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for Clinical Practice Guidelines and
Clinical Decision Support Tools for Rare Diseases

Handbook #10: Methodology for the elaboration of Quality Measures for rare diseases

Prepared by WP-B leader:
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Handbook #10: Methodology for the elaboration of Quality Measures for rare diseases.

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ABBREVIATIONS

AETSA	Andalusian Health Technology Assessment Department
CDSTs	Clinical Decision Support Tools
ClinRO	Clinician-Reported Outcomes
CPGs	Clinical Practice Guidelines
ERN	European Reference Network
FPS	Fundación Pública Andaluza Progreso y Salud
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IACS	Aragon Health Sciences Institute
ICD	International Classification of Diseases
ObsRo	Observer-Reported Outcomes
PerfO	Performance Outcomes
PRO	Patient-Reported Outcomes
PROMs	Patient-Reported Outcome Measures

This handbook provides information on the working group profiles and knowledge to be considered, as well as detailing the key points for the development of Quality Measures and indicators for the monitoring and improving care in rare diseases.

01.

BACKGROUND

With the launching of the first European Reference Network (ERN) in 2017, a care model based on the concentration of knowledge and resources in highly specialised care units for rare diseases became effective in Europe. As of today, 24 European Reference Network work co-ordinately and demand reliable and practical tools, like Clinical Practice Guidelines (CPG) and Clinical Decision Support Tools (CDST) to ensure the safest and most efficient care is provided to patients with rare diseases and carers through the EU.

Nonetheless, there are a number of challenges surrounding the development of CPG and CDST for rare diseases. One of the most relevant barrier is the lack of high-quality evidence, in which the foremost methodological frameworks like GRADE rely on [1].

Therefore, there is a need for specific methodological approaches that can provide reliable and useful Clinical Practice Guidelines (CPGs) and Clinical Decision Support Tools (CDST) for rare diseases to be used by ERNs. The project also aims to provide a common methodology, in order to harmonise the elaboration process of CDST and CPGs in the ERNs.

1.1 | Work Package B: Methodologies for CPGs and CDSTs for Rare Diseases

Work Package B of TENDER NºSANTE/2018/B3/030 pursues the development of methodologies for the prioritisation, appraisal, adaptation, development and implementation of CPGs and CDSTs for rare diseases.

The objective of WP-B of TENDER NºSANTE/2018/B3/030 entails two main steps: Firstly, an analysis of the state of the art on methodologies for CPGs and CDSTs for rare diseases, and secondly, the elaboration of methodological handbook and toolkit for the prioritisation, appraisal, adaptation, development and implementation of CPGs and CDSTs for rare diseases.

It is worth noting that within the scope of WP-B, “rare diseases” is the term used to refer to rare diseases as well as low prevalence complex diseases.

1.2 | Context for Quality Measures development in rare diseases

Quality Measures (QM) are tools that help to measure or quantify healthcare processes, outcomes, patient perceptions, and organisational structure and/or systems that are associated with the ability to provide high-quality health care and/or that relate to one or more quality goals for health care (effective, safe, efficient, patient-centered, equitable, and timely care) [2].

Indicator measurement and monitoring serve many purposes:

- ✓ document the quality of care;
- ✓ make comparisons over time or between places (e.g. hospitals);
- ✓ support accountability, regulation, and accreditation.

The use of indicators enables professionals and organisations to monitor and evaluate what happens to patients as a consequence of how well professionals and organisational systems work to provide for the needs of patients.

QM tools are composed of indicators that should be informative over the health status and sensitive to changes over time. The development of valid and relevant information is a prerequisite for planning efficient health interventions, health services, and allocation of resources.

In the field of rare diseases, information tools have to be tailored to the specific needs and problems. Due to the heterogeneity, the low number of patients/disease and the geographical spread, many indicators used for more common diseases are not applicable. The development of relevant QM tools is crucial for the monitoring of rare disease knowledge progression, health policy and the assessment of the present situation [3].

