CURRENT STATE OF THE ART REGARDING PATIENT EXPERIENCE DATA (PED) / PATIENT REPORTED OUTCOMES (PROs) IN THE CARDIOVASCULAR FIELD

Definition of PED/PROs and what are the advantages?

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February 19th, 2024

ESC
European Society of Cardiology

Disclosures

- Consulting/speaker fees for Medtronic, Boston Scientific, Bristol-Myers-Squibb


Outcomes
Patient
PROMs
PREMs
Data
Reported
Experience
Care
Health
Quality
Access
Instruments
Treatment
Satisfaction
PROs
Well
Life
Survey
Delivery
Healthcare
Impact
Communication
Symptom
Pain
Functional
Status
Functioning
Centered
Coordination
Validated
Interactions
Effectiveness
CAHPS
HRQoL
Burden
Timeliness
Picker
Interviews
Questionnaire
Fatigue
Provider
Personal
Severity
Self
Emotional
Perspectives
Related
Qualitative
PROMIS
Physical
Disease
sF
EQ
5D

Patient experience data in EU medicines development and regulatory decision-making

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Outcome of the workshop on 21st September 2022

- **Patient Experience Data (PED)** are data collected via a variety of patient engagement activities and methodologies to collect patients' experience of their health status, symptoms, disease course, treatment preferences, quality of life and impact of health care. For EU regulators, PED does not only involve quantitative sources of evidence (e.g., patient reported outcomes or patient reported experience measures) but also qualitative sources (i.e., any information obtained as part of patient engagement activities that reflect the wider perspective of patients' experience, for example, the outcome of focus groups, surveys or interviews).

  PED ensures that medicines development and approval has taken account of patients' perspectives and experience in living with a particular condition, and ultimately leads to more patient-relevant decisions.

https://www.ema.europa.eu/en/documents/other/executive-summary-patient-experience-data-eu-medicines-development-and-regulatory-decision-making-workshop_en.pdf

- **Patient Experience Evidence (PEE)** is patient experience data qualified as valid scientific evidence following a scientific assessment. Both PED and PEE are relevant and can complement each other for regulatory purposes; patient data is needed to generate evidence of meaningful outcomes for patients.
- **Patient Engagement[4] (PE)** refers to all activities involving interaction with patients to gather their experience on disease, preferences, outcomes and treatments.
- **Patient Preferences (PPs)** refer to how desirable or acceptable is to patients a given alternative or choice among all the outcomes of a given medicine.
- **Patient Reported Outcomes (PROs)** refer to a health/treatment outcome reported directly by the patient without the interpretation of a clinician or another person.

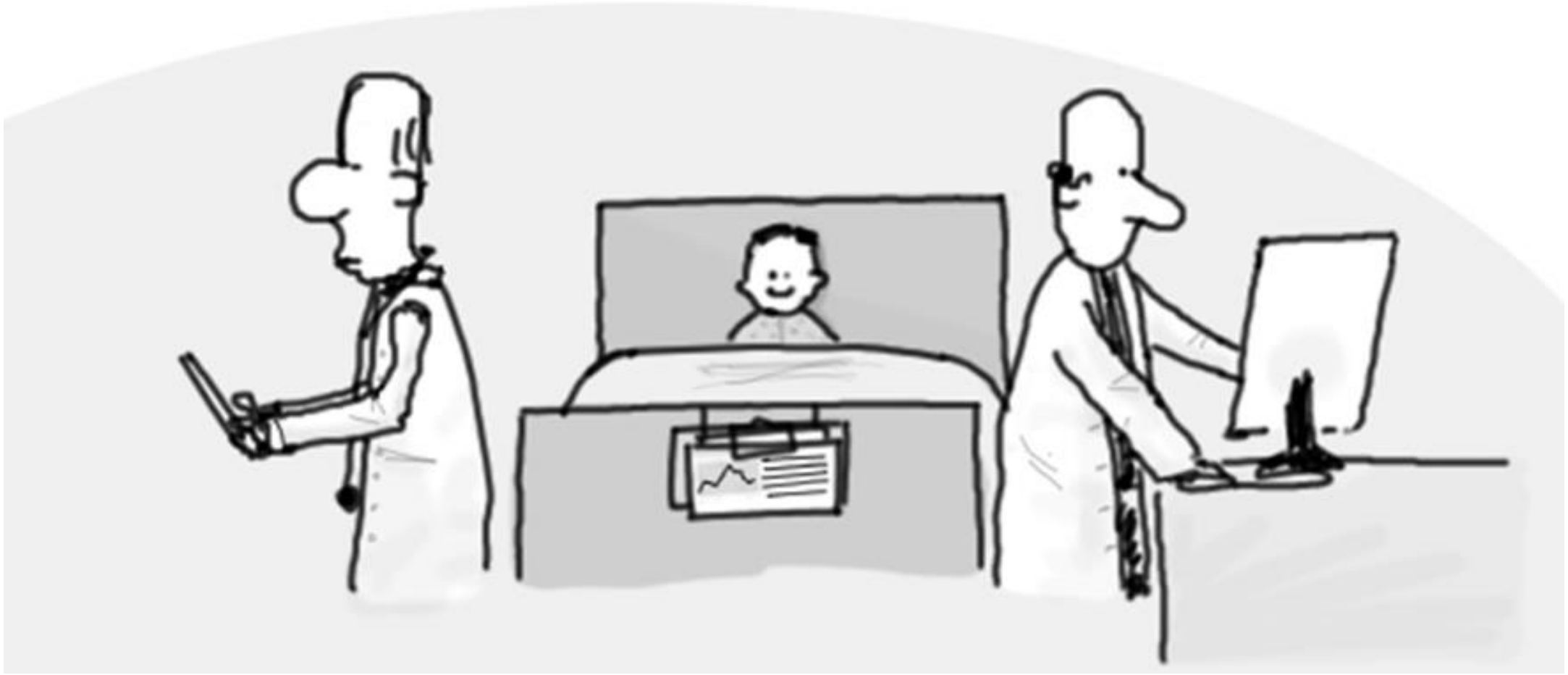
https://www.ema.europa.eu/en/documents/other/executive-summary-patient-experience-data-eu-medicines-development-and-regulatory-decision-making-workshop_en.pdf

U.S. FOOD & DRUG ADMINISTRATION

Patient experience data includes data that provide information about patients' experiences with a disease or condition. Patient experience data can be interpreted as information that captures patients' experiences, perspectives, needs, and priorities related to (but not limited to):

1. the symptoms of their condition and its natural history;
2. the impact of the conditions on their functioning and quality of life;
3. their experience with treatments;
4. input on which outcomes are important to them;
5. patient preferences for outcomes and treatments; and
6. the relative importance of any issue as defined by patients.

Patient experience data is defined in Title III, section 3001 of the 21st Century Cures Act, as amended by section 605 of the FDA Reauthorization Act of 2017 (FDARA)



Patient Experience Data = **Patient centred outcomes**

Patients' perspectives on benefits and risks

- **Clinical benefit**: A ***positive clinically meaningful effect*** of an intervention, i.e., a positive effect on how an individual feels, functions, or survives

  How long a patient lives
  How a patient feels or functions in daily life (includes both improvement as well as prevention/slowing decline)

- **Clinical outcome**: An outcome that describes or reflects how an individual feels, functions or survives

  Assessed using clinical outcome assessments (COAs)

- Careful assessment of patients' views on benefits and risks are an important part of regulatory decision-making

https://www.fda.gov/media/112163/download

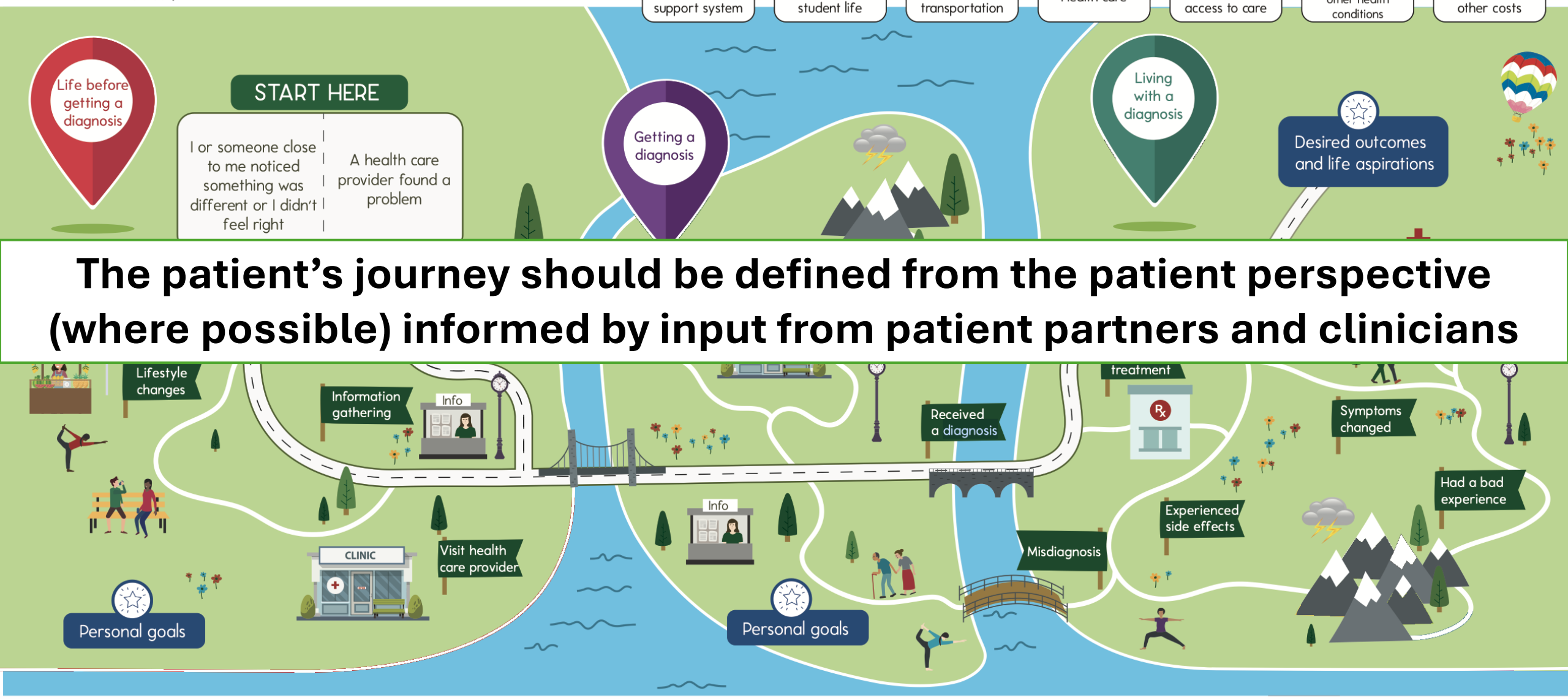
Map My Experience

Every patient has different experiences with their health. This map can be used as a guide to think about your own patient experience from your "starting point," through your diagnosis, to where you are now, and everywhere in between.

