The PSC Partners Patient-Reported Outcomes Measure (PROM) Project: Update from the Research Leads

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PSC PARTNERS SEEKING A CURE

PSC PROM Project: Research Leads

PSC PARTNERS SEEKING A CURE

- PhD in Clinical Psychology
- Liver Disease x 17 years
- Survey and qualitative methods
  - PRO measures
- Patient engagement

Dr. Bryce Reeve

- PhD in Quantitative Psychology
- Survey methodologist
- Developer of NIH PROMIS®
- Professor, Duke University
- Director, Center for Health Measurement

PSC PARTNERS SEEKING A CURE

Report of the PSC Partners Externally-Led Patient-Focused Drug Development (PFDD) Meeting

Public Meeting: October 23, 2020 - Report Date: April 11, 2022

The Symptoms and Daily Impact of PSC that Matter Most to Patients

- **PSC Symptoms That Most Impact Patients' Lives**
  - **Fatigue** – extreme, different from being tired, not remedied by sleep
  - **Pruritus** – unrelenting, uncontrollable itch; often painful, interrupts sleep and slows down or prevents all routine activities
  - **Pain** – chronic, often does not improve with medication, impacts daily life, (abdominal, liver, joint, generalized)
  - **Impaired cognitive function** – "brain fog," loss of identity, memory gaps, inability to function independently
  - **Mental and emotional health issues** – anxiety, depression, post-traumatic stress disorder (PTSD); significant concern for children and young adults with PSC; emotions can intensify physical symptoms
  - **Other symptoms of concern** – insomnia, varices/bleeding varices (enlarged or swollen veins in the esophagus [the tube connecting the throat to the stomach]), loss of appetite/weight loss, nausea/vomiting, as well as the consequences of osteopenia/osteoporosis (bone loss)

https://pscpartners.org/about/the-disease/voice-of-the-patient-report-pfdd-forum.html

PSC PARTNERS SEEKING A CURE

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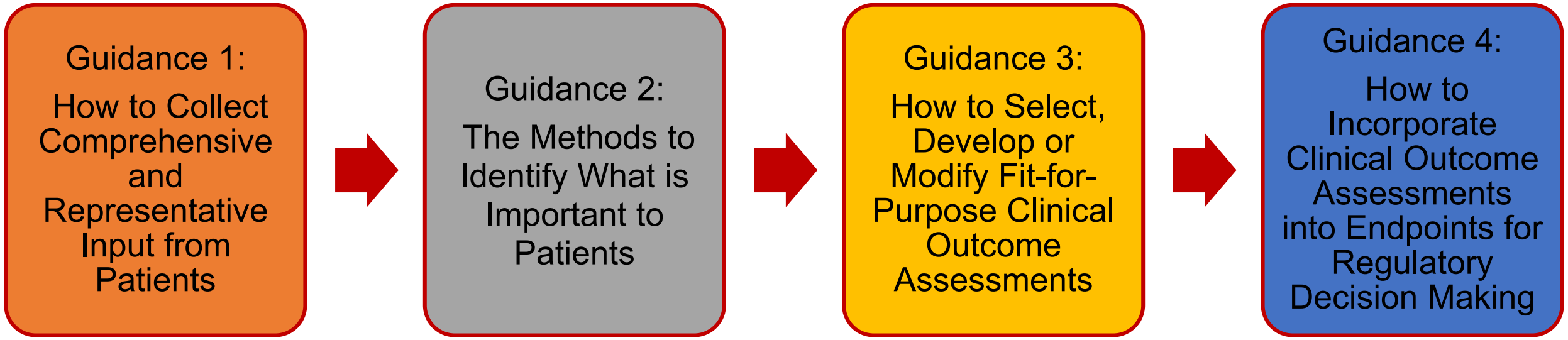
Patients urgently need effective treatments for the symptoms of PSC. The extent, severity, and impact of the symptoms of PSC are still not well-characterized. There are no proven therapies to improve how PSC patients feel and function. Participants vividly described the significant impacts of pruritus, fatigue, and pain, in particular, on their ability to function on a daily basis and on their overall quality of life. Some turn to off-label use of existing medications (e.g., ursodiol, vancomycin) and further studies are needed on the role of these drugs in symptom and/or disease management.

