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COMMENTARY

The increasing complexity of the core outcomes landscape

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Abstract

In this project, we set out to identify ways to increase the uptake of core outcome sets in clinical research. In doing so, we uncovered a growing recognition, across many different health care sectors, of the need for common, relevant outcomes to improve the quality of decision-making. This has led to a plethora of projects, initiatives, and new organizations all intended to develop standardized outcomes and outcome measures for their particular fields. However, the standardized outcome sets developed across siloed initiatives do not carry over to other sectors, such as from research to quality of care. This trend has the potential to lead to confusion and unintended redundancies, as well as wasteful use of both financial and intellectual resources. Better communication and collaboration among different initiatives, and more deliberate alignments of initiative scopes, are needed to ensure a future paradigm in which standards align across contexts where possible and differ for understandable and transparent reasons.

Keywords: Core outcomes; core outcome sets; COS; Standardized outcome sets

1. Introduction

The current lack of relevant or comparable outcomes in clinical research undermines efforts across the health care sector to make evidence-based clinical or health policy decisions and improvements to health care delivery. This is often because outcomes collected across studies for the same disease or treatment are not uniform, or are not measured the same way, making an ''apples to apples'' comparison of important outcomes nearly impossible [1,2]. Available outcomes are also not always meaningful to patients, and may lack relevance to the decision-making at hand. Core outcome sets (COS) for clinical research are agreed-upon standardized collections of outcomes, representing one or more domains of a person's health and function, which should be measured and reported, as a minimum, in all trials for a specific clinical area or condition [3]. The main goal of COS is to promote more relevant and self-consistent bodies of evidence in research.

A critical aspect of COS development methodology should be meaningful patient engagement [4]. Thus, efforts to disseminate and promote uptake of COS in research theoretically align with other efforts to facilitate more relevant and patient-centered research and product development. COS development, including multistakeholder engagement and consensus building, can be rigorous when carried out right. Because of the multistakeholder approach, high-quality COS—those developed using robust methods of meaningful patient and stakeholder engagement, as well as reproducible and transparent processes of consensus building—could potentially offer a transparent vehicle for different organizations to input research priorities and communicate evidence needs and preferences to those conducting and designing research. When COS are broadly adopted in clinical research, we can anticipate better clarity and alignment around relevant outcomes across multiple decision-making authorities, including regulators, payers, and health technology assessors, in addition to patients, clinicians, and other health care decision makers. Yet despite the potential benefits of COS adoption, current uptake of COS in clinical research is varied at best.

2. Approach

We hosted a 1-day, in-person multistakeholder meeting in Baltimore, Maryland, to agree on current challenges related to the uptake of COS in clinical research and to brainstorm possible solutions. Multistakeholder participants represented a range of health care decision makers

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What is new?

Key findings

- This commentary providers readers with a greater understanding of the landscape of initiatives currently developing COS for research and standardized outcome sets for different contexts.

What this adds to what was known?

- This commentary adds more nuanced understanding of the growing number of COS, barriers and facilitators of COS uptake, and potential benefits of greater communication across similar initiatives.

What is the implication and what should change now?

- Creating channels of communication across similar initiatives to avoid redundancies and unnecessary conflicts of standards in the future, promoting awareness of COS, and more research supporting the value of COS for multiple decision makers.

who rely on clinical research findings to shape their work and inform their decisions, including patients, clinicians, payers, regulators, health system administrators, health technology assessors, systematic reviewers, manufacturers, and academia. Participants shared and discussed challenges they faced when making decisions within their respective organizations, with respect to the variability of reported research outcomes. They shared ongoing work within their own organizations that is relevant or similar to COS, and why they thought that work is important. Participants also broke into smaller groups to brainstorm solutions to broader COS adoption in detail.

3. Findings

3.1. There are many different decision-making contexts in health care that use clinical research results

As depicted in Fig. 1, a graphic recording from the stakeholder meeting, these include patients as "the true end user", making evidence-based decisions with their families and doctors about treatment decisions; organizations that design and conduct systematic reviews, aggregating study results to provide a clearer picture of available evidence to help inform multiple stakeholders; providers who struggle to standardize clinical care protocols to achieve clinically meaningful improvements in patient health outcomes; and payers attempting to compare the relative effectiveness and value of similar therapies to inform market access decisions, pricing, formulary tier assignments, or benefit design. Other relevant decision-making contexts include determining the efficacy or effectiveness of health interventions in different populations, monitoring health outcomes over time, and developing clinical practice guidelines. These decisions all stand to improve in quality as the body of evidence becomes more consistent with greater uptake of COS.