Life Factors

As you go along, think about how other "life factors" have played a role in your patient experience, such as:

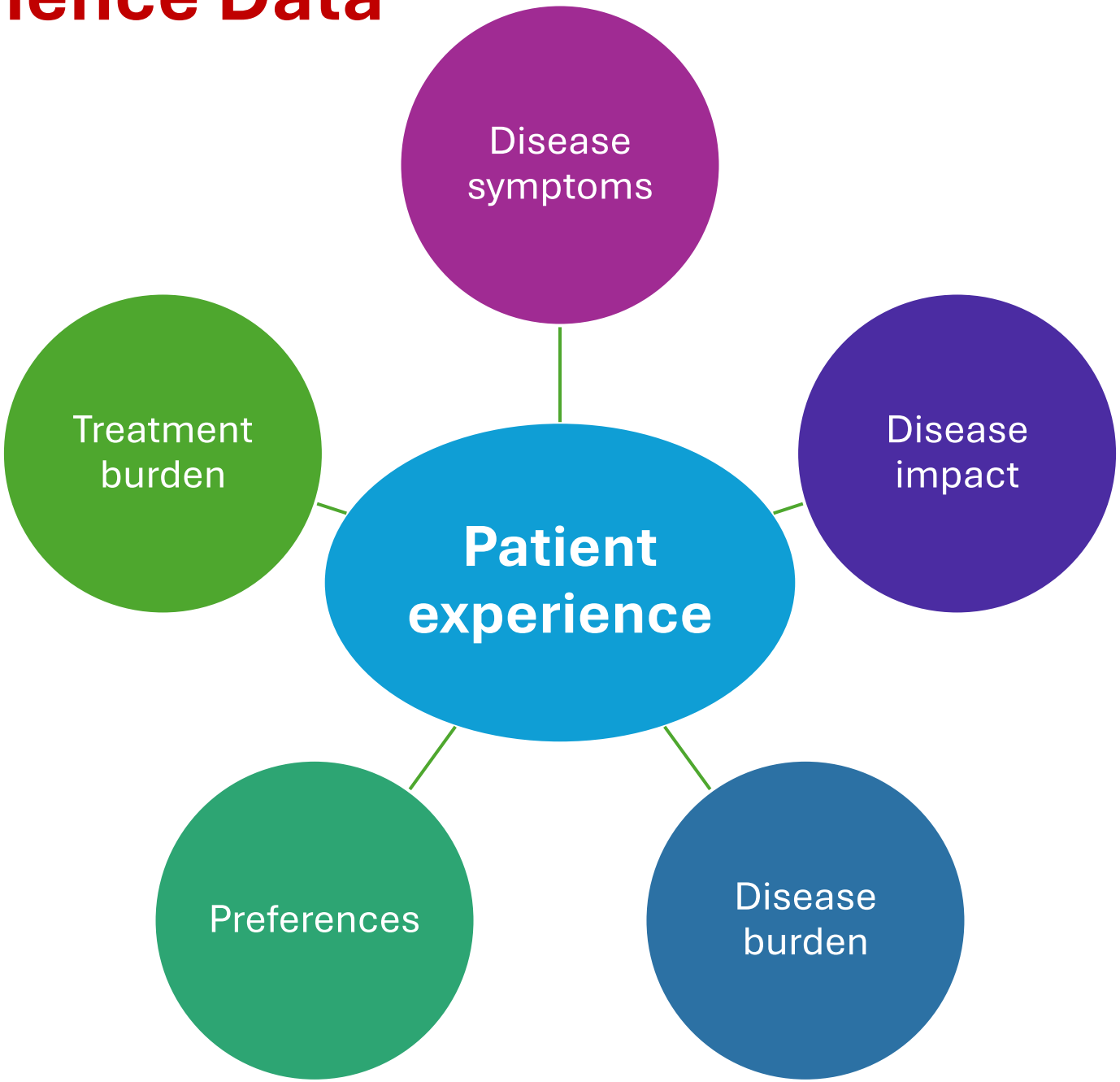
- Family and support system
- Work or student life
- Housing and transportation
- Health care
- Insurance and access to care
- Mental health & other health conditions
- Finances and other costs



The patient's journey should be defined from the patient perspective (where possible) informed by input from patient partners and clinicians

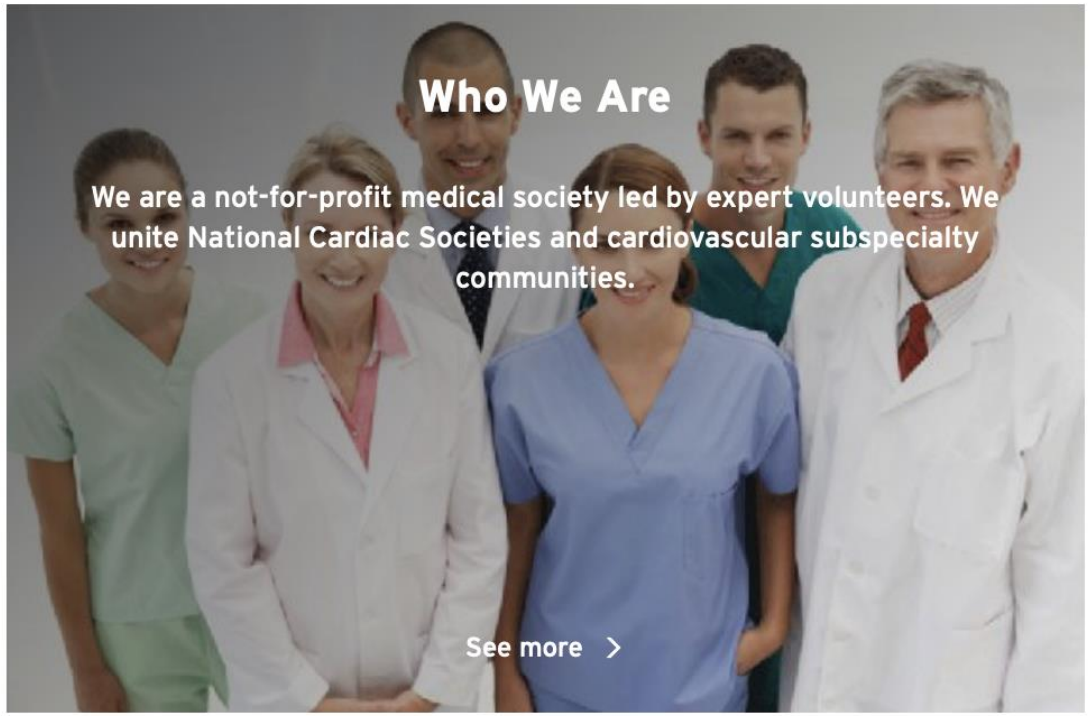
https://nationalhealthcouncil.org/wp-content/uploads/2022/10/PEMT-Map-My-Experience-visual-1_.pdf

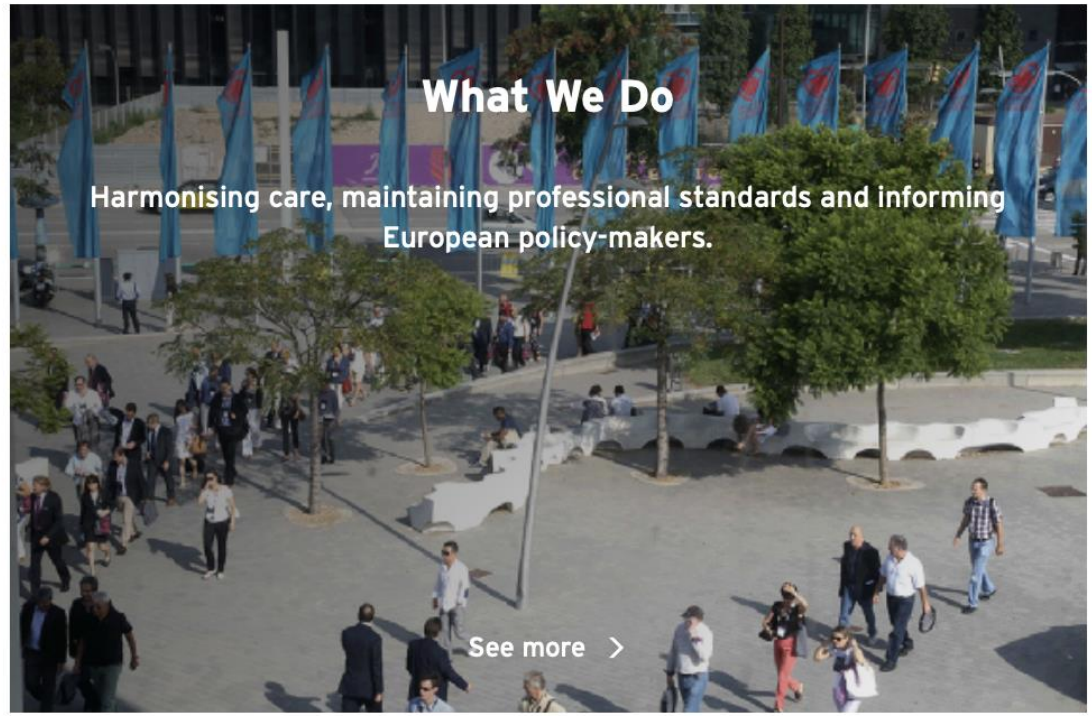
Patient Experience Data



About the European Society of Cardiology

Our mission: To reduce the burden of cardiovascular disease.





The ESC comprises 28 cardiovascular subspecialty communities covering the full spectrum of cardiology.
They include our associations, working groups and councils, enabling us to provide in-depth, expert knowledge to all cardiovascular clinicians and researchers.

ESC
European Society of Cardiology

The ESC Strategic Plan 2023 - 2028

Our Strategic Aims

A Welcoming Society with Fair and Transparent Governance
Nurture inclusivity, diversity and clear structures for collective decision-making

Trusted Knowledge Effectively Delivered
Provision of robust and unbiased, validated information in creative formats via communication channels adapted to the needs and preferences of a global audience

A Membership Experience Rich in Rewards and Benefits
Continue to build a strong community with valued year-round membership benefits for cardiovascular healthcare professionals in ESC National Cardiac Societies and across the world

A Focus on Person-Centred Healthcare
Emphasise the patient perspective in research, training and education, as well as guidelines and scientific documents

High Quality Data and Research
Support of collaborative research and active contributions to high quality data collection

Environmental Sustainability
Mindfulness of the environmental footprint and active pursuit of environmental sustainability across all ESC activities

Future Scenarios

Emphasis on the Patient Perspective
The patient at the heart of all that we do

https://www.escardio.org/The-ESC/What-we-do/strategic-plan

EPF European Patients Forum

Supporting patient-centred innovation: the value of patient experience data

February 2024

The inclusion of patient experience data (PED) at all stages of medicine development and regulatory decision-making ensures that new medicines address the outcomes and preferences that matter to patients. These data are collected to describe patients' experience of their health status, symptoms, disease course, treatment preferences, quality of life and impact of health care[1]. Examples of such data include patient preference studies, large patient surveys, or impacts captured in registries. They ensure that the views and experiences of patients living with a particular condition are taken into account in the development and approval of medicines, ultimately leading to more relevant decisions for patients. The EMA's ongoing work on the generation, collection and use of patient experience data for regulatory purposes, together with the support of the European Medicines Regulatory Network[2], is a crucial step forward. These advancements need to be reflected in the revision of EU pharmaceutical legislation to encourage patient-centred and needs-driven healthcare innovation.

- **Patient experience data are crucial to obtain a full picture of the impacts of a disease on patients and define unmet medical needs.**

The concept of unmet medical need should aim to distinguish innovative medicines that provide tangible and significant added therapeutic value to patients from other new medicines. From the patient's perspective, a medicine that addresses an unmet medical need goes beyond mortality or morbidity considerations. It encompasses the broader impact of the disease, treatment or therapy on the patient's life, and addresses key questions, for example: will this medicine significantly enhance quality of life through e.g. less time spent at the hospital, decreased side effects, reduced symptoms, increased productivity? Will it significantly slow down the progression of a disease? Will it provide a cheaper

https://www.eu-patient.eu/globalassets/20240223-epf-op-ed-on-ped2.pdf

EMA Regulatory Science to 2025

Strategic reflection

https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection_en.pdf

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

3. Human medicines — five strategic goals for regulatory science

3.1 Goal 1: Catalysing the integration of science and technology in medicines development

3.2 Goal 2: Driving collaborative evidence generation improving the scientific quality of evaluations

3.3 Goal 3: Advancing patient-centred access to medicines in partnership with healthcare systems

3.4 Goal 4: Addressing emerging health threats and availability/therapeutic challenges

3.5 Goal 5: Enabling and leveraging research and innovation in regulatory science

https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection_en.pdf

Collecting Patient Experience Data

Anyone can collect patient experience data:

- Patients
- Family members and caregivers – Patient advocacy organizations
- Disease research foundations
- Clinicians
- Researchers
- Medicinal product manufacturers
- etc.

