Development of an international standard set of outcome measures for patients with venous thromboembolism: an International Consortium for Health Outcomes Measurement consensus recommendation

Adam M Gwozdz, Cindy M M de Jong*, Luz Sousa Fialho, Theerawich Likitabhorn, Frieda Sossi, Paula Blancarte Jaber, Anette Arbjerg Højen, Juan I Arcelus, William R Auger, Cihan Ay, Stefano Barco, Marcelo B Gazzana, Julie Bayley, Laurent Bertoletti, Arina ten Cate-Hoek, Alexander T Cohen, Jean M Connors, Jean-Philippe Galanaud, Nicos Labropoulos, Nicole Langlois, Mark H Meissner, Simon Noble, Esther J Nossent, Paula Ponce de León Lovatón, Helia Robert-Ebadi, Rachel P Rosovsky, Noa Smolenaars, Mark Toshner, Cécile Tromeur, Kang-Ling Wang, Eli Westerlund, Kerstin de Wit, Stephen A Black†, Frederikus A Klok†*

Lancet Haematol 2022; 9: e698–706

*These authors contributed equally

†These authors contributed equally

Academic Department of Vascular Surgery, Section of Vascular Risk and Surgery, School of Cardiovascular Medicine and Science (A M Gwozdz MBBS, Prof S A Black MD) **and Department of Haematological Medicine** (A T Cohen MD), **Guy's and Saint Thomas' Hospital, King's College London, London, UK; Academic Section of Vascular Surgery, Department of Surgery and Cancer and Department of Vascular Surgery, Imperial College Healthcare NHS Trust, Imperial College London, London, UK** (A M Gwozdz); **Department of Medicine: Thrombosis and Haemostasis, Leiden University Medical Center, Leiden University, Leiden, Netherlands** (C M M de Jong MD, Prof F A Klok MD); **International Consortium for Health Outcomes Measurement, London, UK** (L Sousa Fialho PhD, F Sossi MSc, P Blancarte Jaber MD); **International Consortium for Health Outcomes Measurement, Boston, MA, USA** (T Likitabhorn MD); **Aalborg Thrombosis Research Unit, Department of Cardiology, Aalborg University Hospital, Aalborg University, Aalborg, Denmark** (A A Højen PhD); **Department of Surgery, University of Granada Medical School, University of Granada, Granada, Spain** (J I Arcelus MD); **Department of Pulmonary Medicine, University of California,**

The International Consortium for Health Outcomes Measurement assembled an international working group of venous thromboembolism experts and patient representatives to develop a standardised minimum set of outcomes and outcome measurements for integration into clinical practice and potentially research to support clinical decision making and benchmarking of quality of care. 15 core outcomes important to patients and health-care professionals were selected and categorised into four domains: patient-reported outcomes, long term consequences of the disease, disease-specific complications, and treatment-related complications. The outcomes and outcome measures were designed to apply to all patients with venous thromboembolism aged 16 years or older. A measurement tool package was selected for inclusion in the core standard set, with a minimum number of items to be measured at predefined timepoints, which capture all core outcomes. Additional measures can be introduced to the user by a cascade opt-in system that allows for further assessment if required. This set of outcomes and measurement tools will facilitate the implementation of the use of patient-centred outcomes in daily practice.

Introduction

Venous thromboembolism, comprising of deep vein thrombosis and pulmonary embolism, affects 1–3% of the population and has an annual incidence of 1–2 per 1000 in high-income countries.[1–3] Approximately 60% of all venous thromboembolism instances present as deep vein thrombosis with the other 40% presenting as pulmonary embolism with or without deep vein thrombosis.[4] The management of venous thromboembolism involves anticoagulation and can be complicated by sequelae, which include recurrent venous thromboembolism, anticoagulant therapy associated bleeding, post-thrombotic syndrome, and post-pulmonary embolism syndrome, with post-thrombotic syndrome and post-pulmonary embolism syndrome affecting 40–50% of all venous thromboembolism survivors.[5–8] Venous thromboembolism has a substantial negative affect on patients' lives, causing a reduced quality of life, a higher prevalence of unemployment, and emotional distress, including anxiety and post-thrombotic panic syndrome.[9–14]

Globally, the management of venous thromboembolism is inconsistent and highly diverse. Not only are there country level differences in health-care systems, availability of resources, and socioreligious circumstances, but guidelines also differ regarding recommendations on risk stratification, management of venous thromboembolism, and long-term follow up, with little consideration to the patients' perspective or values. There are major differences in treatment outcomes, such as, mortality,[15–17] loss of quality-adjusted life years,[18] and chronic thromboembolic pulmonary hypertension (CTEPH)[19] across countries and continents. Other differences involve the use of health-care resources, measured by rate of hospital admissions;[20,21] duration of hospital admission;[21] and use of interventional techniques. Moreover, inability to work due to venous thromboembolism and psychosocial consequences, such as persisting anxiety and depression, which are of considerable importance to the individual patient and society, receive minimal attention in venous thromboembolism patient pathways.[11–14]

There is increasing recognition of the importance of integrating all aspects of health care to focus on the delivery of value-based health care. Value-based health care assesses value by measuring health outcomes against the cost of their delivery, and these approaches lead to improved health outcomes for patients with fewer clinical visits, medical tests, and procedures.[22] Therefore, rather than a system within which clinicians and health-care providers are paid on the basis of the number of health-care services they deliver,[23] a shift to a value-based approach for venous thromboembolism would more directly reward clinicians for helping patients improve their health, reduce the effects and incidence of chronic disease, and live healthier lives in an evidence-based way. A fully standardised approach for value-based health care would include both clinical and patient-reported outcome measures, assessed at fixed timepoints, using well-defined instruments and definitions.

To support improvements in care for patients with venous thromboembolism globally via a value-based health-care approach, the International Consortium for Health Outcomes Measurement (ICHOM) assembled a

geographically diverse working group of 27 clinical or research venous thromboembolism experts and patient representatives from 13 countries in Europe, North America, Latin America, and Asia-Pacific. ICHOM is a not-for-profit organisation that has previously developed 40 standard sets of value-based outcomes for different disease states. The aim of this project was to propose a broadly applicable and easy-to-use standardised minimum set of outcomes for venous thromboembolism patients, including patient-reported outcome measures and clinical outcomes and case-mix factors. The ICHOM-venous thromboembolism set has three specific goals: to standardise and improve the care for individual patients with venous thromboembolism, to facilitate the standardisation of outcomes to make meaningful comparisons across institutions and countries and, to empower patients to manage their disease and seek the optimal care for their individual needs.

