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The WONDER Project

Riordain, Richeal Ni; Farag, Arwa M.; Villa, Alessandro; Robledo-Sierra, Jairo; Delli, Konstantina; Taylor, Jennifer

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EDITORIAL

The World Workshop on Oral Medicine Outcomes Initiative for the Direction of Research Project

The spectrum of conditions managed by Oral Medicine specialists is wide. It includes, among others, ulcerative and vesiculobullous diseases of the oral cavity, orofacial neuropathies, salivary gland disorders, oral complications from cancer therapy, and potentially malignant oral disorders, which may cause severe morbidity and mortality.[1] Due to the chronicity of many of these conditions, most treatments' primary management strategies are typically symptomatic and not curative. The risk-benefit balance for all treatments should be considered before commencement and ideally be accompanied by a high-quality evidence base to support the decisions made by clinicians.

There is a pivotal need to improve the quality of the existing evidence base in Oral Medicine. Meta-analyses of systematic reviews and randomized controlled trials are the pinnacle of the hierarchy of evidence. Various research groups have promoted the development of systematic reviews, most notably the Cochrane Oral Health Group (https://oralhealth.cochrane.org). Specifically for Oral Medicine, Professor Sir David Mason and Dr. Dean Millard founded the World Workshop on Oral Medicine (WWOM) in the 1980s with the goal of establishing international collaborative research groups to explore clinical topics of interest to the Oral Medicine community.[2] Over the last 40 years, numerous high-quality systematic reviews have been published by the WWOM,[3] adding to the evidence base in the specialty. Several of these well-cited systematic reviews have concluded that there is a lack of homogeneity of outcomes used in clinical trials.[4,5] This outcome heterogeneity precludes meaningful meta-analysis and limits the translation of available scientific evidence to guide clinical decision-making.[6] Thus, in January 2020, the World Workshop on Oral Medicine VIII (WWOM VIII) set out to address the inconsistencies in Oral Medicine clinical research outcomes by introducing the **W**orld Workshop on Oral Medicine **O**utcomes I**n**itiative for the **D**irection of **R**esearch (WONDER). This new initiative aims to align Oral Medicine with other medical specialties by developing core outcome sets (COSs) for conditions managed in Oral Medicine clinics. This builds on the pioneering work in Oral Medicine by Taylor et al. and Venda Nova et al., who developed the COS for recurrent aphthous stomatitis[7] and trigeminal neuralgia,[8-10] respectively.

A COS is an agreed standardized set of outcomes that should be minimally measured and reported in all clinical trials of a specific condition.[11] This does not mean that other outcomes cannot be collected, but rather that the COS defines a minimum standard, with the expectation that the primary outcomes will be contained in the COS.[11] Successful COS initiatives have been established in disciplines such as Rheumatology, Dermatology, and Women's and Neonatal Health. The Outcome Measures in Rheumatology (OMERACT), established in 1992, used rigorous methods to support the development of COS for patients with autoimmune and musculoskeletal diseases.[12] The OMERACT now has 35 working groups and over 2250 publications, facilitating meta-analysis and providing robust scientific evidence for numerous rheumatological conditions. The Consortium for Harmonizing Outcomes Research in Dermatology (CHORD) develops, disseminates, and implements COS for clinical trials in Dermatology and builds on the work of the Cochrane Skin Core Outcome Set Initiative (CS-COUSIN), established in 2014.[13,14] Around the same time, the Core Outcomes in Women's and Newborn Health initiative was launched due to identified outcomes heterogeneity limiting meaningful data synthesis. An additional concern was that the outcomes reported in Women's and Newborn health were not always considered relevant or important by patients.[15]

With the increased interest in the development of COS across various health care disciplines, there was a need for a robust and reproducible method that individual working groups could adopt. The Core Outcome Measures in Effectiveness Trials (COMET) initiative (www.comet-initiative.org), an international group of multiple stakeholders, proposed a standardized 2-part methodological framework for developing COS. The initial part determines "what to measure" or the outcome domains in the COS, whereas the second part establishes "how to measure" these core sets of domains.[16] The first 2 projects of WONDER were the development of COS for oral lichen planus (OLP) and dry mouth. These projects determined "what to measure" using the method recommended by COMET[16]: (i) identification of existing knowledge via a systematic review to determine what outcome domains are currently measured, (ii) determination of what measures are important that are being missed based on inputs

from various stakeholders, and (iii) finally the use of a consensus process to determine the COS of domains that should be minimally measured in all future clinical trials.

ORAL LICHEN PLANUS

Oral lichen planus is a chronic inflammatory condition with autoimmune features and is one of the most common oral mucosal diseases affecting nearly 1% of the population worldwide.[17] In its most aggressive forms, OLP causes pain, burning sensation, and discomfort, which may negatively impact the patient's quality of life.

