
NCCN	National Comprehensive Cancer Network
NEST	Needs at the End-of-Life Screening Tool
NEQ	Needs Evaluation Questionnaire
NHNA	Nottingham Health Needs Assessment
NIHDI	National Institute for Health and Disability Insurance
NIHR	National Institute for Health Research
NPCNA	Northwick Park Care Needs Assessment
OCPC	Oncology Clinic Patient Checklist
PCORI	Patient-Centered Outcomes Research Institute
PICOS	Population, Intervention, Comparator, Outcome, Setting
P&P	Paper-and-pencil
PNAT	Patient Needs Assessment Tool
PNAQ	Pharmaceutical Needs Assessment Questionnaire
PNPC	Problems and Needs in Palliative Care
POS	Palliative care Outcome Scale
PSP	Priority Setting Partnership
QALY	Quality-Adjusted Life Year
QoL	Quality of Life
RIZIV	Rijksinstituut voor Ziekte- en Invaliditeitsverzekering
SAQ	Seattle Angina Questionnaire
SCIM	Spinal Cord Independence Measure

SCL-90	Symptom Checklist-90
SCNS	Supportive Care Needs Survey
SDS	Symptom Distress Scale
SF-12	Short-Form 12
SFF	Special Solidarity Funds
SMPH	Summary measure of population health
S.NASA	Salford Needs Assessment Schedule for Adolescents
SNAQ	Southampton Needs Assessment Questionnaire
SPARC	Sheffield Profile for Assessment and Referral to Care
SUN	Service and Needs Assessment
SWLS	Satisfaction with Life Scale
UI	Uncertainty Interval
VAS	Visual analogue scale
VPP	Vlaams Patiëntenplatform
WHO	World Health Organization
WL	Wallonia
YLD	Years of Life lost to Disutility

1 INTRODUCTION

Since several decades, policy makers are taking measures to stimulate demand-driven healthcare systems, especially in the pharmaceutical field. Regulators have established compassionate use and medical need programmes, special schemes to support the registration of pharmaceutical products targeting high unmet medical needs (e.g. PRIME), conditional marketing authorization, orphan designation etc. Drug reimbursement agencies have established programmes for early temporary reimbursement for 'promising' drugs for high unmet medical needs. Several initiatives to support patient-centred decision making in healthcare and healthcare policy have been taken, such as the establishment of an International Consortium for Health Outcomes Measurement (ICHOM) to identify outcomes that matter to patients and develop standard sets of outcome measure[1], and the establishment of the Patient-Centered Outcomes Research Institute (PCORI) in the UK that promotes research that improves patient-relevant outcomes and supports value-based healthcare[2].

The current project emerges from a continued reflection on how to improve the unmet medical need procedure established in 2014 at the National Institute for Health and Disability Insurance (NIHDI – RIZIV – INAMI). The objective of the procedure is to give severely ill patients faster access to promising innovative medicines which have not yet obtained marketing authorization (MA), but are part of an unmet needs or compassionate use programme. The unmet medical needs procedure regulates the early temporary reimbursement of these products. To be eligible for early temporary reimbursement for a cohort of patients, a few conditions must be fulfilled:

- the condition must seriously affect the quality of life or be life-threatening and
- the condition must appear on the list of unmet medical needs, drawn up by the General Council of the NIHDI – RIZIV – INAMI on the advice of the Advisory Committee on Temporary Reimbursement for the use of a medicinal product (CATT/CAIT).

Proposals to include conditions on the list of unmet medical needs can be submitted by the Board of Medical Directors, the Minister(s) of Social Affairs and Public Health and by the manufacturers of medicines. The conditions on the list are ranked by the CATT/CAIT, using a multi-criteria decision approach (MCDA), based on a model proposed by KCE.[3] As unmet need is considered to be a multidimensional concept, consisting of an individual, patient-related, dimension and a societal dimension, a distinction was made between therapeutic need and societal need in the multi-criteria decision model proposed by KCE. The rank of a condition depends on both types of need. As a consequence, a condition can be ranked high if it has an important societal impact, or an important individual impact on the other hand, or both. In the proposed model, these dimensions were not merged and hence two priority lists would be created. As such, a new product could be eligible for entering the unmet medical needs programme due to its high ranking on the therapeutic needs list, societal needs list or both.

Therapeutic need refers to the need **of individual patients** for a treatment or other healthcare solution: solutions that improve patients' quality of life, life expectancy, and overall health. Also the need for a less burdensome or less toxic treatment falls under this category. Therapeutic needs are defined from the perspective of the patients and can be very broad, ranging from a need for a curative treatment to health education. **Societal needs** refer to needs from a broader, **societal (community) perspective**, such as a need for a better treatment for a very common condition, or a treatment as effective but less costly to alleviate its impact on health care expenditures, etc. For example, if a new product could substantially reduce disease-related public expenditures (e.g. because it avoids hospitalisation or lifelong disability) for conditions that are currently very expensive to treat, it meets the societal need to allocate resources more efficiently (obtaining the same outcome for less resources or better outcomes for the same resources).

That the individual and societal dimensions are hard to merge into one single concept is exemplified by the type of criteria that are considered for the appraisal of therapeutic and societal need (see Table 1 for the criteria used in the MCDA proposed by KCE). The therapeutic need criteria are

typically patient-relevant criteria, whereas the societal need criteria are less important from the individual patient's point of view.

Table 1 – Non-exhaustive list of criteria for appraising therapeutic and societal need[3]

Therapeutic need	Societal need
Quality of life with current treatment	Societal cost of condition per patient
Life expectancy with current treatment	Prevalence of condition
Inconvenience of current treatment	

The MCDA applied by the CATT/CAIT uses the same principles but adds a "social vulnerability" criterion (cfr. Table 2). Whereas the KCE proposed criteria weights as measured in the general population,[4] the CATT/CAIT assigned its own weights to the different criteria and established specific scoring rules for each criterion (maximum scores for the 'performance' of a condition on each of the criteria), see Table 2 for the maximum scores and criteria weights.

Table 2 – MCDA applied by the CATT/CAIT to rank order health conditions according to unmet medical need

Criteria	Maximum performance score	Weight
Medical vulnerability		
Impact on life expectancy	3	30
Impact on quality of life	5	50
Rarity	2	20
Disadvantages of actual treatment	2	20
Vulnerable groups		
Pregnant women	1	20
Children	1	
Patient's dignity undermined	1	
Societal impact		
Societal resources (human/financial) required	1	20
Public health issue	1	

By using patient needs as a starting point instead of a specific technology (treatment, management approach, product), the unmet needs approach creates room for creative solutions and broader innovation. For example, patients with heart failure, wearing a pacemaker, could express the need to reduce their anxiety related to the functioning of their pacemaker. Telemonitoring could be a solution to meet this need, but also regular follow-up by a general practitioner or psychologist could offer a solution to patients. Whether telemonitoring or another intervention should be reimbursed for patients with a specific problem of anxiety depends on the level of need (how important this is for patients and how severe the patients' suffering is from this anxiety) but also on factors like price, effectiveness, other benefits, implementation, etc. This contrasts with the current reimbursement procedure, where the starting point is the technology, and it is assessed to which extent patients 'need' this technology.

Patients or patient associations can, as of yet, not submit an application to include a condition on the unmet medical needs list. As a result, most applications come from companies that have a product in their pipeline for a certain condition and want to claim a temporary reimbursement from the NIHDI before the marketing authorisation is granted for the drug. The system for unmet medical needs, which was intended to move to a more demand- or needs-driven reimbursement system in healthcare, therefore remains largely supply-driven. However, as the James Lind Alliance (UK) puts it (emphasis added in italics) "the pharmaceutical and medical technology industries and academia play essential roles in developing and testing new treatments, *but their priorities are not necessarily the same as those of patients and clinicians*."(The James Lind Alliance Guidebook, 2016)[5]

There are different ways to make the system more needs-driven. First, the submission of indications could be extended to patients and healthcare providers. Prerequisite is that patients and providers are aware of this possibility and have easy access to the application procedure. The data requirements should, in that case, not be too high or complex, as the process should be open to all patients. A second possible approach is to establish a new independent entity or charge an existing one to collect data on patient needs in a standardised way. The advantage of a standardised approach is that data is collected on the same variables for different

conditions, which facilitates the ranking of unmet needs later on in the process. Moreover, an independent organisation can make sure that all conditions can be investigated, not only those for which patient advocates exist. The disadvantage is that this approach is time-consuming, and hence the coverage of conditions will inevitably be limited in the short term. Nevertheless, these different approaches can co-exist to create a rich list of unmet needs.

Two organisations submitted, independently, a study proposal related to the identification of patient needs to KCE. First, the Flemish umbrella association of patient organisations, the *Vlaams Patiëntenplatform* (VPP), asked KCE (i) to explore the possibility to let other stakeholders submit proposals to be added to the unmet medical needs list of the CAIT/CATT and (ii) to develop a methodology to identify patient-reported unmet medical needs of patients. Second, the *observatory for chronic diseases* of the NIHDI asked KCE to investigate how patient needs can be identified in a feasible and scientifically valid manner. It asked to reflect on the broader application of the methodology (e.g. in the context of integrated care for chronically ill people). The question of the observatory for chronic diseases goes beyond the unmet medical need procedure of the NIHDI and also asked to consider needs beyond the purely therapeutic needs of patients.

2 OBJECTIVES, RESEARCH QUESTIONS AND SCOPE

2.1 Objectives

In this study, we aim to develop a methodology for identifying **patient needs**, to support initiatives to create a more needs-driven healthcare system. The methodology should consist of a general approach, based on existing data sources, as well as specific needs identification tools. The application of the methodology should result in useful input **for Health Technology Assessment (HTA) and regulatory and reimbursement decision-making processes** for the **assessment of (1) whether a new treatment addresses a therapeutic need of patients and (2) to what extent a new intervention** for which reimbursement is requested **meets the specific needs of patients** (or targets other outcomes that are maybe of secondary importance for patients but are nevertheless used to claim 'added value'). Decision-makers would still need to assess whether the observed effect on the patient-relevant outcome (e.g. in trials) is clinically relevant for patients and -in case of reimbursemend decisions- worth its cost. Moreover, the methodology should provide input to the **creation of a list of patient needs** that allows **innovators and developers** to focus their efforts on those areas where patient needs are highest. Also other stakeholders, such as **patient organisations, sickness funds and healthcare providers,** might benefit from detailed information on patients' highest needs to develop, shape or improve their activities.

We aim to develop a methodology that is sufficiently generic, applicable to a wide range of types, stages and severity of health conditions and the entire population with all its diversity. The methodology should consist of tools and approaches that can be scientifically validated, to ensure different populations are treated in the same evidence-based way. Moreover, we aim at developing a feasible methodology that can be applied in real life and embedded in a structural approach to patient needs identification. To meet these feasibility prerequisites, the methodology should satisfy two main criteria:

- it should be sufficiently generic to allow general applicability to a wide range of conditions;
- it should not be too resource consuming or complicated: as patient needs might, from a macro-perspective, be infinite, the application of the methodology should be relatively easy and not too expensive. If not, it is unlikely that it will be used.

Ideally, an advanced qualitative exploration of the patients' needs is performed in each disease area and patient population by means of qualitative research to obtain detailed information on the precise therapeutic needs of patients. This can be done, for instance, through focus groups or individual interviews with specific patient populations. However, qualitative research is very time-consuming and hence relatively expensive. It is impossible to perform an in-depth qualitative study on the therapeutic needs in *all* patient populations at the same time. Therefore, it is necessary to prioritize health conditions that require further (quantitative and qualitative) research to understand current and relevant patient needs. This study aims to identify a possible approach for this prioritisation exercise. Such an approach, applied by the agency, (research) group or institution mandated to identify patient needs, can exist alongside ad-hoc initiatives of other groups, agencies or institutions to investigate the needs of non-prioritised patient groups.

While there are no scientific arguments to support which group or agency that should get the responsibility to structurally identify patient needs, we can describe the conditions and requirements for this activity. The decision to assign the task to a particular existing group or agency, or establishing a new one, is essentially a political one.

2.2 Research questions

Four research questions have been formulated to achieve the objective of this study to create a methodology for identifying patient needs to support initiatives to create a more needs-driven healthcare system:

- Which methods for identifying patient needs have been described in the literature, and which validated instruments have been used and applied in practice (in Belgium or abroad)?
- Which existing data sources are available to prioritise health conditions for the identification of patient needs?
- What method could be developed to identify patient needs in Belgium, based on the insights from research questions 1 and 2?
- What are the requirements, in terms of human resources and qualification and time, to allow for a systematic identification of patient needs in diverse patient populations in order to embed the information in the health policy system?

2.3 Scope

The main focus of this study is on the identification of therapeutic needs of patients, i.e. needs for which currently no adequate solutions exist yet from the patient's perspective. *Unmet* therapeutic needs can emerge from the non-existence of solutions for experienced health problems or from the lack of reimbursement of existing interventions for the specific indication underlying the unmet need[a]. In the former case, therapeutic innovation is required to meet patients' therapeutic need, either as first treatment or as a better treatment than the existing one(s). In the latter case, appropriateness of extending the reimbursement to new indications will have to be assessed (taking *all* relevant decision parameters into account). Societal need, determined by the budget impact of current standard treatment or care, is out of scope. In the previous KCE report on unmet

[a] Lack of reimbursement often – though not always, cfr cheap over-the-counter products – Implies lack of access and thereby a possible unmet need.

needs assessment[3], therapeutic need was defined as being dependent on the impact of a condition on quality of life (given current treatment or care), inconvenience of current treatment or care and impact on life expectancy. The higher the impact on quality of life, inconvenience or life expectancy, the higher the therapeutic need. The concept was deliberately kept simple, with only three dimensions, to allow for standardised assessment. However, impact on quality of life as well as inconvenience of current treatment can encompass several aspects reflecting the need of patients for a (better) treatment. This is what we would like to develop further in this report.

Issues of access to available treatments and care, and needs resulting from that, were a priori out of scope, unless this lack of access is due to non-reimbursement. However, during the study process, issues of non-use of existing reimbursed treatment or care options were highlighted by the stakeholders in this study's advisory committee, as relevant for policy makers and therefore relevant for the scope of the current project. Indeed, accessibility to healthcare entails more than reimbursement, including geographical accessibility, availability, affordability, or acceptability. The same applies to issues of patient needs that are not directly treatment or healthcare-related, such as information needs, social support needs, spiritual needs, support with daily activities, health education and training, administration, etc. While the initial objective was to focus on therapeutic and healthcare needs only, the advisory committee insisted on taking these other aspects into account. The scope of the study was, therefore, enlarged, at least in the tools developed for the qualitative assessment of the patient needs. Identification of patient needs in a clinical setting, i.e. in individual patient-physician contacts, however, is out of scope for this study.

Given the objective to develop a methodology that consists of tools and approaches that can be scientifically validated, ad-hoc approaches like public hearings or patient involvement in a committee discussing or assessing a single treatment are out of scope.

The objective of this project is to develop a feasible and scientifically valid methodology for identifying patient needs, which can feed HTA, regulatory and reimbursement decision processes and other stakeholders' decision processes. The ultimate aim is to create a more needs-driven healthcare system by defining the gaps (in research, organisation or policy) that need to be filled to meet patients' needs.

Four research questions have been formulated to achieve this objective:

- **Which methods for identifying patient needs have been described in the literature, and which validated instruments have been used and applied in practice (in Belgium or abroad)?**
- **Which existing data sources are available to identify conditions with high unmet needs, on which further qualitative research is desirable to understand better the actual needs of patients?**
- **What method could be developed to identify patient needs in Belgium, based on the insights from the two previous research questions?**
- **What are the requirements, in terms of human resources, expertise and time, to allow for a systematic identification of patient needs in diverse patient populations in order to embed the information in the health policy system?**

3 GENERAL METHODOLOGICAL APPROACH

First, an operational definition of patient needs was developed for this study, based on the literature and our own previous work on unmet medical needs (Chapter 4).

Second, a pragmatic literature review (including grey literature) is performed to identify different approaches to determine patient needs. Both qualitative, quantitative and mixed approaches are studied. The objective is to identify patient needs measurements in Belgium and in other countries, for which purpose, in which population, which instruments have been used and which dimensions are included (Chapter 5).

Third, an overview is made of possible data sources that could be used either to identify patient needs or to identify health conditions with a potential high burden for patients where more in-depth study of patient needs is desirable (Chapter 6). It is explored whether it would be possible to make a identify conditions with high patient needs based on "quantitative" data available in the databases. Given the objective to develop a sustainable methodology, a prerequisite is that the databases are systematically updated and are expected to continue to exist. A good indicator of the burden of a disease is its impact on health-related quality of life (HRQoL). Therefore, specific attention will be given to databases that include quality of life data. The exploration of possible applications of existing databases for identifying heatlh conditions with high needs in the context of prioritization for further qualitative research is done in collaboration with Sciensano (Brecht Devleesschauwer and Rana Charafeddine), who coordinates the Health Interview Surveys in Belgium.

Fourth, a generic questionnaire to measure patient needs is developed (Chapter 7). This could be considered the first part of the qualitative in-depth assessment of patient needs in a specific disease area. A survey allows quantitative analyses and at the same time allows to identify the major domains of unmet needs on which to build for further qualitative assessment. The generic questionnaire is developed based on the domains and items identified in the literature review. An extensive consultation process with patient representatives, using a Delphi panel approach, is set up to ensure the relevance and clarity of the questions asked in the questionnaire.

Fifth, a pilot study is performed in one specific patient population, using the survey developed in Chapter 7 and complemented with qualitative research tools to assess patient needs more in depth. The purpose of the pilot study is to test the feasibility and appropriateness of using an online survey in combination with individual interviews or an online forum to identify patient needs. Moreover, the lessons learnt from the pilot survey allow for improvements in the generic questionnaire developed in Chapter 7.

Throughout the project, the research team was supported by a stakeholder advisory, consisting of experts and stakeholders closely involved in patient needs assessment or already identifying patient needs in Belgium. The technique of "embedded consultation"[b] is applied, involving regular consultation on all aspects of the project. The advisory committee consists of representatives of patients and healthcare users (VPP, LUSS, RaDiOrg, IMA/AIM), the observatory of chronic diseases (part of the NIHDI) and researchers with a background in patient needs research.

[b] https://kce.fgov.be/en/position-of-kce-on-patient-involvement-in-health-care-policy-research

4 DEFINING (UNMET) PATIENT NEEDS

(Unmet) patient needs are a concern from many perspectives, including the individual (e.g. potential pain and disability), policymaking (e.g. allocating healthcare resources to meet the healthcare needs of the population), and societal perspectives (e.g. informal care burdens, economic inactivity due to untreated health care problems).[6] In many countries, the decision on reimbursement of innovative treatments or products is prioritised based on "the level of unmet medical need". Unmet medical need is considered as a sub-category within the broader group of "patient needs". Measuring unmet medical needs is not an easy exercise, because of the lack of an universally accepted definition of the concept and criteria to define unmet medical needs.

The interpretation of unmet medical need varies between different stakeholder groups (such as policymakers, sickness funds, patients, informal caregivers, health technology assessment agencies, pharmaceutical companies, etc.). In this chapter, we will give a conceptual clarification of the construct of unmet medical need, as well as an overview of different possible interpretations, based on three review papers and Belgian and European regulations. Finally, we describe the operational definition used in this study

4.1 Literature

A recent scoping review of 2019 analysed 16 different international definitions of unmet medical need.[7] All of these analysed definitions included one or more of the following elements:

- **Treatment alternatives:** there are no or limited treatment alternatives, or the benefits of existing treatments are insufficient to meet patients' needs.
- **Disease severity or burden of disease:** the condition in question is serious and severe in terms of quality of life, life expectancy, etc.
- **Patient population or disease incidence/prevalence:** if a condition is uncommon, it may not be commercially viable to create good treatment (alternatives) for that particular condition.

Vreman et al.[7] propose some methods for quantification of these different elements:

- For treatment alternatives, the number of alternatives, their effectiveness and their accessibility could be assessed.
- For disease severity and burden of disease, the impact on the quality and duration of life of patients could be assessed.
- For patient population and disease frequency, the incidence and prevalence could be assessed.

According to Allin et al.[8] unmet medical need occurs when an individual does **not receive an available and effective treatment** that could improve his or her health. Building on the literature on the definition of health care needs, the authors identify five types of unmet medical needs:

- **Unperceived medical needs:** individuals are not aware of this unmet need.
- **Subjective, chosen unmet medical needs:** individuals perceive a need but choose not to demand available health services.
- **Subjective, not-chosen unmet medical needs:** individuals perceive a need for, but do not receive health care because of access barriers.
- **Subjective, clinician-validated unmet medical needs:** individuals perceive a need for and access health care, but do not receive appropriate treatment endorsed by clinicians.
- **Subjective unmet medical expectations:** individuals perceive a need for and access health care, but do not perceive the treatment to be suitable.

These types highlight the complexity and multi-dimensional conceptualisation of unmet medical needs (i.e. it cannot be captured by a single indicator or method of measurement), which requires alternative approaches to identify and analyse different aspects of the concept.[6]

Smith et al.[6] suggest to include a dynamic (or longitudinal) perspective in the definition of unmet medical need. If unmet medical needs are measured at one point in time, the long-term consequences of what

happens to those unmet needs is not considered, and yet, this information is important to adequately quantify and respond to unmet medical needs by the health care system. Taking this dynamic perspective in account requires a more detailed evaluation of all types of perceived need that (i) remain completely under the radar of the health care system over time or (ii) are presented now (or at a later date) to a health care provider. By considering what ultimately happens to these perceived needs, three different trajectories are described by Smith et al.[6]:

- **Non-use at any time:** need is perceived, but individual does not at any time convert this need into demand for health care.[c]
- **Delayed (and/or diverted) use:** need is perceived and converted into a demand for health care. However, there is a delay in (i) demanding (e.g. individual waits to see if the health problem gets better before seeking care) and/or (ii) receiving health care (e.g. service availability is limited and individual is placed on a waiting list).
- **Suboptimal use:** need is perceived, converted into a demand, and health care is received. But the level of care is suboptimal (perceived or clinically determined).[d]

In summary, unmet medical needs can be related to limits in the accessibility of health care, patients' lack of awareness of needs, patients' preferences (to not search for or use healthcare) and suboptimal healthcare received because of lack of available effective treatment or care.

4.2 European and Belgian regulations

The European Commission has defined unmet medical needs as "a condition for which **there exists no satisfactory method of diagnosis, prevention or treatment** authorised in the Community or, even if such a method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected".[9] In addition, the European regulation on procedures for the authorisation and supervision of medicinal products for human and veterinary use refer to unmet medical needs as "chronically or seriously debilitating condition or whose condition is considered to be life threatening, and who cannot be treated satisfactorily by an authorised medicinal product". It is the definition currently applied by the European Medicines Agency (EMA). These European operationalisations are broader than the definition utilised in Belgium, in which the focal point lays on "reimbursement". According to the Belgian law of 7 February 2014[10] and Royal decree of 12 May 2014[11] unmet medical needs are defined as a pharmaceutical product for the treatment of a severe or life threatening condition for which **no reimbursed alternative treatment is available**.[12]

4.3 Definition applied in this report

For consistency with previous KCE work on unmet medical needs[12], we will use the concepts of therapeutic needs and – more general – patient needs. Compared to the definitions defined in the literature (see 4.1), **therapeutic needs** refer to "subjective, clinician-validated unmet medical needs"[8], "subjective unmet medical expectations"[8] and "suboptimal healthcare use"[6]. In short, it concerns **needs perceived by the patients that are not met by currently available reimbursed treatments or care, either because they do not exist or because they are not sufficiently effective.**

[c] This trajectory differs from previous traditional survey questions measuring unmet medical needs (e.g. EU-SILC) which focus on non-use at one point in time or a specified time period.

[d] This trajectory is closely related to dimension "Subjective, clinician-validated unmet medical needs" and "Subjective unmet medical expectations" of Allin et al.[8]

Patient needs is a more general concept and encompasses therapeutic need as well as **other needs**, related to the patients' health condition but not strictly healthcare-related. Such needs can refer to social support needs, information and education needs, spiritual needs, financial needs etc. related to the patients' condition. Our concept of "patient needs" closely resembles the concept of "societal health needs" as defined by the Royal College of Physicians and Surgeons of Canada[13]. They define societal health needs as the requirements at the individual, family, community and population levels – across the continuum of care – to achieve physical, cognitive, emotional, social and spiritual wellbeing, taking into account the broad determinants of health.[13] However, because KCE prefers to keep individually perceived needs separated from community and population-level needs, we avoid using the term societal health needs and use therapeutic needs and patient needs as standard terms.

The current study is not limited to *unmet medical needs*, as defined by the European Commission for two main reasons.[12]

- Following the European definition, a need is only really "unmet" when no other alternative is available. However, this is rarely the case. For example, when there is no other curative treatment available for chronic patients, care could be reoriented towards symptomatic treatment or supportive care. From the moment care is provided to patients, this activity should be considered as the alternative to which the new treatment or clinical management strategy should be compared to.
- In complement to this reasoning, need cannot be considered a categorical concept which is "present" or "absent". Need is rather a continuum, with gradations of the extent to which needs are met. Some needs will be more satisfied compared to others, but all needs are important and should, therefore, deserve attention.
- As highlighted by Smith et al.[6], there is a dynamic aspect to unmet medical needs: while patients may express an unmet need at a certain moment in time, it is not certain that that need will remain present in the long term, even without treatment or with insufficiently effective treatement.

The concept "therapeutic need" is more suitable to approach need on a continuum and define gradations. The more effective a treatment, the lower will the therapeutic need be, even if it concerns severe conditions. By defining need this way, it will be possible to identify those conditions that should get priority in terms of investment decisions.

The concept of *patient needs* used in this report encompasses

- **Therapeutic needs: needs perceived by the patients that are not met by currently available reimbursed treatments or care, either because they do not exist, because they are not sufficiently effective or highly burdensome**
- **Other needs related to the patients' health condition**
  - **Healthcare-related needs: access to care (financial, geographical), communication with healthcare providers, …**
  - **Non healthcare-related needs: social support, information, education, spiritual, …**

Patient needs are expressed on a continuum ranging from 'completely unmet' to 'completely met', and are dynamic over time

5 MEASURING HEALTH(CARE)-RELATED PATIENT NEEDS: A PRAGMATIC LITERATURE REVIEW

5.1 Methods

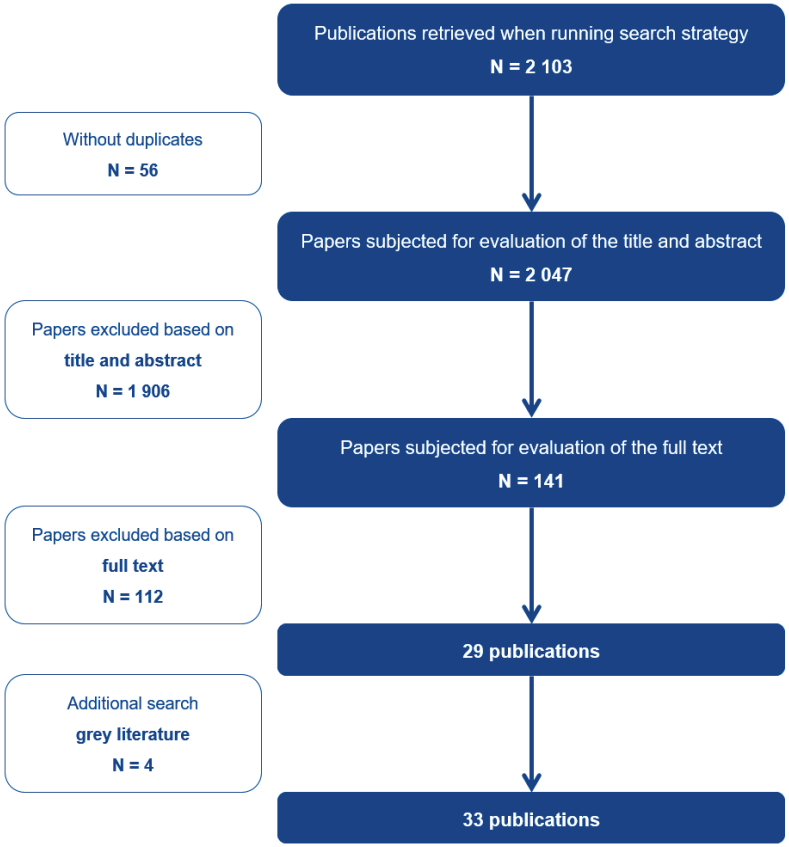
A pragmatic literature review was undertaken to identify methods to measure healthcare-related patient needs. In the literature, the term “unmet medical need” is quite commonly used, even if the underlying concept of investigated needs is larger than the definition of ‘unmet medical needs’ applied by the European Commission. We concentrated in this review on patient needs related to health(care), which encompasses therapeutic needs, but also healthcare information needs, support needs etc. Societal needs was out of scope for this literature review. A detailed overview of the inclusion and exclusion criteria, following the PICOS (Population, Intervention, Comparator, Outcome, Setting) model, is provided in Table 3.

A systematic search was performed using Ovid Medline® across the period 1 January 2000 – 20 January 2020. In addition, only publications written in English, French, or Dutch were included. The detailed search terms and the number of hits for each search strategy are provided in Appendix 1. Table 3 illustrates our search and selection process. In- and exclusion criteria were tested on a set of 100 references by two reviewers (JD and IC). Next, the titles and abstracts of the remaining publications were screened for inclusion by one reviewer (JD). When the relevance of a publication was not clear, full text was retrieved and content examined by both reviewer (JD and IC). Publications meeting inclusion criteria were read and summarised using a structured data extraction form.

Table 3 – Inclusion and exclusion criteria

	Inclusion	Exclusion
P	All patient populations	Studies published before 2000
I	Measurement of healthcare-related patient needs	Measurement of societal need or needs not related to healthcare
C	-	
O	Healthcare-related patient needs	Societal need
S	Evidence from Western countries: EU-28, Iceland, Liechtenstein, Norway, Switzerland, USA, Canada, Australia, and New Zealand	Studies conducted in non-Western countries

Figure 1 – Flow chart of the selection procedure



5.2 Results

Our search strategy of Ovid Medline® identified 2 103 possible relevant publications (2 047 after de-duplication). After applying the inclusion- and exclusion criteria during the screening of titles and abstracts, only 141 publications were left. On the evaluation of the full text, 112 publications were excluded based, resulting in 29 relevant publications. The search of the scientific literature was supplemented by an additional search of grey literature (by searching Google Scholar and snowball searching of the included publications). This additional search gave four relevant publications, increasing the total selection of publications to 33 (Figure 1).

The search revealed 40 approaches that described some form of measurement of health(care)-related patient needs. The nature of the methods could be categorised in three main groups: (i) quantitative methods, (ii) qualitative methods, and (iii) mixed methods. The results section and description of all methods will be structured following this categorisation.

An important observation is that a large proportion of the literature describing quantitative approaches measures patient needs by asking people if they perceived healthcare needs in a certain period of time and did not receive it for some reason. If respondents answer “yes” to this question, they are considered to have experienced an unmet (medical) need. This question is usually followed by the measurement of the reason for this unmet need (e.g. could not afford it, waiting list, too far to travel, etc.). These questions are, for example, part of the EU-SILC (EU Statistics on Income and Living Condition) questionnaire. However, this subjective operationalisation is very broad and quite vague. The response options (with the exception of “other” and “waiting lists were too long”) assume that need was not converted into demand. In other words, the person did not present the need to any health care provider.[6] The answer can vary from unmet needs due to health literacy issues or financial constraints to issues with healthcare organisation on the macro-level. While this operationalisation can be a good starting point for a questionnaire or a focus group, it is not suitable for the in-depth assessment of patient needs.

5.2.1 Quantitative approaches

The majority of the included publications describe quantitative approaches to measure health(care)-related patient needs across a wide variety of health conditions. In total, we identified 30 different quantitative instruments or tools. All these operationalisations are described in more detail below. Psychometric properties of the quantitative assessment tools (in terms of content validity, construct validity and internal consistency reliability) are presented in Table 4.

Table 4 – Overview of the quantitative approaches to measure health(care)-related patient needs

Publication	Approach	Subject	Purpose and population	Country
Allotey (2002) [14]	Disability-Adjusted Life Year (DALY)	Reproductive health	Not specified	Not specified
Albarqouni (2018) [15]		No specific condition	Not specified	PSE
Arnesen (2004) [16]		Developmental disability due to malnutrition and major depression	Children	NOR
Bertram (2013) [17]		Stroke	General population	ZAF
Cassini (2016) [18]		Healthcare-associated pneumonia, healthcare-associated urinary tract infection, surgical site infection, healthcare-associated *Clostridium difficile* infection, healthcare-associated neonatal sepsis, healthcare-associated primary bloodstream infection	Not specified	EU-29 HR
Greden (2001) [19]		Treatment-resistant depression	Not specified	Global
Incerti (2019) [20]		Rheumatoid arthritis, breast cancer, Parkinson's disease, hepatitis C, Chronic Obstructive Pulmonary Disease (COPD)	Not specified	Not specified
Karimkhani (2017) [21]		15 skin diseases	Not specified	IRN and 15 neighbouring countries
Longfield (2013) [22]		Malaria, child survival, HIV, reproductive health	Not specified	Eastern Europe and Laos
Lopez (2006) [23]		No specific conditions	General population	Not specified
Mangen (2013) [24]		Infectious diseases	Not specified	Not specified
McDonald (2017) [25]		Human papillomavirus infection	Not specified	NLD
Phua (2009) [26]		130 health conditions	Not specified	SGP
van den Wijngaard (2015) [27]		Lyme borreliosis	Not specified	NLD
van Lier (2016) [28]		32 infectious diseases	Not specified	NLD

Publication	Approach	Subject	Purpose and population	Country
Vos (2009) [29]		Infectious diseases, cancers, diabetes, cardiovascular disease, mental disorders, chronic respiratory disease	Indigenous Australians (i.e. Aboriginal and Torres Strait Islander people)	AUS
Asadi-Lari (2005) [30]	Camberwell Assessment of Need (CAN)	Severe or long-term mental problems	Measure and define needs of patients with severe or long-term mental problems	GBR
Asadi Lari (2005) [30]	Camberwell Assessment of Need for the Elderly (CANE)		Measure and define needs of elderly with severe or long-term mental health problems	GBR
Stein (2019) [31]				DEU
Aragón Aragón (2017) [32]	Camberwell Assessment of Need Short Assessment Schedule (CANSAS)		Measure and define needs of patients with severe or long-term mental problems (short version of CAN)	GBR
Aragón Aragón (2017) [32]	Nottingham Health Needs Assessment (NHNA)	Cardiovascular disease	Assess health needs of cardiac patients	GBR
Asadi-Lari (2005) [30]				
van Walsem (2017) [33]	Needs and Provision Complexity Scale (NPCS)	Huntington's disease	Assess the unmet needs in health care and social support for patients diagnosed with Huntington's disease	NOR
Aragón Aragón (2017) [32]		Long-term neurological conditions	Measure unmet needs among patients discharged from specialist neurorehabilitation units	GBR
Liker (2009) [34]	Burning Questions and Burning Desires	Gastroesophageal reflux disease (GERD)	Compare the efficacy of GERD therapy from both physicians' and the patients' perspectives	FRA, DEU, JPN, USA, GBR
Lindly (2017) [35]	Consumer Assessment of Healthcare Providers and Systems (CAHPS) Health Plan survey – Child questionnaire	No specific condition	Measure family-centred care (including shared decision making) and unmet health care needs in paediatric care	USA
Richardson (2005, 2007) [36, 37]	Cancer Rehabilitation Evaluation Systems (CARES)	Cancer	Measure rehabilitation needs and QoL, and measure how cancer affects psychosocial, physical and behavioural states among cancer patients	USA
	Cancer Care Monitor (CCM)		Screen high-frequency cancer-related symptoms and assess overall symptom severity and QoL in cancer patients	USA
	Creating better Health Outcomes by Improving Communication about patients' Experiences (CHOICE)		To assess patients' symptoms, functional problems and preferences among outpatient cancer patients before the consultation	NOR

Publication	Approach	Subject	Purpose and population	Country
	Concerns Checklist		To elicit and register main concerns of a wide variety of patient groups	GBR
	Distress Management Tool		Screening tool for rapid assessment among cancer patients	USA
	Needs at the End-of-Life Screening Tool (NEST)		Measure patients' experiences and perspectives regarding their care among patients at end-of-life	USA
	Oncology Clinic Patient Checklist (OCPC)		Systematically assess problems related to cancer and its treatment among adults patients in outpatient clinics	USA
	Patient Needs Assessment Tool (PNAT)		Screen potential problems in physical and psychological functioning in cancer patients	USA
	Problems Checklist		Assess prevalence and severity of psychosocial problems among cancer patients	GBR
	Supportive Care Needs Survey (SCNS)		Assess perceived needs of cancer patients	AUS
	Sheffield Profile for Assessment and Referral to Care (SPARC)		Assess distress caused by advanced illness and screen symptoms/problems to guide referrals to specialist and palliative care for patients with advanced illness	GBR
	Symptoms and Concerns Checklist		Determine prevalence and severity of symptoms and concerns in routine practice as adjuvant to clinical assessment of patients with advanced illness	GBR
Richardson (2005, 2007) [36, 37]	Needs Evaluation Questionnaire (NEQ)		Assessment of informative, psychological and social needs among hospitalised cancer patients	ITA
Asad-Lari (2005) [30]				
Richardson (2005, 2007) [36, 37]	Problems and Needs in Palliative Care instrument (PNPC)		Screen problems of patients' experience in palliative care and their needs for care. To support provision of tailored care to specific demands of individual patients with advanced cancer	NLD
Asad-Lari (2005) [30]				
Asad-Lari (2005) [30]	Needs Assessment Checklist (NAC)	Spinal cord injuries	Assess the rehabilitation outcome measure amongst patients with spinal cord injuries	GBR
	Cardinal Needs Schedule	Severe mental problems	Measure needs for psychiatric and social care amongst patients with severe psychiatric disorders	GBR
		Schizophrenia		GBR

Publication	Approach	Subject	Purpose and population	Country
	Salford Needs Assessment Schedule for Adolescents (S.NASA)	Mental health problems	Assess needs of adolescents with mental health problems	GBR
	Southampton Needs Assessment Questionnaire (SNAQ)	Disability	Identify levels of met need and satisfaction with services provided among patients in rehabilitation, in order to encourage participants to think about their unmet needs.	GBR
	Service and Needs Assessment (SUN)	Multiple sclerosis	Identify unmet needs for people with multiple sclerosis and their carers	GBR, BEL, EST, GRC, ITA
	Care Needs Assessment Pack For Dementia (CARENAPD)	Dementia	Assess the needs of people with dementia and their caregivers in community (and related, e.g. day hospitals) settings	GBR
	Cancer Needs Questionnaire (CNQ)	Cancer	Assess cancer patients' needs using a self-administered cancer-specific questionnaire	AUS
	Elderly Health Care Needs Assessment Questionnaire (EHC-NAQ)	No specific condition	Identify unmet health care needs of older adults	USA

PSE: State of Palestine, NOR: Norway ZAF: South-Africa, HRV: Croatia, IRN: Iran, NLD: Netherlands, SGP: Singapore, AUS: Australia, GBR: United Kingdom, DEU: Germany, FRA: France, JPN: Japan, USA, United States of America, ITA, Italy, BEL: Belgium, EST: Estonia, GRC: Greece

5.2.1.1 Disability-Adjusted Life Year (DALY)

A commonly used metric for assessing therapeutic needs is DALY. This is a measure of overall disease burden, expressed as the number of years lost due to ill health, disability, or early death. DALYs for a disease or health condition are calculated as the sum of Years of Life Lost (YLL) due to premature mortality in the populations and the Years Lost due to Disability (YLD) for people living with the health condition or its consequences.[38, 39]

5.2.1.2 DALY = YLL + YLD

Evidence operationalising patient needs through DALYs usually uses the data collected by the Global Burden of Disease study (GBD).[40] The GBD study is coordinated by the Institute for Health Metrics and Evaluation (IHME) of the University of Washington and aims to describe global descriptive epidemiology using metrics such as DALYs.[41, 41] The most recent GBD wave (2019) included estimates of 369 diseases and injuries in 204 countries and territories.[42] For additional information regarding the GBD study, we refer the reader to paragraph 6.2.1 in Chapter 6.

Box 1 – Example of utilisation of DALY in the Netherlands

Van Lier et al.[28] calculated the national burden of disease estimates (expressed in DALYs) for a set of 32 infectious diseases in the Netherlands for the period 2007 – 2011. The following conditions were included in the study: sexually transmitted infections (e.g. chlamydia, gonorrhea, and hepatitis B infection), vaccine-preventable conditions (e.g. diphtheria, invasive meningococcal disease, measles, rubella, and tetanus), food-related diseases (e.g. campylobacteriosis, hepatitis A infection, salmonellosis, and toxoplasmosis), and respiratory diseases (e.g. influenza, legionellosis, and tuberculosis).

Burden of disease estimates were calculated using the methodology and toolkit (version 0.94) from the Burden of Communicable Diseases in Europe (BCoDE) project. The BCoDE methodology recommends a pathogen-based approach for burden calculation. This focus in this approach is on all health outcomes that can be causally attributed to that specific pathogen. It gives justice to the potential long-term sequelae of infection diseases, and permits a better estimation of the (future) health benefits associated with the prevention of infections.

Burden of disease was calculated based on incidence data.

5.2.1.3 Camberwell Assessment of Need (CAN)

CAN is a family of questionnaires that can be used to assess a wide range of potential problems experienced by people diagnosed with severe or long-term mental health problems.[43] The CAN questionnaires have been developed by King's College London in 1994. New versions of the adult CAN and variants for use with other population groups have been developed by collaborators around the world. Needs are measured within 22 CAN domains: accommodation, food, looking after the home, self-care, day-time activities, physical health, psychotic symptoms, information on condition and treatment, psychological distress, safety to self, safety to others, alcohol, drugs, company, intimate relationships, sexual expression, child care, basic education, telephone, transport, money, and benefits. each domain contains 5 sections: (1) problem severity, (2) amount of help received from friends/relatives, (4) amount of help received from local services, (5) appropriateness of current intervention and satisfaction with amount of help received. Each domain item can be rated on a 3-point Likert scale. The initial developed CAN questionnaire consists of four versions:

- CAN-C: 22-page assessment for clinicians to record needs, support, and an action plan.
- CAN-R: 22-page assessment for research use to record needs, support, and satisfaction.
- CANSAS (Camberwell Assessment of Need Short Assessment Schedule): one-page assessment of needs which can be filled in by either the patient, staff, or carer.
- CANSAS-P: two-page assessment designed for self-completion by patients.

Furthermore, a number of variants of the CAN have been developed internationally:

- CANDID (Camberwell Assessment of Need for Adults with Developmental and Intellectual Disabilities)[44]
- CANE (Camberwell Assessment of Need for the Elderly)[45]
- CANFOR (Camberwell Assessment of Need – Forensic version)[46]
- CAN-M (Camberwell Assessment of Need for Mothers)[47]
- HESPER (Humanitarian Emergency Settings Perceived Needs Scale): a measure that is based on the CANSAS questionnaire and assesses the perceived needs of people affected by large-scale humanitarian emergencies (such as war, conflicts, or major natural disasters). This scale was developed in collaboration between the King's College London and the World Health Organization (WHO).

Box 2 – Example of implementation CANE in Germany

Stein et al.[31] used the CANE assessment tool to study the distribution of met and unmet needs and their association with depression in older age in Germany.

Using a population-representative telephone survey of elderly people, a sample of 845 respondents were assessed via structured clinical interviews. Criteria for participation in the telephone survey were (i) an aged of 75 years or older and (ii) adequate hearing and speech comprehension. Exclusion criteria were (i) problems with hearing, speech, or speech comprehension, (ii) comprehension problems due to cognitive impairment or suspected dementia (which was detected through a screening test for dementia). The CANE assessment tool was

translated and adapted to the German context by the same authors in previous research.[48, 49] For each CANE section and for the four CANE categories (i.e. physical, psychological, environmental, and social needs) a sum score for unmet needs as well as dichotomous variable (0 for no/met needs, 1 for at least one unmet need) was build.

The results of this research revealed most unmet needs in the CANE sections memory, physical health, mobility, eyesight/hearing and communication, and continence. There was no CANE section in which no unmet needs were reported

5.2.1.4 Nottingham Health Needs Assessment (NHNA)

The NHNA questionnaire is specifically developed for health needs assessment among cardiac patients.[50, 51] It was developed based on a literature review, discussions with experts, medical staff and patients and information compiled from patient interviews. The NHNA covers demographic data, employment, mobility and transport, access to local health care facilities, information needs and concerns, availability of carers, current health care, accommodation, education, leisure and social facilities. The tools contains 49 items across five domains: physical needs (8 items), satisfaction (11 items), informational needs (7 items), societal needs (12 items), and concerns (8 items). These items can be rated on a five-point Likert scale (one indicating more needs, five indicating no needs).

5.2.1.5 Needs and Provision Complexity Scale (NPCS)

The NPCS tool has been described/applied in two selected publications for measuring unmet medical needs among patients with long-term neurological conditions.[32, 33] It has also been developed for this target population from 2008 until 2012. First, it measures the patients' needs for healthcare and support services (part A, NPCS-Needs) and, second, to which extend these needs are met through service provision (part B, NPCS-Gets). NPCS-Needs are assessed in a systematic and normative way by the clinician. NPCS-Gets is systematically recorded by the clinician based on information provided by the patient and/or healthcare professional. In its original form, both parts were designed for completion by clinicians. A patient-report version of the NPCS-Gets was subsequently developed and tested for completion by patients and/or their healthcare professionals. The measure includes 15 items with a total score range of 0 – 50 covering low and high levels of needs. These items are divided across 6 subscales representing two domains: (i) health and personal care needs and (ii) social and support needs (both having a score range of 0 – 25). The NPCS can be used at the population level to identify gaps in health service provision. But also on the individual patient level, to monitor needs and provision along the care pathway across time.[33]

Box 3 – Example of implementation NCPS in Norway

Health-Related Quality of Life (HRQoL) of patients with a clinical diagnosis of Huntington's disease was assessed using the EQ-5D-3L. This assessment was complemented by the measurement of unmet needs for health care and social support by the NPCS in order to study the association with HRQoL.[33]

Data was collected through a survey interview, either during study visits in a regional academic medical centre in Oslo or in patients' homes. Interviews were always conducted by the same two experienced clinical raters. NPCS total levels of unmet needs were calculated as the discrepancy between the total level of Needs and Gets: NPCS Needs score – NPCS Gets score = NPCS unmet needs score.

The results regarding unmet needs showed a peak in unmet needs in stage III of Huntington's disease. Levels of unmet needs were lowest for patients in stage I and II. Patients in stage IV and V showed a constant in levels of unmet need, they were higher than those in stage I and II, but lower compared to stage III. In addition, a higher level of unmet needs was associated with lower HRQoL.

5.2.1.6 *Burning Questions and Burning Desires*

Liker et al. (2009)[34] consolidated previously collected data from the Burning Questions and Burning Desires surveys. The Burning Questions survey compared the efficacy of gastroesophageal reflux disease (GERD) therapy between physicians' and patients' perspectives.[52] While the relationship between GERD symptoms and treatment and subjective impact of symptoms was studied in the subsequent Burning Desires survey among patients only.[53, 54] However, we could not retrieve the original survey.

5.2.1.7 *Consumer Assessment of Healthcare Providers and Systems (CAHPS) Health Plan survey*

The CAHPS Health Plan Survey asks US adults and parents of children enrolled in commercial and Medicaid plans to report on and rate their experiences with the health plan.[55] There exist two adult surveys (one for commercial and one for Medicaid plans) and two child surveys (also one for commercial and one for Medicaid plans). The survey is constructed based on four major "composites" that summarise consumer experiences in the areas listed below. The respondents can rate these items on a four-point Likert scale ("never", "sometimes", "usually", or "always").

- Getting needed care (2 items in both surveys)
- Getting care quickly (2 items in both surveys)
- How well doctors communicate (4 items in the adult survey and 5 items in the child survey)
- Health plan information and customer service (2 items in both surveys)

In addition, CAHPS collects four separate global ratings to distinguish important aspects of care. The four questions ask respondents to rate their experiences in the past 6 months with some healthcare professionals or provided care (see below). Ratings are scored on a 0 to 10 scale, where 0 is the "worst possible" and 10 is the "best possible".

- Their personal doctor (1 item in both surveys)
- The specialist they saw most often (1 item in both surveys)
- Health care received from all doctors and other health providers (1 item in both surveys)
- Their health plan (1 item in both surveys)

5.2.1.8 *Cancer Rehabilitation Evaluation Systems (CARES)*

CARES has been also known under a different name in some literature: the Cancer Inventory of Problem Situations (CIPS).[56] It aims to measure rehabilitation needs and Quality of life (QoL), and find out how cancer affects psychosocial, physical and behavioural states in patients with cancer.[36, 37] The long form CARES contains 139 problem statements (in six domains) encountered by cancer patients on a daily basis. These six domains are: physical (26 items), psychosocial (44 items), medical interaction (11 items), sexual (8 items), marital (18 items), and miscellaneous (32 items). Reported items are those of the long form CARES. Patients rate each problem statement on a five-point Likert scale and indicate whether a problem is one that they would like help with (by answering "yes" or "no"). The first 88 items are completed by all patients. The remaining 51 items may not apply to everyone (for example if patients do not receive chemotherapy). However, there is also a short form CARES, which only consists of 59 problem statements.

5.2.1.9 *Cancer Care Monitor (CCM)*

The CCM is a symptom-based scale developed for administration on pen-based computers.[57] The monitor provides a measure to screen high-frequency cancer-related symptoms and to assess overall symptom severity and QoL. It contains 38 items categorised in 6 subscales, all rated on 11-point Likert scale. These subscales are: general physical symptom scale (11 items), treatment side effects scale (8 items), acute distress (4 items), despair (7 items), impaired ambulation (4 items), and impaired performance (4 items).

5.2.1.10 *Creating Better Health Outcomes by Improving Communication about Patients' Experiences (CHOICE)*

The CHOICE questionnaire was designed as an assessment tool for cancer specific symptoms and associated functional problems.[58-60] It can be administered via touch pad computer tablet and has questions and answers tailored to individual responses to problem areas from a potential list of 6 domains (112 items). These domains are: cancer specific symptoms, functional problems, physical, psychosocial, emotional, and spiritual. Plus two global ratings: health and QoL. It asks patients to indicate their agreement or views regarding the severity of their symptoms and needs and rate the importance of their problems.

5.2.1.11 *Concerns Checklist*

The Concern Checklist is a self-assessment tool for cancer patients to identify the concerns they experience.[61] The checklist contains 68 concerns, categorised in 6 main domains: physical concerns (27 items), practical concerns (16 items), emotional concerns (12 items), family or relationship concerns (5 items), spiritual concerns (3 items), information or support (8 items). The respondent also has the possibility to indicate which of the concerns he/she wants to discuss with a key worker, by scoring those concerns on a ten-point Likert scale.

5.2.1.12 *Distress Management Tool*

The National Comprehensive Cancer Network (NCCN) recently published NCCN guidelines for patients for distress to encourage patients to speak with their oncology care team about their distress.[62] The Distress Thermometer, part of the NCCN's guidelines for distress management, enables self-identification of the level of distress on a scale from 0 to 10. Distress scores greater than 4 necessitate referrals to various types of care. The thermometer contains a problem list consisting of 5 categories from which patients can identify sources of distress. These 5 categories are physical problems, emotional problems, practical problems, family problems, and spiritual/religious problems.

5.2.1.13 *Needs at the End-of-Life Screening Tool (NEST)*

NEST is a comprehensive palliative care needs assessment tool consisting of 13 open-ended questions. The instrument screens for palliative care needs among terminally ill patients in four dimensions: (i) social needs, (ii) existential matters, (iii) symptoms (physical and psychological), and (v) therapeutic matters.[63]

5.2.1.14 *Oncology Clinic Patient Checklist (OCPC)*

The aim of the OCPC is to systematically assess problems related to cancer and its treatment among adult patients in outpatient clinics.[36, 37] The checklist is constructed with 86 items in 15 domains plus three open-ended questions. The domains are: information (12 items), fatigue (3 items), pain (3 items), nutrition (7 items), speech and language (4 items), respiration (3 items), bowel and bladder (9 items), transportation (2 items), mobility (5 items), self and home care (8 items), vocational and educational (5 items), interests and activities (6 items), family (5 items), interpersonal relationships (4 items), and emotional (7 items).

5.2.1.15 *Patient Needs Assessment Tool (PNAT)*

The PNAT instrument is an interviewer-rated scale that may be completed through a simple structured interview and screens cancer patients their degree of impairment in several dimensions.[64] These dimensions comprise physical (6 items), psychological (5 items), and social functioning (5 items). Each dimensions is assessed using a five-item scale ranging from no impairment to severe impairment. The instrument has been constructed based on the clinical experience of the authors and a literature review.