Strategy

A project team (FAK, SAB, CMMdJ, AMG, FS, PBJ, TL, and LSF) guided the working group's efforts over 13 months. By drawing on connections within the project team's network and identifying experts in the field of thrombosis through a PubMed search of relevant scientific outputs, experts and patient representatives were engaged to participate in the working group, with the aim of creating a diverse team. In line with other ICHOM working groups, we aimed for a working group of 25–30 people. A broad range of specialties was represented: methodologists and epidemiologists, vascular specialists, pulmonologists, haematologists, angiologists, internists, surgeons, primary care physicians, nurses, and one palliative care physician, one emergency physician, and one psychologist. During the project, three patient representatives participated in the working group, of whom one stopped after contributing to more than half of the development process. The patient representatives all had venous thromboembolism themselves at some point in their life courses. The working group convened through nine video conferences between Jan 7, 2021, and Feb 3, 2022, following a structured process that involved professionals and patients in all meetings. The development of the standard set of outcome measures involved several phases: defining the scope of the project, prioritising and defining outcome domains, evaluating and selecting appropriate outcome measurement tools, and selecting and defining relevant case-mix variables and timepoints.

Identification of potential outcomes and case-mix variables

The project team did a systematic literature review, following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines[24] to identify potentially relevant outcome domains, clinical and patient-reported outcomes, treatment-related complications, and case-mix variables. Appropriate medical subject heading terms and free word searches were used (appendix p 2). The literature search identified 1004 articles. Two reviewers (CMMdJ and AMG) independently screened the articles and selected original research papers in which clinical and patient-reported outcomes were reported in a population of patients with pulmonary embolism or deep vein thrombosis. Any disputes were resolved by a third reviewer (FS). This resulted in the inclusion of 188 articles for full-text review. Patient representatives from the working group participated as a patient advisory group in a separate breakout session to explore their perspectives on which of the various outcomes identified from the literature affected them the most during their day-to-day activities. The predefined criteria by which outcomes were assessed for inclusion in the set were: the frequency of the outcome, the effect on the patients, the potential for modifying the outcome, and the feasibility of measuring the outcome. Variables to be used as case-mix factors, which considers how different risk profiles affect outcomes and allows standardised risk adjustment across different populations, were assessed on relevance, independence, and measurement feasibility. All potentially relevant outcomes and case-mix variables were discussed during the video conferences and put to vote in a three-round modified Delphi process.

Selection of patient-reported outcome measures and definitions

We mapped the standard set outcomes to corresponding patient-reported outcome measures and definitions identified from the literature review. We applied widely used definitions by scientific organisations (eg, International Society on Thrombosis and Haemostasis, World Symposium on Pulmonary Hypertension), in guidelines or applied in studies to define the clinical outcomes. If multiple definitions were found, all were put to vote in the Delphi voting process. We identified original and validation studies on relevant patient-reported outcome measures and evaluated their psychometric quality (ie, validity, reliability, and sensitivity to change), domain coverage, and the feasibility of measurement and implementation. Feasibility considerations included the availability of translations and potential costs associated with the wide implementation of the individual instruments.

Modified Delphi process and open review

Outcome selection was done in an online three-round modified Delphi process. Following each working group video conference, all working group members were required to vote. The consensus process followed the RAND–University of California (Los Angeles, CA) method to reach consensus on which outcomes should be included.[25] The results of each vote were reviewed by the working group during the subsequent video conference. Inclusion in the standard outcome set required that at

San Diego, CA, USA (Prof W R Auger MD); **Clinical Division of Haematology and Haemostaseology, Department of Medicine I, Medical University of Vienna, Vienna, Austria** (Prof C Ay MD); **Department of Angiology, University Hospital Zurich, University of Zurich, Zurich, Switzerland** (S Barco MD); **Centre for Thrombosis and Haemostasis, Johannes Gutenberg University Mainz, Mainz, Germany** (S Barco); **Department of Pulmonology and Thoracic Surgery, Hospital Moinhos de Vento, Porto Alegre, Rio Grande do Sul, Brazil** (M B Gazzana PhD); **National Association of Private Hospitals, Porto Alegre, Rio Grande do Sul, Brazil** (M B Gazzana); **Lincoln Impact Literacy Institute, University of Lincoln, Lincoln, UK** (J Bayley PhD); **Department of Vascular and Therapeutic Medicine** (Prof L Bertoletti MD), **CIC-1408, INSERM** (Prof L Bertoletti), **and French Clinical Research Infrastructure Network [F-CRIN] INNOvenous thromboembolism** (Prof L Bertoletti, C Tromeur MD), **University Hospital of Saint-Étienne, University of Saint-Étienne, Saint-Étienne, France; UMR1059, INSERM, Université Jean-Monnet, Saint-Étienne, France** (Prof L Bertoletti); **Department of Internal Medicine and Pneumology, University Hospital of Brest, Brest, France** (C Tromeur); **Group d'etude de la thrombose de Bretagne Occidentale, Université de Bretagne Occidentale, Brest, France** (C Tromeur); **Heart and Vascular Centre, Maastricht University Medical Centre, Maastricht University, Maastricht, Netherlands** (A ten Cate-Hoek MD); **Hematology Division, Brigham and Women's Hospital** (J M Connors MD) **and Division of Hematology, Department of Medicine, Massachusetts General Hospital** (R P Rosovsky MD), **Harvard Medical School, Harvard University, Boston, MA, USA; Department of Medicine, Sunnybrook Health Sciences Centre and University of Toronto, Toronto, ON, Canada** (J-P Galanaud MD); **Division of Vascular Surgery, Department**