1.3 | The development process of Quality Measures: Main Steps

TASK	•DEFINITION
Composition of the Working Group	•Bring together the profiles with the necessary knowledge for the development.
Defining the concept and perspective	•Definition of the concept to be captured and from which perspectives is going to be measured.
Providing an overview of existing evidence	•Evidence on the causal relationships between measures and improvements should be identified.
Using the evidence for the composition of indicators	•Literature regarding a concept is used to design indicators and define acceptable levels for quality improvement.
Designing indicator specifications	•To stabish valid and reliable methods for the measurement.
Preparing the application of the Quality Measure	•Refining indicator definitions for an specific context of application.

02.

COMPOSITION OF THE WORKING GROUP

The QM working group should be multidisciplinary, as it should represent different perspectives and knowledge [4].

- ✓ Health professionals who are familiar with the concepts or phenomena that are intended to represent in the QM tool, so that they can ensure that appropriate population, units or activities are collected within the indicators together with standards to evaluate whether desirable performance rates are obtained, including members of the corresponding European Reference Network (ERN) and, depending on the disease, any other professional, usually involved in the care of the patient with the rare condition (e.g., a psychologist). Ideally, members of the ERN should be drawn from different parts of Europe, but this will be influenced by the expertise available. For instance, when developing a QM tool for a rare neurological condition diagnosis, it might be relevant to include healthcare professionals involved in different contexts: neurologists, nurses, physiotherapists, etc.
- ✓ Quality of care researchers and health information systems experts. These roles should have experience related to indicator development. For example, what can be the optimal measurement strategies to capture an event, what type of data to obtain from the information systems according to how the information is classified, etc.
- ✓ Methodologists that guarantee the scientific integrity of the indicators that are developed. The indicators that make up a QM tool must be based on evidence. These professionals will carry out a synthesis of the available literature to assess the level of certainty on whether improvements in a clinical indicator will produce consistent and credible improvement in quality of care.
- ✓ Decision-makers at the level of care in which a QM tool is to be used can provide information to the working group on the structure and the conditions for the delivery of healthcare. Precisely, they can be the key role for putting the indicators into practice.
- ✓ Patients and carers can also contribute to the construction of a QM tool. When the term 'patients and carers' is used in this handbook, it is intended to include people with specific rare disease conditions and disabilities and their family members and carers. It also includes members of organisations representing the interests of patients and carers. Patients' perspective should be considered when addressing inclusion/exclusion criteria for indicators. Similarly, patient views may be relevant when evaluating properties of outcome measures.

Once the working group has been selected, relevant meetings, creation of smaller working groups, and those activities required to teamwork should be organised. Working group meetings should be

documented by exhaustive summaries of decisions made by the group.

2.1 | Management of conflict of interest

Potential conflict of interests within the members of QM development group should be carefully identified and duly addressed, following the indications established in WP-A of the TENDER.

03.

QUALITY MEASURES DEVELOPMENT MODEL

There are four main elements that can help when developing a QM tool [4].

- ✓ **Concept: the specific aspect of quality captured by the QM tool.** The working group should define which is the concept that captures a quality aspect. This may be a broad or granular phenomenon (e.g. patient safety vs. referrals of patients with a certain condition between different professionals). The concept is applied at a specific level of the healthcare system, i.e. hospital level, primary care, etc.
- ✓ **Perspective: the point of view from which the QM tool is taken.** Healthcare quality can be viewed from multiple perspectives. There is a system perspective, in which all those resources or actions that are critical to provide care can be considered. This requires, for example, thinking about what clinical processes or activities carried out by professionals are expected to produce particular patients' outcomes (e.g. proportion of patients resected). On the other hand, the patient and carers perspective would require asking about their experiences with a health condition, symptoms or other aspects regarding quality of life.
- ✓ **Method: how is the actual concept measured?** To capture the concept and reflect one or more perspectives, each indicator that is part of a QM tool will incorporate a specific measurement method. This includes several aspects: data sources, indicator type, mathematical specification, inclusion/exclusion criteria, quality standards or thresholds and risk adjustment considerations.
- ✓ **Application: how would the QM tool be used?** A QM tool may be designed for use as a quality improvement tool or as an instrument that allows for the comparison of organisations/units (e.g., comparative reporting or pay for performance). Although a QM tool may be useful in more than one application, some development may require refining indicator definitions for a specific application.