5.2.1.16 *Problems Checklist*

The Problems Checklist has been developed to assess the prevalence and severity of psychosocial problems experienced by cancer patients. Patients are asked to rate on a four-point Likert scale ("not at all" to "very much") the extent to which they had recently had concerns or difficulties in each of 16 items (across 4 domains) of their lives as a result of their illness and/or treatment. These domains are: daily living (4 items), relationships

(5 items), economics (2 items), emotions (3 items), and other (2 items). They could also indicate if the issue did not apply to them, e.g. coping with children.[65, 66]

5.2.1.17 Supportive Care Needs Survey (SCNS)

The SCNS is an instrument to measure needs among cancer patients. There exist two versions of the instrument:

- SCNS-LF59: this is the long-form survey consisting of 59 items comprising the dimensions psychological, health system and information, physical and daily living, patient care and support, and sexuality. It was developed in 1995 following a review of the original Cancer Needs Questionnaire by oncology specialists and further testing with cancer patients.[67]
- SCNS-SF34: further psychometric development was undertaken, leading to the development of the short-from instrument in 2009. A total of 34 items mapped the needs in the dimensions that are identical to those of the longer version.[68]

For each item, respondents are asked to indicate their level of need for help over the last month as a result of having cancer on a five-point Likert scale.[69]

5.2.1.18 Sheffield Profile for Assessment and Referral to care (SPARC)

SPARC is a multidimensional screening tool to assess supportive care and palliative care needs of patients with advanced illnesses, regardless of the health condition. The instrument is developed to be filled in by patients themselves. SPARC is a 45-items instrument categorised in 8 dimensions: (i) communication and information issues, (ii) physical symptoms, (iii) psychological issues, (iv) religious and spiritual issues, (v) independence and activity, (vi) family and social issues, (vii) treatment issues, and (viii) personal issues.

5.2.1.19 Symptoms and Concerns Checklist

The Symptoms and Concerns Checklist is a 29-item self-administered instrument for patients which can be used prior to their consultation with a healthcare professional. Fifteen items relate to physical, psychological or cognitive problems, while the remaining 14 items cover a range of concerns (e.g. self-care, relationships, finance, work, and future). These items can be rated on a 0 to 3 scale (ranging from “not at all” to “very much”). We found this Symptoms and Concerns Checklist as an instrument to measure need among cancer patients. Nonetheless, it can also be used for other patients.

5.2.1.20 Needs Evaluation Questionnaire (NEQ)

The NEQ is a self-administered instrument with 23 dichotomous items that is used both in oncology clinical practice and in research.[70] It was originally developed for use in the hospital setting. However, recent research has also shown that the instrument is an effective tool for outpatient settings.[71]

5.2.1.21 Problems and Needs in Palliative Care instrument (PNPC)

PNPC was specifically designed to assist self-reported needs assessment in the palliative care setting. The original version consists of 6 dimensions with 90 items: (i) activities of daily living and instrumental activities of daily living, (ii) physical symptoms, (iii) role activities, (iv) financial/administrative issues, (v) social issues, and (vi) psychological issues.[72] With its 90 items, however, it is not always practical. This lead to the creation of the shorter version with 33 items in 2007 (including the same 6 dimensions).[73]

5.2.1.22 Needs Assessment Checklist (NAC)

NAC assesses attainment of rehabilitation outcomes among patients with spinal cord injuries through a self-rating of perceived independence during mobilisation and prior to discharge from the hospital.[74] The checklist consist of 199 items categorised in nine rehabilitation domains: activities of daily living (ADL, 29 items), skin management (14 items), bladder management (10 items), bowel management (7 items), mobility (17 items),

wheelchair and equipment (33 items), community preparation (24 items), discharge coordination (32 items), and psychological issues (19 items).

5.2.1.23 Cardinal Needs Schedule

The Cardinal Needs Schedule is a modified version of the previously developed MRC Needs for Care Schedule for measuring needs for psychiatric and social scare amongst patients with severe mental disorders. The MRC Needs for Care Schedule needed some modifications because (i) the assessment procedure needed to be simplified and shortened, rating of needs should systematically take into account the views of patients and their caregivers, and (iii) the procedure needed to define and identify needs in a way that was concise and easy interpretable.[75]

This new structure of the Cardinal Needs Schedule assesses need in three stages[75]:

- Identifying problems: standardised instruments are used to measure the participant's performance in 15 areas of psychiatric and social functioning. These areas of functioning are: psychotic symptoms, underactivity, side-effects, dangerous or destructive, organic symptoms, physical illness, neurotic symptoms, socially embarrassing, domestic skills, money and own affairs, transport and amenities, education, occupation, communication, and hygiene and dressing. Ratings of performance in each area of functioning are then compared with criteria provided by the schedule. If a participant's performance in an area falls below the standard set by these criteria a problem is present.
- Identifying cardinal problems: in this stage, problems (identified in stage 1) are assessed whether they are cardinal problems. A cardinal problem is identified as a need when there are one or more suitable interventions that have not been offered in the past year. The procedure uses three criteria: (i) co-operation criterion (based on patient's view on the problem and desire to be helped), (ii) the caregivers stress criterion (based on the caregiver's view of the problem), and (iii) the severity criterion (based on the nature and severity of the problem).
- Identifying needs: for each kind of cardinal problem there is a list of suitable interventions.

5.2.1.24 Salford Needs Assessment Schedule for Adolescents (S.NASA)

The S.NASA was developed to measure mental health needs among adolescents. Three previously developed adult needs assessment instruments were incorporated and adapted:

- MRC Needs For Care instrument[76]
- Camberwell Assessment of Needs (see 5.2.1.3)[43]
- Cardinal Needs Schedule (see 5.2.1.23)[75]

All three of these needs assessment instruments use decision algorithms to determine final need status. The S.NASA incorporates aspects of all three instruments, though most closely the Cardinal Needs Schedule (especially terminology). S.NASA covers 21 areas of functioning including social, psychiatric, educational and life skills.

5.2.1.25 Southampton Needs Assessment Questionnaire (SNAQ)

The SNAQ has been developed based on a questionnaire that was used by Hampshire social services in 1993 (but was not scientifically validated). It has been used for measuring needs and unmet needs among disabled people. A total of 77 questions are incorporated in the questionnaire with the aim to identify levels of met need and satisfaction with provided services, in order to encourage participants to reflect about their unmet needs. Topics of discussion in the SNAQ are effect of disability on day-to-day life, household situation, medical condition and anticipated progression, employment, social activities, hobbies and recreation, care situation, services, disability organizations, home suitability, adaptations, general mobility, mobility and wheelchairs, equipment, mobility outdoors,

community accessibility, state of affairs of finances, hypothetical increase of income, information, disable person's needs, and caregiver's needs. The SNAQ is completed during a face-to-face interview with a researcher.[77]

5.2.1.26 Service and Needs Assessment (SUN)

The SUN tool has been developed to measure unmet medical needs among disabled patients diagnosed with multiple sclerosis.[78] The instrument consists of almost three identical parts. Part one explores the views of the disabled person, part two the formal or informal caregiver and part three the key health or social care professional (nominated by the disabled person). The introduction section of the questionnaire invites the participant to comment generally on the disabled person's situation and lifestyle in order to encourage consideration of wider personal issues as well as specific "health" or "rehabilitation" needs. The specific areas subsequently explored are mobility (person, home and community), daytime activities (for example hobbies, work and leisure), aids and adaptations, service provision, information and financial matters. At the end of the questionnaire, all participants are asked to list their five most important unmet needs in order of priority. All three parts of the questionnaire also explored the unmet needs of the caregivers as perceived by the three parties.

5.2.1.27 Care Needs Assessment Pack for Dementia (CARENAPD)

The CARENAPD is designed to assess the needs of people with dementia and their caregivers in the community (and related, e.g. day hospitals) settings.[79] It comprises four sections: basic and referral information, separate assessments for the person with dementia and caregiver, and a personal history. The core elements are the needs assessment schedule for the person with dementia and the caregiver assessment. The former is the largest part of the package and comprises seven subscales: health and mobility, self-care and toileting, social interaction, thinking and memory, behaviour and mental state, house care, and community living. This schedule also contains checklists for nutrition and housing and a section to record the views of service users. Subscales are formed of specific items of potential difficulty for people with dementia. For each item, the assessor is asked to indicate need status (none, met or unmet) and for unmet need the type or types of help required (social stimulation/activity, prompting/supervision, doing tasks for the person, aids and adaptations, specialist assessment, counselling for the person, behaviour management, caregiver advice/training, or don't know).

5.2.1.28 Cancer Needs Questionnaire (CNQ)

The short-form CNQ is a 32-item self-administered cancer-specific questionnaire designed to assess patients' needs across several domains: psychological, health information, physical and daily living, patient care and support, and interpersonal communication.[80, 81] Respondents indicate their level of need for help on a five-point Likert scale (1 equalling 'no need: not applicable', 2 equalling 'no need: already satisfied', 3 equalling 'low need for help', 4 equalling 'moderate need for help', and 5 equalling 'high need for help') for each item. Short-form CNQ scores were converted to a score ranging from 0 to 100 where 0 was equivalent to no need and 100 the highest need.[82]

5.2.1.29 Elderly Health Care Needs Assessment Questionnaire (EHC-NAQ)

EHC-NAQ has been developed by Clark et al. (1998)[83] to measure unmet medical needs among elderly in the USA. The questionnaire consists of 54 items generated from a literature review and the Aday et al. (1984)[84] model of access to health care. However, we could not retrieve the original survey.

5.2.2 *Content analysis quantitative approaches*

A word cloud was constructed to visualise the most frequent cited domains included in the quantitative approaches to measure health(care)-related patient needs (Figure 2 and Figure 3). All cited domains in the quantitative approaches were listed and their frequency was counted using R3.6.0. (with the packages “ggplot2”, “snowballC”, "wordcloud", “tm” and “RColorBrewer”). An overview of the domains of each quantitative approach is listed in Figure 2 and Figure 3. The words included in the figures are those that appeared at least three or four times in the quantitative approaches. Prepositions, pronouns, determiners or conjunctions words (i.e. the, at, of, on, or, in, and, an, after, with, for, to, other, others) were excluded from the word cloud, as well as non-informative adjectives (i.e. special and needed) or nouns that were less informative than the adjective associated with them (i.e. needs, dimension, skills, concerns, problems, matters, issues). The size and colour of the words in the figure is proportional to the frequency of their occurrence in the quantitative tools. A histogram with the most frequent cited domains is also available in Appendix 1.5.

Figure 2 – Most frequently cited domains in quantitative approaches (appearing at least 3 times)

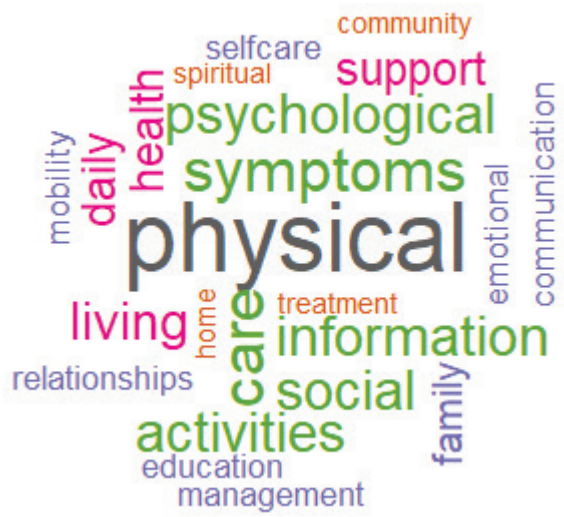


Figure 3 – Most frequently cited domains in quantitative approaches (appearing at least 4 times)

Subsequently the most frequently included domains in these word clouds were categorised into six dimensions based on thematic analysis[e]:

- **Physical dimension:** referring to needs on the physical level and the common demand of physical symptoms relief (such as pain relief);
- **Psychological dimension:** referring to psychological support to deal with emotional problems related to the health condition;
- **Autonomy dimension:** referring to needs concerning daily living and taking care for oneself;
- **Social dimension:** referring to needs related to social interactions with the community or family and building relationships. However, this dimension also entails the need for appropriate information provision and communication;
- **Accessibility dimension:** referring to needs of transportation to access care or several activities, waiting lists, financial accessibility;
- **Spiritual dimension:** referring to needs concerning spiritual issues related to the diagnosis of the condition, such as search for meaning, moral contexts or religious beliefs.

These domains are mainly overlapping with the needs of chronic patients identified in previous KCE research.[85, 86] Nevertheless, important to note is that, it is not because some domains are not listed above, that they could not be relevant to identify needs for some patients groups or certain health conditions. For example, a domain on housing or accommodation may be especially relevant in needs assessment of patients with certain physical disabilities.

5.2.3 Qualitative approaches

We identified four publications in which patient needs are measured using qualitative techniques.[32, 87-89] Three of them utilise individual in-depth interviews with patients or informal caregivers.[87-89] One of the studies strengthens the results of the individual interviews with group discussions.[87] Aragón et al. (2017)[32] describes the method in which patient needs are measured in focus groups with ethnic minority patients diagnosed with colorectal cancer.

[e] This thematic analysis of the word clouds can be consulted in Appendix 1.4.

Table 5 – Overview of the identified qualitative approaches to measure patient needs

Publication	Approach	Subject	Population	Country
Schroedl (2014) [88]	Individual in-depth semi-structured interviews	COPD	Not specified	USA
Tatangelo (2018) [89]	Individual in-depth semi-structured interviews	Dementia	Partner or offspring carers	AUS
Kapiriri (2002) [87]	Individual in-depth structured interviews Nominal group technique	No specific condition	People aged 13 – 55 years	UGA
Aragón Aragón (2017) [32]	Focus groups	Colorectal cancer	Ethnic minority patients	GBR

USA: United States of America, AUS: Australia, UGA: Uganda, GBR: United Kingdom

Box 4 – Example of implementation individual in-depth interviews in USA

Schroedl et al. [88] conducted in-depth semi-structured one-on-one interviews with 20 patients admitted for an acute exacerbation of COPD to an urban academic medical centre in Chicago. Purposive sampling was used to include patients varying in terms of age, race, and sex and interviews were continued until thematic saturation was achieved.

The interview guide was iteratively developed in collaboration between two pneumologists and one clinical health psychologist with expertise in qualitative research:

- **Interview domain 1: experience living with lung disease**

Can you tell me what is wrong with your lungs?

Can you tell me what a typical day is like for you living with your lung disease?

- **Interview domain 2: symptoms**

What kind of symptoms are the most bothersome to you?

How do you make yourself feel better?

- **Interview domain 3: social life and relationships**

Does your lung disease prevent you from doing the things you enjoy? In what way?

- **Interview domain 4: end-of-life**

Do you feel like your doctors have provided you with all the information you need to understand your disease?

Six main themes were identified after the qualitative analysis:

- Understanding of the disease: most participants correctly identified their diagnosis and recognized their symptoms worsening over time. Only half of the participants understood their disease severity and prognosis.
- Symptoms: breathlessness was universal and severe.
- Physical limitations: COPD prevented participation in activities.
- Emotional distress: depressive symptoms and/or anxiety were present amongst most participants.
- Social isolation: most participants identified social limitations and felt confined to their home.

Concerns about the future: half of the participants expressed fear about their future.

5.2.4 Mixed approaches

We identified six studies in which quantitative, qualitative and/or systematic literature reviews were triangulated in order to document patient needs.

Table 6 – Overview of the identified mixed approaches to measure health(care)-related patient needs

Publication	Approach	Subject	Population	Country
Dwyer (2014) [90]	(Online) survey Focus groups	Congenital hypogonadotropic hypogonadism	Men aged 18 – 70 years	CHE
Asad-Lari (2005) [30]		Asthma	Parents of children	NLD
Asad-Lari (2005) [30]	Data analysis Interview with key stakeholders Survey among professionals Additional interviews with professionals Interviews with patients and carers	Palliative care	Not specified	GBR
Aceves (2014) [91]	Literature review	Eosinophilic esophagitis	Not specified	Not specified
Gordon (2015) [92]	Systematic literature review Survey among healthcare professionals/experts	Ulcerative colitis and Crohn's disease	Not specified	GBR FRA
Danese (2019) [93]		Ulcerative colitis	Not specified	Not specified
Papaluca (2015) [94]	Terminology matching	No specific condition	Not specified	Not specified
Jouan-Flahaut (2007) [95]	Epidemiological data Analysis of available therapies Analysis of innovations in clinical trails	Obesity, diabetes mellitus, cardiac insufficiency, breast cancer, colon cancer, melanoma, depression, schizophrenia, multiple sclerosis, Alzheimer, and rheumatoid arthritis	Not specified	FRA

CHE: Switzerland, NLD: Netherlands, GBR: United Kingdom, FRA: France

5.2.4.1 *Combination (online) survey and focus groups*

Dwyer et al. (2014)[90] used a community-based participatory research framework to identify unmet needs of patients with congenital hypogonadotropic hypogonadism. A sequential mixed methods design (including a quantitative and qualitative part) was used: first, in the quantitative part, an online survey was used to collect demographic information and assess healthcare literacy, health information seeking patterns, interactions with healthcare systems/providers, and self-reported adherence to treatment and healthcare. Subsequently, in the qualitative

part, focus groups were used to discuss issues and challenges related to living with the condition, patient-reported coping strategies, and the acceptability of possible online interventions. Questions were derived from the Pender's Health Promotion model[96] and developed with input from patient community leaders.

A similar approach was conducted among parents of children diagnosed with asthma in the Netherlands.[30]

5.2.4.2 *Data-analysis, interview with key stakeholders, survey among professionals, additional interviews with professionals, and interviews with patients and carers*

Wiles et al. (1999)[97] evaluated local palliative care services to identify unmet medical needs and gaps in healthcare provision. This evaluation comprised four elements:

- Identification of providers/agencies providing care for palliative patients, collection of documentation relating to the services identified, collection of data on service use over a one-year period.
- Interviews with key stakeholders involved in providing palliative care services to identify perceived inadequacies of services and gaps in services.
- A questionnaire survey of nurses and general practitioners, combined with additional informal interviews with nurses to identify service usage and perceived inadequacies of specific services and gaps in services.
- Interviews with patients and their informal caregivers to identify their perceptions of need and the extent to which these were perceived as being met.

5.2.4.3 *Literature review*

If there exists a vast body-of-knowledge on health(care)-related patient needs in a specific (health) condition, a literature review can also be used to map all existing health(care)-related patient needs. For example, Aceves et al. (2014)[91] summarised the existing literature on patient needs among patients diagnosed with eosinophilic esophagitis. However, for some rare health conditions, there is not yet substantial evidence on patient needs. This approach can, therefore, not be used for all conditions. Nevertheless, it could be worthwhile to systematically map the literature on patient needs for some important conditions.

5.2.4.4 *Systematic literature review and survey among healthcare professionals/experts*

Two publications combine a systematic literature review with a survey among healthcare professionals and/or experts.[92, 93] Both publications target needs of patients diagnosed with ulcerative colitis (and Crohn's disease).

Box 5 – Example of combination systematic literature review and surveys among experts in Europe

Danese et al.[93] combined an extensive literature review and consensus meeting with experts to identify unmet needs in patients diagnosed with ulcerative colitis and methods to overcome them.

PubMed and the Cochrane Library databases were searched for relevant publications between 2006 – 2016 (relevant publications published later could also be included during the expert panel discussions). The search strategy led to 2 364 publications, of which 92

were included after the selection process. The results of these included publications were used to generate a preliminary set of 15 statements.

Consensus on these preliminary statements was sought from a panel of 14 expert gastroenterologists (from 13 European countries) using a modified Delphi review process, consisting of anonymous surveys followed by face-to-face discussions. In the first round, an anonymous survey invited the experts to score each of the preliminary statements on a 9-point Likert scale (ranging from 1 strongly disagree to 9 strongly agree). Subsequently, median scores and interquartile ranges (IQR) were calculated for each statement. An IQR 7 and above equalled a positive consensus, IQR 3 or less represented negative consensus, and IQR above 3 and less than 7 was considered neutral. Consensus was reached on 11 of the 15 preliminary statements, no consensus was reached on the remaining 4 statements.

In round 2, experts met face-to-face to review the results of the survey and revise wording of the statements were appropriate. Statements that reached consensus in the results of the survey could still be revised after discussion. The wording of 8 of the 11 statements for which consensus was reached were revised. The 4 statements for which no consensus was reached were revised or divided into 2 separate statements, after which they gained consensus. During the face-to-face discussion, an additional 14 areas of unmet medical need were proposed, of which 3 were retained.

The identified needs were categorised in 7 areas:

- impact of ulcerative colitis on patients' daily life;
- importance of early diagnosis and treatment;
- drawbacks of existing treatments;
- urgent need for new treatments;
- disease-, practice or patient-focused unmet needs.

5.2.4.5 Terminology matching

We identified one publication in which therapeutic needs were mapped using terminology matching. Papaluca et al. (2015)[94] matched the terms of chosen disease dictionaries with the therapeutic indication of medicinal products on the market, or of new products in development. This means that only therapeutic needs are identified that can be solved by pharmaceutical products and not by other interventions.

- In the first step, conditions were defined in the Medical for Regulatory Activities (MedDRA) dictionary. The following three levels of the dictionary were considered: the System Organ Classes, the High-Level Group Terms, and the High-Level Terms.
- For the identification of indications covered by approved medicinal products, data from the EudraVigilance Medicinal Product Dictionary (EVMPD) were extracted. This database contains information on medicinal products (since the mandatory reporting of adverse drug reactions since 2001). It also contains a number of medicinal products authorised worldwide. To explore indications covered by new products under development in clinical trials worldwide, the EMA and other external databases were searched.
- Therapeutic indications for which at least one medicinal product was approved were assigned to a MedDRA term at the High-Level Terms level. These were then subtracted from the MedDRA list from the first step: the remaining High-Level Terms constituting a preliminary list of conditions to which authorised products were not associated.
- In the following phase, the scientific literature was reviewed in order to determine whether these preliminary list of conditions were susceptible to standard therapy by pharmaceuticals or by other means (such as surgical intervention or medical devices).
- The remaining High-Level Terms were matched against intended therapeutic indications of medicines under clinical development, from the databases listed above. The final list was the list with white spots in pharmaceutical developments and can be seen as an unmet medical need as defined by the European Commission.

5.2.4.6 *Epidemiological data, analysis of available therapies, and analysis of innovations in clinical trails*

In order to document unmet medical needs for 12 conditions in France, Jouan-Flahault et al. (2007)[95] merged information of four different dimensions:

- Quantitative analysis of epidemiological data, including epidemiological prospective factors to give a prospective overview.
- Analysis of the recommendations for clinical practice concerning the studied condition, in particular in terms of therapeutic strategy, taking into account the place of diseases in public health policy, the objectives adopted for each condition in the French public health law of August 2004 and the public health plans that may be attached to the condition.
- Analysis of the currently available therapies for the different stages of the condition and their place in the therapeutic strategy.
- Identification of the innovations in advanced clinical development (phase III), with a high probability of being made available to patients in the medium-long term.

On the basis of all this information, therapeutic needs were identified by looking for situations where there was a lack of supply, as well as those where improvements were expected in existing therapies.

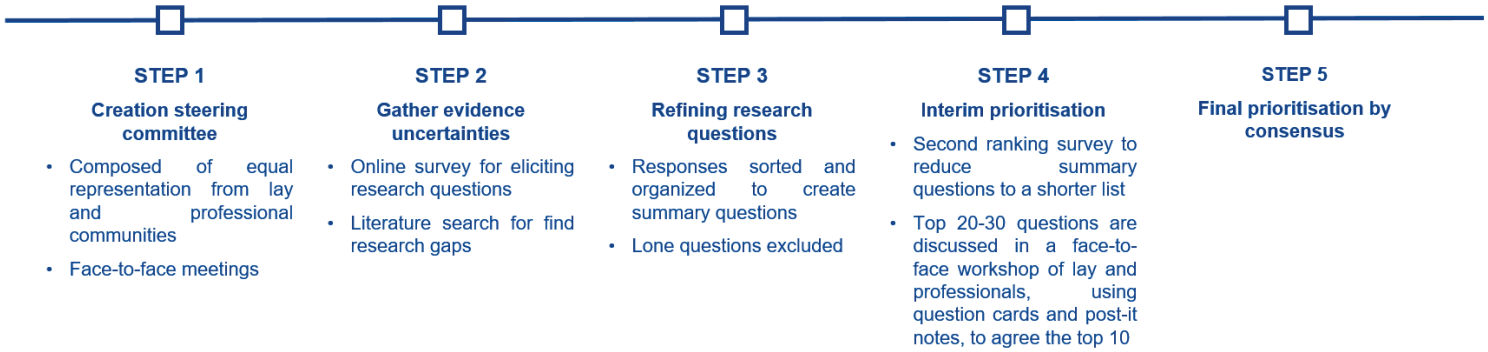
5.2.5 *Additional approaches*

5.2.5.1 *James Lind Alliance Priority Setting Partnerships*

Several publications identified in the initial pragmatic literature search described the James Lind Alliance (JLA) Priority Setting Partnerships (PSPs). Although this JLA PSPs were a recurring method, no included publication used it to assess patient needs. The predominant aim of JLA is to direct future research by identifying and prioritizing evidence gaps or uncertainties. However, we believe that its methodology is a relevant example of a mixed method approach and could also be (partly) used to identify patient needs.

The JLA approach involves a combination of surveys and workshop interactions between patients, carers and health care professionals to identify and agree on a “top ten” list of research questions. The JLA methodology is well defined and usually follows a strict pathway. Figure 4 visualises the JLA methodology procedure.

Figure 4 – Procedure of the James Lind Alliance Priority Setting Partnerships



Source: Authors' own reproduction based on NIHR [5]

Box 6 – Example of implementation James Lind Alliance Priority Setting Partnerships for Type 2 diabetes in the United Kingdom

Finer et al.[98] applied the JLA PSP to identify the "top 10 research priorities" in Type 2 diabetes, involving people living with the condition, their caregivers, and health care professionals.

Creation steering committee

The steering committee of the study comprised of five people living with Type 2 diabetes, five health care professionals (including a dietician, diabetes specialist nurse, general practitioner, and two consultant diabetologists), an information specialist, seven members of the Diabetes UK research and senior leadership team, and a JLA senior advisor. The steering committee met 12 times during the PSP process, in person or through teleconference.

Gather evidence uncertainties

A questionnaire was designed and underwent pretesting and optimisation with a group of Diabetes UK volunteers in terms of acceptability and ease of use. The questionnaire invited respondents to list up to four answers to the question: "What are the questions about Type 2 diabetes you would like to see answered by research?" and also collected basic sociodemographic information. Distribution of the questionnaire was managed by Diabetes UK under the guidance of the steering committee, and was disseminated through existing networks, community champions, wider professional networks, opinion leaders, social media, publications, conferences and specific target groups. The questionnaire resulted in a proposition of 8 227 evidence uncertainties by 2 587 respondents.

In addition, evidence uncertainties were identified from existing research and from recommendations of several scientific report/guidelines.

Refining research questions

The answers of the questionnaire were classified using a Health Research Classification System. Similar questions and uncertainties were grouped and listed by the steering committee to form a list of indicative summary questions, ready for the next stage of the procedure. Submitted questions classified to be "out of scope" were excluded at this stage (i.e. 470 uncertainties). This resulted in 114 indicative summary questions.

Interim prioritisation

A second questionnaire was conducted using the indicative summary questions. Respondents that provided contact details in the first questionnaire were invited by email to complete the second questionnaire. It was distributed through the same networks as mentioned above. Respondents were asked to select the "10 questions that matter the most to them", using a three-stage process, involving: (i) selecting the questions where they thought more research was needed, (ii) selecting the top 10 that were most important, and (iii) putting the top 10 in rank order. There were 1 506 respondents to this second questionnaire.

Total points per research priority were calculated based on all responses and research priorities were subsequently re-ordered from highest to lowest ranking. A final shortlist of 25 questions was produced by the steering committee.

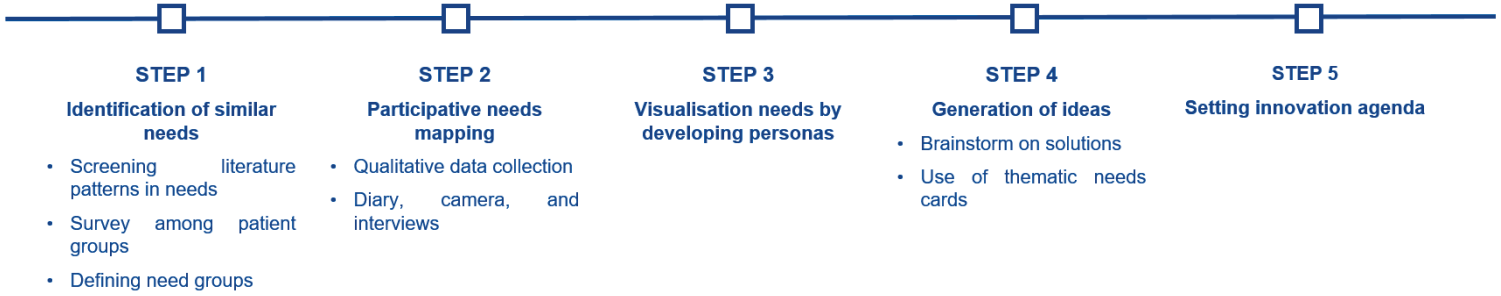
Final priority setting

People living with diabetes, carers, and multidisciplinary health care professionals who had not previously been involved in the procedure were identified through an open call and were invited to attend the final workshop. The workshop was attended by 28 new participants. During this workshop, the nominal group technique was used to build consensus on the final top 10 priorities through group discussions and ranking. The steering committee gave final consideration to the wording of each of the priorities before finalising them.

5.2.5.2 *Participative approach of Vlaams Patiëntenplatform (VPP)*

The VPP conducted a participative study in 2014 with the aim to identify innovation needs of chronic patients and their environment connected with the care offer.[99] An overview of the participative process is visualised in Figure 5. More details of each step and results are described in Box 7.

Figure 5 – Overview participatory process conducted by VPP



Source: Authors' own reproduction based on Becher et al. [99]

Box 7 – Example of implementation participative approach by VPP in Belgium[99]

Step 1

The aim of the first step was to identify similar needs among patient groups (independent from specific pathology). First, the international literature was searched for a typology of needs within the broad domain of chronic conditions. However, no such typology was found.

Therefore, a survey of the member organisations of VPP was initiated. This survey contained question about the clinical picture and possible associated limitations with the condition. More specifically, the questions were inspired by the "International Classification of Functioning, Disability and Health" (ICF) and structured in three domains: (i) disorders of body function, (ii) possibility of participation in daily life and (iii) about location of care provision (48 items in total). The survey had to be completed by an "average patient" from the patient organisation. In total, 67 surveys were returned.

A principal component-analysis of the responses revealed two main dimensions:

- The first and most important dimension captures the relative severity of the chronic condition. Diseases such as Parkinson or Alzheimer and others are accompanied by restrictions on bodily functions and participation in everyday life. For other diseases, such as diabetes or epilepsy, this is relatively less the case. Patients with these conditions can still participate in many ways, provided certain care and support.
- A second dimension makes a distinction between disorders associated with predominantly physical limitations (such as pulmonary hypertension, or kidney disease) and disorders with dominant mental disabilities (such as aphasia, Alzheimer, or bipolar disorder).

In addition, the completed surveys could roughly be divided into four clusters:

- Severe limitations of a predominantly mental nature
- Severe limitations of a predominantly physical nature
- Less severe limitations of a predominantly mental nature
- Less severe limitations of a predominantly physical nature

Step 2

In the second step, patients were recruited to take part in the participative process in order to identify needs ("participatory needs mapping"). Patients completed the same survey as those previously completed by representatives of the member organisations of VPP (i.e. Step 1). Furthermore, they received a diary in which they could document their activities and obstacles/barriers they encountered. Notes in the diary were completed by pictures taken by the patients. Also, two interviews with the patient (or their informal caregiver) were planned.

Step 3

In the following step, the identified needs were visualised by developing eight personas (two for every cluster) which are used for the brainstorming in Step 4.

Step 4

Generating ideas around the personas was done in three short brainstorming sessions. The leading question for the brainstorm was: "What products, services or business models can we develop (or improve) to increase the quality of life of this patient (and informal caregiver)? This brainstorm was structured by 12 thematic need cards per persona. The thematic needs cards entailed domains such as body functions, intellectual tasks and stress, routine tasks and daily activities, communication, mobility, social contact, hobbies and relaxation, technology, self-care, etc. These brainstorm sessions led to a generation of approximately 250 ideas for both products and services to meet the identified needs.

Step 5

- The resulting agenda focused on five coherent areas for innovation:
- Promote self-reliance and self-management;
- Promote recovery and acceptance of illness;
- Promote empathy with and de-stigmatisation of people with disabilities;
- Provide respite for informal caregivers;
- Promote reciprocity.

5.3 Conclusion

This pragmatic literature review identified 40 approaches to measure patient needs, which could be grouped in three main categories:

- **Quantitative methods**: entailing approaches such as DALY and 29 different quantitative instruments or tools for a wide variety of health conditions.
- **Qualitative methods:** in which patient needs are identified through in-depth interviews and/or focus groups.
- **Mixed methods:** a triangulation of methods including quantitative, qualitative and/or systematic literature reviews.

It should be noted that a large proportion of the existing literature using quantitative methods measure unmet medical needs by asking respondents the typical question “Was there any time during the last 12 months when, in your opinion, you needed medical examination or treatment (…) but you did not receive it?”. If respondents answer “yes” to this question, they are considered to have experienced an unmet (medical) need. This question is usually followed by the measurement of the reason for this unmet (medical) need (e.g. could not afford it, waiting list, too far to travel, other). However, this subjective operationalisation is very broad and quite vague. The response options (with the exception of “other” and “waiting lists were too long”) assume that need was not converted into demand. In other words, the person did not present the need to any health care provider.

Furthermore, the majority of the identified quantitative methods are designed to measure patient needs in specific patient groups (such as patients diagnosed with cancer, mental health problems, etc.). This variance in target populations makes it difficult to generalise the instruments. However, it was observed that these identified instruments or tools overlapped in categories or domains. Based on a thematic analysis of these domains, the following main dimensions were identified: (i) physical, (ii) psychological, (iii) autonomy, (iv) social, (v) accessibility, and (vi) spiritual dimension. These dimensions are overlapping with the needs of chronic patients identified in previous KCE research.[85, 86]

In conclusion, based on the results of this pragmatic review, we believe that a triangulation of research methods (including quantitative and qualitative methods) is necessary to identify health(care)-related patient needs in a validated way.

6 HEALTH CONDITIONS WITH MAJOR NEEDS IN BELGIUM: AVAILABLE DATABASES

In this chapter we investigated national and international databases to identify major domains of unmet health needs in Belgium. This identification will allow to orientate the implementation of the survey and subsequent qualitative research to examine the needs of a specific patient group.

As there is no single measure of patient needs in Belgium, we mainly focused on databases and initiatives that potentially include quantitative indicators of quality of life (QoL) (e.g. SF-12, EQ-5D, CASP-12) or summary measures of population health (SMPH) with a QoL component (e.g. Disability-Adjusted Life Years [DALYs], Quality-Adjusted Life Years [QALYs], Years Lived with Disability [YLDs]). SMPH are burden of disease indicators combining multiple dimensions of health (for instance, mortality and morbidity) and therefore have the advantage of combining both the level of - and change in - health. The way those measures are calculated and interpreted is explained below.

We decided to focus on QoL indicators because they are generally derived from a panel or a survey that is representative of the (patient) population and give a good indication of the severity of health loss associated with illness or disability.

6.1 Belgian data sources and initiatives that collect quality of life indicators

6.1.1 The Health Interview Survey

Since 1997, Health Interview Surveys (HIS) have been undertaken every 4 to 5 years by Sciensano, the former Belgian scientific institute of public health. The main objectives of the HIS are to assess the health status of the population and to identify the main health problems as well as the determinants and behaviours that could influence them. The health indicators included in the HIS allow the competent authorities to develop proactive health policies that are adapted to the needs of the population. The last data collection has been organized in 2018 through a face-to-face (F2F) interview and a paper-and-pencil (P&P) self-administered questionnaire (SAQ) covering more sensitive topics.[100] The HIS includes eight main health domains (i.e., health and quality of life, life style, preventive knowledge and practices, mental health and well-being, use of health services, health and society and dental health). In 2018, a health examination survey was conducted with 1 184 participants of the HIS. Most of the results are freely available through various publications and reports gathered on a website[f] and an online interactive analysis tool[g].

This is a cross-sectional household survey, in which participants were selected from the national register through a multistage stratified sample of all persons officially residing in Belgium, without any restrictions on nationality. The sampling design involved a geographical stratification, a selection of municipalities within provinces, households within municipalities, and respondents within households. The net sample size of survey participants was 10 829 and 11 611 individuals in 2013 and 2018, respectively. The participation rate in the survey of 2013 and 2018 was 57.1% and 57.5%, respectively, at household level. The detailed methodology of the survey is described elsewhere.[101] The results are weighted to reflect the composition of the Belgian population. In the HIS, participants older than 15 years are asked to report, amongst others, on

[f] https://his.wiv-isp.be/SitePages/Home.aspx (last access 10 August 2021)

[g] https://hisia.wiv-isp.be/SitePages/Home.aspx (last access 10 August 2021)

diseases and chronic conditions they have suffered from in the last 12 months. In 2013 and 2018, 38 health conditions were included in the survey:

- cardiovascular diseases and risk factors (i.e. myocardial infarction, coronary heart diseases (angina pectoris), high blood pressure (hypertension), high cholesterol level in blood, stroke (cerebral haemorrhage, cerebral thrombosis), narrowing of blood vessels in belly or legs (no varicose veins)),
- chronic lung diseases (i.e. asthma, chronic bronchitis, chronic obstructive pulmonary disease, emphysema),
- musculoskeletal diseases (i.e. osteoarthritis (arthrosis, joint degeneration), rheumatoid arthritis (inflammation of the joints), low back disorder or other chronic back defect, neck disorder or other chronic neck defect),
- endocrine diseases (diabetes, thyroid problems),
- neurological diseases (Parkinson's disease, epilepsy),
- gastrointestinal diseases (i.e. stomach ulcer (gastric or duodenal ulcer), disorder of the large or the small bowel for longer than 3 months, cirrhosis of the liver, liver dysfunction, gall-stones or inflammation of the gall-bladder),
- urogenital diseases (i.e. urinary incontinence, problems in controlling the bladder, stones in the kidney, serious disease of the kidney, other than stones in the kidney, chronic cystitis, prostate complaints),
- eye disease (i.e. glaucoma, cataract, macula degeneration, diabetic retinopathy),
- other on non-specified diseases (i.e. allergy, such as rhinitis, eye inflammation, dermatitis, food allergy or other (allergic asthma excluded), cancer (malignant tumour, also including leukaemia and lymphoma), severe headache such as migraine, depression, chronic fatigue for a period of at least 3 months, osteoporosis, broken hip, serious or chronic skin disease).

These diseases have been selected in the HIS because of their relatively high prevalence in the Belgian population.

In 2018, 29.3% (95% CI: 27.9-30.8) of the population aged 15 years and over reported suffering from an illness or chronic condition(s) which corresponds to a significant increase with regards to the year 2001 (25.1%; 95% CI: 23.9-26.3). These results are partly explained by the ageing of the population. In 2018, the most common reported diseases and conditions in the population were musculoskeletal problems (low back problems, osteoarthritis, arthritis, neck problems), risk factors cardiovascular (hypertension, hypercholesterolemia) and allergies (Table 7). Asthma is not in the top 10, but its prevalence has increased sharply between 2013 and 2018 (2013: 4.3% (95% CI: 3.7-4.9); 2018: 5.8% (95% CI: 5.1-6.4)). Differences in the prevalence of an illness or chronic condition and the ranking is observed between regions, sexes and educational levels (see the HIS website[a,b] for additional results on most prevalent illnesses).

Table 7 – Percentage of the population aged 15 years and over who reported most common illness and chronic conditions in the past 12 months, 2013 & 2018

Diseases	2013	2018
	Weighted % (95% CI)	Weighted % (95% CI)
Low back disorder or other chronic back defect	20.8 (19.6-22.0)	24.8 (23.6-26.0)
Allergy	14.2 (13.1-15.3)	18.7 (17.6-19.8)
Osteoarthritis	16.7 (15.6-17.8)	18.5 (17.4-19.6)
Hypercholesterolemia	16.8 (15.6-17.9)	18.0 (16.9-19.1)
Hypertension	16.5 (15.3-17.6)	17.6 (16.5-18.6)
Neck disorder or other chronic neck defect	11.8 (10.8-12.7)	14.9 (13.8-15.9)
Rheumatoid arthritis	8.1 (7.3-8.9)	7.8 (7.0-8.5)

Data source: Sciensano, CI=Confidence Interval.

Since 2013, the HIS also includes a question on health-related quality of life (HRQoL) using the EQ-5D-5L questionnaire. The EQ-5D includes five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and five severity levels in each dimension (EQ-5D-5L) (see Chapter 5).[102] Belgians included in the HIS are asked to describe their health state by checking the box that corresponds to their level of problems in each dimension. Those scores can be converted in utilities, an important parameter used in QALY estimates (see Box 8).

QALYs are commonly used in economic evaluations of health programs. They are calculated by assigning a utility score from a pre-existing value set to the health state described by a respondent (also called "tariff values"). These tariff values are obtained by collecting utility data for a subset of health states from the general public, e.g. using the time trade-off technique, standard gamble or discrete choice experiments, and modelling these to derive a set of utility values for the entire set. In Belgium, KCE developed a new utility value set for the EQ-5D-5L in 2021.[103] This Belgian EQ-5D-5L value set has been used to estimate the health-related quality of life in HIS 2013 and 2018 (see Box 8).

Box 8 – Quality-adjusted life-year

Quality-adjusted life-year (QALY) is a measure of disease burden, including both the quantity and the quality of life lived. It is commonly used in economic evaluations (cost-effectiveness evaluations) to capture in one metric the most important features of health intervention: its effects on survival measured in terms of life-years, and its effect on quality of life. One QALY equates to one year in perfect health and QALY scores range from 1 (perfect health) to 0 (dead).

The quantity of life, expressed in terms of survival or life expectancy, is a traditional measure that is widely accepted and has few problems of comparison – people are either alive or not.

The quality of life, on the other hand, includes different dimensions of people's health-related quality of life (HRQoL). Several approaches have been developed to generate these HRQoL valuations, referred to as health utilities; for example, standard gamble, time trade-off, scales or multi-attributes instruments.

In 2003 in Belgium, Cleemput et al. developed a valuation set for the EQ-5D-3L, i.e. with 243 potential health states, using visual analogue scale.[104] In 2012, as an intermediary solution, to not impede research being carried out with the more recent EQ-5D-5L descriptive system, a transformation or mapping procedure was proposed by van Hout et al. (2012) to derive an EQ-5D-5L "crosswalk" value set from the available EQ-5D-3L value sets.[105]

In 2021, in order to benefit from the full potential of the EQ-5D-5L, Bouckaert et al. developed a value set specific to the 5L.[103] They used a combination of composite Time Trade-Off (cTTO) and Discrete Choice Experiment (DCE) techniques to derive the new valuation set for 3 125 potential health states. See Bouckaert et al. chapter 2 for additional information on valuation methods.

Each EQ-5D health state is labelled by a code, e.g. 21531, where each digit represents the severity level of a dimension. By convention, the order of dimensions is mobility, self-care, usual activities, pain/discomfort and anxiety/depression.

The utilities that are produced represent the valuations attached to each 3 125 health states on a scale with two anchoring points: 0 and 1. On this scale, 0 is equivalent to being dead and 1 represents the best possible health state. Health states are regarded as being worse than death and can take negative valuations.[106]

Let us take the example of a person who lives 40 years with a disease that reduces his perfect health by 25%. The number of QALYs would be calculated as 1 * 40 * 0.75 = 30 QALYs.

The average Health-Related Quality of Life (HRQoL) score decreased in 2018 (0.79) compared to the score of 2013 (0.81), with 1 reflecting the perfect HRQoL. Among the five dimensions of the HRQoL score, the population aged 15 years and older most often reports problems in the dimensions of pain/discomfort (56.2%) and anxiety/depression (31.5%) (see Table 8).[107]

Table 8 – Evolution of health-related quality of life in Belgium 2013-2018 (based on the EQ-5D-5L), by region

	BE 2013	BE 2018	BXL 2013	BXL 2018	FL 2013	FL 2018	WL 2013	WL 2018
Percentage of the population aged 15 and over who report having ...								
Mobility problems	18.5	19.3	17.2	19.4	18.5	17.4	18.8	22.8
Self-care problems	6.9	6.0	5.4	5.5	7.5	5.7	6.1	6.5
Problems to perform usual activities (e.g. work, study, housework)	17.9	19.4	16.2	17.3	17.0	18.0	20.2	22.6
Pain or discomfort	50.1	56.2	51.3	51.9	47.1	53.0	55.9	63.1
Anxiety or depression	26.5	31.5	37.6	39.7	18.6	22.9	39.8	44.9
Percentage of the population aged 15 and over who ...								
Does not report any health problems	41.5	36.0	37.2	37.1	46.0	40.7	33.5	27.0
Average score in the population aged 15 and over ...								
Health-Related Quality of Life (HRQoL)* (range 0 to 1)	0.86	0.84	0.85	0.84	0.88	0.87	0.83	0.80

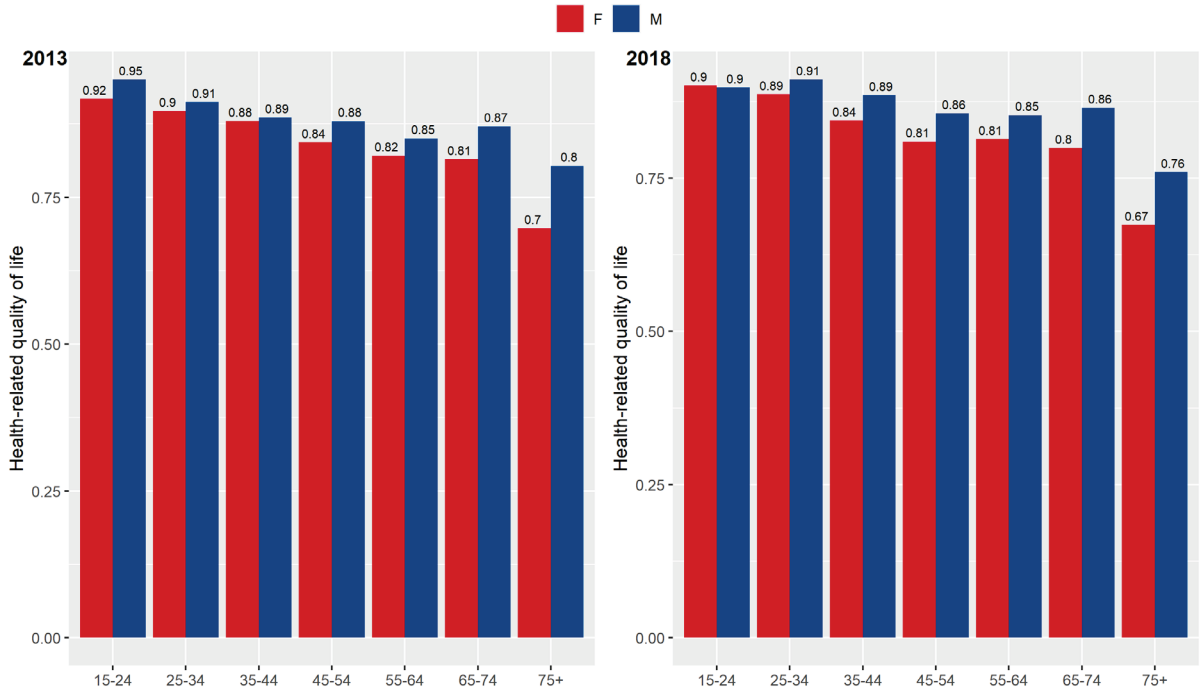
*Data source: HIS 2018, BXL: Brussels, WL: Wallonia, FL: Flanders; *Calculated on the tariff set from Bouckaert et al. 2021[103].*

Socio-demographic factors such as gender, age, region of residence or educational attainment influence the HRQoL results. Figure 6 shows that men consistently reported higher HRQoL scores than women whatever the age-group and the HIS year (except for the age-group 15-24 years in 2018). In 2018, the average score for men (0.87) was significantly higher than for women ($p<0.001$).[108]

Overall the EQ-5D-5L scores decrease with age with a stronger decrease after the age of 70 years (Figure 6).[108] Figure 7 also shows an increase of the EQ-5D-5L score among more educated respondents (Figure 6, 7) and Van Wilder et al. demonstrated a significant effect of educational attainment on EQ-5D-5L score in 2018.[108]

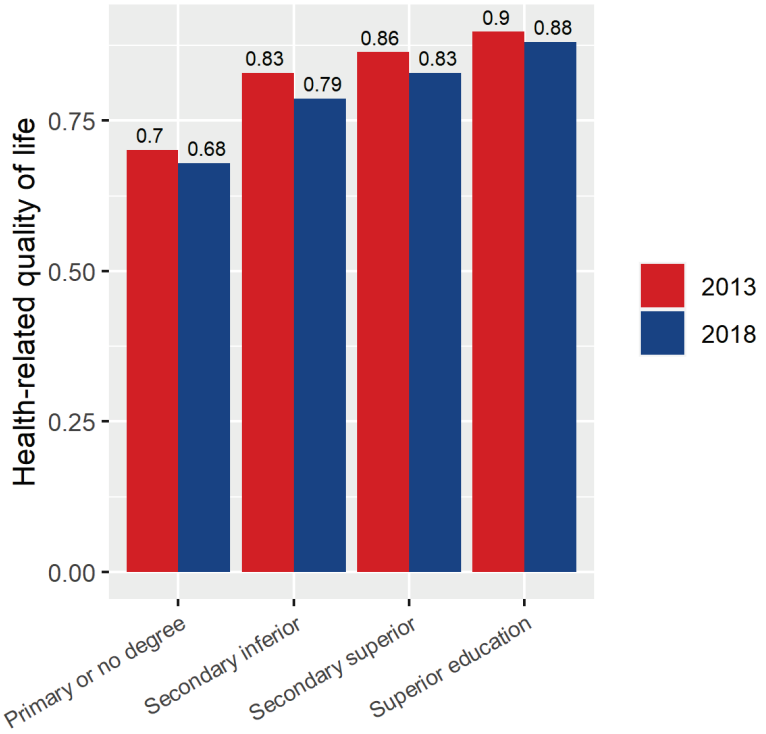
Compared to Flanders (0.87), significantly ($p<0.001$) lower HRQoL scores were estimated for Brussels (0.84) and Wallonia (0.80) in 2018 (Figure 8).[108]

Figure 6 – Average health-related quality of life scores by age, sex and year



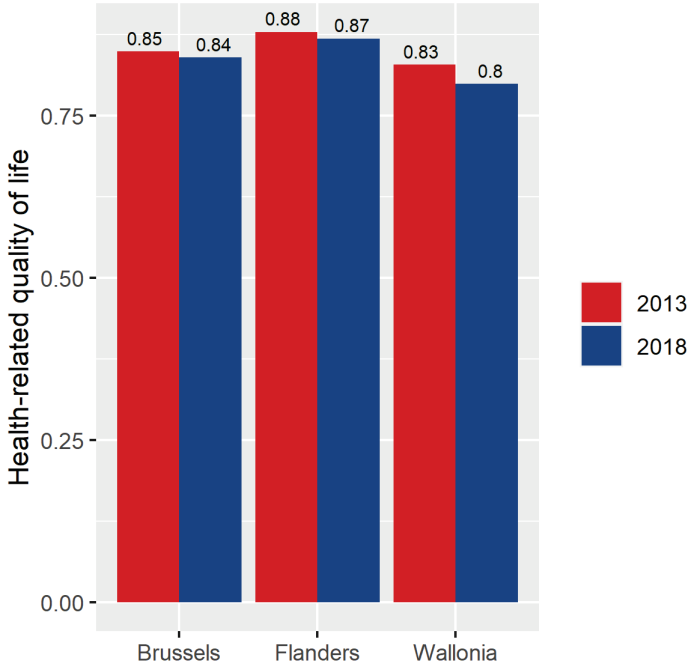
Data source: Sciensano, figure: KCE, HRQoL scores valued from Bouckaert et al. 2021[103].

Figure 7 – Average health-related quality of life scores by level of education and by year



Data source: Sciensano, figure: KCE, HRQoL scores valued from Bouckaert et al. 2021[103].

Figure 8 – Average health-related quality of life score among participants aged 15 years or older, by region and by year



Data source: Sciensano, figure: KCE, HRQoL scores valued from Bouckaert et al. 2021[103].

