Received: 30 October 2018 | Revised: 16 May 2019 | Accepted: 19 May 2019

DOI: 10.1111/cdoe.12477

ORIGINAL ARTICLE

Community Dentistry and Oral Epidemiology WILEY

Prevalence of oral mucosal lesions in population-based studies: A systematic review of the methodological aspects

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Funding information
Meridional Foundation (Passo Fundo – Brazil); Partnerships Program for Education and Training (PAEC) between the Organization of American States (OAS) and the Coimbra Group of Brazilian Universities (CGBU); Coordenação de Aperfeiçoamento de Pessoal de Nível Superior–Brasil (CAPES), Grant/Award Number: 001; Foundation of Rio Grande do Sul — Brazil, Grant/Award Number: DOCFIX 18/2551-0000515-0

Abstract

Objectives: To conduct a systematic review of the literature to evaluate the methodological aspects of population-based studies on the prevalence of oral mucosal lesions (OMLs).

Methods: Two reviewers independently conducted a literature search in three databases (PubMed, Web of Science and Scopus) and extracted data using a standardized form. Data on the following characteristics of the included studies were collected: sample size; age of participants; references used to define the diagnostic criteria, training of the examiners, and data collection; type, grouping and characteristics of the lesions; and lesions excluded and measures of agreement between examiners. Data were analysed descriptively, and data synthesis was performed for each of the studies included in the analysis. A quality analysis of the studies was conducted, and the risk of bias was evaluated.

Results: A total of 29 studies were included in the analysis. Most of the published studies on the prevalence of OMLs were performed in Asian countries. The sample sizes ranged from 255 to 39 206. The World Health Organization guidelines were followed by most of the studies, in terms of design, examiner training and data collection. Approximately 25% of the studies did not determine inter-examiner reliability. Moreover, almost half of the studies included did not report the response rate nor did they present the results with the appropriate confidence intervals.

Conclusions: Several important points need to be improved in population-based studies focusing on the prevalence of OMLs. In particular, these studies should adequately report the response rate and findings, and to a lesser extent, the diagnostic criteria and training of the examiners. We encourage more research in this field and reinforce the importance of standardized studies to facilitate the comparison of different findings. PROSPERO registration number: CRD42018099386.

KEYWORDS
epidemiology, methods, mouth diseases, population, prevalence

1 | INTRODUCTION

The term oral mucosal lesion (OML) refers to any abnormal change in the oral mucosa including changes in the colour or surface, swelling or loss of integrity.[1] OMLs may include common pathologies and developmental defects such as fibromas, mucoceles, candidiasis, leukoplakia, geographic and fissured tongue, Fordyce granules and in rare cases oral cancers.[2-4] It is important to emphasize that this large group of alterations may have clinically relevant implications, such as pain, difficulty in eating and speaking, and also aesthetic problems, which may impact an individual's oral health-related quality of life.[5,6] The prevalence of OMLs in the general population differs across different regions and countries and ranges from 5% to 65%. This high variability may be due to the difference in the methodology employed by the various studies, together with the sociodemographic differences between countries.[1]

Epidemiologic studies of OMLs are not as frequent as studies involving caries or periodontitis.[1,7] The literature has abundant case reports, case series analyses and cross-sectional studies on OMLs conducted in specific settings.[8-10] Most of the latter studies use samples conveniently collected from specialized dental and medical centers,[8,11] as well as from oral pathology reference centers.[10,12] These types of studies are important to understanding the service profiles in relation to the frequency and characteristics of OMLs. However, it is not possible to generalize the findings of these studies, mainly because of the occurrence of selection bias. In contrast, observational studies conducted using representative samples or the entire population allow the determination of the prevalence of the lesions under investigation with a known margin of error.[4,13,14]

Considering the methodology used in observational studies, some important aspects have to be pointed out, such as the use of well-known tools and well-established criteria for the diagnosis and inclusion (and exclusion) of oral lesions; the grouping of the lesions; and the need to report any agreement between examiners.[2,5,15] The standardization of these aspects favours the understanding of the study and the application and reproducibility of the findings.[16] Differences in methodologies including sample selection, diagnostic and inclusion criteria, and other aspects can hinder the systematic analysis of these studies.[1,2,7]

Accordingly, the objective of this study is to evaluate the methodology of population-based studies focusing on the prevalence of OMLs in order to help researchers conduct future studies in this field.

2 | METHODS

This review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA Statement)[17] and is registered in PROSPERO under the number CRD42018099386. The research question addressed in this study was the following: "Which methodological aspects are typically considered in population-based studies on the prevalence of OMLs?".