04.

STEPS IN THE DEVELOPMENT OF QUALITY MEASURES

4.1 | Defining the concept and perspective

The scope of a QM tool will be defined by the concept and the perspective from which it will be measured.

The working group should initially define what will be the scope for a QM tool. That is, what is the concept to be captured and from which perspectives this concept is going to be measured.

Given that the objective of developing a QM tool is the measurement of resources or actions can lead to quality improvements, the concept for a QM tool can be defined by Institute of Medicine framework for quality assessment. This model includes the following six dimensions of the healthcare system [5]:

- ✓ Safe: Avoiding harm to patients from the care that is intended to help them.
- ✓ Effective: Providing services based on scientific knowledge to all who could benefit and refraining from providing services to those not likely to benefit (avoiding underuse and misuse, respectively).
- ✓ Patient-centered: Providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient and carers values guide all clinical decisions.
- ✓ Timely: Reducing waits and sometimes harmful delays for both those who receive and those who give care.
- ✓ Efficient: Avoiding waste, including waste of equipment, supplies, ideas, and energy.
- ✓ Equitable: Providing care that does not vary in quality because of personal characteristics such as gender, ethnicity, geographic location, and socioeconomic status.

Each of these domains can therefore be measured from the perspective of the health system itself, professionals or patients.

For example, an indicator on use of prophylaxis in appropriate patients will be an indicator related to the safety dimension, from the professionals' perspective. Patients and carers' perspective for this indicator would imply knowing their experience when they are subject to that intervention.

4.2 | Providing an overview of existing evidence

QM tools must be supported by existing knowledge from the scientific literature that that establishes the causal relationship between specific resources or processes and desired outcomes or standards. For example, the provision of diagnostic tests is an indicator when supported by evidence that an early diagnosis is related with a better prognosis [6]. This evidence supporting indicators can be derived from CPG or CDST, systematic reviews, clinical trials or original research studies.

In order to provide existing evidence, the following issues should be considered:

- ✓ A systematic literature search should be performed.
    - The research question should be focused on the concept (what is intended to capture) and perspectives (patient and carers, health professional, etc.).
    - The search must be carried out in the main scientific literature databases (PubMed/MEDLINE, Embase, Cochrane Library, etc.) and other relevant sites (e.g., journals, websites, legislation, etc.).
- ✓ Relevant publications for full extraction should be identified using title and abstract screens. Inclusion and exclusion criteria for selecting the evidence should be explicit and coinciding with the concept and perspective considered. For example, if the QM tool is developed for a paediatric condition, the systematic review should have selection criteria that exclude the adult population.
- ✓ Abstract forms or databases allow for the systematic gathering of information and characteristics that may be useful for the development of the QM tool. For example, potential measure specifications (population, observable events, outcome of interest, etc.
- ✓ A critical evaluation of the evidence obtained must be carried out, the method and instruments to carry out this evaluation must be established in advance. In addition, the appropriate instruments for evaluation should be selected according to the type of document retrieved. More information on the evidence synthesis and critical appraisal is provided in Handbook #4: Methodology for the elaboration of CPGs for rare diseases.

Overall, indicators should be based on scientific evidence rather than on expert opinions or clinical experience alone. Notwithstanding, evidence is often scarce in the case of rare diseases and there are also some other formal processes by which the measure may be accepted as a valid marker for quality, such as a formal or informal consensus method. In that case, the lack of evidence must be made explicit and clearly justified. One method frequently used in the development of QM is the RAND/ UCLA Appropriateness Method. Other consensus methods can be consulted in Handbook #5: Methodology for the elaboration of Clinical Consensus Statements for rare diseases [3].