3.2. There are numerous groups developing COS for clinical research

The Core Outcome Measures in Effectiveness Trials (COMET) Initiative collaborates with others to improve the methods standards for developing and reporting COS [6], and serves as a hub for researchers, reviewers, health service users, clinical teams, journal editors, regulators, etc. interested in developing or promoting uptake of COS in clinical research. COMET maintains a searchable repository of ongoing and published COS across many disease areas. One of these disease areas is rheumatology, where the group called Outcome Measures in Rheumatology (OMERACT) has spearheaded methodology and development of COS for over 20 years. In recent years,

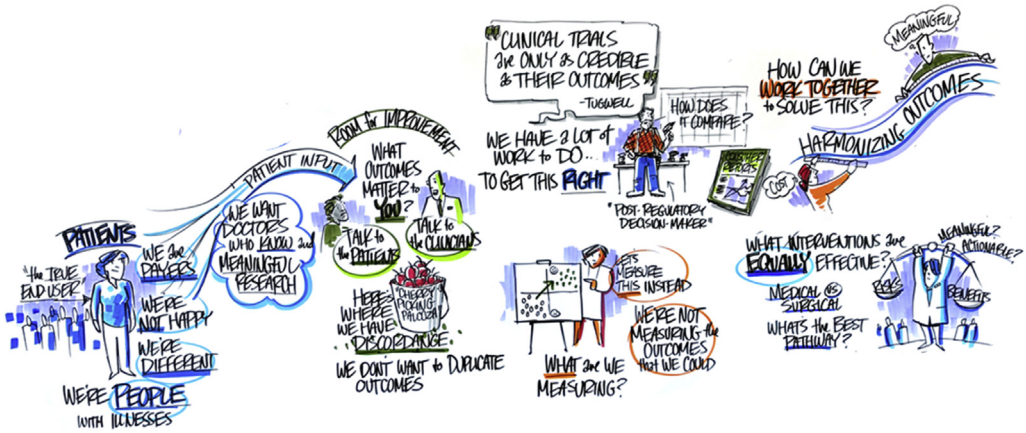

Fig. 1. Graphic recording from stakeholder meeting: current challenges of inconsistent evidence for decision makers. Adapted from Moloney RM, Messner DA, Al Naber J, Tunis SR. "Core outcome sets in clinical research: what are they and how can they help decision makers?" International Society for Pharmacoeconomics and Outcomes Research Annual International Meeting, Baltimore, MD May 2018.

the Center for Medical Technology Policy has begun utilizing the Green Park Collaborative, a neutral multistakeholder platform, to develop COS with focus especially on novel therapies and rare diseases, with broad input from payer, patient, clinician, regulatory, life sciences, and other stakeholder perspectives. The Patient-Centered Outcomes Research Institute has several ongoing initiatives, including a collaboration to explore the need and opportunity to standardize outcomes for real-world oncology research, and a rare disease advisory panel working to develop cross-cutting, patient-centered COS for studies of pediatric rare diseases. The U.S. Food and Drug Administration (FDA) also has several programs relevant to COS, such as a clinical outcomes assessment compendium, and the Patient-Focused Drug Development program. The FDA is also required by legislation to develop a series of four guidance documents describing how the patient voice can be obtained in a rigorous and systematic way that is representative of a population, with additional information about the methods of patient engagement at different stages of research and clinical outcomes assessment. An RFI issued by the FDA on July 31, 2018, solicited input from the public to inform ''planned work to promote development of publicly available standard core sets of Clinical Outcome Assessment (COA) measures for specific disease indications'' [7]. Despite the growing number of published COS, uptake in clinical research remains inconsistent at best. Specific barriers to uptake were identified during key informant interviews and vetted at the multistakeholder meeting. They include the lack of awareness of current COS initiatives and the perceived rise of multiple, sometimes conflicting, standards from decision-making organizations and agencies, which necessitates greater effort for researchers and product developers to navigate and prioritize.