2.1 | Eligibility criteria

Population-based epidemiological studies (type of study) on OML prevalence (outcome) were included in this study. Population-based studies included studies conducted with the entire population of a defined geographical region or with a representative sample of that region.[18,19] Review articles, letters to the editor, case reports, case series and pilot studies were excluded. Furthermore, studies assessing only intraosseous, dental or periodontal lesions (gingivitis and periodontitis); studies focusing on OMLs in specific sites, such as the gum, tongue and lip; studies including individuals with other pathologies (systemic diseases or effects of radiotherapy treatment); and service-based studies were excluded. Studies associated with specific diseases were excluded because the aim of this study was to assess population-based studies that investigated different types of lesions. However, because of their clinical relevance, studies investigating potentially malignant oral disorders were included in the analysis.

2.2 | Electronic searches

Searches were performed in three databases, PubMed, Web of Science and Scopus, and in three languages, English, Spanish and Portuguese. Initially, the search strategy was developed for PubMed (MEDLINE) and adapted to the other databases (Supplementary Table S1). The references cited in the included articles were also reviewed to identify any further relevant articles. Literature searches were carried out until 15 May 2019, by two independent reviewers (KDS and WLOR) without any date restrictions.

2.3 | Study selection

The results of the literature searches were imported into the software Endnote X1 (Thomson Reuters, Philadelphia, PA, USA) to remove duplicates. Two authors independently assessed the titles and abstracts of all of the documents (KDS and WLOR). Documents appearing to meet the inclusion criteria or those with insufficient data in the title and abstract were selected for further analysis. Full-text papers were assessed independently and concomitantly by both reviewers. Any disagreement between the reviewers was solved through discussion until a consensus was reached or by involving a third reviewer (JPAS).

2.4 | Data extraction and synthesis

The reviewers previously discussed all the data that would be collected from the studies and extracted the information in duplicate using a standardized form.

Author names, year of publication, country, sample size and age of participants as well as important methodological aspects, such as diagnostic criteria, type, grouping and characteristics of the lesions, lesions excluded and measures of agreement between the examiners

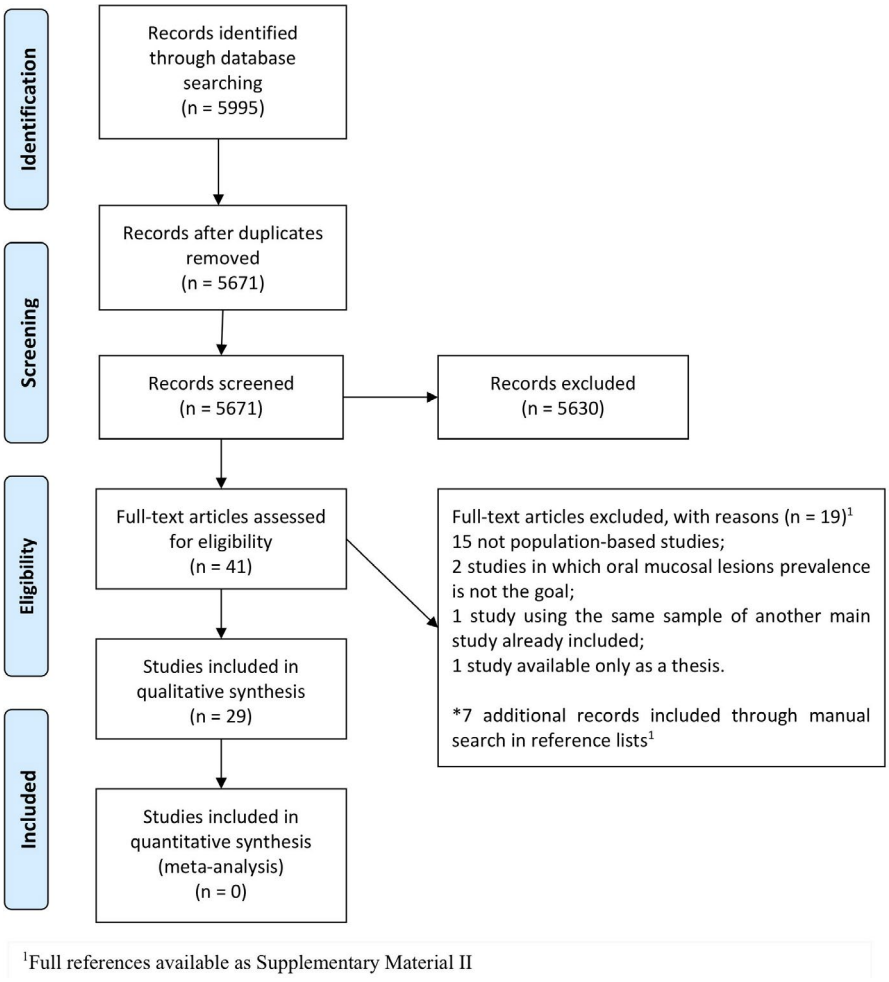

FIGURE 1 Search flow according to the Prisma statement

were collected. The data were analysed descriptively, with the aim of performing data synthesis for each study.

