World Workshop on Oral Medicine VIII: Development of a core outcome set for oral lichen planus: a consensus study

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Objective. A core outcome set (COS) is the minimum agreed-on data set required to be measured in interventional trials. To date, there is no COS for oral lichen planus (OLP). This study describes the final consensus project that brought together the results of the previous stages of the project to develop the COS for OLP.

Study Design. The consensus process followed the Core Outcome Measures in Effectiveness Trials guidelines and involved the agreement of relevant stakeholders, including patients with OLP. Delphi-style clicker sessions were conducted at the World Workshop on Oral Medicine VIII and the 2022 American Academy of Oral Medicine Annual Conference. Attendees were asked to rate the importance of 15 outcome domains previously identified from a systematic review of interventional studies of OLP and a qualitative study of OLP patients. In a subsequent step, a group of OLP patients rated the domains. A further round of interactive consensus led to the final COS.

Results. The consensus processes led to a COS of 11 outcome domains to be measured in future trials on OLP.

Conclusion. The COS developed by consensus will help reduce the heterogeneity of outcomes measured in interventional trials. This will allow future pooling of outcomes and data for meta-analyses. This project showed the effectiveness of a methodology that could be used for future COS development. (Oral Surg Oral Med Oral Pathol Oral Radiol 2023;135:792−803)

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Statement of Clinical Relevance

Using a core outcome set for oral lichen planus would reduce the heterogeneity of outcomes in clinical trials and improve evidence-based interventions. The consensus process described here is the final stage of a three-stage project for developing a core outcome set for oral lichen planus.

Oral lichen planus (OLP) is a chronic inflammatory condition of the oral mucosa with potential malignant transformation.[1-4] It affects approximately 1% of the global population and usually presents in women after the fourth decade of life.[5] The most aggressive forms of OLP can cause pain, soreness, itching, and a burning sensation, which may negatively impact oral function and decrease quality of life.[6,7] The treatment of OLP is intended to reduce symptoms.[8,9] Topical corticosteroids are the gold standard, but other topical, systemic, and non-pharmacological treatments, such as photobiomodulation therapy, are available.[10-13]

Outcomes are variables monitored during a study to reflect the impact of a given intervention on patient health.[14] Systematic reviews on the treatment of OLP have highlighted the heterogeneity in clinician- and patient-reported outcomes among the included studies.[11,15] This heterogeneity makes it difficult to perform meta-analyses and establish the best evidence-based treatment protocol for OLP.[11] Developing a core outcome set (COS) would allow for the pooling of homogenous data for meta-analyses and yield a higher quality of evidence for clinicians to access when making treatment decisions for patients with OLP.[16] However, to date, there is no agreement as to which outcomes should be included in a COS for OLP.

The World Workshop on Oral Medicine (WWOM) Outcomes Initiative for the Direction of Research (WONDER Project) was created to develop a COS for conditions managed by the oral medicine specialty using an established methodology from the Core Outcome Measures in Effectiveness Trials (COMET) group.[14] A three-phase project to develop a COS for OLP was initiated as part of the WWOM VIII) held in Memphis, TN, USA, on May 2 and 3, 2022. The first phase of this project was a systematic review to identify the outcomes collected in interventional studies on OLP (10.1016/j.oooo.2023.01.014). The second phase was a qualitative study of patients with OLP to identify other important patient-reported outcomes (10.1016/j.oooo.2023.02.015). The third phase, presented here, was determining the COS after reaching a consensus among all the stakeholders involved. This study aimed to summarize the findings from the first 2 phases and show how these results were used to inform the final consensus process to determine the COS for future trials of OLP.

MATERIALS AND METHODS

The protocol of this study was previously registered in the COMET Database (https://www.comet-initiative.org/Studies/Details/1558) and followed the COMET guidelines.[14] This study was the third stage of a three-phase project to determine the COS for OLP within the WONDER Project. The methodology for developing the COS followed the established three-phase process of identification of existing knowledge, patient involvement, and the process of reaching consensus.[16]

Identification of Existing Knowledge

A systematic review was undertaken to establish a list of outcomes measured in interventional trials for OLP (10.1016/j.oooo.2023.01.014). This yielded an extensive list of 69 individual outcomes grouped into appropriate domains by the WWOM VIII OLP Working Group (R.M.L-P., M.D.F., S.S.K.R., J.A.V., C.B., H. D., J.R.-S., and J.T.).