4.3 | Using the evidence for the composition of indicators

Literature previously analysed regarding a concept can be used to design different types of indicators and define acceptable levels for quality improvement. Information can be obtained on the structural resources necessary, useful to establish standards for structure indicators (number of healthcare professionals for an action, necessary devices or equipment, etc.), or it could be possible to extract the main characteristics and components on the specific care processes to achieve better outcomes in patients.

Starting from here, according to the Donabedian Model [7, 8], indicators that make up a QM tool can be classified into three types (structure, process and outcome). These three types of indicators are briefly defined below along with a few examples on how the identified evidence would be transferred for the construction of indicators:

4.3.1 | Structure

Structure indicators describe those characteristics or inputs for healthcare. They may represent necessary conditions for the delivery of a given standard of quality of health care [6].

For example, an original study which demonstrates that setting a specific unit for pediatric transplants can produce better patient health outcomes. This implies that this unit must be made up of health professionals from different disciplines with knowledge on specific transplant procedures. On the basis of this evidence, the working group can make a judgment on the specific number of professionals and their desirable characteristics to develop a structure indicator.

4.3.2 | Process

These indicators aim to describe the delivery of appropriate (or inappropriate) healthcare to the relevant population, where appropriateness, as previously mentioned, should be based on clinical evidence of the effectiveness of the process concerned. The processes of care measured should be those demonstrated to cause a higher probability of achieving a desired outcome [6].

For example, the evidence reviewed indicates that active treatment for all patients with a certain condition is important to improve survival and quality of life. According to this, the working group can develop a process indicator for treatment and decide that >70% of patients with that condition should be offered an active treatment [9].

4.3.3 | Outcome

These indicators seek to represent measures of health improvements (or deterioration) attributable to care. When evaluating outcome indicators, the adequacy of controls for differences in case mix or other covariates (e.g. severity of illness) is important, as these factors influence the outcomes and should be appropriately accounted for risk adjustment.

There are different types of outcome indicators depending on the source that provides the information or if this information is subject to an intermediate judgment or interpretation:

- ✓ **Clinical assessment** provides information on the patient's health status based on previous clinical experience, perspective or knowledge. When appropriately defined and developed any of these four categories are accepted as clinical trial endpoints or used for the construction of indicators by the working group [10].
    - **Patient-Reported Outcomes (PRO)** are outcomes where the patient is the rater and assessment rely on patient's direct responses to questions. These responses may be recorded by the patient in a variety of ways (i.e. paper, interviews, questionnaire forms, etc.). Patient direct report can capture a wide range of feelings and functions, as well as provide direct measurement on how patient feels (e.g. anxiety scales).
    - **Clinician-Reported Outcomes (ClinRO)** reflect the evaluation on a patient's condition by a healthcare professional after observation (e.g. pain rating scale).
    - **Observer-Reported Outcomes (ObsRO)** are measured based on an observation by someone other than the patient or the health professional. That is, carers or family living around patient and observing the daily life conditions (e.g. assessment of patient's cognition).
    - **Performance Outcomes (PerfO)** are based on the patient's performance of a defined task that is quantified in a specified way that does not rely on judgment to determine the rating (e.g. distance walked in 6 minutes).

- ✓ **Biomarkers** can be considered as intermediate outcome indicators that reflect changes in biological status that may affect subsequent health outcomes (e.g. protein levels in blood or urine measured by standardised methods). For example, biomarkers that predict the development of pulmonary fibrosis can correlate with the clinical course for patients with systemic sclerosis. The working group could consider an indicator that reflects the proportion of patients above a certain level of a particular pulmonary fibrosis biomarker [11].

4.4 | Designing indicator specifications

When potential indicators that make up a QM tool have been conceptualised, the next step is to design valid and reliable methods for the measurement. In short, how exactly would one measure the concept? This includes several aspects: defining target population, risk adjustment strategy, identifying data sources, mathematical specifications and setting data collection procedures [9, 12].