2.5 | Quality of the included studies

The full text of all of the studies was assessed for methodological quality according to a system devised by Loney et al[20] indicated for population-based studies. One reviewer (KDS) independently assessed the studies based on eight items,[20] as follows: (a) random sample or whole population; (b) unbiased sampling frame; (c) adequate sample size; (d) standard measures; (e) outcome measures by an unbiased assessor; (f) adequate response rate; (g) confidence intervals (CIs), subgroup analysis; and (h) study participants described. Each item received a score of 0 or 1, interpreted as high- and low-risk of bias, respectively.

3 | RESULTS

3.1 | Search strategy

Figure 1 shows a flow chart that summarizes the article selection process according to the PRISMA Statement.[17] A total of 29 studies fulfilled the selection criteria and were included in the qualitative analysis.

3.2 | Descriptive analysis

Table 1 shows the characteristics of the included studies. The first included study was published in 1963[21] and the most recent was published in 2016.[22] Eighteen (62.1%) studies were published in the 21st century.[1,2,4,5,13,14,15,22-32] The distribution of the studies by country and sample size is presented in Figure 2. The sample sizes ranged from 255[33] to 39 206.[34] Four studies were part of larger investigations of general and oral health, the Australian National Survey of Adult Oral Health,[2] the Third German Oral Health Study[30] and the US Third National Health and Nutrition Examination Survey.[13,14] Similarly, three studies were cross-sectional analyses nested in cohort studies conducted in Brazil[4,5] and Sweden.[35]

All studies included both sexes, with nine studies (31.0%)[3,5,14,26,29,32,34,36,37] conducted with children and adolescents (up to 24 years of age)[38] and the same number with adults.[4,24,25,27,30,33,35,39,40] Eleven studies (37.9%)[1,2,13,15,21-23,28,31,41,42] were conducted with both children or adolescents and adults. Most of the references used to conduct the studies (23%-79.3%), in terms of

TABLE 1 Overview of demographic data and methodological aspects of included studies

