

Welcome!

Advancement of patient-focused drug development in Multiple sclerosis

Tap on the buttons below to explore and obtain more information.

Tap on the buttons below to explore 2 new validated, MS-specific patient-reported outcome (PRO) precision measures

PROMIS® Fatigue_{MS} SF8

PROMIS® Physical Function_{MS} SF15

PRO INTRODUCTION

Tap here for a brief **INTRODUCTION** to the PRO concept

WHY

Tap here to learn **WHY** these measures were developed

HOW

Tap here to learn **HOW** these measures were developed in collaboration with the FDA and the iConquerMS and Accelerated Cure Project groups

VALIDATION

Tap here to learn about the **VALIDATION** and alignment of these measures with FDA PRO guidelines

UTILITY

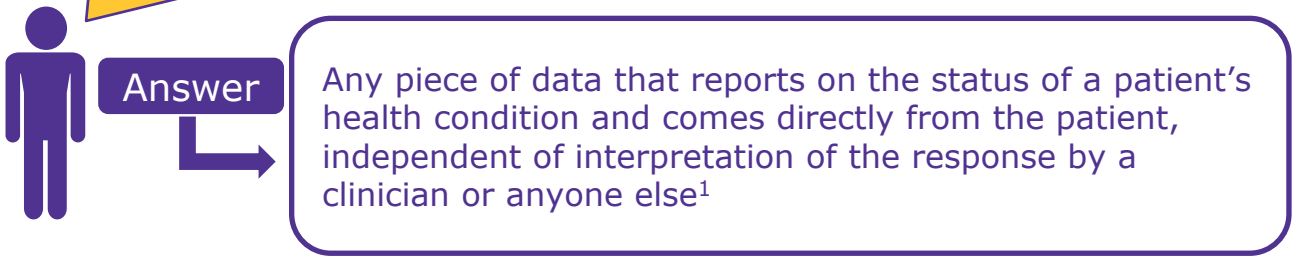
Tap here to learn about the **UTILITY** of the measures and where they can be used





Patient centricity in clinical research What is a patient-reported outcome?

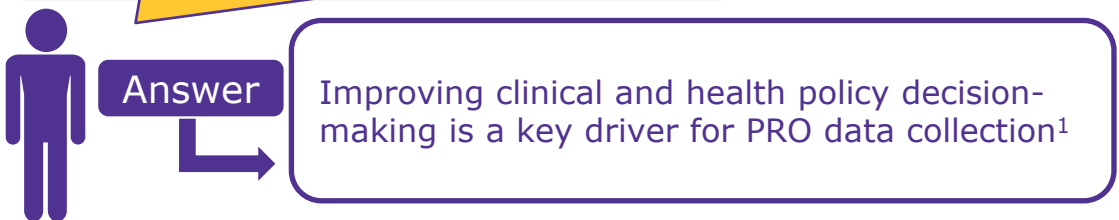
What is a PRO?



How are PROs used?

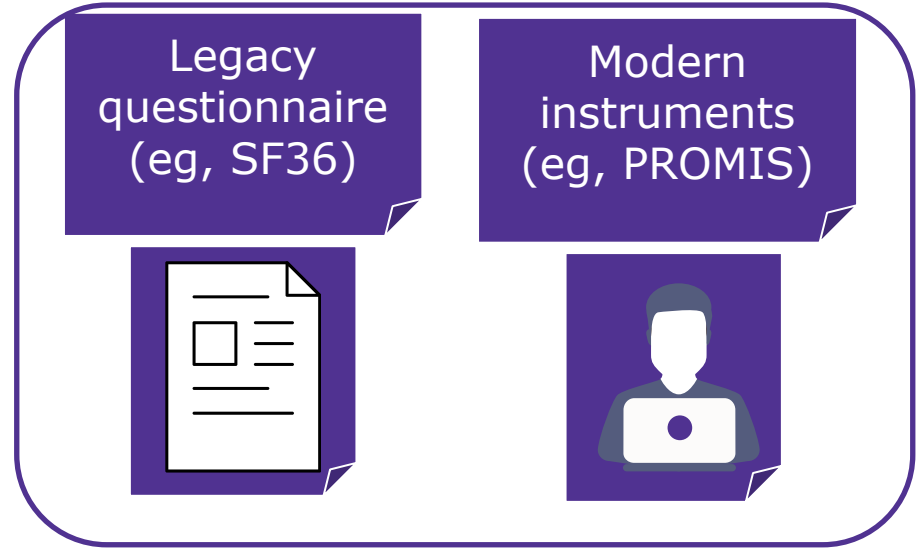


What can PROs help achieve?