of Surgery, Stony Brook Hospital, Stony Brook, NY, USA (Prof N Labropoulos MD); Department of Medicine, Ottawa Hospital Research Institute, Ottawa, ON, Canada (N Langlois MSc); Department of Surgery, University of Washington, Seattle, WA, USA (M H Meissner MD); Marie Curie Palliative Care Research Centre, Cardiff University, Cardiff, UK (Prof S Noble MD); Department of Pulmonary Medicine, Amsterdam Cardiovascular Sciences, Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands (E J Nossent MD); Clínica San Felipe, Jesús María, Peru (P Ponce de León Lovatón MD); Division of Angiology and Haemostasis, Geneva University Hospitals (H Robert-Ebadi MD) and Faculty of Medicine (H Robert-Ebadi), University of Geneva, Geneva, Switzerland; Department of Industrial Design, University of Technology Eindhoven, Eindhoven, Netherlands (N Smolenaars BSc); Heart Lung Research Institute, Department of Medicine, University of Cambridge, Cambridge, UK (M Toshner MD); General Clinical Research Center, Taipei Veterans General Hospital, Taipei, Taiwan (K-L Wang MD); Department of Clinical Sciences, Karolinska Institutet; Danderyd Hospital, Danderyd,

least 80% of the working group voted an item as essential, best instrument, or relevant case-mix variable (represented by a score between seven and nine on a nine-point Likert scale) in either voting round. Outcomes and case-mix variables were excluded if at least 80% of the working group members voted an item as not recommended (scoring between one and three). All inconclusive outcomes were voted on in the final round with 70% consensus required for the outcome to be included; if the 70% majority was not met, the outcome was left out of the final set. For the patient-reported outcome measures and case-mix variables, 70% agreement was required for inclusion. On the basis of the discussion with the working group, a tool package (ie, a combination of instruments to measure the outcomes) with a cascade opt-in system was proposed and included after the voting round that followed the video conference.

To allow for input from people with current or previous venous thromboembolism and professional stakeholders outside of the formal working group, an open review period was held in English before the last working group video conference. The project team contacted English-speaking patients and professional stakeholders outside the project's working group through email and social media. The contacted individuals were shown an overview of the set and asked to provide independent feedback and to rate the importance of outcomes using a nine-point Likert scale, via an online survey. The results of this survey were presented to the working group during the final video conference.

Consensus recommendations

ICHOM set target population and the question of patient subgroups

The outcomes and measures included in the venous thromboembolism standard set were defined for a target population of patients diagnosed with venous thromboembolism aged 16 years and older, including those with incidental venous thromboembolism. Although the working group initially decided that subcategories for patients with cancer-associated venous thromboembolism, pregnant women with venous thromboembolism, and patients at the end of life with venous thromboembolism should be considered, these subgroups were later deselected, because we could not identify any subgroup-specific outcomes not already covered in the overarching set. Of note, separate ICHOM sets are available for pregnancy and several cancers.[26,27] The working group considered these ICHOM sets complementary to the venous thromboembolism set in relevant patients.

Core outcomes in the ICHOM-venous thromboembolism set

After consolidating the literature review findings and focus group meetings, a proposed list of 87 outcomes was identified for discussion and voting, from which the working group selected 15 core outcomes as crucial to patients with venous thromboembolism and health-care professionals (figure 1; table 1; appendix p 3).

The outcomes were categorised into four domains: patient-reported outcomes, long-term consequences of the disease, disease-specific complications, and treatment-related complications. The working group recommended specific patient-reported outcomes in all the following subdomains be captured: disease-specific and general quality of life; functional limitations including the ability to work; pain; dyspnoea; satisfaction with treatment; psychosocial wellbeing including anxiety, depression, and post-thrombotic panic syndrome; and changes in life view. The outcome domain focussing on the long-term consequences of venous thromboembolism was recommended to consist of the following sub-domains: use of

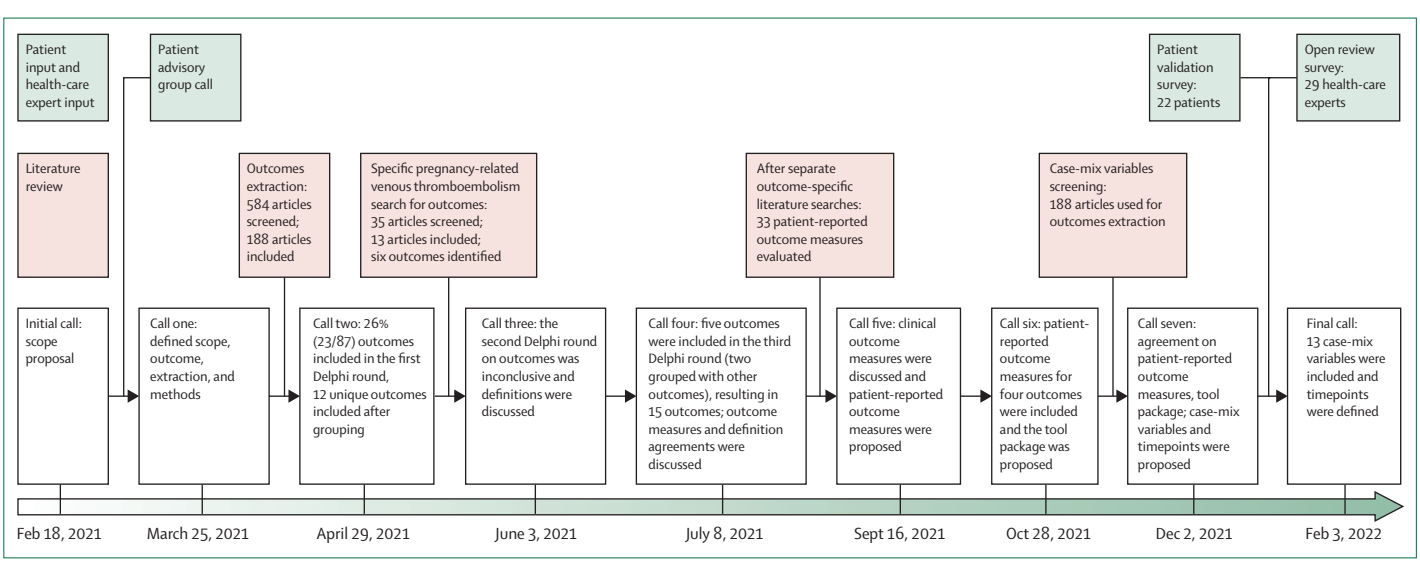

Figure 1: **Development of the ICHOM set of patient-centred outcome measures for venous thromboembolism through a structured working group process**