Author and country (groups)	Sample size (n)[a] and subjects	References adopted[b]	OML type
Witkop & Barros (1963)[21] Chile	1906 All age groups	-	Oral anomalies (not grouped)
Sedano (1975)[36] Argentina	6180 Between 6-15 y	-	Orodental abnormalities (not grouped)
Sawyer et al (1984)[37] Nigeria	2203 Between 10-19 y	-	Oral anomalies (not grouped)
Osterberg et al (1985)[35] Sweden	385 70-y-old adults	Roed-Pedersen & Renstrup (1969)	All (Red, white and hyperplastic lesions, and tongue lesions)
Sedano et al (1989)[3] Mexico	32 022 Between 5-14 y	-	Congenital oral anomalies (not grouped)
Salonen et al (1990)[42] Sweden	920 ≥ 20 y	Axéll (1976, 1984, 1987) + WHO (1978) + Roed-Petersen & Renstrup (1969)	All (Infections, ulcers, whitish lesions, denture-related lesions, tongue lesions, pigmentation, tumour and tumour-like lesions)
Bánóczy & Rigó (1991)[41] Hungary	7820 All age groups	Previous studies of the author + Axéll (1984)+ Roed-Petersen & Renstrup (1969)	Precancerous (Leukoplakia and lichen planus)
Corbet et al (1994)[39] Hong Kong	537 Between 65-74 y	WHO (1980) + Axéll (year not informed) + a colour atlas prepared by one of the authors	All (not grouped)
Kleinman et al (1994)[34] USA	39 206 Between 5-17 y	Pindborg (1985) + Axéll (1976a, 1976b) + Greer (1985) + WHO (1977, 1980) + Roed-Petersen and Renstrup (1969)	All (not grouped)
Zain et al (1997)[40] Malaysia	11 697 ≥ 25 y	WHO (1978, 1980) + Axéll (1976, 1984) + Zain (1996) + Reichart (1987) + Ikeda (1995)	All (not grouped)
MacEntee et al (1998)[33] Canada	255 ≥ 70 years	Axéll (1976)	All (not grouped)
Reichart (2000)[30] Germany	2022 Between 35-44 and 65-74 years	WHO (1980) + Melnick (1993) + Ramanathan (1995) + Axéll (1976) + Zain (1995) + WHO (1995) + Roed-Petersen & Renstrup (1969) + manual prepared by the authors	All (not grouped)
Lin et al (2001)[27] China	3088 Between 35-44 and 65-74 years	WHO (1997) + Axéll (1976, 1984) + atlas prepared by the authors	All (Precancerous lesion and condition, other white lesion, ulcers, lesions related to infection, tongue lesions, tumour, excessive melanin pigmentation, others)
Espinoza et al (2003)[24] Chile	889 > 65 years	WHO (1980, 1997)+Axéll (1976, 1996)	All (not grouped)
Shulman et al (2004)[13] USA	17235 ≥ 17 years	WHO (1980) + NHANES III (1992)	All (Candida related, tobacco-related, acute conditions, tongue conditions, red/white conditions, raised conditions, other conditions)
Shulman (2005)[14] USA	10032 Between 2-17 years	WHO (1980) + NHANES III (1992)	All (Candida related, tobacco-related, acute conditions, tongue conditions, red/white conditions, raised conditions, other conditions)
Chung et al (2005)[23] Taiwan	1075 ≥ 15 y	WHO (1978, 1980) + Axell (1996)	Precancerous (not grouped)
Mumcu et al (2005)[28] Turkey	765 All age groups	WHO (1980, 1997) + Scully (1999)	All (Pigmentation, tongue lesions, denture-related lesions, red mucosal lesions, tumours, white mucosal lesions, recurrent aphthous stomatitis, hypertrophic frenulum, salivary gland diseases, infections, others)
Parlak et al (2006)[29] Turkey	993 Between 13-16 y	WHO (1980)	All (not grouped)

(Continues)

TABLE 1 (Continued)

Author and country (groups)	Sample size (n)[a] and subjects	References adopted[b]	OML type
Splieth et al (2007)[31] Germany	4210 Between 20-79 y	Reichart (1993) + Roed-Petersen & Renstrup (1969)	All (Leukoplakia simplex, leukoplakia verrucosa, leukoplakia erosive, erythroplakia, lichen ruber, ulcer of the oral mucosa, exophytic neoplasia, herpetiform lesion or aphthous lesion, not classifiable, suspicious change of oral mucosa)
Carrard et al (2011)[15] Brazil	1586 ≥ 14 y	WHO (1980) + WHO (1997)	All (Premalignant lesions, proliferative lesions, abscess and fistulas and oral candidiasis)
Jahanbani (2012)[26] Iran	1020 Between 12-15 y	WHO (1980)	All (not grouped)
Ghanaei et al (2013)[25] Iran	1581 > 30 y	WHO (year not informed)	All (White colour lesions and nonwhite lesions)
Tarquinio et al (2013)[4] Brazil	720 24-y-old adults	Hipólito & Martins (2010) + Neville (2009)	All (Pigmented lesions, papules and nodules, white plaque, vesicles and bubbles, erosion, ulcer)
Vieira-Andrade et al (2013)[32] Brazil	541 Between 0-5 y	Bessa (2004) + WHO (1995, 1997)	All (not grouped)
Do et al (2014)[2] Australia	5505 ≥ 15 y	WHO (1977) + Slade (2007)	All (No mucosal pathology, suspected malignancy, ulceration, all other nonulcerated OMLs)
Feng et al (2015)[1] China	11054 All age groups	Do (2014) + WHO (1978, 1997)	All (Tongue lesions, ulcers, infections, whitish lesion, melanin pigmentation, tumour/tumour-like lesion, xerostomia/burning mouth syndrome, pemphigus, others)
Oliveira et al (2015)[5] Brazil	1118 5-y-old children	WHO (1987)	All (Ulcer, papule/nodule, pigmented lesion, erosion, vesicles/blisters, white plaques, indefinite)
Chher et al (2018)[22] Cambodia	1634 > 18 y	WHO (1997)	All White lesions, Red lesions, Pigmented lesions, Ulcerative lesions, Swellings/Exophytic lesions, Other lesions

Note: - Data not reported.
Abbreviation: OML, oral mucosal lesion.
[a]Patients from whom data on oral mucosal lesions were obtained.
[b]References used to conduct the studies. The full references are shown as Data S3.

design, examiners training and data collection, conformed to the World Health Organization (WHO) guidelines, previous research published by the renowned Tony Axéll et al over the years, or both. Moreover, six studies (20.7%)[30,31,34,35,41,42] used previous work by Roed-Petersen and Renstrup[43] for the topographical classification of intra-oral lesions.