PRO, patient-reported outcome; PROMIS, Patient-Reported Outcomes Measurement Information System; SF, short form.

How are PROs collected?¹



PRO data collection is of growing importance for government agencies, pharmaceutical companies, and patient support groups³

1. <https://rethinkingclinicaltrials.org/resources/patient-reported-outcomes-3/#fda-2009>. Accessed January 2020.
2. Kamudoni P, et al. *Living with Chronic Disease: Measuring Important Patient-Reported Outcomes*. New York, NY: Springer Publishing Co; 2018.
3. Nowinski CJ, et al. *Neurotherapeutics*. 2017;14:934-944.



Advancement of patient-focused drug development in multiple sclerosis

New precision measures needed to capture PROs in MS



Endpoints in MS trials have been routinely based on clinician assessments and performance-based outcome measures¹



Recognition of need to incorporate perspective of patients with MS into evaluation of treatment benefit¹



Need for high precision MS-specific measures for main concepts²



Physical function and fatigue were chosen as important concepts in collaboration with the Multiple Sclerosis Working Group (MSWG) of the Critical Path Institute.

The MS Working Group developed standardized PRO measures to assess fatigue and physical function with the aim to meet the requirements for FDA qualification^{2,3}



Existing PRO questionnaires were evaluated. None met all key requirements (ie, content validity, responsiveness, construct validity)^{2,3}



A tailored approach was chosen to increase precision of traditional PRO questionnaires^{4,5}

1. MSWG. Poster presented at: 8th Annual PRO Consortium Workshop; April 26–27, 2017; Bethesda, MD.
2. Martin SA, et al. Poster presented at: ISOQOL 25th Annual Conference; October 24–27, 2018; Dublin, Ireland.
3. MSWG. Poster presented at: 10th Annual PRO Consortium Workshop; April 24–25, 2019; Silver Spring, MD.
4. Jensen RE, et al. *Med Care*. 2015;53:153–159.
5. Oude Voshaar MA, et al. *Rheumatology*. 2015; 54:2221–2229.



Advancement of patient-focused drug development in multiple sclerosis

Innovative collaboration: How were patients engaged?



2
new

PROMIS MS instruments were developed in collaboration with the iConquerMS™ patient-powered research network and the Accelerated Cure Project for Multiple Sclerosis network

iConquerMS™



iConquerMS and EMD Serono collaboration for PFDD

Capturing patient feedback:

- Conceptualization and prioritization of research questions related to disease burden
- Design of clinical trial endpoints (ie, PROs)
- Development and validation of MS PRO measures
- Integration of PRO endpoints into clinical trials (ie, schedule of assessment, burden, training)

