Patient-Centered Core Impacts Sets (PC-CIS): What They Are and What They Are Not

Eleanor M. Perfetto, PhD, MS[1]; Suz Schrandt, JD[2]; Omar A. Escontrías, DrPH, MPH[3]; and Laurie B. Burke, MPH, RPh[1,4]
[1]University of Maryland, School of Pharmacy, Baltimore, MD and independent consultant, Venice, FL
[2]exPPect, Alexandria, VA; [3]National Health Council, Washington, DC, US; [4]LORA Group, Normal, IL

Letter to the Editor

We are writing regarding the Innovations in Pharmacy commentary entitled, "Evidentiary Standards for Patient-Centered Core Impact Value Claims."(1) We thank Dr. Langley for commenting on the National Health Council's work on patient-centered core impact sets (PC-CIS), an initiative spearheaded by the nonprofit organization and its membership with multi-stakeholder representation and input.(2-4) While we have tried to be clear and transparent about the intent of PC-CIS, the commentary made it apparent to us we need to (and will) do more to be explicit about what a PC-CIS is and is not, and its possible downstream uses.

We believe the PC-CIS concept was misrepresented in the commentary and want to provide clarification for readers so they can consider the merits of the initiative for themselves.

1) The commentary refers to core impact measures, and PC-CIS measures and instruments. This is not our terminology. We agree with the commentary author about adhering to good measurement principles and available measurement standards. However, a PC-CIS is not a measure nor set of measures and has not been purported to be.

A PC-CIS is simply a list of the most important impacts patients report that a disease and/or treatment have on their health and daily life, and that of their family and caregivers.(2-4) Impacts are collected from patients as patient experience data (5), typically through qualitative research, e.g., interviews and/or focus groups. It starts by asking patients open-ended questions about how an illness and/or treatments impact their health and lives. Impacts include any reported effect or ramification from a disease or treatment (e.g., pain, fatigue, job loss, out-of-pocket costs for care or drugs, caregiver injury, financial toxicity). The list from patients can be lengthy, "broad and inclusive," capturing the patient voice without restriction.(4) We are unclear why anyone would want to restrict patient reporting as the commentary implies.(1)

The all-inclusive list is narrowed to a prioritized list of what is *most* important to get to the core impacts.(4) That core is informative. We propose the impacts listed in a PC-CIS be used as precursors, qualitative data one collects to inform myriad downstream uses. For example, a PC-CIS could be used to identify the concept of interest (COI)(6-9) for which a measure might then be developed, possibly using the methods discussed in the commentary. Thus, there would eventually be measures developed or identified, informed by a PC-CIS, to capture one or more COIs derived from the impacts listed. But the impacts themselves are measure agnostic and measures will need to be fit-for-purpose depending on the downstream context of use.

Corresponding author: Eleanor M. Perfetto, PhD, MS
University of Maryland, School of Pharmacy**,** Baltimore, MD
Independent consultant, Venice, FL**;**
Email: emperfetto@rx.umaryland.edu

We state outright, in the draft Blueprint for Developing PC-CIS, released by the NHC for public comment during August 2022(4), that measures are downstream from impacts and as such, measurement was not addressed in the draft. The draft Blueprint does not direct readers toward classical or modern approaches and makes no suggestions about ordinal, Likert, or any other type of measure scoring as these are out of scope. It suggests resources for qualitative methods for collecting and prioritizing impacts from patients.

The commentary has sensitized us to the need to further clarify the PC-CIS effort to minimize future confusion. We have added a new section on viewing PC-CIS as a necessary precursor step for downstream uses in the forthcoming release of the updated PC-CIS Blueprint, further stressing PC-CIS are not measures but, as a qualitative precursor, can inform measure development as just one example of a downstream use.

2) The commentary refers to PC-CIS core value sets and value claims. This, again, is not our terminology. We state in the draft Blueprint that PC-CIS are use agnostic.(4) A PC-CIS is not referred to as or intended to be a claim, value claim, or evidence for a claim and nowhere in our documentation do we purport it as such. A medical-product claim must be based on a standard of evidence as defined by the Food and Drug Administration (FDA).(10) PC-CIS are proposed to be created by patient communities to ensure healthcare stakeholders understand what patients experience so stakeholders can leverage that information in their work, regardless of what that work might be.