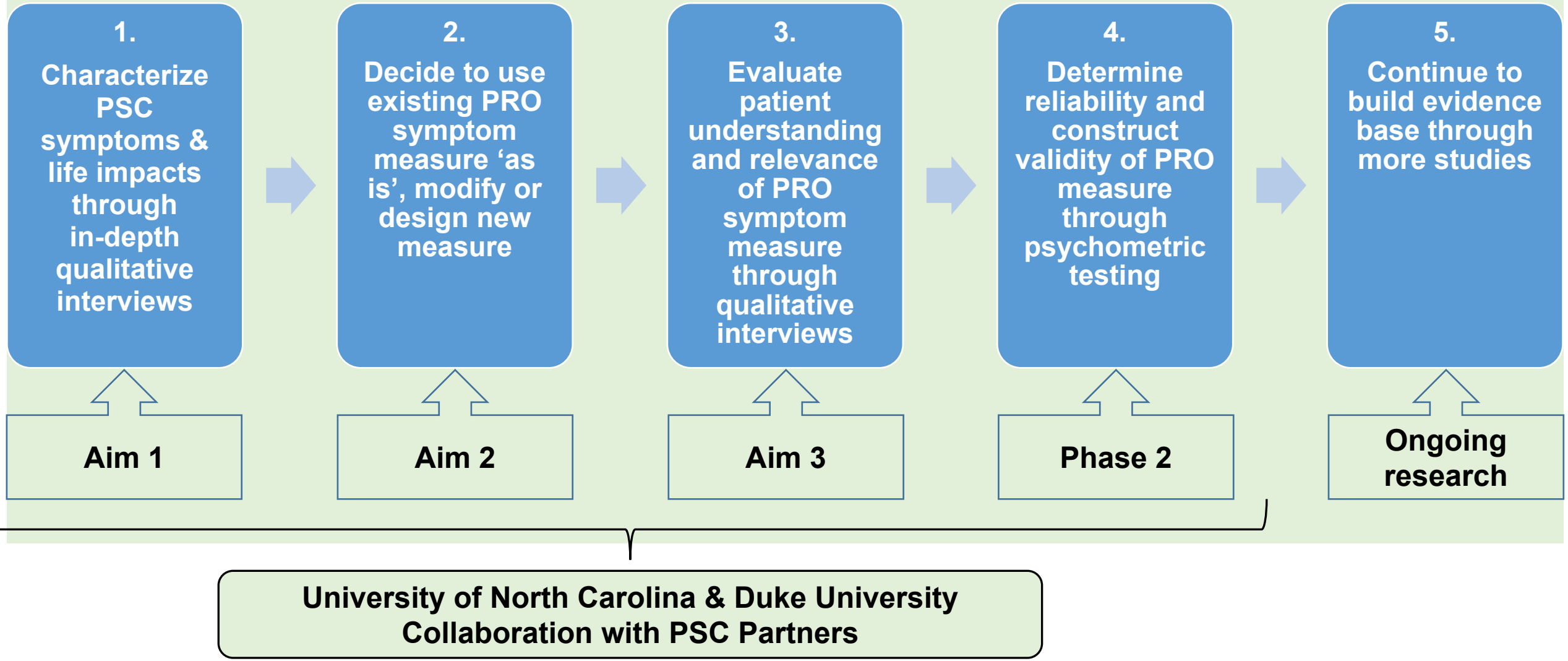
https://pscpartners.org/about/the-disease/voice-of-the-patient-report-pfdd-forum.html

FDA Patient-Focused Drug Development Guidance Series for Enhancing the Incorporation of the Patient's Voice in Medical Product Development and Regulatory Decision Making



https://www.fda.gov/drugs/development-approval-process-drugs/fda-patient-focused-drug-development-guidance-series-enhancing-incorporation-patients-voice-medical

Process to Create PRO Symptom Measures for PSC Trials



Aim 1: **Characterize PSC symptoms & life impacts through in-depth qualitative interviews**

- In-depth individual interviews (“Concept Elicitation”) with a representative sample of patients with PSC who experience symptoms
- Advertise through PSC-Partners and CALiD
- Representative of patients who participate in clinical trials

Aim 2: **Select symptom measures: Existing symptom measure 'as is', modify or design new measure**

- Community Advisory Board (CAB) – PSC-P, patients, clinicians, trialists, survey methodologists, FDA
- Review published literature:
  - Do any existing symptom measures capture the qualities of symptoms described by PSC patients in Aim 1?
  - What is the evidence for its content validity, reliability and construct validity?
  - Has it ever been evaluated in patients with PSC?
  - Does the tool need modification?
- If no PRO symptom measure appears appropriate, we will develop new measure