Patient Involvement

A qualitative study of patients with OLP of varying severity treated with topical or systemic therapy was conducted (10.1016/j.oooo.2023.02.015). Both newly diagnosed and longstanding patients were included, and the duration since diagnosis was considered. Discussion of the outcome measures and experiences of living with OLP yielded a list of outcome domains introduced for patient feedback. The patients agreed on all the domains and added an outcome not previously included.

Consensus Reaching

An international group of experts in Oral Medicine was established with 12 members from 7 countries who had attended the WWOM VIII. The characteristics of the members are shown in Table I. This working group discussed all the domains identified in the first (10.1016/j.oooo.2023.01.014) and second (10.1016/j.oooo.2023.02.015) phases of the project. Once the group assessed the adequacy of these 15 domains, the survey questions for the voting sessions and the information the participants would receive were drafted.

The consensus process was achieved through a four-stage approach. Before conducting the surveys, the participants received verbal and written information explaining the process. Open communication enabled any concerns to be raised.

Stages. STAGE 1: WWOM VIII PARTICIPANTS. The first clicker session was conducted on May 3, 2022, at the WWOM VIII. This was a pilot session to test the process

Table I. Members of the World Workshop on Oral Medicine VIII OLP Expert Working Group

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OLP, oral lichen planus; NHS, National Health Service.

and gain feedback from participants to inform the main consensus process. A group of Oral Medicine experts, all participants in the WWOM VIII (Steering Committee, Consultants, Reviewers, Assistant Reviewers, and Observers), participated in a round of interactive voting.

STAGE 2: 2022 AMERICAN ACADEMY OF ORAL MEDICINE ANNUAL CONFERENCE PARTICIPANTS. The second clicker session was conducted on Friday, May 6, at the 2022 American Academy of Oral Medicine (AAOM) Annual Conference in Memphis, TN, USA. All the participants attending this meeting were invited to vote on the 15 domains using the 9-point Likert scale described below.

STAGE 3: PATIENT FOCUS GROUPS. Ten patients diagnosed with OLP from the Oral Medicine Unit of Cork University Dental School and Hospital, Cork, Ireland, participated in an interactive voting round (10.1016/j.oooo.2023.02.015). They voted on the 15 domains using the same 9-point Likert scale.

STAGE 4: FINAL CONSENSUS. Online interactive meetings were carried out with the WWOM VIII OLP Expert Working Group to discuss the results from the initial 3 stages of voting. A final vote was taken on domains for which support appeared unclear. The domains for inclusion in a COS were determined.

Resources to conduct the clicker sessions. Mentimeter (Mentimeter, Stockholm, Sweden), an eponymous application that can be embedded in presentations to provide real-time feedback, was used to carry out the interactive clicker process. The participants connected to the website via their smartphones or other internet device using a previously established code. The

questions were projected on the presentation slides and could be viewed on the participants' devices. After the participants had identified their continent of origin and current position, they were asked how important they considered each of the previously identified domains using their devices. Once the participants had started voting, the results could be visualized on the presentation slides. After the conclusion of voting for each domain, the data were saved.

Methods of scoring. Using a 9-point Likert scoring system recommended by the Grading of Recommendations Assessment, Development, and Evaluation Working Group for assessing the importance of research evidence[17] allowed the participants to grade the importance of each domain. In this system, a score of 1 to 3 means that an outcome is of limited importance, 4 to 6 that it is important but not critical, and 7 to 9 that it is critical.

Consensus definition. Consensus on including an outcome in the COS was defined as 70% or more of respondents rating it 7 to 9 and <15% rating it 1 to 3. Consensus on the non-inclusion of an outcome in the COS was defined as 70% or more rating it 1 to 3 and <15% rating it 7 to 9. All other distributions of scores were considered to indicate a lack of agreement for the inclusion of a given outcome in the COS.[18]

The arithmetical mean between the response rates of OLP patients and health care providers who attended the 2022 AAOM Annual Conference was calculated to reach a consensus. A final round of voting took place after live interactive discussions among the WWOM VIII OLP Expert Working Group members to establish whether the domains lacking agreement were selected. In this voting stage, the members were instructed to answer "yes/in" or "no/out," depending on whether they felt the domain should be included in the final COS for OLP. Consensus to include an outcome was achieved only when ≥70% participants voted "yes." The final COS did not include outcomes with an agreement of <70%.

Statistical Analysis

Descriptive statistical analysis of the data was performed to determine the number and percentage of participants who voted that an outcome domain was of limited importance, was important but not critical, and was critical. The arithmetical mean of the results obtained at the 2022 AAOM Annual Conference and from patients with OLP was calculated using Microsoft Excel (Microsoft Corp., Redmond, WA, USA).