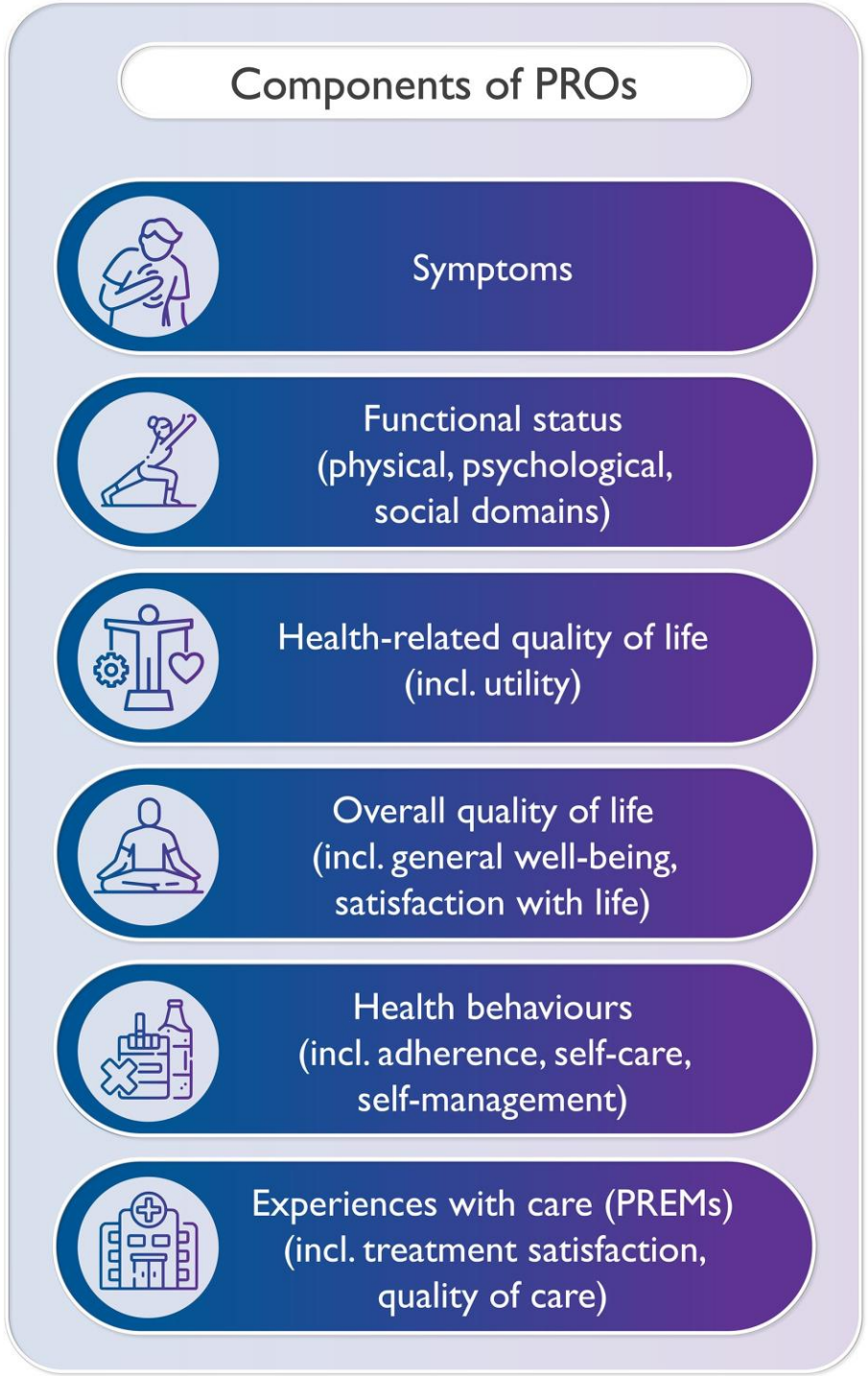
https://www.fda.gov/media/112163/download

Placing patient-reported outcomes at the centre of cardiovascular clinical practice: implications for quality of care and management

A statement of the ESC Association of Cardiovascular Nursing and Allied Professions (ACNAP), the Association for Acute CardioVascular Care (ACVC), European Association of Percutaneous Cardiovascular Interventions (EAPCI), European Association of Preventive Cardiology (EAPC), Heart Failure Association (HFA), European Heart Rhythm Association (EHRA), European Association of Cardiovascular Imaging (EACVI), ESC Regulatory Affairs Committee, ESC Advocacy Committee, ESC Digital Health Committee, ESC Education Committee, and the ESC Patient Forum

SCAN ME

Patient-reported outcomes (PROs) are typically defined as 'any report of the status of a **patient's health condition that comes directly from the patient**, without interpretation of the patient's response by a clinician or anyone else'



Moons P, et al. Eur Heart J 2023 Sep 21;44(36):3405-3422.

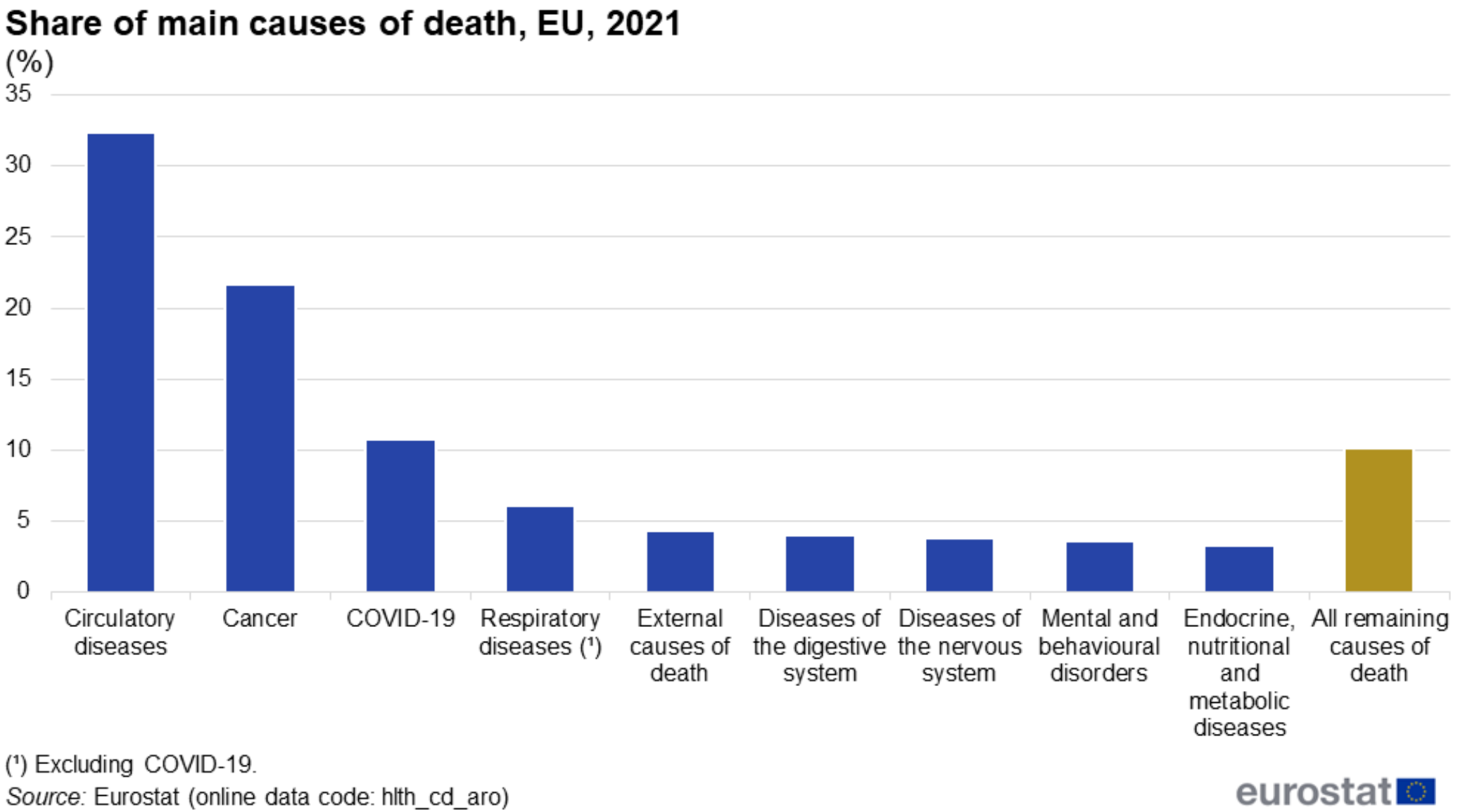
Collecting Patient Experience Data

Qualitative methods

Direct communication to get the patient's perspective (interviews)

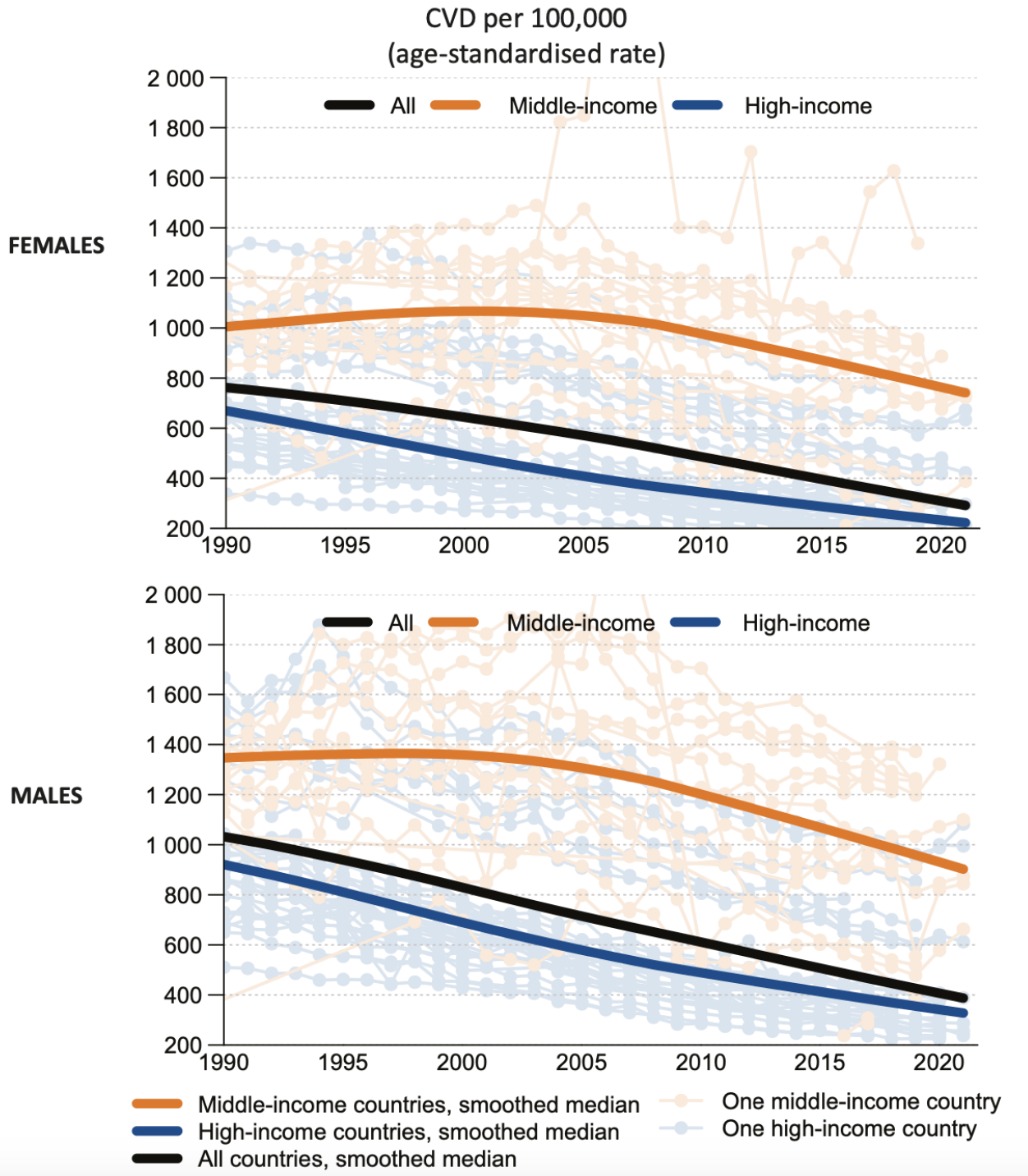
Quantitative methods

Survey/questionnaire to provide numerical result on the patient's perspective (PROMs/PREMs)



https://ec.europa.eu/eurostat/statistics-explained/index.php?title=File:Share_of_main_causes_of_death,_EU,_2021_(%25)_Health2024.png

Age-standardized mortality rate from cardiovascular disease per 100.000 people in females and males in ESC member countries (1990–2021)