Table 9 presents the HRQoL loss indicators (disutilities) for the 38 health conditions included in HIS 2013 and 2018 (see above). HRQoL disabilities can be regarded as the difference in utility score between a reference population and the chronically ill. Data on the reference population was based on the EQ-5D-5L Belgian population norms, i.e. HRQoL data for the average person in the general population in a similar age and/or gender

and/or region group. The disutilities smaller than zero are now set to 0. From these results, QALY losses (see Box 8) have been estimated by multiplying the HRQoL disutilities with the prevalence of the health condition (in the population aged 15 and older). The figures hence represent the total number of QALYs lost in the entire population in one year due to the health conditions.In 2018, loss of HRQoL was mainly driven by cardiac/vascular, age-related and mental diseases. The health conditions with the highest HRQoL loss were myocardial infarction (0.418), stroke (or consequences) (0.365), serious gloom or depression (0.307) and urinary incontinence (0.288). The health conditions with the lowest HRQoL loss were allergy (0.099), high cholesterol level in blood (0.122), high blood pressure (0.128), cataract (0.137) and Serious or chronic skin disease (0.138). In 2013, the health conditions with the highest QoL loss were quite different than in 2018. Indeed, the top five health conditions with the highest HRQoL loss included more various types of conditions and did not include any psychiatric condition. In 2013, myocardial infraction (0.305), chronic fatigue for a period of at least 3 months (0.278), diabetic retinopathy (0.276), cirrhosis of the liver, liver dysfunction (0.275) and serious heart disease (except myocardial infraction) (0.273) and had the highest HRQoL loss. Overall the HRQoL loss range (max 0.418 – min 0.099) is higher in 2018 than in 2013 (max 0.305 – min 0.068) (see Table 9). Note that in general conditions for which there is no or no effective treatment available to fully cure the patients and/or remove all disease-related symptoms rank high on the list, meaning that for these conditions the HRQoL loss is relatively higher than for diseases for which effective curative or symptom-relieving treatments are available.

In 2018, the loss of QALYs was mainly driven by conditions resulting from sedentary live conditions. Indeed, the health conditions with the highest QALYs loss were low back disorder (366 890 QALYs lost), osteoarthritis (319 875 QALYs lost), neck disorder (242 834 QALYs lost), high cholesterol level in blood (218 482 QALYs lost) and serious gloom or depression (214 059 QALYs lost). The disadvantage of using QALYs (instead of HRQoL loss) is that there are highly driven by high prevalence which is not necessarily a good indicator of patient unmet needs. Rarer diseases like macula degeneration (2 645 QALYs) or Parkinson’s disease (6 670) are then relegated to the bottom of the rankings while the impact on patients' HRQoL (and potentially level of unmet needs) is very important. In 2013, the health conditions with the highest number of QALYs lost were more or less the same than in 2018. Low back disorder (287 638 QALYs loss), osteoarthritis (264 716 QALYs), neck disorder (177 691 QALYs), high blood pressure (165 539 QALYs loss) and serious gloom or depression (158 330 QALYs) resulted in the higher number of QALYs lost (see Table 9).

Table 9 – Health Related Quality of Life (HRQoL) loss and QALY loss estimates, 2013 and 2018

Condition	HRQoL loss 2013	Number of QALYs lost 2013	Ranking HRQoL loss 2013	Ranking QALY loss 2013	HRQoL loss 2018	Number of QALYs lost 2018	Ranking HRQoL loss 2018	Ranking QALY loss 2018
Low back disorder	0.143	287 638	28	1	0.150	366 890	30	1
Osteoarthritis	0.164	264 716	23	2	0.177	319 875	24	2
Neck disorder	0.154	177 691	27	3	0.166	242 834	26	3
High cholesterol level in blood	0.095	155 801	36	6	0.122	218 482	37	4
Serious gloom or depression	0.264	158 330	6	5	0.307	214 059	3	5
High blood pressure	0.104	165 539	34	4	0.128	213 915	36	6
Chronic fatigue for a period of at least 3 months	0.278	127 507	2	9	0.267	209 486	6	7
Allergy	0.068	91 681	38	10	0.099	188 030	38	8
Rheumatoid arthritis	0.181	139 287	22	7	0.195	147 473	22	9
Severe headache such as migraine	0.158	135 919	26	8	0.143	144 729	31	10
Urinary incontinence	0.249	80 123	7	11	0.288	122 947	4	11
Disorder of the larger or the small bowel	0.229	55 146	12	16	0.227	100 747	12	12
Chronic bronchitis COPD or emphysema	0.209	74 050	16	13	0.255	93 092	8	13
Thyroid problems	0.097	56 085	35	15	0.140	92 484	32	14
Diabetes	0.131	57 381	30	14	0.160	85 586	27	15
Prostate problems	0.108	45 163	32	19	0.174	83 369	25	16
Asthma	0.115	44 597	31	21	0.151	79 847	29	17
Stomach ulcer	0.212	49 359	15	18	0.234	76 420	11	18
Osteoporosis	0.202	75 684	18	12	0.223	69 357	16	19
Serious heart disease (except myocardial infraction)	0.273	53 489	5	17	0.203	59 899	20	20
Serious or chronic skin disease	0.133	36 944	29	24	0.138	52 508	34	21

Glaucoma	0.163	42 089	24	22	0.160	51 461	28	22
Narrowing of blood vessels in belly or legs (no varicose veins)	0.225	44 944	14	20	0.280	50 416	5	23
Chronic cystitis	0.239	33 079	8	25	0.244	47 409	10	24
Cancer	0.206	39 910	17	23	0.214	45 177	18	25
Myocardial infarction	0.305	27 396	1	27	0.418	27 179	1	26
Coronary heart disease	0.239	27 567	9	26	0.224	26 008	15	27
Stroke (or consequences)	0.183	17 241	21	29	0.365	21 704	2	28
Stones in the kidney	0.106	8 351	33	34	0.216	19 371	17	29
Cirrhosis of the liver, liver dysfunction	0.275	17 924	4	28	0.201	19 058	21	30
Cataract	0.072	7 041	37	36	0.137	17 613	35	31
Serious disease of the kidney, other than stones in the kidney	0.232	14 772	11	31	0.181	17 513	23	32
Epilepsy	0.238	17 017	10	30	0.246	14 792	9	33
Gallstones of inflammation or inflammation of the gall-bladder	0.162	11 269	25	33	0.140	12 803	33	34
Diabetic retinopathy	0.276	2 414	3	38	0.261	10 672	7	35
Broken hip	0.201	7 110	19	35	0.225	9 685	14	36
Parkinson's disease	0.186	6 740	20	37	0.211	6 670	19	37
Macula degeneration	0.228	11 555	13	32	0.226	2 645	13	38

Data source and analysis: Sciensano, HRQoL=Health Related Quality of Life (1 representing the perfect health)

These results should be interpreted with caution because, although being very precious, the HIS data are auto-reported. Also, children aged less than 15 years old are not questioned on this list of conditions, therefore children's unmet needs cannot be assessed using this approach. Finally, the list of conditions includes only a limited number of (common) health conditions, so rare conditions which generally have more unmet needs cannot be examined using the HIS data.

6.1.2 The IMA – AIM database

The Inter-Mutualistic Agency (IMA – AIM) is a partnership of the seven Belgian sickness funds and collects detailed data of the different sickness funds in a common format. An advantage is that the data are exhaustively collected for administrative use. The IMA – AIM collects data on population (i.e. demographic and socio-economic data concerning the members of sickness funds), on health expenses covered by the public health insurance (hence excluding important categories such as over-the-counter drugs and glasses) and on pharmaceutical products expenses in public pharmacies covered by the health insurance, so-called “Pharmanet”. Because IMA – AIM does not have information on patient’s diagnosis, which could be very useful for research or policy makers, INAMI – RIZIV and IMA – AIM started developing pseudo-pathologies based on Pharmanet data in 2016.

The first set of pseudo-pathologies was based on the definitions laid down in the note "Definition Aggregated Diagnosis Groups” (i.e. diagnoses based on the use of certain pharmaceutical products in Pharmanet) of the Health Care Service of the INAMI – RIZIV and used in the framework of financial accountability.[109]

Pseudo-pathologies are actually 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 for all ATC codes in that group is greater than or equal to 90. For some pseudo-pathologies there are also restrictions on age and type of prescriber.[110]

The pseudo-pathologies have been updated and improved at various times by a guidance group and extended with INAMI – RIZIV nomenclature codes (Box 9). Indeed, the original pseudo-pathologies were completely defined on the basis of pharmaceutical products: e.g. diabetes was only based on insulin and for instance not on nomenclature diabetes convention. Therefore there was an underestimation of the number of patients for some pseudo-pathologies.

Box 9 – The INAMI – RIZIV nomenclature

The medical and paramedical services covered by compulsory health insurance in Belgium are listed in a fee schedule, called the ‘nomenclature’, which includes almost 9 000 unique covered services. The list of reimbursable codes contains for each item the required professional qualification of the provider to be eligible for reimbursement, a code-number, a description of the item, a key letter according to the medical specialty, a coefficient and application rules. The coefficient gives for each procedure the relative value compared to other procedures with the same key letter. Multiplying the coefficient by the value of the key letter determines the amount of payment to the provider concerned (i.e. the fee). The type of reimbursable benefits and their amounts (total fee and reimbursement) are determined through a process of negotiations with the various parties involved within INAMI – RIZIV, all within pre-set budgetary limits. The National Commission of Sickness Funds and Providers, the so called ‘Medico-Mut’ (for the doctors) negotiates on the tariffs, and more specifically, on the value of the key letter. The negotiated fee or ‘convention tariff’ is settled in agreements (for physicians and dentists) and conventions (for other healthcare providers).[111]

In 2019, 31 pseudo-pathologies were available in the IMA – AIM database: cardiovascular conditions-General, thrombosis, cardiovascular conditions - Heart disease, chronic obstructive pulmonary disease (COPD) , chronic obstructive pulmonary disease (COPD) (variant A), COPD (variant B), asthma, asthma (variant A), asthma (variant B), cystic fibrosis, diabetes, diabetes with cardiovascular disease, diabetes with insulin, diabetes without insulin, exocrine pancreatic diseases, psoriasis, rheumatoid arthritis, Crohn's disease, Ulcerative colitis, psoriatic arthritis, psychosis in persons 70 years of age and under, psychosis in persons upper 70 years, Parkinson’s disease, epilepsy plus neuropatic pain, HIV, chronic Hepatitis B and C, multiple sclerosis, organ transplantation, Alzheimer’s disease, kidney failure, thyroid conditions, haemophilia, diabetes with insulin (variant A: 30 of age and upper), diabetes with insulin (variant B: under 30 of age).[110]

In the *HISLink* project, Sciensano performed a linkage between Health Interview Survey (HIS) 2013 and IMA – AIM data[h], 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 health care use is lacking, no link between health care 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, health status, lifestyle and health care use. A linkage between the HIS 2018 and IMA – AIM data is also planned.

Considering the specific purposes of the current study on unmet needs, the HIS – IMA – AIM database has several limitations. First, the pseudo-pathologies are, by definition, only developed for patients and pathologies with available treatment, although in some cases the treatment is not sufficiently effective, the unmet therapeutic needs are probably lower than for patients without treatment. Second, to date, the validity of the pseudo-pathologies has only been explored (by Sciensano) for seven pathologies common to the list of HIS 2013 chronic conditions (i.e. diabetes, general cardiovascular disease, Parkinson's disease, thyroid disorders, epilepsy, asthma and COPD). This is not sufficiently broad to make a ranking that can be used to assess unmet needs. Nevertheless, the validity measures showed good agreement for diabetes (Kappa=0.69) and Parkinson's disease (Kappa=0.74), moderate agreement for epilepsy (Kappa=0.46), general cardiovascular disease (Kappa=0.51) and thyroid disorders (Kappa=0.53), low agreement for COPD (Kappa=0.34) and bad agreement for asthma (Kappa=0.16).[112] If, in the future, more HIS chronic diseases can be coupled with pseudo-pathologies, it may be worthwhile to reconsider the use of this dataset. Finally, as 7 795 Belgians answered the question relating to the HRQoL of the HIS 2018 (see section 6.1.1), it is expected that some pseudo-pathologies will include very few or none HIS participants which will render the ranking of the pseudo-pathologies according to unmet need impossible or with a lot of uncertainty.

We therefore excluded the idea of using linked HIS – IMA – AIM database in the frame of this study.

6.1.3 The Belgian cancer registry

Hospitals operating oncology care programs are required by law to participate in cancer registration by providing data to the Belgian Cancer Registry (BCR). [113] The BCR collects, amongst others, data on the incidence and stage of cancer, the localisation of the tumour and the survival rate but does not collect information on quality of life of patients suffering from cancer. The full list of variables available in BCR databases is available in https://kankerregister.org/tumourbank.aspx?PageId=212 . Some results are freely available through an online tool[i] and publications.

Since 2009, the BCR is authorized to link data from its database with IMA – AIM data on cancer-related diagnostic and therapeutic procedures and pharmaceuticals. Through this linkage procedure, the BCR receives details on reimbursed drugs prescribed to the patient, both in the ambulatory setting and during hospitalisation.

Although it has never been done, it is also possible to couple HIS and BCR databases. However, few HIS participants reported having cancer (1.9% in 2013 and 2.4% in 2018, ~400 participants for the two surveys) and dividing these patients by type (and stage) of cancer will result in very few (and probably) heterogeneous patients by cancer type which will negatively impact the external validity of the results. In addition, the HRQoL results for people with cancer depend not only on the type of cancer but also on the stage of cancer and on the treatment received, which implies that these data are available.

We therefore excluded the idea of using linked HIS/BCE database in the frame of this study.

[h] HISLink project, https://www.sciensano.be/en/projects/linkage-health-interview-survey-data-health-insurance-data (last access 11 August 2021)

[i] Belgian Cancer Registry online tool, https://kankerregister.org/default.aspx?PageId=344 (last access 11 August 2021)

6.1.4 The Belgian burden of disease study

In 2016, Sciensano launched the Belgian National Burden of Disease Study (BeBOD) which aims to establish a coherent framework for routinely quantifying the burden of disease in Belgium.[j] To date, results with regards to the burden of cancer in 2018 are available. [114, 115]

Two types of summary measures of population health have been calculated to estimate the burden of cancer, i.e. the number of Years Lived with Disability (YLDs) and the number of YLDs per case. YLDs are calculated by multiplying the prevalence of cancer by the disability weight (DW). A DW of 0 is equivalent to full health, whereas a DW equal to 1 equivalent to death (see section 6.2.1). In BeBOD, DW were extracted from Salomon et al.[116] and prevalence estimates have been derived from the BCR incidence data (see section 6.1.3), using a microsimulation approach. Cancer estimates include (almost) all cancers that are registered by the Belgian Cancer Registry (see section 6.1.3).

In 2018, all cancers resulted in 68 806 YLDs on a population level. The cancers that caused the highest number of YLDs were prostate cancer (11 416 YLDs), malignant neoplasms of skin (9 455 YLDs), breast cancer (8 640 YLDs), colorectal cancer (6 795 YLDs), and bladder cancer (3 577 YLDs). Those results are mainly driven by the high prevalence of these cancers in Belgium. Indeed, these cancers were also included in the top 5 most reported cancers in 2018. Male genital (20 YLDs), heart, mediastinum and pleura (18 YLDs), lip, oral cavity and pharynx (18 YLDs), placenta (8 YLDs) and uterus (7 YLDs) cancers had the lowest impact on Belgian health when using the number of YLDs as measure of burden of cancer (Table 10).

When looking at the impact of cancer at a patient level (i.e. based on the number of YLDs per case) in 2018, the ranking quite different because not driven by the prevalence. Mesothelioma (0.233 YLD per case), unknown primary site cancer (0.184 YLD per case), prostate cancer (0.166 YLD per case), bladder cancer (0.162 YLD per case) and urinary organs cancer (0.151 YLD per case) occupy the first steps of the ranking. This means that these cancers, although some being relatively rare, have a significant impact on patients' quality of life. Bone and articular cartilage of limbs cancer (0.070 YLD per case), malignant melanoma of the skin (0.066 YLD per case), thyroid gland cancer (0.065 YLD per case), testis cancer (0.060 YLD per case) and placenta cancer (0.060 YLDs per case) are the cancer that caused the lowest YLDs per case (Table 10).

The results on the burden of cancer can be further explored via an interactive platform[k]. A publication presenting the non-fatal burden of cancer in Belgium for the period 2004-2018 is also under review. [117]

[j] The Belgian National Burden of Disease Study, https://www.sciensano.be/en/projects/belgian-national-burden-disease-study (last access: 10 August 2021)

[k] https://burden.sciensano.be/shiny/cancer/ (last access : 9 Septembre 2021).

Table 10 – Number of cases, YLDs on population level and YLDs per case by type of cancer, 2018

Cancer type	Number of YLDs population	Number of YLDs per case	Ranking number based on total YLDs population	Ranking number based on YLDs per case
Mesothelioma	202.76	0.223	31	1
Unknown primary site	505.39	0.184	21	2
Prostate	11 415.78	0.166	1	3
Bladder	3577.13	0.162	5	4
Urinary organs, nos*	59.44	0.151	46	5
Pancreas	918.95	0.149	15	6
Myelodysplastic syndromes	980.15	0.148	14	7
Ovary	1086.90	0.147	12	8
Uterus, nos*	7.42	0.146	54	9
Ureter	200.11	0.145	32	10
Lip, oral cavity and pharynx, nos*	17.97	0.143	52	11
Leukemia	2957.49	0.139	6	12
Colorectal	6795.02	0.135	4	13
Oesophagus	741.13	0.131	17	14
Retroperitoneum and peritoneum	93.09	0.129	38	15
Hypopharynx	79.71	0.129	39	16
Trachea, bronchus and lung	2629.87	0.128	7	17
Female genital organs, nos*	111.06	0.127	36	18
Pyriform sinus	170.37	0.124	34	19
Larynx	854.16	0.124	16	20
Gallbladder and biliary tract	241.42	0.123	29	21
Vagina	38.65	0.122	48	22
Nasal cavity and middle ear	65.31	0.120	45	23
Brain and nervous system	643.09	0.119	19	24
Lip and oral cavity	1363.89	0.119	10	25
Liver and intrahepatic bile ducts	558.17	0.118	20	26

Penis	127.74	0.116	35	27
Accessory sinuses	77.30	0.113	42	28
Heart, mediastinum and pleura	18.42	0.110	51	29
Malignant neoplasms of skin	9455.13	0.108	2	30
Male genital organs, nos*	20.07	0.105	50	31
Other pharynx	443.27	0.103	23	32
Soft tissues	438.45	0.103	24	33
Small intestine	376.28	0.102	27	34
Vulva	269.35	0.102	28	35
Breast	8640.39	0.100	3	36
Stomach	1044.04	0.099	13	37
Myeloproliferative neoplasms	480.29	0.099	22	38
Eye and adnexa	185.55	0.098	33	39
Bone and articular cartilage, nos*	77.56	0.097	41	40
Thymus	69.45	0.096	44	41
Anus and anal canal	213.42	0.095	30	42
Nasopharynx	77.94	0.092	40	43
Corpus uteri	1789.45	0.087	8	44
Kaposi's sarcoma	58.05	0.081	47	45
Adrenal gland	93.99	0.079	37	46
Cervix uteri	695.99	0.079	18	47
Hodgkin's disease	412.24	0.072	26	48
Endocrine glands, nos*	37.46	0.070	49	49
Bone and articular cartilage of limbs	71.53	0.070	43	50
Malignant melanoma of skin	1526.87	0.066	9	51
Thyroid gland	1138.16	0.065	11	52
Testis	423.00	0.060	25	53
Placenta	7.90	0.060	53	54

*Data source: Sciensano; *nos=not otherwise specified.*

The main limitation of these results is that they currently only include cancers.

6.1.5 The INAMI – RIZIV unmet medical needs procedure

The unmet medical needs procedure, which became effective in 2016, is intended for pharmaceutical products that have not yet obtained a market license but that treat a major unmet medical need. The program provides temporary financial compensation for such products, provided that they treat an indication that is highly ranked on the list of unmet medical needs established by the INAMI – RIZIV, based on requests to put an indication on the list submitted by manufacturers, the college of medical directors or the ministry of Health and Social Affairs. The list is drawn up annually by a special committee within the INAMI – RIZIV (the “Commission for advice on temporary compensation for the costs a pharmaceutical product” / “Commissie voor advies in geval van tijdelijke tegemoetkoming voor het gebruik van een geneesmiddel” (CATT) / “Commission d’avis en cas d’intervention temporaire pour l’utilisation d’un medicament” (CAIT)) (Table 11).

The KCE was charged by the INAMI – RIZIV to develop the methodology that the committee could use to draw up the list. The full description of the method is available in the KCE report 272.[3] In short, the approach makes a distinction between therapeutic need (from the patient's point of view) and social need and scores are attributed according to explicit criteria. The criteria for therapeutic need are impact of the condition on HRQoL (given current treatment), impact of the condition on life expectancy (given current treatment) and discomfort of the current treatment. The criteria for social need are public expenditure on the condition and frequency of occurrence. The ranking of a condition on the needs lists (there is a separate list for therapeutic and social needs) is driven by the scores on the criteria. A condition that is high in a ranking has scored high on one or more criteria. The way in which this is dealt with in the reimbursement decision is therefore as follows: when a producer applies for reimbursement for a product, it is determined where the indication is on the list. Subsequently, it is evaluated on which criteria the product has an effect and what the relative importance of that criterion was for the ranking of the disorder. If the product has a positive effect on the determining criterion, it is eligible for reimbursement. The next step is to determine how much this financial compensation may amount to. Again, this will have to depend on the place of the disorder in the ranking, but also on the effect of the new treatment on the criteria that were important for the place of the disorder in the ranking.

The ranking of health conditions by the committee happens by means of a multi-criteria decision approach. First, the evidence regarding specific decision criteria is critically assessed. Based on this, the committee members assign a score to each decision criterion. The scores are weighted, using weights assigned to each criterion by the commission (in consensus) and finally the sum of the weighted scores is made.

In 2021, the INAMI – RIZIV list of unmet medical needs included 75 conditions or syndromes. The highest ranked were COVID-19 (score=11.63), newly diagnosed glioblastoma (11.40) and amyotrophic lateral sclerosis (11.34). Half of the conditions included in the list were cancers (53.3%) (Table 11).

Table 11 – INAMI – RIZIV list of unmet medical needs 2021

List of unmet medical needs 2021	Score	Type of disease
Corona Virus Disease 2019 (COVID-19)	11.63	Infectious
Newly diagnosed glioblastoma	11.40	Oncology
Amyotrophic lateral sclerosis	11.34	Neurodegenerative
Acute graft versus host disease	11.25	Transplantation
Locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement	10.63	Oncology
Recurrent glioblastoma	10.58	Oncology
Pancreatic cancer BRCA+	10.56	Oncology
Acid Sphingomyelinase Deficiency	10.54	Rare disease
Neuronal ceroid-lipofuscinosis type 2 (CLN2)	10.40	Neurodegenerative
Malignant pleural mesothelioma	10.34	Oncology
Mesothelioma (L2)	10.22	Oncology
Amyloid light chain amyloidosis	10.14	Other
Duchenne muscular dystrophy	10.02	Neurodegenerative
Selective and early debridement of deep burns in children	9.86	Other
Acute lymphoblastic leukemia (ALL)	9.56	Oncology
Metastatic non-small cell lung cancer (NSCLC) with high, low or no PD-L1 (1L) expression	9.49	Oncology
Locally advanced or metastatic solid tumours related to NTRK gene fusion in adult and pediatric patients	9.45	Oncology
Metastatic uveal melanoma	9.40	Oncology
Treatment of ≥3 lines of HER2-positive metastatic breast cancer (HER2+ mBC) after failure of trastuzumab emtansin (T-DM1)	9.37	Oncology
Recurrent and/or metastasized squamous cell carcinoma of the head and neck (SCCHN) with progression or after platinum-based chemotherapy	9.33	Oncology
Second-line treatment of locally advanced or metastatic urothelial musculo-invasive urothelial cancer	9.25	Oncology
Advanced breast cancer (stage IV) HR-positive HER2-negative with PIK3CA mutation	9.20	Oncology
Chronic graft-versus-host disease	9.20	Transplantation
Unresectable, locally advanced or metastasized papillary renal cell carcinoma MET determined	9.09	Oncology
Recurrent and/or metastatic squamous cell carcinoma of the head and neck	9.08	Oncology
Alfa-mannosidosis	9.06	Neurodegenerative
Newly diagnosed acute myeloid leukemia	9.00	Oncology
Neurofibromatosis 1 (NF1)	8.94	Rare disease
Ovarian Cancer BRCA + (1L)	8.91	Oncology
Metastatic non-small cell lung cancer positive for the BRAF V600E mutation	8.90	Oncology
Metastatic and advanced gastric cancer HER2 + (L2)	8.80	Oncology
Progressive Supranuclear Palsy	8.80	Neurodegenerative

List of unmet medical needs 2021	Score	Type of disease
Small Cell Bronchial Cancer	8.80	Oncology
Relapsed or relapsed diffuse large B-cell lymphoma	8.74	Oncology
Systemic scleroderma and interstitial lung disease (pulmonary fibrosis)	8.60	Oncology
Osteogenesis imperfecta	8.52	Rare disease
Pneumonia in intubated and mechanically ventilated patients	8.51	Infectious
Relapsed or relapsed diffuse large B-cell lymphoma	8.50	Oncology
Chronic Lymphocytic Leukemia in Elderly/Co-morbid patients	8.49	Oncology
Multi-refractory and/or karyotypic multiple myeloma	8.46	Oncology
Metastasized urothelial bladder cancer (1L)	8.37	Oncology
Adjuvant treatment for EGFR-mutated non-small cell lung cancer stage IB-IIIA	8.31	Oncology
Transthyretin-related amyloid cardiomyopathy (TTR-CM)	8.30	Cardiology
BRCA+ metastatic breast cancer	8.28	Oncology
Hepatocellular carcinoma	8.25	Oncology
KRASm+ non-small cell lung cancer	8.18	Oncology
Refractory or relapsing Chronic Lymphocytic Leukemia	8.17	Oncology
HRR+ castration-resistant metastatic carcinoma of the prostate gland	8.14	Oncology
Metastatic colorectal cancer	8.03	Oncology
Dravet's Syndrome	8.02	Rare disease
Advanced cutaneous squamous cell carcinoma	8.00	Oncology
Aggressive systemic mastocytosis	8.00	Rare disease
Myasthenia	7.94	Rare disease
Resectable non-small cell lung cancer at an early or locally advanced stage (neo-adjuvant and adjuvant treatment)	7.89	Oncology
Sickle cell disease	7.80	Hematological
Refractory carcinoid syndrome	7.77	Oncology
Lysosomal acid lipase deficiency	7.62	Rare disease
Lupus nephritis	7.52	Autoimmune
Advanced renal cell carcinoma L2	7.33	Oncology
Sporadic inclusion body myositis (sIBM)	7.22	Degenerative muscle
Alzheimer	6.78	Neurodegenerative
Non-Hodgkin's lymphoma (L1)	6.72	Oncology
Giant Cell Tumor of Soft Tissue	6.57	Oncology
Moderate and severe atopic dermatitis	6.29	Dermatology
Emergency Treatment of a Suspected or Known Opioid Overdose	6.18	Psychiatric
Chronic Heart Failure	6.00	Cardiology

List of unmet medical needs 2021	Score	Type of disease
Episodic cluster headache	5.90	Neurological
Alpha-1-antitrypsin deficiency	5.78	Rare disease
Clostridium difficile infection (prevention of recurrence)	5.24	Infectious disease
Hypogammaglobulinemia (HGG) in the case of solid organ transplantation	5.22	Transplantation
Chronic refractory pain	5.10	Pain
Treatment-resistant depression	4.89	Psychiatric
Hypoparathyroidism	4.16	Hormonal
Chronic refractory cough	4.03	Other
Chronic rhinosinusitis with nasal polyps (CRSwNP)	2.60	Other

Source: INAMI – RIZIV

6.1.6 The Special Solidarity Fund

In Belgium, only drugs with licenced indications (authorized by the European Medicine Agency (EMA) or the national medicines agency FAMHP – FAGG – AFMPS) are eligible for reimbursement. Exceptions and off-label use are possible via the Unmet Medical Needs programme or the Special Solidarity Funds (SSF). In both programs, a commission decides on possible reimbursement on an individual or patient cohort basis.

The SSF receives applications for reimbursement outside the licenced indications, i.e. for products that are on the market for at least one indication but not for the specifically targeted indication (off-label use). The following criteria must be met to be eligible: rare disease, threatening vital functions, no therapeutic alternative, and scientific evidence of effectiveness/value.

In 2019, the most expensive services that have been reimbursed outside the licenced indication were 1) chenodeoxycholic acid (treatment of cholesterol gallstone, > 500 000€), 2) medical expenses, transport and accommodation expenses for the person concerned and accompanying person (250 000-499 000€) and 3) lutetium octreotate therapy (treatment of neuroendocrine tumours, 250 000-499 000€) (see Table 12). Overall the services supported by the SSF are quite varied and cover a range of medical specialisms.

Table 12 – Top 27 most expensive services reimbursed by the Special Solidarity Fund, 2019

Services	Annual cost
Chenodeoxycholic acid (Xenbilox®, Leadiant®, …)	> 500 000€
Medical expenses, transport and accommodation expenses for the person concerned and accompanying person	250 000-499 000€
Lutetium-Octreotate (PRRT)	250 000-499 000€
Treatment for Epidermolysis Bullosa patients	100 000-249 000€
Polyethylene glycol-modified adenosine deaminase (PEG-ADA)	100 000-249 000€
Eculizumab (Soliris®)	100 000-249 000€
Immunoglobulins (Sandoglobuline®, Ivegam®, Multigam®, Privigen®, Octagam®, ...)	100 000-249 000€
Hydroxybutyric acid	100 000-249 000€
Anakinra (Kineret®)	50 000-99 999€
Foscarnet (Foscavir®)	50 000-99 999€
Amfotericine B (Abelcet®, Ambisome®, …)	50 000-99 999€
Cochlear implant	50 000-99 999€
Thiotepa (Tepadina®, Ledertepa®)	50 000-99 999€
Cidofovir (Vistide®, …)	20 000-49 999€
Antithymocyte globuline (Atgam®)	20 000-49 999€
Natriumoxibaat (Xyrem®)	20 000-49 999€
Afamelanotide (Scenesse®)	20 000-49 999€
Peginterferon alfa-2a (Pegasys®)	20 000-49 999€
Fingolimod (Gilenya®)	20 000-49 999€
Filters for LDL apheresis	20 000-49 999€
Brainstem implant	20 000-49 999€
Hersenstimulator (DBS)	10 000-19 999€
Oxybutinine (Ditropan®)	10 000-19 999€
Deflazacort (Calcort®, …)	10 000-19 999€
Macitentan (Opsumit®)	<10 000€
Rituximab (Mabthera®)	<10 000€
Natalizumab (Tysabri®)	<10 000€

Source: The Special Solidarity Fund

With regard to the number of patients, deflazacort (n>50), lutetium-Octreotate (PRRT) (>50) and amfotericine B (Abelcet, Ambisome) were the most frequently services reimbursed by the SSF (see Table 13). If we cross-reference Table 12 and Table 13, 12 services are both costly and frequent with regard to the number of patients: anakinra, chenodeoxycholic acid, cidofovir, cochlear implant, deflazacort, foscarnet, immunoglobulins, lutetium-octreotate (PRRT), oxybutinine, rituximab, thiotepa and treatment for Epidermolysis Bullosa patients. Lutetium octreotate therapy is included in both top 3, this is a costly and frequently reimbursed treatment.

Table 13 – Top 30 services reimbursed by the Special Solidarity Fund with regard to the number of patients, 2019

Services	Number of patients
Deflazacort (Calcort®, ...)	>50
Lutetium-Octreotate (PRRT)	>50
Amfotericine B (Abelcet®, Ambisome®, …)	>50
Oxybutinine (Ditropan®)	20-49
Cidofovir (Vistide®, ...)	20-49
Foscarnet (Foscavir®)	20-49
Anakinra (Kineret®)	20-49
Immunoglobulins (Sandoglobuline®, Ivegam®, Multigam®, Privigen®, Octagam®, ...)	10-19
Peginterferon alfa-2a (Pegasys®)	10-19
Cochlear implant	10-19
Treatment for Epidermolysis Bullosa patients	10-19
Dinutuximab bèta (Qarziba®)	10-19
Hydroxocobalamine (vitamin B12) (magistral)	10-19
Fee for the procedure to create a 3D plan and model (CADCAM)	10-19
Thiotepa (Tepadina®, Ledertepa®)	10-19
Artificial tears and lubricants	10-19
Chenodeoxycholic acid (Xenbilox®,Leadiant®,…)	<10
Neurostimulator	<10
Anal irrigation system	<10
Clofazimine (Lamprene®)	<10
Arm stocking and glove for lymphedema	<10
Stent of the internal carotid artery	<10
Levodopa (Sinemet®)	<10
Medical expenses	<10
Tocilizumab (Roactemra®, ...)	<10
Arm stocking for lymphedema	<10
Bridgework	<10
Fibrinogen (Haemocomplettam®, Riastap®)	<10
Rituximab (Mabthera®)	<10
Dental Implants	<10

Source: The Special Solidarity Fund

Table 12 and Table 13 do not include HRQoL indicators and exact indications of the services reimbursed (for a question of anonymity, given that certain conditions are extremely rare). However, when analysing the treatments, we observe that a large number were related to the treatment of cancers and neurodegenerative diseases.

This makes it challenging to use the SSF data for the identification of the patients with important unmet medical needs in a systematic manner. One possible approach could be to establish a system where the SSF reports on the indications, separately from the products. However we still found interesting to present these data and to use them as parallel information in the elaboration of the selection of health states with potentially highest unmet needs.

6.1.7 *Registries of congenital anomalies, the Belgian Cystic Fibrosis Registry and the Belgian Neuromuscular Disease Registry (BNMDR)*

The registries of congenital anomalies (Antwerpen and Hainaut and Namur)[l], the Belgian Cystic Fibrosis Registry[m] and the Belgian Neuromuscular Disease Registry[n] could have been useful sources of data to define patient needs but they do not include HRQoL indicators.

6.1.8 *SHARE*

SHARE is a panel database of micro data on health, socioeconomic status and social and family networks covering most of the European Union, including Belgium. To date, SHARE has collected 8 panel waves (2004, 2007, 2009, 2011, 2013, 2015, 2017 and 2020) of current living circumstances and retrospective life histories (wave 3 and 7) and on the COVID-19 living situation (wave 8); 3 additional waves are planned until 2024. The more than 150 000 interviews give a broad picture of life after the age of 50 years. SHARE covers the various areas of life, namely health, socioeconomics and social networks, SHARE includes a great variety of information: health variables, physical measures and biomarkers, psychological variables, economic variables and social support variables as well as social network information.

The SHARE target population consists of all persons aged 50 years and over at the time of sampling who have their regular domicile in the respective SHARE countries. The partner of the sampled person is interviewed as well. In Belgium, persons living in institutions are included in the sample. Persons are excluded if they are incarcerated, hospitalised or out of the country during the entire survey period, unable to speak the country's language(s) or have moved to an unknown address. Additional information on the sampling procedure is available in the technical report of Bergmann et al. (2019).[118]

The interviewers used computer-assisted personal interviewing (CAPI) to collect most of the data in all waves. In addition, self-administered questionnaires (drop-off) were handed out in some waves after completion of the CAPI. If a respondent died, end-of-life interviews are conducted face-to-face (CAPI) or by telephone (CATI) with a proxy, collecting the information regarding the respondent's last year of life. Even though SHARE is a panel survey with a core questionnaire stable over time, innovative research questions, physical measurements or modules have been incorporated in each wave.

The quality of life (QOL) measure used in SHARE is CASP-12 (Control Autonomy Self-completion Pleasure, 12 items), which was specifically developed for older people. It is a self-completion questionnaire and spans four derived dimensions of control and autonomy (six items), self-

l Eurocat, https://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=FR&Expert=255824 (last access: 11 August 2021)

m Belgian Cystic Fibrosis Registry, https://www.sciensano.be/en/projects/belgian-cystic-fibrosis-registry (last access: 11 August 2021)

n Belgian Neuromuscular Disease Registry, https://www.sciensano.be/en/belgian-neuromuscular-diseases-registry-bnmdr (last access: 11 August 2021)

realisation (three items) and pleasure (three items).[119, 120] Responds are asked how often they experience certain feelings and situations on a 4-point Likert scale ranging from "never" to "often". For the total score of CASP-12, values range from 12 to 48, with higher scores indicating better quality of life. These scores are subsequently classified into four levels of QOL, where 39-41 indicates very high QOL, 37-39 high QOL, 35-37 moderate QOL and values below 35 low QOL. Examples of items are 'My health stops me from doing the things I want to do' and 'Shortage of money stops me from doing the things I want to do'. CASP has both a 12-item and a more commonly used 19-item version.[121]

The variables that have been selected from the wave 7 SHARE database for Belgium are presented in the Appendix 2.

In 2017, 4 902 patients were included in the SHARE study for Belgium. Mean age was 67.5 (SD 10.4) years and 55.7% were female (see).

Table 14 – Description of the Belgian population included in SHARE wave 7

	Mean (SD) N [%]
Age (n= 4 902)	67.5 (10.4)
<50	55 [1.1]*
50-59	1 212 [27.7]
60-69	1 730 [35.3]
70-79	1 159 [23.6]
80+	756 [15.22]
Female	2 730 [55.7]

*Data source: SHARE, wave 7, *some respondents are younger than 50 because the partner is interviewed as well.*

CASP-12 was available for 4 641 patients for whom the mean QOL score was 26.1 (SD 3.8) which corresponds to 'low QOL'. The median was 26.0 (min 12.0-max 48.0). By dimensions, CASP-3 (i.e. CASP related to only one dimension and 3 items) was the lowest (i.e. corresponding to the lowest QOL) for pleasure (4.6, SD 1.9), followed by self-realization (5.3, SD 2.1), autonomy (7.7, SD 1.7) and control (8.6, SD 2.2) (see Table 15).

Table 15 – CASP-12 results SHARE wave 7

	Mean (SD)	Median	Min	Max
CASP-12 (n= 4 641)	26.1 (3.8)	26.0	12.0	48.0
CASP-3: Pleasure (n= 4 711)	4.6 (1.9)	4.0	3.0	12.0
CASP-3: Self-realization (n= 4 730)	5.3 (2.1)	5.0	3.0	12.0
CASP-3: Autonomy (n= 4 762)	7.7 (1.7)	8.0	3.0	12.0
CASP-3: Control (n= 4 756)	8.6 (2.2)	9.0	3.0	12.0

The average CASP-12 is significantly different between age-groups ($p<0.001$) and more particular between the oldest (80+) and the others age-groups (seeTable 16). There is a weak but positive and significant linear relation ($\beta_1 = 0.05$, $p<0.001$) between age and CASP-12. At each increase of one year of life the CASP-12 increases by 0.05 (see Table 16 and Table 17).

As for the CASP-12, CASP-3 for pleasure, self-realization, autonomy and control were significantly different between age-groups. Overall, oldest respondents reported the highest QOL scores, except for CASP-control for which highest score was reported in the 60-69 years group. Female reported significantly higher CASP scores for pleasure and self-realization than male (pleasure: female 4.7 (SD 1.9) – male 4.5 (SD 1.8), p=0.03 and self-realization: female 5.4 (2.1) – male 5.1 (2.0), p<0.001) whereas male reported higher CASP scores for autonomy and control than female (autonomy: female 7.7 (1.8) – male 7.8 (1.7), p=0.002 and control: female 8.4 (2.2) – male 8.8 (2.1)) (seeTable 16).

Table 16 – Comparison of CASP results by dimension, age and gender.

	CASP-12 Total Mean (SD) n= 4 641	p-value	CASP-3 Pleasure Mean (SD) n= 4 711	p-value	CASP-3 Self-realization Mean (SD) n= 4 730	p-value	CASP-3 Autonomy Mean (SD) n= 4 762	p-value	CASP-3 Control Mean (SD) n= 4 756	p-value
Age-group		<0.001**		0.004**		<0.001**		<0.001**		<0.001**
<50	25.1 (3.6)[80+]		4.7 (1.8)		4.8 (1.9)		6.6 (1.5)		9.1 (1.9)	
50-59	25.8 (3.7)[70-79,80+]		4.7 (1.9)		5.2 (2.0)		7.2 (1.7)		8.7 (2.1)	
60-69	25.8 (3.6)[70-79,80+]		4.5 (1.8)		5.0 (2.0)		7.5 (1.6)		8.8 (2.1)	
70-79	26.3 (3.9)[50-59,60-69,80+]		4.5 (1.8)		5.3 (2.1)		8.0 (1.7)		8.5 (2.2)	
80+	27.3 (4.1)[<50,50-59,60-69,70-79]		4.7 (2.0)		6.1 (2.2)		8.8 (1.7)		7.7 (2.3)	
Gender		0.404*		0.03*		<0.001*		0.002*		<0.001*
Female	26.1 (3.8)		4.7 (1.9)		5.4 (2.1)		7.7 (1.8)		8.4 (2.2)	
Male	26.2 (3.8)		4.5 (1.8)*		5.1 (2.0)		7.8 (1.7)		8.8 (2.1)	

*Data source: SHARE wave 7; *student-t test; ** ANOVA one-way; Tuckey's post-hoc tests: [80+]: significantly different from 80+, [70-79] significantly different from 70-79, [60-69] significantly different from 60-69, [50-59] significantly different from 50-59, [<50]significantly different than <50.*

Table 17 – Parameters of the linear regression between CASP-12 and age (in years)

Variable	DF	Parameter	Standard	t Value	P-value
Intercept	1	22.8828	0.37243	61.44	<0.001
age	1	0.04814	0.00549	8.78	<0.001

Data source: SHARE, Wave 7.

For some diseases, the number of participants was very low (n<50) and were not included in the ranking of the diseases according to CASP results. We were able to rank 16 diseases and among them, cancer (mean CASP-12= 25.9, SD 4.1), hypercholesterolemia (26.1 (3.8)) and high blood pressure or hypertension (26.1 (3.9)) were the top 3 diseases with the lowest QOL (see Table 18).

Table 18 – CASP-12 by health state, SHARE Wave 7, n=4 641

Disease*	N (%)	CASP-12 Mean (SD)	Ranking CASP-12
Cancer in: brain	1 (0.02)	25.0	NA
Cancer in: kidney	1 (0.02)	25.0	NA
Cancer in: cervix	1 (0.02)	25.0	NA
Cancer in: lung	3 (0.06)	25.0 (2.0)	NA
Cancer in: prostate	13 (0.28)	25.4 (2.9)	NA
Cancer in: bladder	2 (0.04)	25.5 (2.1)	NA
Cancer in: skin	5 (0.11)	25.8 (2.6)	NA
Cancer	251 (5.4)	25.9 (4.1)	1
Cancer in: leukaemia	1 (0.02)	26.0 (NA)	NA
Cancer in: other organ	5 (0.11)	26.0 (5.5)	NA
Hypercholesterolemia	1 559 (33.6)	26.1 (3.8)	2
High blood pressure or hypertension	1 676 (36.1)	26.1 (3.9)	3
Other fractures	256 (5.5)	26.1 (4.0)	4
Osteoarthritis/other rheumatism	1 649 (35.5)	26.3 (3.9)	5
Heart attack	452 (9.7)	26.3 (4.0)	6
Diabetes or high blood sugar	549 (11.8)	26.3 (4.1)	7
Stomach or duodenal ulcer, peptic ulcer	256 (5.5)	26.4 (4.0)	8
Rheumatoid arthritis	350 (7.5)	26.4 (4.0)	9
Stroke	169 (3.6)	26.4 (4.3)	10
Cataracts	402 (8.7)	26.5 (3.8)	11
Hip fracture or femoral fracture	96 (2.1)	26.5 (4.4)	12
Chronic kidney disease	87 (1.9)	26.9 (4.0)	13
Chronic lung disease	312 (6.7)	27.0 (4.5)	14
Cancer in: breast	15 (0.3)	27.2 (4.1)	NA
Other affective/emotional disorders	430 (9.3)	27.2 (4.2)	15
Alzheimer's disease, dementia, senility	63 (1.4)	27.9 (4.2)	16

Cancer in: ovary	3 (0.06)	28.3 (7.6)	NA
Parkinson disease	38 (0.82)	28.8 (4.9)	NA
Cancer in: colon or rectum	9 (0.19)	29.4 (3.9)	NA
Cancer in: other pharynx	1 (0.02)	30.0	NA
Cancer in: larynx	1 (0.02)	30.0	NA
Cancer in: stomach	1 (0.02)	31.0	NA
Cancer in: oral cavity	0 (0.0)	NA	NA
Cancer in: thyroid	0 (0.0)	NA	NA
Cancer in: oesophagus	0 (0.0)	NA	NA
Cancer in: liver	0 (0.0)	NA	NA
Cancer in: pancreas	0 (0.0)	NA	NA
Cancer in: testicle	0 (0.0)	NA	NA
Cancer in: endometrium	0 (0.0)	NA	NA
Cancer in: non-hodgkin lymphoma	0 (0.0)	NA	NA

**Disease diagnosed by a doctor. The patient is still embarrassed by the disease at time of interview, NA=Not available*

The main limits of the SHARE results are that they are self-reported and limited to people older than 50 years of age. Also in this database, as in the HIS database, we observe that conditions for which there is no or no effective treatment available to fully cure the patients and/or remove all disease-related symptoms are relatively higher on the list.

6.2 International data sources and initiatives that collect quality of life indicators for Belgium

6.2.1 Global Burden of Disease Study

The Global Burden of Disease (GBD) studies, 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 Global Burden of Disease study.[122]

We collected results of the Global Burden of Disease 2017 (GBD 2017) study for Belgium through the GBD results tool.[o] Detailed information about data, approaches, statistical modelling, and metrics for the GBD 2017 study have been reported elsewhere.[123] The GBD 2017 study used several metrics to quantify health impact of specific disease but for this study we focused on Years Lived with Disability (YLDs) and Disability-Adjusted Life Years (DALYs). YLDs are calculated by multiplying the prevalence of sequelae by their disability weight (DW). A DW of 0 is equivalent to full health, whereas a DW equal to 1 equivalent to death. The DW is meant to capture the severity of functional limitations in different health domains. DWs are derived from a panel of judges (in GBD studies, a panel of more than 60 000 people worldwide) using valuation methods (see Box 10) (in GBD studies, pairwise comparison and population equivalence methods) (see [116] for additional information on DW used in GBD studies). DALYs are the sum of YLLs and YLDs. YLLs are expressing years of life lost and are computed by multiplying the number of deaths for a specific cause in each age-group by a reference life expectancy at that age. The life expectancy at birth in the GBD 2017 reference life table is 86 years for both sexes.

Box 10 – Health state valuation used to derive the DW used in GBD 2017 study

To elicit health state valuations of the 235 health states, two valuation techniques were used: pairwise comparison and population health equivalence.

With **pairwise comparison method**, persons in two alternative health conditions are presented, and participants have to decide whom they regard as being healthier.

Population heath equivalence question ask for a retrospective assessment that compares two hypothetical health programs. The first health program prevented 1 000 people from getting an illness that causes rapid death; the second program prevented 1 500, 2 000, 3 000, 5 000 or 10 000 people from getting an illness that is not fatal but causes the lifelong health problems of one of the selected health states. The respondents are asked to choose with health program they think the greater overall population benefit.

Then paired comparisons are analysed through **probit regression** with indicator variables for each health state that took the value 1 for the first state in a paired comparison, –1 for the second state in a paired comparison, and 0 for all states other than the pair being considered. Then a second step is needed to anchor the resulting estimates onto the 0–1 disability weights scale. The approach relied on a linear regression of the probit coefficients from analysis of paired comparisons on the logit-transformed disability weight estimates derived from interval regression of the population health equivalence responses. Mean values of DW are then estimated on the 0–1 scale using numerical integration. [116]

[o] http://ghdx.healthdata.org/gbd-results-tool (last access: 4 August 2020)

In 2017, estimates of the burden (DALY or YLD) of 293 health conditions were available for Belgium. The highest DALYs were observed for low back pain (217 703 DALYs [95% Uncertainty Interval (UI): 157 043-291 470]), ischemic heart disease (197 552 DALYs [95% UI 184 928-211 242]), lung cancer (143 490 [95% UI 133 262-153 088]), chronic obstructive pulmonary disease (131 998 DALYs [95% UI 120 262-143 530]) and migraine (115 729 DALYs [95%UI 73 888-169 094]. Overall, the ranking is mainly occupied by chronic (e.g. COPD, migraine, diabetes), age-related (e.g. falls, Alzheimer, cancer, hearing loss) or psychiatric diseases (e.g. self-arm, anxiety, depressive disorders) (see Table 19). For most of these diseases, high ranking is explained by their high prevalence among Belgian population.

Excluding the mortality component of the estimates, low back pain (217 703 YLDs [95% UI 133 262-153 088]), migraine (115 729 YLDs [95% UI 73 888-169 094]), diabetes mellitus type 2 (85 526 YLDs [95% UI 57 623-118 550]), falls (79 498 YLDs [95% UI 56 366-109 479]) and neck pain (66 117 YLDs [95% UI 46 095-91 873]) cause the highest burden on population health in 2017. The causes included in the ranking based on the number of YLDs are quite similar than the DALYs one (10 causes are included in both rankings). However, some cardiac/vascular diseases (e.g. ischemic heart disease, ischemic stroke) and cancers (e.g. breast, lung, colon) are no more in the YLDs ranking. This means that the impact of these diseases on population health is mainly driven by early mortality (and number of cases). In the ranking based on the number of YLDs, psychiatric diseases appear (e.g. bipolar disorder, schizophrenia) as having the highest burden on population health (see Table 19).

Finally looking at the number of **YLDs per case** is interesting because it allows to better estimate the impact of a disease at a patient level. In this case, the ranking is totally different from the two previous ones (i.e. based on the number of DALYs or YLDs). Other neurological disorders (i.e. neurological disorders other than Alzheimer's disease and other dementias, Parkinson's disease, epilepsy, multiple sclerosis, motor neuron disease, migraine and tension-type headache), schizophrenia, HIV/AIDS - extensively drug-resistant tuberculosis, HIV/AIDS - multidrug-resistant tuberculosis without extensive drug resistance and HIV/AIDS - drug-susceptible tuberculosis have the highest impact on patient health. Overall, we observe that when using burden estimate at a patient-level (YLD per case), some infectious diseases (e.g. appendicitis, HIV, tuberculosis or neonatal sepsis) appear in the ranking (Table 19).

Table 19 – Top 20 causes of DALY, YLDs and YLD per case in Belgium, 2017

Cause	Number of DALYs	95% UI		Cause	Number of YLDs	95% UI		Cause	Number of YLDs per case	95% UI	
Low back pain	217 703	157 043	291 470	**Low back pain**	217 703	157 043	291 470	**Other neurological disorders**[£]	39.12	54.75	25.11
Ischemic heart disease	197 552	184 928	211 242	**Migraine**	115 729	73 888	169 094	**Schizophrenia**	0.626	0.686	0.53
Tracheal, bronchus, and lung cancer	143 490	133 262	153 088	**Diabetes mellitus type 2**	85 526	57 623	118 550	**HIV/AIDS - Extensively drug-resistant Tuberculosis**	0.410	0.428	0.377
Chronic obstructive pulmonary disease	131 998	120 262	143 530	**Falls**	79 498	56 366	109 479	**HIV/AIDS - Multidrug-resistant Tuberculosis without extensive drug resistance**	0.410	0.428	0.378
Migraine	115 729	73 888	169 094	**Neck pain**	66 117	46 095	91 873	**HIV/AIDS - Drug-susceptible Tuberculosis**	0.409	0.502	0.302
Alzheimer's disease and other dementias	109 713	100 324	119 261	**Major depressive disorder**	64 567	45 299	87 179	**Opioid use disorders**	0.407	0.461	0.33
Falls	107 544	84 752	137 308	**Age-related and other hearing loss**	62 516	43 107	87 338	**Hemolytic disease and other neonatal jaundice**	0.386	0.444	0.318
Diabetes mellitus type 2	100 385	72 410	133 609	**Chronic obstructive pulmonary disease**	56 351	46 435	66 347	**Multidrug-resistant tuberculosis without extensive drug resistance**	0.333	0.347	0.306
Self-harm by other specified means*	73 575	68 451	79 427	**Anxiety disorders**	53 014	37 848	70 547	**Extensively drug-resistant tuberculosis**	0.333	0.348	0.307
Neck pain	66 117	46 095	91 873	**Other musculoskeletal disorders**[$]	33 070	21 161	47 074	**Maternal obstructed labor and uterine rupture**	0.324	0.368	0.272
Major depressive disorder	64 567	45 299	87 179	**Edentulism and severe tooth loss**	25 764	17 256	36 519	**Appendicitis**	0.319	0.429	0.223
Ischemic stroke	62 884	55 582	70 342	**Other cardiovascular and circulatory diseases**[#]	25 647	17 349	35 522	**Other drug use disorders**[§]	0.316	0.401	0.235

Age-related and other hearing loss	62 516	43 107	87 338	**Osteoarthritis**	24 628	12 467	48 670	**Paralytic ileus and intestinal obstruction**	0.312	0.400	0.231
Lower respiratory infections	60 025	55 868	64 873	**Alzheimer's disease and other dementias**	24 330	17 067	32 107	**Neonatal sepsis and other neonatal infections**	0.308	0.360	0.244
Colon and rectum cancer	58 975	54 510	63 722	**Ischemic stroke**	23 972	17 463	30 588	**Neural tube defects**	0.307	0.368	0.239
Breast cancer	53 692	48 402	59 239	**Psoriasis**	23 470	16 596	31 065	**Vascular intestinal disorders**	0.287	0.366	0.212
Anxiety disorders	53 014	37 848	70 547	**Bipolar disorder**	21 002	13 347	30 809	**Pancreatic cancer**	0.278	0.304	0.207
Other cardiovascular and circulatory diseases[#]	47 431	38 888	57 382	**Other unintentional injuries[@]**	20 527	13 635	29 424	**Multiple sclerosis**	0.251	0.296	0.197
Intracerebral hemorrhage	45 025	41 381	48 708	**Schizophrenia**	20 235	15 198	24 969	**Epilepsy**	0.226	0.334	0.155
Other musculoskeletal disorders[$]	36 323	24 250	50 431	**Other mental disorders[%]**	19 953	13 238	27 536	**Acute myeloid leukemia**	0.220	0.256	0.181

*Data source: GBD 2017, UI: Uncertainty Interval, *Self-harm by other specified means than by firearm, [#]Cardiovascular and circulatory diseases other than rheumatic heart disease, ischemic heart disease, stroke, hypertensive heart disease, non-rheumatic valvular heart disease, myocarditis, alcoholic cardiomyopathy, other cardiomyopathy, atrial fibrillation and flutter, aortic aneurysm, peripheral disease or endocarditis, [$]Musculoskeletal disorders other than rheumatoid arthritis, osteoarthritis, low back pain and gout, [@]Unintentional injuries other than exposure to forces of nature, environmental heat and cold exposure, foreign body aspiration and in airway, in eyes or in other body part, falls, drowning, fire, heat, and hot substances, poisonings, exposure to mechanical forces, adverse effects of medical treatments or contact with venomous or non-venomous animal, [%]Mental disorders other than schizophrenia, depressive disorders, bipolar disorder, anxiety disorder, eating disorders, autism spectrum disorders, attention-deficit/hyperactivity disorder, conduct disorder or idiopathic development intellectual disability, [£]Neurological disorders other than Alzheimer's disease and other dementias, Parkinson's disease, epilepsy, multiple sclerosis, motor neuron disease, migraine and tension-type headache, [§]Drug use disorders other than alcohol, opioid, cocaine, amphetamine or cannabis use disorders.*

These results have to be interpreted carefully and cannot replace a national burden of disease study because they suffer from all limitations of GBD 2017 estimates already discussed widely and in detail elsewhere.[124] We summarize the relevant limitations for Belgium focusing on data sources and model used.