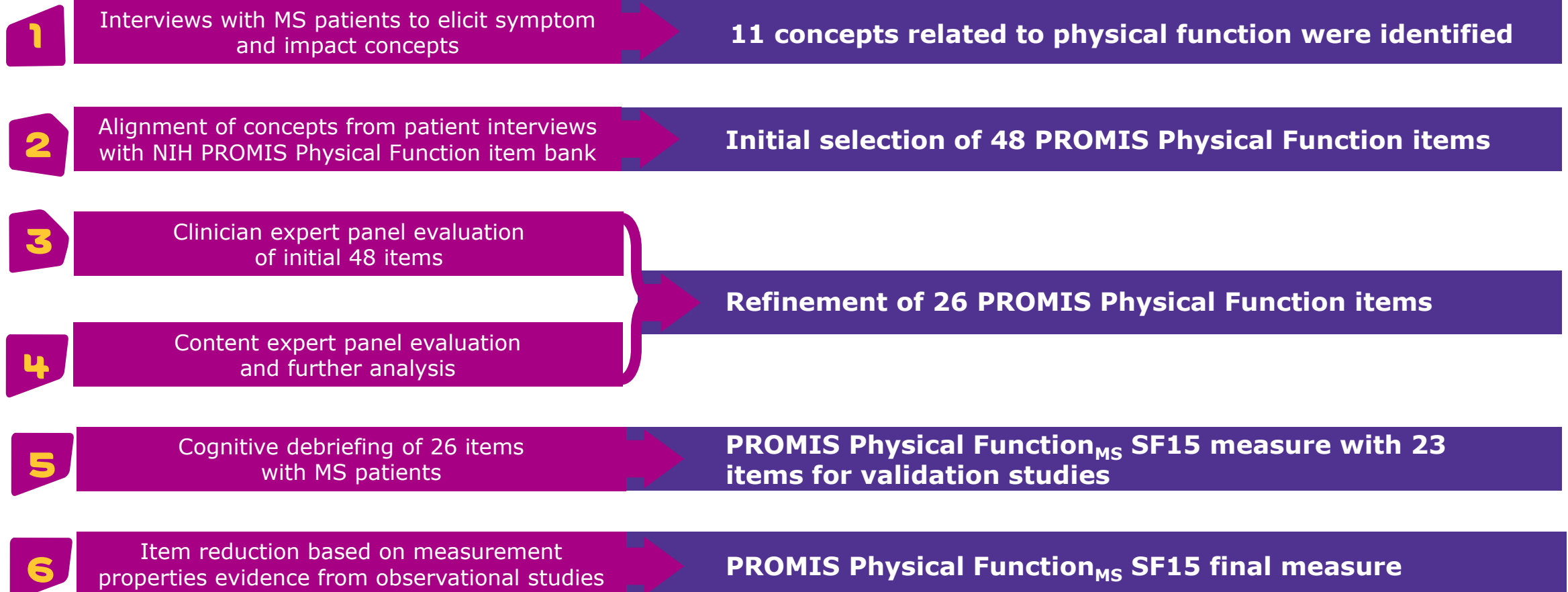


Advancement of patient-focused drug development in multiple sclerosis

Development of PROMIS Physical Function_{MS} Short Form (SF15)



BACK



A similar process was used for the PROMIS Fatigue_{MS} SF8 instrument



Compliant with FDA PRO guidelines
Validated quality PRO measures




Per the FDA, PROs must provide:¹


- **Content validity:** extent to which the concept of interest and the measurement is appropriate and comprehensive for use in the target population¹
- **Reliability:** yield consistent, reproducible estimates of true effect¹
- **Ability to detect change:** sensitive to gains and losses¹

2
 New PROMs

Evidence supports the reliability and validity of the new instruments²⁻⁴
 PROMIS Fatigue_{MS} SF8 and PROMIS Physical Function_{MS} SF15

As part of the validation process, cognitive interviews were conducted with patients with MS to confirm concepts and relevance of items⁵; measurement properties were validated in observational research⁵

Tap here to learn more about the cognitive interview process 

Tap here to learn more about the psychometric validation 

FDA, US Food and Drug Administration; MS, multiple sclerosis; PRO, patient-reported outcome; PROM, patient-reported outcome measure; PROMIS, Patient-Reported Outcomes Measurement Information System; SF, short form.

1. FDA Guidance for Industry. Patient-Reported Outcomes. 2009. Available at: <https://rethinkingclinicaltrials.org/resources/patient-reported-outcomes-3/#fda-2009>. Accessed January 2020.
 2. Kamudoni P. Poster presented at: ISOQOL 26th Annual Conference; October 20-23, 2019; San Diego, CA.
 3. Kamudoni P. Poster presented at: 5th Annual PHO International Conference; October 24-25, 2019; San Diego, CA.
 4. Cook KF, et al. *Qual Life Res.* 2012;21:1021-1030.
 5. Kamudoni P, et al. *Qual Life Res.* 2018;27(S1):S1-S190. [Abstract 1103]





Validated quality PRO measures – additional details

Content validation with cognitive debriefing interviews to confirm content validity of new PROMIS Fatigue_{MS} SF8 and PROMIS Physical Function_{MS} SF15 measures

WHAT WAS DONE?¹

- Cognitive debriefing interviews were conducted with 48 adult patients with MS (RRMS, n=26; PPMS, n=15) recruited from two dedicated qualitative research sites in the US

WHY?^{1,2}

- Assess item relevance and respondent understanding for each individual item
- Assess comprehensiveness of the overall draft PROMIS Fatigue_{MS} and PROMIS Physical Function_{MS} measures
- Assess and perform further item reduction of PROMIS Physical Function_{MS} items



CONFIRMED OUTCOMES^{1,2}

- All items are relevant for patients with MS and are well understood
- Response options and recall periods are suitable for the measures
- Coverage of the most pertinent content for physical function and fatigue in MS



Validated quality PRO measures – additional details **Conduct observational studies to validate measurement properties of PROMIS Fatigue_{MS} SF8 and PROMIS Physical Function_{MS} SF15 measures¹⁻³**

WHAT WAS DONE?