RESULTS

Final Domains

The WWOM VIII OLP Working Group classified the 69 final outcomes obtained from the systematic review into 14 outcome domains. The new and previously unidentified theme, "knowledge and understanding of health care practitioners, family, and friends," was identified in the second phase, which comprised interviews with the OLP patients. Therefore, this domain was added to the 14 previously identified domains, resulting in the following 15 potential domains:

- Appearance of lesions
- Severity of lesions
- Symptoms
- Function
- Social impact
- Psychological impact
- Patient support from family and friends
- Compliance and tolerability
- Overall patient satisfaction
- Adverse events
- Economic impact
- Timelines
- Need for rescue medication
- Biomarkers post-treatment initiation
- Histopathology post-treatment initiation

Drafting of Survey Questions

The WWOM VIII OLP Expert Working Group reviewed and confirmed the final domains identified. Based on these domains, the survey questions (Table II) were drafted to assess the importance of including these domains in future clinical trials on treating OLP. Questions were drafted in the following format: In every future trial testing a treatment for OLP, how important is it to measure, e.g., the appearance of lesions? This format emphasized that such outcomes should be assessed in all clinical studies on treating OLP. Explanatory notes accompanied these questions to help participants relate the domain to the associated outcomes. In addition, an information sheet was handed out before the clicker session so that participants would have sufficient information about the objectives of the project, what a COS means, the stages for defining a COS, the definition of the consensus process, the grading of the questions, and the evaluation of the results (Appendix 1).

Results of the WWOM VIII Clicker Session

Twenty-nine people participated in the clicker session held at the WWOM VIII (Stage 1). Of the 27

Table II. Survey questions for interactive clicker sessions

Q1. In every future trial testing a treatment for OLP, how important is it to measure APPEARANCE OF LESIONS (e.g., red and/or white in color and presence of ulceration)?
Q2. In every future trial testing a treatment for OLP, how important is it to measure the SEVERITY OF LESIONS (e.g., extent and activity)?
Q3. In every future trial testing a treatment for OLP, how important is it to measure SYMPTOMS (e.g., pain, sensitivity, and burning)?
Q4. In every future trial testing a treatment for OLP, how important is it to measure FUNCTION (e.g., eating, speaking, and tooth brushing)?
Q5. In every future trial testing a treatment for OLP, how important is it to measure SOCIAL IMPACT (e.g., interference with work and family life)?
Q6. In every future trial testing a treatment for OLP, how important is it to measure PSYCHOLOGICAL IMPACT (e.g., anxiety and depression)?
Q7. In every future trial testing a treatment for OLP, how important is it to measure PATIENT SUPPORT FROM FAMILY AND FRIENDS?
Q8. In every future trial testing a treatment for OLP, how important is it to measure PATIENT COMPLIANCE AND TOLERABILITY?
Q9. In every future trial testing a treatment for OLP, how important is it to measure OVERALL PATIENT SATISFACTION?
Q10. In every future trial testing a treatment for OLP, how important is it to measure ADVERSE EVENTS (local and/or systemic)?
Q11. In every future trial testing a treatment for OLP, how important is it to measure ECONOMIC IMPACT (e.g., costs)?
Q12. In every future trial testing a treatment for OLP, how important is it to measure TIMELINES (e.g., time to response and duration of effect)?
Q13. In every future trial testing a treatment for OLP, how important is it to measure NEED FOR RESCUE MEDICATION?
Q14. In every future trial testing a treatment for OLP, how important is it to measure BIOMARKERS POST-TREATMENT INITIATION (e.g., blood and saliva tests)?
Q15. In every future trial testing a treatment for OLP, how important is it to measure HISTOPATHOLOGY POST-TREATMENT (e.g., cell changes and cancer development)?

OLP, oral lichen planus.

participants connected at the start of the clicker session, 23 were Oral Medicine specialists, 1 was an Oral Medicine trainee/resident, 2 were practitioners of another dental specialty, and one was an allied health care provider. Two additional participants joined after the collection of baseline demographic characteristics. The session prompted much debate regarding the wording of the questions and the information the participants needed before being able to vote. This pilot session allowed the presentation and clicker voting to be trialed, leading to further improvements in the delivery of the clicker session before the main event.