Timmis A, et al. Eur Heart J 2024 Oct 7;45(38):4019-4062

Burden of Cardiovascular Disease

A record of the death and loss of health due to CV diseases

EPIDEMIOLOGICAL/PUBLIC HEALTH

Morbidity

The number of people in a population who are unwell or disabled, and the severity of their illness or disability

This measures for
Healthy Adjusted Life Years
DALYs – Disability Adjusted Life Years

Mortality

The number of people in a population who die as a result of a specific disease or disability

€ ECONOMIC PERSPECTIVE

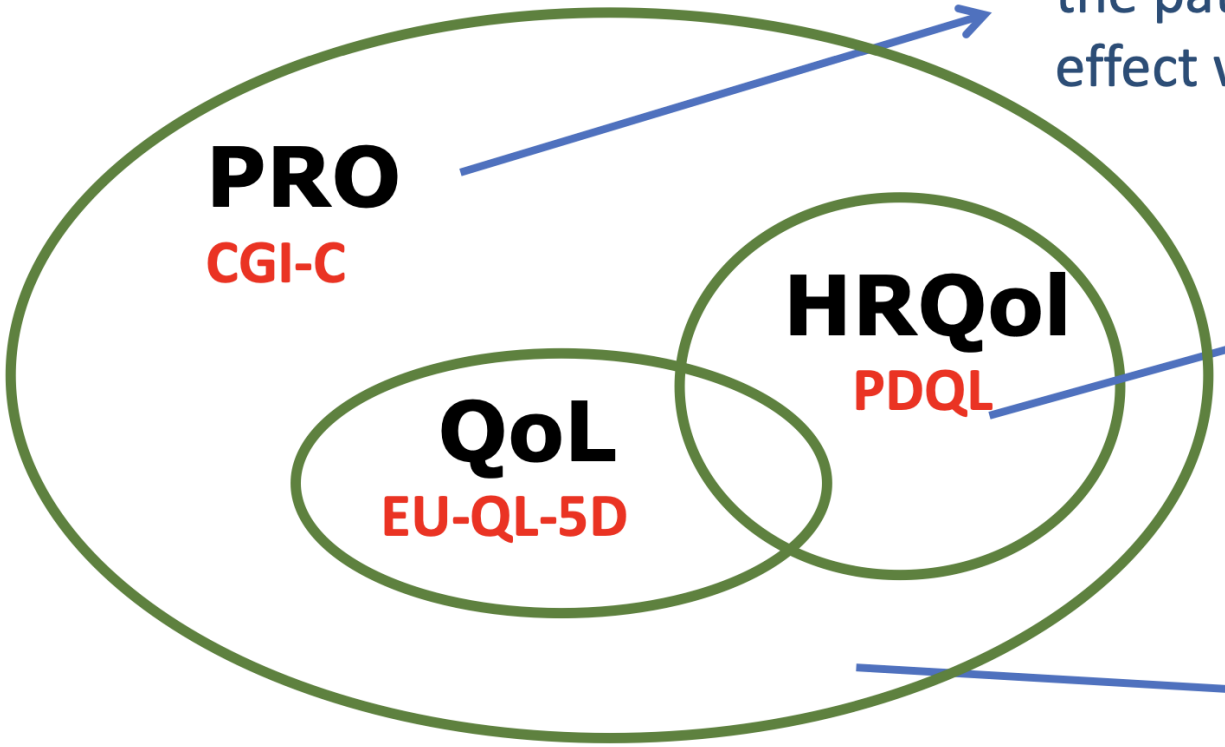
It estimates the economic burden of a specific disease from the societal perspective.

- Identifying the **various cost components** and who bears them
- Measuring the **incidence of different cost components** over the total burden *(healthcare costs, non healthcare costs, productivity losses)*
- Explaining the **costs variability across patients**

The results can effectively help industry, policy-makers, healthcare managers, clinicians and patients to address:

- **Clinical management of the disease**
- **Cost containment measures**
- **Programming healthcare services across centres/regions**
- **Developing new interventions to reduce disease**

Types of quantitative PROs



Any outcome evaluated directly by patient reflecting the patient's perception of a disease and treatment effect without interpretation of physician

HRQoL – Disease specific
Signs and symptoms and their impact on ADL , functioning , well-being

General health status / well-being
e.g., EU-QL-5D: mobility, self-care, usual activities, pain/discomfort and anxiety/depression.

Patient-reported outcomes

Pros

- Independent from physician
- Patient-centred
- Perceived benefit
- What matters
- Open-label they contribute to patient-care decision-making

Cons

- Subjective (ranzomized double-blind studies)
- Can be driven by one sign/symptom
- Not very sensitive to change
- Not always disease specific
- QoL not interchangeable
- High variability

Desirable measurement properties for PROMs

PRO measurements need to be validated:

- Face validity
- Reliability (is the scale reliable ?)
- Content Validity
- Sensitive to change
- Can we determine which xx points change would be of clinical relevance
- Sensitive to detect a treatment effect

https://www.cosmin.nl/tools/guideline-conducting-systematic-review-outcome-measures/?portfolioCats=19

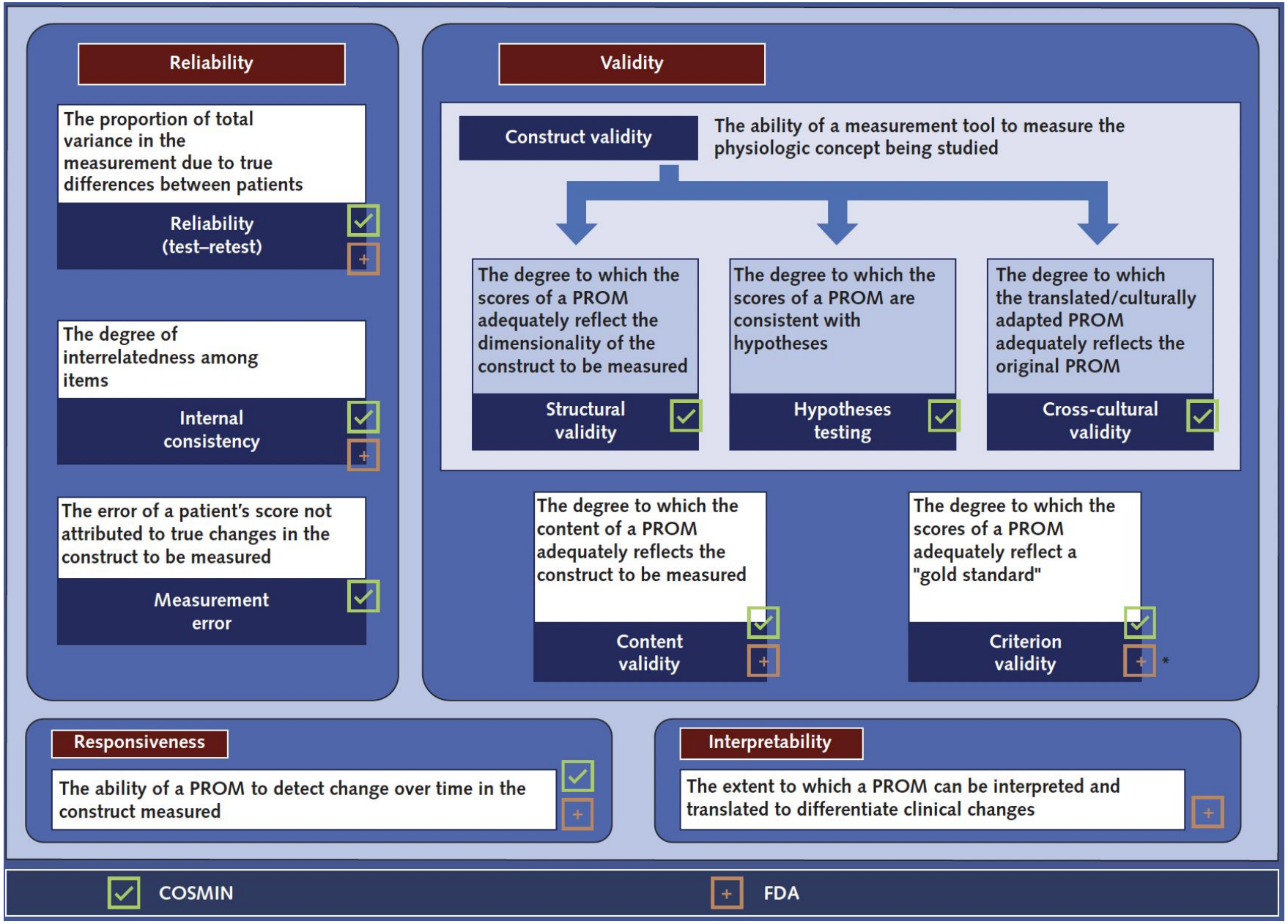
FDA
Medical Device Development Tools (MDDT)

The MDDT program is intended to *facilitate device development by providing an efficient means for collecting the information to support regulatory submissions.*

\# patient-reported outcome measures (PROMs)

- Qualified PROMs can be used across multiple medical device submissions and manufacturers.
- Medical device sponsors can be sure that evidence provided will be accepted without the need to reconfirm the suitability and utility of the tool within the same context of use.

Desirable measurement properties for PROMs

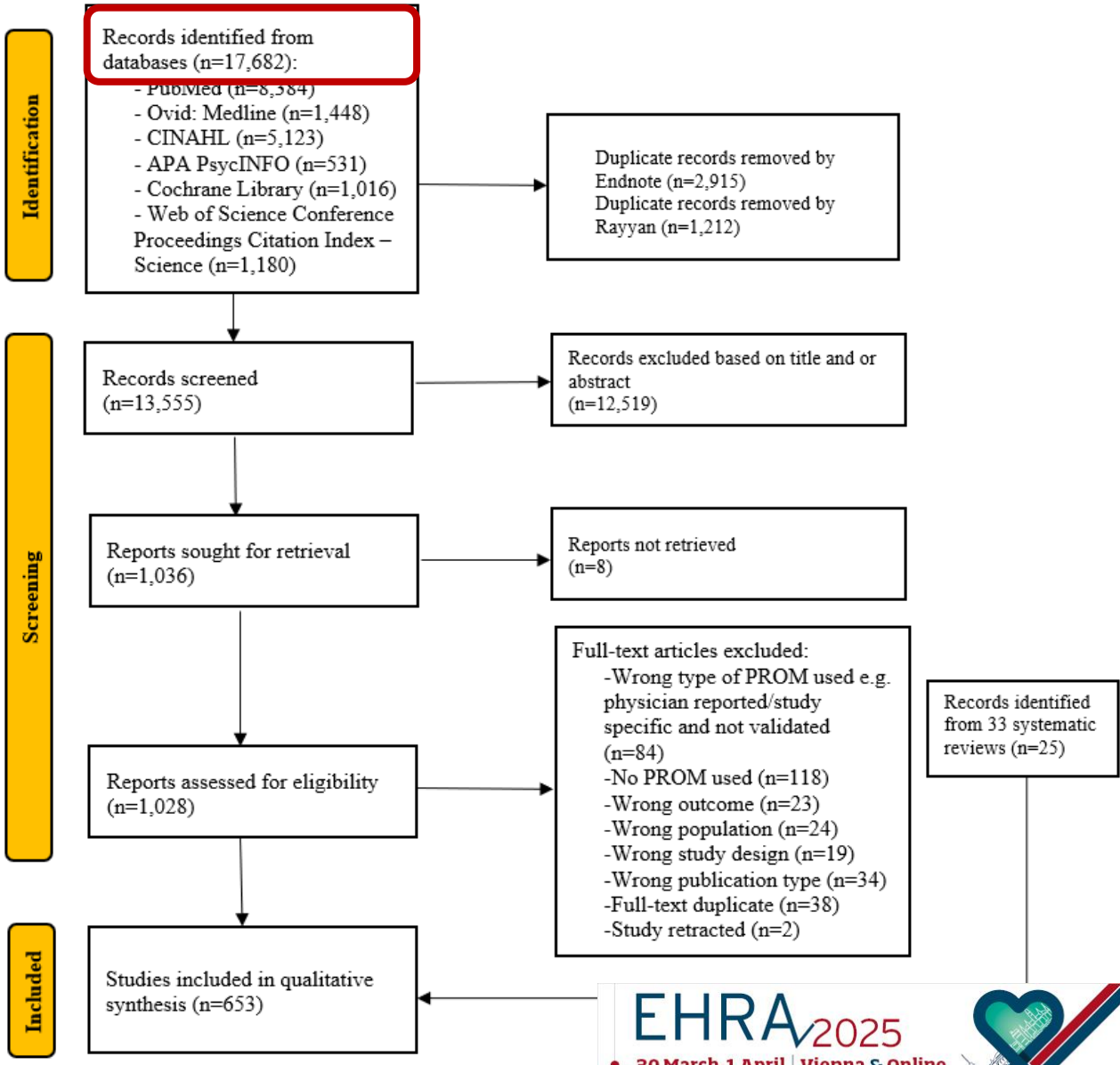


Chew DS, et al. Ann Intern Med. 2022;175:1431-1439.