The majority (27%-93.1%) of the included studies investigated all types of OMLs; however, two studies (6.9%)[23,41] only evaluated "precancerous" oral lesions and were included because of the importance of this group of lesions in the context of OMLs. Four studies (13.8%)[21,36,37] only analysed developmental defects, such as commissural lip pits, Fordyce granules, or fissured and geographic tongue. The clinical diagnoses of OML were grouped in categories (eg, infections, denture-related lesions, tongue lesions) in 15 (51.7%) studies.[1,2,4,5,13,14,15,22,25,27,28,31,35,41,42]

Most studies (26%-89.7%) did not mention the excluded lesions; however, 3 (10.3%)[4,5,24] reported that the developmental defects and other lesions, such as petechiae,[4,5] were not included. Four studies (13.8%)[26,29,30,34] reported that recurrent herpetic lesions and aphthous stomatitis were recorded if observed at the time of examination or through self-reporting.[30,34]

Importantly, only three studies (10.3%) recorded the size,[4,5,14] surface aspect,[14] colour,[14] consistency,[14] associated symptoms[4,14] and duration[4,14] of the lesions. Additionally, three studies (10.3%)[2,4,5] did not use the clinical diagnoses to classify the lesions and considered only the type of mucosal alteration, such as plaque, papule or nodule, vesicle or blister, erosion and ulcer.

With regard to the inter-observer and intra-observer reliability of the clinical assessments in the calibration phase, 16 studies (55.2%)[2-5,15,21,22,24,25,27,29,30,32,34,39,40] performed at least one of these evaluations, while five of them did not report any kappa value.[2,3,21,29,34] For the remaining studies, values ≥0.6 indicated a substantial or good agreement.

3.3 | Quality of the reviewed studies

With respect to methodological quality, almost half of the included studies presented a high risk of bias in particular items, such as "Is the response rate adequate? Are the refusers described?" or "Are the estimates of prevalence or incidence given with confidence intervals and in detail by subgroups, if appropriate?" (Figure 3).