	Measures	Measure at index event	Data source
Patient-reported outcomes			
Quality of life	The PROMIS Scale v1.2—Global Health, PEmb-QoL, and VEINES-QOL questionnaires	No	Patient
Functional limitations (including ability to work)	The Post-VTE Functional Status scale	Yes	Patient
Pain (including symptom severity)	The PROMIS Scale v1.2—Global Health, PEmb-QoL, and VEINES-QOL questionnaires and, if required, the PROMIS Short Form v2.0 Pain Intensity 3a	Yes	Patient
Dyspnoea (including symptom severity)	The PEmb-QoL and PROMIS Short Form v1.0 Dyspnea Severity 10a	Yes	Patient
Psychosocial wellbeing	The PROMIS Scale v1.2—Global Health, PEmb-QoL, and VEINES-QOL questionnaires and, if required, the PHQ-9 and GAD-7 questionnaires	Yes	Patient
Satisfaction with treatment	Measured through the question, "Are you satisfied with your venous thromboembolism treatment?", and, if required, measured using the Anti-Clot Treatment Scale	No	Patient
Changes in life view	Measured through the question, "Have you experienced a change in your expectations, aspirations, values, or perspectives on life opportunities since the diagnosis of venous thromboembolism?"	No	Patient
Long-term consequences of disease			
Use of health-care resources	Number of hospital stays and length of stay; number of emergency room visits; number of non-hospital health-care activities (including general practice, outpatient clinic visits, home health care, and rehabilitation)	Yes	Clinician
Chronic thromboembolic pulmonary hypertension	Clinical diagnosis	No	Clinician
Chronic thromboembolic pulmonary disease	Clinical diagnosis	No	Clinician
Post-thrombotic syndrome	Villalta Score	No	Clinician
Disease-specific complications			
Recurrence	Measured through the question: Has the patient had recurrent venous thromboembolism according to the ISTH definition? with a yes or no answer	Yes	Clinician
Survival	Death regardless of cause	Yes	Clinician
Treatment-related complications			
Bleeding	Measured through the question: Did the patient have any bleeding that was worrisome to the patient or the clinician, impacted daily activities or required medical treatment? with a yes or no answer	Yes	Clinician
Procedure-related complications	Measured through the question: Has the patient experienced an undesirable and/or unintended outcome that is a direct result of a procedure? with a yes or no answer	Yes	Clinician

All measures should be completed at 3 months, 6 months, 1 year, and then annually for as long as the individual is under care. GAD-7=Generalized Anxiety Disorder-7. ISTH=International Society on Thrombosis and Haemostasis. PEmb-QoL=pulmonary embolism quality of life. PHQ-9=Patient Health Questionnaire-9. PROMIS=Patient-Reported Outcome Measurement Information System. PVFS=Post-Venous embolism Functional Status. VEINES-QoL=Venous Insufficiency Epidemiological and Economic Study on Quality of Life. VTE=venous thromboembolism.

Table 1: **Summary of International Consortium for Health Outcomes Measurement venous thromboembolism standard set of outcomes**

health-care resources (eg, hospitalisations, diagnostic tests, and visits to medical professionals such as physiotherapists), chronic thromboembolic pulmonary hypertension (CTEPH), chronic thromboembolic pulmonary disease (CTEPD), and post-thrombotic syndrome. Relevant disease-specific or treatment-related complications included survival (an ICHOM term representative of death), venous thromboembolism recurrence, bleeding, and procedure-related complications.

Optimal instruments to capture these outcomes

The working group decided on a measurement tool package that captures all these core outcomes. Because several of the optimal instruments identified by the working group have partly overlapping questions and domains, a cascade opt-in system was used to ensure that a minimum number of items would capture all core outcomes (figure 2). The measurement tools for the core set include the Patient-Reported Outcomes Measurement Information System (PROMIS) Short Form Global Health,[28] Pulmonary Embolism Quality of Life (PEmb-QoL) questionnaire,[29] Venous Insufficiency Epidemiological and Economic Study on Quality Of Life (VEINES-QOL) questionnaire,[9] and the single item Post-Venous Thromboembolism Functional Status (PVFS) scale,[30] and a single question on treatment satisfaction and changes in life view. If patients indicated the presence of pain, dyspnoea, anxiety, depression, or treatment dissatisfaction (all single questions in the core set of instruments), the cascade opt-in system proposed additional instruments to acquire relevant dimensions and details using PROMIS Short Form v2.0 Pain Intensity 3a,[31] PROMIS Short Form v1.0 Dyspnea Severity 10a,[32] Patient Health Questionnaire-9,[33]

Sweden (E Westerlund PhD); **Department of Emergency Medicine, Queen's University, Kingston, ON, Canada** (K de Wit MBChB); **Departments of Medicine and Health Research Methods, Evidence and Impact, McMaster University, Hamilton, ON, Canada** (K de Wit)

Correspondence to:
Prof Frederikus A Klok, Department of Medicine: Thrombosis and Haemostasis, Leiden University Medical Center, Leiden, 2333 ZA, Netherlands
f.a.klok@lumc.nl

See **Online** for appendix

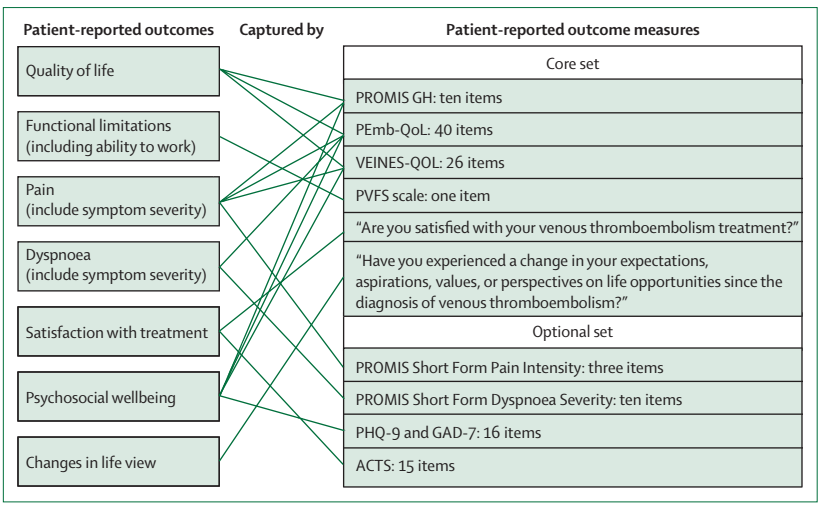

Figure 2: **Overlap between the patient-reported outcomes and patient-reported outcome measures**
By introducing a cascade option (core set *vs* optional set), relevant overlap is mostly avoided. The PROMIS short forms Pain Intensity and Dyspnea Severity are triggered by PROMIS short form GH and PEmb-QoL, respectively. PHQ-9 and GAD-7 are triggered by PROMIS short form GH. ACTS is triggered by the single question on satisfaction with treatment. ACTS=Anti-Clot Treatment Scale. GAD-7=Generalized Anxiety Disorder-7. GH=Global Health. PEmb-QoL=Pulmonary Embolism Quality of Life. PVFS=Post-Venous thromboembolism Functional Status. PHQ-9=Patient Health Questionnaire-9. PROMIS=Patient-Reported Outcomes Measurement Information System. VEINES-QOL=Venous Insufficiency Epidemiological and Economic Study on Quality of Life.

