2nd COMET Network meeting

COMET Initiative North America Network Meeting

Date and venue

April 28, 2014; Center for Medical Technology Policy (CMTP) of Baltimore, MD, USA

Background

The Center for Medical Technology Policy (CMTP) of Baltimore, MD and the Core Outcome Measures in Effectiveness Trials (COMET) Initiative, led from the UK hosted a full day workshop and network meeting on Core Outcome Sets (COS) in Baltimore. CMTP is a non-profit organization that aims to make healthcare more effective and affordable by improving the quality, patient-centeredness and efficiency of clinical research. COMET (www.comet-initiative.org) seeks to foster exchange of ideas, resources, and methodological research in the area of COS.

This network meeting represented the first opportunity in North America for exchange of knowledge and feedback for those involved in COS development and use. The agenda opened with presentations by ten experts currently developing COS for use in clinical trials and other purposes, such as patient care, quality measurement and improvement, and patient-centered outcomes research (PCOR). Each presentation was followed by discussion and feedback from 12 representatives of federal agencies and national organizations with an interest in condition-specific, standardized health outcomes. These included individuals from the FDA, NIH, PCORI, PROMIS, AHRQ, Clinicaltrials.gov, the U.S. Cochrane Center and others.

Meeting Objectives

The objectives of the meeting were to:

1. Promote increased and higher quality work in COS in North America
2. Identify mechanisms to increase the uptake of COS
3. Enable COS developers to share experiences, insights, best practices and challenges
4. Learn about work of federal agencies and other organizations that may be relevant to the development and uptake of COS
5. Learn about the work of COMET
6. Identify opportunities for meeting participants to collaborate following the meeting.

Programme

8:30 am	Refreshments
9:00	Welcome and workshop objectives (Sean Tunis, CMTP)
9:20	COMET Initiative (Paula Williamson, University of Liverpool)
9:40	Presentations from Core Outcome Set developers - 5-7 minute overview of work to date
11:00	Refreshments
11:20	Large group discussion: - best practices - critical success factors - major challenges - potential solution - engaging patients and consumers - promoting uptake
12:35	Lunch
1:15 pm	Comments from public/private organizations with an interests in COS
2:30	Breakout group discussions - identify issues and activities of mutual interest - develop ideas for future work, collaboration
3:00	Refreshments
3:30	Large group discussion: - report back from breakout groups - agree on best ideas for action, collaboration, partnership, etc
4:00	The Way Forward (Paula Williamson, Sean Tunis, Peter Tugwell)
5:00	Meeting close

Attendees

COS Developers	
Jasmohan Bajaj, MD	Virginia Commonwealth University; McGuire VA Medical Center
Wendy Bennett, MD, MPH	Johns Hopkins University School of Medicine
Stephen Mathai, MD, MHS	Johns Hopkins University School of Medicine
Mark Pimentel, MD	Cedars-Sinai Medical Center
John Powers, MD	George Washington University School of Medicine
David Rahn, MD	University of Texas Southwestern Medical Center
Shannon Smith, PhD	University of Rochester Medical Center; ACTIION/IMMPACT
Alkis Togias, MD	Division of Allergy, Immunology, and Transplantation/ National Institute of Allergy and Infectious Diseases (DAIT/NIAID/NIH)
Jilda Vargus-Adams, MD	Cincinnati Children's Hospital Medical Center; University of Cincinnati College of Medicine
James Yao, MD	MD Anderson
Other Organizations	
Amy Abernethy, MD, PhD	Duke Clinical Research Institute (DCRI)
Ethan Basch, MD, MSc	University of North Carolina (UNC)
Kay Dickersin, PhD	US Cochrane Center
David Flum, MD, MPH	Director, Surgical Outcomes Research Center (SOURCE) University of Washington, Department of Surgery
Jason Gerson, PhD	Patient-centered Outcomes Research Institute (PCORI)
William Lawrence, MD, MS	Agency for Healthcare Research & Quality (AHRQ)
Bryan Luce, PhD, MD	Patient-centered Outcomes Research Institute (PCORI)
Elektra Papadopoulos, MD	US Food and Drug Administration (FDA)
Bill Riley, PhD	National Institutes of Health/National Cancer Institute (NIH/NCI); Patient Reported Outcomes Measurement Information System (PROMIS)
Jerry Sheehan, MS	National Institutes of Health/National Library of Medicine (NIH/NLM)
Marc Walton, MD, PhD	FDA Center for Drug Evaluation and Research (FDA)
Becky Williams, PhD	ClinicalTrials.gov/ National Institutes of Health (NIH)

Personnel	
Paula Williamson	Core Outcome Measures in Effectiveness Trials (COMET)
Peter Tugwell, MD, MSc	Core Outcome Measures in Effectiveness Trials (COMET)
Maarten Boers, MSc, MD, PhD	Core Outcome Measures in Effectiveness Trials (COMET)
Elizabeth Gargon, BS	Core Outcome Measures in Effectiveness Trials (COMET)
Sean Tunis, MD, MSc	Center for Medical Technology Policy (CMTP)
Elisabeth Houtsmuller, PhD	Center for Medical Technology Policy (CMTP)
Sandra Hwang	Center for Medical Technology Policy (CMTP)

Key Issues

Throughout the course of the workshop, four primary challenges were identified and discussed by attendees. Three of the four challenges reflect the growing emphasis on the objective of achieving greater "patient-centeredness" in research through COS.