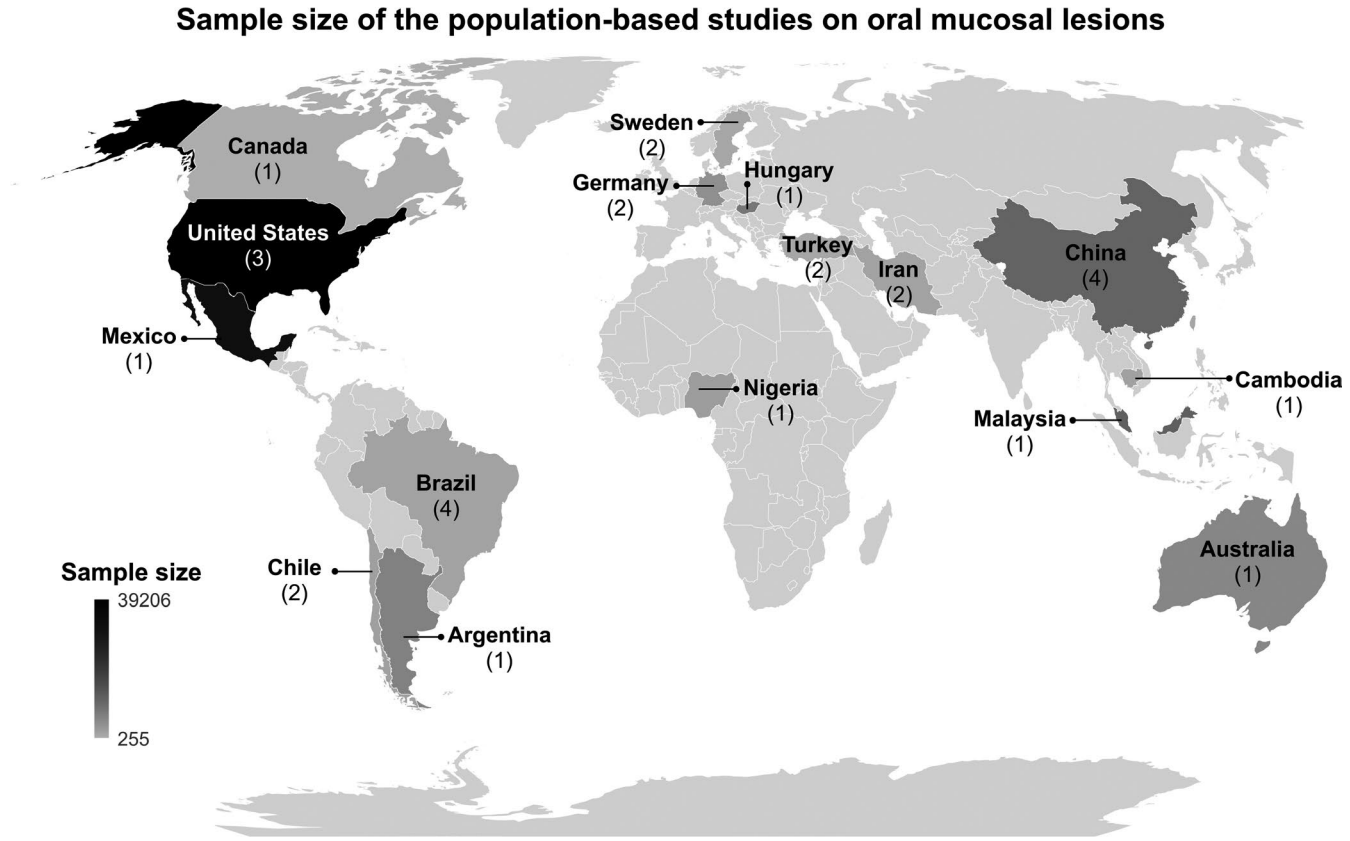

FIGURE 2 Sample size of the population-based studies on OMLs. The data in parenthesis represent the number of studies by country

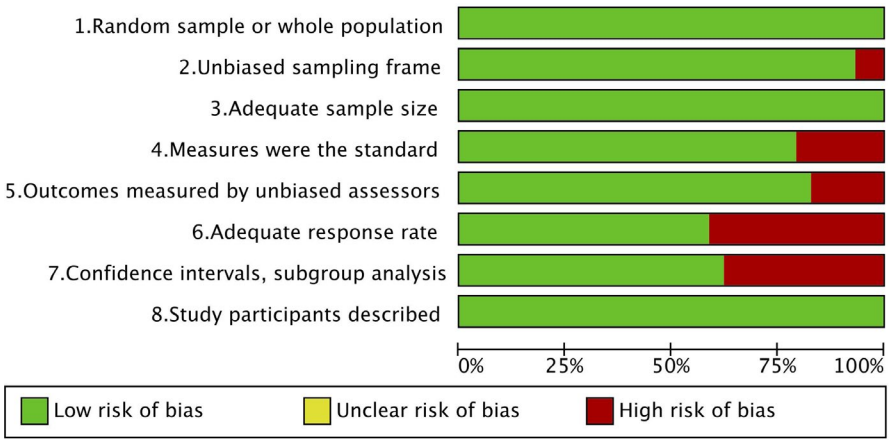

FIGURE 3 Review of authors' judgements regarding each risk of bias item presented as percentages across all included studies, according to Loney et al[20]

4 | DISCUSSION

Population-based studies on the prevalence of OMLs are still scarce in the literature, despite the long period investigated. This systematic review highlights some weaknesses related to the methodology of these studies. The deficiencies are related mainly to the lack of adequate response rates and reports of the refusals and presentation of the results and, to a lesser extent, may be associated with the diagnosis criteria of the lesions under investigation and the training and blinding of the evaluators.

Just over half of the studies herein included[2,4,5,15,22,28,30-35,39-42] reported the response rate and described the reasons for refusal, an important aspect to be considered when analysing the results. Additionally, the inclusion of the confidence intervals is sometimes forgotten,[3,25,27,31,33,35-37,39-41] making it difficult to analyse the precision of the findings.

Two very important aspects that must be taken into consideration when assessing the quality of the studies are the diagnostic criteria and the calibration and blinding of the examiners. The lesions that will be investigated and the training and calibration of the examiners to recognize the included oral conditions are crucial factors in the planning of the study.[44,45] When some lesions are not included or not recognized by the examiners, they can be interpreted as absent or underestimated in a certain population.