In the GBD 2017 study there were no data for some disease sequelae in Belgium. Therefore, data from previous year and from other countries were used to estimate burden of diseases in Belgium. In Global Health Data exchange (GHDx), the IHME catalogue of surveys, censuses, vital statistics, and other health-related data, 873 Belgian sources were reported in and only four referred to the year 2017. In other words, it means that GBD 2017 estimates for Belgium were largely based on data from previous years or from other countries, even non-European countries. Some available data sources, such as the Belgian Cancer Registry, were not used by the IHME in the GBD 2017 estimates. As GBD 2017 Belgian results are based on data from other countries and complex modelling, it is important to not solely rely on GBD estimates and continue to increase investments in national health monitoring and to generate national health status and burden of disease estimates. Second, Bayesian models were used to estimate health metrics of conditions in each country, age, sex and year. The nature of this estimation process means that, without data or powerful covariates, estimated variance might be smaller than the real variance. Results for Belgium have been informed by many available data sources such as vital registration data, surveillance report or studies on specific diseases. UIs provide some information about the extent of available information for Belgium.

Despite these limitations and until the results of the Belgian burden of disease study (see section 6.1.4) become available, GBD results are a good –be it rough- indicator of the health conditions that have the highest impact on Belgian population health. The main advantage of the IHME initiative is that it generates internally consistent estimates, thus allowing for comparisons across countries. However, external validity is not always guaranteed, as evidenced by the differences between different reports. Results ‘per case’ are driven by the availability of effective curative of symptom-relieving treatments, as in other databases described before.

6.3 Final selection of health states with potentially highest patient needs

We selected results and information from five databases, i.e. HIS 2018, the Belgian burden of disease study (cancer) 2018, the GBD study 2017, SHARE 2017 and finally the RIZIV – INAMI unmet needs list 2020, to draw up a list of health conditions that reported the highest burden of disease (at population or patient level) and (health-related) QoL loss and therefore potentially the highest patient needs level (see Table 20).

Table 20 – Databases and initiatives reviewed to estimate health conditions with highest patient needs

Database/initiatives	Main strengths	Main weaknesses	Decision to be included or not in the construction of the list of health conditions with potentially highest patient needs
Health interview survey (HIS)	• Representative of the Belgian population • Large sample size • Includes HRQoL estimates for a number of health conditions	• Self-reported data • Only a limited number of (common) health conditions are evaluated, exclusion of rare conditions • Population under 15 years of age excluded from the question on disease frequency	Included
HIS – IMA – AIM	• Large sample size • Includes HRQoL estimates for a number of health conditions	• Pseudo-pathologies only developed for patients and pathologies with available treatment • The validity of the pseudo-pathologies has only been explored for seven pathologies common to the list of HIS 2013 chronic diseases and showed bad agreement for at least one diagnosis (asthma)	Excluded
Belgian Cancer Registry	• Exhaustive data on the Belgian population suffering from cancer • Coupling HIS/BCR possible	• No quantitative indicators of HRQoL available collected as such in BCR • Only cancer included Linkage HIS/BCR suffering from very low prevalence of cancer reported by HIS participants	Excluded
Belgian burden of disease study	• Includes YLD estimates • Incidence data extracted from BCR (see above)	• Only cancer included, no estimation for other diseases	Included
INAMI – RIZIV's list of unmet medical needs	• List of 75 health conditions estimated • Scores attributed depend (among others criteria) on the impact of the condition on QOL of the patients	• Scores attributed by experts	Included
The Special Solidarity Fund (SSF)	• Requests introduced to the Special Solidary Fund reflect unmet medical needs	• No indicators of HRQoL available • Clinical indications of treatments reimbursed by SSF are not available	(Included)

Registries of congenital anomalies, the Belgian Cystic Fibrosis Registry and the Belgian Neuromuscular Disease Registry (BNMDR)	• /	• No indicators of HRQoL available	Excluded
SHARE	• Includes HRQoL indicator (CASP-12)	• Self-reported data • Limited to people older than 50 years of age	Included
Global Burden of Disease	• SMPH available for a large range of conditions • Comparison across countries is possible	• Estimates are largely based on data from other countries	Included

For HIS 2018, the Belgian burden of disease study (cancer) 2018 and GBD 2017, several indicators of the burden of disease have been retained (number of QALYs lost, HRQoL loss, number of YLDs, number of YLDs per case or number of DALYs) which makes that nine rankings are available to draw up a final list of health conditions.

The results obtained from the different databases and sources are not comparable because the indicators and the methods used to derive them are very different. In addition, the HIS study includes mainly 15 years older population and a selection of 38 health conditions, the Belgian burden of disease study includes only estimates for cancer, the GBD 2017 results are mainly driven by data from other countries and other years and includes a lot of uncertainty, SHARE includes only older than 50 years population and a selection of 16 chronic health conditions and finally unmet needs score are based on “subjective” experts evaluation. As already said previously, the number of QALYs, YLDs and DALYs are heavily influenced by the number of cases (and deaths for DALYs) and may be more valuable to assess healthcare needs on population level than on patient level. Measures such as HRQoL loss, YLD per case, SHARE and unmet needs scores are more valuable for assessing patient needs form the individual perspective. However, both are relevant for the policy maker, who has on the one hand to make sure (structural) decisions are made to improve population health and on the other hand priority is given to interventions that tackled the highest needs of patients (e.g. when decisions are made on the reimbursement of individual products). Therefore, it is still interesting to observe that some similarities of ranking appear between the databases.

We made an arbitrary choice to select the top 20 health conditions (16 for SHARE study) with the highest number of QALYs lost, HRQoL loss, DALYs, YLDs, YLDs per case, unmet needs score and lowest CASP, by database, which gave a total of 176 health conditions (Table 21).

Table 21 – Top 20 health conditions with the highest number of QALYs lost, HRQoL loss, DALY, YLD, YLD per case, unmet needs score and lowest CASP, by database

QALY loss, HIS 2018	HRQoL loss, HIS 2018	YLD, Belgian Burden of Cancer 2018	YLD per case, Belgian Burden of Cancer 2018	DALY, GBD 2017	YLD, GBD 2017	YLD per case, GBD 2017	CASP-12, SHARE 2017	Unmet needs score, RIZIV – INAMI 2021
Low back disorder	Myocardial infarction	Prostate cancer	Mesothelioma	Low back pain	Low back pain	Other neurological disorders[£]	Cancer	Corona Virus Disease 2019 (COVID-19)
Osteoarthritis	Stroke (or consequences)	Malignant neoplasms of skin	Unknown primary site cancer	Ischemic heart disease	Migraine	Schizophrenia	Hypercholesterolemia	Newly diagnosed glioblastoma
Neck disorder	Serious gloom or depression	Breast cancer	Prostate cancer	Tracheal, bronchus, and lung cancer	Diabetes mellitus type 2	HIV/AIDS - Extensively drug-resistant Tuberculosis	High blood pressure or hypertension	Amyotrophic Lateral Sclerosis
High cholesterol level in blood	Urinary incontinence	Colorectal cancer	Bladder cancer	Chronic obstructive pulmonary disease	Falls	HIV/AIDS - Multidrug-resistant Tuberculosis without extensive drug resistance	Other fractures	Acute graft versus host disease
Serious gloom or depression	Narrowing of blood vessels in belly or leg	Bladder cancer	Urinary organs, nos cancer	Migraine	Neck pain	HIV/AIDS - Drug-susceptible Tuberculosis	Osteoarthritis/ other rheumatism	Locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement
High blood pressure	Chronic fatigue for a period of at least	Leukemia	Pancreas cancer	Alzheimer's disease and other dementias	Major depressive disorder	Opioid use disorders	Heart attack	Recurrent glioblastoma
Chronic fatigue for a period of at least 3 months in the past 12 months	Diabetic retinopathy	Trachea, bronchus and lung cancer	myelodysplastic syndromes	Falls	Age-related and other hearing loss	Hemolytic disease and other neonatal jaundice	Diabetes or high blood sugar	Pancreatic cancer BRCA+
Allergy	Chronic bronchitis, COPD or emphysema	Corpus uteri cancer	Ovary cancer	Diabetes mellitus type 2	Chronic obstructive pulmonary disease	Multidrug-resistant tuberculosis	Stomach or duodenal ulcer, peptic ulcer	Acid Sphingomyelinase Deficiency

QALY loss, HIS 2018	HRQoL loss, HIS 2018	YLD, Belgian Burden of Cancer 2018	YLD per case, Belgian Burden of Cancer 2018	DALY, GBD 2017	YLD, GBD 2017	YLD per case, GBD 2017	CASP-12, SHARE 2017	Unmet needs score, RIZIV – INAMI 2021
						without extensive drug resistance		
Rheumatoid arthritis	Epilepsy	Malignant melanoma of skin	Uterus, nos cancer	Self-harm by other specified means*	Anxiety disorders	Extensively drug-resistant tuberculosis	Rheumatoid arthritis	Neuronal ceroid-lipofuscinosis type 2 (CLN2)
Severe headache such as migraine	Chronic cystitis	Lip and oral cavity cancer	Ureter cancer	Neck pain	Other musculoskeletal disorders$	Maternal obstructed labor and uterine rupture	Stroke	Malignant pleural mesothelioma
Urinary incontinence	Stomach ulcer	Thyroid gland cancer	Lip, oral cavity and pharynx, nos cancer	Major depressive disorder	Edentulism and severe tooth loss	Appendicitis	Cataracts	Mesothelioma (L2)
Disorder of the larger or the small bowel	Disorder of the larger or the small bowel	Ovary cancer	Leukemia	Ischemic stroke	Other cardiovascular and circulatory diseases#	Other drug use disorders§	Hip fracture or femoral fracture	Amyloid light chain amyloidosis
Chronic bronchitis, COPD or emphysema	Macula degeneration	Stomach cancer	Colorectal	Age-related and other hearing loss	Osteoarthritis	Paralytic ileus and intestinal obstruction	Chronic kidney disease	Duchenne muscular dystrophy
Thyroid problems	Broken hip	Myelodysplastic syndromes	Oesophagus	Lower respiratory infections	Alzheimer's disease and other dementias	Neonatal sepsis and other neonatal infections	Chronic lung disease	Selective and early debridement of deep burns in children
Diabetes	Coronary heart disease	Pancreas cancer	Retroperitoneum and peritoneum	Colon and rectum cancer	Ischemic stroke	Neural tube defects	Other affective/emotional disorders	Acute lymphoblastic leukemia (ALL)
Prostate problems	Osteoporosis	Larynx cancer	Hypopharynx	Breast cancer	Psoriasis	Vascular intestinal disorders	Alzheimer's disease, dementia, senility	Metastatic non-small cell lung cancer (NSCLC) with high, low or no PD-L1 (1L) expression
Asthma	Stones in the kidney	Oesophagus cancer	Trachea, bronchus and lung cancer	Anxiety disorders	Bipolar disorder	Pancreatic cancer	NA	Locally advanced or metastatic solid tumours related to NTRK gene fusion in adult and pediatric patients

QALY loss, HIS 2018	HRQoL loss, HIS 2018	YLD, Belgian Burden of Cancer 2018	YLD per case, Belgian Burden of Cancer 2018	DALY, GBD 2017	YLD, GBD 2017	YLD per case, GBD 2017	CASP-12, SHARE 2017	Unmet needs score, RIZIV – INAMI 2021
Stomach ulcer	Cancer	Cervix uteri cancer	Female genital organs, nos cancer	Other cardiovascular and circulatory diseases[#]	Other unintentional injuries[@]	Multiple sclerosis	NA	Metastatic uveal melanoma
Osteoporosis	Parkinson's disease	Brain and nervous system cancer	Pyriform sinus cancer	Intracerebral hemorrhage	Schizophrenia	Epilepsy	NA	Treatment of ≥3 lines of HER2-positive metastatic breast cancer (HER2+ mBC) after failure of trastuzumab emtansin (T-DM1)
Serious or chronic skin disease	Serious heart disease (except myocardial	Liver and intrahepatic bile ducts cancer	Larynx cancer	Other musculoskeletal disorders[$]	Other mental disorders[%]	Acute myeloid leukemia	NA	Recurrent and/or metastasized squamous cell carcinoma of the head and neck (SCCHN) with progression or after platinum-based chemotherapy

*NA= Not available, *Self-harm by other specified means than by firearm, [#]Cardiovascular and circulatory diseases other than rheumatic heart disease, ischemic heart disease, stroke, hypertensive heart disease, non-rheumatic valvular heart disease, myocarditis, alcoholic cardiomyopathy, other cardiomyopathy, atrial fibrillation and flutter, aortic aneurysm, peripheral disease or endocarditis, [$]Musculoskeletal disorders other than rheumatoid arthritis, osteoarthritis, low back pain and gout, [@]Unintentional injuries other than exposure to forces of nature, environmental heat and cold exposure, foreign body aspiration and in airway, in eyes or in other body part, falls, drowning, fire, heat, and hot substances, poisonings, exposure to mechanical forces, adverse effects of medical treatments or contact with venomous or non-venomous animal, [%]Mental disorders other than schizophrenia, depressive disorders, bipolar disorder, anxiety disorder, eating disorders, autism spectrum disorders, attention-deficit/hyperactivity disorder, conduct disorder or idiopathic development intellectual disability, [£]Neurological disorders other than Alzheimer's disease and other dementias, Parkinson's disease, epilepsy, multiple sclerosis, motor neuron disease, migraine and tension-type headache, [§]Drug use disorders other than alcohol, opioid, cocaine, amphetamine or cannabis use disorders.*

When deleting the perfect duplicates (n=36), i.e. health conditions with exactly the same label, it remained a list of 140 exclusive health conditions, 32 health conditions from the HIS, 30 cancers from the Belgian burden of disease study, 44 health conditions from GBD study, 20 health conditions from unmet needs RIZIV – INAMI list and 14 health conditions from SHARE (Figure 9).

From the 140 health conditions, 26 additional duplicates have been dropped. The label of those conditions was not exactly the same but expressed the same disease or health state.

From the 116 retained health conditions, we excluded 9 that were defined as "other category" because they did not allow for effective patient selection (i.e. other affective/emotional disorders, other cardiovascular and circulatory diseases, other drug use disorders, other fractures, other ill-defined digestive organs cancer, other mental disorders, other musculoskeletal disorders, other neurological disorders, other unintentional injuries). We also excluded 7 health conditions that were very general and not useful to select patients with highest unmet needs, i.e. cancer, falls, low back disorder, neck disorder, prostate problems, thyroid problems and unknown primary site cancer. A final list of 99 health conditions was retained (Figure 9).

Figure 9 – Selection of the health conditions with highest unmet needs

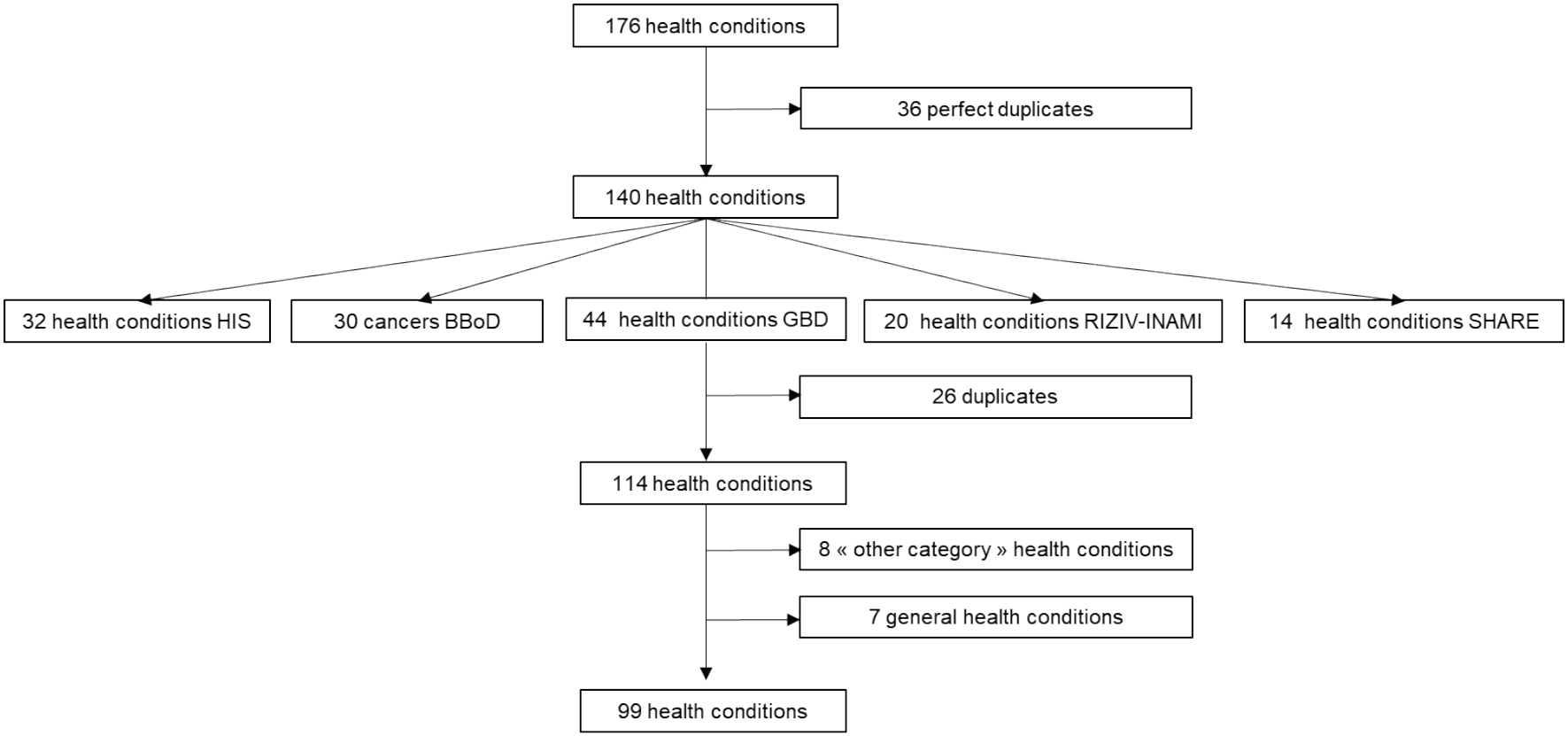


Table 22 presents the list of 99 health conditions with potentially high unmet needs in Belgium. The list is mainly driven by oncological (37 health states, 37.4%), neurological (9 health states, 9.1%) and acute care (8 health states, 8.1%) (Table 23). As highlighted before, conditions for which there are no or no effective treatments available to fully cure the patients and/or remove all disease-related symptoms are generally more likely to be in the top 20 of the list of unmet needs than conditions for which there are effective treatments. These are the conditions for which there is a high therapeutic need. As long as there is no effective treatment available, the healthcare focus will be more on care than on cure. Knowing and understanding the broader patient needs, besides the pure therapeutic need, then become particularly important to ensure patient-centred, value-based and high quality patient care.

Table 22 – Health conditions with potentially high patient needs in Belgium

Health condition	Health domain
Acid Sphingomyelinase Deficiency	Several
Acute graft versus host disease	Several
Age-related and other hearing loss	ENT
Allergy	Several
Alzheimer's disease and other dementias	Neurology
Amyloid light chain amyloidosis	Several
Amyotrophic Lateral Sclerosis	Neurology
Anxiety disorders	Psychiatry
Appendicitis	Acute care
Asthma	Several
Bipolar disorder	Psychiatry
Bladder cancer	Oncology
Brain and nervous system cancer	Oncology
Breast cancer	Oncology
Cataracts	Ophtalmology
Cervix uteri cancer	Oncology
Chronic bronchitis, COPD or emphysema	Pneumology
Chronic cystitis	Urology
Chronic fatigue for a period of at least 3 months in the past 12 months	Several
Chronic kidney disease	Nephrology
Colon and rectum cancer	Oncology
Corona Virus Disease 2019 (COVID-19)	Infectiology
Corpus uteri cancer	Oncology
Diabetes	Endocrino-diabetology
Diabetic retinopathy	Endocrino-diabetology
Disorder of the larger or the small bowel	Gastroenterology

Health condition	Health domain
Duchenne muscular dystrophy	Neurology
Edentulism and severe tooth loss	Dentistry
Epilepsy	Neurology
Extensively drug-resistant tuberculosis	Infectiology
Female genital organs, nos cancer	Oncology
Hemolytic disease and other neonatal jaundice	Hematology
High blood pressure	Cardiology/vascular
High cholesterol level in blood	Several
Hip fracture or femoral fracture	Orthopaedic
HIV/AIDS - Drug-susceptible Tuberculosis	Infectiology
HIV/AIDS - Extensively drug-resistant Tuberculosis	Infectiology
HIV/AIDS - Multidrug-resistant Tuberculosis without extensive drug resistance	Infectiology
Hypopharynx cancer	Oncology
Intracerebral hemorrhage	Acute care
Ischemic heart disease	Cardiology/vascular
Ischemic stroke	Acute care
Larynx cancer	Oncology
(Acute lymphoblastic) Leukemia cancer	Oncology
Lip and oral cavity cancer	Oncology
Lip, oral cavity and pharynx, nos cancer	Oncology
Liver and intrahepatic bile ducts cancer	Oncology
Locally advanced or metastatic solid tumours related to NTRK gene fusion in adult and paediatric patients	Oncology
Locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement	Oncology
Lower respiratory infections	Pneumology
Macula degeneration	Ophtalmology
Malignant melanoma of skin cancer	Oncology
Malignant neoplasms of skin cancer	Oncology
Maternal obstructed labor and uterine rupture	Acute care
(Malignant Pleural) Mesothelioma cancer (L2)	Oncology
Metastatic non-small cell lung cancer (NSCLC) with high, low or no PD-L1 (1L) expression	Oncology
Metastatic uveal melanoma	Oncology
Migraine	Neurology
Multidrug-resistant tuberculosis without extensive drug resistance	Infectiology
Multiple sclerosis	Neurology

Health condition	Health domain
Myelodysplastic syndromes	Oncology
Myocardial infarction	Acute care
Narrowing of blood vessels in belly or leg	Cardiology/vascular
Neonatal sepsis and other neonatal infections	Acute care
Neural tube defects	Neurology
Neuronal ceroid-lipofuscinosis type 2 (CLN2)	Neurology
Newly diagnosed glioblastoma	Oncology
Oesophagus cancer	Oncology
Opioid use disorders	Psychiatry
Osteoarthritis	Rheumatology
Osteoporosis	Rheumatology
Ovary cancer	Oncology
Pancreas cancer (BRCA+ or not)	Oncology
Paralytic ileus and intestinal obstruction	Acute care
Parkinson's disease	Neurology
Prostate cancer	Oncology
Psoriasis	Dermatology
Pyriform sinus cancer	Oncology
Recurrent Glioblastoma	Oncology
Recurrent and/or metastasized squamous cell carcinoma of the head and neck (SCCHN) with progression or after platinum-based chemotherapy	Oncology
Retroperitoneum and peritoneum cancer	Oncology
Rheumatoid arthritis	Rheumatology
Schizophrenia	Psychiatry
Selective and early debridement of deep burns in children	Acute care
Self-harm by other specified means*	Psychiatry
Serious gloom or depression	Psychiatry
Serious heart disease (except myocardial)	Cardiology/vascular
Stomach cancer	Oncology
Stomach ulcer	Gastroenterology
Stones in the kidney	Nephrology
Stroke (or consequences)	Neurology
Thyroid gland cancer	Oncology
Tracheal, bronchus and lung cancer	Oncology

Health condition	Health domain
Treatment of ≥3 lines of HER2-positive metastatic breast cancer (HER2+ mBC) after failure of trastuzumab emtansin (T-DM1)	Oncology
Ureter cancer	Oncology
Urinary incontinence	Urology
Urinary organs, nos cancer	Oncology
Uterus, nos cancer	Oncology
Vascular intestinal disorders	Cardiology/vascular

nos =not otherwise specified.

Table 23 – Number of health conditions retained by health domain

	Frequency	Percentage
Oncology	37	37.4%
Neurology	9	9.1%
Acute care	8	8.1%
Several	7	7.1%
Infectiology	6	6.1%
Psychiatry	6	6.1%
Cardiology/vascular	5	5.1%
Rheumatology	3	3.0%
Nephrology	2	2.0%
Gastroenterology	2	2.0%
Pneumology	2	2.0%
Endocrino-diabetology	2	2.0%
Ophtalmology	2	2.0%
Urology	2	2.0%
Dermatology	1	1.0%
Dentistry	1	1.0%
ENT	1	1.0%
Hematology	1	1.0%
Orthopaedic	1	1.0%

ENT= ears, nose and throat

6.4 Conclusion

We identified 10 national and 1 international data sources and initiatives that potentially include quantitative indicators of (HR)QoL or Summary Measure of Population Health (SMPH) with a HRQoL component (see Table 22). Among these, five (HIS, Belgian Burden of Disease (BeBOD), INAMI – RIZIV, SHARE, GBD) actually included these types of indicators.

Overall, very few national databases or initiatives included HRQoL or SMPH with HRQoL component indicators. Yet these types of population health indicators no longer need to demonstrate that they are a powerful tool for defining health priorities and more specifically, to identify patients with unmet medical needs. Although some national initiatives are in place (for instance the BeBOD study), Belgium is lagging behind compared to other European countries were these types of indicators are already well implemented (e.g. in the Netherlands).

The HIS, BeBOD and GBD included several HRQoL indicators, respectively two, two and three. By adding them with those of INAMI – RIZIV and SHARE, nine indicators were available to identify unmet needs for a total of 176 health conditions. After applying exclusion criteria, 99 health conditions with potentially high unmet needs in Belgium have been identified. The list is mainly driven by oncological, neurological and cardiovascular diseases.

This selection includes a significant number of limitations, among the most important, the various types of indicators used to make the list (DALY, QALY, YLD, etc). Other limitations are related to the exclusion of some people in the database (e.g. HIS and SHARE does not include less than 15 and less than 50 years respectively), the type of data collected (auto-reported data for HIS, SHARE), the area of the data collected (e.g. only oncological diseases for the BeBOD), the definitions of the diseases that are sometimes not specific enough, the rare diseases that are underrepresented in the databases, and the methods used to derive the indicators (e.g. GBD results are derived from data from other countries).

The results presented in the chapter have not been corrected for comorbidities (i.e. the co-occurrence of two or more diseases). Some researchers may argue that to set priorities and compare the impact of health conditions on HRQoL, a crucial issue would be to correct for underlying diseases. Indeed, some studies demonstrated that YLD estimations that do not account for multimorbidity can result in an overestimation of the impact of disease on population health.[125, 126] However, there are several issues when correcting for comorbidities in YLD estimation: the DWs need to be adapted and data on the prevalence (or incidence) of the disease have to be available. There are existing methodologies to adapt DW (additive approach, maximum limit approach, etc) but none is optimal and there is no scientific consensus on the best way to proceed. In addition, when adapting the DWs, prevalence or incidence data of all diseases individuals are suffering from have to be collected. These data should have to be collected from population-based health surveys but because of the large number of possible causes of ill health, it is impossible to measure *all* possible diseases in a population sample.[127] For the disease-specific disutilities (HRQoL loss), we think that by taking observed comorbidities into account the data give a more realistic representation of the burden of disease for patients in real life, as the disutilities presented in this report reflect utility loss in individuals with the specific disease compared to those without the specific disease. Since the HRQoL of an individual is the result of their complete mental and physical state, they also reflect observed comorbidities.

In 2018, the most costly and frequent services reimbursed by the SSF were: anakinra, chenodeoxycholic acid, cidofovir, cochlear implant, deflazacort, foscarnet, immunoglobulins, lutetium-octreotate (PRRT), oxybutinine, rituximab, thiotepa and treatment for Epidermolysis Bullosa patients. It is not possible to know the exact medical indication for which the treatment was reimbursed as this affects a very small number of patients. That said, it is a useful source of information to keep in mind when making choices about unmet medical and therapeutic needs for which a solution should be provided.

Key points

- **Few national databases or initiatives include Health Related Quality of Life (HRQoL) or Summary Measure of Population Health (SMPH) with HRQoL component indicators. We were able to identify four national databases/initiatives (Health Interview Survey (HIS), Belgium Burden Of Disease (BeBOD) study, INAMI – RIZIV unmet needs, SHARE) and one international database (Global Burden of Disease (GBD) study).**
- **The HRQoL or SMPH with HRQoL component indicators vary across databases which increases the difficulty of selecting the health conditions with the highest unmet needs.**
- **Ninety-nine health conditions with potentially high unmet needs in Belgium have been identified, the list is mainly driven by oncological, neurological, acute and psychiatric conditions.**
- **Conditions for which there is a high therapeutic need are generally more likely to rank high on the list of unmet patient needs than conditions for which there are effective treatments. As long as there is no effective (curative or symptom-relieving) treatment available, the healthcare focus will be more on care than on cure. Knowing and understanding the broader patient needs, besides the pure therapeutic need, then become**

particularly important to ensure patient-centred, value-based and high quality patient care.

- **Although it does not include HRQoL indicators, the Special Solidarity Fund (SSF) is an additional source of information to identify patients with unmet needs.**

7 DEVELOPMENT OF A GENERIC QUESTIONNAIRE FOR MEASURING PATIENT NEEDS

This chapter describes the development process of a generic questionnaire for measuring patient needs. The questionnaire is considered as a canvas for future, more condition-specific, patient needs questionnaires.

7.1 Aims

The aim of this part of the study was to

1. **Develop a generic questionnaire for measuring patient needs**, meeting two main requirements:
   - be sufficiently generic to allow applicability to a wide range of health conditions;
   - be accessible/comprehensible and not too 'resource' consuming (in terms of time, cost and/or people)
2. **Evaluate the strengths and weaknesses of the generic questionnaire to identify patient needs**, in terms of feasibility, relevance and appropriateness.

7.2 Methods

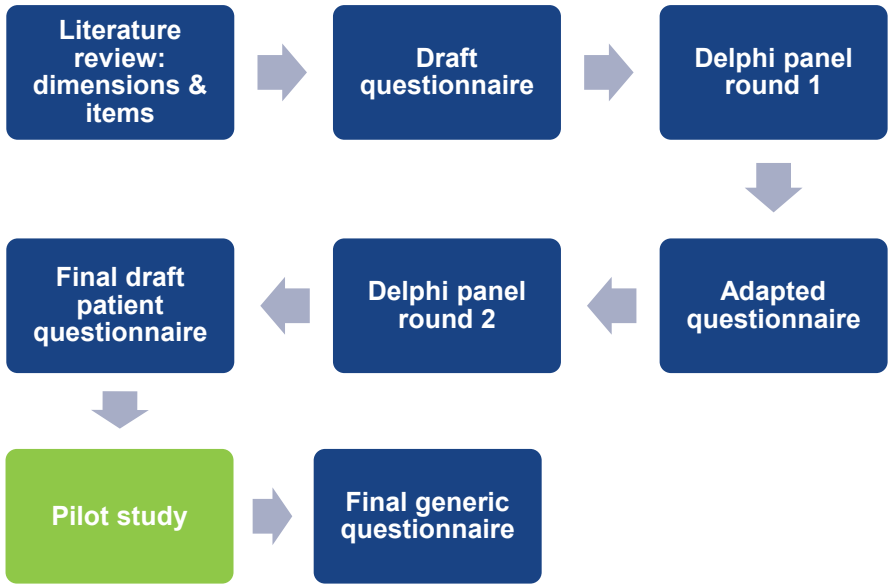
7.2.1 General approach

The first version of generic questionnaire was based on the domains of patient needs and related items identified from the literature (see Chapter 5). To evaluate and test the relevance, clarity and completeness of the questionnaire, we consulted patient representatives (from umbrella organisations of patient associations, sickness funds and the observatory for chronic conditions), through a 2-round Delphi panel. Then, we tested the final draft of the questionnaire during a pilot study (see Chapter 8) and

adapted the draft generic questionnaire based on the lessons learnt from that pilot test.

Figure 10 schematically presents the different steps in the development of the generic patient needs questionnaire. More details on each step are described below.

Figure 10 – Methods and steps used to developed the generic questionnaire



7.2.2 Identification of domains and items

The dimensions identified and included in the draft questionnaire were the following:

- *General information*: includes demographic characteristics of respondents in terms of gender, age and level of education;
- *General health status:* includes the respondents' evaluation of their health status 'at the present time' in general, both descriptive on five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and rated on a visual analogue scale (VAS), using the EQ-5D-5L generic health-related quality of life questionnaire. Each dimension has five response categories, reflecting the experienced level of problems: no problems, slight problems, moderate problems, severe problems, extreme problems. The VAS ranges from 0 (worst imaginable health state) to 100 (best imaginable health state). Additional information included in this dimension relates to co-morbidities, treatment(s) received; care needs patients did not receive and degree of satisfaction with current treatment;
  - *Physical dimension*: encompasses two sub-dimensions
    - *Symptoms:* experience of symptoms (a non-exhaustive list is proposed) in the past six months related to the condition and level of burden of these symptoms;
    - *Side-effects - attitude towards current treatment*: experienced medium and long-term side-effects of their current treatment(s), per treatment;
- *Psychological dimension - attitude towards the condition:* includes respondents' feelings of anger or fear about respondents' treatment(s) (e.g. fear of physical suffering);
- *Autonomy dimension - support network around the person:* relates to respondents' social support network (family or friends) for activities of daily living;

- *Independence & Activities:* relates to respondents' level of anxiety or disturbance during the last six months concerning their lack of autonomy and other difficulties encountered;
- *Social dimension:* encompasses three sub-dimensions :
  - *patient information:* level of information sought and received by patients, willingness to be involved in making choices about treatment;
  - *financial issues:* financial consequences of the condition;
  - *family and social issues:* need to find a trusted person to talk to, expectations towards family (e.g. need for more listening from the family, more support, understanding);
- *Accessibility of care:* includes the use of and access to care (as well as the level of satisfaction) and possible reasons for lack of access;
- *Spiritual dimension:* includes the need for spiritual or religious support.

Original questions from the instruments identified during the literature review were in some cases reformulated to meet the generic nature of the questionnaire. The draft questionnaire was submitted to an experts' panel, using the Delphi panel approach, consisting of patient representatives.

7.2.3 Consultation of patient representatives using a Delphi survey

7.2.3.1 Aim of the Delphi survey

The aim of the Delphi survey was to find consensus on the dimensions and items retained to assess patient needs, and, in particular, to reach consensus on the clarity and relevance of the questions asked and the completeness of the generic questionnaire.

7.2.3.2 Process

Participants

The Delphi panel consisted of patient representatives from umbrella organisations of patient associations (VPP, LUSS and RaDiOrg), sickness funds and the observatory for chronic diseases.

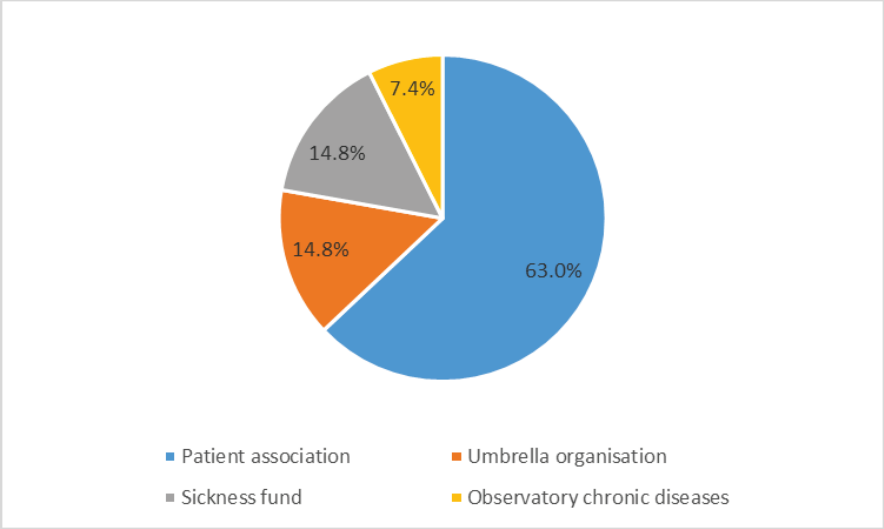
Recruitment of the Delphi panel

The call for participation in the Delphi survey was made by emailing the various directors and presidents of patient associations. All members of the Advisory Committee set up for this project were asked to participate as well (see Chapter 3).

Composition of the Delphi panel

As shown in Figure 11, patient organisations were predominantly represented (63%), followed by representatives of sickness funds and umbrella organisations in equal numbers (15%). Finally, the panel also included representatives of the Observatory for Chronic Diseases of the NIHDI (7%).

Figure 11 – Composition of the Delphi panel



Development of the Delphi survey

The draft questions to be included in the generic patient questionnaire were submitted to the panel in a first Delphi consultation round. A second Delphi round was organized for those items for which no consensus was reached in the first round. KCE decided to limit the Delphi process to two rounds to stay within an acceptable timeframe.

Each question was submitted to the panel in the following way:

- We present the question to be asked to the patient and the response categories, with their precise formulation (*We intend to ask patients the following question: "XXX?"…. We will propose the following answers:"XXX"*)
- We gather the panel's agreement on the inclusion of the question *("Do you agree with this proposed question?"*) with a possibility to grade their level of agreement (or disagreement) (*"Completely agree/ Rather agree/ Rather disagree/ Completely disagree"*)
- When relevant, we ask the panel if they want to add/change anything to the question or response categories (e.g "*Do you have any other categories of responses to suggest?"*)

The questions submitted to the Delphi panel for the two rounds are presented in Appendix 3.

Data collection process

An online platform (LimeSurvey) was used to collect the data from the Delphi panel. Two language versions, Dutch and French, were made available. To test the survey on understandability of the questions, and the user-friendliness of the platform, KCE team members pre-tested the online version in French and Dutch.

The first Delphi round was launched on 04/09/2020 and ran until 15/09/2020. The second round was launched on 09/10/2020 and ran until 23/10/2020. After the initial invitation, one reminder was sent to all invitees, one week before the deadline for completion of the questionnaire.

Analysis

Level of agreement

For questions requiring panel agreement, participants could choose between four response categories:

- Completely agree
- Rather agree
- Rather disagree
- Completely disagree

In line with previous KCE research[128], consensus was considered to exist when 75% or more of respondents 'completely agree' or 'rather agree' with the proposed question and when less than 10% 'completely disagree'. These thresholds are arbitrary because the Delphi approach as such does not impose specific thresholds, but we decided to use similar criteria as

used in previous KCE research, which was also supported by some published Delphi studies.[129, 130] Questions that achieved consensus on the basis of the above rule were not presented in the second round. Suggestions for improvements, rewordings or additions to the validated questions were taken into account in the final version of the questionnaire. In the second round, only the questions that did not reach consensus were revised and presented to the panel.

7.3 Results of the Delphi survey

7.3.1 Results of the first round

At the closure of the survey, 45 records of access to the survey were registered. Of these:

- Seventeen did not complete the questionnaire (n=13) or did not responded to all questions (n=4);
- One respondent was excluded because he did not indicate his/her name in the survey (yet necessary for the invitation to the second round);

Finally, 27 responses were analysed. Consensus was achieved for 29 out of 37 questions in the first round.

Table 24 shows the 37 questions for which consensus was requested from the panel and the associated level of agreement reached in the first round.

At the end of the first round, **eight questions** (i.e. about one fifth of the questions) had not reached consensus and were **submitted to the second round** (Q6, Q12, Q22, Q33, Q44, Q50, Q80, Q92). Q50 on anger or guilty feeling of patients towards family and friends reported the lowest agreement level (only 60 % agreement) (Table 24).

Table 24 – Level of agreement on the 37 questions included in the first Delphi round

Question	Question	Agreement	Total disagreement	CONSENSUS
Q2	We intend to ask patients the following question: "What is your gender?" We will propose the following answers: Male Female Other Do you agree with this question?	89%	0%	YES
Q3	We intend to ask patients the following question: "How old are you?" We will leave a field open for patients to indicate their age. Do you agree with this question?	93%	0%	YES
Q4	We intend to ask patients the following question: "How would you rate your general health?" We will ask them to choose from the following answers: Very good/Good/ Fair Bad/Very bad. Do you agree with this question?	88%	0%	YES
Q5	To assess the general health of patients in more detail, we will ask them to complete the questionnaire below (EQ-5D-5L). Do you agree with this approach?	81%	0%	YES
Q6	**We intend to ask patients the following question: "What disease(s) do you suffer from?" We will leave an open field for patients to indicate their answer. Do you agree with this question?**	**73%**	**0%**	**NO**
Q7	Do you agree with the proposed response mode (open field)?	77%	0%	YES
Q8	We intend to ask patients the following question: "What treatment(s) are you receiving for this disease(s)?" We will leave an open field for patients to indicate their answer. Do you agree with this question?	77%	0%	YES
Q9	Do you agree with the proposed response mode (open field)?	77%	0%	YES
Q10	We intend to ask patients the following question: "In the last six months, did you need health care that you did not receive?" We will offer them a choice of answers: Yes/No. If they answer Yes, we will ask them to specify the type of care and the reason why they did not receive it, including an open field. Do you agree with this question?	85%	0%	YES
Q11	Do you agree with the proposed response mode (open field)?	88%	0%	YES
Q12	**We intend to ask patients the following question: "To what extent do you feel that the medical care you receive meets your needs? We will offer the following answers: Very well/Good/Moderately bad/Very bad. Do you agree with this question?**	**69%**	**0%**	**NO**
Q16	We intend to ask patients the following question: "In the last six months, have you experienced any of the following symptoms related to your illness? How disturbing were these symptoms?" We will offer them a list of symptoms* and the following answers: Very disturbing/ Reasonably disturbing/ Not very disturbing/ Not at all disturbing/ Not applicable. Do you agree with this question?	85%	0%	YES

Question	Question	Agreement	Total disagreement	CONSENSUS
Q18	Do you agree with the types of physical symptoms proposed?	77%	4%	YES
Q22	**We intend to ask patients the following question: "Is your current treatment burdensome for you?" We will offer them the following response categories: Very burdensome/heavy/not burdensome. If the patient answers "Very burdensome" or "Burdensome", we intend to ask them "What is the reason(s)?" We will offer them an open field to state their reason(s). Do you agree with this question?**	**73%**	**0%**	**NO**
Q24	We intend to ask patients the following question: "Have you (had) any side effects from your treatment?" We will offer them the following answer categories: Yes/No. Do you agree with this question?	85%	0%	YES
Q25	If patients answer "Yes" to Q24, we intend to ask them the following question: "List the side effects you experience/have experienced, and indicate how much these side effects bother you in your daily life". We will provide a table for them to indicate for each side effect: Very bothersome / Reasonably bothersome / Not very bothersome / Not at all bothersome / Not applicable. Do you agree with this question?	81%	0%	YES
Q26	Do you agree with the proposed response mode (open field)?	100%	0%	YES
Q29	We intend to ask patients the following question: "Are you concerned about the long-term effects of your treatment?" We will offer them the following answers: Yes/No: If patients answer "Yes", we plan to ask them the following question: "What long-term effects are you most concerned about? "We will leave an open field for them to indicate their answer. Do you agree with this question?	77%	0%	YES
Q33	**We intend to ask patients the following question: "During the past six months, have you experienced any of the following symptoms*?" If so, please indicate how bothersome it was. Very disturbing/ Reasonably disturbing/ Not very disturbing/ Not at all disturbing/ Not applicable. Do you agree with this question?**	**69%**	**0%**	**NO**
Q40	We intend to ask patients the following question: "Do you have feelings of anger or fear about your illness and/or treatment (e.g. fear of physical suffering)?" We will offer them the following answers: Yes/No. Do you agree with this question?	77%	4%	YES
Q44	**We intend to ask patients the following question: "Is there help available for cleaning, cooking and shopping if you need it?" We will offer them the following answers: Yes/No/Not applicable. Do you agree with this question?**	**64%**	**0%**	**NO**

Question	Question	Agreement	Total disagreement	CONSENSUS
Q50	**We intend to ask patients the following question: "Do you have feelings of anger or guilt towards your family and friends?" We will offer them the following answers: Yes/No. Do you agree with this question?**	**60%**	**4%**	**NO**
Q53	We intend to ask patients the following question: "Do your family and/or friends agree with the way your care is organised?" We will offer them the following answers: Yes/No/Don't know/Not applicable. Do you agree with this question?	76%	8%	YES
Q57	We intend to ask patients the following question: "In the last six months, have you been anxious or bothered by the loss of your independence?" We will offer them the following answers: Very much/ Somewhat/Not at all/Not applicable. Do you agree with this question?	76%	0%	YES
Q58	We intend to ask patients the following question: "In the last six months, have you experienced any of the following difficulties[1]: ...". Patients will be given the opportunity to tick one or more boxes. Do you agree with this question?	84%	0%	YES
Q62	Do you agree with the proposed list of difficulties?	80%	0%	YES
Q64	We intend to ask patients the following question: "How clear is the information provided by your carers about what to expect regarding your illness and treatment? We will offer the following responses: Very clear/Reasonably clear/Not very clear/Not at all clear. Do you agree with this question?	80%	0%	YES
Q68	We intend to ask patients the following question: "Have you had one or more of the following needs in the last six months?" We will offer them the following list of needs[2] (...). Patients will have the possibility to choose several answers. If patients have answered that they needed information, we will ask them if they were satisfied with the information they received. Do you agree with this question?	84%	0%	YES
Q69	Do you agree with the proposed list of information needs?	80%	0%	YES
Q71	We intend to ask patients the following question: "Would you like to be more involved in making choices about your treatment?" We will propose the following answers: Yes/No/Not applicable. Do you agree with this question?	80%	0%	YES
Q72	We intend to ask patients the following question: "How much financial hardship does your disease cause you and/or your family?" We will offer the following answers: Very great/Reasonable/Not important/Not at all important/Not applicable. Do you agree with this question?	92%	4%	YES
Q76	We intend to ask patients the following question: "Do you find it difficult to find someone you trust to talk to? We will propose the following answers: Yes/No/Not applicable. Do you agree with this question?	92%	0%	YES

Question	Question	Agreement	Total disagreement	CONSENSUS
Q77	We intend to ask patients the following question: "In the last six months, have you felt any of the following needs[3]? We will ask patients to tick off one or more answers. Do you agree with this question?	92%	0%	YES
Q78	Do you agree with the proposed list of needs?	83%	0%	YES
Q80	**We intend to ask patients the following question: "In the last six months, have you encountered one or more of the following difficulties in accessing medical care (Availability/Geographical accessibility/Financial accessibility/Other (specify)); if so, to what degree (Great difficulty/Some difficulty/No difficulty/Not applicable)?" We will provide a table for them to indicate their answer(s). Do you agree with this question?**	**71%**	**0%**	**NO**
Q86	We plan to ask patients the following question: "In the last six months, how easy was it for you to get the care, tests or treatment you needed?" We will offer them the following answers: Very easy/Moderately easy/Not at all easy. Do you agree with this question?	75%	0%	YES
Q92	**We intend to ask patients the following question: "In the past six months, have you been distressed or bothered by unmet religious or spiritual needs?" We will offer them the following answers: A lot/Moderately/Not at all. Do you agree with this question?**	**67%**	**4%**	**NO**

**In order not to make the table too long, the list of symptoms can be found in Appendix 3. [1]Difficulty preparing meals or cooking/ Difficulty doing light housework/ Difficulty doing heavy housework (cleaning, making beds, gardening)/ Difficulty caring for children or babysitting/ Difficulty with transport (cycling, public transport)/ Difficulty shopping (food or clothes) Difficulty working or studying/ Loss of control over one's own body/ Loss of control over one's own life/ Difficulty filling the day/ Difficulty relaxing/ Difficulty asking for help/ Difficulty making own decisions Other (specify); [2]I needed more information about my diagnosis/ I needed more information about the evolution of my health condition/ I needed more explanations about treatments/ I needed more understandable information/ I needed more information about insurance issues (disability, reimbursement etc.)/ Other (specify); [3]I need more help than my family or other people can give me/ I need to feel more useful in my family, relatives, society?/ I need to talk to people who have the same experience as me/ I need to be reassured by my family, relatives*

7.3.2 *Main reasons for dissensus after the first Delphi round*

In this section, we focus on the eight questions that did not find consensus in the first round (Table 24).

The main reasons of disagreement are described in Box 11 to Box 18.

Q6 - "*What disease(s) do you suffer from*?" Open-ended question (**73% agreement**, see (Table 24).

Box 11 – Main reasons for disagreement on Q6 on other disease(s)

- The term "disease" is too restrictive and sounds too "somatic".
- Prefer the term "disease/disorder".
- Propose a list of diseases/disorders with an "other" category.
- Allow respondents to tick (several) boxes.
- Allow for the possibility of answering "no known diagnosis".
- Allow for the possibility of mentioning the precise name of the disease/disorder if it is known.
- Clarify that the question is about the diseases/disorders that the person currently has.

New proposal for Q6: "What disease(s) or disorder(s) do you suffer from? Here is a generic list of diseases/disorders from which you can tick more than one answer. Please also indicate the precise name of your disease(s)/disorder(s). If you do not know your diagnosis (yet), you can also indicate this." We will propose the generic list of diseases and disorders. As this list is not exhaustive, the choice "other" will also be possible, as well as the choice "no known diagnosis" for people who have not (yet) been diagnosed.

Q12 - "*To what extent do you feel that the medical care you receive meets your needs?*" The following answers were proposed: Very well/Good/Moderately bad/Very bad **(69% agreement**, seeTable 24).

Box 12 – Main reasons for disagreement on Q12 on unmet care needs

- Provide an answer that matches the wording of the question. If "to what extent" is used, the answer should be formulated in quantitative terms (a little, a lot, etc.).
- Harmonise the use of the terms "medical care" and "health care".
- Medical care" refers to somatic aspects, while "health care" is more general and also includes other forms of care (e.g. psychological support).
- Consider also the use of the words "follow-up" and/or "support".
- Clarify whether this refers to the care one is currently receiving, or the care one has received in general.
- Avoid the use of the word "needs" which is too vague and can be interpreted in different ways.

New proposal for Q12: "Are you satisfied with the care, follow-up and support you currently receive for your disease(s)/disorder(s)?" We will offer the following response options: Very satisfied / Satisfied / Moderately satisfied / Not at all satisfied.

Q22 - "*Is your current treatment burdensome for you?*" The following answers were proposed: Very burdensome/heavy/not burdensome. If the patient answers "Very burdensome" or "Burdensome", they were asked to precise the reason **(73% agreement**, seeTable 24).