Scope of COS

COS have the potential to reduce the burden of data collection from patients enrolled in trials by defining a minimum set of standardized core outcomes, including those that are likely to be most patient-centered – outcomes that are often collected directly from patients. Attendees agreed that patients should be engaged in the discussions of COS scope from the earliest stages. There was some discussion of the topic of including caregiver outcomes within the scope of COS for certain conditions.

Other challenges in defining the scope of COS include the variation in presenting symptoms, variation in how people perceive and measure pain and other subjective symptoms, and the difficulty of capturing a full range of important harms and adverse events in COS. It was generally agreed that the domains and outcomes should be identified before moving on to specific metrics and instruments; essentially, the "what" should be clarified before proceeding to the "how."

Quality Standards

As more work is being devoted to the development of COS, it is becoming more apparent that there is considerable variation in the methods by which they are developed, including the technical approaches and processes used. A number of participants commented on this issue, leading to the recognition that it would be useful to have tools that could be used to guide the development and reporting of high quality COS, and to assess the quality of completed COS. Some early stage activity toward this goal is underway within the COMET Initiative. A critical first step will be to identify the domains of quality to be applied when reviewing the process with which a COS has been developed. A mechanism to consistently conduct these quality assessments would be will also need to be explored.

Uptake and dissemination

The dissemination and uptake of COS was also recognized to be a shared topic of interest across the COS developers and other workshop participants. As with primary research, some attention to this issue is helpful to begin early on in the development work. Raising awareness of the existence of COS generally and of ongoing work in specific therapeutic domains is an important first step, and a

major objective of the COMET Initiative generally and this workshop as well. It was informally confirmed by the Baltimore workshop that agency officials, researchers and other experts and stakeholders have limited familiarity with COS.

Strategies to increase awareness will be an important precondition to increased impact. Given the lack of recognized quality standards for COS or a process for identifying those that meet minimal expectations, there is no reason to expect that researchers will have sufficient confidence to adopt any given set of COS. Furthermore, it is common for different research communities to develop their own shared approaches to study design, including outcomes, and they may be reluctant to adopt the recommendations of others, even when their own may not be optimal. COS developers can expect particular resistance when proposing outcomes that differ from those in longstanding use - "legacy" outcomes. Attendees discussed possible strategies to demonstrate the value of high quality COS and monitor their uptake.

One participant expressed the view that stakeholders with significant leverage to promote uptake of COS by researchers would be regulators, payers, research funders, and journal editors. Each of these groups makes a different type of decision informed by the quality of study designs (regulatory approval, reimbursement, project funding, and publication respectively) that could potentially be tied to the use of recognized, high quality COS. Research funders noted that it would be worth considering placing more emphasis on the use of existing COS in the review of research proposals. Clinicaltrials.gov may be able to influence uptake of COS by encouraging researchers to indicate the sources from which the outcomes selected for the study were identified, and perhaps providing information about the availability of the COMET database. Further exploration will be useful to determine what mechanisms might best be pursued to harness the capabilities of clinicaltrials.gov, and the other stakeholders identified as having potential influence on COS uptake.

Stakeholder engagement

The view was expressed that COS development is enhanced by the participation of a full range of stakeholders from the early stages of COS development, including patients, clinicians, payers regulators, research funders and others. At this point, this view is not supported by any empirical evidence, and it is unclear how one would go about demonstrating that this early engagement made for "better" COS. More thought and discussion of this topic would be useful.

There seemed to be very strong consensus that early engagement by patient groups in COS development, and possibly greater leadership of these efforts by patient advocacy organizations, is critically important in this field. Work by the COMET team has documented that the level of involvement of patients varies considerably across COS activities. In addition, while mature COS efforts have accumulated substantial experience engaging patients and consumers, the practices have not been well documented or disseminated.

Regulatory input is potentially important given the very strong influence of regulators on how pharmaceutical companies design their trials. However, COS developers remarked on the difficulty of sustaining ongoing participation of regulatory experts, most likely due to the limited bandwidth of these individuals to engage in external projects, given the potentially huge demand. As the regulatory community gets more engaged in issues such as patient-focused drug development, comparative effectiveness research, and related issues, it may become a higher priority for them to participate in selected activities that have demonstrated a sufficient level of stakeholder participation and potential influence.

The participation of experts from the life sciences industry is clearly valuable from a number of perspectives, including deep technical expertise in specific clinical conditions, and also the importance of this engagement in enhancing the potential for uptake of the COS by these organizations. In addition, these companies have provides substantial resources for COS development in some cases. This obviously raises issues of potential conflict of interest, but good models for managing these conflicts have been developed by OMERACT and other groups, and future activities can be guided by this mature experience.

Federal representatives and other national groups at the workshop generally noted that the discussion triggered many thoughts about potential future collaboration with COS developers. A number of conversations during breaks in the meeting produced some promising early discussions about such collaboration, and we are aware that some of these discussions have continued following the meeting. Developing these ideas further may be promoted by convening a follow up webinar or meeting, with a specific focus on presenting and discussing potential joint activities.

Conclusion

Informal feedback from workshop participants during and after the meeting suggested that the content of the discussions was of high interest, and many participants were eager to find ways to continue the discussion. Following the meeting, there have been a number of interactions between COMET experts and individuals from the FDA, PCORI and NIH. Most people in the room were unaware of many of the other initiatives that were discussed, and recognized that there was a considerable amount of complementary activity going on, with considerable potential for collaboration. The biggest challenge for turning the enthusiasm into some concrete progress is the fact that everyone is busy, and a substantial time commitment would be required to identify and further define the most promising follow up activities to pursue. This will be a focus of discussion between CMTP, COMET, PCORI and others.