After applying the consensus criteria, the results of the clicker session (Table III) showed that the following domains must be included in the COS for OLP based on the voting of the WWOM VIII participants:

- Appearance of lesions
- Severity of lesions
- Symptoms
- Function
- Psychological impact
- Patient compliance and tolerability
- Overall patient satisfaction
- Adverse events
- Timelines

The following domains lacked consensus for inclusion:

- Social impact
- Patient support from family and friends
- Economic impact
- Need for rescue medication
- Biomarkers post-treatment initiation

Only one domain was voted for non-inclusion in the COS:

- Post-treatment initiation histopathology.

Results of the AAOM Annual Conference Meeting Clicker Session

Ninety-six participants participated in the AAOM Annual Conference Meeting clicker session (Stage 2). Of the 84 participants who accessed the voting system at the beginning of the session, 64 were from the United States, 9 were from Europe, 5 were from South America, 5 were from Asia, and 1 was from Australia. Ninety-one participants recorded their current position. Of these, 46 were university or hospital-based Oral Medicine specialists, 12 were general dentists, 10 were dentists within another dental specialty, 9 were Oral Medicine trainees or residents, 7 were Oral Medicine specialists in private practice, 2 were allied health care providers, 1 was a researcher in another specialty, and 4 were practitioners in other specialties or positions.

By applying the consensus criteria, the participants in this clicker session voted that the following domains should be included in the COS for OLP treatment (Table IV):

- Appearance of lesions
- Severity of lesions

Table III. Results of the World Workshop on Oral Medicine VIII clicker session.

Questions	*Limited importance n (%)*	*Unclear importance n (%)*	*Critical importance n (%)*	*No. of participants for each question*	*Consensus*
Q1. In every future trial testing a treatment for OLP, how important is it to measure APPEARANCE OF LESIONS (e.g., red and/or white in color and presence of ulceration)?	3 (11.11)	4 (14.81)	20 (74)	27	Inclusion
Q2. In every future trial testing a treatment for OLP, how important is it to measure SEVERITY OF LESIONS (e.g., extent and activity)?	0	2 (7.14)	26 (92.86)	28	Inclusion
Q3. In every future trial testing a treatment for OLP, how important is it to measure SYMPTOMS (e.g., pain, sensitivity, and burning)?	0	0	27 (100)	27	Inclusion
Q4. In every future trial testing a treatment for OLP, how important is it to measure FUNCTION (e.g., eating, speaking, and tooth brushing)?	1 (3.57)	0	27 (96.43)	28	Inclusion
Q5. In every future trial testing a treatment for OLP, how important is it to measure SOCIAL IMPACT (e.g., interference with work and family life)?	0	9 (32.14)	19 (67.86)	28	Lack of agreement
Q6. In every future trial testing a treatment for OLP, how important is it to measure PSYCHOLOGICAL IMPACT (e.g., anxiety and depression)?	0	5 (18.52)	22 (81.48)	27	Inclusion
Q7. In every future trial testing a treatment for OLP, how important is it to measure PATIENT SUPPORT FROM FAMILY AND FRIENDS?	14 (51.85)	9 (33.33)	4 (14.82)	27	Lack of agreement
Q8. In every future trial testing a treatment for OLP, how important is it to measure PATIENT COMPLIANCE AND TOLERABILITY?	0	2 (7.41)	25 (92.59)	27	Inclusion
Q9. In every future trial testing a treatment for OLP, how important is it to measure OVERALL PATIENT SATISFACTION?	0	8 (29.63)	19 (70.37)	27	Inclusion
Q10. In every future trial testing a treatment for OLP, how important is it to measure ADVERSE EVENTS (local and/or systemic)?	0	0	27 (100)	27	Inclusion
Q11. In every future trial testing a treatment for OLP, how important is it to measure ECONOMIC IMPACT (e.g., costs)?	6 (20.69)	9 (31.03)	14 (48.28)	29	Lack of agreement
Q12. In every future trial testing a treatment for OLP, how important is it to measure TIMELINES (e.g., time to response and duration of effect)?	2 (7.41)	2 (7.41)	23 (85.18)	27	Inclusion
Q13. In every future trial testing a treatment for OLP, how important is it to measure NEED FOR RESCUE MEDICATION?	4 (15.38)	4 (15.38)	18 (69.24)	26	Lack of agreement
Q14. In every future trial testing a treatment for OLP, how important is it to measure BIOMARKERS POST-TREATMENT INITIATION (e.g., blood and saliva tests)?	12 (48)	9 (36)	4 (16)	25	Lack of agreement
Q15. In every future trial testing a treatment for OLP, how important is it to measure HISTOPATHOLOGY POST-TREATMENT INITIATION (e.g., cell changes and cancer development)?	18 (72)	6 (24)	1 (4)	25	No inclusion

OLP, oral lichen planus.