- Observational 52-week prospective longitudinal study from the UK MS register population¹
- A total of 600 patients were assessed¹ (completion rates varied for individual instruments; n=558, physical function and n=384, fatigue)^{2,3}

WHY?¹⁻³

- Assess unidimensionality and known groups validity
- Assess test-retest reliability
- Assess sensitivity to change



CONFIRMED OUTCOMES¹⁻³

Both measures:

- Differentiate between known groups
- Correlates to other PRO measures
- Are unidimensional



PROMIS Fatigue_{MS} SF8^{1,2}

In the past 7 days...

Never Rarely Some-
times Often Always

1. How often were you too tired to think clearly?					
2. How often were you too tired to enjoy life?					
3. How often did you find yourself getting tired easily?					
4. How often did you feel tired even when you hadn't done anything?					
5. How often did you have trouble finishing things because of your fatigue?					
6. How often did you have to push yourself to get things done because of your fatigue?					
7. How often did your fatigue interfere with your social activities?					

- **Recall Period:**
Past 7 days
- **Response Options:**
5-level scale assessing frequency or interference
- **Data Collection Mode:**
Electronic

Tap here to see illustrative example of scoring utilizing PROMIS Fatigue_{MS} SF8



In the past 7 days...

Not at all A little bit Some-
what Quite a bit Very Much

8. To what degree did your fatigue interfere with your physical functioning?					
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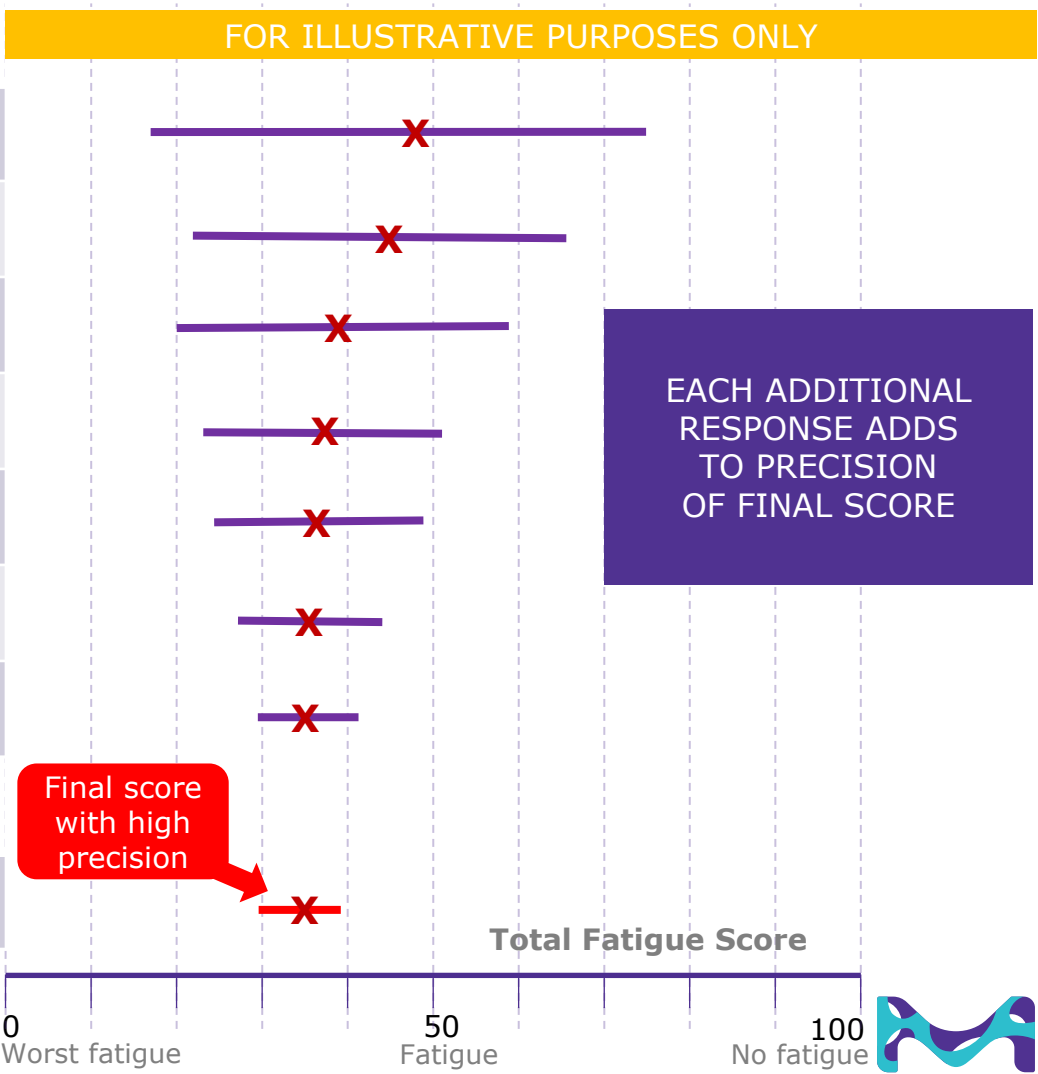