Aim 3: **Is the PRO measure understandable and content valid for PSC patients?**

- Two rounds of individual interviews ("Cognitive Interviews") to evaluate understanding and comprehension of measures: Instructions, recall period, items, response set

In the last 7 days, my itching interfered with my sleep:

None of the time	Some of the time	Most of the time	All of the time

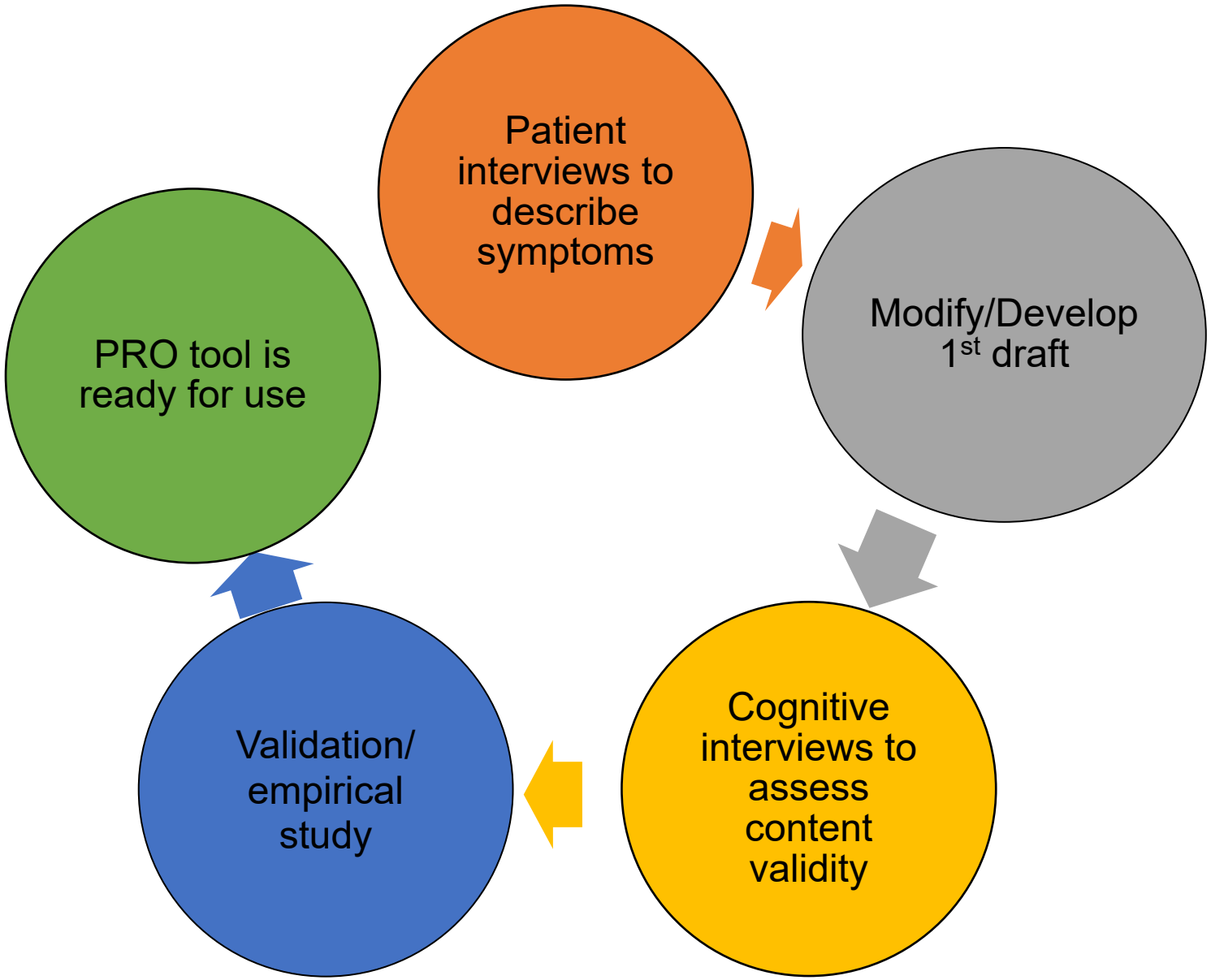
- Interviewer Probes:
  - *Please tell me in your own words what this question means to you?*
  - *Why did you select "most of the time"?*
  - *What days were you thinking of when you answered the question?*

Phase 2: **Determine reliability and validity of PRO symptom measure through psychometric testing**

- Cross-sectional or longitudinal data collection from a large sample of diverse PSC patients.