- Symptoms
- Function
- Psychological impact
- Patient compliance and tolerability
- Overall patient satisfaction
- Adverse events
- Timelines
- Need for rescue medication

The following domains lacked consensus for inclusion:

- Social impact
- Patient support from family and friends
- Economic impact
- Biomarkers post-treatment initiation
- Histopathology post-treatment

Table IV. Results of the 2022 American Academy of Oral Medicine Annual Conference clicker session

Questions	*Limited importance n (%)*	*Unclear importance n (%)*	*Critical importance n (%)*	*No. of participants for each question*	*Consensus*
Q1. In every future trial testing a treatment for OLP, how important is it to measure APPEARANCE OF LESIONS (e.g., red and/or white in color and presence of ulceration)?	1 (1.075)	7 (7.53)	85 (91.40)	93	Inclusion
Q2. In every future trial testing a treatment for OLP, how important is it to measure SEVERITY OF LESIONS (e.g., extent and activity)?	0	1 (1.1)	90 (98.9)	91	Inclusion
Q3. In every future trial testing a treatment for OLP, how important is it to measure SYMPTOMS (e.g., pain, sensitivity, and burning)?	0	2 (2.11)	93 (97.89)	95	Inclusion
Q4. In every future trial testing a treatment for OLP, how important is it to measure FUNCTION (e.g., eating, speaking, and tooth brushing)?	0	9 (9.37)	87 (90.63)	96	Inclusion
Q5. In every future trial testing a treatment for OLP, how important is it to measure SOCIAL IMPACT (e.g., interference with work and family life)?	8 (8.33)	22 (22.92)	66 (68.75)	96	Lack of agreement
Q6. In every future trial testing a treatment for OLP, how important is it to measure PSYCHOLOGICAL IMPACT (e.g., anxiety and depression)?	7 (7.37)	15 (15.79)	73 (76.84)	95	Inclusion
Q7. In every future trial testing a treatment for OLP, how important is it to measure PATIENT SUPPORT FROM FAMILY AND FRIENDS?	27 (29.67)	40 (43.96)	24 (26.37)	91	Lack of agreement
Q8. In every future trial testing a treatment for OLP, how important is it to measure PATIENT COMPLIANCE AND TOLERABILITY?	1 (1.05)	6 (6.32)	88 (92.63)	95	Inclusion
Q9. In every future trial testing a treatment for OLP, how important is it to measure OVERALL PATIENT SATISFACTION?	2 (2.11)	13 (13.68)	80 (84.21)	95	Inclusion
Q10. In every future trial testing a treatment for OLP, how important is it to measure ADVERSE EVENTS (local and/or systemic)?	0	3 (3.16)	92 (96.84)	95	Inclusion
Q11. In every future trial testing a treatment for OLP, how important is it to measure the ECONOMIC IMPACT (e.g., costs)?	16 (16.85)	36 (37.89)	43 (45.26)	95	Lack of agreement
Q12. In every future trial testing a treatment for OLP, how important is it to measure TIMELINES (e.g., time to response and duration of effect)?	2 (2.08)	3 (3.13)	91 (94.79)	96	Inclusion
Q13. In every future trial testing a treatment for OLP, how important is it to measure NEED FOR RESCUE MEDICATION?	8 (8.42)	19 (20)	68 (71.58)	95	Inclusion
Q14. In every future trial testing a treatment for OLP, how important is it to measure BIOMARKERS POST-TREATMENT INITIATION (e.g., blood and saliva tests)?	33 (34.37)	27 (28.13)	36 (37.5)	96	Lack of agreement
Q15. In every future trial testing a treatment for OLP, how important is it to measure HISTOPATHOLOGY POST-TREATMENT INITIATION (e.g., cell changes and cancer development)?	30 (31.58)	22 (23.16)	43 (45.26)	95	Lack of agreement

OLP, oral lichen planus.