Box 13 – Main reasons for disagreement on Q22 in the physical dimension

- Use the word "painful" instead of "burdensome".
- Suggest answering on a scale of 1 to 10 .
- Include the possibility to answer "no treatment".
- Add possibilities for intermediate answers (slightly, moderately, etc.) as in the other questions, to allow for more nuance Specify whether it is the treatment as a whole or its different components (in case of co-morbidities/multiple disorders/multiple treatments. Specify what is meant by treatment(s) (medical or other, reimbursed or not, etc.).
- For the sub-question "for what reasons", suggest a list of possible answers rather than an open field.
- Specify in which sense the word "burdensome" should be taken (financially, medically, psychologically?).

New proposal for Q22: "Do you have a treatment for one or more of your diseases/disorders?" If the patient answers yes, we will ask the following question: "How painful is this/these treatment(s) for you?" We will offer the following response options: Extremely difficult/Very difficult/Somewhat difficult/Not at all difficult. We propose to add a sub-question for people answering 'extremely, very or fairly difficult': "For what reason(s)" (side-effects force me to deal constantly with my illness/my treatment requires a very strict life discipline (timetable, hygiene...) other (specify)).

Q33 - "*During the past six months, have you experienced any of the following symptoms*?" The following answers were proposed: Very disturbing/ Reasonably disturbing/ Not very disturbing/ Not at all disturbing/ Not applicable **(69% agreement**, seeTable 24).

Box 14 – Main reasons for disagreement on Q33 in the psychological dimension

- The list of proposed symptoms is too short.
- Add: stress, anger, aggression, nervous tension, euphoria, irritability, feeling lonely, concentration problems, sadness.
- The distinction between fear and anxiety is not clear.
- The use of the word "symptoms" refers to an illness/disorder, whereas this question seems to be more about general well-being.
- Clarify this confusion, or combine the two questions on symptoms of illness.

New proposal for Q33: to combine this question with the question on symptoms/psychological problems (Mood changes; Fear/Anxiety; Feeling down or depressed; Stress; Anger/aggression; Tension; Euphoria; Feeling abandoned; Sadness; Irritability; Concentration problems...).

Q44 - "*Is there help available for cleaning, cooking and shopping if you need it*?" The following answers were proposed: Yes/No/Not applicable (**64% agreement**, seeTable 24).

Box 15 – Main reasons for disagreement on Q44 in the 'social support network'-dimension

- Add: "sometimes".
- Expand the type of support: personal hygiene, transport, financial support, mobility support, etc.
- Present the different types of assistance in the form of a checklist.
- Rephrase the question so that it is understood that the help needs are related to the disease/disorder.
- If the answer is "No", ask why this aid is not available.

New proposal for Q44: "Do you sometimes need help with basic activities of daily living because of your illness/disorder (e.g. personal hygiene, dressing, mobility, cleaning, eating, etc.)?" We will offer the following response options: Ye s /No. If the answer is yes, we will ask the following sub-question: "Is this help available?" (Yes/No). If the answer is No, we will ask for the reason(s) why this aid is not available (open field).

Q50 - "*Do you have feelings of anger or guilt towards your family and friends*?" The following answers were proposed: Yes/No (**60% agreement, 4% disagreement**, see Table 24).

Box 16 – Main reasons for disagreement on Q50 on feelings towards family and friends

- There is a lot of misunderstanding about this question; its purpose is not clear.
- Explain why it is being asked.
- Give the possibility to answer separately for family and friends.
- Or, on the contrary, mention them all together as "relatives" or "informal carers".
- Give the possibility to answer separately for anger and guilt.
- And why not also gratitude?
- Give the possibility to answer "sometimes" and "not applicable".

Proposal for Q50 to remove the question.

Q80 - "In the last six months, have you encountered one or more of the following difficulties in accessing medical care (Availability/Geographical accessibility/Financial accessibility/Other (specify)); if so, to what degree (Great difficulty/Some difficulty/No difficulty/Not applicable)?" A table will be provide to indicate the answer(s) (**71% agreement**, seeTable 24).

Box 17 – Main reasons for disagreement on Q80 in the 'accessibility of care'-dimension

- Harmonise the use of the terms "medical care" and "health care".
- Clarify the term availability: does it refer to physical accessibility, waiting time, availability of appropriate treatment, availability of competent experts or staff, etc.
- Allow for multiple responses/allow for clarification of which care(s) the responses relate to.
- Risk of collecting only bad experiences and therefore not giving a true picture of the situation.
- Risk of confusion with a very similar question earlier in the questionnaire.

New proposal for Q80: "In the last six months, have you experienced any difficulties in accessing health care? (definition of accessibility provided[p])". If yes, to what degree? We will propose a table[q] to indicate their answer.

Q92 - "In the past six months, have you been distressed or bothered by unmet religious or spiritual needs?" The following answers were proposed: A lot/Moderately/Not at all (**67% agreement and 4% disagreement**, seeTable 24).

[p] This definition is in Appendix 3

[q] Table available in Appendix 3

Box 18 – Main reasons for disagreement on Q92 in the spiritual and religious dimension

- I question the usefulness and relevance of this question.
- This need can be very diverse and difficult to quantify.
- If one does not feel any spiritual or religious need in general, is it "not at all" or should one add: "not applicable", because "not at all" can also correspond to a person who in general has such needs, but who has not had any in the last 6 months
- Same remark as above... to be rephrased.
- What is the added value of this question? Religious or spiritual? Why not more open? Ask for experience of meaning? Experience of the meaning of life or connectivity?
- Religion has no place in a scientific study.
- Do people understand 'spiritual' needs? What is it?

Proposal for Q92 to remove the question.

7.3.3 Results of the second round

At the closure of the online survey for the second round, 20 complete responses were received. The second round consisted of the eight questions for which no consensus was reached in the first round. Of the eight new proposals, half reached consensus.

Table 25 shows, for each question, the new proposal made to the Delphi panel and the level of agreement in the second round.

Table 25 – Level of agreement on the eight questions included in the second Delphi round

Question	New proposal	Agreement	Disagreement	CONSENSUS
Q6	**We intend to ask patients the following question: "What disease(s) or disorder(s) do you suffer from?" Here is a generic list of diseases/disorders from which you can tick more than one answer. Please also indicate the precise name of your disease(s)/disorder(s). If you do not know your diagnosis (yet), you can also indicate this. We will propose the generic list of diseases and disorders below*. As this list is not exhaustive, the choice "other" will also be possible, as well as the choice "no known diagnosis" for people who have not (yet) been diagnosed. Do you agree with this proposal?**	**65%**	**10%**	**NO**
Q12	We intend to ask patients the following question: "Are you satisfied with the care, follow-up and support you currently receive for your disease(s)/disorder(s)?" We will offer the following answers: Very satisfied Satisfied/Moderately satisfied/Not at all satisfied. Do you agree with this proposal?	80%	5%	YES
Q22	We intend to ask patients the following question: "Do you have a treatment for one or more of your diseases/disorders? If the patient answers yes, then we will ask the following question: "How painful is this/these treatment(s) for you?" We will suggest the following answers: Extremely difficult/Very difficult/Somewhat difficult/Not at all difficult. We propose to add a sub-question for people answering 'extremely, very or fairly difficult': "For what reason(s)" (side-effects force me to deal constantly with my illness/my treatment requires a very strict life discipline (timetable, hygiene...) other (specify)). Do you agree with this proposal?	80%	5%	YES

Q33	**We suggest that you combine this question with the question below by adding the following symptoms/psychological problems[1] (...). Do you agree with this proposal?**	**70%**	**10%**	**NO**
Q44	We intend to ask patients the following question: "Do you sometimes need help with basic activities of daily living because of your illness/disorder (e.g. personal hygiene, dressing, mobility, cleaning, eating, etc.)? We will offer them the following answers: Yes/No. If the answer is yes, we will ask them to answer "Yes": If the answer is Yes/No. If the answer is Yes, we will ask the following sub-question: "Is this help available?" (Yes/No). If the answer is No, we will ask for the reason(s) why this aid is not available (open field). Do you agree with the proposal?	80%	5%	YES
Q50	Remove the question	80%	5%	YES
Q80	**We intend to ask patients the following question: "In the last six months, have you experienced any difficulties in accessing health care? (see note below for definition of accessibility[2])". If yes, to what degree? We will propose a table below[3] for them to indicate their answer. Do you agree with this proposal?**	**65%**	**20%**	**NO**
Q92	**Remove the question**	**75%**	**15%**	**NO**

**In order not to make the table too long, the list of diseases can be found in Appendix 3*
[1]Mood changes Fear/Anxiety Feeling down or depressed Stress Anger/aggression Tension Euphoria Feeling abandoned Sadness, Irritability Concentration problems
[2]This definition is in Appendix 3
[3]Table available in Appendix 3

7.3.3.1 Remaining dissensus after the second Delphi round

In this section, we focus on the four remaining points of dissensus of the Delphi panel by exposing the main reasons for disagreement in Box 19 - Box 22. After this second round, we did not submit new proposals to the Delphi panel but directly implemented the suggestions in the questionnaire that was used for the pilot study. The final questionnaire is hence based on the suggestions from the second round *and* the lessons learnt during the pilot study.

- **Q6 b: "*What disease(s) or disorder(s) do you suffer from?"*** A generic list of diseases and disorders was proposed (participants can tick more than one answer). As this list is not exhaustive, the choice "other" is also possible, as well as the choice "no known diagnosis" for people who have not (yet) been diagnosed (**65% agreement and 10% disagreement**, see Table 25).

Box 19 – Main reasons for disagreement on Q6 on other disease(s)

- Leave the possibility to tick more than one box for rare diseases as the patient may have several
- Add "currently" to the list
- Complete the list: neurological disorders, developmental disorders, psychotic disorders, eating disorders, addiction problems, anxiety disorders
- Clearer, less complex formulation of diseases (give examples)
- Delete the term "mental illness" and replace it (psychological vulnerability or otherwise psychological problem).
- Do not give only two categories

- **Q33**: **During the past six months, have you experienced any of the following symptoms?"** A suggestion has been made to combine this question with the question Q44 b (Do you sometimes need help with basic activities of daily living because of your illness/disorder (e.g. personal hygiene, dressing, mobility, cleaning, eating, etc.)?) and by adding the additional symptoms/psychological problems **(70% agreement and 10% disagreement,** see Table 25).

Box 20 – Main reasons for disagreement on Q33 in the psychological dimension

- Keep a question about the patient's general psychological state that is not a symptom
- General well-being mentioned?
- Add psychotic symptoms (e.g. delusions, hallucinations), eating disorders, addictive symptoms
- Maintain the possibility of multiple responses

- **Q80: "I*n the last six months, have you experienced any difficulties in accessing health care*? A definition of accessibility will be available. *If yes, to what degree*?** A table will be proposed for the respondents to add their answers (**65% agreement and 20% disagreement**, see Table 25).

Box 21 – Main reasons for disagreement on Q80 on accessibility of care

- Anticipate the difficulty of travelling (availability and costs)
- Clarify some terms such as qualified care personnel
- Broaden the term to care provider and not only specialist
- Explain (vulgarise) the term geographical accessibility more clearly by nuancing and listing the different types of geographical accessibility. The same applies to waiting times, which can be linked to several factors. Explain also financial accessibility.
- People of low socio-economic status also find it difficult to access health care in other ways because it is complicated, requires a decent level of healthy literacy,
- The 'other' option is essential. for medical reasons, lack of guidance, lack of clarity about where care is available...
- There are differences in the accessibility of different types of care (very important in multi-systemic diseases). Take into consideration that this may exist.
- Unable to give a positive answer to the question on availability

- **Q92 - *"In the past six months, have you been distressed or bothered by unmet religious or spiritual needs?"*** A proposal had been made to delete the question (**75% of agreement and 15% of disagreement**, see Table 25).

Box 22 – Main reasons for disagreement on Q92 in the spiritual dimension

- Keep this dimension never addressed in the surveys
- Use the term resilience or level of spiritual or religious need
- Broaden the scope ("coping strategy")
- Focus the question on the meaning of life? The purpose of life

7.4 Intermediate version of the generic questionnaire before pilot testing

Following the second Delphi round, additional adaptations were made to the generic questionnaire, including:

- simplifying some questions for a better comprehension;
- giving examples when asking for comorbidities instead of using an open field;
- allowing for the selection of different response options instead of just one, in so far as patients could encounter several situations simultaneously (several comorbidities, several treatments, several reasons why a treatment is disturbing, several needs for help with daily activities; several reasons for unaccessibility of care);
- better identifying the person answering: individual patient responding for him/herself, parent responding for a child, informal caregiver or trustee responding for a patient who is not able to respond him/herself.

The intermediate version of the generic questionnaire encompassed nine dimensions (i.e socio-demographic information, general health, co-morbidities, physical and psychological symptoms, healthcare use and access, information, financial consequences, social support) covering 22 questions, and was organised as follows:

- Introduction: informing the patient about the aim of the survey, i.e. to identify their unmet needs in order to propose ways to improve their care and the eligibility criteria for participating in the survey. Eligibility criteria could for instance be: being affected by the condition under consideration or answering on behalf of a child or a person with the condition who is not able to answer the questions him- or herself. In the latter case, respondents are asked to answer *as if* they were the patient.
- *Data confidentiality and informed consent*: explanation of how the confidentiality of patient data is guaranteed, how the data will be processed (i.e. in accordance with the Belgian law of 30 July 2018 on the protection of individuals with regard to the processing of personal data and in accordance with Regulation (EU) 2016/679 of 27 April 2016, which entered into force on 25 May 2018, on the protection of individuals with regard to the processing of personal data and on the free movement of such data). Patient are informed that they have the right to request access to their personal data in order to rectify, delete, transfer or limit its processing, or to object to its processing. Informed consent is requested from patients before they can start filling out the questionnaire.
- *Identification of the respondent*: asks whether the respondent is completing the survey for him/herself or on behalf of someone else. For some conditions or some populations (e.g. children, illiterate patients, patients not familiar with or using modern (ICT) technologies), it is not possible to survey patients directly. We therefore foresaw the possibility that the questionnaire would be completed by a proxy. Instructions are provided on how to complete the survey if it is completed by a respondent on behalf of someone else.
- *General information*: collects general information on the patient, such as gender, age group, province of residence, level of education and employment status before the condition (paid work or not).
- *General health state* : collects data on respondents' health status before (if applicable) and after their condition, using the EQ-5D-5L[r] as quality of life instrument. The EQ-5D-5L asks respondents to describe their health 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

[r] https://euroQoL.org/eq-5d-instruments/eq-5d-5l-about/ (last access: 13 September 2021)

problems, extreme problems). In addition, respondents are asked to score their health state before (if applicable) and after their condition on a visual analogue scale (VAS), ranging from 0 (worst imaginable health state) to 100 (best imaginable health state).

- *Co-morbidities:* describing patients' comorbidities. For this purpose, a non-exhaustive list of the main conditions is proposed, as well as an open field, where respondents could mention other comorbidities that were not included in the list.
- *Physical and psychological symptoms*: collecting data on the physical and psychological symptoms experienced by the patients due to their their illness. A list of possible symptoms, as derived from a literature review and/or consultation with a patient association and/or healthcare professionals, should be proposed, but respondents should be able to add symptoms in an open field. For each symptom, they are asked how burdensome it is.
- *Use and access to care*: collects information on the use of and access to care and the level of satisfaction regarding the care received.
- *Treatments*: address the treatments together with their medium and long-term effects and the level of satisfaction with these treatment(s).
- *Information on the condition*: collects information on the information sought and received by patients, using a non-exhaustive list of possible topics of information, complemented with an open field. Another question on the wish of implication of the respondents was also asked.
- *Financial consequences*: addresses the financial consequences of the condition as well as their nature.
- *Support network around the patient*: collects data on the help needed with some activities of daily living (using a list of activities and an open field). Respondents are also asked by whom this help was provided (formal or informal caregiver).

Where relevant, patients are given the opportunity to give multiple answers. The questionnaire was first developed in French and is available in Appendix 3. The time required to complete the questionnaire was estimated about 15 minutes. The changes made to the generic questionnaire based on the results of the two Delphi panel rounds have been presented to the Advisory Committee in November 2020.

7.5 Lessons learned regarding the patient needs questionnaire

In this section we describe:

- the lessons learned from the Delphi panel, including feedback on the clarity and relevance of the questions, and
- the lessons learned from the pilot testing of the questionnaire in patients with long COVID[s].

The following key observations were made during the Delphi panel and pilot study:

1. Developing a patient needs questionnaire requires good prior knowledge of the condition under investigation. Therefore, a literature review and/or consultation with patient representatives and/or healthcare professionals will often be required;
2. Providing the possibility to let a proxy complete the survey on behalf of a patient is important;
3. A patient needs questionnaire can never be entire generic, adaptation of the questionnaire to the condition in question will always be necessary;

[s] The results of the study are summarized in Chapter 8.

4. It is necessary to be vigilant about the format of the questionnaire (paper or online), because some people may be incomfortable with modern (ICT) technologies;
5. For the recruitment of participants to a patient needs survey, an appropriate strategy should be developed for the dissemination of information about the existence of the survey;
6. Particular attention must be paid to the clarity and unambiguity of the questions;
7. Open-ended questions should be avoided in an questionnaire (and preferred in interviews or discussion forums) in order to facilitate quantitative analysis of the results and to avoid misinterpretation by the researchers.

We elaborate on each of them below.

1. Necessity of performing a literature review and/or consultation with patient representatives and/or healthcare professionals to collect knowledge about the condition

To develop a questionnaire on the needs of patients with a particular condition it is necessary to have sufficient knowledge of the condition, its symptoms and its treatments. In order to collect this information, a review of the literature might be helpful, complemented with consultation of patient representatives (preferably through an association if possible to benefit from collective knowledge about patients' experiences) and/or of health professionals who are familiar with the condition and see patients affected by it.

2. Providing the possibility to let a proxy complete the survey on behalf of a patient

Some populations or conditions cannot be studied if the possibility that the questionnaire is completed by a proxy is not provided. Therefore, this possibility is provided and clear instructions on how to complete the survey as proxy for a patient. The instructions are formulated as follows: "*Please answer all questions as if you were that person. For most questions, you can indicate "I don't know" if you don't know how the person would respond".* Moreover, for an adult patient, it is specified that "*The person you represent is not in a position to make an informed decision to participate at this time. By ticking this box, you are participating in this study based on their likely willingness to participate."*

Specifically children or minors, the instruction is completed by a statement "*By ticking this box you confirm that you are acting in accordance with the presumed wishes of the other parent of the minor you are representing and that you commit to informing him/her as soon as possible."*

With these instructions, we aim at reducing possible weaknesses of assessments by proxy. We are aware that these weaknesses cannot be overcome entirely, but consider it more important to be able to assess all types of conditions and patient populations than to obtain completely unbiased responses.

3. Applicability of the generic questionnaire

The generic questionnaire should never be applied as such, it should be used as a kind of template or basis for a condition-specific questionnaire. Therefore, adaptation to the particular condition under consideration and to the particular population will always be necessary to some extent:

- All **questions related to the specific condition should be made condition-specific**. In many cases, this is relatively straightforward (replacing 'your condition' in the general formulation by the name of the condition under consideration). In other cases, additional elements may need to be added to the questions, following and based on the literature review and expert consultation described in point 1. These elements may, for instance, relate to the overall management of the condition, specific treatments available, treatment side-effects etc.
- The question about the **patient's health status by means of the EQ-5D-5L *before* and *after*** the onset of the condition is generally not relevant for congenital disorders, for which there is no "before" and "after". This type of question is more relevant in the context of acquired conditions with an long-term or short-term impact on patients' health status in terms of mobility, self-care, usual activities and pain/discomfort after onset of the condition. It could apply both to

acute and chronic conditions, as acute conditions might have long-term sequelae (like acute COVID-19).

The merit of the generic questionnaire is, however, that it offers a canvas for the different topics and questions to be addressed and a generic formulation that has been validated by the Delphi panel.

4. The format of the questionnaire should be adapted to the patient population to be reached

The format chosen for filling in the questionnaire is also an important element, as it determines the participation of patients in the survey and might induce a selection bias. For example, if the online format is chosen, like in our pilot study, several difficulties may occur:

- depending on the age of the respondents or their level of comfort with computer tools, an online format might or might not be suitable;
- an online questionnaire might not reach populations who do not have easy access to the Internet, either by choice/lifestyle or because of their precarious situation.

5. The importance of the dissemination of information about the existence of the survey

It is often assumed that it is more difficult to reach the target population when there is no patient association. However, our experience with several means of communication to recruit participants (press conferences, social networks such as Facebook, contact with umbrella organisations) showed that it is possible to recruit a sufficiently large number of participants. Of course, our experience might be biased due to the fact that long COVID was a hot topic at the time of the study, with a lot of media attention. For less frequent conditions, it might still require additional efforts to recruit patients, especially when no patient associations are available. Collaboration with the umbrella organisations of patient associations, individual patients, sickness funds and healthcare providers might be needed in these cases.

6. The questionnaire should consist of clear and unambiguous questions

The Delphi panel highlighted on several occasions questions that were not clear or could be open for different interpretations. This feedback allowed us to modify these questions to make them more clear and unambiguous. Several questions that were originally open-ended (e.g. existence of co-morbidity(ies)) were replaced by a non-exhaustive list of possible answers (with the possibility to choose one or several answers by checking the associated box). An open field was still added to make sure patients could add an answer that was not included in the proposed list.

7. Responses options should be chosen such that they are easily exploitable/analysable by researchers without too much interpretation.

Response options should be chosen such that they are easily exploitable/analysable by researchers without personal interpretation. A non-exhaustive list of responses makes it easier for researchers to analyse the survey responses. At the same time, researchers in this field are well aware that in some cases they might not be able to create an exhaustive list that covers all possible responses, for instance when the symptoms of a condition or side effects of a treatment are very diverse across patients. Given the objective of the questionnaire, to collect information on patient needs we might not be aware of, open fields are often necessary. The drawback of open fields in a questionnaire is that patients can still give answers already included in the list of check-box responses. During the pilot study, this was particularly the case for symptoms or for specialists consulted. The difficulties encountered during the pilot study were:

- answers provided were difficult to interpret because they were too brief;
- responses contained more information than was requested, sometimes related to upcoming questions;
- combined questions (e.g. '*give a side effect'* AND 'say *how bothersome it was'*) were particularly difficult or impossible to analyse when the response option was an open field.

It is difficult to draw a lesson from this. On the one hand, providing an non-exhaustive list has many advantages, one of them being that it is easier for patients to respond to a question (they do not have to write something themselves), another relates to the ease of analysis of the responses (open field responses require recoding, which might be tricky in terms of interpretation).

On the other hand, not foreseeing an open field may leave the respondent unsatisfied if the response that he/she would give is not in the list while deemed very important. Also providing a list that is too long might put people off and result in drop-out. The challenge is to find the right balance between providing pre-defined answers and leaving room for own contributions.

7.6 Final generic questionnaire

In this section we present the final version of the generic questionnaire. The final generic questionnaire is available in Appendix 3.

Between the intermediate and the final version of the questionnaire, **some sections/dimensions remained unchanged** (n=7) because the pilot study did not reveal any issues with them. These sections/dimensions include:

- Data confidentiality and informed consent
- General health state
- Treatment burden/drawback(s)
- Accessibility of care
- Financial impact
- Support network around the patient
- Involvement in the choice of treatment(s)

For **seven other sections/dimensions, adaptations were necessary**. These included:

- General information on the questionnaire
- Information on the health condition
- Co-morbidities
- Symptoms
- Use of care
- Treatments

All adaptations are presented in Table 26 to Table 30, comparing the intermediate version (before pilot study) to the final one (after pilot study). Changes are represented in bold. The parts where changes have been necessary are:

7.6.1 Information box

The questionnaire starts with a box to inform the patients about the aim of the survey and the patient profile sought (Table 26). Several changes have been made to this information box:

- Wording
- Information on the subsequent steps after the survey
- Description of the eligibility criteria for participation
- Clarification of specific term(s) used in the questionnaire

Table 26 – Adaptations performed in the information box, intermediate vs. final version of the questionnaire

Intermediate version	Final version
Thank you for agreeing to participate in our survey.	Thank you for agreeing to participate in our survey.
We would like to use this survey to identify the needs of people with health problems due to *[name of disease]*. The aim of our study is to improve the care of these people.	**Our study aims to identify the needs of people with *[name of the condition]* in order to improve the care of these people.**
You can participate on behalf of a child or a sick person who is not able to answer the questions themselves. In this case, we will ask you to complete the questionnaire from that person's point of view.	**This questionnaire concerns you if :** • **if you are suffering or have been suffering from *[name of the condition]*** • **or if you are speaking on behalf of an adult with *[name of the condition]* who is unable to answer for him- or herself** **or if you are speaking on behalf of a minor with *[name of the condition]***
If you do not have *[name of the disease]*, you cannot fill in this questionnaire.	***[If necessary, clarification of specific term(s) used in the questionnaire]*.**
Before agreeing to participate in this survey, please read the following information about the confidentiality of your data and give your consent to the use of your data.	Before agreeing to participate in this survey, please read the following information about the confidentiality of your data and give your consent to the use of your data.

7.6.2 General information

The question on gender remained unchanged: Changes in this section concerned a clarification on the conditions to fill out the questionnaire and the age of the participants for which the response mode was changed from age ranges to a numeric field to encode the patients' year of birth. For the question about the place of living, the option 'I don't live in Belgium' has been added and several questions regarding the employment status has also been added to explore if the condition has an impact on working. The level of diploma has been more detailed and placed just after the question about the place of living (Table 27).

Table 27 – Adaptations performed in the general information section, intermediate vs. final version of the questionnaire

Intermediate version	Final version
You fill in this questionnaire: □ For yourself □ For another adult (please answer all questions as if you were the person)* □ For a child (please answer all questions as if you were the child)** * Due to his or her clinical situation, the person you represent is not currently considered capable of making an informed decision to participate. By ticking this box, you are participating in this study taking into account his or her likely wishes. ** By ticking this box you confirm that you are acting in accordance with the presumed wishes of the other parent of the minor you are representing and that you undertake to inform him/her as soon as possible.	You complete this questionnaire: □ For yourself □ For another adult (please answer all questions as if you were that person. **For most questions, you can indicate "I don't know" if you don't know how the person would respond**)* □ **For a minor** (please answer all questions as if you were **that minor**. **For most questions, you can indicate "I don't know" if you don't know how the person would respond**)** * **The person you represent is not in a position to make an informed decision to participate at this time. By ticking this box, you are participating in this study based on their likely willingness to participate.** ** By ticking this box you confirm that you are acting in accordance with the presumed wishes of the other parent of the minor you are representing and that you commit to inform him/her as soon as possible.
What is your age group? □ Under 18 years old □ 18-24 years old □ 25-44 years old □ 45-64 years old □ 65-74 years □ 75 years or older	**What is your year of birth?** ***[numeric field]***
In which province do you live? □ Antwerpen □ Limburg □ Oost-Vlaanderen □ Vlaams-Brabant □ West-Vlaanderen □ Brabant Wallon □ Hainaut □ Liège □ Luxembourg □ Namur □ Brussel/Bruxelles	In which province do you live? □ Antwerpen □ Limburg □ Oost-Vlaanderen □ Vlaams-Brabant □ West-Vlaanderen □ Brabant Wallon □ Hainaut □ Liège □ Luxembourg □ Namur □ Brussel/Bruxelles □ **I don't live in Belgium**
What is the highest degree or diploma you have obtained? □ No degree □ Primary education	What is the highest degree or diploma you have obtained **until now**? □ **No diploma / Primary education** □ **Lower secondary education**

Intermediate version	Final version
□ Secondary education □ Higher education of short type □ Higher education of the long type □ Postgraduate degree: doctorate □ Other	□ **Upper secondary education** □ **Higher education of the short type** □ **Higher education of the long type** □ **Other diploma: …….. (open field)** □ **I don't know**
Did you have a paid job before your *[name of disease]*? □ Yes □ No	Did you have a paid job before your *[name of the condition]*? □ Yes □ No **Have you been unable to work (= absent from work for more than one month) because of your *[name of the condition]*?** □ **Yes** □ **No** **If yes, are you back to work?** □ **Yes, I work again as before, the same number of hours per week** □ **Yes, but less than before** □ **No, because my state of health does not allow it** □ **No, for other reason(s): ……** **What is your main professional status?** □ **Worker** □ **Employee** □ **Self-employed** □ **Unemployed** □ **Student** □ **Retired** □ **Disability**

7.6.3 A specific section on the condition

To be able to put the responses of the patients in context, it is important to include a section on the duration of the patients' experience with the condition studied and diagnosis of the condition or any other information that might be relevant for the identification of patients' needs. This new section was added in the context of the pilot project as the research team was interested in:

- The diagnosis (or not) and the type of test performed ;
- The existence of persistent symptoms and their duration;
- Hospital stays and their duration;
- Intensive care unit stays.

In the final generic questionnaire, this is addressed as follows:

Since how long approximately do you have *[name of the condition]*?

- □ **Since birth**
- □ **Since [numeric field] week(s)**
- □ **Since [numeric field] month(s)**
- □ **Since [numeric field] year(s)**

For conditions experienced in the past that are no longer present, the question needs to be adapted to "Approximately for how long have you had [name of the condition]"

Have you, at any time, been diagnosed with *[name of the condition*] by a healthcare professional?

- □ **Yes**
- □ **No**
- □ **There was no diagnostic approach available at the time of my *[name of the condition*].**

Have you ever been hospitalised because of your *[name of the condition]?*

- □ **Yes**
- □ **No**
- □ **I don't know**

If yes, what was the duration (in days) of your last hospitalisation? *[numerical field]*

How many times have you been hospitalised in the last year (0 being possible)?

[numerical field]

Although the section on general health status remains unchanged, it should be noted that, depending on the health condition and if deemed relevant, the questions from the EQ-5D-5L could be asked twice, i.e. before and after the onset of the condition. In the case of long COVID, it was considered relevant to assess the impact COVID-19 and long COVID had on patients' HRQoL because the needs of patients might be correlated with this impact.

7.6.4 Other health problems

In this section, the phrasing of the question has been changed to make it more clear to respondents that the question relates to co-morbidities. In addition, some disease categories were rephrased (Table 28).

Table 28 – Adaptations performed in the 'Co-morbidities'-section, intermediate vs. final version of the generic questionnaire

Intermediate version	Final version
Do you suffer from another illness than *[name of the disease]*?	**Do you also suffer from any other health problem?**
□ Yes	□ Yes
□ No	□ No
□ I don't know	□ I don't know
If yes, here is a list of disease categories from which you can tick several responses. Please also indicate the precise name of your disease if you know it. If you do not (yet) know your diagnosis, you can also indicate this.	If yes, here is a list of health problem categories. You can tick one or more responses.
	Please also specify name of your condition if you know it.
	If you do not (yet) know your diagnosis, you can also indicate this.
	(several answers possible)
□ **Haematological (blood) and immune diseases** (more specifically: …..)	□ **Heart or blood vessel disease** (more specifically: …..)
□ **Endocrine, nutritional or metabolic disease** (more specifically: …..)	□ Respiratory tract disease (more specifically: …..)
□ **Mental and behavioural disorders** (more specifically: …..)	□ Digestive tract disease (more specifically: …..)
□ **Nervous system disease** (more specifically: …..)	□ Skin disease (more specifically: …..)
□ Disease of the eye disease and its appendages (more specifically: …..)	□ Disease of the locomotor system (bones, joints, muscles) (more specifically: …..)
□ Disease of the ear or vestibular system (more specifically: …..)	□ **Mental Health Disorder** (more specifically: …..)
□ **Circulatory tract diseases** (more specifically: …..)	□ Haematological (blood) or immune disease (more specifically: …..)
□ **Respiratory tract disease** (more specifically: …..)	□ Endocrine, nutritional or metabolic disease (more specifically: …..)
□ Digestive tract disease (more specifically: …..)	□ Nervous system disease (more specifically: …..)
□ Skin disease (more specifically: …..)	□ Eye disease and its appendages (more specifically: …..)
□ Disease of the locomotor system (bones, joints, muscles) (more specifically: …..)	□ Disease of the ear or vestibular system (more specifically: …..)
□ Disease of the genitourinary system (more specifically: …..)	□ Disease of the genitourinary system (more specifically: …..)
□ Other (more specifically: …..)	□ Multi-system disease (more specifically: …..)
□ No known diagnosis	□ Other
	□ No known diagnosis

7.6.5 Symptoms (physical and psychological)

The same questions and answers have been maintained but it seemed to be more relevant to adapt the list of symptoms according to the patients' condition (by adding specific ones). Moreover, to facilitate the analysis of the burden of the symptoms, we deleted the option to introduce free text under the response category 'other'.

7.6.6 Healthcare use and access to care

The questions relating to the healthcare use and access to care were, in the final version of the generic questionnaire, grouped into one single dimension. Concerning the access to care, the changes compared to the intermediate version concerned the formulation of the question and the restriction to 'access in the last 12 months' to avoid recall bias. Furthermore, as mentioned above, in order to facilitate the analysis of the results, the open field after the answer 'other' was removed. Other modifications concerned the type of specialists consulted (Table 29).

Table 29 – Questions/answers retained in the section 'Use of care' for the final generic questionnaire

Intermediate version	Final version
Did you not receive the care related to (name of the disease), which you needed for your disease? This could be treatment, consultation, medical tests, rehabilitation or other. ☐ **Yes** ☐ **No** If yes, for what reason(s)? □ Distance between home and place of care □ Transport problem (no public transport nearby, no personal vehicle, unable to drive your own vehicle, no one to take you to your care) □ Lack of competent staff to give you the care you need □ Very long waiting times □ Difficulties in paying for care □ Fear of medical tests, hospital or other □ Lack of time because of work, childcare or others □ Other reason (Specify ……)	**In the last 12 months, was there any care for your [name of your condition] that you did not get while you needed it?** This could be treatment, consultation, medical tests, rehabilitation or other. ☐ Yes ☐ No ☐ **I don't know** If yes, for what reason(s)? **(several answers possible)** □ Distance between home and place of care □ Transport problem (no public transport nearby, no personal vehicle, unable to drive your own vehicle, no one to take you to your care) □ Lack of competent staff to give you the care you need □ Very long waiting times □ Difficulties in paying for care □ Fear of medical tests, hospital or other □ Lack of time because of work, childcare or others ☐ **Lack of information** ☐ **Other**
What types of care providers have you been in contact with as part of your *[name of the disease]*? (several answers possible) □ General practitioner	What types of care providers have you been in contact with due to your *[name of the condition]*? (several answers possible) □ General practitioner □ Emergency Department Team

□ Emergency Department Team □ Team of a revalidation centre □ Hospital □ Psychologist □ Psychiatrist □ Physiotherapist □ Specialist doctor □ Other (specify……) □ Other (specify……) □ Other (specify……)	□ Team of a revalidation centre □ Physiotherapist □ **Nurse at home** □ Psychologist □ **Logopedist** □ **Social worker** □ **Specialist doctor** □ **Cardiologist** □ **Pneumologist** □ **Gastroenterologist** □ **Rheumatologist** □ **Specialist in Physical Medicine and Rehabilitation** □ **Neurologist** □ **Psychiatrist** □ **Infectious Disease Specialist** □ **General Internist (General Internal Medicine)** □ **Geriatrician** □ **Pediatrician** □ **Nose, Throat and Ear (ENT) Specialist** □ **Ophthalmologist** □ **Dermatologist** □ Other
How satisfied are or have you been with their services? □ Very satisfied □ Satisfied □ Moderately satisfied □ Not at all satisfied	**(For each type of provider) Please indicate how satisfied you are / were with their services.** □ **Very satisfied** □ **Satisfied** □ **Slightly satisfied** □ **Not satisfied**

7.6.7 Treatment

In the “Treatment”-dimension, the final generic questionnaire distinguishes between prescribed and over-the-counter medicinal treatments as well as supplements such as vitamins, homeopathy, naturopathy, etc. (Table 30).

The question in the intermediate version on the level of satisfaction with patient follow-up was removed as it appeared to be redundant with the question on the level of satisfaction of health professionals. Questions relating to the burden of treatment and adverse effects have also been modified.

Table 30 – Questions/answers retained in the section 'Treatments' for the final generic questionnaire

Intermediate version	Final version
Are you receiving treatment (medication or other) for your *[name of the disease]*? □ Yes □ No □ I don't know If yes, which treatment(s) and how satisfied are you with this/these treatment(s) (several answers possible)? □ Very satisfied □ Satisfied □ Moderately satisfied □ Not at all satisfied	**Are you taking (or have you taken) any treatment for your *[name of the condition]*?** □ Yes □ No □ I don't know If yes, which ones and with what degree of satisfaction? □ **A prescription drug** □ **An over-the-counter medicine** □ **Physiotherapy** □ **Surgical intervention** **Per indicated response:** □ **Very satisfied** □ **Satisfied** □ **Slightly satisfied** □ **Not satisfied**
How burdensome is the treatment you receive to treat (name of the condition)? □ **Extremely** burdensome □ **Very** burdensome □ **Quite** burdensome □ **Not** burdensome **at all**	How burdensome is/**was** the treatment(s) you receive/**have received** for your ***[name of the disease]***? □ Very burdensome □ Quite burdensome □ Slightly burdensome □ Not burdensome
If extremely burdensome, very burdensome and somewhat burdensome, for what reason(s)? □ Because of the side effects □ it requires me to constantly deal with my illness/treatment □ it requires a very strict life discipline (schedules, hygiene...) □ other (specify).....	If extremely burdensome, very burdensome and somewhat burdensome : For what reason(s)? (several answers possible) □ Because of the side effects □ Because it forces me to constantly deal with my illness/treatment □ Because it demands a very strict life discipline (timetable, hygiene...) □ **Because I have been on the treatment(s) for a long time** □ Other

Does your treatment for (name of condition) cause or has it caused you any adverse effects?

□ Yes
□ No
□ Don't know

If yes, please list the side effect(s) and indicate whether they are bothersome.

	Very disturbing	Reasonably disturbing	Not very disturbing	Not at all disturbing
….				
….				
….				

If you experience(d) any side effects when treating your *[name of the condition]*, indicate to what extent each of these are/were disturbing.

	Very disturbing	**Rather disturbing**	**Slightly disturbing**	**Not disturbing**
□Headache				
□Nausea and/or vomiting				
□Constipation and/or diarrhoea				
□Fatigue or exhaustion				
Table to be adapted depending on the condition under consideration				

Are you satisfied with the follow-up and support you currently receive for *[name of the disease]*?

□ **Very satisfied**
□ **Satisfied**
□ **Moderately satisfied, why ?.....**
□ **Not at all satisfied, why ?.....**

This question was removed because already covered by question on satisfaction with healthcare provider services.

7.6.8 Extra box

An extra open field box was added in the final version to allow patients to add needs they had not been able to express in the other questions. Therefore, the following question was added:

Are there one or more other important needs that you were unable to express in the questionnaire?

□ **Yes**

□ **No**

If, yes, which one(s) ? (open field)

……..

8 PILOT STUDY

8.1 Aim

To test whether our general methodological approach was able to identify patient needs in a real life situation, we performed a pilot study in a specific patient population in on specific patient population.

8.2 Method

The pilot study encompassed **four phases**:

1. the choice of a particular health condition and patient population;
2. the **adaptation of the data collection approach** to the population of interest, including the data collection tools;
3. the **data collection phase**, triangulating three methods, i.e. an online survey, individual interviews and an asynchronous online discussion forum; and
4. the **data analysis phase**.

We concluded the pilot study with a methodological reflection (see chapter 9) to assess the appropriateness and feasibility of the proposed overall methodological approach to identify patient's needs.

8.2.1 Choice of a particular health condition and patient population

We decided to test our approach with patients who developed long-term health problems after COVID-19 (i.e. "long COVID"). The choice for this patient population was made for the following reasons:

- KCE received a request from the patient umbrella organisation LUSS to carry out a study on patients with long COVID. Therefore, it seemed relevant and efficient to test our approach while meeting the objectives of another KCE study;
- the population of long COVID patients is potentially large, allowing to test the online forum with a sufficient number of participants. Online fora for qualitative data collection is relatively new. The application in the pilot study would allow to test the advantages and disadvantages of this approach.

8.2.2 Adaptation of the data collection approach

8.2.2.1 Online survey

Aim

The aim of the online survey was to investigate the characteristics and (unmet) needs of people who developed long-term health problems after COVID-19 (called 'long COVID').

Questionnaire development

Adaptation steps

To adapt the generic questionnaire to the particular population of patients suffering from long COVID, we undertook the following steps:

- We adapted the items and the questions to the scope and objectives of the study context;
- We did a quick scan of the literature on patients' experiences with long COVID (see references);
- We performed a pragmatic review about the epidemiology of long COVID (definition; prevalence; range and frequency of symptoms; risk factors);
- The questionnaire, initially developed in French, has been translated to Dutch by KCE researchers. A detailed comparison of the two versions was carried out to ensure that both versions were identical in terms of structure and content;

- Subsequently, both versions were proofread by KCE team members, two representatives of the patient umbrella organisations (one French-speaking from LUSS and one Dutch-speaking from VPP) and a researcher from Sciensano;
- The two language versions were imported in an online platform (LimeSurvey). In order to pre-test the survey on understandability of the questions and the user-friendliness, five non-scientific citizens with different ages and backgrounds in terms of education and socio-economic status were recruited for this pre-test. The online questionnaire was adapted based on their feedback;
- Finally, KCE team members pre-tested the online versions in French and Dutch.

Before launching the questionnaire, the research protocol, including the questionnaire, was submitted to and approved by the ethical committee of the 'Cliniques Universitaires de Bruxelles' (P2020/704 / B40620200000319). The approval was valid from 15/01/2021 till 30/11/2021.

Content

The final questionnaire consisted of 33 questions, organised around the following five main topics:

- *General information*: a distinction was made between people who were answering for themselves, for another adult (unable to answer the questionnaire him/herself) or for a minor. The other questions in this section related to demographic characteristics of the respondents: gender, age, place of residence (province), level of education and employment status (paid employment, disability, health sector employment);
- *Acute episode of COVID-19*: this section was designed to provide information on the respondents' experience during the acute phase of COVID-19: how and by whom they were diagnosed; whether they were hospitalised (general COVID or on intensive care unit; with or without ventilation) and the duration of their hospitalisation; presence and duration of COVID-19 symptoms;
- *General health status*: this section aimed at comparing respondents' health status before and after COVID-19[t], using the EQ-5D-5L[u] as quality of life instrument. The EQ-5D-5L asks respondents to describe their health status on five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each item had five response categories, reflecting the level of problems experienced in each dimension (no problems, slight problems, moderate problems, severe problems, extreme problems). In addition, respondents are asked to score their health state before and after COVID-19 on a visual analogue scale (VAS), ranging from 0 (worst imaginable health state) to 100 (best imaginable health state);
- *Other illnesses*: the aim of this section was to find out whether respondents had comorbidities and if so, which one(s). For this purpose, a non-exhaustive list was proposed, as well as an open field, where respondents could mention other comorbidities that were not included in the list;

Long COVID: the questions in this section aimed at describing the physical, psychological and care consequences of long COVID. The questions addressed the symptoms (physical and psychological) experienced by the respondents; the use of and access to care; the

[t] The generic questionnaire did only foresee to question the health status once. Since long COVID is preceded by an acute phase the health status might have changed rapidly. Therefore it was decided to ask the current perceived health status as well as the health status before COVID-19.

[u] https://euroQoL.org/eq-5d-instruments/eq-5d-5l-about/ (last access: 18 June 2021)

financial consequences of long COVID; the level of information sought and received by the respondents; social support network around them and the treatments together with their medium and long-term effects. Table 31 gives an overview of the adaptations made to the generic questionnaire to make it long COVID-specific.

Table 31 – Adaptations from the generic questionnaire

Generic questionnaire	Long COVID questionnaire
9 dimensions	10 dimensions
22 questions	33 questions
Generic introduction: • General questionnaire	Adapted introduction: • Explaining context of survey • Purposes of the survey
Generic questions	Condition-specific questions (e.g. using "long COVID" instead of "your condition")
Generic response categories	Adding condition-specific response categories (e.g. specific symptoms)
	Adding long COVID-specific questions to meet survey objectives

For most questions, respondents were given a choice of answers (often based on the literature) but they were also given the opportunity to add elements in an open field. For several questions, respondents were asked to indicate their level of satisfaction. In many cases, responses to specific questions led to sub-questions (e.g. when the respondent indicated 'Yes', he/she had to specify his/her answer).

At the end of the questionnaire, participants were asked if they were willing to participate in the online discussion forum or an individual face-to-face interview.

The entire questionnaire submitted is available in Appendix 4.

Participants

Respondents had to meet the following criteria to be eligible for participation in the survey:

- been infected with COVID-19 (self-declared or based on a test);
- not or no longer being hospitalised at the time of the survey;
- having, at the time of the survey, long COVID symptoms or having had COVID symptoms for more than 4 weeks after the onset of COVID-19;
- living in Belgium.

When the respondent represented another adult (who met the inclusion criterion but was unable to respond his- or herself because of his/her health condition) or a minor who met the inclusion criteria, he/she had to respond *as if* the patient he/she represented would answer the questionnaire.

Recruitment of the participants

Several communication channels (KCE website, e-mailing, social networks and general media, long COVID patient support groups) were used us to reach the target population of our study. The call for participation included a link to a page on the KCE website, where the same text was available and the link to the survey and informed consent was accessible. Patients who recognised themselves in the description of the call for participation could directly access the online survey via the link on the KCE webpage. In addition, we have asked the sickness funds, the umbrella organisations of patient associations (LUSS and VPP) and the general media (press conference, COVID-19 crisis centre) to share the information.

8.2.3 Data collection

The online survey was launched in Limesurvey on 27/01/2021 and ran until 14/02/2021.

8.2.4 Data Analysis

Open field responses were analysed using thematic coding and afterwards recoded into existing categories where possible. For reported comorbidities, for example, open-ended responses were merged with existing categories (i.e. categories proposed in the online questionnaire) and if not possible, new categories were created based on the literature and/or after consultation of researchers. In addition, comments that did not really relate to the question posed were classified as 'Not applicable'.

Afterwards, statistical analysis had been performed. Detailed method and results are available in the KCE report 344.[131]

8.2.4.1 Qualitative approach

Aim

In this section, we describe the qualitative approach that aimed at deepening the understanding (based on the online survey – see Chapter 7) of the patients' perspectives on the management of long COVID and of their needs. This qualitative approach is complementary to the online survey.

Methods

Participants

Participants were recruited from the respondents to the online survey. This choice was made because long COVID is an umbrella term, including a heterogeneous patient population without clear clinical criteria and covering all age groups. In addition, at the time of the study recruitment the healthcare services covering the care for these patients were (if available at all) unclear, not allowing to recruit patients via contacts with healthcare professionals. The respondents to the online survey (see Chapter 7) were offered the opportunity to participate in either an online forum or an individual interview.

The use of different qualitative data collection methods had the aim of increasing the participation rate, cover a wide range of patient profiles and limit the selection bias due to (lack of) digital literacy and/or (aversion to) written communication. It also allowed to assess and compare the advantages and disadvantages of two different qualitative data collection techniques, one in which the experience of the KCE team is broad (i.e. interviews) and one that is relatively new to us as a data collection tool (i.e. online forum).

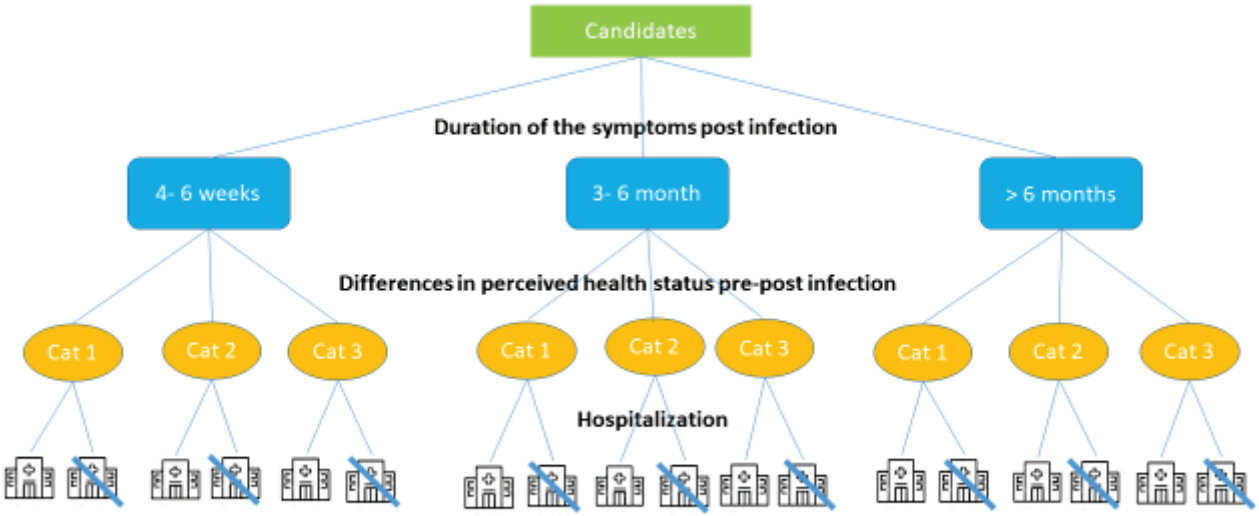
Selection of the participants for the interviews

We planned to conduct a maximum of 36 individual interviews, 18 in French and 18 in Dutch. In order to achieve a maximum of variation in respondent profiles, the researchers prioritised the recruitment of participants who agreed to participate to the interview from each language group according to the following segmentation criteria.

- Duration of symptoms since onset of acute COVID-19: short: 4-12 weeks / mid: 3-6 months / long: > 6 months;
- Difference in perceived health-related quality of life score on the visual analogue scale (VAS) before and after COVID-19, divided into tertiles
- Hospitalisation during acute COVID-19 phase versus no hospitalisation.

We excluded patients who had been admitted to the intensive care unit, to avoid bias in the results due to symptoms and needs related to the post-intensive care syndrome rather than to long COVID.

Figure 12 – Segmentation of the candidates for interviews



In each segment of the online survey (Figure 12) participants registering for the interview, maximum 3 participants were randomly selected: one effective and 2 substitutes (if available).

Selection of the participants for the forum

Online fora have the advantage that they can include larger sample sizes than face-to-face research, which allows researchers to gain access to a wider range of experiences. However, some researchers prefer smaller groups to stay true to the aims of qualitative research and gain a deeper understanding of the experiences of a smaller sample of people.[132] We decided to limit the number of participants in the forum to 200 (100 in the French forum and 100 in the Dutch forum) to allow for a realistic management of the forum posts (e.g. interaction, surveillance on respecting the pre-defined rules, etc.) with regard to the means allocated to the research.

It was foreseen that in case too many people wanted to participate in the forum, the researchers could select patients in order to obtain a balanced sample. The following criteria were used to make the selection (if required):

the duration of the symptoms (4-12 weeks / >12 weeks), whether or not they were hospitalised, and whether or not they were active in the labour market before their illness. In addition, it was foreseen to further balance the sample for gender, age and place of residence (province).

Contact procedure

Participants selected to participate in the interviews first received a phone call to confirm whether they were still willing to participate and to schedule the interview. Once they agreed, they received the confirmation and informed consent form by e-mail. In this email they also had access to an explanation of the login procedure via Zoom® and a video explaining how to sign the informed consent with Adobe® sign.

If participants changed their mind or if they did not respond to three phone call attempts, the substitute with the same profile (if any) was contacted. Candidates who were not selected were contacted by e-mail to explain the reason for exclusion or to place potential participants on a back-up list in case of withdrawal or need to contact specific additional profiles (according to the first analysis of the material, in order to ensure data sufficiency).

The participants selected to participate in the forum received an email confirming their selection one week prior to the launch of the forum, together with the explanation on how to connect to the forum.

Data collection

Data collection tools

The topics covered during the interviews and the forum were derived from a literature review on the unmet needs of patients with long COVID[133-138], social networks discussions and the main concerns reported by the participants in the online survey.[131]

The **interview guide** was first developed in French and afterwards translated to Dutch by KCE researchers. A comparison of the two versions was carried out to ensure that both versions were identical in terms of structure and content. Subsequently, both versions were proofread by team members and two representatives of patient umbrella organisations (one French-speaking from LUSS and one Dutch-speaking from VPP).

The final interview guides are presented in Appendix 4. They cover the following topics:

- Perceived health status before COVID-19
- Symptoms of long COVID
- Diagnosis and treatment of long COVID
- Information and support network
- Relationships with the medical profession
- Long COVID and work
- Social and family relations

The forum was conducted via the **Moodle ™ platform**.

Several actions were undertaken to ensure the effective functioning of the forum:

- The establishment of a charter of good behavior to be signed by participants before accessing the discussion forum (like the inform consent).
- The possibility to communicate with another forum participant on a one-by-one basis was removed from the MoodleTM platform as part of this project. The reason for this was twofold: first, we wanted to focus on the discussions that were regulated by the two moderators; and second, we wanted to avoid that important information exchanged between forum participants could not be captured by the KCE researchers and moderators.
- The use of a generic e-mail address dedicated to KCE forums (forum@kce.be) to centralize communication between KCE researchers and forum participants.
- Via the generic email address, a weekly e-mail was sent to all participants to stimulate their participation and to inform them if a new theme was launched on the forum.