3.3. There are also a growing number of initiatives resembling COS development but intended for use in health care contexts other than clinical research

While the term ''core outcome set'' originated in the clinical research context [8], there are now a growing number of initiatives across health care contexts that similarly emphasize standardizing outcomes and the way outcomes are measured to better inform decision-making (Fig. 2) [5]. These organizations reach beyond the scope of clinical research, to quality improvement and performance measurement, increasing their level of activity in defining valid, reliable, and meaningful measures of quality and patient outcomes. For example: The International Consortium for Health Outcomes Measurement (ICHOM) is working to develop core outcome measures sets for conditions to help assess value in the international health care market and inform purchasing decisions. The Centers for Medicare and Medicaid Services (CMS) Division of Quality Measurement is looking to engage with patients, families, and clinicians to develop standard measures with strong evidence base for public reporting on provider performance in a way that will help identify and address key performance gaps in U.S. health care delivery, across specific care delivery settings, such as hospitals, outpatient settings, and sites participating in quality-based payment programs. Finally, although it does not develop measures specifically, the National Quality Forum evaluates outcome measures and their underlying evidence base for their appropriate designation and use as standards for measuring quality of care.

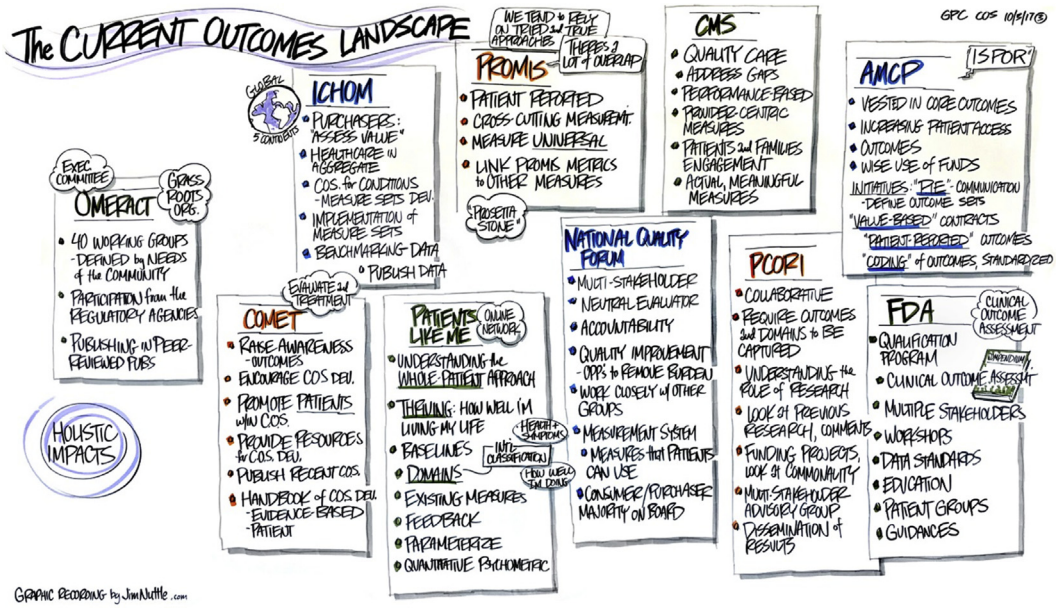

Fig. 2. Graphic recording from stakeholder meeting: key players in the current outcomes landscape.

The fact that there is a growing trend toward outcomes standardization across health care sectors suggests that many different stakeholder organizations perceive the benefit of doing so. Consider the potential importance of outcome standardization in the context of value assessment. A fundamental definition of ''value'' in health care is the improvement in outcomes relative to the cost of care. In this context, the articulation of outcomes meaningful to patients and other stakeholders is key to defining value for any product or service in health care. For value to be operationalized coherently in new agreements that involve accountability for costs and quality (e.g., alternative payment models), a minimum set of consistently collected patient/stakeholder-important outcomes is an essential mechanism to determine the value of care. While not all the outcomes selected for these different purposes readily translate between contexts, these siloed initiatives (Fig. 2) are moving forward without full attention to ensuring coordination wherever possible. At the stakeholder meeting, participants worried that payment for value and provider accountability in health care are moving the environment toward more fragmentation of outcome measures into siloes created by professional societies and organizations engaged in negotiations over quality metrics and payment.

Greater appreciation of the potential downfalls of this siloed environment led some stakeholders to articulate a new shared sense of urgency to devoting greater attention to increasing communication and awareness across initiatives. There was a common sense of apprehension that if groups continue down their own paths toward standardization without forging channels of communication and dialog, researchers and product developers may eventually face many different standards that would likely compete against each other. In that version of the future, there would be greater challenges for researchers and manufacturers; they would have to divert greater resources to consider and balance multiple obligations to meet unmatched standards across different agencies and decision-making bodies. This paradigm could severely slow innovation, working against the original intent of COS for research, and outcomes standardization more broadly.

4. Recommendations

Based on the findings described previously, we offer the following recommendations to improve awareness and uptake of COS while minimizing duplication of efforts across different initiatives and health care sectors.