Patient Group Consensus

Ten OLP patients participated in the group consensus session (Stage 3). Considering the consensus criteria, the patients felt the following outcome domains should be included in the COS for the treatment of OLP (Table V):

- Appearance of lesions
- Severity of lesions
- Symptoms
- Function
- Social impact
- Psychological impact
- Patient compliance and tolerability
- Overall patient satisfaction
- Timelines

Table V. Results of patient focus group voting

Questions	*Limited importance n (%)*	*Unclear importance n (%)*	*Critical importance n (%)*	*No. of participants for each question*	*Consensus*
Q1. In every future trial testing a treatment for OLP, how important is it to measure APPEARANCE OF LESIONS (e.g., red and/or white in color and ulceration)?	0	2 (20)	8 (80)	10	Inclusion
Q2. In every future trial testing a treatment for OLP, how important is it to measure SEVERITY OF LESIONS (e.g., extent and activity)?	0	2 (20)	90 (80)	10	Inclusion
Q3. In every future trial testing a treatment for OLP, how important is it to measure SYMPTOMS (e.g., pain, sensitivity, and burning)?	0	0	10 (100)	10	Inclusion
Q4. In every future trial testing a treatment for OLP, how important is it to measure FUNCTION (e.g., eating, speaking, and tooth brushing)?	0	2 (20)	8 (80)	10	Inclusion
Q5. In every future trial testing a treatment for OLP, how important is it to measure SOCIAL IMPACT (e.g., interference with work and family life)?	0	2 (20)	8 (80)	10	Inclusion
Q6. In every future trial testing a treatment for OLP, how important is it to measure PSYCHOLOGICAL IMPACT (e.g., anxiety and depression)?	0	3 (30)	7 (70)	10	Inclusion
Q7. In every future trial testing a treatment for OLP, how important is it to measure PATIENT SUPPORT FROM FAMILY AND FRIENDS?	4 (40)	2 (20)	4 (40)	10	Lack of agreement
Q8. In every future trial testing a treatment for OLP, how important is it to measure PATIENT COMPLIANCE AND TOLERABILITY?	0	2 (20)	8 (80)	10	Inclusion
Q9. In every future trial testing a treatment for OLP, how important is it to measure OVERALL PATIENT SATISFACTION?	0	0	10 (100)	10	Inclusion
Q10. In every future trial testing a treatment for OLP, how important is it to measure ADVERSE EVENTS (local and/or systemic)?	2 (20)	4 (40)	4 (40)	10	Lack of agreement
Q11. In every future trial testing a treatment for OLP, how important is it to measure ECONOMIC IMPACT (e.g., costs)?	0	6 (60)	4 (40)	10	Lack of agreement
Q12. In every future trial testing a treatment for OLP, how important is it to measure TIMELINES (e.g., time to response and duration of effect)?	0	2 (20)	8 (80)	10	Inclusion
Q13. In every future trial testing a treatment for OLP, how important is it to measure NEED FOR RESCUE MEDICATION?	1 (10)	4 (40)	5 (50)	10	Lack of agreement
Q14. In every future trial testing a treatment for OLP, how important is it to measure BIOMARKERS POST-TREATMENT INITIATION (e.g., blood and saliva tests)?	6 (60)	4 (40)	0	10	Lack of agreement
Q15. In every future trial testing a treatment for OLP, how important is it to measure HISTOPATHOLOGY POST-TREATMENT INITIATION (e.g., cell changes, cancer development)?	5 (50)	5 (50)	0	10	Lack of agreement

OLP, oral lichen planus.

The following domains lacked consensus for inclusion:

- Support from family and friends
- Economic impact
- Adverse events
- Need for rescue medication
- Biomarkers post-treatment initiation
- Histopathology post-treatment initiation

Average of the AAOM Conference and Patient Results

The voting results from the 2022 AAOM Annual Conference were compared with those from the OLP patient group. Despite the difference in sizes, an equal weighting was given to each group to ensure that the patients' opinions were supported throughout the process. A consensus was achieved to include the following domains in the COS (Table VI):