- The possibility for moderators to delete or anonymize information such as telephone numbers, names and addresses of healthcare providers or facilities.

The moderators and research team received training in forum facilitation and moderation from an external company (Tree Company).

The **topic guide for the forum** was developed based on the interview guide. The following six themes were proposed to participants:

- Theme 1: Symptoms of long COVID
- Theme 2: Diagnosis and Treatment of long COVID
- Theme 3: Information and support network
- Theme 4: Relationships with medical professionals
- Theme 5: Long COVID and work
- Theme 6: Social and family relations

The 7th and final theme concerned the participants' most important needs.

DEVELOPMENT

For each theme, one or more open-ended questions were foreseen. These were written in French and translated into Dutch by a Dutch-speaking researcher from the team. Questions were discussed within the team to judge their relevance and clarity in both languages. The two moderators then had the chance to familiarize with the different themes. In addition, in order to facilitate moderation, the research team proposed stimuli questions to the moderators.

PRE-TEST

In a first step, the themes and associated questions were discussed.

In a second step, the themes were implemented in the online version via the Moodle platform. KCE researchers, the moderators and the trainer (Tree Company) tested it using every forum's user profile (participants, moderators, administrators).

The online forum was then adapted according to the comments to get a final version.

FINAL DISCUSSIONS TOPICS

Table 32 summarises the different retained themes and their related sub-topics. The full questionnaire is available in Appendix 4.

Table 32 – Final themes and associated sub-topics

Themes	Sub-topics
Theme 1: Symptoms of long COVID	Most disturbing symptoms
Theme 2: Diagnosis and treatment of long COVID	Difficulties with diagnosis Difficulties with treatment Unresolved symptoms Use of alternative, non-conventional treatments
Theme 3: Information and support network	Difficulties in finding information Missing information Impact of missing information Searching for missing information
Theme 4: Relationships with medical professionals	Relationships with caregivers and healthcare professionals
Theme 5: Long COVID and work	Difficulties at the professional level
Theme 6: Social and family relations	Impact of long COVID on social and family relationships
Essential needs	

Data collection process

Due to the sanitary context of the COVID-19 pandemic we had to organise the data collection in a safe ('remote') way. Therefore, **interviews** were organised via an electronic format.

Interviews were conducted via Zoom© by 2 French-speaking researchers and by two Dutch-speaking researchers. The interviews lasted 1 to 1.5 hours.

Each interview was recorded and transcribed verbatim by an external company. All names of participants, institutions or care providers were removed during transcription.

For the **forum**, the participants received an email informing them that the online forum was open on the day the forum was launched.

To access the forum questions, potential participants had to confirm informed consent after registering on the platform.

The different themes of the forum were opened one after the other according to a predefined schedule (Table 33). For asynchronous online fora, the study duration depends on the speed of the discussions.

"Williams identified asynchronous online focus group studies ranging in duration from one to twenty-four weeks (mean study duration was nine weeks)." (Williams, 2012, p. 376[132]) with an average duration of four weeks. The study duration also depends on the intensity of the interactions.[132] Given the time constrains, the forum remained open for just over three weeks.

Table 33 – Calendar of the online forum

Date	Action
1st of March 2021	LAUNCH OF THE PLATFORM Theme 1: Treatment of long COVID-19 Theme 2: Symptoms of long COVID-19
8th of March 2021	Theme 3: Information and support network Theme 4: Relationships with the medical professionals
15th of March 2021	Theme 5: Long COVID and work Theme 6: Social and family relations
19th of March	Essential needs
26th of March	Closure of the online forum and sending of a 'satisfaction' survey for participants and non-participants

The discussions on the forum have been moderated by a collaborator from the two largest Belgian umbrella associations of patients organisations, i.e. the "Ligue de Usagers de Soins de Santé" (LUSS) for the French-speaking part and the "Vlaams Patiëntenplatform" (VPP) for the Dutch-speaking part.

The KCE researchers and moderators communicated about the forum throughout its duration via a Teams group, set up as a support platform specifically for this purpose. In addition, ad hoc meetings were organised to discuss the way the forum works, and potential issues.

Data analysis

We performed a qualitative thematic inductive analysis on the transcripts of the interviews and the export of the discussions of forum using NVIVO software which allows structuring the collected information and facilitates the analysis by the researchers.

All the French-speaking material (transcripts of interviews and export of the discussion of the forum) was coded by one native French-speaking researcher and all the Dutch-speaking material by two native Dutch-

speaking researchers. The three researchers met several times to build a final common nodes tree. It served as structure for the reporting of the results. Each interview was considered as a unit, as was each forum.

8.3 Results: identification of the needs of long COVID patients

8.3.1 Participants

8.3.1.1 Online survey

1 320 participants were retained for the analysis from the online. The majority of respondents were women (74.8%) and from Flanders (59.0%). The most represented provinces among the participants were Antwerpen (16.5%), Oost-Vlaanderen (13.0%) and Vlaams-Brabant (13.2%). There was a relatively large proportion of people with a high level of education (non-university higher education (30.5%); university education (25.4%)) and who had paid work before acute COVID-19 (82.0%). Most of the respondents (97.1%) answered the online questionnaire for themselves and only a minority for another adult (1.8%) or a child (1.1%). More than 80% of the respondents were in paid employment before being infected with SARS-COV-2 and 30% were working in the health sector (38% were nurses). Additional information about the participants to the online survey are available in KCE report 344 on long COVID.[131]

8.3.1.2 Interviews

We carried out 33 interviews: 52% in Dutch and 48% in French. Most participants were female. Two participants responded in the name of a relative. The full description of the participants to the interviews is available in Appendix 4.

Table 34 – Description of the participants to the interviews (N=33)

	N
Socio-demographic information	
Respondent participating for	
him-/herself	31
another adult	1
a minor	1
Gender	
Women	20
Men	13
Language	
Dutch	19
French	14
Age	
< 18y	1
18-30 y	2
31-40 y	10
41-50 y	10
51-60	6
>60 y	4
Region	
Flanders	19
Wallonia	11
Brussels	3
Paid job (Yes)	18
Education level	
Doctorate with thesis	1
Master's degree	11
Bachelor's degree	1
Non-university higher education of the short type	12
Upper secondary education or general secondary education at the 3rd level	5
Primary education	1
No diploma	2

COVID Issues	
Hospitalized (Yes)	12
Duration of the symptoms	
4-12 weeks	13
12 weeks – 6 months	10
> 6 months	10
VAS difference before and after COVID	
Tertile1	11
Tertile2	11
Tertile3	11

8.3.1.3 Forum

In total, 167 participants (12.7%) to the online survey wanted to participate to the forum: 68 French-speaking and 99 Dutch-speaking. Although they were all invited to participate, 101 effectively participated (60.5%). For four participants, it was not possible to link the online survey database to the forum database. The contact email was used to link the two databases (online survey to forum), but these four participants used different contact emails during the online survey and the forum, which made impossible to link these participants to their socio-demographic characteristics (reported in the online survey only). The majority of forum participants were women (77.3%) and highly educated (40.3%) (Table 35).

Table 35 – Description of the participants to the forum (N= 97)*

	N (%)
Socio-demographic information	
Status of respondent	
Hi/herself	96 (99.0)
Another adult	1 (1.0)
A minor	0 (0.0)
Gender	
Women	75 (77.3)
Men	22 (22.7)
Language	
Dutch	54 (55.7)
French	43 (44.3)
Age (Fr, n=43)	
< 18y	0 (0.0)
18-30 y	3 (7.0)
31-40 y	7 (16.3)
41-50 y	20 (46.5)
51-60	8 (18.6)
>60 y	5 (11.6)
Age (Nl, n=54)	
< 18y	0 (0.0)
18-24 y	0 (0.0)
25-44 y	25 (46.3)
45-64 y	26 (48.1)
65-74 y	1 (1.9)
> 75 y	2 (3.7)
Region	**N (%)**
Flanders	54 (55.7)
Wallonia	33 (34.0)
Brussels	10 (10.3)
Paid job (Yes)	78 (80.4)
Education level	**N (%)**
Doctorate with thesis	2 (2.1)
University education, bachelor's, engineer or master's degree	32 (33)
Non-university higher education of the long type, master's degree at a university	5 (5.2)
Non-university higher education of the short type	25 (25.8)
Academic baccalaureate	7 (7.2)

Post-secondary non-tertiary	9 (9.3)
Upper secondary education or general secondary education at the 3rd level	12 (12.4)
Lower secondary education or 1st or 2nd level secondary education	5 (5.2)
Primary education	0 (0.0)
No diploma	0 (0.0)
Other diploma	0 (0.0)
I don't know	0 (0.0)
Number of comorbidities	
None	56 (57.7)
1 to 2	26 (26.8)
3 to 4	13 (13.4)
5 or more	2 (2.1)
VAS after-Vas before (mean; DS)	27.0 (16.2)
COVID Issues	
Hospitalized (Yes)	22 (22.7)
Duration	
1 to 2 weeks	4 (18.2)
< 1 week	9 (40.9)
> 2 weeks	9 (40.9)
Intensive care (Yes)	9 (40.9)
Respiratory assistance (Yes)	7 (77.8)
Duration of the symptoms	
4-12 weeks	14 (14.4)
12 weeks – 6 months	30 (30.9)
> 6 months	53 (54.6)
VAS difference before and after COVID	
Tertile1	45 (46.39)
Tertile2	31 (31.96)
Tertile3	21 (21.65)

** For 4 participants no match (FR n=2, NL n=2) was possible between the online Limesurvey and the forum*

8.3.2 Patient needs

In this section, we present the main results of the survey (online survey, face-to-face interviews and forum) regarding patients' needs[v]. The detailed results regarding long COVID are available in KCE report 344.[131]

About one in three respondents reported having experienced unmet needs. Among them, the most frequently reported were informational needs (52%), need for staff competent in the domain of COVID-19 and long COVID (24%), and accessibility to care (23%).

A clear need for more information and 'recognition'

Respondents to the survey highlighted a clear need for more and better information on long COVID, with 60% reporting issues with the information received. The main areas for which these respondents require more information are: changes in their health state (74%), the long COVID condition (68%), and treatment possibilities (62%). Many patients also expressed a need to talk about long COVID with healthcare professionals (32%) and other long COVID patients (27%). Patients want to be informed correctly (e.g. when lab tests or medical imaging cannot explain their symptoms, about the evolving scientific insights) by the public authorities and healthcare professionals. Patients (both in interviews and forum) indicated that they wanted correct information (knowns and unknowns) and want to be kept informed about the evolving medical and scientific insights in long COVID. This information will not only empower them, it will also take away some fears (e.g. uncertainty about the future).

During the interviews and the forum the terminology 'need to be recognized' was frequently used. This did not only refer to the need to be 'officially or administratively recognised' to be eligible for some benefits (e.g. access to certain conventions, long COVID recognised as an occupational disease, access to same financial protection mechanisms in the national health insurance as other chronic ill patients, etc.). The, by

[v] The following text is extracted from the short report long COVID (https://kce.fgov.be/sites/default/files/atoms/files/KCE_344C_Long_Covid_Short_report_2.pdf)

patients voiced need to be recognised as a 'long COVID patient', is for a large part also to be understood as a demand to be taken seriously (e.g. by decision makers, by the medical community, by research and clinicians, by the general public, by employers) and a need to create awareness about this new condition (both in the medical community as in the general public). Patients reported the need to explain that this condition can affect people of all age categories and after a mild or severe infection. Several patients stressed the importance to provide information (to the general public as well as the medical community) that long COVID is not a problem restricted to patients who have been hospitalised. This is a 'misunderstanding' which causes many problems to patients who were never hospitalised for COVID-19.

Patients expressed the need to invest in more and better information about long COVID to support the medical community and the general public (e.g. to facilitate diagnoses by standardised measurement instruments; to enable them to inform patients correctly, central website about the relevant scientific insights, etc.). This could also help to change the attitude of some healthcare professionals (e.g. those who are currently minimizing the symptoms), and smoothen the care trajectory (e.g. less time lost before correct referrals are made).

A need for improvement in the way healthcare professionals listen to the needs and experiences of long COVID patients

Even if it is not a therapeutic need, the first step in the care of the patient and the first unmet need in their pathway is that healthcare professionals listen to them. Patients demand to be taken seriously and state that this will require a change in the attitude of some healthcare professionals. They should be more open to listen to patient experiences. In addition it is important that, especially because this concerns a new medical condition with many unknowns, they are open-minded and curious enough to find explanations and solutions. Patients also stated that they find it important that healthcare professionals are honest and say that they do not know what is happening instead of immediately labelling it as a 'psychosomatic' condition. Patients reported that it is important to them that they get the feeling during their contacts with healthcare professionals that they listen to them in a sincere way and are open to what their patient suggests. Healthcare professionals need to work in a context that facilitates this (e.g. some patients indicated that there is currently insufficient time during consultations; tele-consultations have benefits but also limitations to express feelings).

Healthcare services adapted to the long COVID population: multidisciplinary & tailored to patients' needs

During the patient interviews as well as on the online forum, several suggestions were given to improve healthcare services for long COVID patients.

Patients expressed the need for the development of a multidisciplinary, holistic and coordinated approach of their long COVID based on a clear pathway including the diagnostic work up, the treatment, rehabilitation as re-integration at work. They need to be listened in their difficulties and guided through their pathway by staff competent in the long COVID domain. Nowadays they have the feeling to be forgotten in a landscape where care is insufficiently coordinated. It is forcing them to take the initiative a go and look around for medical care (e.g. by contacting several medical specialists).

The statements of patients reveal a need for organization of care. Indeed, patients stated that post-COVID clinics with multidisciplinary teams with specific long COVID expertise will have to be developed covering both the diagnoses as the management of long COVID. A specific point of attention that was mentioned was their accessibility for children (a forgotten group of long COVID patients). Patients also suggested to develop multidisciplinary conventions (analogue as is done for other chronic conditions such as diabetes) to give them access to multidisciplinary expertise (e.g. social workers, psychologists, dieticians, …) which are current not or insufficiently reimbursed.

Multidisciplinary and tailored care also require investments in decision support and professional development

Patients also reported a need to support healthcare professionals to develop expertise within this domain and to guide them in their decision making process. This will require, for instance, that clinic criteria for long

COVID diagnosis (symptoms and examinations) are defined. Patients indicated that such definition should also take into account patients with long COVID symptoms without a positive PCR results (e.g. many patients, especially during the first wave, were untested but present with a clinically the same symptoms). Patients mentioned besides the need to develop a care pathway also a need to develop instruments for physicians that allow to classify and follow-up the evolution of symptoms should be developed.

Investment in research

Patients are aware that this is a domain under development. As such they showed a lot of understanding for the fact that the healthcare professionals do not know the answers either. Therefore they recommended to invest in research on long COVID to allow a better understanding of the underlying mechanisms, its treatment & management, and organizational requirements (e.g. type of healthcare services). A specific need was voiced by a group of patients to invest in treatments to deal with cognitive and concentration problems (also called brain fog).

Social support needs

Patients indicated that due to their long COVID also their relatives experience a burden (e.g. taking over household activities) point to a need to provide professional support to relieve them (partly).

Need to share experiences with peers

Patients feel a need to share experiences with peers. Several patient support and social media groups exist. While this helps some patients (e.g. to be reassured that their symptoms are real and they are not alone, to get inormation about available healthcare services) this is not always the case. Patients staed that information is often unfiletered (e.g. no quality assurance check) and can also can overwhelm them resulting in an insecure and anxious feeling. They expressed a need of peer groups (in person and social networks) with the support and involvement of healthcare professionals. Nevertheless, “official” self-help groups which also involve healthcare professionals, even on Facebook or by Teams, should allow to interact in an anonymous way. Otherwise patients might be afraid to answer (e.g. because of a potential the reaction of their treating physician).

Measures to deal with the financial impact of long COVID

More than one in three respondents (37%) reported to experience a financial impact because of long COVID due to loss of income, medical expenses or a combination of both. As stated above patients reported that they want access to financial protection mechanisms (e.g. statute of chronic disease, maximum billing) as is done for other chronic conditions. In addition some patients pointed to the need to expand the reimbursement of specific services (e.g. expand the duration and number of physiotherapy sessions, access to multidisciplinary rehabilitation for patients without a hospitalization, expand reimbursed sessions with a psychologist).

Indeed, the early and expanded reimbursement of psychological was an important theme for several reasons (e.g. to deal with post-traumatic stress related to their acute COVID-19; to help them to accept the situation, think about the perspectives to live with the condition and manage the feelings of guilt; to deal with feelings of anxiety and depression). Respondents stressed that psychological support is in the first place required to help them to deal with the long COVID. This need should, according to patients, not be understood as a treatment for a psychological condition. Patients indicated that they prefer that psychological support is proposed to them at different time points. Early after the acute phase of COVID-19, but also regularly during follow-up. After all, patients might feel they do not need psychological support (or do not have the energy for it) at one moment in time, but this feeling might change when symptoms last. The limited reimbursed (often in combination with income loss) create a financial barrier to access psychological care.

Administrative support

Patients mentioned the need for help with administrative tasks when they are discharged from hospital. It is usually foreseen in the hospital for the elderly (e.g. via social worker) but it should be also available for young or single people. Patients see also a role for sickness funds but expect more efficiency and flexibility from them.

In the section below, an in-depth reflection on the advantages and disadvantages of the different methods for studying patient needs is developed.

Key points – Identification of patient needs

The online survey (i.e. the questionnaire previously developed to identify unmet needs) allowed us to quantify the needs but we can easily conclude that it is not sufficient to identify patients' needs.

The forum and the interview allow us to contextualize these needs and to study them more deeply. For the long COVID population these are:

- **Need of information**
- **Need of 'recognition'**
- **Needs related to the relationship with healthcare providers, i.e.improvement in the way healthcare professionals listen to the needs and experiences of long COVID patients**
- **Need for healthcare services adapted to the long COVID population: multidisciplinary & tailored to patients' needs. That requires investments in decision support and professional development.**
- **Need for more research on long COVID**
- **Need to share experiences with peers**
- **Need for measures to deal with the financial implications of living with long COVID**

Need for administrative support

9 METHODOLOGICAL REFLECTIONS AFTER THE PILOT

9.1 Aim

In order to verify what seems to be the best method to capture patient needs, we complete the investigation by comparing the content of the different data collection methods, by questioning the candidates to the forum and by interviewing the forum's moderators.
This part investigates mainly the forum-related aspects because they are rather new to us: indeed, KCE is used to collect qualitative data by interviewing people face-to-face or via online surveys and less frequently by online asynchronous discussion.

9.2 Methods

We combined different approaches to nourish our methodological reflection: learnings from the literature, analysis the type of results obtained during the pilot project on long COVID, and data collection among registered participants to the forum and forum moderators.

9.2.1 Literature review

A rapid literature search was conducted in March-April 2021 to retrieve scientific information regarding the use of online forums for qualitative research. The focus was put on methodological issues, descriptions of approaches and points of attention for the use of online forums. First, Pubmed, ERIC and Sociological Abstracts was searched to retrieve information; second, a Google search was conducted to find additional documents; and third, a snowball approach was applied to identify missing key-papers. Because of the rapidly changing nature of the internet, recent publications were preferred and papers up to maximum 15 years old were included. Search terms used were, amongst others: 'online forum", 'chat*', 'bulletin board', online focus group', 'comparison', 'difference', 'qualitative research', 'synchronous', 'asynchronous'.

9.2.2 Results of the online survey, interviews and forum

We analysed the information obtained from the three data collection techniques (i.e. online survey, interviews and forum) in terms of content (type of results) and form (tone). We compared the content of the Nvivo codes used in the forum and the interviews. In addition we coded the transcripts of the forum to identify communication styles, i.e. specific ways used by the participants to express themselves in such platform.

9.2.3 Survey among registered participants to the forum

In order to get input on the motivation to participate in a data collection activity via a forum and participants' experience with it, two online surveys (Limesurvey) were sent to the candidates for the forum:

- 1 for people who eventually did not participate (n=42)
- 1 for effective participants (n=57)

The questionnaires are presented in Appendix 5.

9.2.4 Interviews with the moderator of the forum

To catch the impressions of the moderators regarding their experience with the forum we performed an individual online semi-structured face-to-face interview with each moderator (1 Dutch-speaking and 1 French-speaking). The topics discussed were:

- The general satisfaction and experience with the content of the discussions
- The general satisfaction and experience with the moderation of an online forum
- The general satisfaction and experience with the technical aspects of the platform
- Suggestions for improvement

9.3 Results

9.3.1 Advantages and disadvantages of online fora as a means of qualitative research compared to classic data collection methods according to the literature

9.3.1.1 Advantages

From our literature review we identified the following advantages of using a bespoke asynchronous forum to collect data:

- An important feature of the online fora is the perception for the participants of anonymity. Anonymity is described to have a disinhibiting effect on participants, social desirability is diminished and "the exchange of 'true' attitudes and opinions is encouraged"(Rodham, 2006 p.95).[139] Due to the anonymity of the internet, it facilitates the expression of a true self. "Expressing aspects of the self that might be taboo or stigmatized often has negative social consequences.(Williams, 2012 p.374) "[132]. The 'online disinhibition effect' can be especially advantageous when the topic is of a sensitive or stigmatizing nature.[132]
- Using written communication (e.g. text-messaging, instant messaging, online fora, and social networking websites) is preferred by many people to communicate their experiences.[140]
- Using written language can allow for greater inclusion of participants in studies.[132]
- Online fora can be used to research individuals who might otherwise be difficult to reach, such as those living with a rare illness, those who have not sought professional help for a health issue[141, 142] or geographically dispersed samples, at little cost.[142, 143]
- Messages posted in online forums can be read anywhere using an internet connection together with web browser software, without needing any special software.(Smedley, 2021 p.39[141])

- The physical distance between researcher and participants in virtual research can serve to reduce unequal power relations. “Reduced power relations amongst participants can allow less confident participants to feel comfortable about contributing to discussions, thus enabling voices that might normally be silenced to be present”(Williams, 2012 p.372).[132]
- Online focus groups can potentially use larger sample sizes than face-to-face studies, allowing researchers to have access to a wider range of experiences.[132]
- Forum messages are automatically stored in easily-accessible archives. Researchers can search through these archived collections of previously-posted discussions to identify messages that are relevant to the research topic.[141]
- Studies may be cheaper and quicker to conduct by avoiding the time and costs associated with recruiting participants and conducting surveys or interviews[141, 144].
- Using online forums eliminates need to transcribe data (cost & time saving). Because the conversations exist already in digital format, transcribing audio material is not necessary.[145] “Automatic transcripts directly printed out from the online forum site are an asset of the online forum method, which can increase the credibility of the data.”(Im, 2006 p.5)[144].

9.3.1.2 Disadvantages

We identified the following disadvantages from the literature:

- Some qualitative researchers state that “online discussions could never achieve the level of dialogue and “meaningful discourse” of a face-to-face context”(Williams, 2012 p.371), but others disagree with this view ant state that written communication “should not be underestimated in its capacity to induce strong feelings and reactions”(Williams, 2012 p.371).[132]
- “The inability to request or certainly obtain clarification or elaboration from those posting to forums may give rise to ambiguity and misunderstanding further exacerbated by missing words, spelling errors and strange punctuation which characterize this kind of informal communication”(Jowett, 2015 p.3).[146]
- Anonymity of online forums complicates analysis as there is normally only little sociodemographic information available about the users.[146] Information (such as age and gender) may be inferred from the content of posts (e.g. from the name used), but there is often no way of verifying this information.[141, 146]
- “The absence of social cues within messages may make it difficult for researchers to understand the intended meaning of messages, particularly if they are read out-of-context.”(Smedley, 2021 p.39)[141]
- Internet access, although its’ use is widely spread, is not distributed equally across the population.[141]
- Some individuals use forums when they are feeling particularly bad, and then stop posting messages when they feel better. “This may lead to a bias, where some issues are overrepresented and others are underrepresented “(Smedley, 2021 p.39)[141]. Moreover, “anonymous posting can result in a tendency to make more extreme statements on the internet than they would in face-to-face situations, due to de-individuation effects” (Latkovikj, 2020 p.51)[145]. This might hamper transferability of the study results.[144]

9.3.1.3 Conclusion

Scientific literature is quite unanimous regarding the use of online forums for qualitative data collection: When planning a qualitative online forum study, the first thing to do would be to check if the research purposes and questions actually require the study to be an online forum study. Although the use of online forums could be viewed as innovative, the method has some inherent limitations due to its unique characteristics. “*If a conventional research method works well for the research purpose and questions, there is no need to conduct an online forum study that has a number of shortcomings such as lack of theoretical saturation and difficulties in trust building*.”(Im, 2012 p.5)[147] However, it is a good alternative with several advantages for specific groups compared to

traditional approaches. Reasons to choose for an online forum are, among others, geographical distance, study cost, time load, stigma of participants or difficulties discussing sensitive topics with strangers.[147]

9.3.2 Output emerging from the different methods in the pilot study

9.3.2.1 Participants

To identify which type of respondent were 'caught' by a data collection method or another, we compared the profiles of the candidates for the interview with those for the forum. These features were available through the data of the online survey.

Statistical analysis

Univariate and multivariate logistic regression analyses have been conducted to investigate the factors associated with the candidate status (to be a candidate for the forum or the interview versus not to be a candidate) and with the type of candidate (to be a candidate for the forum versus to be a candidate for the interview).

In univariate analysis the status of the respondent (responded to the online survey for him/herself, another adult or a minor), gender (women, men, other), language (Dutch, French), age groups (fr: 18-40,51-60,>60; nl:18-44,45-64,>65 years), region (Flanders, Wallonia, Brussels), paid job (yes/no), educational level (primary/no diploma, lower secondary, upper secondary, short type, long type), the number of co-morbidities prior to COVID-19, delta (VAS after-VAS before COVID infection), hospitalisation in acute COVID phase (yes/no), hospitalisation in ICU (yes/no), respiratory assistance among patients hospitalised in ICU (yes/no), duration of symptoms (short, mid, long) and beta (EQ-5D-5L before – EQ-5D-5L after) have been introduced in the models.

In multivariate analysis of the candidate status, delta, hospitalisation in acute COVID phase, duration of symptoms, and beta have been corrected for age, paid job and educational level in the French-speaking population and for paid job and educational level in the Dutch-speaking population.

In multivariate analysis of the candidate type, delta and beta have been adjusted for education level.

The statistical analyses were performed with SAS Enterprise Guide (7.1). A p-value below 0.05 was considered as significant.

Candidate versus not candidate for the forum or the interview

Table 36 shows the results of the univariate analysis comparing candidates for the qualitative part after the online survey to those who were not candidate.

Table 36 – Comparison of the participants to the online survey who were candidate for the qualitative data collection (forum or interview) and those who are not candidate

	Not candidate for forum or interview n=812 N (%)	Candidate for forum or interview n=508 N (%)	OR	95% CI		p-value
Status of respondent						
Him/herself (ref)	782 (96.3)	500 (98.4)				
Another adult	20 (2.5)	4 (0.8)	NA			
A minor	10 (1.2)	4 (0.8)	NA			
Gender						
Women (ref)	595 (73.3)	392 (77.2)				
Men	216 (26.6)	115 (22.6)	0.81	0.62	1.05	0.557
Other	1 (0.12)	1 (0.2)	NA			
Language						
Dutch (ref)	490 (60.3)	229 (48.1)				
French	322 (39.7)	279 (54.9)	1.25	1.00	1.56	0.052
Age (Fr)						
18-40 (ref)	112 (34.8)	63 (27.5)				
41-50	113 (35.1)	94 (41.1)	1.48	0.98	2.23	0.193
51-60	47 (14.6)	47 (20.5)	1.78	1.07	2.96	**0.037**
>60	50 (15.5)	25 (10.9)	0.89	0.50	1.57	0.096
Age (Nl)						
18-44 (ref)	227 (46.3)	152 (545)				
45-64	234 (47.8)	112 (40.1)	0.72	0.53	0.97	0.309
>65	29 (5.9)	15 (5.4)	0.77	0.40	1.49	0.783
Region						
Flanders (ref)	493 (60.7)	286 (56.3)				
Wallonia	242 (29.8)	156 (30.7)	1.11	0.87	1.43	0.515
Brussels	77 (9.5)	66 (13.0)	1.48	1.03	2.12	0.060
Paid job (Yes)	647 (79.7)	429 (84.5)	1.39	1.03	1.86	**0.030**
Education level[$]						
Long type	244 (30.5)	199 (39.6)	1.09	0.50	2.35	**0.008**
Short type	310 (38.8)	188 (37.4)	0.81	0.37	1.75	0.739
Upper secondary	187 (23.4)	88 (17.5)	0.63	0.29	1.38	0.141
Lower secondary	42 (5.3)	16 (3.2)	0.51	0.20	1.31	0.091
Primary (or no diploma) (ref)	16 (2.0)	12 (2.4)				
Number of comorbidities						
None (ref)	517 (63.7)	324 (63.8)				

	Not candidate for forum or interview n=812 N (%)	Candidate for forum or interview n=508 N (%)	OR	95% CI		p-value
1 to 2	200 (24.6)	110 (21.7)	0.88	0.67	1.15	0.062
3 to 4	68 (8.4)	49 (9.7)	1.15	0.78	1.70	0.804
5 or more	27 (3.3)	25 (4.9)	1.48	0.84	2.59	0.179
COVID Issues						
VAS after-Vas before mean (Delta); [DS]	22.7 [16.0]	30.5 [17.6]	1.03	1.02	1.04	**<0.001**
Hospitalised (Yes)	83 (10.2)	91 (17.9)	1.92	1.39	2.64	**<0.001**
Duration						
< 1 week (ref)	29 (34.9)	30 (33.0)				
1 to 2 weeks	33 (37.8)	32 (35.2)	0.94	0.46	1.90	0.506
> 2 weeks	21 (25.3)	29 (31.9)	1.34	0.63	2.85	0.342
ICU (yes)	20 (24.1)	33 (36.3)	1.79	0.93	3.47	0.083
Respiratory assistance (Yes)	14 (70.0)	25 (75.8)	1.34	0.39	4.65	0.645
Duration of the symptoms						
4-12 weeks(ref)	192 (23.7)	75 (14.8)				
12 weeks – 6 months	299 (36.9)	268 (52.8)	1.32	0.96	1.84	0.281
> 6 months	319 (39.4)	165 (32.5)	2.29	1.68	3.14	**<0.001**
Beta° mean [SD]	0.27 [0.23]	0.37 [0.25]	5.91	3.68	9.48	**<0.001**

°Beta= EQ-5D after-EQ-5D-before (expressed as an absolute value) valued using new value set[103] ; CI= Confidence Interval; OR=Odds Ratio; SD=Standard Deviation; NA=Not Applicable

In univariate analysis, we observed that being aged 51-60 years (among French-speaking) (OR 1.78 (95% CI 1.07-2.96)), having a paid job (OR 1.39 (95% CI 1.03-1.60)) and being highly educated (OR 1.09 (95% CI 0.50-2.35)) significantly increased the chance for being a candidate for the forum of the interview.

From the perspective of experiences with COVID-19, patients who have been more affected by the condition are more likely to be candidates. Indeed, having been hospitalised (OR 1.92 (95% CI 1.39-2.64), having a higher delta (OR 1.03 (95%CI 1.02-1.04)), having symptoms for more than 6 months (OR 2.86 (95% CI 2.17-3.77)) and a higher beta (i.e. a greater impact of COVID on quality of life) (OR 5.91 (95% CI (3.68-9.48)) significantly increased the chances of being a candidate for the forum or the interview (Table 36).

By adjusting factors related to COVID experience for age, paid job status and education status, the conclusion remained the same (Table 37).

Table 37 – Factors associated with being a candidate for the qualitative part of the study (forum or interview), multivariate logistic regression, by language

	OR*	95% CI		p-value
FRENCH-speaking				
VAS after-Vas before	1.03	1.02	1.05	**<0.001**
Hospitalisation (No=ref)	2.14	1.16	3.96	**0.015**
Duration of the symptoms				
4-12 weeks (ref)				
12 weeks – 6 months	3.04	1.82	5.10	0.884
> 6 months	1.70	1.04	2.78	**<0.001**
|EQ-5D after-EQ-5D-before|	6.52	2.98	14.27	**<0.001**
DUTCH speaking	**OR****	**95% CI**		**p-value**
VAS after-Vas before	1.03	1.02	1.04	**<0.001**
Hospitalisation (No=ref)	2.21	1.47	3.31	**<0.001**
Duration of the symptoms				
4-12 weeks (ref)				
12 weeks – 6 months	1.02	0.65	1.61	0.073
> 6 months	1.99	1.32	3.01	**<0.001**
|EQ-5D after-EQ-5D-before|	7.70	4.08	14.53	**<0.001**

** Adjusted for age, paid job and education level (see Table 36); ** Adjusted for paid job and education level (see Table 36); CI= Confidence Interval; OR=Odds Ratio*

Candidate versus not candidate for the forum versus candidate the interview

Table 38 shows the results of the univariate analysis comparing participants candidates to the interviews and participants candidates to the forum

Table 38 – Comparison of the participants for the forum and for the interviews

	Candidate for forum n=167 N (%)	Candidate for interview N=341 N (%)	OR*	95% CI		p-value *
Status of respondent						
Him/herself (ref)	166 (99.4)	334 (98.0)				
Another adult	1 (0.6)	3 (0.9)	NA			
A minor	0 (0.0)	4 (1.2)	NA			
Gender						
Women (ref)	130 (77.8)	262 (76.8)				
Men	36 (21.6)	79 (23.2)	1.09	0.70	1.70	0.709
Other	1 (0.6)	0 (0.0)	NA			
Language						
Dutch (ref)	99 (59.3)	180 (52.8)				
French	68 (40.7)	161 (47.2)	1.30	0.90	1.90	0.167
Age (Fr)						
18-40 (ref)	18 (26.5)	45 (28.0)				
41-50	29 (42.7)	65 (40.4)	0.90	0.45	1.81	0.744
51-60	14 (20.6)	33 (20.5)	0.94	0.41	2.16	0.932
>60	7 (10.3)	18 (11.2)	1.03	0.37	2.88	0.859
Age (Nl)						
18-44 (ref)	52 (52.2)	100 (55.6)				
45-64	43 (43.4)	69 (38.3)	0.83	0.50	1.39	0.319
>65	4 (4.1)	11 (6.1)	1.43	0.43	4.71	0.454
Region						
Flanders (ref)	95 (56.9)	191 (56.0)				
Wallonia	52 (31.1)	104 (30.5)	1.00	0.66	1.51	0.748
Brussels	20 (12.0)	46 (13.5)	1.14	0.64	2.04	0.634
Paid job (Yes)	140 (83.8)	289 (84.8)	1.07	0.65	1.78	0.789

Education level[$]						
Long type	59 (35.5)	140 (41.5)	0.79	0.21	3.03	0.104
Short type	55 (33.1)	133 (39.5)	0.81	0.21	3.09	0.090
Upper secondary	39 (23.5)	49 (14.5)	0.42	0.11	1.65	0.245
Lower secondary	10 (6.0)	6 (1.8)	0.20	0.04	1.04	**0.020**
Primary (or no diploma) (ref)	3 (1.8)	9 (2.7)				
Number of comorbidities (cat)						
None (ref)	103 (61.7)	221 (64.8)				
1 to 2	35 (21.0)	75 (22.0)	1.00	0.63	1.59	0.510
>2	29 (17.4)	45 (13.2)	0.72	0.43	1.22	0.224
COVID Issues						
VAS after-Vas before mean (Delta); [DS]	26.8 [16.2]	32.3 [18.1]	1.02	1.01	1.03	**0.001**
Hospitalised (Yes)	27 (16.2)	64 (18.8)	1.20	0.73	1.96	0.473
Duration						
< 1 week (ref)	5 (18.5)	27 (42.2)				
1 to 2 weeks	11 (40.7)	19 (29.7)	3.13	0.93	10.48	**0.036**
> 2 weeks	11 (40.7)	18 (28.1)	0.95	0.33	2.72	0.204
Intensive care (Yes)	11 (40.7)	22 (34.4)	0.76	0.30	1.92	0.564
Respiratory assistance (Yes)	9 (81.8)	16 (72.7)	0.59	0.10	3.57	0.568
Duration of the symptoms						
4-12 weeks(ref)	28 (16.8)	47 (13.8)				
12 weeks – 6 months	49 (29.3)	116 (34.0)	1.41	0.79	2.51	0.229
> 6 months	90 (53.9)	178 (52.2)	1.18	0.69	2.01	0.968
Beta° mean [SD]	0.34 [0.24]	0.39 [0.25]	2.52	1.16	5.48	**0.019**

°Beta= EQ-5D after-EQ-5D-before, (expressed as an absolute value) valued using new value set[103] ; CI= Confidence Interval; OR=Odds Ratio; NA=Not applicable

In univariate analysis, we observed that being highly educated decreased the chance for being a candidate for the interview compared to having no or a primary school diploma (OR 0.20 (95% CI 0.04-1.04)) (Table 38).

From the perspective of experiences with COVID-19, the higher the impact of the condition on QOL, the higher is the chance for participants to be a candidate for the interview. Indeed, the higher the delta (OR 1.02 (95%CI 1.02-1.03)) or the beta (OR 2.52 (95% CI (1.16-5.48)), the higher is the chance of being a candidate for the interview (Table 38). Participants who were hospitalised for 1 to 2 weeks were also more likely to be candidates for the interview (OR 3.13 (95% CI 0.93-10.48)) than patients hospitalised for less than a week.

By adjusting factors related to COVID experience for educational level, the conclusion remained the same (Table 39).

Table 39 – Factors associated with being a candidate for the forum vs interview, multivariate logistic regression (ref=forum)

	OR*	95% CI		p-value
Hospitalisation duration				
< 1 week (ref)				
1 to 2 weeks	6.04	1.47	24.80	0.011
> 2 weeks	1.43	0.45	4.53	0.305
VAS after-VAS before	1.02	1.01	1.03	**0.002**
Beta°	2.90	1.31	6.44	**0.009**

** Adjusted for education level (Table 38), °Beta= EQ-5D after-EQ-5D-before (expressed as an absolute value) valued using new value set[103] ; CI= Confidence Interval; OR=Odds Ratio*

9.3.2.2 Content and diversity

Methodological preamble

Before examining the content of information and its diversity according to each data collection method, it is important to remember how the material was analysed: First, all interview transcripts were imported into Nvivo©. Each interview then constitutes a recording unit. Secondly, the entire forum discussion for each language was imported into the software, without being possible to identify precisely which participant contributed what information. A forum is therefore also considered a recording unit. We therefore collected identifiable information from 35 data sources, i.e. 33 interviews and 2 forums.

All the French-speaking material was coded by one researcher and, because of internal human resources availability, the Dutch-speaking material by two researchers. Each researcher coded inductively the material with primary codes, i.e. a precise description of extracts from the material, in his own mother tongue. Because the interviews were ready to analyse before the forum, the researchers began with these data sources.

Afterwards, the Dutch researchers discussed their respective coding and arrived at a common 'primary' coding. This codebook was then discussed between the three researchers. However, the primary codes remained in their original language. The French-speaking researcher proposed to group the primary codes into categories. This proposal was discussed and the final classification revised jointly by the three researchers. The results were described by one and reviewed by all researchers.

In total, 49 categories were created from the first coding (Table 40), in which 13 were directly referring to patients' needs, 1 to the relatives' needs and one to the health care providers' needs. The other categories described the patients before COVID-19, the health condition, their experience with the condition and the impact of it as well as their experience with the health care services.

Table 40 – Codes categories

Description of the patient and the condition	Description of the experience with condition	Description of the health care services	Needs	Other
• Before COVID-19 • COVID-19 Acute phase • Disease metaphor • Symptoms • Treatment	• Diagnosis establishment • School • Treatment effectiveness • Evolution • Healing process • Financial impact • Psychological impact • Impact on professional life • Impact on life at work • Administrative burden • Recognition • Reintegration • Relationship with others	• Access to health care services • Coordination of care • Reliability of information • Professional illness • Patients are understanding • Patients are proactive • Taking it seriously • Relationship with doctors • Relationship with other caregivers • Follow-up • Post-COVID Unit	• Needs for assistance • Needs for treatment • Needs to work • Needs for lost doctors and carers • Needs to evolve • Needs for diagnosis • Needs for explanations • Needs for administrative information • Needs for information on long COVID • Administrative needs • Needs for information about the evolution of the condition • Relatives' needs • Needs for recognition • Needs for support • Need for physician specialized in (long) COVID	• suggestions for improvement • Social networks • Patient theory about the long COVID • Vaccination

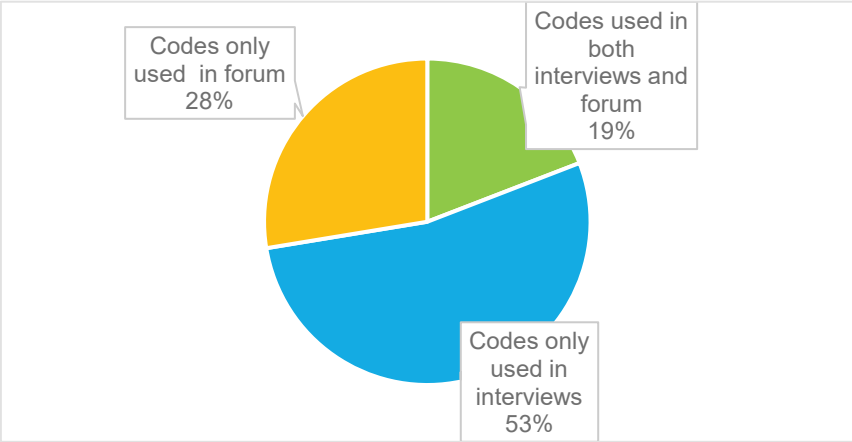
Content and diversity of the data collection results

We calculated the number of primary codes related to patient needs that were built during the content analysis of the French-speaking interviews and the French-speaking forum discussions. We only used this material for our analysis because all the material in French was coded by one and the same researcher, while the material in Dutch was coded by two different researchers. This choice allows to avoid interpretation bias. Moreover, it allowed us to perform the analysis in a shorter timeframe, allowing for a more efficient allocation of KCE resources.

The analyses were thus carried out on the responses of 14 interviewees and 43 participants to the forum.

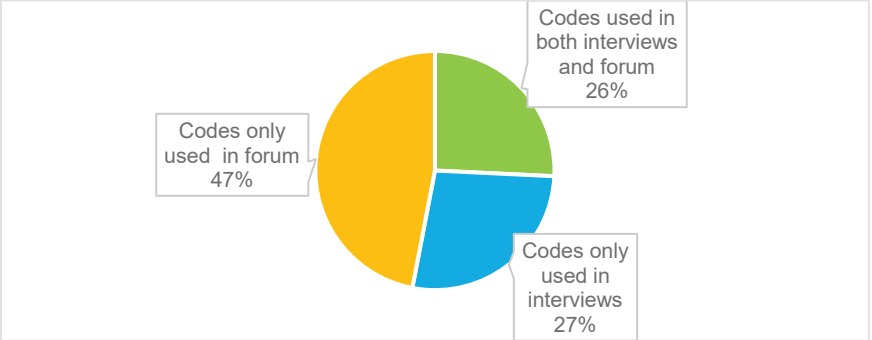
In total, 627 primary codes were created. About half of them were used only in the analysis of the interviews, about a third only for the analysis of the forum and a fifth for both the interviews and the forum discussion (Figure 13).

Figure 13 – Proportion of the primary codes specific or common for each data collection method (N=627)



If we focus on the patient needs, we can see that 66 codes have been created, almost half of which via the forum (Figure 14).

Figure 14 – Proportion of primary codes referring to patient needs (not including the respondents' suggestions for improvement of their care) (N=66)



By comparing the two figures above, it appears that the forum has led to the creation of more primary codes specifically related to patient needs. Nevertheless, because we assume that to understand patient needs we need to have more information on their experience with the condition than the specific codes related to the needs, we performed a deeper analysis on all material of qualitative data.

For this, we counted the number of codes per category present in the French speaking corpus of analysis according the data collection method used and ranked the categories according to the number of primary codes they cover.

This allows us to identify which type of information is mainly captured by each data collection method (Table 41). It is a global approach of the material. We attributed a colour to each category that appears in multiple column in order to compare them.

Table 41 – Top 10 categories of codes according to the sub-codes numbers per data collection

Top 10 codes interviews		Top 10 codes forum		Top 10 common codes	
Symptoms	50	Symptoms	53	Symptoms	23
Follow-up	46	Suggestions for improvement	49	Suggestions for improvement	12
Treatment	42	Relationship with physicians	20	Need info on long COVID	9
Health care pathways	35	Impact on professional life	18	Treatment	9
Psychological impact	24	Need for info on long COVID	17	Diagnosis establishment	8
Impact on professional life	23	Psychological impact	16	Impact on professional life	7
Diagnosis establishment	23	Treatment	15	Psychological impact	7
Relationship with physicians	21	Proactive attitude of patient regarding disease management	15	Relationship with others	6
Need for info on long COVID	18	Diagnosis establishment	14	Social networks	5
Proactive attitude of patient regarding disease management	17	Relationship with others	10	Proactive attitude of patient regarding disease management	4

From a first general look at the table it appears that all the categories with the most information diversity, i.e. the highest number of 'primary' codes, in the forum are also found in the top 10 categories with common codes or in the top 10 categories of interviews. Two categories strongly represented in the interviews are neither included in the top 10 codes per category of the forum nor in common: ‘follow-up’ and ‘pathways’. This means that the interviews offered a greater diversity of information for the description of the ‘follow-up of the patients’ and the ‘pathways taken during their condition’.

Both methods allowed to identify a lot of symptoms, treatments, psychological impact, impact on professional life, information on the establishment of the diagnosis, information needs and the proactive attitude of the patients regarding the management of the condition (diagnosis, treatment, etc) with additional ones that were brought through each methods separately. Both methods were also useful to catch the majority of the codes related to the importance of social networks for long COVID patients.

The large number of participants in the forum allowed to increase the variability of the responses and the possibilities to reach data saturation. Nevertheless, if we compare the number of primary codes in each category, we see that in our corpus of analysis, almost the same number of additional codes are furnished by either the interviews or the forum only **for** the **symptoms**, the **information needs** and the description of the **proactivity** of the patients. This suggest that for such type of information both data collection methods are complementary, without any preference.

To identify the **treatments**, the **psychological impact**, the **impact on professional life**, and the information on the **establishment of the diagnosis**, we retrieved more diverse information from the interviews than

from the forum. This suggests then that choosing for interviews instead of a forum could deliver more information on these aspects.

Finally, more tracks or **suggestions for improvements** were highlighted by the forum than by the interviews. This could be explained by the higher number of participants and probably also to the time for reflection. Respondents of the interviews were not really prepared to give suggestions for improvement, they gave more spontaneous ideas, ideas that were probably more in line with their own priorities. The forum, on the other hand, allowed for a broader and longer brainstorming, as participants had more time to reflect and react on the ideas of others.

Because of the semi-structured feature of the interviews, it is probable that response are more led by the story of the respondents an, in consequence that it probably produces more codes in a same category

If we isolate the categories only containing primary codes in one or in the other data collection method (Table 42), it appears that the interviews contributed to slightly more categories than the forum.

Table 42 – Specific categories comprising no common primary codes per type of data collection

Codes only in interviews	Codes only in the forum
• Access • Before COVID-19* • Administrative needs • Need for explanations • Need for physician specialized in (long)COVID • School • Treatment efficiency • Evolution of the condition • Post-COVID Unit	• Diagnostic needs • Needs of relatives • Need for recognition • Healing process • Patient theory about the long COVID

The type of categories seems to be partly related to the interview guide/list of topics to be discussed. For example, it is not surprising that interviews are the only data sources to provide specific additional codes about patients' health before COVID-19 because the interviewer used the question about the patients' health status before COVID-19 as an ice-breaker at the beginning of the interview. Such an ice-breaker question was not used in the forum and thus the forum did not contribute to this category. This is not a problem in itself as this topic was not part of the research questions. On the contrary, although it is very important to start the conversation in a way that is fluid and easy for the interviewee (the purpose of the ice-breaker questions) and although it gives context to the interview, this statement illustrates the amount of information that is less necessary to process when using an interview, compared to a forum.

Another example is the category 'post-COVID unit', also present only in the interviews. It covers the knowledge of and experience with post-COVID units existing in some hospitals. This information was brought up during the interviews while there was less place to talk about it in the forum because the topic proposed in the forum focused on the difficulties with treatment for long COVID rather than on the possible treatments themselves.

Another aspect is the composition of the participants: the category related to the school being only present in the interviews is justified by the fact that no parents of minor child participated in the forum.

Finally, the format of the data collection explained the presence of specific categories: the written asynchronous data collection allows to present theories about the mechanisms of long COVID, the evolution of the condition , etc and link to (scientific) websites which was not 'encouraged' by an interviewer during a conversation in face to face.

Limits of our analysis

A first limit is that our analysis is based only on the French language material. Although it is unlikely that there are major differences between the two language groups, it cannot be excluded that Dutch speakers have a different way of interacting depending on whether the data collection is oral or written and synchronous or asynchronous.

Secondly, it should be kept in mind that the interviews were coded before the forum. Given the very dense and repetitive nature of the answers given

during the forum, it is possible that a certain amount of coding fatigue may have set in and that the coding density of the forum would have been higher if it had taken place first. Moreover, this fatigue is accentuated by the large amount of information (sometimes very long) that is somewhat outside the scope of the study.

To conclude, the lessons learned from these analyses should therefore be seen as a first exploratory approach to the material.

9.3.2.3 Communication aspects

In contrast to individual interviews, the forum is a place where exchanges between participants are allowed and encouraged. Moreover, because it is a written medium, some ways to communicate are specifically used. We identified particularities in the way that information was given.

Content and tone

The way to interact could probably explain why some participants enjoyed participating in a forum or why some of them were frustrated.

Some posts are directly addressed to the other participants. In these posts we identified several types of messages, i.e. invitation to celebrate life, expression of messages of hope, commiseration, encouragements, making jokes, expressing their gratitude for alleviating their feeling of isolation, thanking the other participants (and researchers) for having had the opportunity to read similar experiences to their own, which is a source of comfort or reassurance.

The forum is an opportunity for participants to interact with researchers. Some of them took the opportunity to ask the researchers to get in touch with their network to deepen certain aspects of the research or to contact Sciensano to improve the research. Others asked questions about how responses will be handled. Finally some participants suggested improvements for future similar forums.

If we look at the content of the exchanges in the light of the interactions that took place, we can see that the participants exchanged ideas on what to try or 'tips', that they gave or exchanged information they had found themselves or received from others (doctors, experts, etc.), websites to visit, and that they invited some to join support groups or to have more personal contacts outside the forum. Some took the opportunity to explain their theories, presented as being validated by experts in the field, to others. The forum was also an opportunity for some to initiate a broader discussion, out of the initial scope of the foreseen topic.

The discussions were also a way for some to search for recognition, for their condition and experiences, as well as for the presented theories.

Nevertheless, the forum as it was conceived and conducted, was also a source of frustration for some participants. They expressed frustration at the lack of response from other participants to their posts or the lack of responses from researchers.

Note that the comments regarding the tone and the content described here can also be present in a (focus/group) interview.

Process

We identified some specificities during the gathering of the data by the forum itself:

First, some participants needed to introduce themselves to the others, to justify why they were participating, to apologize because they were questioning their legitimacy to intervene in the discussion, or to introduce themselves as “non-expert (but …)”.

During the forum, some participants got the opportunity to realize that some of their symptoms are probably due to the condition, while they originally did not identify them as long COVID-related, or to realize to what extend long COVID impacts other patients.

From the moderator-side, in many cases, they asked for clarification on some contributions of participants but get no reaction.

Output form

The responses to the forum were either long and very detailed or very short and less elaborated.

The language was (obviously) rather ‘more formal.

Some participants reused answers given in other subjects, copying and pasting the same answer several times. Some copy-pasted extracts of their personal diary.

Key points

- **Being aged 51-60 years, having a paid job and being highly educated increased the chance to be willing to participate in the additional qualitative step of the study. Also having been more affected by the condition, i.e. having been hospitalised, experiencing a higher impact of COVID-19 on quality of life and, having symptoms for more than 6 months.**
- **Being highly educated decreased the chance for being a candidate for the interview.**
- **The higher the impact of the condition on QOL, the higher is the chance for participants to be a candidate for the interview.**
- **Interviews or forum both contribute to identify information on patient needs.**
- **The format of the data collection, the more or less structured feature as well as the written/spoken media lead to different categories of codes.**
- **Data collection via a forum identify more diversity in the information related to the patient needs.**
- **Data collection via forum generate more suggestions for improvement**
- **Interviews give a more complete history of the patient but used alone, it allows to identify only about half of the patient needs.**

  Diversity in collected information is in general increased by increasing the number of respondents. In this sense, the results of the forum led to more diversity in the responses but were less able to identify the context of the responses than the interviews.