A general lack of standardization makes it difficult to compare the findings of different studies. In addition, the adoption of unclear diagnostic criteria compromises the validity of the results. In this way, the marked variation in the reported prevalence of OMLs among studies appears to be predominantly related to the differences in the methodologies employed, and to a lesser degree to the geographical settings and sociodemographic characteristics of the population.[16,29]

Overall, the literature regarding the prevalence of OMLs in population-based studies is limited,[1] although the WHO encourages publications on the subject.[44] The difficulties, in terms of cost and logistics, of conducting large population-based studies are well-known.[14,44] We observed that OML prevalence studies with larger samples were able to secure government funding and were part of major investigations conducted not only on oral health but also on general health. The ideal scenario would be to evaluate populations as a whole; however, cross-sectional studies with adequate sample sizes and design are suitable to determine the prevalence of OMLs. Cross-sectional studies with a representative sample of an entire population cannot replace high-cost population studies, but are certainly able to validate their findings. As can be seen in Figure 2, the importance of this topic is highlighted by the fact that even low-income countries have published research related to the prevalence of OMLs.

Asian countries have published the highest number of population-based studies regarding the prevalence of OMLs. The high rate of oral cancers in some Asian countries seems to favour researches on the subject.[23] South American countries are the next in ranking, with Brazil publishing four out of seven studies. The birth cohort studies of Pelotas/Brazil were important for the consolidation of this number and also serve as well-designed studies that can be used as references.[46]

An important aspect to consider is the age of target population. Traumatic OMLs, such as mucoceles and traumatic ulcers, and infectious OMLs, such as fistulae and herpetic infections, may be more frequent in children than in adults.[14,32] Similarly, denture and tobacco-related lesions, such as stomatitis, hyperplasia and leukoplakia, affect adults more frequently.[13] In addition, the overall prevalence of OML tends to be higher as age increases. These differences should be taken into account when comparing the prevalence of different studies and in the study design when defining the clinical diagnoses that will be investigated. Considerably, more attention should be paid to more prevalent lesions in a specific age group during training and calibration of examiners. We believe that the division observed in studies between children or adults is not a limitation of them, but it could be an important strategy in the study design when it is not possible to investigate all age groups or when the objective of the study is to determine the prevalence of the lesions in a specific age range of the population.

With regard to diagnoses such as Fordyce granules, fissured and geographic tongue, and exostosis, which belong to a group known as developmental defects or variations in normal anatomy,[3,32,37] it is important to consider the differences in OML prevalence that can arise from the decision to include or not include this group.[4,39] Because of their relatively common occurrence, the overall prevalence of OMLs may be higher in certain populations if developmental alterations are included.[25,26,32] It is noteworthy that most of these conditions require no treatment and have little relevance in terms of oral health[4]; however, the great majority of the studies have included these conditions. This fact justifies their inclusion in future studies in order to better compare them. Additionally, the knowledge of the distribution of these changes in specific populations can help health professionals to provide appropriate guidance on oral health to individuals.

Similarly, the inclusion of transient and recurrent oral conditions, such as recurrent aphthous ulceration and herpetic infection, may increase the OML prevalence in the populations studied. This systematic review found only four studies that included these lesions.[26,29,30,34] There are two ways of investigating their prevalence: through clinical examination and through self-reported lifetime history. Clinical examination leads to underestimation of their true prevalence due to the transient and recurrent nature of these diseases. However, self-report studies are prone to measurement validity errors and generally observe a higher prevalence than studies using clinical examinations.[29,30,34] Based on these limitations, researchers should carefully consider the inclusion of transient and recurrent lesions in cross-sectional surveys, even though their inclusion would be an important factor, since they can be very common in some age groups. We believe that the best option is to exclude these oral conditions, owing to the difficulties associated with their evaluation and also to better compare different studies.

In addition, it is important to encourage the use of specific clinical diagnoses rather than to classify the conditions according to the type of mucosal alteration. Three studies included in this review classified the pathologies in the latter form. Besides the difficulty in comparing them with others in the literature, there is no detailed information about the clinical diagnosis associated with these lesions described as maculae, plaques, papules or nodules, vesicles or blisters, and erosions or ulcerations.[2,4,5] A papule or nodule, for example, may represent a reactive or infectious lesion; an erosion may represent a traumatic, allergic or infectious process, or even a potentially malignant or malignant alteration.[4]

Moreover, differences in the prevalence of OMLs can be observed depending on the grouping of the lesions. Usually, the groups present slight variations, such as the inclusion of candidiasis in denture-related lesions group[28] or in the infectious group[1] or in the group of red or white lesions,[25,35] which implies different prevalence outcomes of the groups, and, in the latter example, may generate distortion of the prevalence of potentially malignant lesions.