Generalized Anxiety Disorder-7 questionnaire,[34] and the Anti-Clot Treatment Scale.[35]

Long-term consequences of disease and complications are health-care professional reported. Definitions of these outcomes were primarily derived from the International Society on Thrombosis and Haemostasis set of common data elements for venous thromboembolism research.[36]

Baseline characteristics and case-mix variables relevant to the ICHOM set

The working group selected the most important baseline characteristics and case-mix variables to allow standardised risk adjustment across different populations. The working group identified several patient demographics, measures for baseline health status, and treatment-related factors that affected outcomes included in the core standard set (table 2). The demographic risk-adjustment factors selected for inclusion were age, sex, race, ethnicity, and educational attainment. The clinical risk-adjustment factors (ie, baseline and treatment-related) include BMI, comorbidities according to the Self-Administered Comorbidities Questionnaire,[37] history of venous thromboembolism, high risk or massive pulmonary embolism, phlegmasia, unprovoked venous thromboembolism, actual use of antithrombotic medication, and specific interventions for the treatment of venous thromboembolism.

Final set

For the **final ICHOM standard set** see https://connect.ichom.org/patient-centered-outcome-measures/venous-thromboembolism/

The final ICHOM standard set of patient-centred outcome measures for patients with venous thromboembolism including relevant timepoints is shown in figure 3. Of the recommended patient-reported outcome measures, quality of life, treatment satisfaction, and changes in life view are not to be captured at baseline. The PVFS scale can be used to assess the pre-venous thromboembolism functional status for comparison.

This set was subjected to open review by 22 people with lived experience of venous thromboembolism and 29 expert professionals who completed an online survey. Most the participants who had a history of venous thromboembolism were aged 46–60 years, six (27%) patients had pulmonary embolism at some point in their life course, five (23%) had deep vein thrombosis, and 11 (50%) had both pulmonary embolism and deep vein thrombosis. The 29 health-care professionals were mostly physicians (90%; 26 of 29); two (7%) were researchers and one (3%) was a health-care administrator. At least 65% of individuals with lived experience of venous thromboembolism and health-care professionals rated 12 of the 15 core outcomes in the standard set as essential. For the other three outcomes, there was discrepancy between the two groups. The outcome of CTEPH was rated as essential by ten (50%; two individuals did not rate this outcome) of those with lived experience of venous thromboembolism, and CTEPD by nine (45%; two individuals did not rate this outcome), while 24 (83%) of the 29 health-care professionals rated CTEPH as essential, and 23 (79%) CTEPD. By contrast, the outcome changes in life view was rated as essential by 48% of professionals, while 70% of those with lived experience considered this outcome to be essential.

21 (95%) of the 22 individuals with lived experience of the disease felt that the proposed outcomes broadly captured all the important aspects that matter most to patients with venous thromboembolism, and that applying the set and collecting the information would be helpful to support patient care. Health-care professionals were asked to provide feedback on the entire set. 92–100% of professionals rated the included patient-reported outcome measures, clinical outcome measures, and case-mix variables as essential, and 88–100% rated the timepoints proposed to measure the outcomes and variables as essential. Additionally, four professionals who completed the survey commented that the set might have too many instruments and measurements. After discussion and consideration by the working group during the final video conference, all outcomes, and their capture at the proposed timepoints, were considered crucial, with the core set of selected instruments and additional instruments via the cascade opt-in system.

The set has several limitations that need to be acknowledged. Despite considerable efforts to engage venous thromboembolism experts from Asia and Africa, and despite the diversity of our team in terms of nationality, culture, and religion, the majority of working group members live in Europe and North America, which could have affected the decision-making process. Furthermore, the patient-reported outcome measures included in the

	Details to be recorded	Timing	Reporting source
Demographic factors			
Birth year	Year of birth as YYYY	Index event	Clinical, patient reported, or administrative data
Sex	Sex at birth	Index event	Clinical, patient reported, or administrative data
Race	The biological race of the person	Index event	Patient reported
Ethnicity	The cultural ethnicity of the person that they most closely identify with	Index event	Patient reported
Educational attainment	Highest level of education completed based on local standard definitions of education levels; to compare against the International Standard Classification of Education	Index event	Patient reported
Baseline health status			
Body-mass index	Calculated in kg per m^2	Index event, 1 year, and annually*	Clinical
Previous history of venous thromboembolism	Yes or no	Index event	Clinical
Comorbidities	Based on the Self-Administered Comorbidities Questionnaire	Index event, 1 year, and annually*	Patient reported
High risk or massive pulmonary embolism	Yes or no	Index event	Clinical
Phlegmasia	Yes or no	Index event	Clinical
Unprovoked venous thromboembolism	Yes or no	Index event	Clinical
Treatment-related factors			
Antithrombotic treatment	Yes or no; generic name of the drug; dose; medical indication; drug class	Index event, 3 months, 6 months, 1 year, and annually*	Clinical
Underwent interventional treatment for venous thromboembolism	Yes or no	Index event, 3 months, 6 months, 1 year, and annually*	Clinical

*For as long as the patient is under care.

Table 2: **Case-mix variables included in the ICHOM set of patient-centred outcome measures for venous thromboembolism**

standard set were developed in Europe or North America and have little country-specific or region-specific validation (ie, validation of the translated version), which is a major limitation of this set and other standard outcome sets.