4.4.1 | Define target population

The target population refers to the patient group whose care the clinical indicator is designed to assess. In order to define it, the following aspects should be determined:

- ✓ Specific inclusion and exclusion criteria. Describe upper or lower age limits, gender or specific conditions.
- ✓ Whether the selection should be based on confirmed diagnoses, symptoms or sings. Indicate which definitions will be used for each case.
- ✓ Whether prevalent or incident cases (or both) are included.
- ✓ Time period for measurement.

4.4.2 | Determine adjustment strategy

Since indicator results often vary due to factors outside the control of the system, such as comorbidities or severity of illness, and these factors often vary systematically, risk adjustment has to be applied in order to make fair comparisons. This ensure that any observed differences in indicator levels can be attributed to the interventions and not to differences between the populations included [12].

- ✓ During literature review, potential risk factors (age, gender, comorbidities, or patient characteristics etc.) should be identified and clearly described.
- ✓ Assess whether the potential risk factors that have been identified are quantifiable and it is possible to obtain data to incorporate them into the indicator. It has to be acknowledged that clinical data with the detail necessary for comprehensive risk adjustment is often lacking, especially at the international level. Nevertheless, an effort should be made to adjust indicators to the degree possible and the limitations should be kept in mind when interpreting results [6].
- ✓ An alternative approach to risk adjustment is risk stratification. That is, patients who are subject of measurement are divided into two or more groups according to their expected risk of the process or outcome of interest. For example, setting “percentage of high-risk patients who have pressure sores” and the “percentage of low risk patients who have pressure sores” as separate indicators. However, reporting stratified data typically requires larger sample sizes than reporting aggregated data, or else stratum-specific estimates of performance are unreliable.

4.4.3 | Identifying data sources

Once the clinical indicators have been defined, target population determined and factors for risk adjustments derived, the working group should state how the data should be obtained. It is important to know the available data sources and how they are organized, have information on what variables are collected and how they are organized. In this way, later, the most appropriate mathematical artefact can be developed to collect the information from the indicators.

There are different sources of information that can be useful to obtain data on which the indicators are based. They are reviewed below with reference to their particular use [13, 14].

- ✓ **Health system data:** These are computerised hospital files where the patient diagnosis is coded usually using the International Classification of Diseases (ICD). They are clinical tools, adapted to counting patients who are using healthcare services. They are intended to be used by healthcare managers, however, sometimes are used for research purposes. In the field of rare diseases their use is limited as the ICD does not yet provide specific codes. This should change with the release of ICD-11 [15]. For example, Hospital discharges and length of stay statistics from Eurostat.
- ✓ **Healthcare provider's/system databases:** These are defined as permanent registrations of patient information in a systematic way, carried out by one healthcare provider or specific regional healthcare system on the basis of their referrals. These databases sometimes do not provide a true representation of the general population, usually biased towards more severe cases. They may be not suitable for collecting epidemiologic data, but they may be adequate to know how the care processes take place in certain types of patients, establishing criteria and geographical delimitation.
- ✓ **Patient registries:** They constitute key instruments for the development of clinical research in the field of rare diseases, and the improvement of patient care and healthcare planning as well as social, economic and quality of life outcomes. Patient registries usually pool scarce data for epidemiological and/or clinical research. Although they are vital to facilitate the planning of appropriate to support the enrolment of patients and to keep track for implementation activities, these registries should be taken with caution, since there is a multiplicity of registration for different conditions and types of patients that are not always aggregated in the same databases. Nevertheless, well-structured patient registries without information overlapping could be a useful tool for evidence generation in the future.
- ✓ **Data collected ad-hoc:** Data can also be obtained from targeted population or staff involved within the implementation of a CPG or CDST at offering the possibility to answer one or more specific questions. This is one shot data gathering, which may be repeated in at another time. The data collected is in the exact format required for the analysis. This implies an adequate definition of the population included and proper planning of what information is to be collected and how its analysis will be carried out.
- ✓ **Cohort data:** This is a concrete form of the data collected on purpose (ad-hoc) for a specific analysis. Data collection can be transversal (all defined patients or professionals involved registered once) or longitudinal (data collected at different points in time for the same participant). For rare disease clinical research, cohorts are highly desirable as they are usually the only way to collect enough data to allow a proper analysis, due to the very small number of cases.