It is also interesting to identify the characteristics of the lesions found.[16] This review showed that very few studies report the characteristics of the different lesions.[4,5,13,14] Detailed data on size, colour, consistency, surface aspect, associated symptoms and time of onset are important in order to better identify the clinical characteristics of the different lesions presented. Better identification of the oral lesions may help with the differential diagnoses and in the establishment of the final diagnosis. Moreover, it is important to emphasize that the location of an oral lesion is often critical in determining its differential diagnosis.[47]

TABLE 2 Summary of the important aspects related to the design of population-based studies on the prevalence of OMLs

Recognized references to be adopted	Points to be observed
1. Guide to the epidemiology and diagnosis of oral mucosal diseases and conditions (1980), by WHO 2. Oral Health Surveys—Basic Methods (2013), by WHO[47]	1. Select a clinical diagnosis taking into account the age of the participants and geographic and cultural differences between the populations 2. Report data on examiner concordance 3. Cite the excluded alterations, such as developmental changes or petechiae 4. Present the response rate and the reasons for the refusals 5. Present the results appropriately with the confidence intervals

Abbreviation: WHO, World Health Organization.

Another relevant aspect is to encourage examiner training and calibration, so that the conditions are viewed in a similar way by different individuals who perform the clinical examinations.[4,5] This step is admittedly challenging, because the same pathology may have different clinical presentations in distinct patients, the conditions can present at different stages of their manifestation, and the site of occurrence may differ.[16] In fact, some lesions such as mucoceles and fibrous hyperplasia can be easily diagnosed by their clinical characteristics, but other conditions such as lichen planus and reactive gingival lesions may require histopathological analysis to establish the final diagnosis, because they are diagnosed clinically with less accuracy.[14,16] Moreover, the rarity of some oral conditions may hinder the replication of the examinations during calibration, and the process sometimes has to be done through the analysis of photographs.[14]

These reasons may explain, in part, why only slightly more than half of the studies have calibrated examiners and evaluated intra- and/or inter-examiner agreement, despite the importance of such a step. The calibration process can be easier in population-based studies that investigate a single or a group of OMLs, such as potentially malignant oral disorders in adults and older people or when the aim is to investigate specific associated/risk factors.[23,41] Although this process is a challenge in population-based surveys that investigate the overall prevalence of OMLs,[14,16] these studies are more relevant and allow determination of the general prevalence of OMLs.

Greater standardization of the methods used in population-based studies on the prevalence of OMLs may enhance reproducibility of the studies and facilitate comparison of the findings from different populations.[16,44,45] The most current version of the WHO guidelines is the "Oral health surveys: basic methods - 5th edition (2013)",[45] which can be used in conjunction with the "Guide to epidemiology and diagnosis of oral mucosal diseases and conditions (1980)",[44] also from the WHO. Table 2 summarizes the important aspects to be noted in future studies when designing population-based investigations of OML prevalence and associations.

We conclude that the use of a standard methodology can be improved, mainly in relation to the determination of the response rates and the presentation of the data to include the confidence intervals, as well as the performance of standard measurements by unbiased assessors. The variations in the methodologies of these studies were able to influence the prevalence of OMLs, thus making comparisons between them difficult. The WHO guidelines should be used by researchers to increase the quality, validity and reproducibility of their studies. We hope that further studies on the subject will be better designed and contribute to knowledge of the occurrence of OMLs in different populations and settings.

ACKNOWLEDGEMENTS

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior—Brasil (CAPES)—Finance Code 001. KDS is funded by CAPES and WLOR by the Foundation of Rio Grande do Sul - Brazil (DOCFIX 18/2551-0000515-0). JPAS is funded by Partnerships Program for Education and Training (PAEC) between the Organization of American States (OAS) and the Coimbra Group of Brazilian Universities (CGBU). RSO is funded in part by Meridional Foundation (Passo Fundo—Brazil) and in part by Capes.

AUTHOR CONTRIBUTIONS

KDS, WLOR, RSO and SBCT participated in the conception and design of the study. KDS and WLOR drafted the article. WLOR, RSO and JPAS assisted in the acquisition, analysis and interpretation of data, and revised the article for important intellectual content. FFD, MBC and SBCT participated in the analysis and interpretation of data, and revised the article for important intellectual content. All authors approved the final version of the article to be published.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: da Silva KD, Rosa WLDOD, Sarkis-Onofre R, et al. Prevalence of oral mucosal lesions in population-based studies: A systematic review of the methodological aspects. *Community Dent Oral Epidemiol*. 2019;00:1–10. https://doi.org/10.1111/cdoe.12477