1) Promote better awareness of COS using a focused message of patient-centeredness and transparency. Efforts to promote awareness of COS should recognize that COS could provide a baseline of consistency across different contexts. COS, by their nature, offer a potential vehicle by which health systems leaders, clinical guideline developers, and payers can guarantee a consistent influx of patient preferences and values into health care decisions across the range of decision-making. COS can also offer a vehicle to foster greater transparency and agreement between agencies responsible for regulatory decisions, coverage, health technology assessment and/or research funding, who can all rally behind the mantle of patient-centeredness, despite different missions and directives.
2) Open channels of communication between organizations that do similar work. There may be potential in the future for a network dedicated to linking and facilitating collaboration between these organizations. In the near term, a feasible first step is to simply start by creating channels of communication. This could be accomplished with minimal effort, either as a standalone platform or hosted by an existing platform such as the COMET initiative, and by identifying organizations and contact persons who should be included in outreach and engagement efforts going forward, perhaps even dedicating an index of contacts or an informal social network for like-minded outcome or measure standardization groups—for example, connecting groups working in rheumatology to contacts from OMERACT, or groups working in kidney disease to contacts from the SONG (Standardised Outcomes in Nephrology) initiative. A potential vehicle for creating these channels of communication may be the Red Hat Group, an early collaboration among several leading COS-development organizations, including OMERACT, COMET, the Green Park Collaborative, ICHOM, CSG-COUSIN, and GRADE. While in its formative stage, this collaboration may serve as a pilot for growing connections and sharing knowledge related to COS.
3) Engage broader representation of ''post-regulatory decision makers'' such as payers, health system leaders, health technology assessors, and clinical guideline developers in COS development. Greater representation in COS development enables greater opportunity for stakeholders to identify and call attention to variable fitness of COS in different contexts of use. Furthermore, COS developers keen to facilitate uptake of their COS should be proactive in seeking out stakeholder input and collaboration opportunities. Broadening the scope and starting the efforts of knowledge translation earlier in the COS development process will maximize the impact of targeted outreach aimed to minimize redundancies in standards.
4) Conduct more empirical research to support the adoption of COS. While recognizing that direct translation of outcomes across contexts will not always be feasible, a conscious assessment of similarities and essential differences may lead to opportunities for greater (even if partial) harmonization of outcomes

intended across different contexts. These are the types of questions that should be asked and answered with empirical research:

a. What are the different contexts for which standardized outcomes and outcome measures would benefit decision makers?
b. What characteristics define ''good'' (relevant, appropriate, or useful) outcomes for each of those contexts?
c. How well do existing COS meet those characteristics, or criteria?
d. What empirical evidence is needed to demonstrate that COS meet those criteria?

For example, in the context of quality and provider accountability, measures should link patient outcomes impacted by health care delivery to improvement activities that are associated with improved results. In other words, those outcomes-based measures should be actionable from a provider perspective, associated with cost savings or the potential for cost savings, and measured within a feasible amount of time to keep up with health system decision-making. Other questions that may help identify and develop stakeholder engagement, COS development, and knowledge translation plans may include

e. Do existing COS assumptions about available data and reporting requirements match the feasibility or reality of those contexts?
f. What are other barriers to COS uptake?
g. Which organizations are key players to promoting uptake in those contexts?
h. What groups are doing parallel work in the same disease area?

5. Discussion

As evidenced by Fig. 2, the outcomes measurement landscape is complex. The degree of overlap between different initiatives is not yet entirely clear. There are sometimes multiple standards developed for the same disease, but intended for different contexts, which could be compared and vetted by stakeholders. The different groups working to standardize outcomes point to a need for greater understanding of contextual differences and overlaps. With our limited knowledge, we can only articulate limited examples of areas that could be harmonized because we still lack an understanding of how best to align these different efforts. These contexts differ in terms of available data sources, appropriate measures and situation-specific measurement instruments.

At a time when CMS and private payers are starting to explore and develop their own definitions of core quality and clinical outcomes in different models for payment and accountability, the availability of already existing, patient-informed COS begs the question: would existing COS meet their needs, or do they need to spend time and resources developing a whole other set of standard outcomes?

CRediT authorship contribution statement

Rachael M. Moloney: Conceptualization, Methodology, Data curation, Writing - original draft, Project administration. **Donna A. Messner:** Conceptualization, Methodology, Writing - review & editing, Supervision, Funding acquisition. **Sean R. Tunis:** Conceptualization, Methodology, Writing - review & editing, Funding acquisition.

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