Implementation

The final set is now available online for use within clinical practice and potentially research. After signing up for free through ICHOM Connect, all materials related to the set (ie, a flyer, reference guide, and data dictionary) can be downloaded. By signing up before downloading the materials, all users can be contacted when an updated version of the set is published. Although we have drawn on publicly accessible tools where possible, to implement the set, colleagues must first assess what technology, informatics, and access infrastructures are available within an individual health-care institution or regional health-care system. We advise preparing an implementation plan in the relevant context, with a roll out phase including pilot data collection and refinement of the workflow, ahead of implementing the full set for all patients within our stated scope. From here, data can be collected on every patient according to the defined timepoints for measurement of the outcomes. The Data Dictionary (part of the online Reference Guide) gives all details to guide data collection and supports the implementation of outcome measurement as consistently as possible, which is crucial to make comparisons across institutions and countries.

Embedding patient-reported outcome measures into electronic health records would ease cross-care integration into clinical practice and enhance routine measurement of patient-reported outcomes. Furthermore, in recognition of the time challenges of completing patient-reported outcome measures, incorporating them as digital measures could provide the necessary flexibility to automatically direct patients and providers to the relevant questions (through the cascade opt-in system), shortening the time needed to complete the questionnaires. We are aware of the need to minimise data collection to avoid burden on both health-care providers and patients but recognise the need to encompass all important outcomes for meaningful comparisons. The feasibility of the measurement and implementation of these outcome measures were considered during the working group discussions and selection of outcome measures, as were the realities of being a patient with venous thromboembolism or a health-care provider. So

For **ICHOM Connect registration** see https://connect.ichom.org/registration/individual-free/

For **ICHOM Connect portal** see https://connect.ichom.org/

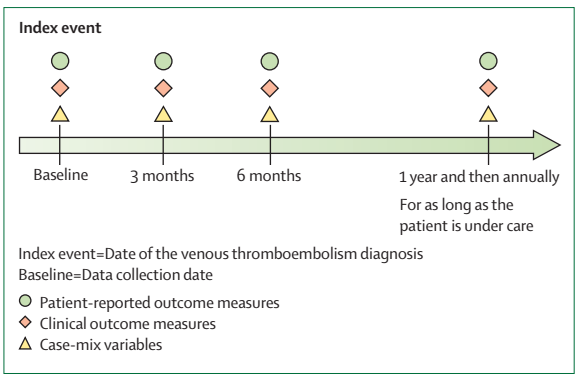

Figure 3: **The final ICHOM standard set of outcome measures for patients with venous thromboembolism including relevant timepoints**
Of the recommended patient-reported outcome measures, quality of life, treatment satisfaction, and changes in life view are not to be captured at baseline. The Post-Venous thromboembolism Functional Status scale can be used to assess the pre-venous thromboembolism functional status for comparison. Data collection starts at the time of diagnosis. A new timeline should be started if the patient has a recurrent venous thromboembolism event. More details about patient-reported outcome measures, clinical outcome measures, and case-mix variables can be found in the ICHOM venous thromboembolism Reference Guide.

Search strategy and selection criteria

During the development process of the standardised set of outcomes, literature searches were done using appropriate medical subject heading terms and search terms. Potentially relevant outcome domains and clinical and patient-reported outcomes were identified through a literature search of PubMed, done on March 8, 2021, with search terms capturing "venous thromboembolism", combined with terms covering "patient reported outcome measures" (and terms with "patient relevant") and "treatment outcome", in "adults" and "adolescents" (papers studying children [younger than 16 years] were excluded). Papers published in English between March 8, 2011, and March 8, 2021, were reviewed. Original research papers in which clinical and patient-reported outcomes were reported in a population of patients with pulmonary embolism or deep vein thrombosis were included for full-text review to identify outcomes. Separate outcome-specific literature searches were done to identify potentially relevant patient-reported outcome measures using the same criteria.

For **ICHOM Implementation frequently asked questions** see https://www.ichom.org/faqs/#implementation

For **a map of the implementation of ICHOM sets of patient-centred outcome measures** see https://www.ichom.org/global-set-implementation/

far, ICHOM has developed more than 40 standard sets. Because ICHOM sets are publicly available, it is difficult to track implementation precisely; even so, implementation of at least one ICHOM set has been reported for 650 institutions and 13 registries across 32 countries, highlighting the success of existing ICHOM standard sets. Implementation studies[38–42] have been done for different ICHOM sets, showing the feasibility of implementing ICHOM sets. Help and support with implementation and with the measurement of outcomes and the application of patient-reported outcome measures is provided by ICHOM. Because the set includes existing outcome measures that best capture the recommended outcomes, the tools should be interpreted according to the original scoring manuals. To enquire about support or to contact other ICHOM Connect members, the online ICHOM Connect portal can be visited. Of note, the questionnaires can be easily included in an online survey that will also facilitate the correct postprocessing and interpretation of the patient-reported outcome measures.

Although the aim is to achieve a globally adopted standard set, we recognise that there are different resources, digital infrastructures, and health-care contexts in low-income, middle-income, and high-income countries that can affect the speed and success of implementation. Training and education, commitment, and enabling attitudes of health-care professionals are believed to facilitate implementation,[43] which can offset more structural challenges within the health-care system. The patient-reported outcome measures suggested in our standard set do not require a fee or license, can be completed on paper, and can be implemented with minimum resources. Nonetheless, implementation in low-income and middle-income countries poses more challenges than in most high-income countries. ICHOM and the working group will continuously promote global use of the standard set and provide help to local institutions where possible. Also, if a desired translation is not available, ICHOM provides guidance in translating patient-reported outcome measures following a defined process in accordance with the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Principles of Good Practice.[44]

Conclusion

On the basis of the principles of evidence-based medicine: integrating patients' values, best available evidence, and medical expertise; we have developed a consensus recommendation for a standardised minimum set of outcomes that cover all of the aspects of venous thromboembolism treatment and clinical course that matter most to patients and health-care professionals: ICHOM-venous thromboembolism. As with all ICHOM sets, the process of development is unique through the extensive engagement of patient representatives in all steps and decisions. Following the focus groups, several outcomes that had previously not been studied in venous thromboembolism were considered relevant and therefore were included in the final set (eg, changes in life view). The working group targets integration of the standard set into routine clinical practice and, potentially, research. The substantial patient involvement in the development phase of the set is expected to improve patient compliance to completing the instruments in daily practice. We anticipate that the introduction of this set will contribute substantially towards increasing value in venous thromboembolism care. Health-care professionals and policy makers will be able to use these measures to identify effective, high-value practices in the

therapeutic management and in follow-up of venous thromboembolism patients, which in turn helps to better target efforts towards quality improvement. Moreover, implementation of this set will empower patients with venous thromboembolism to actively participate in their care and, together with involved professionals, make better informed decisions about health-care options.