Patient-reported outcome measures for atrial fibrillation: systematic review and evaluation of psychometric properties of symptom severity measures

Ogendo JJ, Darma A, Mihajlovic M, Arbelo E, Lane DA.

- Six bibliographic databases searched from inception until 2 February 2024
- Full-text publications in all languages
- ≥1 measurement property of PROMs in AF patients
- Aged ≥18 years
- PROSPERO ID: CRD42024523340
- Measurement properties appraised using Consensus based Standards for the selection of health Measurement Instruments (COSMIN) recommendations



PROMs identified

HRQoL

AFEQT*
AFImpact*
AFQLQ*
AF-QoL*
ASTA**
AQoL♦
Dartmouth COOP chart♦
CAST-QoL**
C-CAP**
DUKE♦
EQ-5D♦
EQ-5D-3L♦
EQ-5D-5L♦
HSQ♦
IIRS♦
MHIQ♦
NHP♦
PPAQ^
PROMIS global health♦
PROMIS-29♦
QLAF*
QLAFv2*
QDIS-MCC¤
Q-LES-Q♦
QLI♦
QLI-CV#
SF-12♦
SF-12v2♦
SF-36♦
SF-36v2♦
SF-6♦
SF-8♦
SIP♦
SRH♦
VR-36♦
WHO-5♦
WHOQoL-BREF♦

Physical function

ADL♦
BADL♦
DASI♦
IADL♦
KPS♦
OARS♦
PROMIS-Bank Physical Function♦
Rosow-Breslau Functional Health Scale♦
WHODAS 2.0♦

Emotional function

ASI♦
BDI♦
BDI-II♦
BDI-SF♦
CES-D♦
CAQ#
GAD-7♦
GDS♦
HADS♦
HAM-A♦
HAM-D♦
MDI♦
MOCS-A♦
PGWB♦
PHQ-8♦
PHQ-9♦
POMS♦
PSS-10♦
SAS♦
SCL-90♦
SCL-92♦
SDS♦
STAI♦
WI♦
Whooley depression screener♦

Cognitive function

MMSE♦
MoCA♦
PROMIS cognitive function♦
SPMSQ♦
T-MoCA♦
TICS-m♦

Symptom severity

AF6*
AFS/B*
AFSS*
AFSymp*
LARQ*
MAFSI*
SCL**

Exercise tolerance

GPAQ♦
Specific activity scale♦
IPAQ♦
IPAQ-SF♦
LTPA♦
Phone-FITT♦
SGPALS♦
YPAS♦

Ability to work

SPS♦
WPAI♦

Languages identified: Argentinian Spanish, Brazilian Portuguese, Chinese, Cantonese, Danish, Dutch, English, French, German, Greek, Indonesian, Japanese, Italian, Korean, Mandarin, Malay, Norwegian, Persian, Polish, Portuguese, Spanish, Swedish and Turkish

PROM	PROM development	Content validity	Structural validity	Internal consistency	Reliability	Cross-cultural validity	Criterion validity	Construct validity	Responsiveness
AFSymp[41]			?	+	+			+	
AFS/B[42]			?	?	?			?	
AFSS[43-45]				-	?			-	
ASTA[53-58]			?	+	+			+	
AF6[46,47]			+	+	+		?	?	?
SCL[48-50]			?	+			?	-	

Certainty in quality of evidence	
High	
Moderate	
Low	
Very low	
Not assessed	

Measurement property	
Sufficient	+
Indeterminate	?
Insufficient	-

Modified grading of recommendations, assessment development and evaluation (GRADE) ratings

Patient-Reported Outcome Measures in Cardiovascular Disease: An Evidence Map of the Psychometric Properties of Health Status Instruments

Table 1. Adherence of PROM Validation Process to FDA Recommendations*

Instrument	Content Validity	Test-Retest Reliability	Internal Consistency	Construct Validity	Responsiveness	Interpretability	Fulfilled All FDA Recommendations
Arrhythmia							
AF-6	X	X	X	X	X	X	X
AFEQT	X	X	X	X	X	X	X
AFQLQ	X	X	X	X	X		
AF-QoL	X	X	X	X	X	X	X
AFImpact	X	X	X	X	X		
ASTA HRQoL	X		X	X			
ISQL		X	X	X			
OHQ	X	X	X	X	X	X	X
PPAQ	X		X				
QLAF		X	X	X	X		
Coronary artery disease							
APQLQ			X	X	X		
CLASP		X	X	X	X		
CROQ	X	X	X	X	X		
HCS			X	X			
MacNew	X	X	X	X	X	X	X
MIDAS	X		X	X			
QLICD-CHD	X	X	X	X	X		
SAQ		X	X	X	X	X	

Chew DS, et al. Ann Intern Med. 2022;175:1431-1439.

Table 1. Adherence of PROM Validation Process to FDA Recommendations*

Instrument	Content Validity	Test–Retest Reliability	Internal Consistency	Construct Validity	Responsiveness	Interpretability	Fulfilled All FDA Recommendations
Heart failure							
CaReQoL CHF	X	X	X	X			
CHAT	X		X	X			
CHF-PROM	X		X	X		X	
CHFQ	X	X	X	X	X	X	X
HF-FSA	X						
HFSPS	X		X	X	X		
HFFSI	X		X	X			
KAPQ-HF	X	X	X	X			
KCCQ	X	X	X	X	X	X	X
LVD-36	X	X	X	X	X		
MDASI-HF	X		X	X			
MSAS-HF	X	X	X	X	X		
MLHFQ	X	X	X	X	X	X	X
PROMIS-Plus-HF	X	X	X	X	X		
QLQ-SHF	X	X	X	X	X		
SDHFQ				X	X		
General cardiovascular populations							
CD-QOL	X		X	X			
CHP	X	X	X	X			
HeartQoL	X	X	X	X	X		
LIFEWARE CAI				X			
MILQ	X	X	X	X			
QLI-C	X		X		X		
Other cardiac populations							
ACHD PRO	X	X	X	X			
CHD-TAAQOL	X		X	X	X		
IDCV	X		X	X			
QOLVAD	X	X	X	X	X		
TASQ	X		X	X	X		

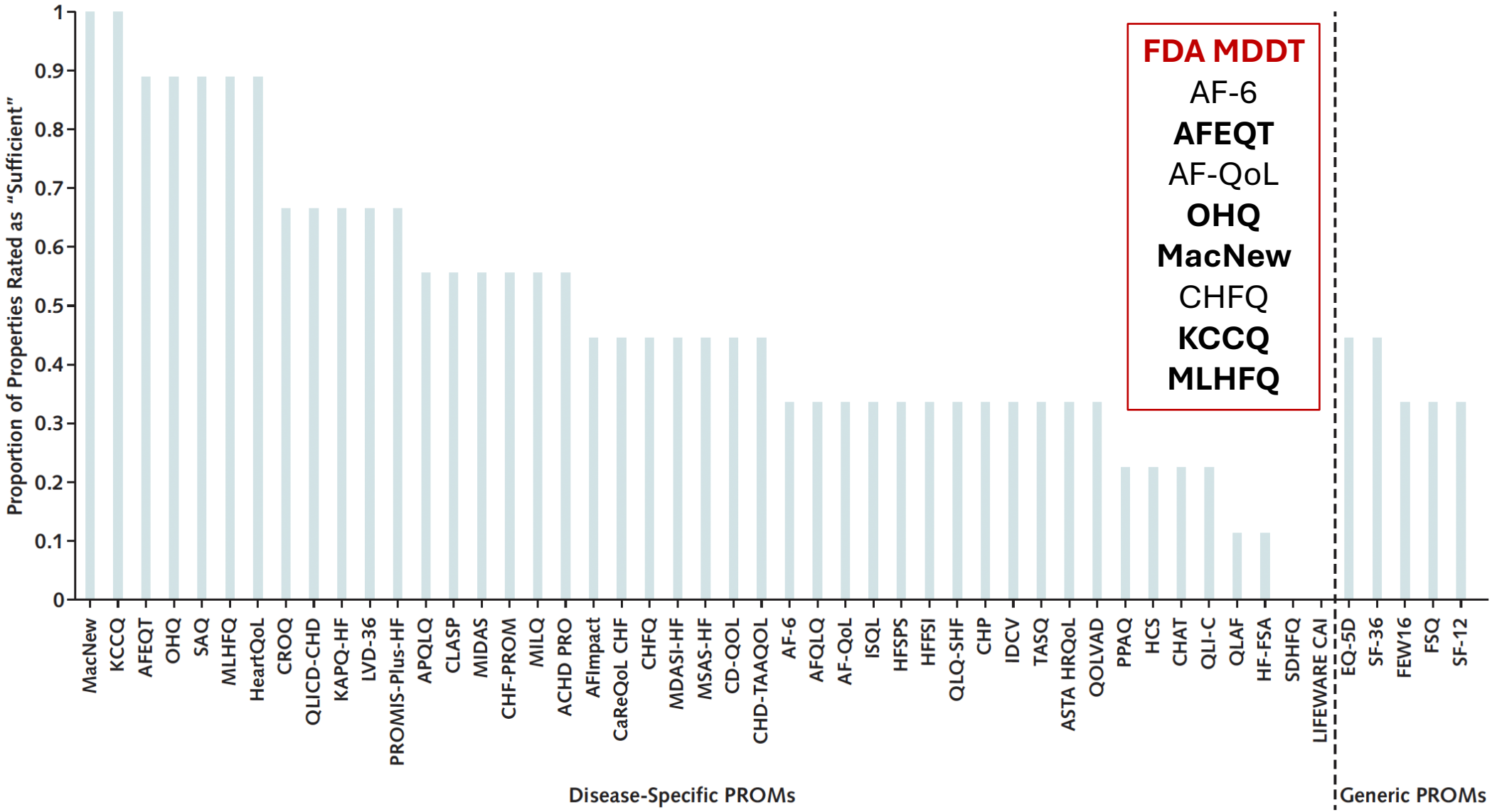
Chew DS, et al. Ann Intern Med. 2022;175:1431-1439.