PROMIS Fatigue_{MS} SF8^{1,2}

In the past 7 days...	Never	Rarely	Sometimes	Often	Always
1. How often were you too tired to think clearly?			✓		
2. How often were you too tired to enjoy life?			✓		
3. How often did you find yourself getting tired easily?				✓	
4. How often did you feel tired even when you hadn't done anything?		✓			
5. How often did you have trouble finishing things because of your fatigue?			✓		
6. How often did you have to push yourself to get things done because of your fatigue?				✓	
7. How often did your fatigue interfere with your social activities?				✓	

In the past 7 days...	Not at all	A little bit	Somewhat	Quite a bit	Very Much
8. To what degree did your fatigue interfere with your physical functioning?			✓		



Final score with high precision





PROMIS Physical Function_{MS} SF15^{1,2}

	Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
1. Are you able to carry a laundry basket up a flight of stairs?					
2. Are you able to stand without losing your balance for several minutes?					
3. Are you able to get up from the floor from lying on your back without help?					
4. Are you able to hold a plate full of food?					
5. Are you able to dress yourself, including tying shoelaces and buttoning your clothes?					
6. Are you able to run errands and shop?					
7. Are you able to push open a heavy door?					
8. Are you able to exercise hard for half an hour?					
9. Are you able to walk with a heavy backpack (about 10 lbs/5 kgs) for 20 minutes					
	Not at all	Very little	Somewhat	Quite a lot	Cannot do
10. Does your health now limit you in hiking a couple of miles (3 km) on uneven surfaces, including hills?					
11. Does your health now limit you in climbing several flights of stairs?					
12. Does your health now limit you in doing moderate work around the house like vacuuming, sweeping floors, or carrying in groceries?					
13. Does your health now limit you in doing vigorous activities, such as running, lifting heavy objects, participating in strenuous sports?					
	No difficulty	A little difficulty	Some difficulty	A lot of difficulty	Cannot do
14. How much DIFFICULTY do you currently have walking on uneven surfaces (eg, grass, dirt road, or sidewalk)?					
15. How much DIFFICULTY do you currently have standing up from a low, soft couch?					

- **Recall Period:**
No recall period
- **Response Options:**
5-level scale
- **Data Collection Mode:**
Electronic

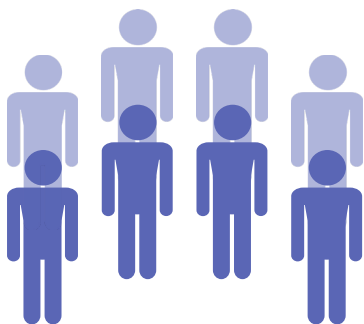




Utility of new instruments in clinical research

Where will PROMIS Fatigue_{MS} and PROMIS Physical Function_{MS} be incorporated?

Ongoing and future EMD Serono-sponsored clinical trials in MS



Can also be incorporated in other clinical research in MS outside of EMD Serono-sponsored trials



PROMIS measures are already used in clinical practice in other disease states^{1,2}

- **Needs assessment** (eg, screening)
- **Shared decision-making** (eg, expected functional improvement from total knee replacement vs physical therapy)
- **Symptom management** (eg, monitoring unexpected changes in severity of fatigue or functional problems)
- **Outcomes assessment** (eg, regular assessment of fatigue or physical function after starting a new treatment)
- **Quality improvement** (eg, monitoring symptom prevalence within a healthcare system, changes over time)



Anticipated increase in use with continued qualification of instruments²