- Perform statistical evaluations
  - Internal consistency and test-retest reliability
  - Association of PRO measure scores with other collected clinical and PRO data
  - Change in scores over time consistent with theory

First - Establish ***content*** and ***empirical*** validity of the measure



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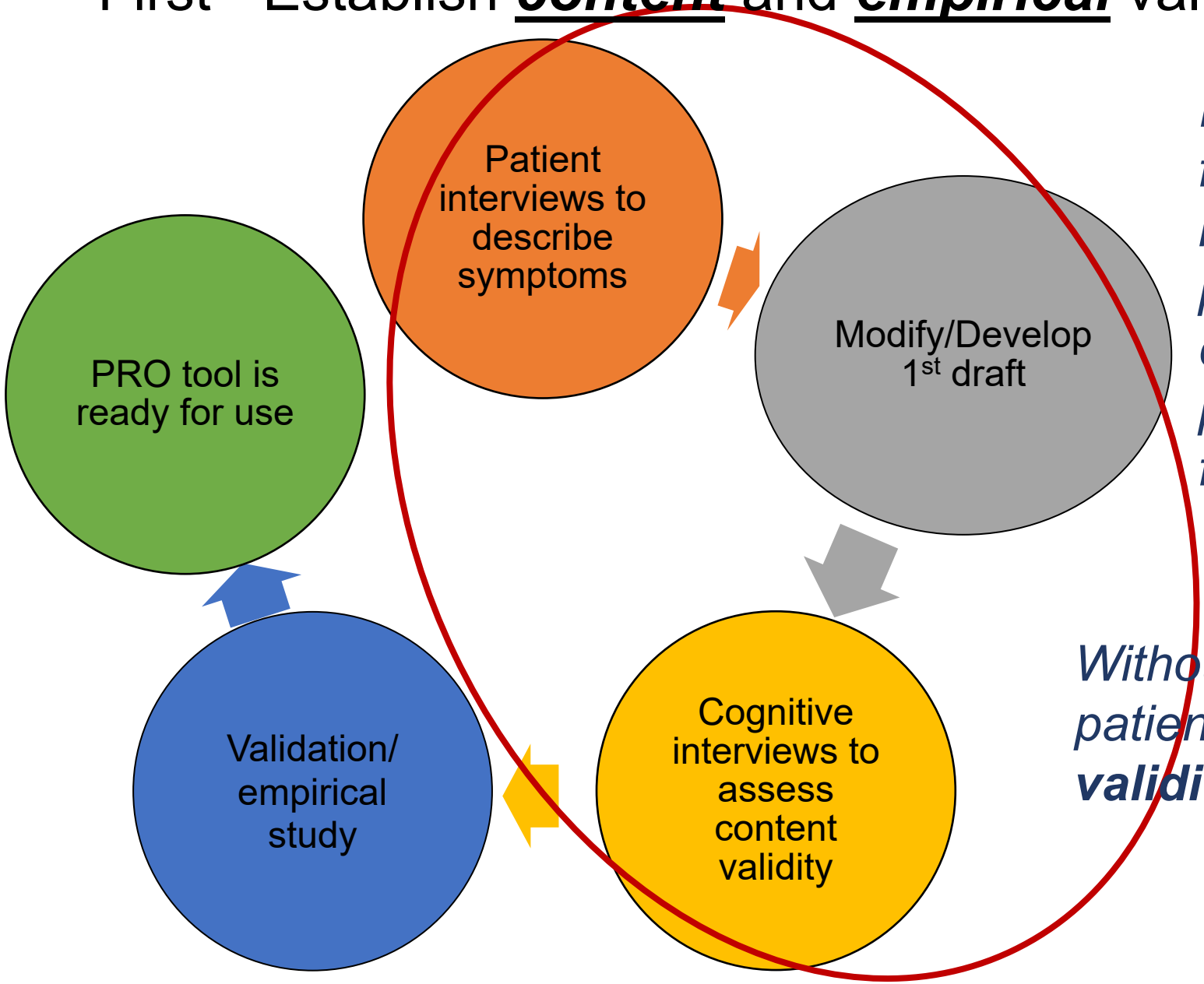

It is this combination of input from the target population in item generation + evaluation of patient understanding through cognitive interviewing that provides the required evidence for content validity

Patrick et al; Value in Health, 2011

Without adequate documentation of patient input, a PRO tool's ***content validity is*** *questionable*

https://www.fda.gov/media/116277/download