4.4.4 | *Mathematical specifications*

Discussion among clinical and information systems experts within the working group is necessary to establish specifications of the indicators that are part of a QM tools. Specifically, the following points are important:

- ✓ Take into account the inclusion criteria that have been previously established.
- ✓ The mathematical construction of the indicators must be consistent with the evidence reviewed in previous phases of the development of the QM tool.
- ✓ Indicators should be adapted to the available data sources.
- ✓ Protocols on standards and threshold values should be established.
- ✓ A plan for handling missing data should be developed.

Regarding the mathematical specification, it is possible to use different artefacts according to the needs of the indicators [12]:

- ✓ **Proportions and percentages:** Most indicators are constructed as proportions or percentages, where the denominator represents the number of persons treated during a defined time period who were at risk of, or eligible for, the numerator event. The numerator then represents the number of persons in the denominator who received the appropriate diagnostic test or treatment (e.g., aspirin for heart attack), or the number who experienced an adverse outcome. Percentage indicators are bounded between 0% and 100%, which facilitates comparison of performance across measures and sites. The major drawback of the proportion/percentage approach is that it ignores interesting variation among those who are categorised as "yes" or "no," such as the relative severity of a complication.
- ✓ **Ratios:** A ratio describes the relationship between two numbers in terms of how many times one of the numbers is contained within the other. For example, number of beds per 1,000 inhabitants.
- ✓ **Means and medians:** Capture specific details of care better than proportion or percentage measures. It may be possible to distinguish differences in performance using mean or median values that could not be distinguished using proportion or percentages that have a category-based nature. The standards or thresholds for means and medians must me clearly explained, because it is not always apparent whether lower or higher values represent better care.
- ✓ **Counts:** A few indicators are reported simply as counts of events or adverse outcomes. The population and criteria for an event to be counted should be specified. These indicators are intended for promoting transparency and not to compare performance across settings/services.

4.5 | Preparing the application of the Quality Measures

The final QM tool development consideration is the anticipated application of the indicators. Although measures may be useful in more than one application, some development may require refining indicator definitions for a specific application [12].

The appropriate application of a QM tool is partially informed by indicator validation efforts:

- ✓ Ensure that the population that was initially established from the evidence reviewed is the one that is collected in the real-world context.
- ✓ Check existing population distributions to ensure that the indicator results reflect actual activity.
- ✓ Consider what are clinically significant differences among groups rather than simply statistically

significant differences

- ✓ Check whether the indicators are sensitive to changes in the population, processes or health outcomes
- ✓ Ensure that the characteristics and factors included in the risk adjustment models are being correctly collected.

05.

BEST PRACTICES FOR DEVELOPING A QUALITY

Based on all the information provided, a checklist for the development of QM tools is proposed (see Annex 7.1). This list is based on a publication that collects good practices in the development of PROMs [16], which has been adapted for general use in the development of any type of indicator in such a way that working group can check all the steps in the elaboration process (information on which the measurement is based, objectives, concept to be measured, measurement plan, etc.).

Key issues

- Quality Measures (QM) are tools that help to quantify healthcare processes, outcomes, patient perceptions, and organisational structure and/or systems. The development of relevant QM tools is crucial for the monitoring of rare disease knowledge progression, health policy and the assessment of the present situation.
- The QM working group should be multidisciplinary, as it should represent different perspectives and knowledge.
- There are four main elements that should be taken into account when developing a QM tool: concept, perspective, method and application.
- The key steps to follow for developing a QM tool are:
  - Define and establish the concept and perspective of QM.
  - Provide an overview of the existing evidence.
  - Use the evidence to build indicators. These indicators can be of structure, process or results.
  - define the methodological specifications of the indicator (population, data sources, mathematical artifact).
  - Prepare the QM application in context.