Table VI. Average of patient and clinician voting results

Questions	*Limited importance (%)*	*Unclear importance (%)*	*Critical importance (%)*	*Consensus*
Q1. In every future trial testing a treatment for OLP, how important is it to measure APPEARANCE OF LESIONS (e.g., red and/or white in color and ulceration)?	0.54	13.77	85.70	Inclusion
Q2. In every future trial testing a treatment for OLP, how important is it to measure SEVERITY OF LESIONS (e.g., extent and activity)?	0	10.55	89.45	Inclusion
Q3. In every future trial testing a treatment for OLP, how important is it to measure SYMPTOMS (e.g., pain, sensitivity, and burning)?	0	1.06	98.95	Inclusion
Q4. In every future trial testing a treatment for OLP, how important is it to measure FUNCTION (e.g., eating, speaking, and tooth brushing)?	0	14.69	85.32	Inclusion
Q5. In every future trial testing a treatment for OLP, how important is it to measure SOCIAL IMPACT (e.g., interference with work and family life)?	4.17	21.46	74.38	Inclusion
Q6. In every future trial testing a treatment for OLP, how important is it to measure PSYCHOLOGICAL IMPACT (e.g., anxiety and depression)?	3.69	22.90	73.42	Inclusion
Q7. In every future trial testing a treatment for OLP, how important is it to measure PATIENT SUPPORT FROM FAMILY AND FRIENDS?	34.84	31.98	33.19	Lack of agreement
Q8. In every future trial testing a treatment for OLP, how important is it to measure PATIENT COMPLIANCE AND TOLERABILITY?	0.53	13.16	86.32	Inclusion
Q9. In every future trial testing a treatment for OLP, how important is it to measure OVERALL PATIENT SATISFACTION?	1.06	6.84	92.11	Inclusion
Q10. In every future trial testing a treatment for OLP, how important is it to measure ADVERSE EVENTS (local and/or systemic)?	10	21.58	68.42	Lack of agreement
Q11. In every future trial testing a treatment for OLP, how important is it to measure ECONOMIC IMPACT (e.g., costs)?	8.43	48.95	42.63	Lack of agreement
Q12. In every future trial testing a treatment for OLP, how important is it to measure TIMELINES (e.g., time to response and duration of effect)?	1.04	11.57	87.40	Inclusion
Q13. In every future trial testing a treatment for OLP, how important is it to measure NEED FOR RESCUE MEDICATION?	9.21	30.00	60.79	Lack of agreement
Q14. In every future trial testing a treatment for OLP, how important is it to measure BIOMARKERS POST-TREATMENT INITIATION (e.g., blood and saliva tests)?	47.19	34.07	18.75	Lack of agreement
Q15. In every future trial testing a treatment for OLP, how important is it to measure HISTOPATHOLOGY POST-TREATMENT INITIATION (e.g., cell changes and cancer development)?	40.79	36.58	22.63	Lack of agreement

OLP, oral lichen planus.

- Appearance of lesions
- Severity of lesions
- Symptoms
- Function
- Social impact
- Psychological impact
- Patient compliance and tolerability
- Overall patient satisfaction
- Timelines

The other domains lacked consensus for inclusion.

Final Consensus Stage

An interactive online meeting was held to discuss the results to date further and reach a consensus for the unknown domains. The 12 WWOM VIII OLP Expert Working Group members and 3 additional investigators (H.D., A.F., and C.H.) attended, and the 6 unclear domains were discussed with a final in/out voting.

Subsequent discussions and rounds of voting resolved disagreements. This led to the following final list of included domains for the COS for OLP (Figure 1):

- Appearance of lesions
- Severity of lesions
- Symptoms
- Function
- Social impact
- Psychological impact
- Patient compliance and tolerability

Fig. 1. Final list of domains included in core outcome set for oral lichen planus. OLP, oral lichen planus.

- Overall patient satisfaction
- Adverse events
- Timelines
- Need for rescue medication

DISCUSSION

The lack of high-quality evidence for interventions in Oral Medicine is secondary to various methodological limitations in trials, including the heterogeneity of outcome measures. Therefore, using a COS that aims to reduce the heterogeneity of outcomes measured will lead to the pooling of data for meta-analysis. Medical, surgical, and dental specialties have been working within this research area supported by the COMET initiative. (www.comet-initiative.org). Although there is variety in the methodology used for COS development, the following areas are universally accepted: 1) identification of existing knowledge, 2) patient involvement, and 3) consensus.

The WWOM registered the WONDER project with the COMET initiative in 2020 to develop a COS for OLP and dry mouth as part of the WWOM VIII. This promoted a unique opportunity to develop a concise methodology for developing COS projects in Oral Medicine and to perform a live interactive process via clickers at an international meeting of experts. The final consensus stages involved patients with OLP and health care providers worldwide who attended the WWOM VIII and the 2022 AAOM Annual Conference. The results of this consensus made it possible to determine which outcome domains should be part of the COS for evaluating the treatment of OLP.

There are various methods for gaining consensus as part of COS development. In most cases, large-scale Delphi questionnaires or expert panel meetings are used.[14] There are several issues to consider when conducting a large-scale Delphi consensus, including the lack of live interaction among stakeholders, the cost of running the studies, and the time-consuming nature of online or paper questionnaires. These issues increase the risk of participant attrition, a significant disadvantage of this technique.