Table 1. Adherence of PROM Validation Process to FDA Recommendations*

Instrument	Content Validity	Test-Retest Reliability	Internal Consistency	Construct Validity	Responsiveness	Interpretability	Fulfilled All FDA Recommendations
Generic PROMs validated in cardiovascular disease populations							
EQ-5D			X	X	X		
FEW16			X	X	X		
FSQ		X	X	X			
SF-12		X	X	X	X		
SF-36			X	X		X	

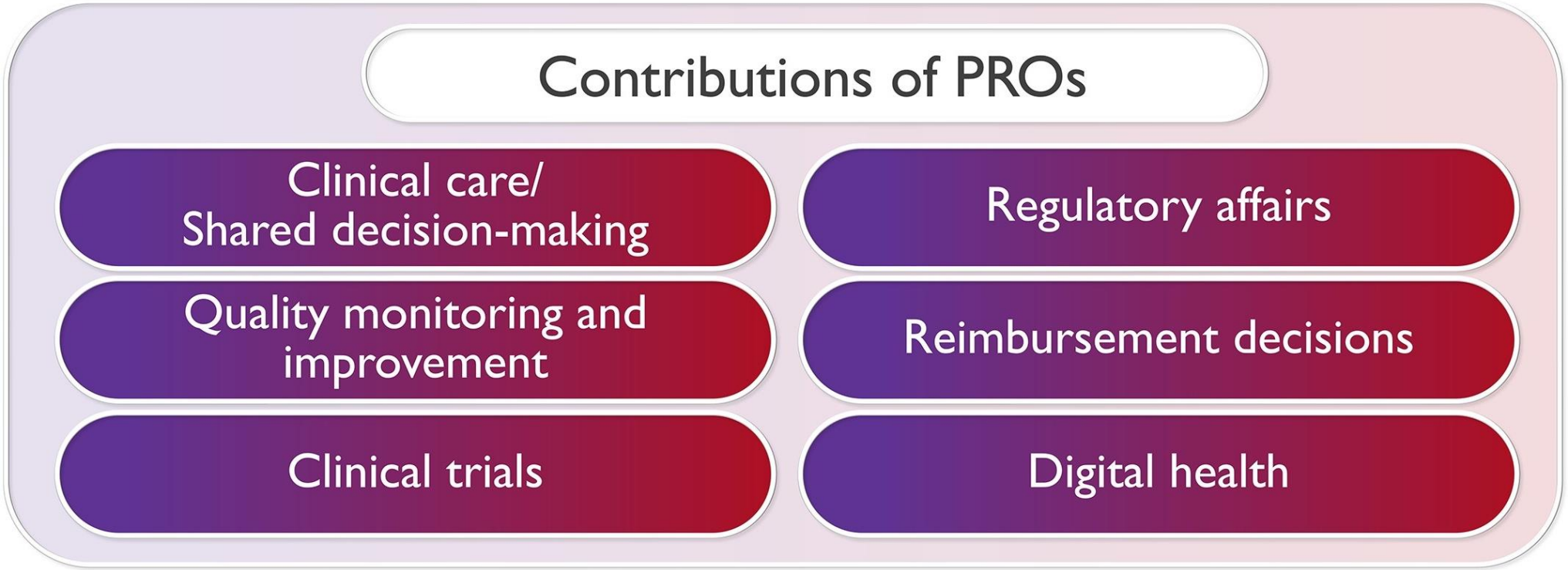
Chew DS, et al. Ann Intern Med. 2022;175:1431-1439.

Appendix Figure 3. Proportion of psychometric properties ranked as "sufficient" as per COSMIN criteria for optimal measurement properties.



Chew DS, et al. Ann Intern Med. 2022;175:1431-1439.

Uses of patient experience data



Moons P, et al. Eur Heart J 2023 Sep 21;44(36):3405-3422.

Recommendations on PROMs for conformity assessment and post-market surveillance

CORE-MD

Coordinating Research and Evidence for Medical Devices

Table 1. Relation between stakeholders and uses of PROMs

Stakeholder	Uses of PROMs
Health system policymakers / system managers	• Compare outcomes at a local regional, provincial and international level as well as over time. • Compare different models of care and clinical pathways (e.g. referral patterns). • Support health service allocation decisions ('value-based' care). • Inform quality improvement initiatives.
Healthcare organizations	• Monitor organization and provider performance. • Conduct comparisons with peer organizations. • Inform quality improvement initiatives.
Healthcare providers	• Provide feedback to inform care plan. • Provide evidence on improved or maintained health of patients. • Improve clinician-patient communication. • Facilitate performance comparisons with expected standards. • Facilitate comparative effectiveness research.
Patients	• Provide opportunity to give feedback regarding treatment, care processes and preferences. • Increase awareness of expected outcomes of care. • Enhance communication with providers. • Increase involvement in care planning and decision-making.

What is the regulatory utility of patient-reported outcomes?

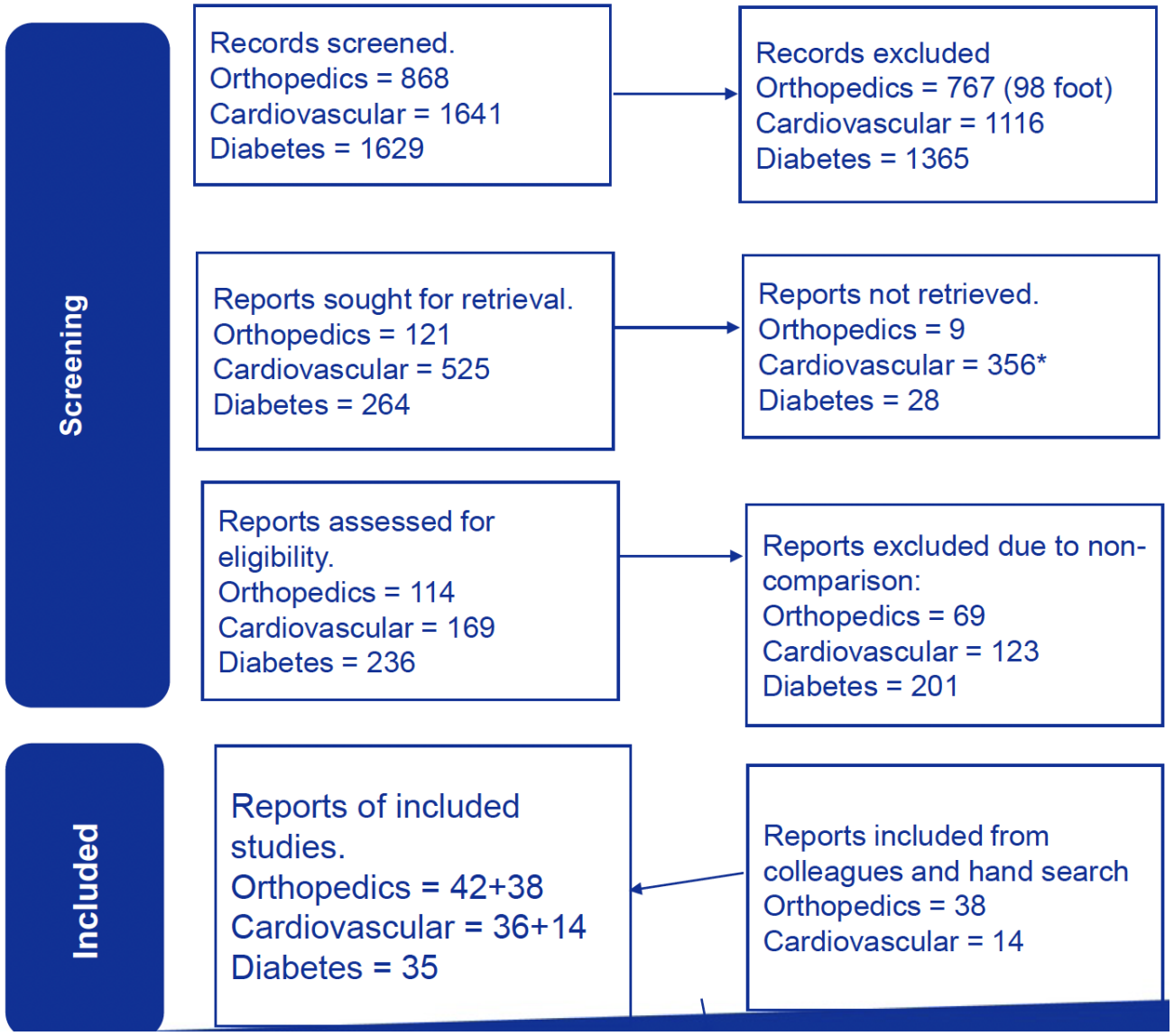
NIHR | National Institute for Health Research

PROSPERO
International prospective register of systematic reviews

An Integrative Systematic Review of Patient Reported Outcome Measures (PROMs) Used to Evaluate Orthopedic, Cardiovascular and Diabetes High Risk Implantable Medical Devices.

Objectives:

- To analyse the use of Patient-Reported Outcome Measures (PROMs) in trials, studies, of high-risk cardiovascular, orthopaedic, and diabetic medical devices.
- To provide the perspective of patients on their high-risk medical devices.



CORE-MD
Coordinating Research and Evidence for Medical Devices

https://www.core-md.eu/results/

Figure 3. Orthopaedics word cloud of primary concepts measured by F

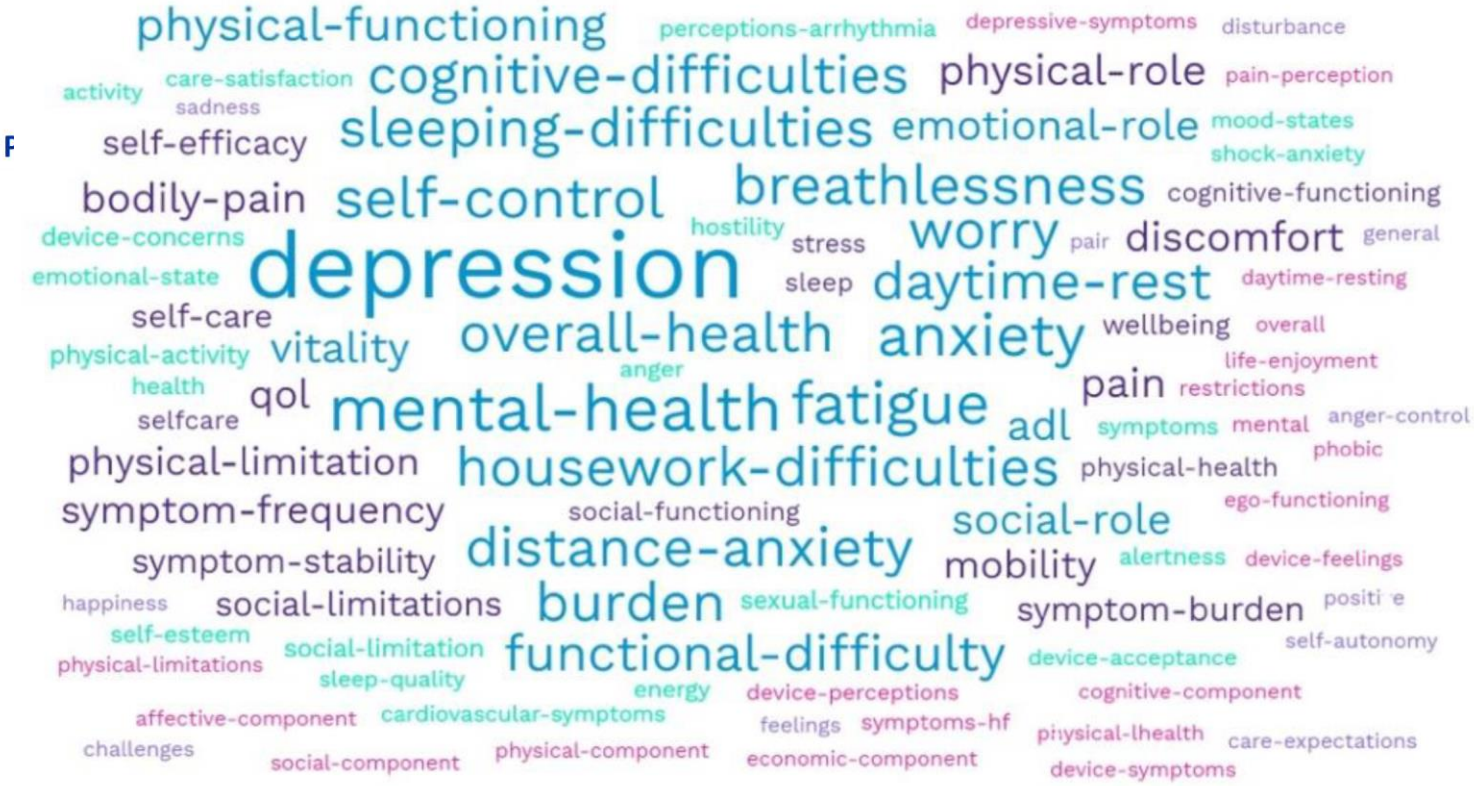


Figure 4. Cardiovascular word cloud of primary concepts measured by PROMs

Table 5. Characteristics of the selected populations for detailed study

	Cardiovascular	Orthopaedics	Diabetes
Number of studies (adult/child)	48/2	80	15/20
RCTs with PROM as prime	11 (22%)	17 (21%)	10 (28%)
RCTs with PROM as secondary	8 (16%)	24 (30%)	4 (11%)
Observation studies	21 (42%)	7 (9%)	12 (34%)
Registry studies	1 (2%)	5 (6%)	0
Retrospective studies	7 (14%)	20 (25%)	9 (26%)
Mean (sd) sample size			
RCT PROM primary	214(259)	86(24)	90
RCT PROM secondary	133(162)	159(123)	84
Mean age (sd) RCT/PROM primary	68(7)	67(9)	2 and 68 years
Mean age (sd) age RCT/PROM secondary	64(8)	69(9)	2 and 68 years
Year of study			
2000-2014	31	26	
2015-2023	19	54	35
Region of primary contact			
Europe	21	59	19
America/Canada	20	9	11
Asia/Middle East	5	2	1
Australia/NZ	1	7	4
Africa	0	0	