- **The forum gave the opportunity to participants to communicate with each other and it had a positive impact on their feelings. However it can also be a source of frustration because of wrong expectations.**
- **The forum leads to several unclarified ideas because the respondents did not react to the triggering questions of the moderator.**

9.3.3 Results from the evaluation survey

9.3.3.1 Participants' characteristics

Figure 15 – Participants to the evaluation survey

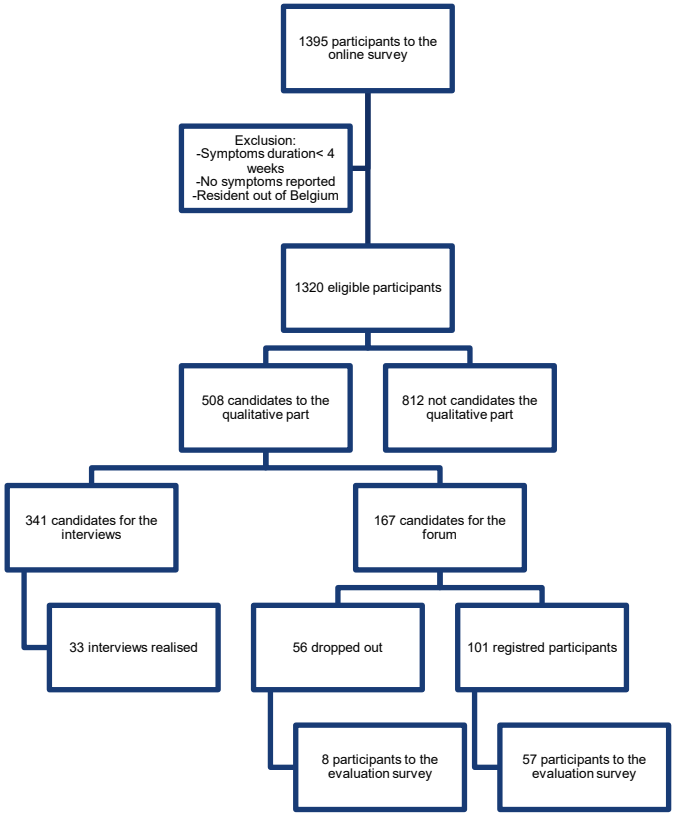


Table 43 – Characteristics of the participants to the evaluation online survey

	% (N)
Gender	
Women	29.6% (38)
Men	70.4% (16)
Other	0.0% (0)
Language	
Dutch	38.60% (22)
French	61.40%(35)
Age (years)	
<25	0.0% (0)
25-44	40.7% (22)
45-64	53.7% (29)
65-74	3.7% (2)
75 and +	1.9% (1)

9.3.3.2 Lessons learned about the data collection via an online forum in the pilot project

The results of the survey allow us to identify the reasons to opt for participating to an online forum versus an interview and to specify how people used the forum (technically and for what purposes).

Attitude of the participants towards an online forum

Reasons to opt for forum rather than for interview

The motivations to participate in a forum rather than in an interview reported by the respondents are:

- The asynchronous organisation :
  The possibility to participate when you like –i.e. as often as you like, at the time you like, when you see a possibility with no previous schedule– was anticipated as a positive feature of the forum. This flexibility is appreciated in general and particularly by long COVID patients who suffer from fatigue, lack of energy and brain fog. Some respondents opt for the forum because they were not available for an individual interview.
  The asynchronousity of the forum also allows to take time for reflection.
- A forum better suits their personality or personal features:
  A forum allows to remain anonymous, which is valuable for some people, particularly because some people do not want to be identified as 'complaining'. For shy people, this way to collect data is an opportunity to express themselves safely. Finally, some people are not sure to be sufficiently legitime to participate, because they consider their symptoms as rather light compared to those of other people.
- The written format:
  Firstly, by answering in writing, people do not feel obligied to justify themselves when they do not want to. In the long COVID population, this aspect is very relevant because patients suffer from incomprehension and often feel that they are not taken seriously. They thus feel that they frequently have to justify themselves. Secondly, for long COVID patients who have voice troubles, the written way is obviously an easier way to participate. Finaly, some repodents are already used to participating in discussion fora or group discussions (via Facebook, etc.) and hence feel comfortable with this way of expression.
- The group format :
  By opting for the forum, participants opted for a group approach compared to an individual approach. Participants underlined that this way of contributing to the data collection process was an opportunity to understand what other people experience, to get information in general about the condition, the treatments, etc., to feel less alone, which could decrease anxiety for some people. In addition, they expected to get information about other people's experiences, valued participating in a collective research activity, hoped to situate themselves among the other patients ("Am I alone to have this symptom, is my situation worse or better that the others?"). Some of them saw an opportunity to make contact with other patients.
- The interactivity :
  Related to the group format, participants reported valuing the interactivity feature of the forum : They expressed a desire to exchange information about long COVID (symptoms, treatment, etc.), to exchange experiences, particularly with people who understand. This aspect is obviousely related to their frustration of not being taken seriously by the entourage. Some of them saw in the forum an opportunity to help other people. The interactivity is, in addition, a means to enhance more creativity in finding solutions.
- Other:
  While we have clearly proposed to chose between an interview and a forum, it appears that some participants were not aware of the possibility to be interviewed. Finaly, some people were indifferent between participating in an interview of the forum.

Preferences

Results show that there is (are) no specific preferred day(s) to connect to the forum space. While some people prefer to connect at the end of the day, a large part of the participants did not have a prefered time of the day to contribute to the forum.

Table 44 – Preferred day to connect to the online forum (several answers possible)

Day	n
Monday	3
Tuesday	3
Wednesday	2
Thursday	2
Friday	2
Saturday	4
Sunday	5
No preference	40

Table 45 – Preferred time of the day to connect to the forum

Time	n
No preference	22
20h – 23h	14
17h – 20h	8
7h – 9h	5

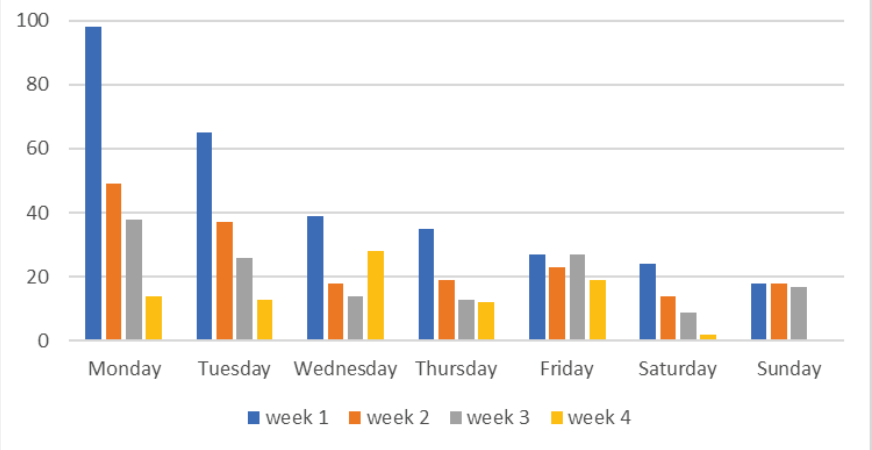
Way to participate in the forum

Our rapid online survey on the experience with the forum clarified the way people participated. While we asked participants to connect at least 3 times a week to enhance interactivity, the majority of the respondents admitted to have connected once a week or less.

Participation

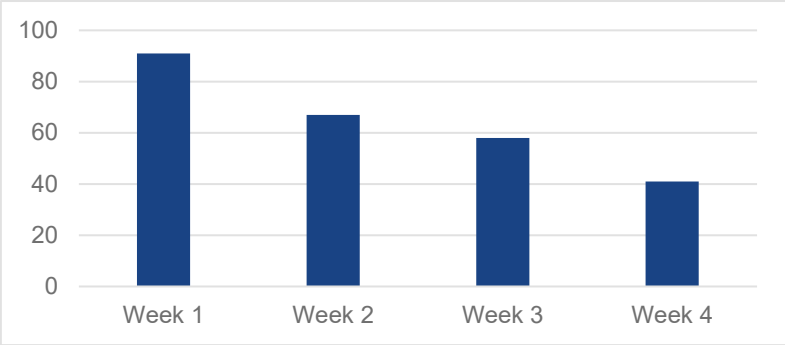
Figure 16 shows that participants connected rather on the Monday and that the number of connections decreased during the week, excepted for the 4th one. This is explained by the fact that new topics were posted at the beginning if the week, excepted for the last one where we posted on the Wednesday too.

Figure 16 – Number of connections to the forum per day and week



The decreasing participation is related to the decreasing number of participants per week (Figure 17).

Figure 17 – Number of participants in the forum per week



When we asked how often participants logged on to the forum, we state that only around one third of them respected the requirement. Many of them have been connected only once a week or less (Figure 18). Moreover they reported that they did not post a reaction at each connection (Figure 19).

Figure 18 – Self-reported rythm of connections to the forum per participant

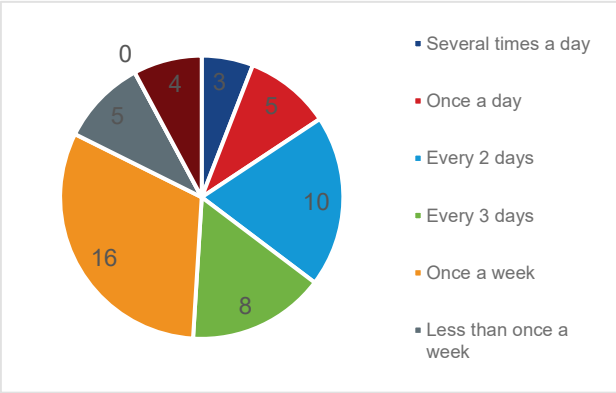
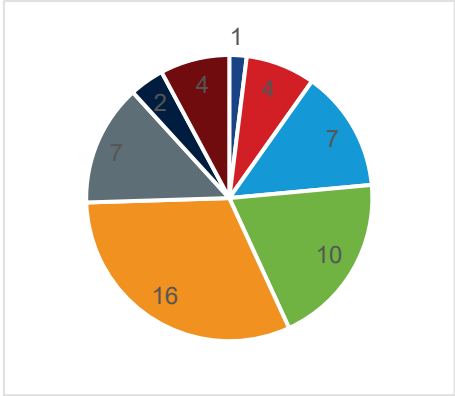
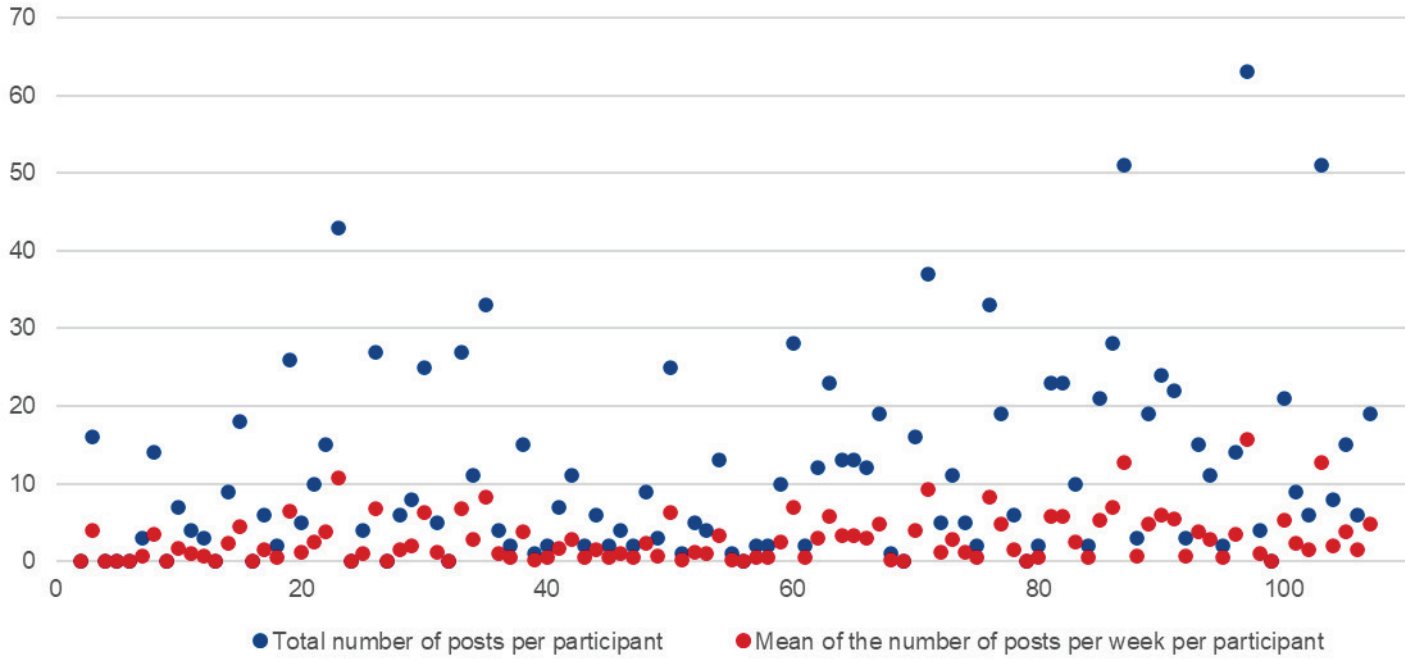


Figure 19 – Self-reported rythm of posts in the forum per participant



From the statistics of the forum itself (Figure 20) we learn that people posted till 63 reactions, i.e. 15 posts per week in average.

Figure 20 – Number of posts in the forum by participants (total and mean per week)



Drop-out

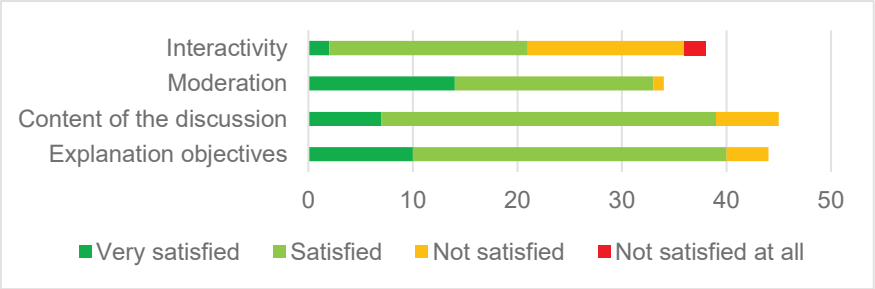
Sixty-eight persons had registered for participation in the forum but finally did not contribute. Among those who dropped out, only 8 responded to our post-forum survey. These people explained that they changed their mind because they were too tired to participate (n=3), too ill (n=1), finally did not have time to contribute (n=2), forgot about it (n=1) or experienced technical issues to register to the forum (n=1).

Satisfaction and experiences of the participants towards the online forum

We asked the participants their level of satisfaction with the forum according to several features (Figure 21). In general, the majority of the participants was satisfied with the forum. The objectives were well explained, they appreciated the content of the discussion and, for those who answered the question, the moderation. Regarding this last aspect we would like to state that a large part of the respondents preferred not to

answer this question, maybe because it is directly related to a person and not to the tool.

Figure 21 – Satisfaction of the participants with different forum features



People who were not really satisfied with the explanation of the objectives pointed out that they were not convinced that such a data collection could be helpful, because it is not based on scientific evidence or because of what they have read in the forum.

> *« Au vu des échanges dans ce forum, je ne comprends pas à quoi pourra servir le contenu de ce forum pour la suite de la prise en charge. »*
>
> *"Ik heb niets aan te merken op de uitleg en de doelstellingen van het forum, dus ben ik daar tevreden over. Veel zal nu afhangen van wat u in de toekomst zult doen met de resultaten van het forum."*

Moderation was appreciated: both the presence of the moderators as well as their human and empathy skills. Nevertheless, some participants expected more interventions from the moderators to generate interaction. More generally, some of them regretted the rules they had to stick to: they do not understand why, in a closed discussion, posts containing names of institutions or healthcare professionals were not allowed.

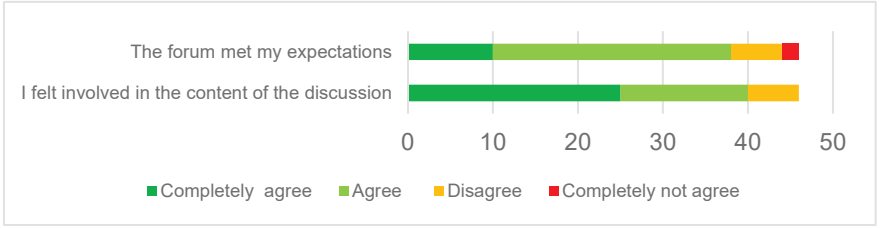
A large group of participants were not satisfied (and a few "not satisfied at all") with the interactivity on the forum. For example, one participant felt like 'talking in a vacuum'. Indeed, while one person compared the forum to the heavy discussions within the Facebook group, another expected exchanges with scientists or physicians and one participant regretted not having found ideas to be helped. Nevertheless, these two last kinds of interaction were not pursued by the forum in the context of this data collecting exercise. Regarding the content of the discussions: people who were satisfied explained that they recognised themselves in the posts. People who were less satisfied, mentioned the repetitiveness of some posts, the too large amount information, and the lack of interactivity. Suggestions to opt next time for a social media forum or open questions were proposed.

> *« Bien que le format du forum soit très bien fait, ce n'est pas très motivant car cela prend beaucoup de temps de découvrir l'ensemble des informations qui sont postées sur le forum par d'autres. »*
>
> *« C'est souvent redondant et il y a des personnes qui écrivent beaucoup. Cela prend du temps pour lire. ».*

A participant emitted the hypothesis that it was not easy to interact because, while all the participants had different journey, they met the same difficulties. Without diversity in views or experiences, interactions are often less extensive.

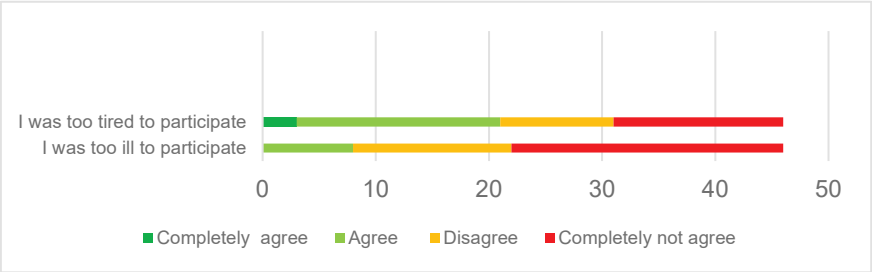
These aspects explained probably partly why a few people considered that the forum did not meet their expectations or why they did not really feel involved in the discussions (Figure 22).

Figure 22 – Experience with the forum



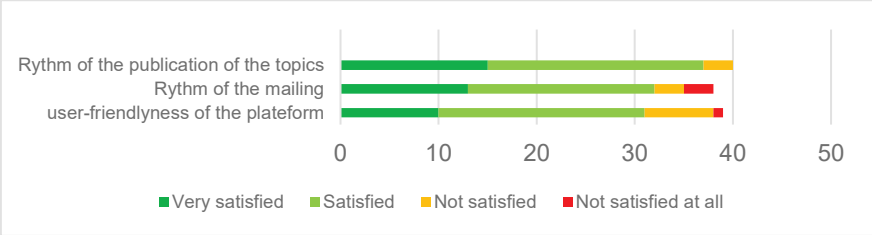
To enhance the interaction, possibilities to deepen answers and the discussions in general, we asked participants to visit the forum at least three times a week. It appears from the results (Figure 23) that this rhythm was too heavy for nearly the half of the respondents, and that, in the same proportion, tiredness was an issue. Also, more than half of the participants missed time to participate. Illness had also limited participation in the discussion be it for a smaller group of participants.

Figure 23 – Experience with the connections to the forum



Regarding the way the forum was scheduled and presented, Figure 24 shows that participants were in general satisfied with the duration of the forum, as well as the rhythm of the publication announcing the availability of new discussion topics.

Figure 24 – Satisfaction regarding the process of the forum



Unsatisfied persons seem to have missed the emails. Also the rhythm of the publication of new topics was appreciated because participants had time to reflect before posting or reacting and felt no pressure. The planning announced in advance allowed to clarify the functioning of the forum. Regarding the total duration of the forum, it was generally appreciated, while some participants had preferred more time, suggesting a permanent opening. Others considered it too long.

The platform we used was mentioned by some as not being user-friendly, because of the layout and the not so intuitive navigation. The platform did not stimulate interaction, for instance because there were no clear alerts when a reaction to a post was given.

Advantages, disadvantages and suggestions for improvement of the data collection by an online forum

Perceived **advantages** after having participated in the forum were:

- The format is convenient because:
  - It gives liberty of time and tempo
  - It gives the possibility to reflect before answering
  - It is possible to exchange information and ideas with other participants
  - It is possible to express yourself
  - It could be a means to vent your feelings
  - It gives structure to the topics
  - It is easy to organise your own thoughts
  - It allows to avoid missing something
  - It allows to review and correct your answers
  - It is easy to participate, also for people who are tired or are unable to move
  - It allows collection of data in a difficult sanitary context
  - It allows interaction with other patients

- It offers a safe environment to share sensitive data, thanks to the presensence of moderators

- Personal enrichment
  - It is a means to learn
  - It is a means to get information
  - It gives the feeling to be less alone
  - It allows getting to know others' experiences
  - It gives confidence or reinsurance because of the presence of people with similar experiences
  - It gives energy
  - It gives the feeling to be recognized
  - It allows improving the scientific knowledge about the condition
- Objective
  - It gives the opportunity to be heard
  - It gives the opportunity to be taken into consideration
  - It gives hope that something will (rapidly) be done to meet the patients' needs

Perceived **disadvantages** after having participated in the forum were:

- Related to the consequences for the participants:
  - It increases physical discomfort because typing is not easy
  - Reading about problems you do not experience yourself (yet) or you had not linked to the condition could create discomfort or fear
  - It creates fatigue
  - It is an extra medium to follow (by other participants)
  - It is not clear what will be done with the answers
  - There is no personal follow up or solution from the research team
- Related to the format
  - It is difficult in case of brain fog
  - It is time demanding (for 3 connections per week)
  - It is less easy to exchange or interact than in a classical discussion
  - It is less 'human' than a face-to face interaction
  - Typing seems less efficient
  - The motivation to partcipate rapidly descreases
  - It is distant

Disadvantges of data collection for a scientific report notified but not related to the format of the forum include

- The long delay between the data collection and the publication of the report
- There being other surveys and research projects abroad that are more advanced

Some participants made **suggestions** to improve the forum as a data collection tool :

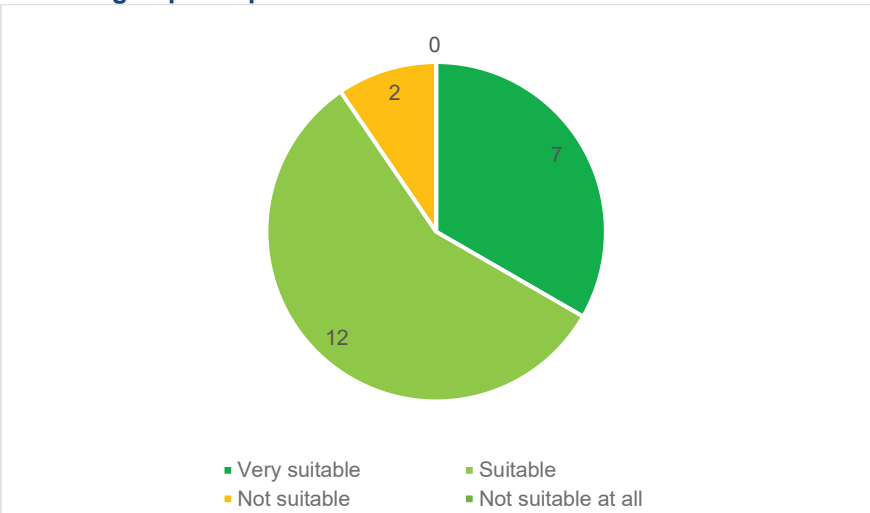
- To add researchers to allow for a more rapid and personnalised follow-up, and to increase the presence on the forum
- To opt for a more user-friendly platform, also more adapted to a smartphone
- To make all subjects available at start to allow people to choose where they will put their energy and priorities
- Identification of keywords to allow people to go immediately to the topic of their interest
- To better enhance interactions

- To increase the frequency of reminders per email
- To require less connections
- To keep the forum open longer
- To change the design: only open questions
- To have a medical advisor on board in the forum
- To give the opportunity to participants to ask medical questions to a physician, outside the forum

Suitability of an online forum to identify patient's needs

The very large majority of our sample of participants found that an online forum is a suitable way to identify patients' needs (Figure 25)

Figure 25 – Perceived suitability of a forum to identify patients' needs according to participants of the forum



Key messages

- **A forum is perceived as an adequate means to identify patient needs**
- **Participants were generaly satisfied with this way of data collection**
- **A forum has several advantages for the participants because of the written asynchronous nature and the potential group dynamics**
- **Perceived disadvantages of a forum are related to the content of the discussion (emotional, energy demanding…) and the lack of interactivity**
- **People are not active in the same way (rhythm of connections, posts)**
- **Keeping participants active in a forum during several weeks is challenging**
- **The number of required connections should be low (2 seems to be a maximum)**

9.3.4 The moderators' perception on a data collection via an online forum

We interviewed separately the 2 moderators. We heard common reflections on their both experiences but also differences due to their personality.

9.3.4.1 Quality of the data

The moderators reported that the forum produced a large amount of information. However, one moderator questioned the richness of the data and the added value of the method because the lack of interactivity between the participants and between the participants and the moderator. An hypothesis is that questions might be too directive, too structured.

Lack of spontaneity of the responses was underlined. But in another way the time to reflect for the participants and the possibility to nuance their answers was perceived as an advantage.

9.3.4.2 The moderation

Working remotely is an advantage: it is easy to connect, it is not necessary for the researcher and/or for the participants to travel. And that is more compatible with the other professional tasks. Moderators have blocked time in their agenda and did not found difficult to manage the moderation in combination with the rest of their work. Moreover, directly having accessible output was appreciated.

Nevertheless, for one moderator, it was very frustrating to not have face-to-face relationship with the respondent. The absence of non-verbal communication was difficult to manage. It was also difficult to know when exactly relaunch a question or deepen a response, particularly to keep the discussion in the study scope. In that way, skills in qualitative research is clearly required to guarantee that the discussion follow the right track. Because of the medical content of the discussion, medical skills would have been an added value to be sure to have understood certain responses.

The moderators noticed that some participants had inadequate expectations of what will happened in the forum. These frustrations were difficult to manage.

Moderators were invited to connect 3 hours a day what was enough regarding the participants who respected well the rules. However moderators remarked that participants did not connect as frequently as what was required.

The interactivity with the KCE team via a separated platform was appreciated.

9.3.4.3 Technical aspects

It was not easy to identify the new posts in the quantity of the discussions. New interventions should be more visual, in bold for example. This could contribute for better interactivity among all participants and facilitate targeted relaunches. A menu on the side of the platform with themes and sub themes would be appreciated to facilitate navigation through the discussions.

It should be advisable to make the signal of the reactions (actually a bell at the top of the screen) more visible.

Key messages

- **According to the moderator, a forum deliver much information on patient needs**
- **According to their personality and skills, moderators felt more or less confortable with their task.**
- **Skills in mediation, qualitative research and medical background are advisable**
- **Two to three hours per day are sufficient, better divided in several short period foreseen in the agenda**
- **Plateform should be improved to facilitate the identification of the new posts and enhance interactivity**
- **Objectives of the discussion should be clarified to avoid inadequate expectations**
- **Communication with the research team is advisable**

9.3.5 Comparison between online survey, forum and interviews

Based on the results from the previous part and the features of each method, we compared what is required and what could be expected using the different methods we used in this study (Table 46). We added information on online focus groups to give a complete picture of what is possible. The information comes from our expertise and particularly our experience with online focus groups carried on the study on somatic care in psychiatry.[148]

Table 46 – Comparison of online methods to identify patient needs

	Online survey	Online asynchro-nous Forum	Individual online interviews	Online focus groups
Process / preparation				
Material				
For the researcher and the participants	Access to internet	Access toternet	PC, laptop, smartphone, or tablet with microphone and camera & good internet connection	PC, laptop, smartphone, or tablet with microphone and camera & good internet connection
Interface*	Limesurvey©	Moodle© or other	Zoom© or other	Zoom© or other
Human resources				
Technical support	No	Yes	No	No
Data collection tool conception	Researcher with skills in surveys	Researcher with skills in qualitative data collection	Researcher with skills in qualitative data collection	Researcher with skills in qualitative data collection
Required skills	Survey	Qualitative data collection	Qualitative data collection	Qualitative data collection
Cost	/	- Training of moderators - Platform	Training of interviewers	-Training of interviewers -Platform
During data collection				
Human resources				
Technical support	No	Hotline	No	No
During the data collection	No	At least 1 moderator	1 interviewer	1 interviewer + 1 note taker / observer
Required skills	N.A.	Written moderation (some knowledge on the topic)	Oral moderation	Oral moderation
N of participants in the data collection time lapse	Unlimited	Unlimited	Limited	Limited
Guarantee of the ID of the respondent	No	No	Yes	Yes
Spontaneity of responses	No	No	Yes	Yes
Power relation between researcher and participants	NA	Reduced	Possible	Possible
Power relation between participants	No	Possible	No	Possible
Guarantee to get response when needed	Yes	No	Yes	Yes

	Online survey	Online asynchro-nous Forum	Individual online interviews	Online focus groups
Influence moderator / interviewer in the responses	No	Yes	Yes	Yes
Non-verbal communication	No	Limited: using capital letters, punctuation, emoticons, emojis	Yes	Yes
Output				
Type of output	Quantitative data Some qualitative data	Written qualitative data	Oral qualitative data	Oral qualitative data
Availability of the corpus of analysis (raw data)	Direct	Direct	Time for the transcription	Time for the transcription
Human resources and skills	Quantitative data analyst Qualitative data analyst	Qualitative data analyst	Qualitative data analyst	Qualitative data analyst
Costs	No	No	Transcriptions	Transcriptions
Quality of the output				
Possibility to quantify answers	Yes	Not appropriate	Not appropriate	Not appropriate
Possibility to get deepen responses	No	Limited	Yes	Yes
Possibility to have reached unexpected answers	Limited	Limited	Yes	Yes

Table 46 shows that each method has advantages and inconveniences to estimate the needs of patients.

We were forced to use online data collection methods due to the sanitary situation. Nevertheless it is interesting to compare the process, the duration of data collection and the outputs differences between a 'real' face to face qualitative data collection and an 'online one. This comparison is presented in Table 47.

Table 47 – Features of face-to-face and online synchronous qualitative data collection methods

	Face-to-face	Online (synchronous)
Process / preparation		
Material		
For the researcher	(Video) recorder	Zoom©, Teams©, etc.
For the participant	None	PC, laptop, smartphone, or tablet with microphone and camera & good internet connection
Human resources		
Technical support	No	No
Data collection tool conception	Researcher with skills in qualitative data collection	Researcher with skills in qualitative data collection
Required skills	Qualitative data collection	Qualitative data collection
Cost	- Training of moderators -Traveling costs	- Training of moderators - Platform (if focus group)
During data collection		
Human resources		
Technical support	No	No
During the data collection	At least 1 moderator	At least 1 moderator
Required skills	Oral moderation (Some knowledge on the topic)	Oral moderation (Some knowledge on the topic)
Number of participants in the data collection time	Max 12 participants per focus groups	Max 6 participants per focus groups
Guarantee of the ID of the respondent	Yes	Yes
Spontaneity of responses	Yes	Yes
Power relation between researcher and participants	Reduced	Reduced
Power relation between participants	Possible	Possible
Guarantee to get response when needed	Yes	Yes
Influence in the moderator/interviewer in the responses	Yes	Yes
Non-verbal communication	Full body language	Partial body language
Output		
Type of output	Sound (& video) recording	Sound & video recording

	Face-to-face	Online (synchronous)
Availability of the corpus of analysis (raw data)	Time for the transcriptions	Time for transcription
Human resources and skills	Qualitative data analyst	Qualitative data analyst
Costs	Transcriptions	Transcriptions
Quality of the output		
Possibility to get deepened responses	Yes	Yes
Possibility of unexpected answers	Yes	Yes

N.A. Not applicable

Here also, we state that according to the purpose of the data collection, the population and the available resources, one approach or the other could be more or less appropriate.

9.4 Discussion and conclusion

Our evaluation showed that both online fora a and interviews are suitable techniques for identifying patient needs. It is impossible to check whether these techniques can catch all patient needs, as there is no gold standard for identifying patient needs. In general, we can conclude that each of the methods has its limits, requirements, advantages and disadvantages. These depend on the population, the illness, the resources allocated to the study. For example, if a forum is set up to stimulate interaction between participants, it will not be successful in areas where there is a lot of consensus on the issues experienced by patients. If all patients have approximately the same needs, interaction will be limited. An alternative could be considered, like an online questionnaire with large open-ended questions for example, but we have no idea on the attractiveness of such format compared to a forum. Moreover, analysing responses to open-ended questions is challenging, as demonstrated by the online survey in long COVID patients.

If a discussion platform is used, the objectives should be clear from the start, attention should be paid to the qualities and skills of the moderators, the technical aspects of the platform, the schedule for the publication of new discussion topics and the duration of the forum.

Our methodological reflections have some limitations.

We performed only a quick literature review, results are non-exhaustive.

We based our reflections on only one research topic, long COVID, a new condition, consequence of a pandemic, with much ongoing research and very few medical knowledge, and a large group of respondents. Collecting information on smaller groups of patients, suffering from a better known pathology, chronic, acute or even an orphan, might result in other findings and considerations.

We had only online collected data. This means that only people who were able to manage with computer equipment and who had an internet connection could be included in the study. It was hence not possible to measure the influence of the digital divide on the participation to the study and the results of the different data collection methods. It also hampered the comparison between an online versus face-to-face approach ‘on the field’.

While we originally intended to test the appropriateness of collecting data on patient needs via a forum only, the combination of the long COVID study report and this study has allowed us to focus more closely on certain methodological aspects. While this opportunity certainly has had an added value for our reflections, we should acknowledge that comparing an individual approach (interviews) with one group approach (forum) has limitations. Ideally two group data collection approaches (i.e. focus group and forum) should be compared to the individual approach to identify more

clearly what emerges from the interaction between the participants versus from individual interviews.

Another limitation of our study is that content analysis occurred only on the French-speaking material (as explained in section 9.3.2).

Regarding the process of the evaluation of the forum, we faced a large number of non-respondents, particularly in the group of candidates who finally did not participate in the forum. This did not allow us to document in-depth the reasons for candidates' changing their mind between the online survey and the start of the forum discussion.

Moreover, the interviews with the moderators of the forum were carried out by a member of the research team who was involved in the building of the survey, the forum and the interviews. There is therefore a risk of bias of desirability that had potentially interfered in the responses.

10 SUMMARY OF FINDINGS

The definition and identification of patient needs is a challenge identified by many health authorities and healthcare decision makers. The European Medicines Agency (EMA) uses the concept of unmet medical need to take decisions on conditional marketing authorisation and accelerated assessment[149], the new European Pharmaceutical strategy[150;w], adopted on 25th November 2020, explicitly refers in its primary objectives to addressing unmet medical needs, and healthcare payers have used the concept to decide on early temporary reimbursement of pharmaceutical products[x].

The European Commission has defined unmet medical needs as "a condition for which there exists no satisfactory method of diagnosis, prevention or treatment authorised in the Community or, even if such a method exists, in relation to which the medicinal product concerned will be of major therapeutic advantage to those affected".[9] In addition, EMA refers to unmet medical needs as "chronically or seriously debilitating condition or whose condition is considered to be life threatening, and who cannot be treated satisfactorily by an authorised medicinal product". The NIHDI, logically taking a reimbursement perspective, defines unmet medical needs as "a severe or life threatening condition for which no reimbursed alternative treatment is available".(Belgian law of 7 February 2014[10] and Royal decree of 12 May 2014[11])

For consistency with previous KCE work on unmet medical needs[12], we used the concepts of therapeutic needs and -more general- patient needs. **Therapeutic needs** refer to clinical needs or needs directly related to (health)care. They encompass subjective, clinician-validated medical needs[8], subjective medical expectations that are not met[8] and clinically determined medical expectations that are not met[6]. In short, it concerns needs perceived by the patients that are not met by currently available

w pharma-strategy_report_en.pdf (europa.eu)

x See, for example, Onbeantwoorde medische behoeften - Unmet Medical Need - RIZIV (fgov.be) and Besoin médical non rencontré - Unmet Medical Need - INAMI (fgov.be)

reimbursed treatments or care, either because they do not exist or because they are not sufficiently effective.

Patient needs is a more general concept and encompasses therapeutic need as well as other needs, related to the patients' health condition but not strictly healthcare-related. Such needs can refer to social support needs, information and education needs, spiritual needs, financial needs etc. related to the patients' condition.

Budgetary pressure on the healthcare system makes it increasingly important to target resources to the areas with the highest unmet needs. In 2016, KCE published a report on how to assess therapeutic and societal needs, using a multi-criteria decision approach (MCDA).[3] This approach defined therapeutic needs based on three criteria: impact of the condition on life expectancy after providing standard of care treatment, impact of the condition on quality of life with the current standard of care, and the inconvenience of the current standard of care for the patient. These three criteria are often insufficient to capture all patient needs or to understand the actual implication of the stated impact on quality of life or inconvenience of treatment. A frequently cited example is fatigue: some generic health-related quality of life instruments, like the EQ-5D-5L, do not include fatigue as a separate dimension, while it might be very important and impactful for patients' quality of life. Moreover, quality of life and inconvenience of current treatment are multi-dimensional concepts in themselves. To be most informative for decision making, it is important to have in-depth knowledge on which dimensions are most affected and why. The current study complements the previous one, by specifying how patient needs can be identified directly from patients, to either complement the criteria for the MCDA and/or better understand the actual breadth of the included criteria.

The objective of this project was to develop a feasible and scientifically valid methodology for identifying real patient needs, as perceived by the patients themselves (or by a proxy on behalf of a patient, if patients are not able to express themselves), which can feed in the decision processes at RIZIV – INAMI, but can also serve other purposes and other objectives of different stakeholders in healthcare, like researchers, research funders, patient organisations, sickness funds, etc. The ultimate aim is to contribute to the creation of a more needs-driven healthcare system by defining the gaps in research or current policy that need to be filled to meet patients' needs.

The literature review revealed three categories of approaches to collect data on patient needs: quantitative, qualitative and mixed approaches. In all categories, we focused on scientific approaches, involving the application of scientifically validated methods. Approaches like public hearings or involving patients in committees as witnesses are not included in our scope. The mixed approach, combining quantitative techniques such as surveys with qualitative techniques such as interviews or focus groups, supported by scientific literature review, is the most comprehensive and promising approach to fully capture patients' needs. Therefore, we built further on this approach to develop our methodology.

Based on the review, we identified six dimensions of patient needs:

- **Physical dimension:** referring to needs on the physical level and the common demand of physical symptoms relief (such as pain relief);
- **Psychological dimension:** referring to psychological support to deal with emotional problems related to the health condition;
- **Autonomy:** referring to needs concerning daily living and taking care for oneself;
- **Social dimension:** referring to needs related to social interactions with the community or family and building relationships. This dimension also encompasses the need for appropriate information and communication;
- **Accessibility:** referring to needs of transportation to access care or several activities, waiting lists, financial accessibility;
- **Spiritual dimension:** referring to needs concerning spiritual issues related to the diagnosis of the condition, such as search for meaning, moral contexts or religious beliefs.

These dimensions were included in a generic patient needs questionnaire, developed in collaboration with patient representatives. The questions

were derived from the questionnaires included in the literature review, from which we know that they have been validated and tested psychometrically. A two-round Delphi process was used to arrive at an intermediate version. The questionnaire has been translated to Dutch and French by KCE. During the development of the questionnaire, a few challenges were identified. First, it proved difficult to create a generic questionnaire, that is sufficiently broad to allow all types of patients to express their needs and at the same time not too extensive or complicated to ensure it is still feasible for patients to complete the survey. Second, it became clear that the generic questionnaire would require at least some adaptation for each specific condition. We recommend, however, not to add too many questions or change the framing of the questions to maintain validity and feasibility. The objective is to use a similar questionnaire across health conditions and populations, to ensure equal treatment of different populations and minimise bias introduced by the researchers in surveying patients on their needs. If more in-depth information is needed -e.g. to be able to translate the findings of the patient needs study to concrete (policy) measures or actions- it should be taken up in the qualitative part of the data collection exercise. Of course, in all instances where the questions refer to the generic term 'your condition', this term could be replaced with the name of the condition under consideration.

The patient survey and two qualitative data collection techniques to obtain more in-depth information on the quantitative outcomes resulting from the survey (online forum and interviews) were tested during a pilot study in patients suffering from long-term sequelae after COVID-19. The objective of the pilot study was to assess whether the questionnaire is applicable, useful and effective in identifying patient needs; whether an online forum helps to collect in-depth qualitative information on the needs emerging from the survey. The online forum is a rather new technique for qualitative data collection for KCE. The opportunity was taken in this study to test the feasibility and added value of such a forum compared to individual interviews.

Concerning the questionnaire, we learned from the Delphi panel and the pilot study that:

- Developing a patient needs questionnaire requires good prior knowledge of the condition under investigation. Therefore, a literature review and/or consultation with patient representatives and/or healthcare professionals will be required
- Providing the possibility to let a proxy complete the survey on behalf of a patient is important;
- A patient needs questionnaire can never be entirely generic, adaptation of the questionnaire to the condition in question will always be necessary
- It is necessary to be vigilant about the format of the questionnaire (paper and/or online), because some people may be incomfortable with modern (ICT) technologies
- For the recruitment of participants to a patient needs survey, an appropriate strategy should be developed for the dissemination of information about the existence of the survey
- Particular attention must be paid to the clarity and unambiguity of the questions
- Open-ended questions should be avoided in a questionnaire as they are difficult to include in a quantitative analysis. The coding of free text answers always requires some kind of interpretation from the researcher and might thus introduce bias in the quantitative results (due to e.g. misinterpretation of the free text by the researchers).
- When an exhaustive list of response categories cannot be provided, the respondent should be able to answer "other", but the examination of what this entails should happen using qualitative research techniques (e.g. interviews or discussion forums).
- It is difficult for patients to make a distinction between symptoms of their condition and side-effects of the treatment.

These learnings led to adaptations in the generic questionnaire. The final version of the generic questionnaire is provided in Appendix 3 and as a

separate document. The questionnaire is available in three language versions.

Concerning the online forum as a tool for collecting qualitative data on patient needs, we learned from the pilot survey that:

- A forum allows to identify a lot of information on patient needs;
- The majority of the participants in the forum was satisfied with this approach to data collection and on the overall content of the discussion;
- In the case of long COVID, the invitation to participate in a qualitative research project, subsequent to completing an online survey, attracted relatively more highly educated and working patients and patients more impacted by the condition;
- Among the candidates for the qualitative part of the long COVID study, candidates for the forum were relatively less educated and less impacted by the condition than candidates for the interviews;
- Compared to data collection via individual interviews, the forum identified partly the same needs. Nevertheless each data collection technique generated different types of information:
    - Interviews delivered a more complete history, including the context of the responses but only about half of the patient needs,
    - The forum generated more diversity in the information related to the patient needs and more suggestions for improvement of the patients' situation. This is probably due to the higher number of respondents.
      Unfortunately, the lack of interactivity during the forum and the fact that the respondents did not always react to the triggering questions of the moderator led to several unclarified ideas.
- In order to reach an efficient data collection via an online forum, some attention points have been highlighted by our pilot exercise:
    - Expectations of the patients participating in a forum have to be clearly framed in order to avoid frustration.
    - Moderators' skills and affinity with the method are important: a background in mediation, qualitative research is advisable, as well as a basic understanding of the medical aspects of the health condition under consideration (or the possibility to rely on a medical expert in case of questions). Affinity with written communication is necessary.
    - The platform used for the forum has to be user-friendly and enhance interactivity.
    - Discussion between the moderators and the research team is advisable to swiftly tackle any issues or concerns.
- A period of 3 weeks for the data collection, with prior communication about the planning for the posting of new topics, is appropriate.
- Asking the participants to connect at least every 3 days seems to be appropriate.
- Moderators have to spend 2 to 3 hours per day on their task.

While these lessons are valid for the long COVID case, they might have to be adapted according to the condition being studied.

The exercise as described above (i.e. quantitative and qualitative data collection) is time consuming, and some kind of prioritization will be required to start the patient needs identification activities. Therefore, we examined different databases and initiatives that could help to identify health conditions with high unmet needs, which could help in the prioritization process. Besides the individual patient needs due to the impact of a condition on quality of life and the inconvenience of the current treatment, also the impact on life expectancy matters. By comparing the impact of disease on life expectancy and quality of life, compared to non-ill population with the same characteristics (i.e. the population 'norms'), the

severity or burden of disease can be estimated.[y] The Belgian Health Interview Survey, Belgian Burden of Disease study, Global Burden of Disease (GBD) study, SHARE and NIHDI (unmet needs) databases were identified as useful. From these databases, 99 health conditions with potentially high unmet needs have been identified, mainly oncological, neurological and cardiovascular diseases. However, it should be noted that each of these databases has its strengths and weaknesses for the defined purpose. For example, the number of diseases is limited and usually defined in broad terms (encompassing several health conditions), rare conditions are most often not included, indicators are sometimes attributed by experts only, (very) young people are sometimes excluded from the database and the method used to derive the indicators is limited (e.g. GBD results are derived from data from other countries). An interesting finding from the analysis of the databases was that conditions for which there are little (effective) treatments available -and hence there are high therapeutic needs- often rank high on the unmet needs lists derived from the databases. This implies that pending on the development of such treatments, the 'other' needs of patients, e.g. the care-related needs, become more important to ensure patient-centred, value-based and high quality patient care. This emphasises the importance of *asking* patients about these needs (by means of a survey and/or qualitative research), besides identifying the therapeutic needs based on existing databases.

11 SUGGESTED IMPLEMENTATION APPROACH

11.1 How to implement a patient identification programme?

It is not realistic to expect from individual patients, citizens or healthcare professionals that they perform extensive in-depth quantitative and qualitative research on patient needs for the purpose of creating an evidence-based list of patient needs. It seems more appropriate to assign this responsibility to a scientific organisation that has and/or can attract people with the right competences to set up and execute or coordinate the required studies to collect the evidence on patient needs. To ensure that an organisation takes up this responsibility, we consider two possible scenarios: either to mandate an existing organisation with a new mission or to establish a new unit.

11.2 How to use the data

The implementation approach suggested in this chapter is independent of the scenario that is eventually chosen. The objective of the responsible organisation would be to collect detailed, in-depth evidence on patient needs for several conditions, that can serve as an input for several instances that need this evidence to develop their activities. The most obvious user of the output of patient needs studies seems to be the NIHDI, in the context of its unmet medical needs programme or in the context of reimbursement decisions. However, other stakeholders will also benefit from the evidence on patient needs. For example, it will help companies, researchers and research funders to prioritize their research activities; patient organisations and sickness funds to develop communication strategies and/or (public) information campaigns, the European Medicines Agency to assess whether a new medicinal product meets the most

[y] We leave aside whether the disease burden should be expressed in terms of proportional or absolute shortfall (loss of healthy life due to disease compared to full health, either in relative or in absolute terms), as described by Stolk et al.[151, 152]. The biggest difference between the two is the influence of the age of the patients. This is a normative choice and both have their strengths and weaknesses.

important needs of patients; and many other stakeholders in the healthcare or welfare sector to develop or improve their activities. In the study on long COVID, for instance, patients highlighted that the lack of information on the health condition is a major issue, both from the healthcare providers' perspective and from the societal perspective. They do not feel recognized and felt that they had to justify themselves repeatedly for being ill. Sickness funds and patient organisations could help to increase the awareness around the condition.

Table 48 describes a few concrete and possibly immediate applications for decision making processes of some stakeholders. The list is not exhaustive, however, as it is very well imaginable that other, e.g. also regional, agencies could make use of the evidence generated by the patient needs identification projects.

Because of the broad relevance of the patient needs evidence, it is important to involve stakeholders in the full process, from identification of priority areas for further research on needs, to dissemination of the in-depth study results.

Table 48 – Some possible applications of the evidence on patient needs

Stakeholder	Evidence on patient needs as input for
European Medicines Agency (EMA)	Assessing candidates for the PRIME scheme[z] Assessing whether a new medicinal product targets and meets the most important needs of patients with a specific condition
NIHDI – Advisory Committee on Temporary Reimbursement for the use of a medicinal product (CATT/CAIT)	Creating a rank ordered list of health conditions according to their level of unmet needs
NIHDI – Drug Reimbursement Committee (CTG/CRM), Medical Devices Reimbursement Committee (CTIIM/CRIDMI), other services where reimbursement decisions are discussed	Reimbursement decisions: to assess whether a new medical product, service, intervention or management programme meets the most important needs of patients
Federal Public Service Health, Food Chain Safety and Environment	Prioritizing policy measures in patient-related themes
Medical product developers	Prioritizing R&D activities: focussing on the areas with the highest unmet needs Targeting development activities within a disease area to the most important needs of patients with a specific condition
Patient organisations and sickness funds	Developing a communication strategy towards decision makers, healthcare professionals, product developers, other patients, … Develop information campaigns and educational material (written, online, oral) for patients

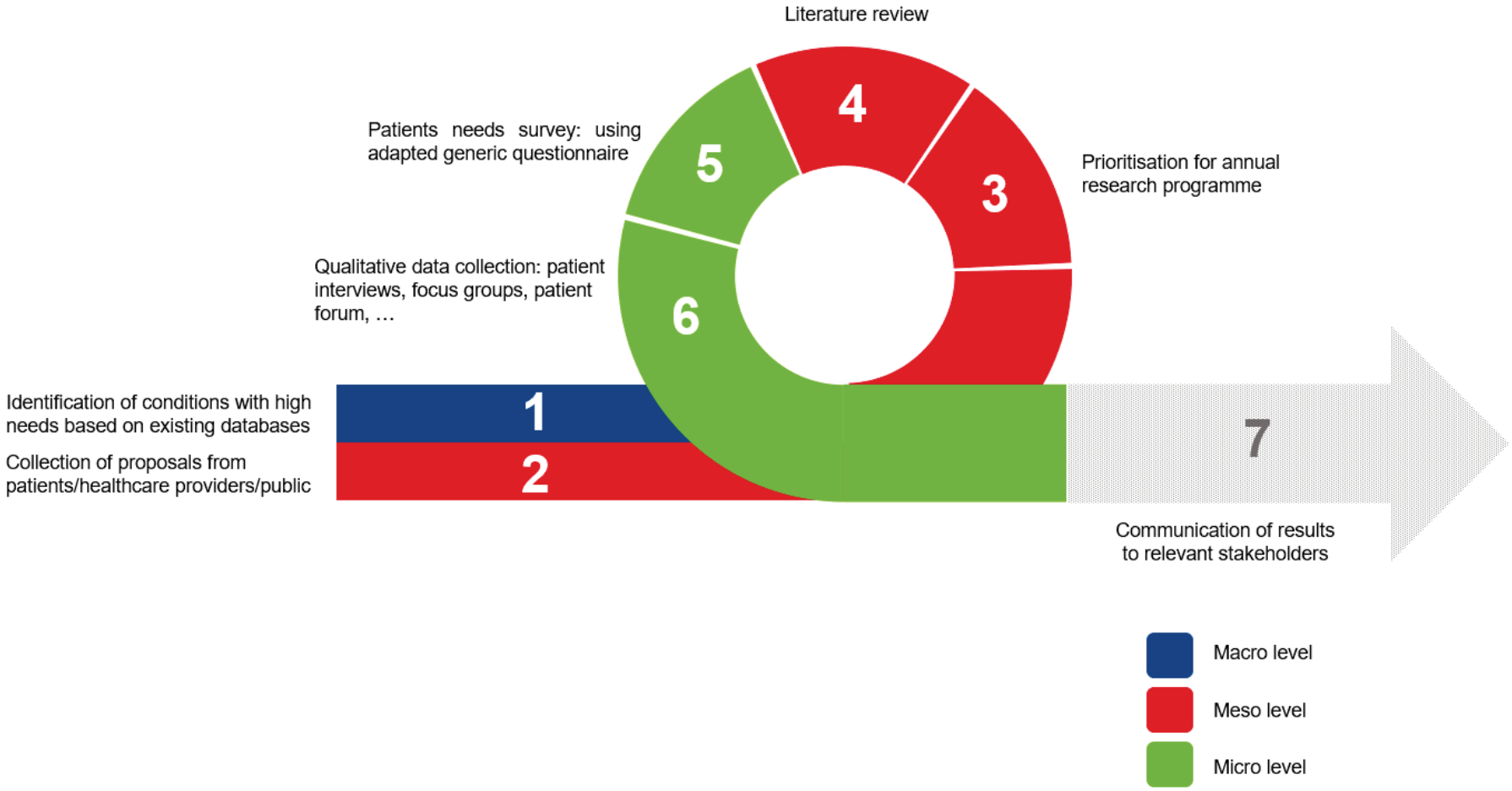
[z] https://www.ema.europa.eu/en/documents/other/european-medicines-agency-guidance-applicants-seeking-access-prime-scheme_en.pdf

Researchers	Prioritizing (bio-para)medical research: focussing on the areas with the highest unmet needs Targeting development activities within a disease area to the most important needs of patients with a specific condition
Research funders	Allocating funds to projects that address or target populations with high needs or address important needs in a specific population
Healthcare providers	Improving daily practice to address aspects of the condition or treatment impacting heavily on patients' life with the patient, aspects they might not immediately have thought of themselves

11.3 How could the data collection be organised?

We suggest a 7-step approach to identify patient needs, encompassing a macro-, meso- and micro perspective (Figure 26).