Following the COMET Initiative, the first step in developing a COS for OLP was identifying the outcomes used in previous interventional studies. For this purpose, a systematic review was conducted to identify all primary and secondary outcomes reported in OLP interventional studies over the past 2 decades.[18] In the second step, the outcomes (n = 69) identified in the systematic review were brought to focus groups of patients with OLP to identify other relevant outcomes through synergistic discussions between individuals with different disease experiences.[19] Thereafter, the individual outcomes identified through these 2 processes were categorized into outcome domains (n = 15) by various working groups. In the third and final step, a consensus was achieved among the stakeholders (i.e., clinicians, researchers, and patients) on 11 outcome domains to be included in the COS for OLP through various voting procedures, including a Delphi clicker session that occurred during the American Academy of Oral Medicine Annual Conference held in Memphis, USA, in May 2022.[20]

DRY MOUTH

Dry mouth is a common condition that can significantly impair oral health, speaking, eating, and the overall quality of life and increase the economic burden associated with using health care services.[21,22] The term dry mouth encompasses xerostomia, salivary gland hypofunction, and hyposalivation. The reported prevalence among the general population varies considerably from 5.5% to 46%.[23,24] As the population ages, the prevalence of dry mouth is likely to increase, yet the condition appears to remain underrecognized and undertreated.[21,25]

To allow the development of COS for dry mouth following the suggested steps of the COMET Initiative,[26] 2 systematic reviews were conducted to explore the existing outcomes and outcome measures for salivary gland hypofunction[27] and xerostomia.[28] At the same time, qualitative interviews with patients experiencing dry mouth were performed to identify outcomes that are important to them.[29]

The project identified 22 outcome domains through the 2 systematic reviews and the patient focus groups. The domains were presented to the attendees of the American Academy of Oral Medicine Annual Conference held in Memphis, USA, in May 2022 as a Delphi Survey, as well as to patient focus groups. Consequently, a consensus was reached for 12 outcome domains to be included in the COS for dry mouth.[30]

FUTURE DIRECTIONS

With the establishment of the COS of domains for OLP and dry mouth, the WONDER projects will progress to the second stage of development, which is how to best measure the domains. This phase of development will include systematically reviewing the literature for existing measurement instruments or tools for each of the outcome domains in the COS, assessing the quality and suitability of these instruments for use in the specific patient population, and using a consensus process, once again, to make recommendations as to which instruments should be used as a minimum in future trials in OLP and dry mouth.[11] Methodological guidance will be sought from the Consensus-based Standards for the selection of health Measurement Instruments initiative (http://www.cosmin.nl/) to determine the quality and suitability of the instruments. This will allow a robust evaluation of the psychometric properties of the instruments under consideration, ensuring that the tools will be valid and reliable for use in trials for interventions on OLP and dry mouth.

The role of the WWOM, specifically in the context of the WONDER projects, will require not only the development of the COS of domains and instrument recommendations but also the promotion of COS adoption by researchers, funding bodies, and regulators. Once the final consensus has been reached on the minimum set of instruments that will allow the recording of the COS, it is critical to disseminate the COS and promote its use among researchers and clinicians in the future. When considering dissemination and incorporation into research, the plan is to evaluate how well the previously published COS from other medical disciplines have been incorporated into clinical trials. There is evidence from Rheumatology that over 80% of trials evaluating pharmacologic interventions in rheumatoid arthritis have incorporated the COS developed by the OMERACT initiative.[31] This increased uptake of the COS in clinical trials was directly influenced by recommendations coming from agencies such as the Food and Drug Administration and the European Medicines Agency.[31]

In conclusion, it is the hope of the WWOM that the WONDER initiative will promote homogeneity of outcome measurement in Oral Medicine research. This will facilitate the pooling of study results and, hence,

allow for meta-analysis of data, leading to a higher-quality evidence base and, consequently, the most robust clinical decision-making in the future.

DECLARATION OF INTEREST

None.

Richeal Ni Riordain, MBBS, BDS, MA (Higher Ed), PhD, MFD, FFD, FDS(OM),*
Cork University Dental School and Hospital, University College Cork, Cork, Ireland
Arwa M. Farag, BDS, DMSc,
Department of Oral Diagnostic Sciences, Faculty of Dentistry, King Abdulaziz University Jeddah, Saudi Arabia
Department of Diagnostic Sciences, Oral Medicine Division, Tufts University School of Dental Medicine, Boston, MA, USA
Alessandro Villa, DDS, PhD, MPH,
Miami Cancer Institute, Baptist Health South Florida, Miami, FL, USA
Department of Translational Medicine, Herbert Wertheim College of Medicine, Florida International University, FL, USA
Department of Orofacial Sciences, University of California San Francisco, San Francisco, CA, USA
Jairo Robledo-Sierra, DDS, MSc, PhD,
Faculty of Dentistry, CES University, Medellin, Colombia
Konstantina Delli, DDS, MSc, PhD,
Department of Oral and Maxillofacial Surgery, University of Groningen, University Medical Center Groningen, Groningen, Netherlands
Jennifer Taylor, BDS, MBChB, PhD, MFDSRCS, FDS(OM)
Department of Oral Medicine, Glasgow Dental Hospital and School, Glasgow, UK

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