As mentioned, PC-CIS can inform thinking about measure development. If a PC-CIS-informed outcome measure is developed and subsequently used in trials, the trial data could theoretically serve as the evidentiary basis for a claim. However, that is an example of a downstream use of a PC-CIS, not the PC-CIS itself. A PC-CIS can be leveraged to inform other downstream activities, not just Clinical Outcomes Assessment (COA) development or data capture to support claims. They

DOI: https://doi.org/10.24926/iip.v14i1.5264

might inform quality-of-care measure development, value and health technology assessment, clinical-trial endpoint selection, etc.(2, 4) We view the examples cited in the commentary, the Food and Drug Administration's Pilot Program for Standard Core Clinical Outcome Assessments, and ICHOM's disease-specific core outcome sets,(1) as examples of downstream uses that could be informed by a PC-CIS.

3) PC-CIS is in direct alignment with past and current FDA guidance on COA development, dating as far back as 2009.(6-9) Guidance states that patient input informs selection of the COI for a measure. That is, you need to figure out what the "thing" is you want to measure when you want to assess the clinical benefit of a treatment. PC-CIS could help inform that thinking by supporting COI selection and rationale, as depicted in the recently updated FDA COA Roadmap and described in new draft guidance.(9) PC-CIS capture information that can help researchers zero in on one or more target COIs for outcome measurement. FDA expects patient engagement in COI selection and COA development. A PC-CIS is a proposed efficient mechanism for making needed qualitative data widely available to researchers, a mechanism that has not existed to date. Again, we agree that standards exist for measure development. But, we know of no such existing standards for PC-CIS and, in fact, no PC-CIS are available to date (though pilots are in process).

Consider this hypothetical example. Osteoarthritis patients tell us through qualitative research that the impacts they experience from OA are pain, stiffness, stigma, and out-of-pocket costs. They report pain as most important and pain "constancy" throughout the day and night as having the most impact on their everyday lives. Knowing this information, a patient-reported outcome (PRO) measure for use in an intervention study is then developed using sound methods and focused on the COI, pain "constancy." Further, data collected using the sound measure will become available to inform clinical, regulatory, value, and/or formulary conversations. It is a chain of events that starts with understanding the most important impacts.(2) In fact, "impacts" is the term used in the 21st Century Cures Act, which directed the FDA to prepare four patient-focused drug development guidances based on patient experience data.[1](5,7-9)

It is a long road between identifying impacts patients report, to informing COI selection, to finally arriving at a measure that is well defined and reliable for a specific context of use.

4) The commentary contends PC-CIS will not be useful to formulary or other healthcare decision makers. We view these decisions as important downstream uses. For example, it should be noted that lack of measures and data on core impacts can be informative. One anecdotal report by a patient with kidney disease illustrates this point. The patient participated in a focus group to inform selection of outcomes (not specific measures) that should be collected in future trials. Fatigue was stated as a most-important impact by every patient in the group -- but was not included in the resulting list of what should be measured. When asked why, researchers said it was "too hard" to measure.

It is critical to avoid the scenario of researchers or others selecting a COI because it is easy or gives the answers someone wants – rather than measuring what is important to patients. Thus, a publicly available and well-disseminated PC-CIS could help improve that accountability.

When examining evidence (e.g., such as in a drug dossier) the question that should be asked is: What was the rationale for choosing the measure(s) and endpoint(s) used in these studies?(9) A lack of provided rationale is telling, as is a rationale that veers from what might be listed in a PC-CIS for the disease. The methods used in a study could be exemplary, but study findings are not useful if focused on unimportant or simply convenient concepts. Thus, when available, PC-CIS can and should be considered in measure and evidence evaluation.

5) The author also refers to the list of impacts in a PC-CIS as a "wish list." Patients do not wish for the sometimes-horrific impacts disease and treatment have on their lives. Patients often wish for these impacts to just go away. The thing that is most important to patients if often the desire to return to normal or wellness.

PC-CIS are proposed simply to qualitatively capture what patients tell us is important and we should be doing a better job of listening rather than suggesting it is "premature" to be attentive to the patient voice. We contend that one of the reasons the current evidentiary foundation is weak is because we have done a poor job listening to patients in general. PC-CIS is offered as one proposed mechanism for remedying that.

We wanted to provide clarification about PC-CIS, an initiative we believe has the potential to be very impactful for the future. The draft Blueprint is being updated based upon comments received during the public open-comment period and through a PCORI-funded dialogue meeting held August, 2022. The update will be available in early 2023. We encourage anyone interested to follow the progress of the NHC's PC-CIS initiative at https://nationalhealthcouncil.org/a-blueprint-for-developing-patient-centered-core-impact-sets-pc-cis/.