06.

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7.

ANNEXES

ANNEX 7.1 | Quality Measures development checklist

A checklist is presented in which to follow the steps and the information detailed along the indicator development process. An example is provided using an indicator on "proportion of patients with brain (or central nervous system) cancer presenting with seizures at diagnosis who are seen by a neurologist or a nurse with expertise in epilepsy management" (QPI 11 – seizure management) which is part of a QM tool on Cancer Quality Performance developed by Scottish Cancer Taskforce from NHS Scotland [17].

1. A rationale for measuring should be described	In this section the working group must provide the necessary evidence and justification for the development of the QM tool. For example, in the case of seizure management indicator, evidence from CPGs is provided to support that diagnosis of epilepsy is more accurate when made by a medical practitioner who specialises in epilepsy.
Is a knowledge gap described and justified?	
Is there evidence that the QM tool is meaningful and important to stakeholders (patients, health professionals, etc.)?	
How does this data collection and reporting in particular address the gap?	
Are the data sources selected the most appropriate source to collect information?	
2. The intended context of use should be described and justified	It should be explained what is expected from the development of this measure. For example, increasing the number of health professionals with training in epilepsy management in the setting/context produces more accurate diagnoses and this leads to better patient outcomes.
Is the intended context of use clearly described and justified?	
How is information from the indicator expected to inform change in practice or improve performance in the context of use?	
How will the indicators improve understanding of performance in the intended context of use?	
3. The QM should be adequately developed for the intended context of use, including demonstration of meaningfulness and importance (as well as adequate psychometric properties in the case of PRO)	Description of the measurement configuration must be reported, including how the measurement will be validated, the standardised classifications that will be

Is the underlying concept to be measured clearly identified?	used to identify the analysis population, inclusion and exclusion criteria, etc. For example, whether the collection of data will be piloted on a small number of patient records should be explained as a method to identify any anomalies or difficulties with data collection.
Is there prior or planned qualitative work with potential stakeholders (or patients in the case of PRO) demonstrating understanding of terminology of the underlying concept of interest?	
Is there evidence of adequate properties of the indicator, including validity and reliability, meaningfulness of score changes in a comparable population?	
4. There should be planed work for demonstrating that it is sensitive to change and clinically actionable	The time in which changes in the measure are expected should be specified and how these changes will be detected. Depending on the type of measurement, if there are limit values or standards to be reached In the same example, it is stated that indicator will be kept under regular review and be responsive to changes in clinical practice and emerging evidence. The indicator is a proportion so it will be censored between 0 and 100.
Has the measure been shown to detect changes over time or differences between groups, practices or procedures?	
Does the measure detect changes in clinical actions or decisions?	
Is there evidence that there is not a floor or ceiling effect of the indicator?	
5. There should be a recommended analysis plan, including risk adjustment, missing data approach, etc.	The indicator analysis plan must be detailed and what variables will be essential (risk adjustments or stratification according to different types of patients). In the case of epilepsy indicator, it has been indicated that tolerance within the target level of the measure is designed to account for factors of patient choice.
Is there a well-justified a priori risk adjustment or stratification strategy based on evidence?	
Is there a plan to adjust analysis for case mix or response bias?	
What are sample sizes or minimum data collection necessary for planned analysis?	
6. There should be a recommended framework for interpreting the results, including units of analysis and meaningful score thresholds	How the measurement is operationalised, in which units the data will be taken and how they will be processed to obtain the indicator In this case, the indicator type is a proportion. that desired value is a higher score and target is stated at 95%.
What unit of analysis is recommended (e.g. hospital, individual practice, patient-level, etc.)	
What measurement artefact should be used to reflect the concept (e.g. percentages, rations, mean, etc.)?	
7. There should be a recommended approach for reporting and disseminating results	Information on reports, periodicity, what data will be provided, etc. must be clarified.
Is there a suggested approach for presenting reports to professionals or patients?	

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