This study used a face-to-face meeting method, taking advantage of access to the WWOM VIII and the 2020 AAOM Annual Conference. The 2 meetings provided an opportunity to engage with and elicit the opinions of a broad group of Oral Medicine experts who may otherwise have found it difficult to participate in such a project. The first consensus stage was a pilot run of the clicker session with a group of Oral Medicine specialists. This gave the participants a chance to trial the technology and the timings. The interactive nature of the pilot process allowed participants to give live feedback and suggestions relating to the outcomes

under discussion and to consider the patients' viewpoints from the preliminary patient focus groups. After this, an information sheet about the project was uploaded (Appendix 1) to the AAOM Annual Conference app, and paper copies were distributed throughout the lecture hall. This gave participants a brief synopsis of the project to prepare them for the voting process. The results from the clicker session were saved, and the process was later repeated with the patient focus group.

The patients' opinions were included throughout the process by taking both the patients' voting outcomes and the AAOM Conference voting results and weighing them equally. After further discussion on the remaining 6 unclear outcomes, the patients voted none to be of critical importance.

- Support from family and friends
- Economic impact
- Adverse events
- Need for rescue medication
- Biomarkers post-treatment initiation
- Histopathology post-treatment initiation

At the final discussion, clear unanimous voting was easily achieved for the exclusion of the domains "histopathology post-treatment initiation" and "support from family and friends," as well as for the inclusion of "adverse events" and "need for rescue medication." When the domain "economic impact" was discussed, it was expressed that it would be interpreted differently depending on geographic location. For example, the cost of medication would not be a consideration for patients in a country with free access to health care, but it would be a consideration for health care providers and patients in a private or health insurance setting. It was decided that treatment efficacy should be judged on the clinical effect on patients and that economic considerations would only be required if a specific treatment was found to be successful. Although this domain could be added to the COS in particular trials, it would not be necessary for every trial, so it was not included in the final COS.

The domain "biomarkers post-treatment initiation" also prompted debate. As a domain in the context of an outcome measure for OLP, "biomarkers" was chosen to cover all possible measurable biological outcomes, such as blood tests or saliva tests. Examples of biomarkers include everything from pulse rate and blood pressure through basic chemistries to more complex laboratory tests of blood and other tissues.[14] However, a biomarker itself could be confused with the *measurement* of a particular biomarker for OLP, which does not currently exist. It was decided that if a biological test was required to measure the effect of treatment, then it would be specific to the treatment and should not be necessary for all potential treatments in a trial setting. As such, this domain was not included in the final COS.

Although this COS was developed following the recommendations from COMET, it has several limitations as a project. Ideally, a consensus process should involve a wide variety of stakeholders, including patients, specialists (practitioners of Oral Medicine, Oral Pathology, and dentistry), researchers (with experience in trials), and industry (pharmaceutical companies with trial experience). In this study, no industry or pharmaceutical companies were involved. Although only 10 patients voted, compared to the 96 participants at the clicker event, the patients' opinions were supported throughout the process. Nevertheless, the patients were enrolled from only one unit in Cork, Ireland, and including patients' opinions from other geographic locations may have led to differing results. Most AAOM Annual Conference and WWOM VIII participants in this consensus process were clinicians from the United States. A worldwide approach would have increased the external validity of the opinions expressed during the clicker process. Lastly, although most participants answered all the questions in the sessions, the results showed that not all participants answered all the questions in the clicker sessions, possibly due to delays or loss of internet connection.

CONCLUSIONS

Outcome measures are an important way of assessing a treatment effect. There are a variety of considerations when choosing outcome measures, including *what* to measure, *how* to measure it, and *when* to measure it. A COS is an agreed minimum set of outcomes that should be measured in all future treatment trials for a particular condition, and COS development is a way of improving our future evidence base by reducing heterogeneity. This COS for OLP, developed by consensus, aims to improve the future evidence base for treating OLP. In addition, the methodology developed for this project could guide future COS projects for other conditions managed by the Oral Medicine specialty.

According to the results of this consensus, future clinical trials on the treatment of OLP should include outcomes that evaluate the appearance of lesions, the severity of lesions, symptoms, function, social impact, psychological impact, patient compliance and tolerability, overall patient satisfaction, adverse events, timelines, and need for rescue medication. This consensus has established *what* should be measured. The next stage is to agree on *how* to measure it and *when* to measure it, specifically the timing of each step in measurement, in the projects that follow in the future. Completing this stage requires achieving consensus on which measurement tools to use. The project that pursues this aim should

follow the methodology and guidance of the Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN).

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DECLARATION OF COMPETING INTEREST

None.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.oooo.2023.01.013.

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