Contributors

AMG, CMMdJ, and FAK wrote the draft of this Review. All authors contributed to the working group discussions and online voting, provided important intellectual content, reviewed and edited the manuscript, and all have approved the manuscript's final version.

Declaration of interests

AAH reports research grants from The Danish Heart Foundation and The Novo Nordisk Foundation, consulting fees from Bayer and The Bristol-Myers Squibb-Pfizer Alliance, speaker bureaus from Bayer, The Bristol-Myers Squibb-Pfizer Alliance, and Merck Sharp & Dohme, and role as vice chair of special interest group venous thromboembolism of Danish Nurses' Council. JIA reports honoraria from Sanofi and Rovi for educational activities, and research funding from Sanofi and Bayer AG. WRA reports payment or honoraria from Bayer Pharmaceuticals, support for attending meeting from Bayer Pharmaceuticals, and participation as Clinical Advisor for Janssen. CA received personal fees for lectures and participation in advisory boards from Bayer, Bristol Myers Squibb, Daiichi-Sankyo, Pfizer, and Sanofi. SB reports unrestricted scientific grants from Bayer, INARI, Boston Scientific, Medtronic, Bard, SANOFI, and Concept Medical; consulting fees from INARI, Bayer, Boston Scientific, and Concept Medical; and travel financial support for attending meetings from Bayer and Daiichi Sankyo. LB reports personal fees and non-financial support from Aspen, personal fees and non-financial support from Bayer, Bristol Myers Squibb-Pfizer, Leo Pharma, and Johnson and Johnson; grants, personal fees and non-financial support from Merck Sharp & Dohme, outside the submitted work. ATC reports grants from Alexion Pharmaceuticals, Bayer Pharma AG, and Bristol Myers Squibb-Pfizer, consulting fees from Alexion Pharmaceuticals, Bayer Pharma AG, and Bristol Myers Squibb-Pfizer, and payments from Alexion Pharmaceuticals, Bayer Pharma AG, and Bristol Myers Squibb-Pfizer, all fees paid to his company. HR-E reports speaker's honoraria from Bayer and Daichi-Sankyo, and support for attending meetings and travel from Bayer. RPR reports consulting fees from Bristol Myers Squibb, Janssen, Inari, Penumbra, Abbott, and research grants paid to her institution from Bristol Myers Squibb and Janssen, all outside the scope of this paper. CT reports honoraria from Riche Bayer, Astra Zeneca, Actelion, and Janssen. K-LW reports honoraria from Bayer, Boehringer Ingelheim, Daiichi-Sankyo, and Pfizer for Continuing Medical Education lectures. SAB reports consulting fees from Boston Scientific, Gore, Becton Dickinson, Cook, Phillips, Vesper, Veryan, Vetex, and Medtronic; honoraria from Boston Scientific, Gore, Becton Dickinson, Cook, Philips, Vesper, Veryan, Vetex, and Medtronic; research grants from Boston Scientific and Medtronic that are paid to his institution; is on the advisory board for Philips, Medtronic, Gore, and Boston Scientific. FAK reports research grants from Bayer, Bristol-Myers Squibb, Boehringer-Ingelheim, Merck Sharp & Dohme, Leo Pharma, Daiichi-Sankyo, Actelion, The Netherlands Organisation for Health Research and Development, The Dutch Thrombosis Association, The Dutch Heart Foundation, and the Horizon Europe Program, all outside the submitted work and paid to his institution. All other authors declare no competing interests.

Acknowledgments

This project was supported from unrestricted grants from Bayer, Boston Scientific, The Dutch Thrombosis Association, Leiden University Medical Center, Leo Pharma, and King's College London. The European Society for Vascular Surgery, the North American Thrombosis Forum, the Swiss Society of Angiology, and the Italian Society of Hemostasis and Thrombosis expressed written support of the project or accepted the project as a formal society's project. JB and NS were the patient representatives of our working group.

References

1 Huisman MV, Barco S, Cannegieter SC, et al. Pulmonary embolism. *Nat Rev Dis Primers* 2018; **4:** 18028.
2 Wolberg AS, Rosendaal FR, Weitz JI, et al. Venous thrombosis. *Nat Rev Dis Primers* 2015; **1:** 15006.
3 Naess IA, Christiansen SC, Romundstad P, Cannegieter SC, Rosendaal FR, Hammerstrøm J. Incidence and mortality of venous thrombosis: a population-based study. *J Thromb Haemost* 2007; **5:** 692–99.
4 Heit JA, Spencer FA, White RH. The epidemiology of venous thromboembolism. *J Thromb Thrombolysis* 2016; **41:** 3–14.
5 Rabinovich A, Kahn SR. The postthrombotic syndrome: current evidence and future challenges. *J Thromb Haemost* 2017; **15:** 230–41.
6 Delcroix M, Torbicki A, Gopalan D, et al. ERS statement on chronic thromboembolic pulmonary hypertension. *Eur Respir J* 2021; **57:** 2002828.
7 Klok FA, van der Hulle T, den Exter PL, Lankeit M, Huisman MV, Konstantinides S. The post-PE syndrome: a new concept for chronic complications of pulmonary embolism. *Blood Rev* 2014; **28:** 221–26.
8 Kahn SR, Comerota AJ, Cushman M, et al. The postthrombotic syndrome: evidence-based prevention, diagnosis, and treatment strategies: a scientific statement from the American Heart Association. *Circulation* 2014; **130:** 1636–61.
9 Kahn SR, Ducruet T, Lamping DL, et al. Prospective evaluation of health-related quality of life in patients with deep venous thrombosis. *Arch Intern Med* 2005; **165:** 1173–78.
10 Klok FA, van Kralingen KW, van Dijk AP, et al. Quality of life in long-term survivors of acute pulmonary embolism. *Chest* 2010; **138:** 1432–40.
11 Hunter R, Noble S, Lewis S, Bennett P. Long-term psychosocial impact of venous thromboembolism: a qualitative study in the community. *BMJ Open* 2019; **9:** e024805.
12 Hunter R, Lewis S, Noble S, Rance J, Bennett PD. "Post-thrombotic panic syndrome": a thematic analysis of the experience of venous thromboembolism. *Br J Health Psychol* 2017; **22:** 8–25.
13 Tran A, Redley M, de Wit K. The psychological impact of pulmonary embolism: a mixed-methods study. *Res Pract Thromb Haemost* 2021; **5:** 301–07.
14 Jørgensen H, Horváth-Puhó E, Laugesen K, Brækkan S, Hansen JB, Sørensen HT. Risk of a permanent work-related disability pension after incident venous thromboembolism in Denmark: a population-based cohort study. *PLoS Med* 2021; **18:** e1003770.
15 Barco S, Mahmoudpour SH, Valerio L, et al. Trends in mortality related to pulmonary embolism in the European Region, 2000–15: analysis of vital registration data from the WHO Mortality Database. *Lancet Respir Med* 2020; **8:** 277–87.
16 Barco S, Valerio L, Ageno W, et al. Age-sex specific pulmonary embolism-related mortality in the USA and Canada, 2000–18: an analysis of the WHO Mortality Database and of the CDC Multiple Cause of Death database. *Lancet Respir Med* 2021; **9:** 33–42.
17 Barco S, Valerio L, Gallo A, et al. Global reporting of pulmonary embolism-related deaths in the World Health Organization mortality database: vital registration data from 123 countries. *Res Pract Thromb Haemost* 2021; **5:** e12520.
18 Wendelboe AM, Raskob GE. Global burden of thrombosis: epidemiologic aspects. *Circ Res* 2016; **118:** 1340–47.
19 Leber L, Beaudet A, Muller A. Epidemiology of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension: identification of the most accurate estimates from a systematic literature review. *Pulm Circ* 2021; **11:** 2045894020977300.
20 van der Wall SJ, Hendriks SV, Huisman MV, Klok FA. Home treatment of acute pulmonary embolism: state of the art in 2018. *Curr Opin Pulm Med* 2018; **24:** 425–31.
21 Klok FA, Huisman MV. When I treat a patient with acute pulmonary embolism at home. *Hematology Am Soc Hematol Educ Program* 2020; **2020:** 190–94.
22 Stowell C, Ackerman C. Better value in health care requires focusing on outcomes. 2015. https://hbr.org/2015/09/better-value-in-health-care-requires-focusing-on-outcomes (accessed 9 May, 2022).
23 Porter ME. What is value in health care? *N Engl J Med* 2010; **363:** 2477–81.