[1]21st Century Cures Act states the FDA will develop guidance that will address… "approaches to identifying and developing methods to measure *impacts* to patients that will help facilitate collection of patient experience data in clinical trials…"

DOI: https://doi.org/10.24926/iip.v14i1.5264

Acknowledgement: The PC-CIS initiative is being conducted by the National Health Council and has been funded by the EveryLife Foundation for Rare Diseases, the Innovation and Value Initiative, Amgen, Edwards, Johnson & Johnson, Merck, Novartis, PhRMA, Research Consortium for Health Care Value Assessment, Takeda. No funding was received or used for the preparation of this letter.

Declaration of author disclosures:

Dr. Perfetto is a Professor at the University of Maryland School of Pharmacy and an independent consultant. Dr. Perfetto was previously an employee of and is a current consultant to the National Health Council, a nonprofit, membership organization that receives dues, sponsorships, and grants. For a complete list of members, sponsors, and funders, see: www.nationalhealthhcouncil.org. In addition, Dr. Perfetto has past and ongoing research support and contracts from various non-profit organizations and for-profit companies that are unrelated to this work.

Suz Schrandt, JD, is the Founder and CEO of ExPPect; she serves as a consultant to the National Health Council on the Patient-Centered Core Impact Set Blueprint Initiative. Unrelated to this paper she has received funding from FACTORx, Research Triangle Institute, the Food and Drug Administration, the National Institutes of Arthritis and Musculoskeletal and Skin Diseases, the Monell Center, and the Society to Improve Diagnosis in Medicine.

Omar A. Escontrías, DrPH, MPH, is Vice President, Research, Education, and Programs at the National Health Council, a nonprofit, membership organization that receives dues, sponsorships, and grants. For a complete list of members, sponsors, and funders, see: www.nationalhealthhcouncil.org

Laurie B. Burke, Founder, LORA Group, and Affiliate Associate Professor, University of Maryland, Baltimore. Ms. Burke has past and ongoing research support and contracts from various non-profit organizations and for-profit companies that are unrelated to this work.

The opinions expressed in this paper are those of the authors.

References

1. Langley P. Evidentiary Standards for Patient-Centered Core Impact (PC-CIS) Value Claims. *InovPharm* 2022;13(3): No. 15.
2. Perfetto, E.M., Oehrlein, E.M., Love, T.R. *et al.* Patient-Centered Core Impact Sets: What They are and Why We Need Them. *Patient* 15, 619–627 (2022). https://doi.org/10.1007/s40271-022-00583-x
3. Perfetto, E.M., Love, T.R., Oehrlein, E.M., *et al.* A Blueprint To Advance Patient-Centered Core Impact Sets. Health Affairs Forefront June 14, 2022. Accessed on Nov 7, 2022 at 10.1377/forefront.20220610.963313
4. The National Health Council. A Blueprint for Developing Patient-Centered Core Impact Sets (PC-CIS). Accessed on Nov 7, 2022 at https://nationalhealthcouncil.org/a-blueprint-for-developing-patient-centered-core-impact-sets-pc-cis
5. Public Law 114–255 114th Congress. Title 1, Sections 3001 and 3002. Accessed Nov 7, 2022 at https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf
6. Food and Drug Administration. Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. December 2009. Access on Nov 7, 2022 at https://www.fda.gov/media/77832/download
7. Food and Drug Administration. Patient-Focused Drug Development: Collecting Comprehensive and Representative Input. Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders. Accessed Nov.7, 2022 at https://www.fda.gov/media/139088/download
8. Food and Drug Administration. Patient-Focused Drug Development: Methods to Identify What Is Important to Patients. Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders. Accessed Nov.7, 2022 at https://www.fda.gov/media/131230/download
9. Food and Drug Administration. Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments. DRAFT Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders. Accessed Nov.7, 2022 at https://www.fda.gov/media/159500/download
10. US Code of Federal Regulations, TITLE 21--FOOD AND DRUGS CHAPTER I--FOOD AND DRUG ADMINISTRATION DEPARTMENT OF HEALTH AND HUMAN SERVICES, SUBCHAPTER C - DRUGS: GENERAL, PART 202 -- PRESCRIPTION DRUG ADVERTISING. Accessed Nov 7, 2022 at https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-202