Figure 26 – Proposed model for patient needs identification in Belgium



Step 1 involves the **identification of health conditions** for which further in-depth data collection should be performed to identify the specific patient needs. This step is a necessity in the context of limited resources to perform the activities. **Data from large databases** like the Belgian Burden of Disease database, the Belgian Health Interview Survey, the database from the unmet medical needs programme and the special solidarity fund of the NIHDI, the Global Burden of Disease database and SHARE can be used in this exercise. To ensure maximal relevance of the results for the Belgian context, we recommend the use of Belgian databases where possible. Despite the limitations of each of the databases, they can provide a first rough indication of areas where the impact of disease on health-related quality of life is high (see chapter 6). In the future, other relevant Belgian databases, currently still under construction, should also be taken into account.

Impact indicators used to identify areas with high patient needs may reflect the burden of the condition for the individual patients (e.g. impact on HRQoL) and/or for the population (e.g. total number of QALYs lost in the population due to the condition). Both are relevant, but one should be careful not to focus on population indicators only, because these are often heavily determined by the prevalence of the condition. Therefore, we recommend to prioritize both conditions with a high individual impact and conditions with a high population impact and balance the two for the in-depth qualitative research.

Life-threatening and severely debilitating conditions for which no treatment (curative or symptom control) is currently available are automatically high on the patient needs list. No treatment' means: there are no ways to help the patient survive or live a decent life (with acceptable discomfort). The identification of such conditions could be based on an assessment of the indications of pharmaceuticals that received conditional marketing authorization (EMA), orphan designation (EMA) or early temporary reimbursement (NIHDI), which were included in the PRIME scheme (EMA), a medical needs or compassionate use programme (FAMHP) or for which reimbursement was granted to individual patients in the context of the Special Solidarity Fund (NIHDI). An assessment of the indications is still needed, because not all these indications will be life-threatening *and* severely pharmaceuticals *and* have no treatment (symptom control or curative). For many conditions, however, effective symptom control management options are available. For these conditions, assessing the level of need is less obvious and requires more research (see next steps).

Step 2 involves the request for **proposals from patients or patient organisations, healthcare providers and the general public**. The importance of this step is to cope with the limitations of the databases studied in Step 1, i.e. varying HRQoL indicators, limited and varying number of heatlh conditions and high-level definition of health conditions. Patients, patient organisations, healthcare professionals and the general public could submit proposals within the high-level priority domains defined in Step 1, or in other domains. Specifically for rare conditions or conditions for which no patient associations exists, this latter possibility should remain open. Moreover, the submissions could relate to a specific outcome or symptom that can occur in different underlying diseases (e.g. paralysis), thereby expanding the scope from a purely disease-oriented approach to a condition-oriented approach. The responsible organisation should develop a procedure on how, when and how frequent the public call for proposals will be launched.

Step 3 involves the selection of specific conditions for the **development of the annual programme** of the responsible organisation. The output of steps 1 and 2 together form the input for step 3. The selection procedure could be similar to the selection procedure for research projects in research organisations like KCE – i.e. based on a set of pre-defined prioritisation criteria and independent review of proposals. In the selection, an appropriate balance between highly prevalent, less prevalent and rare conditions might have to be sought. In the establishment of the selection criteria, such ethical considerations (i.e. not to disadvantage patients with less prevalent conditions), should be taken into account. The responsible unit should develop a procedure specifying how conditions are selected for the annual programme, including the selection criteria, assessment of proposals (how and by whom), ranking and final decision. This process should be repeated every year, including updated information from the databases (step 1) and new topic proposals (step 2). Topics may come back the following year if they were not retained in a previous year.

Step 4 involves, for the selected conditions, a **review of the literature** on the needs of patients with the condition. The objectives of the literature review are: (1) to identify existing evidence on patient needs and the burden of the condition, (2) collect information on the available treatments, their effectiveness and the inconvenience of current treatment; and (3) collect input for the required modifications to the generic patient needs questionnaire (see step 4).

It is – as researcher or policy maker – very important to be sufficiently informed about a condition, its treatments or management strategies and evidence gaps to be able to take informed decisions. Similarly, this information is of crucial importance to understand and interpret patient needs. The James Lind Alliance builds on this principle to identify priorities for research, based on patient input.[5]

The review encompasses different parts. The first part should describe **the clinical evidence** about the condition and its treatment: what are the currently available treatment options, what is their effectiveness, what is the level of evidence, what is the level of heterogeneity in effectiveness amongst sub-groups of the patient population? The second part should be about the patient needs, given the clinical state of the art. This part encompasses a review of **patient-based evidence** about patient needs, e.g. based on surveys, interviews, focus groups. Note that it is important in this step to critically assess this literature, not only on scientific rigour but also on applicability to the Belgian context. For example, it might be that the results of a focus group performed in Australia are not applicable to the Belgian context because the availability of treatments or the standard of care is different between Australia and Belgium.

Other initiatives focused on the national Belgian context could provide useful information as well in this step. For example, PaRIS, the Patient-Reported Indicators Surveys, is an ongoing project of the OECD focusing on patient-reported outcome measures (PROMs) and Patient-reported experience measures (PREMs) in primary healthcare of patients living with chronic conditions in primary healthcare.[aa] The objective of the project is to collect internationally comparable data on PROMs and PREMs. Questionnaires are now being pilot tested in different countries, including Belgium. In 2022, the project will be implemented. Results are expected by the end of 2022. As several questions in the draft questionnaires are similar to the questions in our generic questionnaire, it is worthwhile to closely follow the PaRIS initiative to identify unmet needs criteria in the PaRIS surveys that could nourish the unmet needs identified on a national level using our generic questionnaire. This would allow for a much broader evidence base on unmet needs.

The responsible organisation will have to develop a process note on which databases to search, how to summarize the evidence and how to translate the findings from the literature into modifications to the generic questionnaire (Step 5).

Step 5 involves the **collection of Belgian data by means of a survey**. In this study, we developed a generic survey for collecting data on patient needs. This generic survey should be considered as an advanced template, which needs to be adapted to the specific condition under investigation. Based on the literature review (Step 4), for instance, specific needs might be identified that are not included in the generic questionnaire but are still very relevant for the exercise. Specific questions on these needs can be added to the questionnaire. We recommend, however, not to add too many questions or change the framing of the questions to maintain validity and feasibility. The objective is to use a similar questionnaire across health conditions and populations, to ensure equal treatment of different populations and minimise bias introduced by the researchers in surveying patients on their needs. If more in-depth information is needed -e.g. to be able to translate the findings of the patient needs study to concrete (policy) measures or actions- it should be taken up in the qualitative part of the data collection exercise.

Also the project of the *Vlaams Patiëntenplatform (VPP)* relating to the innovation needs of chronic patients is worth mentioning in this context[99], see Chapter 5. It can help to identify the cluster of the condition under

[aa] https://www.oecd.org/health/paris/ (last access: 13 October 2021)

consideration and offer a starting point for the adaptation of the generic questionnaire. For example, when investigating the needs of patients with a neuromuscular condition, falling in the cluster of severe limitations of a predominantly physical nature, specific attention should be paid to the physical symptoms. Hence the questions on physical limitations might be more elaborate than the questions on mental issues, and even additional specific questions might need to be added to the generic questionnaire on the specific consequences of these physical limitations. The most appropriate data collection approach (i.e. the choice of the medium: online, on paper, self-completed or with the help of the third party) also has to be considered seriously.

The responsible organisation will have to develop a process note on:

- how to adapt the generic patient questionnaire to the patient population: who should review, guidance on patient involvement, whether pre-testing and pilot testing is required and by how many people, etc.;
- how to recruit patients for completing the patient needs' survey, which partners could help with the recruitment (sickness funds, patient organisations, health care professionals, …), respecting the rules stipulated in the General Data Protection Regulation (GDPR)) and principles of ethical conduct of research;
- how to collect the data: how to administer the questionnaire, how to select the most appropriate technique for the collection of the qualitative data, whether different techniques have to be combined, etc., to ensure that the full target population is reached, including patients with limited digital literacy, and patients who do not receive healthcare.;
- data management, respecting the rules of the GDPR;
- how to analyse the quantitative data (descriptive statistics, correlations, multivariate analyses, etc);
- how to treat the free text responses: (re)code or take further to next step, where in-depth qualitative exploration of responses to the survey is performed;
- how to analyse the qualitative data.

In **Step 6**, the needs identified through the survey are **further explored via qualitative research techniques**, such as individual interviews, focus groups, an online forum, etc. The choice of the technique will depend on the patient population, their preferences and abilities. It might be worthwhile also to include healthcare providers and caregivers in this step as key informants, especially if they experience large needs themselves due to the condition of the patients or if the patients have limited ability to express themselves. The responsible organisation will have to develop a process note to clear out how the choice of a technique can be made, when and how patients, healthcare providers and caregivers should be involved, etc. The process note on patient involvement of KCE can serve as a source of inspiration.[128]

Step 7 involves the **communication of the results to the relevant stakeholders** to allow them to use the collected information. Relevant stakeholders include healthcare policy makers, NIHDI, sickness funds, patient organisations, healthcare providers, medical product companies, research funding agencies and several regional organisations that might benefit from the results to improve their policies and activities.

In order to make it feasible for the stakeholders to use the information, the wealth of information generated by the five steps must be brought together in a manageable format. For instance, NIHDI needs to integrate the information in its assessment and appraisal procedures. It requires a clear format that allows to assess and appraise the level of need of a specific patient population, compared to other patient populations. Therefore, a table format, as proposed in the context of the previous KCE report on medical needs, seems to be the most straightforward option.

A tool for assessing and reporting the quality of evidence on – amongst others – patient-reported outcomes and inconvenience of treatment was provided and is still available on the web-site of KCE (link). The submission template for putting conditions on the unmet medical needs list of the

NIHDI (published on the same webpage) or for submitting reimbursement requests should ideally be updated with information on patients' needs. For an adequate use of the data in reimbursement decisions of the NIHDI, it is not only necessary that evidence-based indicators of patient needs are included in the reimbursement request file of a health intervention, but also the proof of the effect of the intervention on these indicators. This requires the systematic collection of data on patient needs indicators, including in clinical trials.

This would allow for a more accurate assessment and appraisal of the level of therapeutic need and subsequently a more needs-based appraisal of new products to treat a specific condition.

The responsible organisation will have to develop a process note on the communication and dissemination of the results of the patient needs studies to the diverse relevant stakeholders. The process notes should for instance describe the role of specific stakeholders in the dissemination of the results, and give guidance on how to decide on the format by which the results are published and made available to stakeholders.

Stakeholder involvement will be important in steps 5 to 7 of this process. The process notes of KCE on stakeholder involvement can serve as a source of inspiration on how to organize stakeholder involvement in this context.[153] Specific attention should be given to the involvement of patient representatives (with experiential knowledge), as this will be essential for a good outcome of patient needs research.[154]

11.4 What does it take to perform a patient needs study?

In terms of expertise needed, based on our experience during the pilot project, we recommend the involvement of people with:

- quantitative research skills (including a data analyst), for the database analyses, as well as the analysis of the data collected through the patient survey
- qualitative research skills for designing and performing the qualitative research, including people with specific skills required for specific qualitative data collection techniques (e.g. interviewing skills, oral moderation skills for moderating (focus) group discussions or written moderation skills for moderating an online forum) and people with sociological research skills to interpret the qualitative results and put them into (contextual) perspective
- medical, para-medical and public health expertise to interpret the results of the databases analyses, interpret the open field responses of the patients in the survey, interpret the results of the literature review and contribute to the adaptation of the generic questionnaire
- literature review skills to perform the literature review according to the state of the art methodology for literature reviews
- communication expertise for informing potential survey participants about the existence of the survey, (actively) communicating the results to relevant stakeholders
- skills for organizing and implementing the patient survey, including ICT aspects, sending out invitations for the survey and for the qualitative data collection (interviews, focus groups, …), contacting people for organizing the interviews/focus groups/…

Besides human resources, financial resources are needed for e.g. presents for participants in the survey and/or qualitative data collection, licenses for online tools (e.g. for the survey, forum, online interviews, online focus groups, …), subcontracting (e.g. if part of the study -e.g. literature review, data collection- is outsourced to an external partner)

For the management of a unit responsible for the evidence generation on patient needs, a programme manager responsible for the organisation and planning of the year programme, including the call for proposals, is needed.

It is also important to involve patients and/or their representatives throughout the process, as well as healthcare providers and any other stakeholders.

For illustration, the pilot study on long COVID required about 285 person days (Table 49). Financial resources amounted to €8 000 for training in moderation, use of the forum platform, expert consultation. It needs to be

emphasized, however, that the estimate of human resource use includes learning time. The estimate does not include the literature review because long COVID was a very specific case, on which little scientific literature on patient needs and experiences was published at the time of our pilot study. We relied mainly on the input from the clinical literature review (performed by a medical doctor), a review of the messages found in the press and on social media and patient organisations to adapt the generic questionnaire.

Table 49 – Resource use pilot study "identification of Long COVID patient needs"

Expertise	Estimated number of person days
Survey development (i.e. adaptation of generic questionnaire to long COVID), including literature review	70
Quantitative analysis, including data cleaning, recoding and reporting	50
Interview guide and forum development	15
Qualitative data collection by means of interviews and online forum	50
Qualitative data analysis	80
ICT support	4
Project management and meetings (internal and external)	16
TOTAL	**285**

12 DISCUSSION

12.1 Societal implications of our study

This study proposes a methodology to identify the needs of patients with conditions that have high individual and societal burden. It will allow to make healthcare and healthcare policy more needs-driven. Multiple initiatives with intentions in this direction already exist at the **federal level** to make the **healthcare system more needs-driven and patient-centred**, such as the compassionate use and medical need programme of the FAMHP, the unmet medical needs programme of the NIHDI, the special solidarity fund and the observatory for chronic diseases. However, the actors often lack the data to fully exploit the possibilities of the initiatives. With this proposal, we want to contribute to the evidence-base of needs-driven decision making in Belgium. By taking patient needs into account in reimbursement decisions, the NIHDI and the Minister of Health can improve efficiency in the healthcare sector: the more the focus is on the high patient needs, the higher the possible gains in patients' health or quality of life and hence the better the outcome for a given amount of resources.

Patient-centeredness is an important value in the Belgian system and is considered to be a component of high quality healthcare. By using evidence on patient needs, patients' care and experiences can be improved and become more patient-centred. It will allow for better therapeutic management and thus -depending on the results of the patient needs studies- allow to develop actions that decrease the burden of disease (e.g. DALYs, YLDS, ...) on the population, decrease costs (related to care, replacement income, etc.) and pressure on social security, improve (re)integration into the labour market, reduce the pressure on family carers, etc. We are also convinced that the identification of patient needs in the way we propose, will not only serve the FAMHP and the NIHDI but also many other stakeholders, both at the policy and operational level and both nationally and internationally.

On the **international level**, there are opportunities to use the proposed approach as well. The European Medicines Agency has established the

PRIME scheme to reinforce scientific and regulatory support to stimulate development and enable accelerated assessment of new medicines targeting high unmet medical needs. The assessment of the level of unmet medical needs can be supported by the evidence collected as proposed in the current study. Collaborations with agencies or units with a similar mission in other countries might be considered. Collaboration would allow to investigate more conditions. Especially for rare conditions this might be important. Collaboration might increase the number of patient-participants in the survey and qualitative research.

12.2 Strengths and weaknesses of the study

For the first time, a 7-step methodology to assess patient needs has been developed. These results were achieved through close collaboration with patients associations (VPP, LUSS, RaDiOrg), sickness funds, patient organisations and other health institutions (e.g. Sciensano, NIHDI) during all the different stages of the project..

The generic questionnaire was developed using a Delphi methodology (with two rounds), pre-tested by stakeholders and tested on patients. Yet, adaptation to specific health conditions will always be necessary.

Most of the steps included in this approach have been tested under real-life conditions on a large population of patients suffering from long COVID. This allowed us to really appreciate the difficulties of applying such a method, the resources needed and to adjust it to make it as realistic as possible. The emergence of a new health condition, called “long COVID”, created a double opportunity for our study. First, by selecting this topic for our pilot study, we had to adapt our questionnaire to a new, rather unknown condition. Second, because of the prevalence of the condition and the ‘hot topic’-nature of it, the online survey attracted many participants. This allowed us to collect enough data to make quantitative analysis on the survey and recruit enough candidates to test the use of an online discussion forum (i.e. its implementation and results), besides a more traditional qualitative data collection approach (interviews). The comparison of the methods made us realise, for example, that the two qualitative methods did not necessarily attract the same types of patients and that they were therefore complementary.

This study also has some weaknesses. For instance, the pragmatic review identified the most used methods to assess patient needs. This identification was used as input for the 7-step implementation model and to identify the fundamental dimensions to be included in the generic questionnaire. However, we did not make an in-depth assessment of the identified methods by comparing them amongst each other or assess their complementarity. The databases identified to make a prioritisation of 99 conditions with potential high needs include a significant number of limitations, among the most important, the various types of indicators used to prioritise (population or individual level), the exclusion of some people and conditions (e.g. rare diseases) and the methods used to derive the indicators. The strengths and weaknesses of the different databases available to prioritise conditions with potentially high needs are described in detail in Chapter 6.

The proposed approach was only tested on a sample of patients suffering from long COVID that was mainly represented by women, adults (35-65 years) and highly educated patients. The tool may therefore need further adaptation if it is to be applied to children, elderly or less educated people.

The needs identification may also be more complex if the approach is applied to a group of diseases rather than to one single disease. In addition, the long COVID is a new condition, not really acute nor chronic (yet). It is not representative of all the types of conditions.

In the qualitative data collection step, only an online asynchronous forum and interviews have been applied. However other techniques (e.g. focus groups, diaries, brainstorming, thematic needs cared, etc.) exist to gather data on patient needs.[155] Some have been applied in Belgium by VPP and proven their applicability for identifying innovation needs.[99]

12.3 Future research

The proof of the pudding will be in the eating. We propose an operational approach to identifying patient needs in a more systematic manner and describe roughly what is required to create the appropriate environment for such an activity. Several procedures developed by KCE can serve as a source of inspiration to develop this new mission (literature review, qualitative research, patient involvement, stakeholder involvement). The process notes and the KCE process book are freely available and can be used by any organisation getting this mission (link)[bb]. Adaptation of the process notes to the specific mission will be required, and the responsible organisation will have to learn by doing and update the notes accordingly. Lessons can also be learnt from other initiatives with a similar or related purpose, like the James Lind Alliance.

Further research on the appropriateness of different techniques for qualitative data collection, in function of the patient population, is welcome as well. It would help to develop guidance for researchers on how to choose the appropriate methods and define the required resources and competences.

Initiatives to assess the burden of diseases at a national and individual level should be further promoted. The presence of epidemiological indicators integrating both prevalence, mortality, morbidity, duration and impact on quality of life (e.g. DALYs) of conditions, diseases or risk factors are still far too scarce in existing national databases or initiatives. These data are of great value as they allow to compare the impact of conditions on the population health, to prioritise them and to concentrate efforts on those that have the greatest impact. This information makes it possible to set up better oriented health policies and also to potentially measure their impact. At present, only the BBoD study (Sciensano) is really working in this direction. Other existing initiatives and/or databases should be encouraged to collect this type of indicator in a systematic way (e.g. the cancer registry).

---

bb https://processbook.kce.fgov.be/

APPENDICES

See separate files.

REFERENCES

1. ICHOM. International Consortium for Health Outcomes Measurement. [Web page]. [cited 10th November]. Available from: https://www.ichom.org/
2. PCORI. Patient-centered Outcomes Research Institute. [Web page]. [cited 10th November]. Available from: https://www.pcori.org/
3. Cleemput I, Devriese S, Christiaens W, Kohn L. Multi-criteria decision analysis for the appraisal of medical needs: a pilot study. Health Services Research (HSR). Brussels: Belgian Health Care Knowledge Centre (KCE); 2016 28/06/2016. KCE Reports 272 Available from: http://kce.fgov.be/sites/default/files/page_documents/KCE_272_Unmet_needs_Report2.pdf
4. Cleemput I, Devriese S, Kohn L, Devos C, van Til J, Groothuis-Oudshoorn K, et al. Incorporating societal preferences in reimbursement decisions - Relative importance of decision criteria according to Belgian citizens Health Services Research (HSR). Brussels: Belgian Health Care Knowledge Centre (KCE); 2014 22/12/2014. KCE Reports 234 Available from: http://kce.fgov.be/sites/default/files/page_documents/KCE_234_reimbursement_decisions_Report.pdf
5. National Institute for Health Research. The James Lind Alliance Guidebook. 2020. Available from: http://www.jla.nihr.ac.uk/jla-guidebook/
6. Smith S, Connolly S. Re-thinking unmet need for health care: introducing a dynamic perspective. Health Econ Policy Law. 2020;15:440-57.
7. Vreman RA, Heikkinen I, Schuurman A, Sapede C, Llinares Garcia J, Hedberg N, et al. Unmet medical need: an introduction to definitions and stakeholder perceptions. Value Health. 2019;22(11):1275-82.

8. Allin S, Grignon M, Le Grand J. Subjective unmet need and utilization of health care services in Canada: what are the equity implications? Social Science & Medicine. 2010;70:465-72.

9. Commission Regulation (EC). No 507/2006 of 29 March 2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC). European Parliament.

10. 7 Februari 2014 - Wet houdende diverse bepalingen inzake de toegankelijkheid van de gezondheidszorg / 7 Février 2014 - Loi portant des dispositions diverses en matière d'accessibilité aux soins de santé, Belgisch Staatsblad / Moniteur Belge 2014.

11. 12 MEI 2014. - Koninklijk besluit tot uitvoering van de artikelen 25 en volgende van de wet betreffende de verplichte verzekering voor geneeskundige verzorging en uitkeringen / 12 MAI 2014. - Arrêté royal portant exécution des articles 25 et suivants de la loi relative à l'assurance obligatoire soins de santé et indemnités, 2014.

12. Cleemput I, Devriese S, Christiaens W, Kohn L. Multi-criteria decision analysis for the appraisal of medical needs: a pilot study. Brussels: Belgian Health Care Knowledge Centre; 2016. KCE report 272

13. Royal College of Physicians and Surgeons of Canada. Defining societal health needs. Ottawa: Royal College of Physicians and Surgeons of Canada; 2012.

14. Allotey PA, Reidpath DD. Objectivity in priority setting tools in reproductive health: context and the DALY. Reproductive Health Matters. 2002;10(20):38-46.

15. Albarqouni L, Elessi K, Abu-Rmeileh NME. A comparison between health research output and burden of disease in Arab countries: evidence from Palestine. Health Research Policy & Systems. 2018;16(1):25.

16. Arnesen T, Kapiriri L. Can the value choices in DALYs influence global priority-setting? Health Policy. 2004;70(2):137-49.

17. Bertram MY, Katzenellenbogen J, Vos T, Bradshaw D, Hofman KJ. The disability adjusted life years due to stroke in South Africa in 2008. International Journal of Stroke. 2013;8 Suppl A100:76-80.

18. Cassini A, Plachouras D, Eckmanns T, Abu Sin M, Blank HP, Ducomble T, et al. Burden of Six Healthcare-Associated Infections on European Population Health: Estimating Incidence-Based Disability-Adjusted Life Years through a Population Prevalence-Based Modelling Study. PLoS Medicine / Public Library of Science. 2016;13(10):e1002150.

19. Greden JF. The burden of disease for treatment-resistant depression. Journal of Clinical Psychiatry. 2001;62 Suppl 16:26-31.

20. Incerti D, Borowne J, Baker CL, Makinson G, Goren A, Willke R, et al. An empirical tool for estimating the share of unmet need due to healthcare inefficiencies, suboptimal access, and lack of effective technologies. BMC Health Serv Res. 2019;19(113).

21. Karimkhani C, Dellavalle RP, Karimi SM, Rahimi-Movaghar V, Pourmalek F, Kiadaliri AA, et al. Burden of Skin and Subcutaneous Diseases in Iran and Neighboring Countries: Results from the Global Burden of Disease Study 2015. Archives of Iranian Medicine. 2017;20(7):429-40.

22. Longfield K, Smith B, Gray R, Ngamkitpaiboon L, Vielot N. Putting health metrics into practice: using the disability-adjusted life year for strategic decision making. BMC Public Health. 2013;13 Suppl 2:S2.

23. Lopez AD, Mathers CD. Measuring the global burden of disease and epidemiological transitions: 2002-2030. Annals of Tropical Medicine & Parasitology. 2006;100(5-6):481-99.

24. Mangen MJ, Plass D, Havelaar AH, Gibbons CL, Cassini A, Muhlberger N, et al. The pathogen- and incidence-based DALY approach: an appropriate [corrected] methodology for estimating the burden of infectious diseases. PLoS ONE [Electronic Resource]. 2013;8(11):e79740.

25. McDonald SA, Qendri V, Berkhof J, de Melker HE, Bogaards JA. Disease burden of human papillomavirus infection in the Netherlands, 1989-2014: the gap between females and males is diminishing. Cancer Causes & Control. 2017;28(3):203-14.

26. Phua HP, Chua AV, Ma S, Heng D, Chew SK. Singapore's burden of disease and injury 2004. Singapore Medical Journal. 2009;50(5):468-78.

27. van den Wijngaard CC, Hofhuis A, Harms MG, Haagsma JA, Wong A, de Wit GA, et al. The burden of Lyme borreliosis expressed in disability-adjusted life years. European Journal of Public Health. 2015;25(6):1071-8.

28. van Lier A, McDonald SA, Bouwknegt M, group EPI, Kretzschmar ME, Havelaar AH, et al. Disease Burden of 32 Infectious Diseases in the Netherlands, 2007-2011. PLoS ONE [Electronic Resource]. 2016;11(4):e0153106.

29. Vos T, Barker B, Begg S, Stanley L, Lopez AD. Burden of disease and injury in Aboriginal and Torres Strait Islander Peoples: the Indigenous health gap. International Journal of Epidemiology. 2009;38(2):470-7.

30. Asadi-Lari M, Gray D. Health needs assessment tools: progress and potential. Int J Technol Assess Health Care. 2005;21(3):288-97.

31. Stein J, Liegert P, Dorow M, Konig HH, Riedel-Heller SG. Unmet health care needs in old age and their association with depression - results of a population-representative survey. Journal of Affective Disorders. 2019;245:998-1006.

32. Aragón Aragón MJ, Chalkly M, Goddard M. Defining and measuring unmet need to guide healthcare funding: identifying and filling the gap. York: University of York; 2017.

33. van Walsem MR, Howe EI, Ruud GA, Frich JC, Andelic N. Health-related quality of life and unmet healthcare needs in Huntington's disease. Health & Quality of Life Outcomes. 2017;15(1):6.

34. Liker HR, Ducrotte P, Malfertheiner P. Unmet medical needs among patients with gastroesophageal reflux disease: a foundation for improving management in primary care. Digestive Diseases. 2009;27(1):62-7.

35. Lindly OJ, Geldhof GJ, Acock AC, Sakuma KK, Zuckerman KE, Thorburn S. Family-Centered Care Measurement and Associations With Unmet Health Care Need Among US Children. Academic pediatrics. 2017;17(6):656-64.

36. Richardson A, Medina J, Richardson A, Sitzia J, Brown V. Patients' needs assessment tools in cancer care: principles and practices. London: King's College London; 2005.

37. Richardson A, Medina J, Brown V, Sitzia J. Patients' needs assessment in cancer care: a review of assessment tools. Support Care Cancer. 2007;15:1125-44.

38. Devleesschauwer B, Havelaar AH, Maertens de Noordhout C, Haagsma JA, Praet N, Dorny P, et al. Calculating disability-adjusted life years to quantify burden of disease. International Journal of Public Health. 2014;59:565-69.

39. Devleesschauwer B, Havelaar AH, Maertens de Noordhout C, Haagsma JA, Praet N, Dorny P, et al. DALY calculation in practice: a stepwise approach. International Journal of Public Health. 2014;59(571-74).

40. Institute for Health Metrics and Evaluation (IHME). Global Burden of Disease Study. In. Washington.

41. Institute for Health Metrics and Evaluation (IHME). Protocol for the Global Burden of Diseases, Injuries, and Risk Factors study (GBD). Seattle: University of Washington; 2018.

42. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. 2020(10258):1204-22.

43. Slade M, Thornicroft G, Loftus L, Phelan M, Wykes T. Adult Camberwell Assessment of Need (CAN). Royal College of Psychiatrists; 1999.

44. Xenitidis K, Slade M, Thornicroft G, Bouras N. CANDID: Camberwell Assessment of Need for Adults with Developmental and Intellectual Disabilities. Royal College of Psychiatrists; 2003.

45. Orrell M, Hancock G. CANE: Camberwell Assessment of Need for the Elderly: A Needs Assessment for Older Mental Health Service Users. Royal College of Psychiatrists; 2004.

46. Thomas S, Harty MA, Parrott J, McCrone P, Slade M, Thornicroft G. CANFOR: Camberwell Assessment of Need – Forensic Version. Royal College of Psychiatrists; 2003.

47. Howard L, Hunt K, Slade M, O'Keane V, Seneviratne T, Leese M, et al. CAN-M: Camberwell Assessment of Need for Mothers. Royal College of Psychiatrists; 2008.

48. Stein J, Luppa M, König HH, Riedel-Heller SG. Assessing met and unmet needs in the oldest-old and psychometric properties of the German version of the Camberwell Assessment of Need for the Elderly (CANE)–a pilot study. International Psychogeriatrics. 2014;26(2):285-95.

49. Stein J, Luppa M, König HH, Riedel-Heller SG. The German version of the Camberwell Assessment of Need for the Elderly (CANE): evaluation of content validity and adaptation to the German-speaking context. International Psychogeriatrics. 2015;27(11):1919-26.

50. Asadi-Lari M, Packman C, Gray D. Unmet health needs in patients with coronary heart disease: implications and potential for improvement in caring services. Health and Quality of Life Outcomes. 2003;1(1):26.

51. Asadi-Lari M, Packman C, Gray D. Psychometric properties of a new health needs analysis tool designed for cardiac patients. Public Health. 2005;119(7):590-98.

52. Jones R, Armstrong D, Malfertheiner P, Ducrotté P. Does the treeatment of gastroesophageal reflux disease (GERD) meet patients' needs? A survey-based study. Curr Med Res Opin. 2006;22:657-62.

53. Ducrotté P, Liker HR. How do people with gastro-oesophageal reflux disease perceive their disease? Results of a multinational survey. Curr Med Res Opin. 2007;23:2857-65.

54. Jones R, Liker HR, Ducrotté P. Relationship between symptoms, subjective well-being and medication use in gastro-oesopgeal reflux disease. Int J Clin Pract. 2007;61:1301-07.

55. Agency for Healthcare Research and Quality. CAHPS Health Plan Survey: methodology. Rockville: Agency for Healthcare Research and Quality; 2019.

56. Coscarelli A, Heinrich RL. Cancer Rehabilitation Evaluation System (CARES): manual. 1988.

57. Fortner B, Okon T, Schwartzberg L, Tauer K, Houts AC. The Cancer Care Monitor: psychometric content evaluation and pilot testing of a computer administered system for symptom screening and quality of life in adult cancer patients. J Pain Symptom Manage. 2003;26(6):1077-92.

58. Ruland CM. Decision support for patient preference-based care planning: effects on nursing care and patient outcomes. J Am Med Inform Assoc. 1999;6(4):304-12.

59. Ruland CM. Handheld technology to improve patient care: evaluating a support system for preference-based care planning at the bedside. J Am Med Inform Assoc. 2002;9(2):192-201.

60. Ruland CM, White T, Stevens M, Fanciullo G, Khilani SM. Effects of a computerized system to support shared decision making in symptom management of cancer patients: preliminary results. J Am Med Inform Assoc. 2003;10(6):573-79.

61. Macmillan Cancer Support. Concerns Checklist. London: Macmillan Cancer Support; 2017.

62. National Comprehensive Cancer Network. NCCN Guidelines for Patients: Distress. Version 1.2017. 2017.

63. Emanuel LL, Alpert HR, Emanuel EE. Concise screening questions for clinical assessments of terminal care: the needs near the end-of-life care screening tool. J Palliat Med. 2001;4(4):465-75.

64. Coyle N, Goldstein ML, Passik S, Fishman B, Portenoy R. Development and validation of a patient needs assessment tool (PNAT) for oncology clinicians. Cancer Nurs. 1996;19:81-92.

65. Cull A, Stewart M, Altman DG. Assessment of and intervention for psychosocial problems in routine oncology practice. British Journal of Cancer. 1995;72(1):229-35.

66. Wright EP, Selby PJ, Gould A, Cull A. Detecting social problems in cancer patients. Journal of the Psychological, Social and Behavioral Dimensions of Cancer. 2001;10(3):242-50.

67. Bonevski B, Sanson-Fisher RW, Girgis A, Burton L, Cook P, Boyes A, et al. Evaluation of an instrument to assess the needs of patients with cancer. Cancer. 2000;88(1):217-25.

68. Boyes A, Girgis A, Lecathelinais C. Brief assessment of adult cancer patients' perceived needs: development and validation of the 34-item Supportive Care Needs Survey (SCNS-SF34). Journal of Evaluation in Clinical Practice. 2009;15(4):602-6.

69. McElduff P, Boyes A, Zucca A, Girgis A. The Supportive Care Needs Survey: A guide to administration, scoring and analysis. Newcastle: Centre for Health Research & Psycho-Oncology; 2004.

70. Tamburini M, Gangeri L, Brunelli C, Beltrami E, Boeri P, Borreani C, et al. Assessment of hospitalised cancer patients' needs by the Needs Evaluation Questionnaire. Annals of Oncology. 2000;11:31-7.

71. Bonacchi A, Miccinesi G, Galli S, Primi C, Chiesi F, Lippi D, et al. Use of the Needs Evaluation Questionnaire with cancer outpatients. Support Care Cancer. 2016;24(8):3507-15.

72. Osse BHP, Vernooij MJFJ, Schadé E, Grol RPTM. Towards a new clinical tool for needs assessment in the palliative care of cancer patients: the PNPC instrument. Journal of Pain and Symptom Management. 2004;28(4):329-41.

73. Osse BHP, Vernooij-Dassen MJFJ, Schadé E, Grol RPTM. A practical instrument to explore patients' needs in palliative care: the Problems and Needs in Palliative Care questionnaire – short version. Palliative Medicine. 2007;21:391-99.

74. Kennedy P, Hamilton LR. The Needs Assessment Checklist: A Clinical Approach to Measuring Outcome. Spinal Cord. 1999;37(2):136-9.

75. Marshall M, Hogg LI, Gath DH, Lockwood A. The Cardinal Needs Schedule - a modified version of the MRC Needs for Care Assessment Schedule. Psychological Medicine. 1995;25:605-17.

76. Brewin CR, Wing JK, Mangen SP, Brugha TS, MacCarthy B. Principles and practice of measuring needs in the long-term mentally ill : the MRC need for care assessment. Psychological Medicine. 1987;17:971-81.

77. Kersten P, McLellan L, George S, Smith J. The Southampton Needs Assessment Questionnaire (SNAQ): a valid tool for assessing the rehabilitation needs of disabled people. Clincial Rehabilitation. 2000;14:641-50.

78. Kersten P, McLellan DL, Gross-Paju K, Grigoriadis N, Bencivenga R, Beneton C, et al. A questionnaire assessment of unmet needs for rehabilitation services and resources for people with multiple sclerosis: results of a pilot survey in five European countries. Clin Rehabil. 2000;14(1):42-9.

79. McWalter G, Toner H, McWalter A, Eastwood J, Marshall M, Turvey T. A community needs assessment: the care needs

assessment pack for dementia (CarenapD)—its development, reliability and validity. International Journal of Geriatric Psychiatry. 1998;13(1):16-22.

80. Foot G, Sanson-Fisher R. Measuring the unmet needs of people living with cancer. Cancer Forum. 1995;19(131-35).

81. Sanson-Fisher R, Girgis A, Boyes A, Bonevski B, Burton L, Cook P. The unmet supportive care needs of patients with cancer. Supportive Care Review Group. Cancer. 2000;88:226-37.

82. Cossich T, Schofield P, McLachlan SA. Validation of the cancer needs questionnaire (CNQ) short-form version in an ambulatory cancer setting. Qual Life Res. 2004;13(7):1225-33.

83. Clarck D, Dellasega C. Unmet health care needs: comparison of rural and urban senior center attendees. Journal of Gerontological Nursing. 1998;24(12):24-33.

84. Aday LA, Andersen RM. The national profile of access to medical care: where do we stand? Amercian Journal of Public Health. 1984;74(12):1331-39.

85. Keirse E, Benguin C, Desmet M, Deveugele M, Menten J, Simoens S, et al. Organisation of palliative care in Belgium. Brussels: Belgian Health Care Knowledge Centre (KCE); 2009. KCE Report 115C

86. Paulus D, Van den Heede K, Mertens R. Position paper: organisation of care for chronic patients in Belgium. Brussels: Belgian Health Care Knowledge Centre (KCE); 2012. 190C

87. Kapiriri L, Norheim OF. Whose priorities count? Comparison of community-identified health problems and Burden-of-Disease-assessed health priorities in a district in Uganda. Health Expectations. 2002;5(1):55-62.

88. Schroedl CJ, Yount SE, Szmuilowicz E, Hutchison PJ, Rosenberg SR, Kalhan R. A qualitative study of unmet healthcare needs in chronic obstructive pulmonary disease. A potential role for specialist palliative care? Annals of the American Thoracic Society. 2014;11(9):1433-8.

89. Tatangelo G, McCabe M, Macleod A, You E. "I just don't focus on my needs." The unmet health needs of partner and offspring caregivers of people with dementia: A qualitative study. International Journal of Nursing Studies. 2018;77:8-14.

90. Dwyer AA, Quinton R, Morin D, Pitteloud N. Identifying the unmet health needs of patients with congenital hypogonadotropic hypogonadism using a web-based needs assessment: implications for online interventions and peer-to-peer support. Orphanet Journal Of Rare Diseases. 2014;9:83.

91. Aceves SS. Unmet therapeutic needs in eosinophilic esophagitis. Digestive Diseases. 2014;32(1-2):143-8.

92. Gordon JP, McEwan PC, Maguire A, Sugrue DM, Puelles J. Characterizing unmet medical need and the potential role of new biologic treatment options in patients with ulcerative colitis and Crohn's disease: a systematic review and clinician surveys. European Journal of Gastroenterology & Hepatology. 2015;27(7):804-12.

93. Danese S, Allez M, van Bodegraven AA, Dotan I, Gisbert JP, Hart A, et al. Unmet Medical Needs in Ulcerative Colitis: An Expert Group Consensus. Digestive Diseases. 2019;37(4):266-83.

94. Papaluca M, Greco M, Tognana E, Ehmann F, Saint-Raymond A. White spots in pharmaceutical pipelines-EMA identifies potential areas of unmet medical needs. Expert Review of Clinical Pharmacology. 2015;8(3):353-60.

95. Jouan-Flahault C, Billon N, Castaigne A, Henry YD, Omnes C, Puech A, et al. [State of unmet medical needs in France in 2006: necessity of reinforcing research effort]. Therapie. 2007;62(5):393-415.

96. Pender NJ. Health promotion model manual. University of Michigan; 2011.

97. Wiles R, Payne S, Jarrett N. Improving palliative care services: a pragmatic model for evaluating services and assessing unmet need. Palliative Medicine. 1999;13:131-7.

98. Finer S, Robb P, Cowan K, Daly A, Shah K, Farmer A. Setting the top 10 research priorities to improve the health of people with Type 2 diabetes: a Diabetes UK-James Lind Alliance Priority Setting Partnership. Diabetic Medicine. 2018;35(7):862-70.

99. Becher K, Rohden C, Vandenbroeck P, Van den Hende W. Een patiëntgedreven innovatie-agenda. Vlaams Patiëntenplatform; 2014.

100. Sciensano. Health Interview Survey [Web page].Brussels, Belgium;2018 [cited 10 April 2020]. Available from: https://his.wiv-isp.be/SitePages/Home.aspx

101. Demarest S, Van der Heyden J, Charafeddine R, Drieskens S, Gisle L, Tafforeau J. Methodological basics and evolution of the Belgian health interview survey 1997–2008. Archives of Public Health. 2013;71(1):1-10.

102. EuroQol. EQ-5D. The Netherlands; 2020.

103. Bouckaert N, Gerkens S, Devriese S, Cleemput I. An EQ-5D-5L value set for Belgium – How to value health-related quality of life? Health Services Research (HSR). Brussel: Belgian Health Care Knowledge Centre (KCE); 2021 07/2021. KCE Reports 342 Available from: https://kce.fgov.be/sites/default/files/atoms/files/KCE_342_EQ-5D-5L_value_set_for_Belgium_Report_1.pdf

104. Cleemput I. A social preference valuations set for EQ-5D health states in Flanders, Belgium. The European Journal of Health Economics. 2010;11(2):205-13.

105. Van Hout B, Janssen M, Feng Y-S, Kohlmann T, Busschbach J, Golicki D, et al. Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets. Value in health. 2012;15(5):708-15.

106. Gray AM, Clarke PM, Wolstenholme JL, Wordsworth S. Applied methods of cost-effectiveness analysis in healthcare. Oxford University Press; 2011.

107. Charafeddine R, Braekman E, Van der Heyden J. Enquête de santé 2018 : Qualité de vie liée à la santé. Brussels, Belgium: Sciensano; 2018. Numéro de rapport: D/2019/14.440/30

108. Van Wilder L, Charafeddine R, Beutels P, Bruyndonckx R, Cleemput I, Demarest S, et al. Belgian population norms for the EQ-5D-5L, 2018. Quality of Life Research. 2021:1-11.

109. Arrêté royal du 4 mai 2012 fixant la méthode de calcul de la clé de répartition normative et les caractéristiques des paramètres en vue de l'application de la responsabilité financière définitive des organismes assureurs pour les années 2008 et suivantes, 2012. Available from: http://www.ejustice.just.fgov.be/eli/arrete/2012/05/04/2012022220/justel

110. IMA – AIM. Echantillon permanente steekproef. Bruxelles: InterMutualist Agency 2019. EPS R13 - FLAGS Release 20190201 NL Available from: https://IMA – AIM.be/IMG/pdf/eps_r13_-_flags_release_20190201_nl_-_vs2.pdf

111. Leroy R, De Gendt C, Stordeur S, Silversmit G, Verleye L, Schillemans V, et al. Quality indicators for the management of head and neck squamous cell carcinoma. Health Services Research (HSR). Brussels: Belgian Health Care Knowledge Centre (KCE); 2019 01/2019. KCE Reports 305 (305) Available from: https://kce.fgov.be/sites/default/files/atoms/files/KCE_305_Quality_indicators_Head_and_neck_Report.pdf

112. Berete F, Vander Heyden J, Demarest S, Tafforeau J. Projet Hislink. Couplage des données de l'enquête national de santé par interview 2013 (HIS) avec les données de l'agence intermutualiste (IMA). Bruxelles, Belgique: Sciensano; 2019.

113. Loi du 13 décembre 2006 portant dispositions diverses en matière de santé, Moniteur Belge 2006. Available from: https://www.ejustice.just.fgov.be/cgi_loi/change_lg.pl?language=fr&la=F&cn=2006121335&table_name=loi

114. Devleesschauwer B. Country Report: the Belgian National Burden of Disease Study 2020. European Journal of Public Health. 2018;28(suppl_4):cky213. 830.

115. Gorasso V, Silversmit G, Arbyn M, Cornez A, De Pauw R, De Smedt D, et al. The non-fatal burden of cancer in Belgium, 2004–2018. 2021.

116. Salomon JA, Haagsma JA, Davis A, de Noordhout CM, Polinder S, Havelaar AH, et al. Disability weights for the Global Burden of Disease 2013 study. The Lancet Global Health. 2015;3(11):e712-e23.

117. Gorasso V, Silversmit G, Arbyn M, Speybroeck N. The non-fatal burden of cancer in Belgium, 2004-2018. Under review. 2021.

118. Bergmann M, Thorsten K, De Luca G, Scherpenzeel A. Survey participation in the Survey of Health, Ageing and Retirement in Europe (SHARE), Wave 1-7. Based on Release 7.0.0. Munich: SHARE-ERIC; 2019. SHARE Working Paper Series 41-2019 Available from: http://www.share-project.org/fileadmin/pdf_documentation/Working_Paper_Series/WP_Series_41_2019_Bergmann_et_al.pdf

119. Hyde M, Wiggins RD, Higgs P, Blane DB. A measure of quality of life in early old age: the theory, development and properties of a needs satisfaction model (CASP-19). Aging & mental health. 2003;7(3):186-94.

120. Wiggins RD, Netuveli G, Hyde M, Higgs P, Blane D. The evaluation of a self-enumerated scale of quality of life (CASP-19) in the context of research on ageing: A combination of exploratory and confirmatory approaches. Social Indicators Research. 2008;89(1):61-77.

121. Howel D. Interpreting and evaluating the CASP-19 quality of life measure in older people. Age and ageing. 2012;41(5):612-7.

122. Murray CJ, Lopez AD, Organization WH. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020: summary. World Health Organization; 1996.

123. James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. 2018;392(10159):1789-858.

124. de Noordhout CM, Van Oyen H, Speybroeck N, Devleesschauwer B. Changes in health in Belgium, 1990–2016: a benchmarking analysis based on the global burden of disease 2016 study. BMC public health. 2018;18(1):1-13.

125. Mathers CD, Iburg KM, Begg S. Adjusting for dependent comorbidity in the calculation of healthy life expectancy. Population Health Metrics. 2006;4(1):1-12.

126. Hilderink HB, Plasmans MH, Snijders BE, Boshuizen HC, Poos MR, van Gool CH. Accounting for multimorbidity can affect the estimation of the Burden of Disease: a comparison of approaches. Archives of Public Health. 2016;74(1):1-16.

127. van den Akker M, Buntinx F, Roos S, Knottnerus JA. Problems in determining occurrence rates of multimorbidity. Journal of clinical epidemiology. 2001;54(7):675-9.

128. Kohn L, Dauvrin M, Cleemput I. Patient involvement in policy research at KCE: process note. Health Services Research (HSR). Brussel: Belgian Health Care Knowledge Centre (KCE); 2021 06/2021. KCE Reports 340 Available from: https://kce.fgov.be/sites/default/files/atoms/files/KCE_340_Process%20Note_Patient_Involvement_Report2.pdf

129. Santaguida PL, Oliver D, Gilsing A, Lamarche L, Griffith LE, Mangin D, et al. Delphi consensus on core criteria set selecting among health-related outcome measures (HROM) in primary health care. J Clin Epidemiol. 2020;127:105-16.

130. Diamond IR, Grant RC, Feldman BM, Pencharz PB, Ling SC, Moore AM, et al. Defining consensus: a systematic review recommends methodologic criteria for reporting of Delphi studies. J Clin Epidemiol. 2014;67(4):401-9.

131. Castanares-Zapatero D, Kohn L, Dauvrin M, Detollenaere J, Maertens de Noordhout C, Primus C, et al. Long COVID: Pathophysiology – epidemiology and patient needs. Health Services Research (HSR). Brussels: Belgian Health Care Knowledge Centre (KCE); 2021. KCE Reports (344) Available from: https://kce.fgov.be/sites/default/files/atoms/files/KCE_344_Long_Covid_scientific_report.pdf

132. Williams S, Clausen MG, Robertson A, Peacock S, McPherson K. Methodological Reflections on the Use of Asynchronous Online Focus Groups in Health Research. International Journal of Qualitative Methods. 2012;11(4):368-83.

133. Anonymous. COVID-19 rapid guideline: managing the long-term effects of COVID-19. Review. NICE; 2020 2020-12-18. NICE Guideline (NG188) Available from: https://www.nice.org.uk/guidance/ng188

134. Vaes AW, Machado FVC, Meys R, Delbressine JM, Goertz YMJ, Van Herck M, et al. Care Dependency in Non-Hospitalized Patients with COVID-19. J Clin Med. 2020;9(9).

135. Greenhalgh T, Knight M, A'Court C, Buxton M, Husain L. Management of post-acute covid-19 in primary care. BMJ (Clinical research ed.). 2020;370:m3026.

136. Maxwell E. Living with COVID-19: A dynamic review of the evidence around ongoing Covid19 symptoms (often called Long Covid). National Institute for Health Research (NIHR); 2020. NIHR Themed Review Available from: https://evidence.nihr.ac.uk/wp-content/uploads/2020/10/Living-with-Covid-Themed-Review-October-2020.pdf

137. Kingstone T, Taylor AK, O'Donnell CA, Atherton H, Blane DN, Chew-Graham CA. Finding the 'right' GP: a qualitative study of the experiences of people with long-COVID. BJGP Open. 2020;4(5).

138. Greenhalgh T, Knight M. Long COVID: A Primer for Family Physicians. American family physician. 2020;102(12):716-7.

139. Rodham K, Gavin J. The Ethics of Using the Internet to Collect Qualitative Research Data. Research Ethics. 2006;2(3):92-7.

140. Turkle S. Alone together: Why we expect more from technology and less fro each other. New York: Basic Books 2011.

141. Smedley RM, Coulson NS. A practical guide to analysing online support forums. Qualitative Research in Psychology. 2021;18(1):76-103.

142. Salvador PTCdO, Alves KYA, Rodrigues CCFM, Oliveira LVE. Online data collection strategies used in qualitative research of the health field: a scoping review. Rev Gaucha Enferm. 2020;41:e20190297.

143. Tates K, Zwaanswijk M, Otten R, van Dulmen S, Hoogerbrugge PM, Kamps WA, et al. Online focus groups as a tool to collect data in hard-to-include populations: examples from paediatric oncology. BMC Med Res Methodol. 2009;9:15.

144. Im E-O, Chee W. An online forum as a qualitative research method: practical issues. Nurs Res. 2006;55(4):267-73.

145. Latkovikj MT, Ppovska MB. Online research about online research: advantages and disadvantages. E-methodology. 2020;6(6):13.

146. Jowett A. A case for using online discussion forums in critical psychological research. Qualitative Research in Psychology. 2015;12(3):11.

147. Im E-O, Chee W. Practical guidelines for qualitative research using online forums. Comput Inform Nurs. 2012;30(11):604-11.

148. Jespers V, Christiaens W, Kohn L, Savoye I, Mistiaen P. Somatic health care in a psychiatric setting. Health Services Research (HSR). Belgian Health Care Knowledge Centre (KCE); 2021 03/2021. KCE Reports 338 Available from: https://kce.fgov.be/sites/default/files/atoms/files/KCE_338_Psychosomatic_Report_2.pdf

149. Llinares J. Unmet medical need; definitions and need for clarity.: European Medicines Agency; 2017.

150. European Commission. Pharmaceutical Strategy for Europe. 2020 Available from: https://ec.europa.eu/health/sites/default/files/human-use/docs/pharma-strategy_report_en.pdf

151. Stolk EA, Pickee SJ, Ament AH, Busschbach JJ. Equity in health care prioritisation: an empirical inquiry into social value. Health Policy. 2005;74(3):343-55.

152. Stolk EA, van Donselaar G, Brouwer WB, Busschbach JJ. Reconciliation of economic concerns and health policy: illustration of an equity adjustment procedure using proportional shortfall. Pharmacoeconomics. 2004;22(17):1097-107.

153. Piérart J, Léonard C, Chalon PX, Daue F, Mertens R. Stakeholder Involvement in KCE working processes. Method. Brussels: Belgian Health Care Knowledge Centre (KCE); 2012 20120402. KCE Reports 174 (D/2012/10.273/11) Available from: https://kce.fgov.be/sites/default/files/page_documents/KCE_174C_stakeholder%20involvement_in_KCE_working_processes.pdf

154. Cleemput I, Dauvrin M, Kohn L, Mistiaen P, Christiaens W, Léonard C. Position of KCE on patient involvement in health care policy research. Method. Brussels: Belgian Health Care Knowledge Center (KCE); 2019 11/2019. KCE Reports 320 Available from: https://kce.fgov.be/sites/default/files/atoms/files/KCE_320_Patient_involvement_health_care_policy_research_Report_2.pdf

155. Kohn L, Christiaens W. The use of Qualitative Research Methods in KCE studies. Method. Brussels: Belgian Health Care Knowledge Centre (KCE); 2012. KCE Reports 187 (D/2012/10.273/68) Available from: https://kce.fgov.be/sites/default/files/page_documents/KCE_187C_qualitative_research_methods.pdf