24 Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021; **372:** n71.

25 Fitch K. The RAND/UCLA appropriateness method user's manual. Santa Monica, CA: RAND, 2001.

26 Ong WL, Schouwenburg MG, van Bommel ACM, et al. A standard set of value-based patient-centered outcomes for breast cancer: the International Consortium for Health Outcomes Measurement (ICHOM) initiative. *JAMA Oncol* 2017; **3:** 677–85.

27 Nijagal MA, Wissig S, Stowell C, et al. Standardized outcome measures for pregnancy and childbirth, an ICHOM proposal. *BMC Health Serv Res* 2018; **18:** 953.

28 Hays RD, Bjorner JB, Revicki DA, Spritzer KL, Cella D. Development of physical and mental health summary scores from the patient-reported outcomes measurement information system (PROMIS) global items. *Qual Life Res* 2009; **18:** 873–80.

29 Klok FA, Cohn DM, Middeldorp S, et al. Quality of life after pulmonary embolism: validation of the PEmb-QoL Questionnaire. *J Thromb Haemost* 2010; **8:** 523–32.

30 Boon G, Barco S, Bertoletti L, et al. Measuring functional limitations after venous thromboembolism: optimization of the Post-venous thromboembolism Functional Status (PVFS) Scale. *Thromb Res* 2020; **190:** 45–51.

31 Cella D, Choi SW, Condon DM, et al. PROMIS adult health profiles: efficient short-form measures of seven health domains. *Value Health* 2019; **22:** 537–44.

32 Choi SW, Victorson DE, Yount S, Anton S, Cella D. Development of a conceptual framework and calibrated item banks to measure patient-reported dyspnea severity and related functional limitations. *Value Health* 2011; **14:** 291–306.

33 Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001; **16:** 606–13.

34 Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006; **166:** 1092–97.

35 Cano SJ, Lamping DL, Bamber L, Smith S. The Anti-Clot Treatment Scale (ACTS) in clinical trials: cross-cultural validation in venous thromboembolism patients. *Health Qual Life Outcomes* 2012; **10:** 120.

36 Le Gal G, Carrier M, Castellucci LA, et al. Development and implementation of common data elements for venous thromboembolism research: on behalf of SSC Subcommittee on official communication from the SSC of the ISTH. *J Thromb Haemost* 2021; **19:** 297–303.

37 Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Rheum* 2003; **49:** 156–63.

38 Ackerman IN, Cavka B, Lippa J, Bucknill A. The feasibility of implementing the ICHOM Standard Set for Hip and Knee Osteoarthritis: a mixed-methods evaluation in public and private hospital settings. *J Patient Rep Outcomes* 2018; **2:** 32.

39 Niazi SK, Spaulding A, Vargas E, et al. Feasibility Study of three-phase implementation of international consortium for health outcomes measurement depression and anxiety standard set in an outpatient consultation-liaison psychiatry practice. *Psychosomatics* 2020; **61:** 8–18.

40 Laureij LT, Been JV, Lugtenberg M, et al. Exploring the applicability of the pregnancy and childbirth outcome set: a mixed methods study. *Patient Educ Couns* 2020; **103:** 642–51.

41 Depla AL, Ernst-Smelt HE, Poels M, Crombag NM, Franx A, Bekker MN. A feasibility study of implementing a patient-centered outcome set for pregnancy and childbirth. *Health Sci Rep* 2020; **3:** e168.

42 Queirós L, Redondo P, França M, et al. Implementing ICHOM standard set for cataract surgery at IPO-Porto (Portugal): clinical outcomes, quality of life and costs. *BMC Ophthalmol* 2021; **21:** 119.

43 Moore L, Britten N, Lydahl D, Naldemirci Ö, Elam M, Wolf A. Barriers and facilitators to the implementation of person-centred care in different healthcare contexts. *Scand J Caring Sci* 2017; **31:** 662–73.

44 Wild D, Grove A, Martin M, et al. Principles of good practice for the translation and cultural adaptation process for Patient-Reported Outcomes (PRO) Measures: report of the ISPOR Task Force for Translation and Cultural Adaptation. *Value Health* 2005; **8:** 94–104.