Many PROMS being used: orthopedic device trials

GENERIC PROMS	freq	Pre-mkt	Core set	CONDITON SPECIFIC	freq	Pre-mkt	Core set
EQ-5D	25		X	Western Ontario and McMaster Universities Arthritis Index (WOMAC)	16	X	
SF-12 (VR-12)	9		X	Oxford Knee Score (OKS)	12		
SF-36	6	X		Oxford Hip Score (OHS)	11		
				Harris Hip Score (HHS)	9		
Non-validated / single item				Knee Injury and Osteoarthritis Outcome Score (KOOS)	9	X	X
Satisfaction VAS	18		X	Hip Disability and Osteoarthritis Outcome Score (HOOS)	7	X	X
Numeric pain rating scale	37	X	X	UCLA activity /function score	5		
VAS rating of disability	1			KSS expectation / satisfaction	2		
Disability index: self-admin	1			Forgotten Joint Score	1		
Questions about noise	1			Paffenbarger physical activity	1		
Unnamed questionnaire	1			Intermittent and Constant Osteoarthritis Pain (*ICOAP*)	1		

PROMS in cardiovascular devices

ADULT GENERIC	freq	Pre-mkt	Core set	ADULT CONDITION SPECFIC	freq	Pre-mkt	Core set
SF-36	17	#		**Kansas City Cardiomyopathy Questionnaire** KCCQ*	4	#	#
SF-12	3		#	**Minnesota Living with Heart Failure Questionnaire** MLHFQ*	1	#	
EQ-5D	6	#		KCCQ-12	1		
HADS	5			Seattle Angina Questionnaire	1	#	
EQ-VAS	2			EuroQoL-HF	1		
State-Trait Anxiety Inventory (STAI)	2			Cardiac Anxiety Questionnaire (CAQ)	1		
PHQ-9	1		#	**MODIFIED for children**			
Profile of Mood States (POMS)	1			Patient scar assessment questionnaire (PSAQ)	1		
Quality of Well Being Schedule	1	#					
WHOQoL-Bref	1						
Satisfaction	1						
MODIFIED				**DEVICE SPECIFIC**			
"A short QoL questionnaire"	1			Florida Patient Acceptance Survey (FPAS)	3		
Karolinska questionnaire	1			Florida Shock Anxiety Scale (*FSAS*)	1		
NHQ /SF-36	1			Implanted Device Adjustment Scale (IDAS)	2		

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*MDDT qualified

https://www.core-md.eu/results/

Table 6. Frequency of types of PROM used

Medical specialty	Number of types of PROMs used	Types of PROM instruments		
		Generic	Condition-specific	Device specific PROM
Cardiovascular n=50	79	51	23	5
Orthopaedics n=80	130	56	80	
Diabetes n=35	125	25	99	1

Medical specialty	Pain	Satisfaction	QoL			
			Overall QoL	Emotional	Physical	Social
Cardiovascular	6%	14%	74%	88%	80%	62%
Orthopaedics	61%	27%	71%	40%	100%	40%
Diabetes		47%	100%	33%		

Other aspects of the utility

- different ways to identify important change
- follow-up schedules

PROMS	Significant or important change	Baseline	6 Weeks	3 Mths	6 Mths	9 Mths	12 Mths	24 Mths	36 Mths Annually Thereafter
Subjective pain VAS (Clement 2021)	20-point (on a 100-point scale) improvement / unstated/trend	X	X	X	X		X	X	X
OKS (Moorthy 2020)	published MCID values	X			X			X	
SF-36 Mental and Physical Component Scores (Baktir et al 2016; Beaupré 2007;)	Statistically significant mean improvement from baseline	**X**	X	X	**X**		**X**	X	X
KCCQ (Lefevre et al. 2010)	using 0.05 as the minimum clinically important difference (MCID).	X					X		
MLHF (Acker et al. 2006)	Mean difference (<0.05)	X		X	X	X	x		
Florida Patient	cut-off score of 67			X					

Table 11. Mean months in follow-up

Medical specialty	All studies	PROMs as primary outcome	PROMs as secondary outcome
Cardiovascular	16	10	25
Orthopaedics	42	34	43

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https://www.core-md.eu/results/

Qualitative assessment

Table 19. Ranking of important domains relating to medical devices

Rank (1=most important, 10=least important)	Criteria
1	• Safety and performance of the device
2	• Concerns about misfunctioning
3	• Security
4	• Control of the device
5	• Comfort
6	• Replacement of the device
7	• Noise • Size • Feeling under the skin
8	• Shape
9	• Appearance of the device
10	• Colour

Qualitative assessment

Results on the use of PROMs

- Limited familiarity with PROMs
- Co-creation and feedback pathways
- Frequency of PROM use

  Approximately every 3-6 months or 2-4 times a year. This frequency would adequately capture changing opinions, emotions, and outcomes over time

- Detail and format of PROM questionnaires:

  Max imum10-15 mins, preferrably online

How are PROMs used in device evaluation and regulatory decision-making?

- PROM instruments contribute to understanding of the **real-world effects**, **satisfaction and acceptance** (eg KCCQ, FPAS).
- PROMs are also used to identify **adverse events** and events that occur outside of the normal clinical visit times (eg MLHFQ).
- PROMs as **intermediate endpoints**.
- PROMs may also have utility for:
  - selection of clinical study subjects or to stratify patient population by predicted risk;
  - study population enrichment;
  - defining adverse events developing post-market surveillance methodologies

Challenges to incorporating PROs in trials

Table 2 How PRO assessment can become unnecessarily burdensome for trial participants and staff

Unnecessary burden on participants	Unnecessary burden on trial staff

• Questionnaires may be too long
• Questions may be
  ◦ Repetitive (particularly if multiple questionnaires are used and these assess the same or similar concepts)
  ◦ Irrelevant to the participant's condition
  ◦ Intrusive (of a personal nature) for some participants
  ◦ Poorly worded (eg, single questions may address multiple concepts)
  ◦ Difficult; ie, wording may include difficult terminology for some participants or may be targeted at the incorrect reading level (lower reading levels are typically recommended)
• PRO assessments may be too frequent, causing even brief questionnaires to become burdensome
• Response options may be unclear (ie, scale numbers provided without scale anchors [not at all – very much]
• The mode of administration may be burdensome to participants (eg, if the participants must attend the clinic simply to complete a questionnaire, or log-in procedures for online assessment may be difficult for some participants)
• Participants may not understand the purpose for PRO assessment if this is not explained to them, which may contribute to feelings of burden
	• Trial staff do not understand the purpose of PRO assessment due to poor training
	• PRO data are collected but never analyzed or reported
	• Trial staff need to provide high levels of assistance to participants due to a poorly chosen questionnaire, poorly worded questions, or difficult or time-intensive administration method
	• Assessments are too long, frequent, or repetitive
	• The return method involves scanning a double-sided or stapled booklet[41]

Abbreviation: PRO, patient-reported outcomes.

BURDENSOME

Mercieca-Bebber, R, et al. Patient Relat Outcome Meas 2018 Nov 1:9:353-367.

Challenges to incorporating PROs in trials

- **Budget and time** challenges related to **generating sufficient evidence** for a PRO, process barriers, such as protocol implementation and site training.
- **Lack of psychometric evidence** - requiring further studies making it more time-consuming and costly to include PROs in trials.
- Lack of clarity about evidence requirements: Stakeholders are uncertain about:
  - what and how much evidence is necessary
  - the priorities for PROM evidence generation
- Availability of **PRO interpretation guidelines** of the results.

PROs in clinical trials

- PRO endpoints should be decided *a priori* and included in the ethical review and the trial registration.
- Trial committees should have PRO expertise.
- Patients should be involved in selecting suitable PRO instruments.
- Guidance for the use, analysis, and interpretation of PROs in clinical trials should be developed.
- Recommendations for designing, analysing and reporting PRO findings should be used (e.g. SPIRIT-PRO; CONSORT-PRO).
- PRO Alerts are advised to capture issues that require prompt intervention.

PROs for regulatory purposes

- Minimal requirements for PROMs suitable for regulatory purposes should be developed.
- Minimal clinically important differences (MCID) should be determined for all PROMs that are (to be) used for regulatory purposes.
- Existing EU guidance on the clinical evaluation of medical devices[218] and the recommendations from the International Standardization Organization[219] should be revised to include specific advice concerning PROs.

PROs for reimbursement and health economics purposes

- The use of a broad range of PROs (i.e. functional status, symptoms, activities of daily living, empowerment) in informing reimbursement decisions should be further evaluated.
- Consensus has to be reached among patients, clinicians, and decision-makers on choosing the appropriate PROMs.
- Reimbursements based on PROs should account for risk adjustments and case mixes.
- Health Technology Assessment (HTA) should consider both generic and disease-specific measures in order to allow comparisons across conditions as well as to capture specificities of a particular disease.
- International consensus on adequate data-gathering methods ought to be reached to promote integrated PRO assessment in health decision-making across countries.

Moons P, et al. Eur Heart J 2023 Sep 21;44(36):3405-3422.

PFMD.org
Made WITH Patients

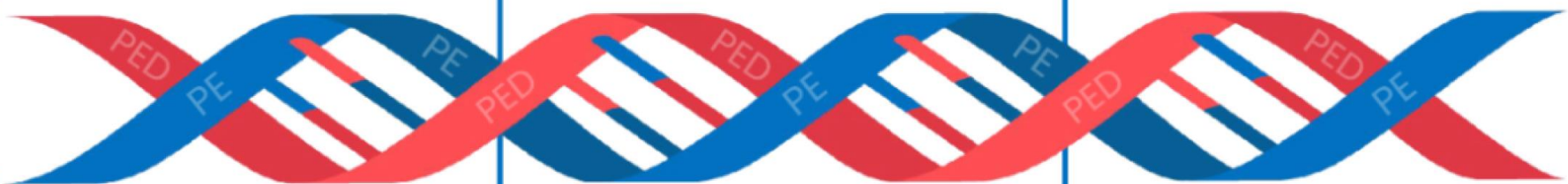
Patient experience data does not 'replace' patient engagement

The generation and collection of data from patients' experiences across all aspects of their lives

Patient Experience Data

Patient Engagement

Active and meaningful involvement of patients in developing medicines and delivery of care



Contextualize:

Ensure patient participation in decision-making processes

Provides context and understanding of the results

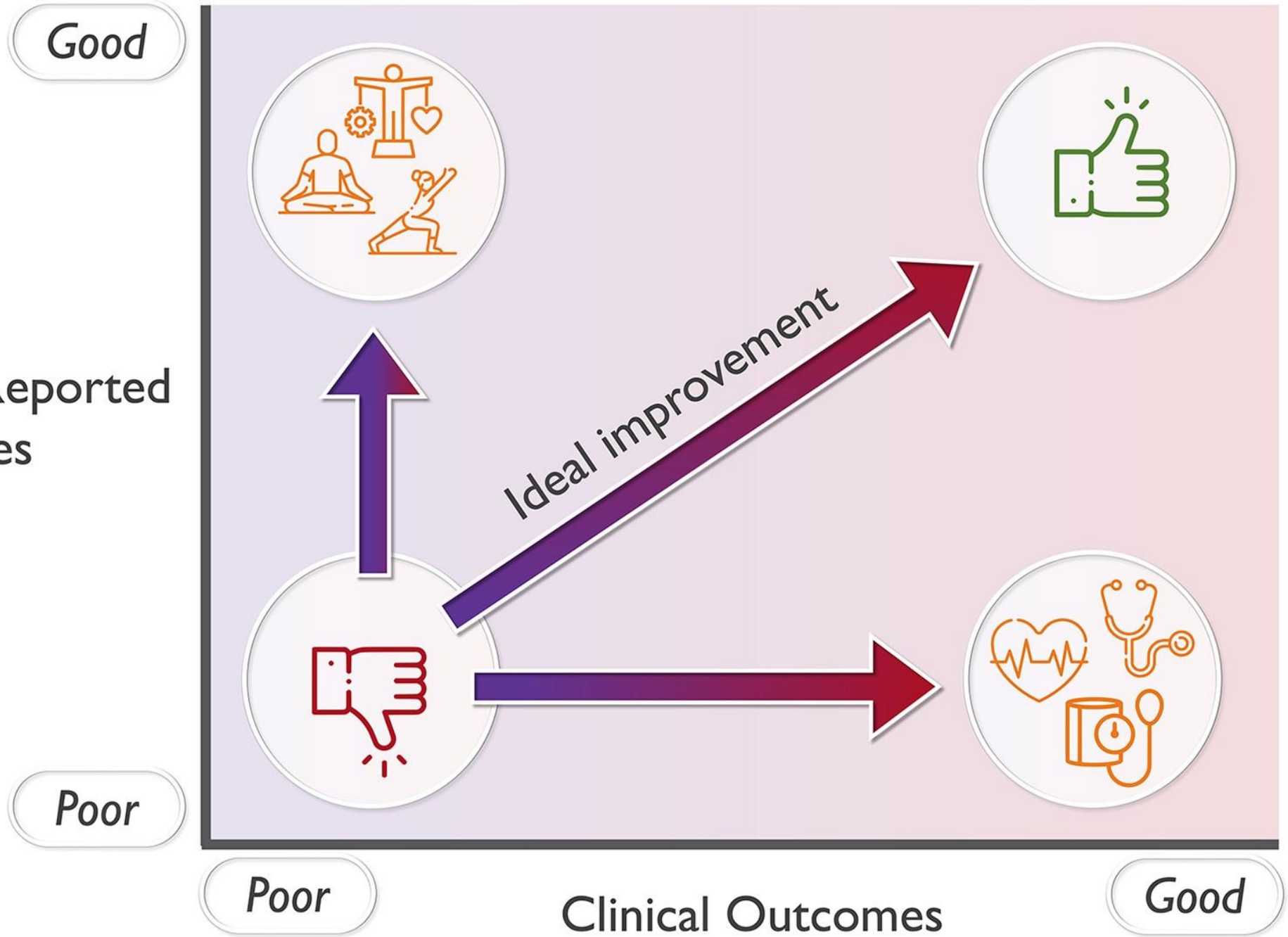
Co-create:

Ensures PED is focused on patient-meaningful topics

Co-design evidence generation to ensure it is meaningful

Patient Experience Data needs patient engagement throughout

https://patientfocusedmedicine.org/patient-experience-data/



Moons P, et al. Eur Heart J 2023 Sep 21;44(36):3405-3422.

The challenges facing healthcare systems

	The widespread problem	Our ambitious solution
1	Healthcare **spending under pressure and inefficient at the same time.** OECD estimates that 20% of healthcare expenditure is wasted[4]	Standardise PRO measurements to create **transparency** of burden of disease and outcomes and to increase healthcare **efficiency**
2	**Patient Voice is not being heard** by providers, payers and regulators	Equip patients with tools to **measure outcomes in a standardised way** and use them to improve clinical care both at a patient and population level
3	Lack of trust and incentives in sharing valuable health data **limits ability to harness digital technologies** to accelerate R&D and create evidence of value for innovation	Create an **ethical framework around data governance** to establish trust and enable data sharing to advance health science and policy

https://health-outcomes-observatory.eu/wp-content/uploads/2023/10/The-Health-Outcomes-Observatory-The-Power-of-Patient-Reported-Outcomes.pdf

Standardised PROs

Patients

- **Tracking personal measures** about their condition, such as symptom severity or functional status over time
- **Having richer and more productive** dialogues with their HCP
- **Better understanding** the burden of disease, comparing it to others with the same condition and assessing the quality of care they receive

Healthcare Providers

- **Accessing** structured patient-reported information
- **Accessing** the patient-reported data between consultations
- **Having more effective discussions** with patients and enabling better, data-driven decision making and personalisation of patient care
- **Gaining an overview** of their patients, the patients' views and preferences, and being able to (anonymously) benchmark with similar patients in other practices

Regulators and HTAs

- **Having access** to high-quality, trustworthy outcomes data, particularly for newly approved medicines and high-cost/high-value treatments
- **Incorporating patients' PROs and PROMs** in their analyses to highlight areas for potential improvements in healthcare, thus contributing to value based health care

https://health-outcomes-observatory.eu/wp-content/uploads/2023/10/The-Health-Outcomes-Observatory-The-Power-of-Patient-Reported-Outcomes.pdf

Standardised PROs

Health Authorities

- **Supplementing existing data sources** improve understanding of the burden of disease and the performance of the healthcare system
- **Enabling health authorities** to compare different patient pathways and select the most efficient ones, optimising patient outcomes and costs
- **Promoting outcomes-based** pricing and reimbursement negotiations, including outcomes-based contracting

Researchers

- **Running research studies** using the H2O infrastructure and/or data to inform health policy and/or medical science
- **Assessing the impact** of new therapies on the patient population
- **Conducting randomised studies** on standardised RWE to inform medical science and regulatory decision making

Industry

- **Enabling outcomes** based decision making in health policy
- **Creating** an enabling infrastructure for VBHC
- **Improving** patient centricity

https://health-outcomes-observatory.eu/wp-content/uploads/2023/10/The-Health-Outcomes-Observatory-The-Power-of-Patient-Reported-Outcomes.pdf

Standardised PROs

Using structured PROs as a way of communication between HCPs, patients and their carers enables an evidence-based discussion. It creates a common language that amplifies the patient voice in an entirely new way, driving better clinical outcomes

Better patient outcomes

When all parts of the health system have access to standardised PRO data, they see the impact of care across multiple disease areas and populations, giving an unprecedented overview of the real needs of patients and providing an objective way of targeting the pain points in the system

Sustainable Health Care Systems

Innovation in life sciences

Systematic collection of standardised, structured PROs paired with clinical outcomes can inform design of clinical trials, provide insights into standard of care, reveal patients needs and advance scientific knowledge

Sustainable Health Care companies

Standardised PROs paired with clinical outcomes, can become a new window into the patient experience and outcomes allowing better business decisions to meet unmet patient needs but also allow evidence generation to assess effectiveness of various interventions.

https://health-outcomes-observatory.eu/wp-content/uploads/2023/10/The-Health-Outcomes-Observatory-The-Power-of-Patient-Reported-Outcomes.pdf

COMMENTARY

Building a Value-Based Care Infrastructure in Europe: The Health Outcomes Observatory

Leaders at the European Union's Innovative Medicines Initiative are developing a large-scale multi-stakeholder international ecosystem to incorporate patient-reported outcomes and measures to improve patient engagement and drive value.

Authors: Tanja Stamm, PhD, Dr. rer. biol. hum., Mag. phil., MSc, MBA, Nick Bott, PsyD, Rob Thwaites, MA, Erika Mosor, MSc, PhD, Margaret R. Andrews, MPH, Joris Borgdorff, PhD, Yolima Cossio-Gil, MD, MPH, +17, and Meni Styliadou, LLM Author Info & Affiliations

NEJM Catalyst | June 9, 2021 |

Cardiometabolic

ADULT OBESITY

ATRIAL FIBRILLATION

CORONARY ARTERY DISEASE

DIABETES

HEART FAILURE

HEART VALVE DISEASE

HYPERTENSION IN LOW- AND MIDDLE-INCOME COUNTRIES

STROKE

VENOUS THROMBOEMBOLISM

CONGENITAL HEART DISEASE

ICHOM
International Consortium for Health Outcomes Measurement

ICHOM
International Consortium for
Health Outcomes Measurement

Heart failure

Coronary artery disease

Atrial fibrillation

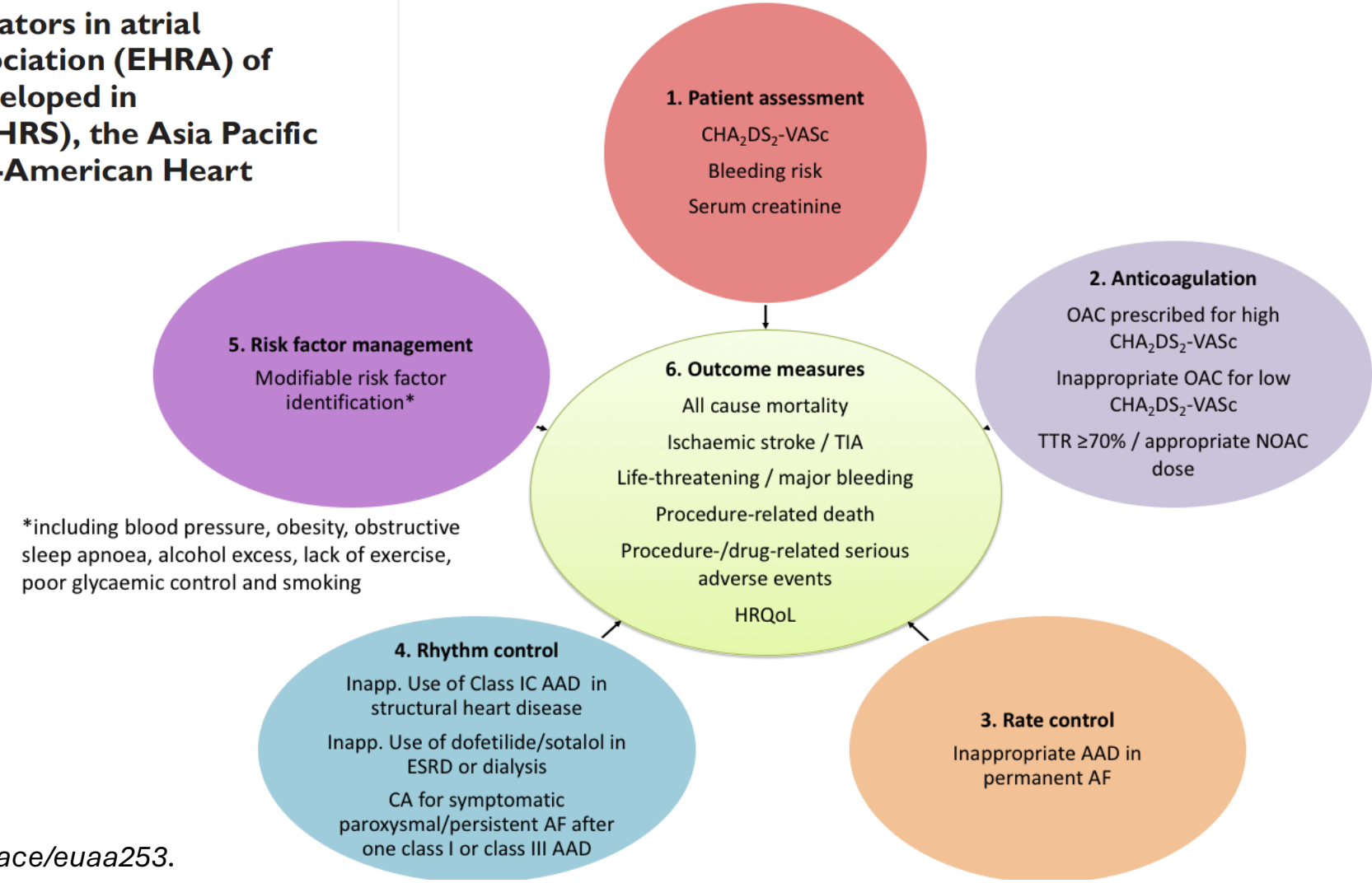
Heart valve disease

ESC European Society of Cardiology
Europace (2020) **00**, 1–17
doi:10.1093/europace/euaa253

GUIDELINES

Quality indicators for the care and outcomes of adults with atrial fibrillation

Task Force for the development of quality indicators in atrial fibrillation of the European Heart Rhythm Association (EHRA) of the European Society of Cardiology (ESC): Developed in collaboration with the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS), and the Latin-American Heart Rhythm Society (LAHRS)



Arbelo E et al. EP Europace 2020. DOI: 10.1093/europace/euaa253.

Summary

- **Patient engagement** is **critical** throughout the care process (and in medical product development).
- **Patient experience data (PED)** can provide useful information to patients, prescribers, regulators and other stakeholders.
- Despite growing recognition on the value of **PED/PROs** for the development of therapies, **implementation remains challenging**.
- **Methodological robustness** (double-blind, RCT), **standardised measures** and **consistency of outcome reporting** are paramount.
- **Regulatory requirements** for PED remain to be defined.
- **Need greater participation of patients** in the selection, analysis and interpretation of PED.

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